Abstracts

ESOPHAGUS

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Relationship Between Diabetes Mellitus and Adenocarcinoma of the Esophagus and Gastric Cardia
Joel H. Rubenstein, M.D., Jennifer Davis, M.H.S.A., Jorge A. Marrero, M.D., John M. Inadomi, M.D.
Puyallup Division, Digestive Health Specialists, PS, Puyallup, WA.

Purpose: Obesity is a risk factor for adenocarcinomas of the esophagus and gastric cardia. Diabetes mellitus might mediate that association. This is the largest study to date to evaluate the association. We aimed to estimate the risk of diabetes mellitus on the development of adenocarcinoma of distal esophagus and gastric cardia beyond that of gastroesophageal reflux disease.

Methods: A case-control study was performed using a national administrative database of the Veterans Administration.

Results: 311 cases of cancer and 10,154 controls were identified. Gender, age, and race were risks for cancer. Diabetes was diagnosed in 36% of cases, and 32% of controls (p = 0.15). Diabetic complications were diagnosed in 14% of cases and 13% of controls (p = 0.60). Multiple logistic regression confirmed the absence of an association between cancer and diabetes (odds ratio 1.1, 95% confidence interval 0.8 – 1.5) or diabetic complications (odds ratio 0.8, 95% confidence interval 0.6 – 1.3).

Conclusions: Within the limitations of this case-control study, there is no evidence of an association between diabetes and adenocarcinoma of the esophagus or gastric cardia among U.S. veterans with gastroesophageal reflux disease.

Clinical Presentation, Endoscopic Findings and Treatment of Eosinophilic Esophagitis in Adults: An Analysis of 61 Consecutive Cases
Lin Huang, M.D., Ph.D., Angela C. Fields, M.D., Thomas E. Reinertson, M.D.† The Puyallup Division, Digestive Health Specialists, PS, Puyallup, WA.

Purpose: Eosinophilic esophagitis is a chronic inflammatory disorder of the esophagus characterized by heavy infiltration of eosinophils of the esophagus. The etiology, pathogenesis, natural history and optimal treatment of eosinophilic esophagitis in adults are unknown. Here we present the largest case series of eosinophilic esophagitis in adults to date, and to provide evidence that eosinophilic esophagitis in adults is related to gastroesophageal reflux disease (GERD).

Methods: In our group practice of 20 gastroenterologists, we identified a total of 61 consecutive adult patients with a histological diagnosis of eosinophilic esophagitis from our pathology database between 2002 and 2004. The medical records of these patients were reviewed. Data on clinical presentation, endoscopic findings, treatment, and response to treatment were collected and analyzed.

Results: Among the 61 patients with a histological diagnosis of eosinophilic esophagitis, 38 patients (60%) presented with solid food dysphagia and 12 patients (20%) had a history of food impaction. Twenty-five patients (41%) presented symptoms of GERD, either with (14 patients) or without (11 patients) concurrent dysphagia, as their main complaints. The classical endoscopic finding of ringed esophagus was present in only 32 patients (52%), and 8 patients (13%) had normal esophagus at endoscopy. In parallel with the abundance of clinical symptoms of GERD, endoscopic findings associated with GERD were common, with hiatal hernia present in 30 patients (49%), reflux esophagitis in 11 patients (18%), peptic stricture in 4 patients (7%), and Barrett’s esophagus in 2 patients. While esophageal dilation, either alone or in conjunction with treatment with a proton pump inhibitor (PPI), was effective in relieving dysphagia, medical treatment with a PPI alone without dilation also resulted in resolution of dysphagia in all 9 patients whose follow-up information was available.

Conclusions: The presence of clinical and endoscopic features of GERD and the response to treatment with proton pump inhibitors in many of our patients strongly implicate GERD in the pathogenesis of eosinophilic esophagitis in adults. In adult patients with eosinophilic esophagitis who present with dysphagia, we suggest treatment with a PPI before performing esophageal dilation.

The Vulcan Syndrome – Asymptomatic Healthy Volunteers with Pathologic Esophageal Acid Exposure
Jerry D. Gardner, M.D.,* Sheldon Sloan, M.D., Malcolm Robinson, M.D., Phillip B. Miner, Jr., M.D.
Aim: To examine the distributions of values for esophageal acidity in normal and GERD subjects, paying particular attention to high values from normal subjects.

Methods: Esophageal pH was recorded for 24 hours in 26 asymptomatic healthy control subjects on 2 separate occasions 1 week apart, and in...
The Association of Barrett’s Esophagus and Body Mass Index
Daniel J. Stein, M.D., Hashem B. El-Serag, M.D., John Kaczynski, M.D., Jennifer R. Kramer, Ph.D., Richard E. Sampliner, M.D.* Section of Gastroenterology, Southern Arizona VA HealthCare System, Tucson, AZ and Sections of Gastroenterology and Health Services Research, Houston Center for Quality of Care and Utilization Studies, Baylor College of Medicine, Houston, TX.

Purpose: Obesity is a recognized risk factor for esophageal adenocarcinoma. Its relationship to Barrett’s esophagus (BE) is less well defined.

Aim: Examine the relationship between the presence and length of BE to weight, height, and body mass index (BMI).

Methods: A retrospective cross-sectional study of male patients undergoing upper endoscopy at SAVAHCS between 1998 and 2004 was conducted. BE was diagnosed by one endoscopist using standardized (ACG guidelines) endoscopic (columnar appearing distal esophagus) and histologic (intestinal metaplasia) criteria. The non-BE patients had normal esophageal mucosa at endoscopy. Chart review was performed for demographics, history of malignancy, death, and weight and height within 1 year of the endoscopy. Patients with BE and without BE were compared for demographic features, weight, height and BMI. Multivariate logistic regression analysis was conducted to examine the association of BMI and weight with BE, and analysis of covariance was used to examine the effect of BMI and weight on length of BE.

Results: 65 patients newly diagnosed with BE and 385 non-BE patients who did not have any recorded malignancy were compared. BE patients had a higher mean BMI (29.8 ± 28, p = 0.03) and greater mean weight (206 lb vs. 190 lb, p = 0.005). There was no significant difference in height. Multivariate logistic regression adjusted for race and age showed an association between BE and BMI, both when categorized and continuous BMI: 25–30 (vs. <25) odds ratio 2.38, p = 0.03 and BMI >30 (vs. <30) odds ratio 2.45, p = 0.03. For each 10 pound increase in weight or 5-point increase in BMI there was a 10 and 15% increased risk of BE, respectively (p = 0.002 and p = 0.01). There was no significant correlation between the length of BE and BMI.

Conclusions: Obesity is associated with a greater than 2-fold increase in the risk of BE, providing another possible risk factor in the development of BE. BMI was not associated with BE length.

The Prevalence of Gastroesophageal Reflux in Extra Thoracic Airway Obstruction
Eric R. Frizzell, M.D., Roy Wang, M.D.,* Inku Hwang, M.D., Corrine Maydonovich, B.S., Joyce Garovich-Uena, B.S. Gastroenterology, Walter Reed Army Medical Center, Washington, DC; Speech Pathology, Walter Reed Army Medical Center, Washington, DC and Pulmonary, Walter Reed Army Medical Center, Washington, DC.

Purpose: This is a prospective prevalence study of GER in patients diagnosed with Extra Thoracic Airway Obstruction (ETAO).

Background: ETAO is a debilitating disorder, in which sufferers develop dysfunctional vocal cord movement, blocking inspiration. The diagnosis is defined by wheezing not due to asthma, with no response to beta agonist medications and closure of the vocal cords during inspiration documented on laryngoscopy. Currently the standard of care is counseling and speech training to learn to control the rate of breathing and relax the vocal cords. The prevalence of ETAO is estimated at 3–5% of all patients diagnosed with asthma and may be higher in patients who are more physically fit.

There is a small but growing body of evidence that ETAO triggers include post-nasal drip, airborne irritants and GER in addition to stress and increased ventilation. The prevalence of GER in asthma is 60–80% in most studies. There have been no studies to determine the prevalence of GER in ETAO. We assessed the prevalence of GER and patient characteristics in patients with ETAO using the BRAVO pH monitor.
Purpose: The presence of intestinal type goblet cells (ITGC) is essential for the diagnosis of Barrett’s metaplasia (BM). However, we have seen cases diagnosed as BM based solely on the presence of columnar cells that: (a) resemble ITGC, or (b) that show positive staining with Alcian blue (AB). The clinical significance of goblet cell mimickers (GCM) is unknown. The purpose of this study is to determine: (1) the prevalence of GCM in esophageal biopsies; (2) their association with ITGC; and (3) whether GCM or positive staining with Alcian blue is associated with a significant risk for malignant progression.

Methods: Initial biopsies from 78 patients with a mean follow-up of 72 months and with original diagnosis of BM negative for dysplasia were reviewed and re-classified into 3 categories: (1) ITGC, (2) GCM, or (3) “gastric” if they lacked ITGC and GCM. Additional sections of cases with available tissue were stained with AB at pH 2.5. Statistical analysis was performed using the Kaplan-Meier method and the log rank test for statistical significance.

Results: GCM were present in 35 cases, and were associated with ITGC in the same biopsy in 23 (66%) of these cases. ITGC were present in 56 cases, and the remaining 10 were “gastric.” Only the presence of ITGC was identified on routine H&E-stained sections.

Conclusions: In this preliminary report, the incidence of GER in ETAO was 42%, lower than commonly reported in asthma. To date there were no significant predictors of GER in ETAO patients. While empiric GER treatment may be reasonable as adjunctive therapy in ETAO, GER is likely not the primary trigger of ETAO symptoms.
charts of all the patients who had capsule esophageal pH monitoring at Park Ridge Hospital between January and May 2005. The Bravo pH system was used on all patients. Failure was defined as non-attachment of the pH capsule to the esophagus. Data on demographic variables and comorbidities were collected.

**Results:** The mean age of the total sample (N = 36) was 45.4 ± 13.7 years. 69.4% were women. 94% were Caucasians and 5.6% African Americans. 44.4% had prior diagnosis of GERD, 86.1% were on a PPI (proton pump inhibitor) prior to study, 22% had normal endoscopic findings, 44.4% had hiatal hernia, 11.1% had esophagitis and 11.1% had gastritis. 50% had non-gastrointestinal indications for pH monitoring such as cough, hoarseness of voice and atypical chest pain. 52.8% had pH capsule placed by the new method 2 and the mean duration was 8.72 ± 3.72 minutes. 47.2% had the standard method 1 with a mean duration of 17.8 ± 16.64 minutes. The difference in duration of both methods is 9.03 minutes (P = 0.07). There was no re-attempt in method 2 and three in method 1 (P = 0.052). There was one failure in method 2 and three failures in method 1 (P = 0.208).

**Conclusions:** This data suggests that placement of capsule under direct endoscopic visualization has a better outcome as measured by the lesser duration, number of attempts and failure rate. These differences were not statistically significant probably due to the small sample size. A large randomized prospective study is planned to confirm these findings.

**Dx-1 – A New Device for Detecting Supraesophageal Gastric Reflux (SEGR)**


**Gastroenterology, Digestive Diseases, Chula Vista, CA; Medical Device, Respiratory Technology Corporation, San Diego, CA and Mathematics, San Diego State University, San Diego, CA.**

**Purpose:** Clinical and animal data have documented deleterious effects of acid pH < 4 (AGR) and weakly acid pH 4–7 (WAGR) gastroesophageal reflux, even in small amounts, when above the UES. Despite recognition of multiple manifestations of SEGR, characterization, identification and response to therapy have evaded understanding due to lack of a suitable detection device.

**Aim:** Evaluate the Dx-1 minimally invasive catheter utilizing an auto-briding ionic flow pH sensor, designed to work in the posterior oropharynx, for detection of SEGR, using standard 24hr triple sensor pH catheter(24PH) for verification.

**Methods:** Patients in a GI practice (GW) with chronic symptoms likely due to SEGR, off reflux meds 4–7days, underwent 24PH with 2 esophageal (E) and 1 pharyngeal (P) sensor (Sandhill PH10-V) positioned with the LES Indicator at 5 cm < LES, 5 cm < UES and 1 cm > UES. The 1.5 mm nasopharyngeal catheter (Dx1-ResTech) was placed at the oropharynx behind the uvula, above patient’s discomfort position. Tracings from all 4 synchronized pH inputs & patient diary were analyzed graphically on a single screen, excluding meals +5 min. SEGR event definition: rapid pH drops at the Dx-1 sensor, >3 S.D. from 60 sec baseline, sequential to drops in pH <4 in 24 pH sensors, then classified as AGR/WAGR. S.I. <50%:

**Results:** 8 patients, 1M, 7F, avg. age 64 (49–75): 6 cough, 1 loss enamel, 1 sleep apnea/cough, 4 had normal 24PH. There were 14 Dx-1 SEGR events in 6 pts, one AGR (pH 3.5), and 13 (93%) WAGR (pH 4.5–6.5, avg = 5.7) Dx-1 events were near vertical, gradual return to baseline & synchronous to E pH drops (low E: 11 AGR & 3 WAGR; P: 7 AGR & 7 WAGR). These 14 SEGR events were 4.3% of # pH events, at the lower E (329). Seven P events didn’t reach the Dx-1, 6 in 1 pt where P sensor possibly misplaced distal to UES. The avg pH values increased 43% from E to P, 21% from P to Dx-1. S.I.+ 83% at E, 33% at Mid E, 0 at P/6pts.

**Conclusions:** (A) SEGR exists in the oropharynx, detectable by Dx1. (B) There is a gradient of increasing pH from E to oropharynx, the latter rarely <4.

**Pantoprazole 40 mg Is as Effective as Esomeprazole 40 mg To Relieve Symptoms of Gastroesophageal Reflux Disease (GERD) after 4 Weeks of Treatment and Superior Regarding Preventing of Symptomatic Relapse**

Dirk Glatzel, M.D., Mouwafeg Abdel-Qader, M.D., Gudrun Gatz, M.D., Bernd Pfaffengerber, Ph.D., Peter Sander, Ph.D.*, Private, Practice, Hannover, Germany; Private, Practice, Winsen, Germany and Department of Gastroenterology, ALTANA Pharma AG, Konstanz, Germany.

**Purpose:** Symptom relief assessed with the validated reflux questionnaire ReQuestTM and symptomatic relapse during a 7 days post-treatment phase was compared in patients with erosive GERD treated with pantoprazole 40 mg (PANTO) or esomeprazole 40 mg (ESO).

**Methods:** In this randomized, double-blind, multicenter, parallel-group comparison conducted in Germany 561 patients (ITT) with endoscopically confirmed GERD grade A-D (LA Classification) received either PANTO (n = 284) 40 mg or ESO (n = 277) 40 mg once daily over a period of 4 weeks followed by a post-treatment period of 7 days without medication. For assessment of GERD-symptomatology, patients completed the ReQuestTM daily. Symptom relief was achieved if the score of the validated subscale ReQuestTM-GI fell below a pre-defined GERD symptom threshold. The primary efficacy variable was the mean score of the ReQuestTM-GI of the last 3 days of treatment. Non-inferiority of PANTO compared with ESO was tested by means of Hodges-Lehmann estimation, using a one-sided 97.5%-Confidence-Interval (CI) according to Moses. A non-inferiority margin of 1.725 (i.e. the pre-defined GERD symptom threshold) was assumed. In the post-treatment period, the maximum ReQuestTM-GI sum score was determined and tested using the two-sided Median Two-Sample Test. For the same period, the rate of patients above the GERD symptom threshold was tested using the two-sided Fisher’s Exact Test to characterize the clinically relevant symptomatic relapse.

**Results:** The median ITT values (PP) of the mean scores of ReQuestTM-GI during the last 3 days of active treatment were 0.24 (0.22) in the PANTO and 0.31 (0.30) in the ESO group (97.5% CI: −∞; + 0.010 (0.008)). Non-inferiority was concluded since the upper bound of the CI was below the non-inferiority margin. During the post-treatment phase the median values (PP) of the maximum ReQuestTM-GI sum scores were 1.44 in the PANTO group and 2.18 in the ESO group (p = 0.0313). Furthermore, 46% in the PANTO and 54% in the ESO group showed a symptomatic relevant relapse in the post-treatment phase (p = 0.022).

**Conclusions:** PANTO 40 mg is at least as effective as ESO 40 mg for symptom relief of GERD after 4 weeks of treatment. In the 7-day post-treatment phase without medication, patients in the PANTO group experienced significantly fewer symptomatic relapses.

**Eosinophilic Esophagitis in Adults: Is It Really a Rare Disease?**

Sripathi R. Kethu, M.D.*, Division of Gastroenterology, Brown Medical School and Rhode Island Hospital, Providence, RI.

**Purpose:** Eosinophilic esophagitis (EE) is increasingly recognized as an important cause of dysphagia in adults. However, the true prevalence of EE in adult patients who present with dysphagia is unknown. The aim of the present study was to estimate the frequency of EE as the underlying cause of dysphagia in adults.

**Methods:** All patients who underwent upper endoscopy by a single gastroenterologist for the evaluation of dysphagia over an 18-month period (Oct 2003 to Mar 2005) were included in the study. Because of the increasing reports of EE in the recent literature, esophageal biopsies were

[C] Redefinition of significant pH events above the UES as% or >3 S.D. pH drops merits consideration; further Dx-1 studies should aid understanding SEGR.
obtained routinely in patients who had no anatomic abnormality that could explain the cause of dysphagia and/or if they had any features suggestive of eosinophilic esophagitis (mucosal furrows, corrugations, adherent whitish plaques, fragile esophageal mucosa or so called crepe-paper mucosa). Two random biopsy samples are taken at each level, from the mid and lower esophagus. The diagnosis of eosinophilic esophagitis was based on the presence of >24 eosinophils per high power field.

**Results:** A total of 454 upper endoscopies were performed during the study period. Thirty-eight patients underwent upper gastrointestinal endoscopy for the evaluation of dysphagia. No apparent anatomical abnormality was found in 16 of them (42%), 10 male and 6 female. Five of these patients (all white male, age range: 18–49, mean age:31) were found to have EE; these patients constituted 13% of the total patients who were evaluated for dysphagia. Two of the 5 patients had peripheral eosinophilia (40%). No cause for dysphagia was found in 28% of patients after the endoscopy and esophageal biopsies. In subgroup analysis, among men who had no obvious anatomic abnormality such as a stricture, schatzki’s ring, cancer, or esophagitis that could be the source of their symptoms, 5 out of 10 patients (50%) had biopsies diagnostic of EE.

**Conclusions:** EE should no longer be considered a rare cause of dysphagia in adults. Routine esophageal biopsies should be performed in patients with dysphagia who have no obvious endoscopic anatomical abnormalities that could explain their dysphagia, especially if they are male. If these findings are confirmed in large prospective studies, increased awareness of eosinophilic esophagitis in adults will likely avoid unnecessary further investigations after a “negative” upper endoscopy.

**Endoscopic Ultrasonography with Fine Needle Aspiration (EUS-FNA) for Esophageal Cancer Staging and Its Impact on Therapy: A Survey of Gastroenterologists**

Kevin J Peifer, M.D., Steven A. Edmundowicz, M.D., Dayna S. Early, M.D., Riad Azar, M.D.* Division of Gastroenterology, Washington University School of Medicine, Saint Louis, MO.

**Purpose:** To assess the perception of gastroenterologists who perform EUS-FNA for esophageal cancer staging and the impact of nodal involvement on therapeutic decisions.

**Methods:** A 15 question survey was distributed via email to gastroenterologists who perform EUS. This survey included questions related to clinical practice, referral patterns and communication with surgeons. Clinical vignettes were used to assess if EUS-FNA of lymph nodes changed therapeutic decisions made by thoracic surgeons.

**Results:** 77 gastroenterologists responded to the survey (31%). 68% personally perform more than 20 staging EUS procedures per year for esophageal cancer. Nearly 80% stated their institution used EUS-FNA for esophageal cancer staging in more than 60% of cases. All respondents felt it was important to directly communicate with a thoracic surgeon. 43% felt this communication should occur after the procedure, while another 41% believe communication both before and after the procedure is ideal. Over 95% felt EUS with or without FNA was the most accurate T- and N-staging test. Over 75% thought a pre-EUS PET scan is useful, particularly in identifying areas for FNA. Less than 25% of endoscopic ultrasonographers surveyed will always dilate a stricture to complete a EUS staging procedure, where as 45% will consider performing dilation on a case by case basis. All respondents consider FNA of an abnormal appearing lymph node, although only 55% will perform FNA in all such cases. If EUS-FNA found either a positive celiac or gastrohepatic ligament lymph node in a patient with a proximal esophageal cancer, the majority of respondents (92% and 65% respectively) felt this represents metastatic disease that precludes esophagectomy. 56%, 64% and 48% answered that positive proximal para-esophageal, gastrohepatic ligament and celiac lymph nodes respectively did not prevent esophagectomy for patients with distal esophageal cancer.

**Conclusions:** EUS-FNA has become widely utilized for accurate staging and directing therapy for esophageal cancer. Significant variability in practice patterns exists between gastroenterologists who perform EUS. Based on this survey, direct communication between the endoscopic ultrasonographer and the thoracic surgeon before and after EUS may help with decisions related to FNA and dilution encountered during the EUS exam as well as decisions pertaining to ultimate appropriateness of esophagectomy.

**Clinical Study on Pathophysiology of Endoscopic-Negative GERD**

Toshikiro Konagaya, M.D.∗, Toshihiko Hayakawa, M.D., Hiroshi Kaneko, M.D., Yasushi Funaki, M.D., Akihito Kasahara, M.D., Shinichi Kakamu, M.D. Gastroenterology, Aichi Medical University, Nagakute, Aichi, Japan.

**Purpose:** The underlying mechanisms for symptoms in patients with endoscopy-negative GERD (EN-GERD) remain unclear. Proton pump inhibitors (PPI) are not always effective for relief from reflux symptoms. It was reported that prokinetics drug improved heartburn in patients of functional dyspepsia (FD). To analyze pathophysiology of EN-GERD in the view of gastric acid secretion and emptying, and long-term outcome.

**Methods:** Fifty-two EN-GERD patients with chief complaint of ‘heartburn’ (38 males: mean age; 56.1 yr) gave informed consent to entry this study. GERD related symptoms intake (by QUEST, cut off: 6 points), upper gastrointestinal endoscopy, 24-h gastroesophageal pH monitoring, and gastric emptying test were performed. pH monitoring was performed under hospitalization. Gastric emptying time was determined by the paracetamol method. In 47 out of 52 subjects, prescription, symptoms and endoscopic findings were followed up for at least 1 yr (average; 1,347 d).

**Results:** Grades of endoscopic esophagitis were classified according to the Los Angeles classification into none (Grade O; 12 cases), mild (Grade A & B; 20), and severe (Grade C & D; 20). No correlation with esophagitis grades were determined in gender, age, QUEST score, and H. pylori status. In accordance with esophagitis grades, prevalence of hiatus hernia of the esophagus and grade of gastric mucosal atrophy were significantly higher. Lower gastro-esophageal reflux and higher gastric pH > 3 holding time ratio were observed in EN-GERD. Lower pepsinogen I/I ratio were observed in patients with none esophagitis, but gastrin concentration showed no difference among the groups. Delayed gastric emptying was observed in patients with EN-GERD as compared with either those with esophagitis or healthy volunteers (P < 0.05). Among 37 esophagitis, PPI (18 cases), H2 blocker (15), and prokinetics (1) were prescribed with no recurrence and symptom-free. In 10 EN-GERD, prokinetics alone was effective in 4 cases and PPI was needed in 2. One patients in EN-GERD developed esophagitis (Grade A).

**Conclusions:** The diagnostic characteristics of EN-GERD involve less acid reflux to the esophagus and low gastric acidity accompanied by mucosal atrophy together with delayed gastric emptying. Taking the advantage of prokinetics in EN-GERD into consideration, EN-GERD should be categorized into (dysmotility-like) FD rather than endoscopy-positive esophagitis.

**Tale of Two Cancers: Continued Changes in the Incidence of Esophageal and Gastric Adenocarcinoma**


**Purpose:** The incidence rates of esophageal and gastric adenocarcinoma (ACa) have been changing over the past 30 years. Time trends in the incidence of ACa of the esophagogastric junction (EGJ) are not as well known as this area is difficult for large databases to define. Aim: To estimate changes by decade in specific incidence of esophageal and gastric ACa from 1971–2000.

**Methods:** Using the unique data resources of the Rochester Epidemiology Project, all cases of gastric and esophageal ACa in Olmsted County, Minnesota between 1971 and 2000 were identified. The complete inpatient and outpatient records of each case were reviewed and the specific site (distal
stomach, proximal stomach, EGJ and esophagus) was identified using consistent criteria. Incidence rates were estimated directly and age and sex adjusted to US white 2000 population figures. Age, gender and calendar year effects were evaluated using Poisson regression.

Results: A total of N = 183 cases were identified. The site and decade specific incidence rates are given in Table I. The incidence of distal stomach ACa declined and esophageal ACa increased. Furthermore the incidence of proximal stomach ACa was stable while EGJ increased significantly. In the most recent decade, the incidence of esophageal ACa was numerically higher than stomach ACa.

Table 1. Gastric and Esophageal Incidence Rates 1971–2000. Age & Sex-Adjusted Rates Adjusted to US White Census 2000, Rates are per 100,000 Person-Years of Follow-up

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<tbody>
<tr>
<td>Esophageal</td>
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<tr>
<td>Esophagus</td>
<td>0.4 (0.0,1.1)</td>
<td>0.7 (0.1,1.4)</td>
<td>2.5 (1.4,3.6)</td>
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<tr>
<td>EGJ</td>
<td>0.6 (0.0,1.2)</td>
<td>1.9 (0.8,2.9)</td>
<td>2.2 (1.2,3.1)</td>
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<tr>
<td>Overall</td>
<td>1.0 (0.2,1.9)</td>
<td>2.6 (1.4,3.9)</td>
<td>4.7 (3.2,6.1)</td>
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<tr>
<td>Stomach</td>
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<tr>
<td>Cardia/Fundus</td>
<td>1.3 (0.4,2.3)</td>
<td>1.8 (0.8,2.8)</td>
<td>0.8 (0.2,1.3)</td>
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<tr>
<td>Distal</td>
<td>6.8 (4.5,9.1)</td>
<td>2.9 (1.6,4.2)</td>
<td>2.1 (1.2,3.1)</td>
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<tr>
<td>Diffuse</td>
<td>1.2 (0.3,3.0)</td>
<td>0.7 (0.1,1.2)</td>
<td>0.4 (0.0,0.8)</td>
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<tr>
<td>Overall</td>
<td>9.3 (6.7,11.9)</td>
<td>5.3 (3.6,7.1)</td>
<td>3.3 (2.1,4.5)</td>
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Conclusions: In this population, esophageal ACa is now as common as gastric ACa. The complete medical records available for individual review in this study lead to very accurate site-specific identification which allows one to note that proximal gastric ACa incidence remains unchanged while the incidence of EGJ ACa is increasing.

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Association of Barrett's Esophagus and Colon Adenomas
Deepa K. Shah, M.D., Richard Gerkin, M.D., Francisco C. Ramirez, M.D., Michele A. Young, M.D.* Internal Medicine, Banner Good Samaritan, Phoenix, AZ and Gastroenterology, Carl Hayden VA Medical Center, Phoenix, AZ.

Purpose: Barrett's esophagus and colonic adenomas share similar genetic alterations and environmental risk factors. A similar dysplasia to carcinoma sequence is seen in both premalignant conditions, thus the aim is to determine whether Barrett's esophagus is associated with adenomatous lesions in the colon.

Methods: A review of the endoscopic database at a VA medical center was performed from January 1997 to April 2005. The first two hundred patients that were men with Barrett's esophagus on upper endoscopy and histological confirmation and had a complete colonoscopy with an adequate prep were included. Two hundred patients with symptoms of reflux and no evidence of Barrett's esophagus or erosive esophagitis meeting the same criteria comprised the control group. The number, size and histology of each polyp was recorded. Advanced neoplasia was defined as one or a combination of adenoma ≥ 10 mm, villous component, HGD, or invasive carcinoma. Chi square was used to compare proportional data whereas, the student's t-test was used to compare means.

Results: There were 200 patients with Barrett's esophagus, mean age 60.8 ± 0.6 and 200 controls, mean age 59.8 ± 0.8. The BMI's of the Barrett's esophagus and control group were 28.7 ± 0.4 and 29.3 ± 0.4, respectively. 61% of the patients had short segment Barrett's esophagus and 39% had long segment. Characteristics of adenomatous lesions in Barrett's patients and controls are shown below.

Conclusions: Barrett's esophagus patients had significantly higher adenomas than in the controls. There was a trend toward more adenomas per patient in the Barrett's esophagus patients than in the controls. There was a trend toward a greater number of advanced neoplasms in the Barrett’s esophagus group compared with the controls.

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Histological Changes of Lower Esophagus Transiently Occur One Month after Helicobacter pylori Eradication, but Will Recover within 12 Months
Masanori Toyoda, Nobuo Aoyama,* Daisuke Shirasaka, Iwaya Miki, Yoshinori Morita Department of Clinical Molecular Medicine, Division of Diabetes, Digestive and Kidney Diseases, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan and Department of Endoscopy, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan.

Purpose: Although the association between newly diagnosed reflux esophagitis and Helicobacter pylori (H. pylori) eradication has been reported, there are few reports that examined esophagitis histologically both before and after eradication. This study evaluated the histological changes in lower esophagus before and after eradication therapy.

Methods: Histological evaluation of lower esophagus in 55 subjects (25 without endoscopically reflux esophagitis with H. pylori, 13 with mild esophagitis without H. pylori and 17 normal controls without H. pylori) were analyzed before, 1 and 12 months after H. pylori eradication. Basal layer zone thickness, height of papillae, Ki-67 index were used as histological evaluation of esophagitis.

Results: One month after eradication, basal zone thickness and Ki-67 index significantly increased (p < 0.05, respectively). Papillar height also increased although not significantly. Twelve months after eradication, basal zone thickness and papillar height return to the levels before eradication. The same tendency was found in Ki-67 index, although its recovery was not absolute during 12 months. In H. pylori positive subjects without endoscopically reflux esophagitis, the histological findings were not different from those in H. pylori negative controls, regardless of eradication. In H. pylori negative subjects with esophagitis, all histological parameters showed significantly high levels compared to those in H. pylori positive subjects without esophagitis before and after eradication, and those in normal controls (p < 0.05).

Conclusions: H. pylori eradication may cause histological esophagitis during a short observation period. However, its histological change may possibly recover 12 months after eradication.

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Proton Pump Inhibitors Are Associated with Reduced Incidence of Esophageal Malignant Tumors in Patients with Gastro-Esophageal Reflux Disease
Vikas Khurana, M.D.,* Gloria Caldito, Ph.D., Jamie S. Barkin, M.D. Gastroenterology and Hepatology, Overton Brooks VA Medical Center, Shreveport, LA; Biometry, Louisiana State University Health Science Center at Shreveport, Shreveport, LA and Division of Gastroenterology, University of Miami/ Mt. Sinai Medical Center, Miami, FL.
Two mechanisms contributing to gastric cardia adenocarcinoma are thought of tumor originating in the gastric cardia, later spreading to the esophagus. Adenocarcinoma, however may occur in the absence of Barrett’s metaplastic Barrett’s esophageal mucosa finally developing into adenocarcinoma. Evolution of esophageal adenocarcinoma usually begins with GERD, leading to aggressive acid suppression. Combined multichannel intraluminal

Panendoscopy-Gastroesophageal Junction Adenocarcinoma in a Patient without Barrett’s Mucosa

Sobia Ali, M.D.,* Ganapathi Parameswaran, M.D., Tarun Kothari, M.D. Internal Medicine, Unity Health System, Rochester, NY.

Purpose: We report the occurrence of Panendoscopy-gastroesophageal adenocarcinoma in a patient without Barrett’s mucosa. We believe this is the first reported case of this clinical entity. Although several case reports have been published about distal esophageal and gastroesophageal adenocarcinoma, none have reported pan-esophageal adenocarcinoma on the initial presentation, in absence of Barrett’s mucosa. 56 year old male presented with complaints of dysphagia and odynophagia for two weeks, and a 25lb weight loss in the last two months. Past medical history included hypertension, but no history of GERD, or tobacco use. The patient underwent an upper GI series, showing numerous superficial ulcerations involving the entire esophagus. Subsequently an upper gastrointestinal endoscopy was performed, showing an ulcerated mass at the cardia of stomach and severe ulcerative esophagitis involving the entire esophagus. Biopsies were taken, from the thoracic esophagus till the gastric mass in 7 places, each at 3-4 cm intervals. Biopsy results showed poorly differentiated adenocarcinoma in all specimens. No evidence of Barrett’s mucosa was found and a stain was negative for H. pylori. An abdominal CT scan showed extensive metastatic disease. The patient was referred to an oncologist for further workup. Esophageal adenocarcinoma represents 50% of all esophageal carcinomas. Evolution of esophageal adenocarcinoma usually begins with GERD, leading to metaplastic Barrett’s esophageal mucosa finally developing into adenocarcinoma. Adenocarcinoma, however may occur in the absence of Barrett’s mucosa, as was the case with our patient. We believe the patient had spread of tumor originating in the gastric cardia, later spreading to the esophagus. Two mechanisms contributing to gastric cardia adenocarcinoma are thought to be H. pylori, and the resultant effects of GERD induced damage, both, not seen in our patient. Studies have shown up to 40% of patients diagnosed with esophageal adenocarcinoma may not have any reported symptoms of GERD. On reviewing case reports of esophageal adenocarcinoma and time of onset of symptoms, we found that these patients had involvement of only the distal esophagus at time of presentation. Interestingly, our patient in spite of this extensive involvement, remained asymptomatic until the very end. Our literature search revealed no prior reports of such extensive disease, with such a time compressed clinical course. The rapidity of spread of tumor in this case raises the question of surveillance endoscopy.

Does Combined Multichannel Intraluminal Impedance and pH Help with the Diagnosis of Refractory GERD?

Subhrajit Maji, M.D., Wissak Pakk, M.D., Steven Shy, M.D., Michael F. Vaez, M.D., Ph.D.* Department of Gastroenterology and Hepatology, Cleveland Clinic Foundation, Cleveland, OH.

Purpose: Persistent acid or non-acid reflux has been implicated as a cause of typical or atypical gastroesophageal reflux (GERD) symptoms refractory to aggressive acid suppression. Combined multichannel intraluminal...
impedance and pH (MII-pH) allows evaluation of both acid and non-acid reflux events. However the clinical utility of MII-pH in this patient population has not been well established.

Methods: A prospective cohort study of patients with refractory GERD symptoms was performed. Patients with typical symptoms of heartburn and regurgitation or atypical symptoms of hoarseness, throat clearing, sore throat, cough, chest pain and globus who are unresponsive to twice-daily (BID) proton pump inhibitor (PPI) therapy were included. All patients underwent MII-pH on therapy. The impedance measuring segments were positioned at 3, 5, 7, 9, 15, and 17 cm above LES and the pH sensor at 5 cm above LES. Normal values for MII-pH: Distal reflux events – total ≤73, acid ≤55, non-acid ≤1; Proximal reflux events – total ≤31, acid ≤28, non-acid ≤1.

Results: Total of 42 patients were enrolled. 15 patients had atypical symptoms only and 27 had typical symptoms with or without atypical symptoms. Symptom prevalence: hoarseness (53.3%), chest pain (33.3%), cough (15.3%), throat symptoms (40%), heartburn (70.3%) and regurgitation (66.7%). None of the patients with only atypical symptoms (0 of 15, 0%) had abnormal MII-pH. In contrast, 9 of 27 (33%) patients with typical symptoms had abnormal MII-pH. (p < 0.02) In this group, the predominant symptom in patients with abnormal MII-pH was regurgitation (7 of 9, 78%) while regurgitation was present in 6 of 18 (33%) patients with normal MII-pH. (p < 0.05). Additionally, 5 of 9 (56%) patients with abnormal MII-pH (4 had symptom of regurgitation) underwent surgical fundoplication and had complete symptom resolution post fundoplication.

Conclusions: MII-pH is unlikely to be clinically useful in patients with atypical symptoms refractory to aggressive acid suppression. However, it may be useful in those who have typical symptoms. In this group, regurgitation may be predictive of abnormal MII-pH.

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The Impact and Yield of Upper Endoscopy in a Diverse Population with Refractory GERD
Reezwana Chowdhury, B.A., Josh Olstein, M.D., Fritz Francois, M.D.* Medicine, Division of Gastroenterology, NYU School of Medicine, New York, NY.

Purpose: Several studies have suggested that EGD may alter the management of patients with reflux symptoms. It remains unclear whether the benefit of EGD is consistent across ethnic groups given the lower prevalence of Barrett’s esophagus in minority populations. The aim of this study was to determine the yield of EGD and its impact on the management of GERD in a multi-ethnic cohort with refractory symptoms.

Methods: All ambulatory patients who completed upper endoscopy for heartburn between July 2002 and December 2004 in a large municipal hospital were reviewed. The study cohort consisted only of patients with persistent heartburn despite at least 6 weeks of PPI therapy. Pre-procedure demographic and clinical data was collected and patients were grouped according to the presence of alarm symptoms (dysphagia, odynophagia, GI bleeding, weight loss, or iron deficiency anemia). Reflux complications were defined as grade 2 or above esophagitis, Barrett’s esophagus ≥3 cm, or esophageal stricture. GERD management was considered to be altered if there was a change in antisecretory therapy, stricture dilation, Barrett’s surveillance initiated, or referral to surgery.

Results: A total of 263 patients (mean age 53 ± 12 years) met inclusion criteria of which 33 (13.6%) were Caucasian, 21 (8.6%) were African-American, 149 (61.3%) were Hispanic, and 40 (16.5%) were Asian or of Middle Eastern descent. Although reflux complications (RC) were highest among Caucasians compared to non-Caucasians, the difference was not significant (15% vs. 14%; p = 0.83). The prevalence of RC in the 78 patients with alarm symptoms was not significantly different from the 185 patients without alarm symptoms (13% vs. 15% p = 0.69). EGD altered GERD management in 35% of patients although only 14% of individuals had RC. The 34 patients with RC were significantly more likely to have any alteration in management compared to the 229 patients without RC (56% vs. 31% p = 0.006). Although the prevalence of RC did not differ according to gender, among those with RC women were significantly more likely to have alteration in management when compared to men (72% vs. 38%; p = 0.042).

Conclusions: In this diverse population with refractory GERD, reflux complications did not differ according to gender, ethnicity or the presence of alarm symptoms. EGD significantly altered management especially in women with esophageal findings. Further studies to evaluate predictors of reflux complications and gender differences in management in multi-ethnic populations are warranted.

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Suture Location Impacts Clinical Outcome for Endoscopic Treatment of Gastroesophageal Reflux Disease
Julia J. Liu, M.D., Peter J. Kahrilas, M.D., Xin Li, B.S., Rie Maurer, M.S., David L. Carr-Locke, M.D., John R. Saltzman, M.D.* Gastroenterology, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA and Gastroenterology, Northwestern University, Chicago, IL.

Purpose: Endoscopic treatments for gastroesophageal reflux disease (GERD) have variable long-term success rates, however the reason for such variability in response rates is unclear. The aim of this study was to determine the effects of location and number of sutures on clinical outcome in patients undergoing endoscopic treatment for GERD.

Methods: Patients with persistent GERD symptoms despite medical therapy and undergoing endoscopic anti-reflux treatment with more than one year follow up were included. Endoscopic suturing of the gastroesophageal junction (GEJ) was done using commercially available endoscopic suturing devices. Sutures were placed within 2 cm distal to the squamo-columnar junction in a circumferential fashion. The number of sutures was recorded and the locations of the sutures were documented according to the face clock position at the GEJ. Greater curve sutures were at the 6 o’clock position and lesser curve sutures were at the 12 o’clock position. Complete symptom resolution was defined as absence of heartburn and regurgitation symptoms at the longest available follow up. The association between number of sutures, suture location (combination of lesser and greater curve, or lesser curvature or greater curvature) and symptom resolution was examined using Fisher’s exact test.

Results: Forty-two patients (26F/16M) with a mean follow up of 20 months were included in the analysis. Thirteen patients (31%) achieved complete symptom resolution. Sixteen patients had placement of three sutures, 24 patients had placement of two sutures, and 2 patients had placement of one suture. The number of sutures did not correlate with clinical outcome. Patients with a combination of lesser and greater curve, or lesser curvature or greater curvature and symptom resolution was examined using Fisher’s exact test.

Conclusions: A combination of greater and lesser curve sutures at the gastroesophageal junction was associated with the best long-term clinical outcome of endoscopic treatment for gastroesophageal reflux disease. Future larger studies will be needed to confirm this finding and to determine the optimal suture placement configuration.

24
Regression of Barrett’s Esophagus with High Dose Proton Pump Inhibitor Therapy
Kart A. Barrett, DO*. Family Practice, Battle Creek Health System, Athens, MI.
Purpose: To evaluate the therapeutic effect of high dose Proton Pump Inhibitors (PPI's) in the regression of specialized intestinal metaplasia of the distal esophagus (Barrett's Esophagus = BE).

Methods: I reported (Vol. 93, No. 9, Suppl., 2003) on five consecutive cases of endoscopically biopsy confirmed BE that had regressed to “no BE identified” at yearly surveillance endoscopy. I now have identified five more similarly treated cases. Patients were treated with high dose PPI to the end point of total supression of atypical, extraluminal, supraesophageal GERD signs and symptoms. Patients were encouraged to abstain from caffeine, mints and fatty foods. Weight loss was encouraged as was elevating the head of the bed, sleeping on the left side and avoidance of late evening meals. All patients took PPIs in dosage range of 160 mg to 360 mg daily titrated to total symptom supression.

Results: At follow up endoscopy all 5 patients who had previously demonstrated specialized intestinal metaplasia were symptomatically improved. They had biopsy results that were free of any evidence of histologic BE. Four of the five patients have been diagnosed with Obstructive Sleep Apnea Syndrome(OSAS).

Conclusions: Barrett’s Esophagus can regress with high dose Proton Pump Inhibitor therapy and lifestyle alterations when the end point of therapy is total supression of extraluminal, atypical GERD symptoms.OSAS is commonly encountered in GERD patients.

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Clinical Utility and Acceptance of Esophageal Capsule Endoscopy for Evaluation of Patients with Chronic Heartburn Not Seeking Traditional Care

Purpose: Chronic heartburn affects as many as 10 million US citizens over 50 years of age. Many individuals may not seek medical care as a result of milder symptoms or reluctance to undergo an invasive procedure. This study evaluates the utility and acceptance of esophageal capsule endoscopy (ECE) in patients with chronic heartburn who are not seeking traditional medical care.

Methods: Subjects with a minimum of 2 episodes of heartburn a week during the past 6 months were recruited from the community. Subjects who had undergone an upper endoscopy within 5 years or had dysphagia were excluded. Subjects completed a pre-study questionnaire to determine heartburn day and nocturnal frequency, duration, use of medications and impact on QOL prior to undergoing ECE. Data is presented on the first 13 of 40 subjects.

Results: Six subjects reported discussing their heartburn with their primary physician, and 9 were using daily or almost daily heartburn medication.

Barrett’s esophagus (BE) appearing mucosa was seen in 6 subjects, and 5 had esophagitis (LA Class A/B/4; LA Class C/D/1). Two subjects had non-obstructing esophageal strictures and one subject had findings suggestive of an esophageal carcinoma. The majority of subjects responded that they would consider undergoing an endoscopy evaluation if the ECE showed significant abnormal findings. Nine of the 11 subjects over 50 years of age had undergone a colonoscopy for cancer screening in the past. Other measures of heartburn symptoms are summarized in Table #1.

Table 1.

<table>
<thead>
<tr>
<th>Non-BE (n = 7)</th>
<th>BE (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>61</td>
</tr>
<tr>
<td>Male:Female Ratio</td>
<td>4.3:4.2</td>
</tr>
<tr>
<td>Duration (1:&lt; 1 yr; 2:1–5 yrs; 3:3–5 yrs)</td>
<td>2.4</td>
</tr>
<tr>
<td>Frequency (1:Occasional; 2:Most days; 3:Daily)</td>
<td>1.7</td>
</tr>
<tr>
<td>Nocturnal (0:Never; 1:Occasional; 2:Most nights)</td>
<td>0.7</td>
</tr>
<tr>
<td>Impact on QOL (0:None; 1:Minimal; 2:Moderate; 3:Severe)</td>
<td>2</td>
</tr>
</tbody>
</table>

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Comparative Study Between Life Style Modifications and Sucralfate on Pregnant Women’s Heartburn
Ali Mohbnaifar, M.D., Parvin Saalari, R.N., M.P.H., Mahnaz Akbari, M.P.H., Mohammad Forivar, M.D. Gastroenterology, Mashhad University Medical School, Mashhad, Islamic Republic of Iran; Midwifer and Nursing School of Nursing and Midwifery, Mashhad, Islamic Republic of Iran; Public Health, School of Nursing and Midwifery, Mashhad, Islamic Republic of Iran and Gastroenterology, Boston University Medical School, Boston, M.A.

Purpose: 30 to 80 percent of pregnant women suffer from heartburn. This study was done to compare the effect of education about life style modifications and Sucralfate therapy.

Methods: This is a triple-blind clinical study involving 78 pregnant women suffering from frequent daily heartburn. By multiple stage sampling method in three groups “placebo,” Sucralfate” and “life style modifications”. At first, clinical evaluation of the average of the last three days of heart burn done. And an interview was performed to acquire information pertaining to their personal characteristics, fertility, health, and behavioral habits. After delivering medicine to its specific group and providing necessary training by educational group, after one week clinical evaluation was done again for analyzing the normal distributed parameters were used and for non normal distributed variables non parametric statistics were utilized.

Results: Finding showed that there were significance difference between mean of times (Placebo P = 0.002), (Sucralfate P = 0.032), (training P < 0.0001), intensity (placebo P = 0.003), (Sucralfate P = 0.020), (training P < 0.0001), duration (placebo P < 0.0001), (Sucralfate P < 0.0001), (training P <0.0001) before and after treatment. Decreasing of frequency of radiation rate after treatment were (26.1% in placebo group, 41.7% in sucral fate group and 82.6% in training group.) There were a positive linear relationship between acquired degree of education and the rate of improvement, that were for intensity (P = 0.008 R = 0.5), times (P = 0.024 R = 0.4) and duration (P = 0.011 R = 0.2).

Conclusions: Life style modification is an efficient method in treating heartburn of pregnant women, but for providing a point of view about sucral fate, it needs further research.

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Gatifloxacin-Containing Sequential Therapy for H. pylori Infection
David Y. Graham, M.D.,∗ Suhaib Abudayyeh Abudayyeh, M.D., Hala El-Zimaitly, M.D., Jill Hoffman, PA-C, Antonie R. Opekun, PA-C. Medicine, Michael E. DeBakey VAMC, Houston, TX and Baylor College of Medicine, Houston, TX.

Purpose: The success rate of anti-H. pylori therapy has continued to fall in part due to increasing resistance.

Aim: To test the sequential combination of high dose PPI-amoxicillin followed by the addition of gatifloxacin for H. pylori infection.

Methods: This was a pilot study where patients with active H. pylori infection received sequential therapy consisting of 40 mg of omeprazole and 1 g amoxicillin t.i.d. for 12 days. Both naive and treatment failures were eligible. On days 6 through 12 gatifloxacin (400 mg in the a.m.) was added to produce a triple therapy. Outcome was assessed by UBT or
endoscopy with histology and culture done 4–6 weeks after ending antibiotic therapy.

**Results:** To date, the cure rate has been 100% among those who received all three drugs. One patient stopped therapy after receiving only the PPI plus amoxicillin and therapy was unsuccessful. Side effects consist of mild diarrhea/loose stools in 25%. Another patient in whom gastritis had been contraindicated received 40 mg of esomeprazole and 1 g amoxicillin t.i.d. for 12 days and then metronidazole 500 mg t.i.d on days 6 through 12 and the infection was treated successfully.

**Conclusions:** Sequential therapy using the combination of high dose PPI and amoxicillin (the German therapy) followed by the addition of metronidazole appears to be an excellent first or second line therapy for *H. pylori* infections.

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### Evaluation of Dysphagia after Laparoscopic Antireflux Surgery in Patients with Ineffective Esophageal Motility

**Purpose:** Persistent post-operative dysphagia is common in patients who undergo antireflux operations. In order to avoid post-operative dysphagia the operation has been tailored according to the preoperative esophageal manometric findings at the cost of decreased efficacy. To evaluate and compare the incidence and severity of dysphagia in patients with ineffective esophageal motility who underwent either a Toupet or Nissen fundoplication Versus patients with normal esophageal motility who underwent a Nissen fundoplication.

**Methods:** A retrospective review was done of 47 patients who underwent a laparoscopic antireflux procedure over a 4 year period. Among these 10 patients had ineffective esophageal motility, 5 of them had a Nissen and the other 5 had a Toupet procedure. These 10 patients were compared with 10 other patients with normal esophageal body motility who underwent a Nissen procedure. All patients were interviewed post-operatively after an interval of 4–6 years. Their symptoms were recorded on a dysphagia score ranging from 0–13.

**Results:** Among the 5 patients with ineffective motility who underwent a Nissen fundoplication 0(0%) complained of dysphagia, average score 0.8 and maximum score 1. Among the 5 patients with ineffective motility who underwent a Toupet fundoplication 3(60%) complained of dysphagia, average score 3.6 and maximum score 6. Among the 10 patients with normal esophageal body motility who underwent a Nissen procedure all patients were interviewed post-operatively after an interval of 4–6 years. Their symptoms were recorded on a dysphagia score ranging from 0–13.

**Conclusions:** Laparoscopic Nissen fundoplication can be safely performed in patients with ineffective esophageal motility and the antireflux procedure does not have to be modified on the basis of preoperative esophageal body motility.

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### Ineffective or “Insignificant” Esophageal Motility Disorder in Gastroesophageal Reflux Disease (GERD)

**Purpose:** Ineffective esophageal motility (IEM) is a common finding in patients with GERD. Laparoscopic nissen fundoplication (LNF) is the surgical treatment of choice for GERD. However, dysphagia may be reported following surgery. Patients with IEM may have dysphagia pre-surgically secondary to their underlying motility disorder, which may worsen after LNF. We aimed to evaluate the prevalence of IEM in GERD, and compare symptoms of dysphagia pre- and post LNF in IEM vs non-IEM patients.

**Methods:** LNFs performed between Jan and Dec 2004 were evaluated. Of 36 patient records, 35 completed esophageal manometry study (Solid-state esophageal manometry was performed following an overnight fast) and pre-op symptom assessment questionnaire. Seventeen patients completed pH-metry, and 34 completed EGD. All patients had a post-op follow up at 1 to 8 months.

**Results:** Thirty six fundoplications were performed; 33 laparoscopic and 3 open. Indications included GERD (30), achalasia (4), and paraesophageal hernia (13) and large hiatal hernia (2) repairs (median age 61 y, range 21–85; 21 F: 34 Caucasian, 2 Hispanic). Thirty (83%) patients had either subjective or objective GERD (EGD/pH); 9 of 30 (30%) had IEM on manometry tracings (4 [13%] in subjective reflux only, 0 in objective reflux only, and 5 [17%] in both). IEM and non-IEM groups did not differ in age, gender, or race (64y ± 12; 80% F; 100% Caucasian vs 59y ± 14; 59% F; 91% Caucasian). Pre- and post-op dysphagia was noted in 30% and 40%, respectively, in IEM group and 50% (OR 0.43 [0.9, 2.1]) and 43% (OR 0.96 [0.21, 4.4]), respectively, in non-IEM group. Three of 9 (33%) IEMs had either symptomatic paraesophageal hernia or large hiatal hernia. Six of 9 (67%) IEMs had reduced lower esophageal sphincter pressures. Interestingly, 2 of 6 Toupet’s were performed in GERD patients with IEM, which resulted in relief of pre-op dysphagia.

**Conclusions:** Ineffective esophageal motility may be a common finding in gastroesophageal reflux disease; however, the clinical significance remains unclear as the rate of pre- and post-op dysphagia did not differ between IEM vs non-IEM group. Well-designed prospective studies are needed to better elucidate the impact of esophageal dysmotility disorders on outcomes following esophageal surgery for GERD.

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### Prevalence of Gastroesophageal Reflux in Native Americans

**Purpose:** A recent Gallup survey found that 40% of Americans suffer from heartburn at least once a month. The American population is heterogenous, and thus the prevalence of gastroesophageal reflux (GER) should be expected to vary among these different population groups.

**Aim:** To determine the prevalence of GER in Native Americans (NA).

**Methods:** Patients from an Indian Medical Center attending primary care clinics were asked to complete a survey regarding the presence and frequency of heartburn and regurgitation. For comparison purposes, pts attending a VA Medical Center primary care clinics (a population mostly Caucasian) were also surveyed regarding the above symptoms of GER. For the NA population their primary residence (urban vs. rural) was also recorded. Demographic data was obtained in both the NA and VA populations.

**Results:** A total of 1553 NA (representing over 25 tribes) and 1004 VA pts completed the survey. Demographics are shown in table 1.

<table>
<thead>
<tr>
<th>Population Demographics</th>
<th>NA (all)</th>
<th>NA (Rural)</th>
<th>NA (Urban)</th>
<th>VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1553</td>
<td>292</td>
<td>1261</td>
<td>1004</td>
</tr>
<tr>
<td>Age</td>
<td>43.3 ± 0.4*</td>
<td>49.0 ± 0.9</td>
<td>42.0 ± 0.4</td>
<td>59.4 ± 0.4*</td>
</tr>
<tr>
<td>Men</td>
<td>537</td>
<td>104</td>
<td>433</td>
<td>930</td>
</tr>
<tr>
<td>Age Men</td>
<td>45.8 ± 0.7*</td>
<td>50.7 ± 1.6</td>
<td>43.8 ± 0.8</td>
<td>60.0 ± 0.5*</td>
</tr>
<tr>
<td>Women</td>
<td>1016</td>
<td>188</td>
<td>828</td>
<td>78</td>
</tr>
<tr>
<td>Age Women</td>
<td>43.1 ± 0.5*</td>
<td>48.1 ± 1.2</td>
<td>41.1 ± 0.5</td>
<td>51.5 ± 1.4*</td>
</tr>
<tr>
<td>Older 65</td>
<td>166*</td>
<td>59</td>
<td>107</td>
<td>336*</td>
</tr>
<tr>
<td>Younger 65</td>
<td>1387*</td>
<td>233</td>
<td>1154</td>
<td>670*</td>
</tr>
</tbody>
</table>

*p < 0.05 NA vs. VA pts.*
Percent of pts (NA and VA) reporting heartburn and regurgitation are shown in table 2.

<table>
<thead>
<tr>
<th>GER Symptoms</th>
<th>NA (all)</th>
<th>NA (Rural)</th>
<th>NA (Urban)</th>
<th>VA (all)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn (all)</td>
<td>53%*</td>
<td>50%</td>
<td>55%</td>
<td>67%*</td>
</tr>
<tr>
<td>Heartburn (Men)</td>
<td>55%*</td>
<td>57%</td>
<td>54%</td>
<td>67%*</td>
</tr>
<tr>
<td>Heartburn (Women)</td>
<td>52%*</td>
<td>47%</td>
<td>53%</td>
<td>77%*</td>
</tr>
<tr>
<td>Heartburn (&gt;65 y)</td>
<td>50%**</td>
<td>47%</td>
<td>50%</td>
<td>65%**</td>
</tr>
<tr>
<td>Heartburn (&lt;65 y)</td>
<td>54%*</td>
<td>52%</td>
<td>54%</td>
<td>72%*</td>
</tr>
<tr>
<td>Regurgitation (all)</td>
<td>45%*</td>
<td>41%</td>
<td>46%</td>
<td>62%*</td>
</tr>
<tr>
<td>Regurgitation (Men)</td>
<td>44%*</td>
<td>36%</td>
<td>46%</td>
<td>61%*</td>
</tr>
<tr>
<td>Regurgitation (Women)</td>
<td>45%*</td>
<td>44%</td>
<td>46%</td>
<td>72%*</td>
</tr>
<tr>
<td>Regurgitation (&gt;65 y)</td>
<td>49%*</td>
<td>34%</td>
<td>39%</td>
<td>65%*</td>
</tr>
<tr>
<td>Regurgitation (&lt;65 y)</td>
<td>54%*</td>
<td>42%</td>
<td>47%</td>
<td>72%*</td>
</tr>
</tbody>
</table>

*p < 0.0001; ** p < 0.05 NA vs. VA pts.

Regarding the frequency of GER symptoms, VA pts reported more daily heartburn (40%) and regurgitation (40%) compared to the NA (32% and 38%, respectively) pts. This difference, however only approached statistical significance (p = 0.1).

Conclusions:
(1) NA report heartburn less often than VA pts, regardless of age and gender.
(2) NA experience less daily heartburn than VA pts.
(3) The difference in GER prevalence between NA and VA populations needs to be explored further.

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The Prevalence and Characteristics of Gastric Pathology in Refractory GERD Patients Undergoing Upper Endoscopy
Josh Olstein, M.D., Reezwana Chowdhury, B.A., Fritz Francois, M.D.*
Medicine, Division of Gastroenterology, NYU School of Medicine, New York, NY.

Purpose: The sensitivity of EGD for detecting relevant esophageal disease in patients with refractory reflux symptoms has been reported to be low. It remains unclear whether the incidental discovery of gastric pathology increases the overall yield of EGD in this population. The aim of this study was to evaluate the prevalence and characteristics of gastric pathology detected by endoscopy in a multi-ethnic population with refractory reflux symptoms.

Methods: Patients evaluated with EGD for heartburn between July 2002 and December 2004 in a large municipal hospital were reviewed. The study population consisted only of patients with persistent heartburn despite at least 8 weeks of PPI therapy. Pre-procedure demographic and clinical data was collected and patients were grouped according to the presence of alarm symptoms (dysphagia, odynophagia, GI bleeding, weight loss, or iron deficiency anemia). Reflux complications were defined as: grade 2 or above esophagitis, Barrett’s esophagus >3cm, or esophageal stricture. Significant gastroduodenal findings were defined as: gastric ulceration, gastric cancer, duodenal ulceration, duodenal cancer, or H. pylori positivity.

Results: A total of 263 patients (mean age 53 ± 12 years) met inclusion criteria of which 33 (13.6%) were Caucasian, 21 (8.6%) were African American, 149 (61.3%) were Hispanic, and 40 (16.5%) were Asian or of Middle Eastern descent. Reflux complications were present in 14% of individuals, while 35% had gastroduodenal pathologies, and 3% of the group had both. Alarm symptoms as defined did not predict gastric findings, although the 38 patients with nausea & vomiting had a higher prevalence of gastric pathology compared to the 154 without nausea & vomiting (55% vs. 32%, p = 0.006). The most frequent gastric finding was H. pylori colonization in 39% of individuals. Patients with reflux complications had a significantly lower prevalence of H. pylori colonization compared to the group without reflux-related findings (20% vs. 43% p = 0.017). This negative association remained significant in multivariate logistic regression analysis after controlling for age, gender, and ethnicity (OR 0.37; 95% CI 0.14 to 0.96; p = 0.043).

Conclusions: In this diverse population with refractory GERD, the overall yield of EGD was increased more than twofold by the incidental detection of gastric pathology. H. pylori colonization was negatively associated with reflux complications, while the presence of nausea & vomiting was predictive for gastric pathology.

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Absence of Correlation between Heartburn Symptoms and Acid Reflux in Patients with Classic Heartburn Symptoms
Richard C. Nodurft, M.D., Chutima Zhao, R.N., Ravinder K. Mittal, M.D.*
Gastroenterology, Scripps Clinic, La Jolla, CA and Gastroenterology, University of California San Diego, San Diego, CA.

Purpose: To investigate whether symptoms of heartburn correlate with documented acid reflux events in a subgroup of patients with classic, chronic heartburn and an “acid-sensitive” esophagus as defined by a positive Bernstein test.

Methods: Twenty-eight patients were identified by a trained physician to have symptoms of classic, chronic heartburn occurring on a daily basis. Bernstein testing was performed followed by prolonged esophageal pH monitoring, during which patients self-reported symptoms of heartburn. The relationship between symptoms of heartburn and acid reflux events was reported as a symptom index (SI).

Results: Thirteen patients (46%) had a positive Bernstein test while 15 (54%) had a negative test. Twenty-one patients reported heartburn symptoms during prolonged esophageal pH monitoring. In the Bernstein-positive group and 13 in the Bernstein-negative group.

<table>
<thead>
<tr>
<th>Bernstein- Positive Group</th>
<th>Bernstein- Negative Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Patients with a SI ≥50%</td>
<td>25% (2/8)</td>
</tr>
<tr>
<td>Mean Symptom Index</td>
<td>26.2% (±37.9)</td>
</tr>
</tbody>
</table>

Results based on 21 patients who reported symptoms of heartburn during pH monitoring.

Conclusions: Even in patients who report “classic” symptoms of heartburn and in whom a Bernstein test confirms sensitivity to acid, the correlation between heartburn symptoms and objective acid reflux is poor. This finding suggests that other factors besides reflux of gastric acid may be involved in the generation of heartburn symptoms in many patients.

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Higher Incidence of Erosive Reflux Disease in ICU Patients Than in Regular Floor Patients
Yoosun Han, M.D., Mahmoud Barrie, M.D., Marc D. Rosenberg, M.D., Qiang Cai, M.D.* Medicine, Emory University School of Medicine, Atlanta, GA.

Purpose: Gastroesophageal reflux disease (GERD) is a very common disease that affects 20–50% of adults in Western Countries. The disease can be divided into three clinical categories: nonerosive reflux disease (NERD), erosive reflux disease (ERD), and Barrett’s esophagus. Why do some patients with GERD have NERD and others have ERD? We do not have the answer for this question at the present time. The aim of this study is to determine risk factors for ERD.

Methods: We tallied all in-hospital esophagogastroduodenoscopy (EGD) with diagnosis of ERD in the year of 2004. We reviewed all patients information regarding patient’s age, gender, prior history of GERD, general healthy conditions, dietary history, etc to find the potential risks for ERD.
Results: In 2004, we had 455 in-patients EGD. ERD was reported in 21 patients (excluded other than reflux esophagitis, such as candidiasis, pill esophagitis, etc.). Among the 455 patients, 165 were Intensive Care Unit (ICU) patients, the rest of 290 patients were in the regular floor. 16 patients in the ICU group had ERD; only 5 in the regular floor group had ERD. Therefore, the rate of ERD in this in-patient population was 4.6%(21/455), with 9.7%(16/165) and 1.7%(5/290) in the ICU patients and floor patients respectively. ICU patients had higher incidence of ERD than regular floor patients, even though ICU patients received histamine 2-receptor inhibitors more than the regular floor patients. Other factors, such as age, gender, history of GERD, etc. were not associated factors for ERD.

Conclusions: ICU patients are prone to have ERD despite receiving intravenously histamine 2-receptor inhibitors. Proton pump inhibitor prophylaxis may be better for those patients to prevent ERD.

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Intrasession Variability and Reproducibility of BRAVO pH-metry Following Sedated and Unsedated Capsule Placement
Michele M. Moirano, P.A.-C., Michael D. Crowell, Ph.D., ∗ H. Jae Kim, M.D., Virender K. Sharma, M.D. Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Scottsdale, AZ.

Purpose: Esophageal 24-hr pH-metry is a useful test for the diagnosis of gastroesophageal reflux disease. Recent advances have resulted in the approval of the BRAVO capsule pH-metry. The BRAVO is a radiotelemetry, catheter-free pH system that provides prolonged, 48-hr assessment of esophageal pH. The capsule is most often placed during EGD with the patient is sedated, which may lead to increased variability between recording day 1 and recording day 2. We have developed a method for placing the capsule orally in un sedated patients.

Aim: The aim of this study was to determine the concordance of data between the first and second 24-hr recording periods in sedated vs unsedated patients using Bravo.

Methods: Consecutive patients (n = 87; 42 UnSed [24F & 18M], 45 Sed [25F & 20M]) were studied over two continuous 24-hr freely ambulating periods. All patients were studied following an overnight fast, but were encouraged to follow their standard diet and activities during the study. The concordance between the two 24-hr periods was evaluated in Sed vs Unsed patients using Pearson Correlation Coefficients. Between group differences in pH-metry parameters were evaluated controlling for acid medication use via Multivariate ANOVA with significance set at the p < 0.05 level.

Results: No differences were noted between groups for age or gender. The BRAVO capsule detached from the mucosa prior to study completion in 2 Sed and no Unsed patients. These were not included in the statistical analyses. Overall, no significant group or group x days effects were found. Significant correlations were identified between the two 24-hr recording periods for both the Sed and Unsed groups. However, variability was higher and correlations lower in the Sed group compared to the Unsed group.

Conclusions: The Bravo pH monitoring system proved to be a safe and well-tolerated technique for measuring esophageal acid exposure for prolonged periods in unrestricted patients. No significant differences were found between sedated, endoscopic placement and un sedated placement of the BRAVO capsule. However, less variability and higher reproducibility was noted between the two measurement days following unsedated capsule placement.

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Prevalence of Eosinophilic Esophagitis among Patients Presenting with Dysphagia to a Community Gastroenterology Practice
David A. Zink, M.D., Kimberly Tosch, M.D., C. Chang, M.D., Tusar K. Desai, M.D. ∗ Division of Gastroenterology and Hepatology, William Beaumont Hospital, Royal Oak, MI and Department of Pathology, William Beaumont Hospital, Royal Oak, MI.

Purpose: Dysphagia is a common symptom of eosinophilic esophagitis (EE). No reports exist regarding the prevalence of EE in patients presenting with dysphagia. The aim of our study was to assess the prevalence of (EE) among patients presenting with dysphagia to a community gastroenterology group.

Methods: Clinical, endoscopic, histologic and radiologic records were reviewed from a consecutive series of patients presenting with undiagnosed solid food dysphagia to a community-based gastroenterologist. EE was defined as more than 20 eosinophils/hpf in esophageal biopsies. Esophageal motility disorders were diagnosed by barium esophagram and/or esophageal manometry and/or scintigraphy. Patients with a documented history of esophageal food impaction, malignancy, HIV infection, dementia and oropharyngeal dysphagia were excluded.

Results: Over a 2-year period 95 patients (42 men and 53 women) who met study criteria were evaluated for dysphagia (Table 1). We diagnosed EE in 15 patients (12 men and 3 women). All patients diagnosed with EE had been treated with proton pump inhibitors for at least 10 days prior to diagnosis. Seven of the subjects had both a Schatzki ring and EE. Barrett’s esophagus was an uncommon finding in patients with dysphagia (n = 5).

Table 1. Diagnostic Findings in Patients with Dysphagia

<table>
<thead>
<tr>
<th>Findings</th>
<th>Total Patients</th>
<th>Patients &lt; age 60 (n = 38)</th>
<th>Patients ≥ age 60 (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EE</td>
<td>15</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Schatzki Ring (7 with EE)</td>
<td>36</td>
<td>14</td>
<td>22</td>
</tr>
<tr>
<td>Achalasia</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Non-specific dysmotility</td>
<td>8</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Barrett’s esophagus</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Benign Esophageal Stricture (1 with EE)</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Erosive Esophagitis</td>
<td>12</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>No finding</td>
<td>33</td>
<td>8</td>
<td>25</td>
</tr>
</tbody>
</table>

*Total adds to greater than 95 because some patients had more than one finding.

Conclusions: We found EE in approximately 16% of patients presenting with solid food dysphagia. It is particularly common among patients under age 60. A high index of suspicion for EE should be maintained when evaluating causes of dysphagia.

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Dyspeptic Symptoms and Maximal Tolerated Volume during a Water Drinking Test in Post-Nissen Fundoplication Patients
Jose M. Remes-Troche, M.D., Aldo Montano-Loza, M.D., Julio Martinez-Salgado, M.D., Miguel F. Herrera, M.D., Miguel A. Valdivinos-Diaz, M.D. ∗ Gastroenterology, INCMNSZ, Mexico City, Mexico and Surgery, INCMNSZ, Mexico City, Mexico.

Purpose: After Nissen fundoplication (NF), about 30% of patients develop dyspeptic symptoms (DS). NF may cause motor and sensitive disorders in the proximal stomach that could be responsible for DS. The water drinking test (WDT) has demonstrated to discriminate healthy subjects from dyspeptic patients. Our aim was to evaluate the prevalence of DS and maximal tolerated volume (MTV) with WDT in patients with NF.

Methods: We evaluated 18 post surgical patients with NF by laparoscopic techniques having >6 months after surgery and were compared with 18 healthy volunteers (HV) and 18 functional dyspepsia (FD) patients (Rome II). All subjects answered the Nepean FD questionnaire and underwent WDT at a 15 mL/min ingestion rate. Severity of DS (abdominal pain, distension, early satiety and nausea) was evaluated with a 5 point Likert scale at baseline and every 5 minutes during the WDT. The MTV was considered as the inability to continue drinking water.

Results: There were no gender, age or IMC differences between the 3 groups. Nine (50%) patients with NF developed dyspeptic symptoms after the surgical procedure. The MTV for patients with symptoms after NF
was significantly lower than HV and NF patients without symptoms but similar to FD patients \((p = 0.001, Figure\ 1)\). Symptoms scores for NF patients were significantly higher than HV but similar to FD patients. A significant negative correlation was found between MTV and Nepean index \((p = 0.01, Figure\ 2)\).

Methods: In the last few months, patients with grade 4 ERD confirmed by esophagogastroduodenoscopy (EGD) were enrolled in the study. The patients were randomly divided into 2 groups. Group 1 received Protonix 80 mg IV bolus, followed by 8 mg/hour IV drip for 72 hours. Group 2 received Protonix 40 mg IV once a day for 72 hrs. Both groups then received Protonix 40 mg by mouth once a day after the initial 72 hrs. About 7 days after the initial EGD, a repeat EGD was performed for the patients in both groups.

Results: Six patients were identified by EGD in our hospital during the study period. Those patients were ICU patients. They all had IV histamine 2-receptor inhibitors for prophylaxis. Two patients refused the study, the other four were enrolled. In day 7 after the initial EGD, ERD completely resolved in three patients (2 patients in Group 1, 1 patient in Group 2), partially resolved in one patient (Group 2 patient).

Conclusions: ICU patients are prone to have ERD despite receiving intravenously histamine 2-receptor inhibitors. Histamine 2-receptor inhibitors may not be sufficient prophylaxis for ERD in ICU patients. Proton pump inhibitors intravenously may be better for those patients to prevent ERD. Continuous IV infusion of Protonix for 72 hours at the beginning may heal ERD faster than once a day injection. Although more study is still undergoing, this preliminary data indicated that if rapid healing of ERD is needed in certain patients, Protonix given through continuous IV infusion for the initial 72 hours should be considered.

Conclusions: Patients underwent NF who develop FD symptoms, have a lower MTV and higher frequency of symptoms during WDT. These results suggest that NF may diminish gastric accommodation and maybe induce proximal stomach hypersensitivity. [figure1] [figure2]

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Intravenous Protonix, Not Histamine 2-Receptor Inhibitors, to Prevent Erosive Esophagitis in ICU Patients
Yoosun Ham, M.D., Jae W. Nam, M.D., Mahmoud Barrie, M.D., Marc D. Rosenberg, M.D., Qiang Cai, M.D.∗ Medicine, Emory University School of Medicine, Atlanta, GA.

Purpose: Gastroesophageal reflux disease (GERD) is a very common disease that affects 20–50% of adults in Western Countries. The disease can be divided into three clinical categories: nonerosive reflux disease (NERD), erosive reflux disease (ERD), and Barrett’s esophagus. Our prior retrospective study showed patients in Intensive Care Unit (ICU) were prone to have ERD, despite using of histamine 2-receptor inhibitors as prophylaxis. The aim of this study is to examine whether Protonix given through continuous intravenous (IV) infusion for 72 hours is superior to Protonix given through once a day IV injection in treatment of ERD.

Methods: In the last few months, patients with grade 4 ERD confirmed by esophagogastroduodenoscopy (EGD) were enrolled in the study. The patients were randomly divided into 2 groups. Group 1 received Protonix 80 mg IV bolus, followed by 8 mg/hour IV drip for 72 hours. Group 2 received Protonix 40 mg IV once a day for 72 hrs. Both groups then received Protonix 40 mg by mouth once a day after the initial 72 hrs. About 7 days after the initial EGD, a repeat EGD was performed for the patients in both groups.

Results: Six patients were identified by EGD in our hospital during the study period. Those patients were ICU patients. They all had IV histamine 2-receptor inhibitors for prophylaxis. Two patients refused the study, the other four were enrolled. In day 7 after the initial EGD, ERD completely resolved in three patients (2 patients in Group 1, 1 patient in Group 2), partially resolved in one patient (Group 2 patient).

Conclusions: ICU patients are prone to have ERD despite receiving intravenously histamine 2-receptor inhibitors. Histamine 2-receptor inhibitors may not be sufficient prophylaxis for ERD in ICU patients. Proton pump inhibitors intravenously may be better for those patients to prevent ERD. Continuous IV infusion of Protonix for 72 hours at the beginning may heal ERD faster than once a day injection. Although more study is still undergoing, this preliminary data indicated that if rapid healing of ERD is needed in certain patients, Protonix given through continuous IV infusion for the initial 72 hours should be considered.

Conclusions: Patients underwent NF who develop FD symptoms, have a lower MTV and higher frequency of symptoms during WDT. These results suggest that NF may diminish gastric accommodation and maybe induce proximal stomach hypersensitivity. [figure1] [figure2]

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Continuous 48-hr Esophageal pH-metry in Obese Patients with Gastroesophageal Reflux Symptoms Compared to Non-Obese Patients
Michael D. Crowell, Ph.D.∗, Anton G. Decker, M.D., V. Ann Schetter, B.S.N, Michele M. Moinano, P.A-C., H. Jae Kim, M.D., Virender K. Sharma, M.D. Gastroenterology, Mayo Clinic College of Medicine, Scottsdale, AZ.

Purpose: Obesity is a risk factor for GERD symptoms and esophageal erosions, however data from 24-hour, catheter-based pH studies have been inconsistent. Patient discomfort and interference with normal diet and activities may limit catheter-based testing systems. The recently developed BRAVO® wireless pH-metry system is designed to reduce these limitations and to provide prolonged, continuous recording of esophageal pH for up to 48 hours.

Aim. We compared 48-hr esophageal pH-metry in obese (OB) and non-obese (NO) patients referred for complaints of heartburn.

Methods: 87 patients with GERD symptoms were studied over a continuous 48h period. Patients were separated into 2 groups by weight (NO < 30 kg/m2; n = 64; or OB ≥ 30 kg/m2; n = 23). The pH telemetry capsule was positioned transorally 6 cm above the squamocolumnar junction using endoscopic measurement or 5 cm above the upper margin of the LES using manometric measurements. Patients maintained a diary of activities throughout the study period. Data between groups and days were evaluated using Two-Way, Repeated Measures ANOVA controlling for PPI usage.

Results: OB and NO groups did not differ in age or gender (57 ± 17 yrs; 58 ± 14 yrs; 52% F vs. 58 ± 17 yrs; 52% F). BMI was significantly greater in OB compared to NO patients (34.2 ± 3.8 vs 25.0 ± 2.8 kg/m2). No group differences were seen in acid exposure on Day 1 (% pH < 4.0 = 4.4 ± 0.63 vs 3.5 ± 1.8), but acid exposure was significantly elevated in the OB group (% pH < 4.0 = 8.02 ± 1.5) compared to NO (% pH < 4.0 = 4.1±1.1) on Day 2. Acid exposure was highest in both groups during the awake, upright periods (p < 0.05). The DeMeester score for Day 2 was also significantly higher in the OB group (28.7 ± 41.0) compared to the NO group (12.0 ± 16.8). Patterns of variability differed between groups. OB patients showed increased percent time pH < 4.0 from the 1st to the 2nd 24h period, whereas NO patients showed a decrease.

Conclusions: Gastroesophageal acid reflux was greater in obese patients with GERD symptoms compared to non-obese patients. These differences were primarily noted during the second 24h recording and may be due to altered daily activities. Increased variability in esophageal acid exposure in obese patients supports the use of more prolonged pH studies in subsets of GERD patients.
Long Term Outcomes Following Treatment of High Grade Dysplasia in Barrett’s Esophagus: Comparison of Endoscopic and Surgical Treatment Cohorts
Ganapathy A. Prasad, M.D., Kenneth K. Wang, M.D.,* Michel WongKeeSong, M.D., Navtej S. Buttar, M.D., Lori Lutze, CCRP, Lynn Borkenhagen, R.N., Sarah Papenfuss Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

Purpose: Photodynamic therapy (PDTP for High Grade Dysplasia (HGD) in Barrett’s Esophagus (BE)) is an FDA approved alternative to esophagectomy. Critical information for clinical decision making regarding overall survival of patients followed long-term after these therapies has not been available. Our aim is to determine long term survival of a cohort of patients with HGD treated with PDT compared to patients treated with esophagectomy.

Methods: We reviewed records of patients seen at Mayo Clinic for HGD between 1994 and 2005. Data was abstracted from a prospectively maintained database for those that had PDT. PDT was performed by a single investigator, using 630 nm light administered using a bare cylindrical diffusing fiber or a centering balloon, 48 hours following the intravenous administration of a photosensitizer. Light dosages were between 150–200 J/cm fiber. Drug doses were equivalent to 2 mg/kg of sodium porfimer. Esophagectomy was performed by either transthoral or trans-thoracic approaches by experienced surgeons. We excluded all patients with evidence of cancer on biopsies. Vital status and death date information was queried using an institutionally approved internet research and location service. Statistical analysis was performed using Kaplan Meier curves and Cox proportional hazards ratios.

Results: 129 patients (65%) were treated by PDT and 71 (35%) were treated by esophagectomy. The mean age of patients undergoing PDT was older than that of patients undergoing surgery (64.6 versus 60.3, p = 0.0076). Gender distribution was comparable (males 87% versus 94%, p = 0.1). There were 17 total deaths. Overall mortality in the PDT group was 9% (11/129), compared with 8.5% (6/71) in the surgery group, over a median follow up of 57.4 months (Interquartile range 3.03, 129.7) in the PDT group and 63.4 months (IQR 34.8, 82.6) in the surgery group. Overall survival was similar between the 2 groups (Wilcoxon test = 0.0924, p = 0.76). On univariate analysis, neither age, nor treatment modality (PDT or surgery) were significant predictors of mortality. Treatment modality was also not a significant predictor of mortality on multivariate analysis, after adjusting for age and gender.

Conclusions: Overall mortality and long-term survival in patients with HGD treated with PDT appears to be comparable to that of patients treated with esophagectomy.

Abdominal Obesity Is an Independent Risk Factor for Endoscopic Reflux Esophagitis in Korean People
Mun Su Kang, M.D., Dong Il Park, M.D.,* Se Yong Oh, M.D., Tae Woo Yoo, M.D., Jung Ho Park, M.D., Hong Joo Kim, M.D., Yong Kyun Cho, M.D., Chong Il Sohn, M.D., Woo Kyu Jeon, M.D., Byung Ik Kim, M.D. Internal Medicine, KangBuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea.

Purpose: The relationship between reflux esophagitis and obesity is controversial in Korea, because morbid obesity (BMI > 30 kg/m^2) is less common than Western countries. The aim of this study is to evaluate the relationship between obesity and endoscopic reflux esophagitis in Korean people.

Methods: 2457 subjects who visited our health center for a general check-up including EGD during the period from September 2004 to April 2005 were enrolled. All of them were given a questionnaire about physical activity, smoking, consumption of alcohol, consumption of beverage, weekly symptom of heartburn or acid regurgitation, use of drugs, and other medical or surgical history. The subjects were classified into three groups by BMI: nonobese (<25 kg/m^2), obese (25–30 kg/m^2) and severe obese (>30 kg/m^2). And abdominal obesity was defined by waist circumference (>80 cm in women and >90 cm in men). Reflux esophagitis was diagnosed by EGD according to the LA classification (≥LA-A). Univariate analyses of various risk factors for reflux esophagitis was performed by using χ^2 test, and then multiple logistic regression analyses was used to examine relationship between reflux esophagitis and obesity.

Results: After exclusion of subjects who had gastric surgery, analysis was done on 2310 subjects (mean age was 44 ± 9 years and 31.3% was women). 28.8% was obese, 2.4% was severe obese, and 23.5% had abdominal obesity. The prevalence of endoscopic reflux esophagitis was 6.7% and significantly higher in men than in women (8.7% vs. 2.1%, p < 0.001). There was a dose-response relationship between prevalence of reflux esophagitis and BMI (5.7%, 8.2%, and 15.5% in <25, 25–30, and >30, respectively, p = 0.002). Waist circumference (11.2% vs. 5.2%, p < 0.001), hiatal hernia (42.6% vs. 5.8%, p < 0.001), current smoking (9.5% vs. 5.3%, p < 0.001), physical activity (7.6% vs. 4.2%, p = 0.002), use of hypertensive medications (12.7% vs. 6.1%, p = 0.005), and use of aspirin or NSAIDs (15.2% vs. 6.3%, p = 0.001) were significantly related with reflux esophagitis. After adjustment for sex, hiatal hernia, current smoking, physical activity, use of hypertensive medications, and use of aspirin or NSAIDs, only waist circumference remained as an independent risk factor for reflux esophagitis (adjusted OR 1.9, 95% CI 1.3–2.9, p = 0.002).

Conclusions: Abdominal obesity is an independent risk factor for reflux esophagitis in Korean people.

The Clinical Utility of Esophageal Manometry
Brian E. Lacy, Ph.D., M.D.,* Lisa Paquette, R.N., Douglas Robertson, M.D., Julia Weiss, MA, David Bauer, B.A., Maurice L. Kelley, Jr., M.D. Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH; Medicine, White River Junction VA Medical Center, White River Junction, VT and Biostatistics, Dartmouth Medical School, Hanover, NH.

Purpose: Esophageal manometry (EM) is routinely ordered in the evaluation of patients (Pts) with dysphagia, chest pain (CP), and gastroesophageal reflux disease (GERD), although the clinical utility of EM is unknown.

Methods: Prior to performing EM, referring physicians prospectively completed a questionnaire requesting: primary and secondary indications for the test; primary and secondary symptoms; duration of symptoms; results of previous testing; and medication use. Two weeks after test results were provided to the referring physician, a follow-up questionnaire was sent asking whether EM provided new information, altered the Pt’s diagnosis, or changed Pt management. EM were classified using standard criteria. Demographic information was obtained from the Pt.

Results: During a 6 month period, 303 EM were performed and 152 (50.2%) fully completed questionnaires were returned providing data for further analysis. Mean age at time of manometry was 52; 53% were women. Primary reason for requesting EM was dysphagia (33%), followed by the need to accurately place pH probe or BRAVO (29%), acid reflux symptoms (13%), and CP (10%). In the evaluation of their symptoms, 74% of Pts had undergone prior EGD, while 41% underwent barium swallow. Overall, 35% of EM were normal; 22% in dysphagia, 40% in CP, and 25% in GERD. Physicians reported that EM provided new information in 86% of cases for both dysphagia and CP, and 100% of cases for GERD. Results of EM led to a change in diagnosis 48% of the time for dysphagia, 21% of the time for CP, and 20% of the time for GERD. Results of EM led to a change in management 60% of the time for dysphagia, 43% for CP, and 45% of the time for GERD.

Conclusions: EM is a clinically useful test as it frequently provides new information and leads to a change in diagnosis and/or change in management. It is most helpful in patients with the primary complaint of dysphagia.

A Novel Method Comparing Multidose Delivery of Proton Pump Inhibitors (PPI’s) Via Enteral Feeding Tubes: An In Vitro Study
Adedamola Lufadeju, M.D., Nelson Tajong, M.D., Philip O. Katz, M.D.,* Division of Gastroenterology, Albert Einstein Medical Center, Philadelphia, PA.
Effect of Single Doses of Rabeprazole 20 mg and Pantoprazole 40 mg on 24-Hour Intraesophageal Acidity in Gastroesophageal Reflux Disease (GERD) Patients with Nocturnal Heartburn


Purpose: PPIs with rapid and prolonged control of acid secretion may be useful for treating nocturnal GERD symptoms. This study compared the antisecretory effects of single doses of rabeprazole sodium (RAB) 20 mg and pantoprazole sodium (PAN) 40 mg tablets in patients with a clinical diagnosis of GERD and a history of nocturnal heartburn (≥1 episode/wk).

Methods: This open-label, randomized, 2-way crossover comparison enrolled H pylori–negative subjects to receive RAB 20 mg and PAN 40 mg (single oral doses) in the morning (≥14-day washout). Intragastric pH was measured from 24 h before (day 0) until 24 h after dosing (day 1). Patients fasted from 2200 h the evening before until ~0900 h on day 0 and 1, and had standard meals/drinks 1, 4, and 10 h after dosing on day 1 and at corresponding times on day 0. Primary end point was 24-h area under intragastric pH-time curve (AUC0–24) on days 0 and 1. Secondary end points included AUC for 0–5, 5–11, 11–14, and 14–24 h; % time pH >3 and >4 over 24 h and for 0–14 and 14–24 h; and safety/tolerability.

Results: 31 patients (male, n = 19; mean age, 44 yr) were enrolled (evaluable population, n = 29). Preliminary results show that day-1 mean intragastric pH AUC0–24 was significantly higher for RAB vs PAN: 319,692 vs 259,921 pH units/sec, respectively (evaluable population; P ≤ 0.0001). In the ITT and evaluable (Table 1) populations, mean pH AUC was significantly higher for RAB (P ≤ 0.024) in all time intervals studied, including overnight (14–24 h). Mean day 1% time pH >3 and >4 was significantly higher for RAB (P ≤ 0.004) during the 24 h after dosing and all time intervals (ITT and evaluable populations). Both treatments were well tolerated.

Conclusions: Overall and during all time intervals, including overnight, a single oral dose of RAB 20 mg increased intragastric pH more than did PAN 40 mg in GERD patients with nocturnal heartburn. Research supported by Eisai Ltd., London, UK; Eisai Inc., Teaneck, NJ, USA; and Janssen Pharmaceutica Inc., Titusville, NJ, USA.

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To Study the Incidence of Barrett’s Esophagus in Patients with Liver Cirrhosis

Nadeem Anwar, M.D., Neelima Komatinneni, M.D., Savant Mehta, M.D., Dominic Nompelaggi, M.D.* Medicine, UMass Memorial Medical Center, Worcester, MA.

Purpose: GERD is increasing in the general population. In cirrhotic patients, incidence may even be higher because of the use of alcohol, presence of ascites and use of drugs like beta-blockers, which reduce the LES pressure. de la Pena et al showed that the sclerotic used for sclerotherapy provokes GERD. COX-2 gene is overexpressed in patients with cirrhosis and hypothetically may worsen GERD (Grover et al). In patients with esophageal varices, esophageal transit time is delayed and GERD is common in up to 64% of the patients (Fass R et al). Sclerotherapy can decrease the mean amplitude of esophageal contractions and normal peristalsis may be occasionally replaced by non-propagating simultaneous contractions that may cause chest pain and/or dysphagia in the absence of stricture. Cirrhotics have screening EGD’s to evaluate for esophageal and gastric varices. The investigators have noted an increased incidence of high-grade dysplasia in cirrhotics. We hypothesize that there may be an increased risk of Barrett’s esophagitis in patients with cirrhosis.

Methods: Inclusion criteria: All patients with biopsy proven cirrhosis who underwent EGD’s at UMass between 1/1/98 to 6/30/03 and control patients who underwent EGD in the month of April 2004 for any other indication.

Exclusion criteria: Inability to find the patients in the Meditech system. Also, patients with known Barrettts who presented for a surveillance EGD were excluded.

Data collection: 249 cirrhotics and 153 controls met the criteria. The control group was divided into two groups, namely subjects with symptoms of GERD (pain, heartburn) and those with all other indications for the EGD.

Results: In the cirrhotic group (ages 17 to 82 years, 80 females,168 males), 19/249 had endoscopic appearance of Barrettts esophagus, with 14/19 having had a biopsy. 8/14(3.2%) patients had biopsy findings consistent with Barrettts esophagus. In the controls with GERD symptoms (ages 29–80 years, 26 females, 10 males), 2/37 had endoscopic Barrettts, with 1 with positive biopsy (2.7). In the third group (ages 22–83 years, 51 males and 54 females), 3/105 had endoscopic appearance but only 1/3 (0.95%) had biopsy proven Barrettts.

Conclusions: This data supports the hypothesis that patients with cirrhosis may be at increased risk of developing Barrettts esophagus. A larger, prospective study is needed. If this relationship can be proven, it might become a standard of care to regularly screen cirrhotic patients for Barrettts esophagus.

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Frequency of GERD in Patients with Pulmonary Symptoms as Assessed by pH Testing with Impedance

Dawn D. Ferguson, M.D., Kenneth R. Devault, M.D.,* Mark E. Stark, M.D., Ernest P. Bouzas, M.D., Sami B. Achem, M.D. Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL.

Purpose: Gastroesophageal reflux disease (GERD) has been implicated as an etiology for a variety of pulmonary diseases and complaints. Traditionally, esophageal pH testing has been the gold-standard for evaluating GERD in these patients. However, patients with pulmonary disease may be affected by
both acid and non-acid reflux and pH testing with impedance allows for the evaluation of these two entities. We aimed to evaluate the utility of pH testing with impedance for patients with pulmonary diseases and complaints. **Methods:** The records of all patients with pulmonary complaints who were referred for pH testing with impedance to our motility laboratory between April of 2004 and May of 2005 at Mayo Clinic Jacksonville were reviewed. Patients’ age, gender, pulmonary disease or complaint, medication use and pH testing with impedance were recorded. A pH test was considered abnormal if the esophageal acid contact time was greater than 4.6% of the total time tested. Non-acid reflux was diagnosed as >72 episodes of liquid reflux but with normal pH testing. **Results:** There were 17 patients who had pH testing with impedance and pulmonary complaints. Overall, 10/17 (58%) had some evidence of reflux (acid or non-acid); 6/17 (35%) had non-acid reflux and negative pH testing; 4/17 had positive acid reflux (2 were off of acid suppressing medications and 2 were on twice daily proton-pump inhibitors). Of the 17 patients, six had IPF, five had COPD, three had chronic cough, one had cryptogenic restrictive bronchiolitis, one had asthma and one pulmonary hypertension. Only 2 patients were not on acid suppressing medications, and both of them had positive pH testing. **Conclusions:** pH and impedance testing in patients with respiratory complaints is a useful tool to diagnose reflux in this population. This technique identified additional potential mechanisms (i.e. non-acid reflux) that may play an important role in the pathogenesis of respiratory symptoms in these subjects.

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### An Exploratory Open Label Trial of Tegaserod in Non-Erosive GERD Patients with Incomplete Response to PPI’s

*Sheila Rodriguez-Stanley, Ph.D., Maggie Wolff, B.S., Howard M. Proskin, Ph.D., Ivan Bottoli, M.D., Jeffrey Kralstein, M.D., Philip B. Miner, M.D.*  
*Gastroenterology, The Oklahoma Foundation for Digestive Research, Oklahoma City, OK; Howard M Proskin and Associates, Inc, Rochester, NY and Novartis Pharmaceuticals, East Hanover, NJ.*

**Purpose:** Forty to 50% of patients treated with PPI’s for non-erosive GERD (NERD) have persistent upper gastrointestinal symptoms. A previous study has shown that tegaserod improves variables of mechanical hypersensitivity and symptoms in patients with functional heartburn, suggesting tegaserod may be useful in symptomatic NERD. **Aim:** To determine if addition of tegaserod (6mg BID) to a prescribed PPI regimen improves: (1) Global GERD assessments and (2) occurrence, frequency, severity and distress of 10 upper gastrointestinal symptoms. **Methods:** This 4-week open-label, randomized, two-center, parallel-group pilot study followed a 4-week screening and 2-week baseline period. NERD patients on stable PPI’s for at least 30 days with persistent symptoms were eligible. Treatments were: PPI + tegaserod 6 mg bid (Teg) or PPI alone in a 2:1 allocation. Patients completed weekly and end of treatment global symptom assessments. A GERD Symptom Assessment Questionnaire (GSAQ) was completed at screening and after treatment. A Global Composite Index Score (GCIS) was calculated from the GSAQ. Within-treatment changes from baseline were evaluated using paired t-tests. Between treatment comparisons employed analyses of covariance for continuous parameters, van Elteren’s test for ordinal parameters, and Cochran-Mantel-Haenszel tests for dichotomous parameters. **Results:** Forty-one patients were evaluated (Age 21–63 yrs; 20 Males, 21 Females; n = 27 Teg + PPI; n = 14 PPI). Between treatment comparisons of global GERD assessments vs. pre-study were significant for Teg + PPI at week 1 (p = 0.02) and week 3 (p = 0.03). Occurrence of heartburn/acid reflux, regurgitation, abdominal bloating and nausea were improved at the final visit by Teg + PPI vs PPI alone (all p < 0.05). Frequency, severity and bothersomeness of regurgitation and nausea were improved at the final visit by Teg + PPI vs PPI alone (all p < 0.05). Teg + PPI improved the GCIS from baseline to the final visit (p = 0.0002). Tegaserod was well tolerated, with no serious adverse events reported. **Conclusions:** Tegaserod in combination with a PPI significantly improved several global and individual symptom assessments in NERD patients with incomplete relief from PPI’s. Data from this trial justifies investigation of the potential utility of tegaserod in patients with NERD.

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### Idiopathic Subglottic Stenosis and Gastroesophageal Reflux (GER): The Chicken, the Egg, . . . the Enigma

*Kathryn A. Peterson, M.D., M. Sci.,* Panagiotis Panagiotakis, M.D., John Fang, M.D., Mark Elstad, M.D., Marshall Smith, M.D.  
*Gastroenterology, University of Utah, Salt Lake City, UT; Pulmonary Medicine, University of Utah, Salt Lake City, UT and Otolaryngology, University of Utah, Salt Lake City, UT.*

**Purpose:** Previous studies have inferred a relationship between gastroesophageal reflux (GER) and idiopathic subglottic stenosis (SGS). We propose to look at the relationship between GER and all SGS patients to determine whether the onset of SGS is directly related to GER or whether GER may be a manifestation of SGS and it’s associated airway obstruction. **Methods:** A retrospective chart review was performed on all patients seen within the University of Utah’s Airway clinic between 1/2001 and 1/2005. Patient data abstracted (when available) included age, gender, symptoms of GER, EGD findings, pH probe findings, date of laser dilations, and dates of treatment with proton pump inhibitors or fundoplication. Both non-idiopathic and idiopathic patients were assessed. Univariable analysis of pH results between groups was then made. Additionally, when available frequency of dilations before and after therapy for GER were also evaluated in both groups. **Results:** A total of 55 patients were identified. 27 idiopathic SGS patients and 7 non-idiopathic patients were found to have undergone dual channel pH probes. All idiopathic patients were female while 5/7 of non-idiopathic patients were female. 17/27 idiopathic SGS patients had positive pH probes as compared to 5/7 non-idiopathic SGS patients (63% vs 71%, p > 0.05). 8/34 (24%) SGS patients had abnormal pH detected only in the proximal sensor. In those who did, only 2/8 idiopathic patients described having heartburn before the onset of their pulmonary symptoms. All non-idiopathic patients developed heartburn symptoms after the diagnosis of SGS. Interestingly, the frequency of dilations appeared to decrease in patients treated with PPI or fundoplication therapy. **Conclusions:** Although the numbers are small, this retrospective study argues that the increased prevalence of GER in SGS is more likely related to the presence of SGS itself. There is no difference in prevalence of GER between the idiopathic and non-idiopathic SGS groups. Additionally, from those few patients who described GER, it appears that the majority of these patients developed GER after the onset of their stenosis. Interestingly, however, if the fact that the frequency of dilations for the SGS appeared to decrease after the initiation of anti-reflux therapy. This, however, needs to be further investigated in prospective studies.

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### Persistent Non-Cardiac Chest Pain in Patients on PPI Therapy: Prevalence, Prescribing Patterns and Results of pH Testing at a Tertiary Referral Center

*Sami R. Achem, M.D.,* Dawn D. Ferguson, M.D., Beate Hugl, M.D., Herbert Wolfens, M.D., Mark Stark, M.D., Ernest Bouras, M.D., Kenneth R. Devault, M.D.  
*Gastroenterology, Mayo Clinic, Jacksonville, FL and Department of Surgery, Mayo Clinic, Jacksonville, FL.*

**Purpose:** Gastro-esophageal reflux (GERD) occurs in 22–66% of patients with non-cardiac chest pain (NCCP). Proton pump inhibitors (PPIs) are widely available and are commonly prescribed as initial empirical therapeutic strategy for NCCP. Little is known about the patients who continue to experience chest pain despite PPI therapy and whether pH testing may offer additional information in this population.
Aims: To determine the prevalence of PPI use, describe prescribing PPI practices, and evaluate the diagnostic utility of pH testing in patients with persistent NCCP.

Methods: We reviewed consecutive patients with recurrent chest pain that received a PPI trial prior to their referral to our institution over a 2-year span. We determined the type and number of PPI trials prior to their referral to our institution. The results of 24-hour pH testing were also examined. GERD was diagnosed by abnormal acid contact time on pH testing.

Results: During the study period 130 patients were evaluated for NCCP, mean age 56.9 (range 23–90 years); 34.5% male, 65.5% female. Prior to referral to our center, 80 (61.5%) of these patients had received a PPI trial. At least, 20 (25%) had received 2 PPI trials and 6 (7.5%) received at least three PPI trials. The most commonly prescribed PPI prior to referral was omeprazole in 41 (54.6%) cases;esomeprazole was used in 18 (24%). All patients were asked to have 24-hour ambulatory pH testing and 59/80 (73.7%) consented. pH results were categorized to patients ON or OFF PPI therapy. The results were grouped as follows:

<table>
<thead>
<tr>
<th>pH Results</th>
<th>PPI Status</th>
<th>Number (%)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>ON therapy</td>
<td>11/59 (14%)</td>
<td>Acid unlikely source of pain</td>
</tr>
<tr>
<td>Normal</td>
<td>OFF therapy</td>
<td>25/59 (42%)</td>
<td>Acid unlikely “original” source of pain</td>
</tr>
<tr>
<td>Abnormal</td>
<td>ON therapy</td>
<td>5/59 (8.4%)</td>
<td>Insufficient acid inhibition, acid possible source of pain</td>
</tr>
<tr>
<td>Abnormal</td>
<td>OFF therapy</td>
<td>18/59 (30.5%)</td>
<td>Undetermined, acid questionable source of pain</td>
</tr>
</tbody>
</table>

Conclusions: In patients referred for evaluation of persistent chest pain to a tertiary center as many as half these patients have received a PPI trial and over 25% at least two different trials. pH testing in these patients indicates that persistent acid reflux occurs in only the minority (8%) of these patients. Failure to respond to PPI trials should prompt search for other non-acid related sources of chest pain.

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Esophagogastroduodenoscopy (EGD) Clearance for Transesophageal Echocardiogram (TEE) in Patients with Esophageal Disease

David Lee, M.D., Kostas Sideridis, M.D., Nakechand Pooran, M.D.* Division of Gastroenterology, Long Island Jewish Medical Center, New Hyde Park, NY.

Purpose: TEE is more sensitive than transthoracic echocardiography (TTE) in evaluating valvular heart disease and cardiac thrombus. Complication rates for TEE are reported to be 0.88%. If a patient history is suggestive of gastroesophageal disease, evaluation of the esophagus prior to TEE may be indicated. To investigate whether EGD is warranted prior to TEE we recorded EGD findings, TEE findings and complications.

Methods: We prospectively followed 36 patients (18F, 18M) who were referred for esophageal evaluation prior to TEE at Long Island Jewish Hospital from 2003–2005. We recorded why esophageal evaluation was requested, EGD findings, TEE results, and for any complications occurring during hospitalization.

Results: The mean age was 60 years. Six patients (16.7%) were referred for evaluation because of gastroesophageal reflux disease, 9 (25%) complained of dysphagia, 8 (22.2%) had a history of cirrhosis or alcohol abuse, and 13 (36.1%) had anemia or guaiac positive stools. EGD findings were normal in 6 patients (16.7%), 5 (13.9%) had esophagitis, 13 (36.1%) had peptic ulcer disease or non-specific gastritis, and 8 (22.2%) had a hiatal hernia. Five patients (13.9%) who were evaluated by EGD did not have a TEE. Only 2 patients (5.4%) were cancelled due to EGD findings (tortuous esophagus, esophageal varices), while the remaining 3 patients (8.1%) were cancelled due to unsuccessful intubation by the TEE scope. There was no complication among those who successfully had TEE.

Conclusions: Although majority of the patients had endoscopic findings on EGD, these findings rarely precluded performing a TEE. TEE is a relatively safe procedure, and an EGD prior may be unnecessary. Larger studies are needed to validate these results and to investigate criteria for the use of EGD in patients undergoing TEE.

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A Prospective Single Center Long-Term Follow up Study of Barrett’s Esophagus on Proton Pump Inhibitor Therapy: 1989–2005

Prasun K. Jalal, M.D., Kostas Sideridis, DO, Simmy Bank, M.D.* Division of Gastroenterology, Long Island Jewish Medical Center–Albert Einstein College of Medicine, New Hyde Park, NY.

Purpose: The aim of this study was to evaluate the esophageal and gastric findings in patients with Barrett’s esophagus on long term PPI therapy in our center.

Methods: 61 patients with biopsy proven Barrett’s esophagus on continuous PPI therapy have been followed as follows: 2 for 16 years, 18 for 15 years, 30 for 14 years, 2 for 13 years, 6 for 12 years, 3 for 11 years. Initially omeprazole was used on alternate days because of the “black box” warning. Thereafter, 53 patients are maintained on a daily dose of PPI (Omeprazole 20 mg or esomeprazole 40 mg twice daily in 27 patients and once daily in 26 patients). 8 patients remained on an alternate day regime. Surveillance endoscopies (3 months to 2 years) with esophageal and gastric biopsies have been performed in all.

Results: Non-Esophagogastric Events: 7 patients (11.5%) have died from non-esophagogastric causes and 17 (28%) have developed unrelated diseases.

Esophagogastric Findings: Esophageal- one patient with once daily dose of PPI developed high grade dysplasia (1.7%) after 5 years of follow up, but refused surgery and has remained on endoscopic follow up. Another patient had low grade dysplasia on biopsy, remained on twice daily PPI and repeat biopsies are consistently negative for dysplasia. 4 patients had recurrent grade B or C esophagitis that responded to an increased dose of PPI. Gastric – 20 patients (30%) developed gastric fundic polyps (2 to more than 100) after more than 2 years of PPI therapy. One patient developed a large (3 × 3 cm) adenomatous polyp with severe dysplasia requiring endoscopic resection and follow up did not show recurrence.

Conclusions: A single center 12–15 year (cumulative 853 person-years) prospective follow up of patients with Barrett’s esophagus on continuous PPI therapy revealed very low incidence of dysplasia (one case) and no carcinoma. Gastric polyps are common on PPI therapy and one patient had high grade dysplastic gastric adenoma. The high mortality and morbidity (39.5% in this group) from unrelated causes in patients with Barrett’s esophagus favor a conservative approach; however, continued surveillance of both esophageal and gastric status would seem prudent on long term PPI therapy.
Esophageal Dilation of Benign Strictures: Do Published Articles Follow the Rule of Three?
Peter W. Simpson, M.D.* Digestive Diseases, UCLA, Los Angeles, CA.

Purpose: The purposes of this study were to determine if published studies of dilation of benign esophageal strictures with Savary dilators or balloons follow the rule of 3 (that no more than 3 dilators be passed after resistance is encountered – 2 mm effective dilation), and to compare the reported complication rates between studies.

Methods: A systemic review of all papers describing esophageal dilation of benign esophageal strictures using Savary or balloon catheters was conducted. Exclusion criteria were inability to determine dilation protocol or complications, rings, webs, malignant strictures, achalasia, steroid injection, stents, or pediatric patients. Information on stricture type, dilation protocol, and complications was abstracted.

Results: 23 articles described balloon dilation in a total of 771 patients. None of these described dilation protocols which were consistent with the rule of 3 (2 mm dilation). A single study dilated patients by only 3 mm at a time, while most fully dilated patients to at least 15 or 20 mm in the initial session. 3 perforations were reported; no relationship between dilation protocol and complications could be established.

9 articles described Savary dilation in a total of 502 patients. 5 of these articles described a protocol more aggressive than the rule of 3 would dictate, though few dilated fully during the first session. 5 perforations were reported, 4 of these were guidewire perforations in a single study of strictures due to caustic ingestion. All perforations occurred in studies dilating more aggressively that the rule of 3 would dictate.

Conclusions: Despite the widely quoted rule of 3, most authors elected to treat patients more rapidly that this would dictate with both Savary dilators and balloons. No randomized controlled trials of this maxim exist, nor would they be feasible, given the rarity of complications. The apparently higher perforation rate with rapid Savary dilation is driven entirely by guidewire perforations in one series. If we accept that these are not a function of the number of dilators used in a single session, then no relationship between dilation protocol and perforation rate is seen with either Savary dilators or balloons. The overall small number of patients described and multiple possible confounders make it difficult to draw strong conclusions from this study; however, it is apparent that no evidence for increased safety with the rule of 3 exists for Savary or balloon dilation of benign strictures.

Efficacy of Baclofen in Chronic Cough
Kathryn A. Peterson, M.D., M.Sci.,* John Fang, M.D., Wayne Samuelson, M.D. Gastroenterology, University of Utah, Salt Lake City, UT and Pulmonary, University of Utah, Salt Lake City, UT.

Purpose: Gastroesophageal reflux is a common contributor to cough. Many patients will respond only partially to aggressive acid suppression, indicating other etiologies to such cough, such as asthma, sinus disease, and microaspiration. We propose to analyze the efficacy of Baclofen, a GABA-B agonist, in the treatment of chronic cough, persistent despite acid suppression.

Methods: A retrospective chart review was performed on all patients seen in the asthma clinic from 8/2003 to 1/2005 at the University of Utah. The search was limited to those patients who were on acid suppression with continued cough. Patients must have had a cough of at least 8 weeks duration. Asthma patients were included in the analysis. Data abstracted included age, gender, length of cough, medications, documentation of improvement of cough, pH, impedance, and manometry results, and outcomes after fundoplication or Enteryx therapy. The response to Baclofen was documented prior to abstracting the pH/Manometry data.

Results: A total of 27 patients were identified. 19 (70%) patients described improvement of their cough after initiation of Baclofen. 2 patients (7%) could not tolerate the side effects of Baclofen and discontinued the medication. 6 patients (22%) did not improve with Baclofen. A total of 26 patients had either pH testing or impedance testing performed for analysis of cough. All patients who described improvement demonstrated abnormal amounts of acid or non-acid reflux on pH/impedance testing. From the non-responders, 2 had no evidence of abnormal reflux on pH/impedance testing, 2 had normal manometry results (nutcracker and DES) with elevated LES pressures, and 1 was found to have a nearly obstructing tumor in her proximal duodenum. 8 patients had been referred further for either Enteryx therapy or fundoplication after the Baclofen. All patients described either substantial or near-complete resolution of cough after these procedures.

Conclusions: Baclofen therapy appears to be an effective way to treat chronic cough suspicious for gastroesophageal reflux. Baclofen may provide partial relief of cough in patients with pathologic reflux. A response to Baclofen appears to indicate a continued contribution of gastroesophageal reflux to the cough. Finally, patients who respond to Baclofen appear to demonstrate remarkable improvement after fundoplication or Enteryx therapy. Baclofen may be helpful in identify patients who suffer from cough due to persistent acid/non-acid reflux.

Guanylc Cyclase C (GC-C): A Potential Biomarker for Barrett's Esophagus (BE)
Pradnya Mittoo, M.D., Alessandro Bombonati, M.D., David Loren, M.D., Rhonda Walters, Juan Palazzo, M.D., Stephanie Schulz, Ph.D., Scott Waldman, M.D.* Department of Gastroenterology, Thomas Jefferson University Hospital, Philadelphia, PA; Department of Pharmacology, Thomas Jefferson University Hospital, Philadelphia, PA and Department of Pathology, Thomas Jefferson University Hospital, Philadelphia, PA.

Purpose: BE is a premalignant condition that predisposes patients to esophageal adenocarcinoma (AC). Studies have demonstrated that accuracy of presumptive endoscopic or histological suspicion of BE was low at follow-up. Thus, there is a need for diagnostic biomarkers that can identify patients at risk for developing BE and, ultimately, AC. GC-C is a receptor selectively expressed in apical membranes of epithelial cells from the duodenum to the rectum, but not by normal esophageal or gastric mucosa in humans. Recent studies revealed that GC-C is an immunohistochemical marker of intestinal metaplasia (IM), dysplasia and AC in the upper GI tract. The purpose of the study was to evaluate the expression of GC-C protein along the continuum of neoplastic transformation in the esophagus, from IM through AC, by immunohistochemistry (IHC).

Methods: 26 biopsies with BE, 15 with low grade dysplasia (LGD), 6 with high grade dysplasia (HGD) and 3 with AC arising in BE were evaluated. 6 biopsies of normal gastroesophageal junction (GEJ) and 6 of cardiac-type mucosa (CTM) without IM also were evaluated. Paraaffin-embedded specimens were stained for GC-C employing purified IgG from rabbits immunized with a peptide derived from human GC-C. Epithelial cells exhibiting apical membrane staining were considered positive for GC-C expression.

Results: GC-C was expressed in 26/26 (100%) cases of BE, 15/15 (100%) cases of LGD, 4/6 (67%) cases of HGD and 1/3 (33%) cases of AC. In contrast, 6 normal GEJ and 6 CTM did not stain. Normal squamous epithelia were negative in all cases.

Conclusions: GC-C IHC is 100% sensitive for BE and LGD, since it was consistently expressed in all areas of IM and LGD. Similarly, GC-C IHC is 100% specific for BE and LGD, staining was absent in normal GEJ, CTM, and normal squamous epithelia. As tissues progressed along the continuum of neoplastic transformation to HGD and AC, the detection of GC-C declined, suggesting that the expression of this marker may be down-regulated in later stages of tumorigenesis. Future studies will continue to define the utility of GC-C as a prognostic marker for the initiation of neoplastic transformation (BE), and as a diagnostic marker for the progression of tumorigenesis (LGD,HGD,AC) in the upper GI tract.
A One-Step Endoscopic/Laryngoscopic Therapy for Pharyngoesophageal Disconnect
Stacie Vela, M.D., Branden S. Hunter, M.D., Terry A. Day, M.D., Brenda J. Hoffman, M.D.* Division of Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, SC.

Purpose: Complete pharyngoesophageal disconnect is a rare complication of radiation therapy for head and neck malignancies. Surgery has been the mainstay of treatment for this condition. Lew et al (Head and Neck, Feb 2004) described a combined endoscopic/laryngoscopic approach to establishing luminal patency using a stiff guidewire. However, repeated dilation may be required to achieve maximum diameter, and the restenosis rate for radiation-induced strictures has been high. Mitomycin-C has been used with success in the prevention of recurrent laryngeal and tracheal stenosis and is thought to have an antiproliferative effect. We describe a novel one-step method of reconnection, dilation, and treatment for pharyngoesophageal disconnect.

Methods: Retrograde endoscopy through an existing gastrostomy tube tract is performed to the level of the disconnected proximal esophagus. Direct laryngoscopy is performed at the same time to visualize the light source below. An EUS needle (Echotip, Wilson Cook Corp) is advanced by the laryngoscopist with endoscopic guidance. A 0.35 mm ERCP guidewire (Jagwire, Microvasive corp) is passed through the EUS needle into the esophagus and grasped with a forceps. The wire is pulled back thru the gastrostomy and fixed in place. Savary style dilators are then passed per os, serially from the smallest to a minimum of 51 Fr. Before removing the guidewire, mitomycin-C pledgets are applied via laryngoscopy.

Results: Six patients with pharyngoesophageal disconnect after radiation therapy for head and neck malignancies underwent the combined procedure. Luminal patency was achieved in all patients, and all were able to progress to teaching for self dilation. One patient suffered a minimal localized esophageal perforation for which conservative management was used. Luminal patency was maintained in all patients with follow-up to 12 months after the initial procedure.

Conclusions: This combined one-step approach offers a less invasive and technically superior option to surgery. Dilation in one setting to 51 Fr can be performed with minimal complications. The EUS needle allows for a controlled puncture and passage of a guidewire. Despite their prior disconnect, these patients can be taught to perform self-dilation to prevent or delay recurrence without forming false tracts. Mitomycin-C topical treatments may provide an antiproliferative effect for radiation-induced strictures, however further long term studies are warranted.

Eosinophilic Esophagitis: The Ochsner Clinic Experience
K. Shiva Kumar, M.D., James W Smith, M.D.* Division of Gastroenterology, Ochsner Clinic, New Orleans, LA.

Purpose: Eosinophilic Esophagitis (EE) is an increasingly recognized entity that often presents with intermittent solid food dysphagia. The clinical features, natural history and therapy of EE are yet to be fully characterized. We describe our experience with EE in a tertiary referral center.

Aim: To describe the clinicopathologic features and outcomes following therapy of all patients with EE seen at Ochsner Clinic over a two year period.

Methods: All patients diagnosed with EE over a two-year period from July 2003 – June 2005 were included. Only patients with eosinophilic infiltration greater than 20 per high power field (hpf) in biopsies obtained from mid-esophageal body (20 cm) were included. Clinical, demographic, pathology and treatment data was collected.

Results: There were 8 patients with EE over the study period. Six were male. Seven had intermittent solid food dysphagia, two of whom presented with food impaction. One was asymptomatic. Mean age at diagnosis was 35 yrs (range 26–50). Diagnosis was delayed for a mean of 3 years following onset of symptoms (range 0–8 yrs). Endoscopic features included “ringed” appearance of the esophagus in seven and linear furrows in one. All patients had biopsies from the mid-esophagus (20 cm) that constituted the basis for diagnosis. Extent of eosinophil infiltration ranged from 25 to more than 80 hpf. Four patients had an atopic predisposition. Median duration of follow up was 7 months (range 2–20). Five patients were treated with swallowed fluticasone. Complete symptom resolution was noted in all after 3 months. Recurrence was noted in one after cessation of therapy, with prompt resolution on re-institution of therapy. No complications of therapy were observed. One patient underwent periodic dilation with improvement in symptoms. No complications were described during endoscopy, although mucosal tearing with passage of the endoscope was seen in one. Peripheral eosinophilia was seen only in two, as high as 31% in one (absolute eosinophil count 2800). This patient was asymptomatic. Serum IgE level was elevated only in one patient.

Conclusions: In this small series of EE, male predominance and younger age at onset was noted. Diagnosis is often delayed and clinicians should recognize EE as a cause of unexplained intermittent solid food dysphagia. Presenting symptoms range from food impaction to asymptomatic EE diagnosed incidentally during endoscopy. Swallowed steroids appear to be a safe and effective therapeutic option. Approach to patients with asymptomatic eosinophilic infiltration of the esophagus remains to be clarified.
Does the Catheter-Free Bravo™ pH Capsule Alter Esophageal Motor Function?
Qing Zhang, M.D., Ph.D., Christopher T. Boniquit, B.S., Sudip K. Ghosh, Ph.D., John E. Pandalofino, M.D., Andrew F. Jarosz, Peter J. Kahrilas, M.D.* Gastroenterology, Feinberg School of Medicine, Northwestern University, Chicago, IL.

Purpose: Whether attachment of the Bravo™ catheter-free pH monitoring system alters esophageal motility has yet to determined. The aim of this study was to assess the effect of the Bravo™ capsule on esophageal motor function using high-resolution manometry (HRM) before and after placement.

Methods: 10 controls (5 males, age 20–54) were studied. A solid-state manometric assembly with 36 circumferential sensors spaced 1 cm apart was positioned to record from the hypopharynx to the stomach (Sierra Scientific Inc). Esophageal manometry studies were performed before and ≥12 hours after the Bravo™ capsule placement. The subjects performed 5 5-ml water swallows in both upright and supine positions. Two 5-ml barium swallow were also performed in 6 subjects under fluoroscopy synchronized with manometry recordings.

Results: There was no significant change in basal LES pressure, LES relaxation pressure or peristaltic function before and after Bravo™ placement in both positions (Table). However, a noticeable 1.5 cm high-pressure focus was noted during peristalsis at the location of the capsule during fluoroscopy. The mean peristaltic pressure at the Bravo™ capsule attachment site was increased in both positions, however, statistical significance was only reached in the upright position (Upright, 59.4 ± 10.5 mmHg vs. 134.1 ± 20.2 mmHg, p = 0.005; Supine, 111 ± 15 mmHg vs. 141.3 ± 19.8 mmHg, p > 0.2). Five out of ten subjects reported symptoms during eating (foreign body sensation, chest pain). Although the median pressure increase at the attachment site was noted during peristalsis at the location of the capsule during fluoroscopy, there was no significant change in basal LES pressure, LES relaxation pressure or peristaltic function before and after Bravo™ placement in both positions (Table).

Table: Esophageal Manometric Parameters Before and After Bravo™ Placement

<table>
<thead>
<tr>
<th>Basal LES pressure (mmHg)</th>
<th>LES relaxation pressure</th>
<th>Peristaltic amplitude 8 cm above LES</th>
<th>Peristaltic success rate (%)</th>
<th>Peristaltic Velocity (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Bravo 14.7 (5.9)</td>
<td>7.9 (3.1)</td>
<td>95.6 (54)</td>
<td>100 (0)</td>
<td>2.1 (0.3)</td>
</tr>
<tr>
<td>Post-Bravo 18.5 (7.5)</td>
<td>8.6 (2.8)</td>
<td>103.6 (53)</td>
<td>96 (12)</td>
<td>2.2 (0.2)</td>
</tr>
</tbody>
</table>

Conclusions: Bravo™ placement does not alter standard manometric parameters assessing esophageal function. The regional manometric changes noted at the capsule attachment site are relegated to a short segment of the esophagus and should not alter bolus clearance. However, this short area of increased peristaltic amplitude may be an important factor in determining individual’s comfort during the recording period.

Comparison of the Wireless (Bravo) pH Monitoring Device Parameters Before and After the Traditional 24 hr pH Monitoring in the Evaluation of Gastroesophageal Reflux Disease
Isam Daboul, M.D., Janaki ram P. Earla, M.D.* Gastroenterology, Dept of Internal Medicine, Medical University of Ohio, Toledo, OH.

Purpose: Before the development of the wireless pH monitoring device (capsule), the evaluation of patients with presumed GERD was performed by a 24 hr intranarial inserted pH probe. The traditional 24 hr dual channel probe is capable of directly evaluating the pH in the esophagus. This function has also been demonstrated equally with the use of a wireless device called as ‘Bravo capsule’ which is endoscopically inserted into the esophagus. The tolerability of this procedure and validity of the pH recordings has been already studied and was found to be valid.

DeMeester (DM) score is an index used by clinicians to determine the degree of severity of GERD both on traditional 24 hr pH monitoring, as well as wireless pH monitoring.

To evaluate the usefulness of the DM score as a reflection of severity of GERD in both techniques, this study was undertaken to retrospectively analyze the pH monitoring parameters in both 24 hr dual channel pH and wireless capsule pH studies, in patients with clinical manifestations of GERD.

Methods: In this study we evaluated the pH monitoring parameters such as number of refluxes, number of long refluxes, the duration of longest reflux, period of time with pH < 4 and fraction of the time of pH < 4, which are used as variables in the compilation of the DM score. These variables were analyzed and compared with the parameters of the pH monitoring readings, who had wireless pH monitoring technique.

Results: The statistical analysis, showed that the wireless pH monitoring group had a stronger correlation of DM score with the parameters like the number of total refluxes (0.79), total time of pH < 4 (0.88) and total fraction time of pH < 4 (0.93) and was found significant when compared with the traditional 24 hr pH monitoring group, which showed a correlation with the number of total refluxes (0.58), total time of pH < 4 (0.86) and total fraction time of pH < 4 (0.87).

Conclusions: There is stronger correlation of the DM score with the individual parameters in the pH recording by wireless technique when compared with the traditional 24 hr method.

Prevalence of GERD and Its Effect on Quality of Life in a Large Cohort of Patient with Obstructive Sleep Apena
Bryan Green, M.D., Michael Thorn, DrPH, J Barry O'Connor, M.D.* GI, Digestive Disease Group, Greenville, SC; Statis, Statistical Resources Inc., Durham, NC and Medicine, Duke University Medical Center, Durham, NC.

Purpose: Determine the prevalence of GERD and its effect on quality of life in a large cohort of patients with sleep apnea.

Methods: 362 consecutive patients presenting for a nocturnal polysomnography (sleep study) between June 2003 and January 2005 completed self-administered questionnaires including demographics, GERD symptom frequency and severity within the previous week, GERD medication use and SF-36 prior to their sleep study. A respiratory disturbance index (RDI) ≥ 15 was used to define the presence of obstructive sleep apnea (OSA). GERD frequency was defined as the number of days and/or nights with GERD symptoms within the previous week. GERD severity scale was 0 (none) to 5 (very severe).

Results: Patients not meeting RDI criteria for OSA and those having a titration sleep study were excluded. Data on 168 patients were analyzed. Mean age was 50.8 years (SD 13.5; range 23–83). Gender: 64.9% male, 35.1% female. Race: 60.1% white, 39.9% non-white. Mean RDI = 26.8 (normal <15; SD 25.9). Daytime and nighttime GERD symptoms were experienced an average of 1.8 days (26%) and 1.6 nights (23%) respectively during the previous week. Daytime GERD severity was moderate or severe in 24% while nighttime GERD severity was moderate or severe in 31% during the previous week. Compared to the US general population, our OSA patient had a much lower QOL score in all subscales of the SF-36 (except
Conclusions: GERD symptoms are common and frequently severe in patients with OSA. A substantial minority of patients with OSA use H2-RAs or PPIs. QOL is severely impaired in OSA. Coexistent moderate/severe night-time GERD with OSA is associated with even worse QOL. All patients with sleep apnea should be evaluated for GERD. This study was supported by an AstraZeneca ISS grant.

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The Gene Expression Profile of Cardiac Intestinal Metaplasia Is Similar to Barrett's Esophagus, Not Gastric Intestinal Metaplasia

Daniel S. Oh, M.D., Steven R. DeMeester, M.D.*, Koji Tanaka, M.D., Paul Marjoram, Ph.D., Daniel Vollbohmer, M.D., Hidekazu Karamochi, M.D., Jeffrey Hagen, M.D., Peter Danenberg, Ph.D., Kathleen Danenberg, B.Sc., Cedric Brenner, M.D., John Lingham, M.D., Parakrama Chandrasoma, M.D., Tom R. DeMeester, M.D. Dept of Surgery, University of Southern California, Los Angeles, CA; Dept of Preventive Medicine; Dept of Pathology and Response Genetics Inc, Los Angeles, CA.

Purpose: The etiology and significance of cardiac intestinal metaplasia (CIM) is disputed. CIM may represent a form of Barrett's esophagus (BE) due to reflux or could reflect generalized gastric intestinal metaplasia (GIM) due to H. pylori. The aim of this study was to utilize gene expression data to compare CIM to BE and GIM.

Methods: Biopsies were first classified by endoscopic and histologic criteria as CIM (n = 40), BE (n = 26), or GIM (n = 23). The squamocolumnar and gastroesophageal junctions were aligned in CIM patients. H. pylori status was tested in antral biopsies of all patients. After laser-capture microdissection, quantitative RT-PCR was used to measure the expression of a panel of 9 genes tested in antral biopsies of all patients. After laser-capture microdissection, quantitative RT-PCR was used to measure the expression of a panel of 9 genes that has been shown to differentiate BE from other foregut mucosa (Cox2, Cdx1, Cdx2, VEGF, TSP1, Survivin, TIMP1, Bcl2, CTNNB1). Next, cluster analysis using linear discriminant analysis of logged expression data was used to classify samples into groups based solely on similarity of gene expression. Cluster analysis was performed for 3 groups (CIM vs BE vs GIM) and 2 groups (CIM+BE vs GIM).

Results: Median BE length was 4.5 cm. There was no difference in H. pylori infection among groups (p = 0.68). Three group clustering had a misclassification rate of 0.39 (p = 0.001); most errors occurred between CIM and BE (Table 1). Two group clustering had a misclassification rate of 0.18 (p<0.001) (Table 2).[figure1]

Table 1

<table>
<thead>
<tr>
<th>Actual Group</th>
<th>Predicted Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE</td>
<td>CIM</td>
</tr>
<tr>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>0</td>
<td>17</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Actual Group</th>
<th>Predicted Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE + CIM</td>
<td>GIM</td>
</tr>
<tr>
<td>6</td>
<td>17</td>
</tr>
</tbody>
</table>

Conclusions: The gene expression profiles of CIM and BE were similar in 91% of patients and differed significantly from that of GIM. Those with misclassification of CIM as GIM may have an alternate etiology such as H. pylori. The similar gene expression profile of CIM and BE suggests a shared reflux etiology in the majority of patients and calls into question the perception that CIM is an innocuous process.
**Purpose:** Esophageal food impaction (FI) is a distressing condition that requires urgent endoscopic intervention, with a recurrence rate of about 20%. Knowledge of factors predisposing to recurrent FI may enable the initiation of preventive measures that minimize the risk of recurrence. The aim of this exploratory study was to identify factors associated with recurrent FI.

**Methods:** Medical records of all patients undergoing emergent endoscopy for FI at Mayo Clinic Rochester (MCR) from 1989 to 2000 were reviewed. Cases and controls used MCR as their primary health care provider and resided within 50 miles of MCR. Cases were defined as presenting with recurrent FI requiring endoscopic intervention within 5 years of the index event; controls had no recurrent FI within 5 years of the index event. Several variables from patient demographics, medical history, endoscopic findings and therapy, and follow up data were extracted for analysis. Statistical significance was determined with $\chi^2$ tests and t-tests for univariate analyses and stepwise logistic regression for multivariate analyses.

**Results:** 52 cases and 124 controls were identified. The most common causes of FI were Schatzki’s ring (cases 39%; controls 32%) and peptic stricture (cases 31%; controls 33% [p = NS]. Cases and controls were similar with respect to age, gender and BMI. Dentures were worn by 32% of cases and 39% of controls [p = NS]. GERD was present in 35% of cases and 23% of controls [p = NS]. Esophageal dilation was performed at the index FI in 37% cases and 38% controls [p = NS]. Results of multiple logistic regression analyses are shown in the table.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-food impaction follow up by physician</td>
<td>0.38</td>
<td>0.18, 0.80</td>
<td>0.01</td>
</tr>
<tr>
<td>Presence of Diaphragmatic Hernia</td>
<td>2.65</td>
<td>1.19, 5.89</td>
<td>0.02</td>
</tr>
<tr>
<td>Disimpaction by piecemeal extraction</td>
<td>2.32</td>
<td>1.09, 4.97</td>
<td>0.03</td>
</tr>
<tr>
<td>Esophageal biopsies taken at index FI</td>
<td>3.69</td>
<td>1.41, 9.66</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**Conclusions:** The presence of a DH, complexity of endoscopic disimpaction technique (piecemeal extraction) and lack of follow-up were associated with recurrent FI. The collection of esophageal biopsies as a positive variable suggests a visibly more severe esophageal disorder as a potential cause of recurrent FI. This study provides preliminary data for the development of a FI Severity Score and management algorithm to reduce the risk of recurrent FI.

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Dysphagia Lusoria in the Adult: Clinical Findings and Diagnostic Approach

Lex Denysenko, B.A., Marc S. Levine, M.D., Gary R. Lichtenstein, M.D.*
School of Medicine, University of Pennsylvania, Philadelphia, PA; Division of Gastrointestinal Radiology, Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA; and Division of Gastroenterology, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA.

**Purpose:** Derived from the Latin *lusus naturae* and first described by Bayford in 1794, dysphagia lusoria (DL) can arise from any aortic arch anomaly compressing the esophagus, and the most common of these is the aberrant right subclavian artery (ARSA). A majority of cases present in infancy and are treated with surgery. DL first presenting in adulthood is exceedingly rare and not well characterized. Small case reports have described adult-onset DL in patients who were treated nonsurgically. We report our experience, and discuss the importance of performing video cine esophagography in the setting of a patient with dysphagia and an unrevealing esophagogastrodudenoscopy (EGD).

**Methods:** A computer-generated search of the radiology records of a tertiary care hospital center was performed (keywords: aberrant or anomalous and subclavian) for the period of 1996–2005. IRB approval was obtained for this study. The results were screened for confirmation of the vascular anomaly and for dysphagia. Cases for which the dysphagia could be attributed to other pathology were not included in our analysis. Clinical information, including age at diagnosis, duration of symptoms, prior studies, and treatments was gathered by chart review and patient follow-up.

**Results:** Lusorian arteries were found in a total of 193 patients who underwent barium swallow or computed tomography (CT) of the chest. DL not attributable to any other cause was identified in 28 cases. 26 had an ARSA,
one had an aberrant left subclavian artery, and one had a right-sided aortic arch. Mean age at diagnosis was 51 yrs (range 25–75 yrs). 25 were female. 17 patients reported dyspepsia in addition to dysphagia. The imaging modality that first yielded diagnosis was barium swallow (n = 19), CT (n = 8) or magnetic resonance imaging (n = 1). An extrinsic mass compressing on the esophagus was found in only 2 of 13 cases evaluated by EGD.

**Conclusions:** DL can present in adulthood, and cases not severe enough to warrant surgery often go unrecognized for years. When episodic solid food dysphagia is present in the setting of an unremarkable EGD, radiographic imaging is merited to help explain the etiology. A CT and / or barium swallow might be considered in these cases to help explain the etiology of the dysphagia.

### Combined Multichannel Intraluminal Impedance and pH Ambulatory Reflux Monitoring in Symptomatic GERD Patients on Acid Suppression Therapy: Confusion or Clarification?

**Saad F. Jazrawi, M.D., Nicholas M. Gualtieri, M.D., Anthony A. Starpoli, M.D.∗ Gastroenterology, St. Vincents Catholic Medical Center-Manhattan New York Medical College, New York, NY.**

**Purpose:** Persistent GERD symptoms despite acid suppression therapy present a diagnostic and therapeutic challenge to the clinician. 24 hrs multichannel intraluminal impedance combined with pH monitoring (MII-pH) is an important new tool for the GERD evaluation. The goal of the study is to define the symptomatology among patients who are still on PPI.

**Methods:** A retrospective look of our cohort (10/03–6/05) that had MII-pH. Symptoms were either typical (regurgitation, heartburn and belching) or atypical (the rest). We studied reflux in terms of symptom index (SI+ when >50%), and the more specific symptom association probability (SAP+ when >95%). 30 patients were identified on PPI. 15 men and 15 women, average age (46yr). We noted 6 patients reported one symptom while 12 reported 2 and another 12 patients reported 3 main symptoms for a total 66 symptoms.

<table>
<thead>
<tr>
<th>SI table</th>
<th>SI+ total</th>
<th>SI+: acidic reflux</th>
<th>SI+: nonacidic reflux</th>
</tr>
</thead>
<tbody>
<tr>
<td>belch</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>heartburn</td>
<td>8</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>regurgitation</td>
<td>11</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>abdominal pain</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>chest pain</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>cough</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>dysphagia</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>hoarseness</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>throat pain</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Those are symptoms reported by 25 patients.

**Results:** Acidic events noted among 7/27 patients (25.9%) with typical symptoms and 4/23 with atypical one (17.4%). SI+ was noted in 31 symptomatic patients while SAP+ was noted in 13. The concordance rate for SAP with SI is 5/15 (33.3%) for acidic reflux vs 9/21 (42.8%) for nonacidic reflux (distribution seen in tables 1 and 2). When comparing typical symptoms to atypical one, SI+ was noted in 21/39 (53.8%) vs 10/27 (37%), while for SAP+ was 11/39 (28.2%) vs 2/27 (7.4%). Heartburn, regurgitation, belching and cough were the only symptoms to have SAP+ among our cohort.

<table>
<thead>
<tr>
<th>SAP table</th>
<th>SAP+ total</th>
<th>SAP+: acidic reflux</th>
<th>SAP+: nonacidic reflux</th>
</tr>
</thead>
<tbody>
<tr>
<td>heartburn</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>belch</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>regurgitation</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>cough</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

These symptoms were noted by 13 patients.

### The Acute Effects of Nicotine on the Esophagus of Smokers and Non-Smokers

**Jigna Thakore, M.D., N. Gopalswamy, M.D., David Brown, R.N., Sangeeta Agrawal, M.D.∗ Gastroenterology, Veterans Administration Medical Center, Dayton, OH and Gastroenterology, Wright State University, Dayton, OH.**

**Purpose:** Cigarette smoking has been linked to a decrease in lower esophageal sphincter (LES) tone and an increase in gastroesophageal reflux symptoms. There have been no prospective studies comparing the effects of nicotine on the esophageal motility of smokers and non-smokers. We conducted a prospective study that measured baseline and post-nicotine LES pressure, LES relaxation, and esophageal body motility in chronic smokers and non-smokers.

**Methods:** Esophageal manometry using solid state catheter was performed at baseline and after a 14 mg transdermal nicotine patch on nine smokers and seven non-smokers. The baseline and post-nicotine LES pressure, lower esophageal residual pressure, distal esophageal amplitude, and percent peristalsis were compared within each group and between the two groups using Wilcoxon Signed Rank Sum Test.

**Results:** Among the smokers, there was no significant decrease in the lower LES tone and LES residual pressure after nicotine patch placement (1-tailed p = 0.84 and 1-tailed p = 0.45 respectively). The distal esophageal amplitude and percent peristalsis were also not significantly different before and after nicotine exposure among smokers (p = 1 and p = 1 respectively).

In the non-smokers, no significant decrease in LES tone and LES residual pressure was found after nicotine exposure (1-tailed p = 0.29 and 1-tailed p = 0.34 respectively). Also, there was no significant difference in the distal esophageal amplitude and percent peristalsis before and after nicotine patch placement (p = 0.289 and p = 0.5 respectively).

When comparing the smokers with non-smokers, baseline LES tone, LES residual pressure, distal esophageal amplitude, and percent peristalsis were not significantly different. These parameters did not change significantly after nicotine exposure in smokers compared to non-smokers.

**Conclusions:** Our study showed that nicotine had no statistically significant effect on the esophageal motility of smokers and non-smokers.

### Barrett’s Esophagus and Esophageal Adenocarcinoma in South Carolina in 2003: Geographic Analysis of Prevalence and Effect of Availability of a Gastroenterologist

**Noah M. DeVicente, M.D., Marcelo F. Vela, M.D.∗ Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, SC.**

**Purpose:** The incidence of Esophageal Adenocarcinoma (EA) is rapidly rising. Diagnosing Barrett’s Esophagus (BE), a precursor of EA, is important because it enables surveillance and detection of malignancy at a curable stage. Geographic analyses of BE and EA prevalence that consider the effect of gastroenterologist availability are lacking. Our aim was to assess geographic variation in 2003 BE and EA prevalence across South Carolina (SC) counties, examine effect of GI availability and compare gender/ethnic variation to published data.

**Methods:** 2003 number of EA cases (ICD-9 search) and number of gastroenterologists, and population demographics for each county from SC Office of Statistics. 2003 number of EA cases per county from SC Cancer Registry. Geographic distribution and relationships among BE/EA prevalence and GIs (no. doctors/100,000 population) studied by Geographic Information System for Epidemiological Studies (ArcView 3.x).
Conclusions: Availability of a GI may impact BE diagnosis/prevalence in different SC geographic areas. Rates appear higher for females compared to literature. Undetected BE in regions with limited access to GI may lead to higher EA prevalence. If supported by further studies, these data can be used to determine need of GIs and endoscopic centers in specific geographic areas. Five-year data analysis in progress.[figure1]
defined as a mean increase from baseline of ≥ 1 complete spontaneous bowel movement (CSBM) per week. All patients reported re-treatment with topical steroids at three year follow-up; preliminary responses suggest that a majority of patients require repeated treatment. Furthermore, a number also experience food impaction requiring endoscopic therapy despite the topical steroid treatment. It seems over the long term, topical steroids may not modify the symptoms or need for endoscopic treatment of food impaction in eosinophilic esophagitis.

Conclusions: In these CC pts, a history of other GI disorders (NUD and GERD) was common (23%) and did not alter the response to T in pts with both GERD and dyspepsia. P rates tended to be slightly lower in the UGI condition subgroups, most pronounced for pts with dyspepsia vs non-dyspepsia (not significant). OR tended to be higher in the UGI condition subgroups vs those without.

Tegaserod (N = 882) Placebo (N = 863)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Response wks 1–4</th>
<th>OR p value</th>
<th>Response wks 1–12</th>
<th>OR p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non GERD</td>
<td>305/719 (42)</td>
<td>2.37 &lt;.0001</td>
<td>10/27 (37)</td>
<td>3.38 .20</td>
</tr>
<tr>
<td>GERD</td>
<td>61/158 (39)</td>
<td>2.20 .0055</td>
<td>6/15 (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Non NUD</td>
<td>340/813 (42)</td>
<td>2.23 &lt;.0001</td>
<td>12/24 (50)</td>
<td>2.72 .04</td>
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<tr>
<td>NUD</td>
<td>26/64 (41)</td>
<td>2.06 &lt;.0001</td>
<td>12/24 (50)</td>
<td>2.28 &lt;.0001</td>
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<tr>
<td>Non both</td>
<td>356/850 (42)</td>
<td>2.28 &lt;.0001</td>
<td>10/27 (37)</td>
<td>3.38 .20</td>
</tr>
<tr>
<td>Both</td>
<td>102/271 (45)</td>
<td>2.16 &lt;.0001</td>
<td>28/64 (44)</td>
<td>5.00 .0013</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Condition</th>
<th>Response wks 1–4</th>
<th>OR p value</th>
<th>Response wks 1–12</th>
<th>OR p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non GERD</td>
<td>322/719 (45)</td>
<td>2.16 &lt;.0001</td>
<td>10/27 (37)</td>
<td>3.38 .20</td>
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<tr>
<td>GERD</td>
<td>64/158 (40)</td>
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<td>6/15 (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Non NUD</td>
<td>358/813 (44)</td>
<td>2.06 &lt;.0001</td>
<td>12/24 (50)</td>
<td>2.28 &lt;.0001</td>
</tr>
<tr>
<td>NUD</td>
<td>28/64 (44)</td>
<td>5.00 .0013</td>
<td>12/24 (50)</td>
<td>2.28 &lt;.0001</td>
</tr>
<tr>
<td>Non both</td>
<td>377/850 (44)</td>
<td>2.17 &lt;.0001</td>
<td>10/27 (37)</td>
<td>3.38 .20</td>
</tr>
<tr>
<td>Both</td>
<td>9/27 (33)</td>
<td>2.49 .23</td>
<td>6/26 (23)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Eosinophilic esophagitis is an increasingly recognized cause of dysphagia and food impaction in adults. The diagnosis is suggested by subtle endoscopic findings including a ringed or furrowed esophagus, and confirmed with esophageal biopsies revealing dense eosinophilic infiltrates. Topical steroids are increasingly used for treatment. However, at three year follow-up, preliminary responses suggest that a majority of patients require repeated treatment. Furthermore, a number also experience food impaction requiring endoscopic therapy despite the topical steroid treatment. It seems over the long term, topical steroids may not modify the symptoms or need for endoscopic treatment of food impaction in eosinophilic esophagitis.

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Improved pH-Metry and Symptom Scores 3 mo post-ENTERYX®:
Interim US Randomized Controlled Trial Results

Richard I. Rothstein, M.D., Yang K. Chen, M.D., Thomas F. Mendolia, DO, Lawrence B. Cohen, M.D., Jacques Desiere, M.D., T. Raymond Foley, M.D., David A. Johnson, M.D., Guido Costamagna, M.D., M. Brian Fennerty, M.D., Prateek Sharma, M.D., William Snape, Jr., M.D., Steven A. Edmundowicz, M.D., Glen A. Lehman, M.D.*, Peter J. Kahrials, M.D. Dept. Gastro., Dartmouth-Hitchcock Medical Center, Lebanon, NH; U. Colorado Hospital, Aurora, CO; NW Piedmont Clinical Research, Elkin, NC; Mt. Sinai Hospital, New York, NY; Erasme Hospital, Brussels, Belgium; Regional Gastroenterology Associates, Lancaster, PA; Eastern VA School of Medicine, Norfolk, VA; U. Cattolica del Sacro Cuore, Rome, Italy; Oregon Health Sciences U., Portland, OR; VA Medical Center, Kansas City, MO; CA Pacific Medical Center, San Francisco, CA; Washington U., St. Louis, MO; Indiana U. Medical Center, Indianapolis, IN and Northwestern U., Chicago, IL.

Purpose: To compare pH-metry and GERD-HRQL scores in ENTERYX treated (EG) vs control (CG) groups.

Methods: PPI-dependent and responsive pts were randomized to either EG or CG. CG pts underwent endoscopy; DMSO was sprayed on distal esophagus. 3 mo post initial procedure, EG pts w/ GERD-HRQL score >11 (off PPIs) were eligible for retreatment; CG pts who were off PPIs with GERD-HRQL ≥ 20 and pH <4.0 were eligible for crossover to ENTERYX. pH-metry success was defined as either total time pH ≤ 4.0 reduced ≥ 5% of total time were eligible for crossover to ENTERYX. pH-metry success was defined as either total time pH ≤ 4.0 reduced ≥ 5% of total time or pH ≤ 4.0 reduced ≥ 50% from baseline. GERD-HRQL score success was defined as either a score of ≤ 11 or an improvement from baseline ≥ 9 points.

Results: Interim 3-mo data were available for 62 pts (31/group). To date, 61% (19/31) of CG pts crossed over and 13% (4/31) of EG pts were retreated. These initial results reflect outcomes from one ENTERYX treatment. Mean change from baseline (CFB) in pH-metry (% total time pH ≥ 4.0) was −4.3% in EG, vs −0.5% in CG (p < 0.05). pH-metry success was achieved by 50% of EG vs 23% of CG (p < 0.05). EG had more patients achieve GERD-HRQL heartburn score success (83% vs 54%, p < 0.05) and had larger mean CFB for GERD-HRQL heartburn (−14.9 vs −9.2, p < 0.05) than the CG. Conclusion: At 3 mo, ENTERYX Procedure significantly improves pH-metry and GERD-HRQL measures vs control. Furthermore, the proportion of pts eligible for retreatment/crossover was lower in the ENTERYX group than in controls, despite similar eligibility criteria. These results confirm the true effect of ENTERYX in the treatment of GERD.

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ENTERYX® Procedure: 12-Month Follow-Up of GERD Symptoms and Treatment Satisfaction

Michael Brown, M.D., David A. Johnson, M.D., Ron Pruitt, M.D., Robert A. Ganz, M.D., Martin Radwin, M.D., Thomas Mendolia, DO, Nishim Vakil, M.D., Christopher J. Gostout, M.D., Mark DeLegge, M.D., Douglas K. Pleskow, M.D., Yang K. Chen, M.D.* Department of Gastroenterology, Rush University Medical Center, Chicago, IL; Eastern Virginia Medical School, Norfolk, VA; Nashville Medical Research Institute, Nashville, TN; Abbott-Northwestern Hospital, Minneapolis, MN: Pioneer Valley Hospital.
Purpose: To evaluate GERD symptoms and treatment satisfaction prior to and during 12 months following the ENTERYX Procedure.

Methods: Patients with GERD, responsive to PPIs participated in two ongoing post-market studies to evaluate treatment outcomes with the ENTERYX Procedure. GERD symptoms (Velanovich GERD-HRQL) and treatment satisfaction were assessed at baseline on PPIs and months 1, 6, 12, 24, and 36 post-procedure. Treatment satisfaction regarding symptom control, relief, freedom to eat and drink, sleep improvement, and overall rating was assessed using a GERD-specific questionnaire. Paired t-tests comparing baseline and follow-up scores were performed for evaluable patients.

Results: 59% (202/343), and 18% (61/343) of patients have completed 6 and 12-month follow-up respectively. Mean age is 49 ± 13.2 years; 49% of patients is male. Prior to treatment, mean GERD-HRQL score for the 199 patients with 6-month follow-up was 19.7 compared to 9.6 at 6 months (p < 0.05; 95% CI: 8.6, 11.5). For the 60 patients with 12-month follow-up, mean baseline GERD-HRQL score was 20.6 compared to 13.0 at 12 months (p < 0.05; 95% CI: 4.5, 10.8). Treatment satisfaction results are presented below.

### Median Scores

<table>
<thead>
<tr>
<th>Symptom Control</th>
<th>N Baseline</th>
<th>Month 6*</th>
<th>N Baseline</th>
<th>Month 12*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom relief</td>
<td>196</td>
<td>3.0</td>
<td>4.0</td>
<td>57</td>
</tr>
<tr>
<td>Freedom to eat/drink</td>
<td>197</td>
<td>3.0</td>
<td>4.0</td>
<td>57</td>
</tr>
<tr>
<td>Sleep improvement</td>
<td>197</td>
<td>4.0</td>
<td>4.0</td>
<td>57</td>
</tr>
<tr>
<td>Overall rating</td>
<td>196</td>
<td>3.0</td>
<td>4.0</td>
<td>57</td>
</tr>
</tbody>
</table>

(1 = Poor, 2 = Fair, 3 = Good, 4 = Very Good, 5 = Excellent) *p < 0.05.

Conclusions: Interim data from these ongoing post-market studies suggest that following ENTERYX, patients are more satisfied with treatment benefits and have improved GERD symptoms as compared to baseline on PPIs.

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**Eosinophilic Esophagitis in Adolescents – Entity Should Be Known to Adult Gastroenterologists**

Juan F. Villalona, M.D., Thomas Rossi, M.D., Marilyn R. Brown, M.D., Ashok Shah, M.D., Philip Katzman, M.D., Jay Matur, M.D. Pediatric and Adult Gastroenterology, University of Rochester Medical Center, Rochester, NY.

**Purpose:** A majority of adolescent patients are scoped for esophageal symptoms by adult gastroenterologists. The eosinophilic esophagitis (EE) should be in the differential diagnosis of patients with esophageal symptoms in these patients. This study was done in collaboration with the pediatric gastroenterologists to study the occurrence of EE, its symptomatology and endoscopic findings.

30 adolescent patients with EE were studied to evaluate their symptoms, endoscopic findings and relationship to allergy. All of these patients met the accepted criteria for the diagnosis of eosinophilic esophagitis (EE).

**Methods:** 30 charts of patient with the diagnosis of EE were reviewed for sex, age at presentation, onset of symptoms, specific symptoms, pH probe test results, endoscopic findings, RAST tests (if done) and biopsy results.

**Results:** There were 22 (73%) males and 8 (27%) females. The predominant symptoms were dysphagia in 21 (70%) patients, heartburn in 16 (53%) patients, food impaction in 14 (47%) patients, and abdominal pain in 13 (43%) patients. 22 patients with EE had a pH probe study of which 17 (77%) tested positive, 19 (63%) had allergies to food, medications or environmental allergies. RAST test was done in 22 (73%) of cases and 13 (59%) were positive. The common allergic food was milk. The most common endoscopic finding was linear grooves in 14 (47%), white spots in 8 (27%) and rings in 5 (17%) of cases. The biopsy revealed 15 to 80 eosinophils/HPF in 26 (87%) cases. There was eosinophilic gastroenteritis in 5 (10.4%) cases. 27(90%) of the cases responded to elimination of allergen and flucortisone.

**Conclusions:** Adult gastroenterologists should be aware of this entity as they will be treating a majority of these adolescents with esophageal symptoms. Dysphagia, heart burn, food impaction and abdominal pain were common presenting symptoms. The characteristic endoscopic and biopsy findings are diagnostic of EE. A majority of patients responded to elimination of allergen and flucortisone.

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**Endoscopic Full-Thickness Plication for the Treatment of GERD:**

**3-Year Multicenter Results**

Douglas E. Pleskow, M.D., Richard I. Rothstein, M.D., Simon K. Lo, M.D., Robert H. Hayes, M.D., Richard A. Kozarek, M.D., Gregory B. Huber, M.D., Christopher J. Gustout, M.D., Anthony J. Lenbo, M.D.* Gastroenterology, Beth Israel Deaconess Medical Center, Boston, MA; Gastroenterology, Dartmouth Hitchcock Medical Center, Lebanon, NH; Gastroenterology, Cedars Sinai Medical Center, Los Angeles, CA; Gastroenterology, Virginia Mason Clinic, Seattle, WA; Gastroenterology, St. Michael’s Hospital, Toronto, ON, Canada; Gastroenterology, Mayo Clinic, Rochester, MN and Gastroenterology, Medical University of South Carolina, Charleston, SC.

**Purpose:** The Plicator (NDO Surgical, Inc., Mansfield, MA) delivers a transmural suture through the gastric cardia under direct endoscopic visualization. The resulting serosal tissue apposition restructures the valvular mechanism of the gastroesophageal (GE) junction. Previously published studies have shown the Plicator procedure effective in reducing GERD symptoms and medication use at 1-year post-plication.

**Aim:** To assess the long-term safety and efficacy of endoscopic full-thickness plication for the treatment of symptomatic GERD.

**Methods:** Sixty-four patients with chronic heartburn requiring maintenance daily anti-secretory therapy received a single, endoscopically placed, full-thickness plication in the gastric cardia 1cm below the GE junction. Re-treatments were not permitted. Study exclusions included hiatal hernia > 2 cm, Grades III and IV esophagitis, and Barrett’s esophagus. Patients were evaluated for GERD symptoms and medication use at baseline, 12-months, and 36-months post-plication.

**Results:** Twenty patients have completed the 36-month follow-up; additional data collection is in process. All procedure-related adverse events occurred acutely, as previously reported, and no new adverse events were observed during extended follow-up. At 3-years post-procedure, 63% (12/19) of PPI dependent patients remained off daily PPI. Treatment effect remained stable from the 12 to 36-month follow-up intervals, with only 4/20 patients showing an increase in medication requirements. At 3-years post-procedure, mean GERD-HRQL scores remained improved versus baseline off meds (20.8 vs. 11.9) and were comparable to baseline on-meds values (11.9 vs. 11.8).

**Conclusions:** Endoscopic full-thickness plication can effectively reduce symptoms and medication use associated with GERD out to at least 3-years post-procedure.

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**Unresolved Upper Gastrointestinal (UGI) and Extraesophageal (EE) Symptoms in Gastroesophageal Reflux Disease (GERD) Patients Despite Chronic Proton Pump Inhibitor (PPI) Therapy**

D. Earnest, M.D., A. Lenbo, M.D., J. Novick, M.D., H. Proskin, M.D., M. Rojavin, M.D. Novartis Pharmaceuticals Corp, East Hanover, NJ; Beth Israel Deaconess Medical Center, Boston, MA; Charm City Research, Towson, MD and HM Proskin & Associates, Rochester, NY.
Detection of *H. pylori* at Distal Esophageal Mucosa by a Novel Multiplex PCR Assay

Xiangwen Meng, Ph.D., Hongjin Zhang, Ph.D., Tat-Kin Tsang, M.D.*
Evanston Northwestern Healthcare, Northwestern University Feinberg School of Medicine, Evanston, IL.

**Purpose:** Many factors have been reported to affect the ability to identify *H. pylori* in clinical practice. These include the type of tests used, the experience of the pathologist, the number of biopsy samples, and the location from which they were taken. *H. pylori* is a highly motile and most commonly lives in the mucous layer of the gastric epithelium. Motility, by way of flagella, enables the organism to easily travel within the mucous layer. *H. pylori* in the esophagus is found only in areas of Barrett’s esophagus. In order to determine the prevalence of Helicobacter pylori infection at antral gastric and esophageal mucosa and its correlation with the multiplex PCR findings, a prospective study was performed with a novel one-step multiplex PCR method in 102 patients with dyspepsia symptoms.

**Methods:** This study was performed in 102 patients with dyspepsia symptoms undergoing endoscopy in Evanston Northwestern Healthcare. Six specimens, 2 from the corpus, 2 from the antrum and 2 from the distal esophageal, were collected from each patient by endoscopy for extracted DNA and was performed the one-step multiplex PCR.

**Results:** Helicobacter pylori was found on the biopsy specimens of the gastric antrum/corpus and distal esophagus in 43% (44/102) and 32% (33/102), respectively. The combinative positive results of the three locations were achieved 53%.

**Conclusions:** Our results indicate that the *H. pylori* could live in the distal esophagus since some cases have positive *H. pylori* in the esophagus but not in the stomach. (Although false positive results may be obtained, the samples of distal esophagus due to contamination from the gastric antrum/corpus in the process of endoscopy or because of the hyper sensitivity of the PCR method) Therefore multiple biopsies, especially the specimens from distal esophagus may be needed for the diagnosis of *H. pylori* infection in some situation.

Endoscopic Mucosal Resection (EMR) for High Grade Dysplasia (HGD) and Early Esophageal Cancer

Emad Y. Rahmani, M.D.,* Kathy L. Arney, R.N., Carolyn Turpin, R.N.
Department of Medicine, Division of Gastroenterology, Indiana University School of Medicine, Indianapolis, IN.

**Purpose:** Endoscopic mucosal resection (EMR) is considered a major advance in minimally invasive surgery in the gastrointestinal tract. EMR is particularly appealing in the management of high-grade dysplasia in Barrett’s esophagus which has been a difficult area in clinical decision-making. This utility of endoscopic therapy is based on the notion that there is no lymph node metastasis in high-grade dysplasia and very low rate of metastasis in invasive cancer confined to the mucosa. Endoscopic ablative therapies like photodynamic therapy have been successful for high-grade dysplasia

Interobserver Variation among Gastroenterologists with “PillCam” Esophageal Capsule

Gulam Khan, M.D., Ira Mayer, M.D., Joel Albert, M.D., Jian Jun Li, M.D., William Erber, M.D., Scott Tenner, M.D., M.P.H.* Division of Gastroenterology, Maimonides Medical Center, Brooklyn, NY.

**Purpose:** Gastro-esophageal reflux disease (GERD) is a common entity. Erosive esophagitis, esophageal ulcers and Barrett’s esophagus are found in 10 – 20% of patients with heartburn. As patients with Barrett’s esophagus have 0.5% per patient-year risk of developing esophageal adenocarcinoma, endoscopy is recommended for surveillance. Although endoscopy is safe, there are rare risks including perforation and complications from sedation. A new ingestible “PillCam” esophageal capsule recently approved for the evaluation of esophageal disease may offer an alternative office-based approach to visualize the esophagus without sedation. However, unlike endoscopy which allows repetitive movements by the endoscopist to review an area, the esophageal capsule passes capturing selected images that are reviewed at a later period of time. The ability of gastroenterologists using the esophageal capsule to define pathology has not clearly been established. In addition, interpretation of the images may vary.

**Methods:** In order to determine the accuracy and assess for interobserver variation of esophageal capsule endoscopy in the evaluation of GERD, 6 patients underwent esophageal capsule endoscopy within 24 hours of standard endoscopy, which served as the “gold standard”. The images were then reviewed by four gastroenterologists who were unaware of the original endoscopy findings. The gastroenterologists were asked to report the degree of esophagitis (LA Class), the presence of esophageal ulcers, Barrett’s esophagus, hiatal hernia and nodules/submucosal masses.

**Results:** Six patients were included in the study allowing 24 esophageal capsule reports to be collected from the gastroenterologists. Of the six patients included, 3 had normal exams, 2 had Barrett’s esophagus and 1 had erosive esophagitis/esophageal ulcers. All four gastroenterologists were able to identify the presence of Barrett’s esophagus and esophageal ulcers. However, there was no correlation in the degree of esophagitis (LA Class), the length of Barrett’s esophagus and the size of the hiatal hernia. In addition, a nodule in Barrett’s mucosa was not appreciated by 2/4 gastroenterologists.

**Conclusions:** Although the “PillCam” esophageal capsule can assist in the identification of Barrett’s esophagus, significant limitations exist which may affect the accuracy of this new technology, including difficulty in assessing the length of the hiatal hernia, the length of Barrett’s mucosa and the degree of esophagitis.
in Barrett's esophagus. However, important limitation of such therapy is the lack of pathology specimen confirming that disease is confined to the mucosa and uncertainty of complete ablation especially where the disease might be deeper than superficial mucosa.

Methods: Patients: During the period of January 2002 to May 2005, 52 patients had 183 EMR for the treatment of esophageal lesions. There were 39 males and 13 females, mean age was 70 (34–86). The indications were endoscopic resection of HGD (n = 24), early cancer (n = 27), endoscopic resection of a lesion which pathology biopsy was not conclusive (n = 1). Methods: EMR was performed using submucosal injection of either normal saline or dextrose 50% along with methylène blue. EMR kit (Olympus) was used to excise the specimen. Mean size of resected specimen was 1.2 cm (0.5–2.0). Different specimen bottles were used for the lesion versus the surroundings. Mean number of specimen per patient was 4 (range 1–6). All patients underwent meticulous staging including EUS, CT and PET scan.

Results: Complete endoscopic excision was achieved in fifty patients. Cancer extending to the lateral margin of the specimen was seen in (n = 8). HGD extending to the margin of the surrounding tissue was seen in (n = 14). Tumor was upgraded from T1 to T2 was seen in 2 patients, while it was downgraded from T1 to HGD in 5, and to LGD in one patient. Photodynamic therapy was used in 21 patients to ablate residual HGD/T1 cancer. Follow up for up to 3 years revealed HGD± T1 cancer-free in all but three patients. Two patients died from progressive disease and one from unrelated cancer.

Conclusions: EMR with or without other modality should be considered as a treatment option in all esophageal HGD or superficial adenocarcinoma patients.

S50 Abstracts

80 Esophageal pH Monitoring Using a Wireless System: A Single Center’s Experience
Jay P. Babich, M.D., Michael Sullivan, DO, James H. Grendell, M.D., Maureen Stampe, R.N., Kavita R. Kongara, M.D.* Division of Gastroenterology, Winthrop Univ. Hospital, Mineola, NY

Purpose: Traditional catheter-based esophageal pH testing is limited by patient discomfort and inconvenience. A catheter-free pH monitoring system has become available. The aim of this study was to report our experience with this wireless pH-monitoring device over a 48 hr period in patients with typical and extraesophageal manifestations of GERD.

Methods: Medical records of consecutive patients undergoing wireless pH monitoring at our institution were reviewed.

Results: 90 patients (58 F/32 M, mean age 50) underwent wireless pH monitoring between 7/2003 and 6/2005. Indications for the study were typical reflux symptoms (laryngitis, hoarseness, globus, and abnormal throat sensations (25%). (28%); pulmonary symptoms (chronic cough, asthma) (16%); ENT symptoms (sore throat, hoarseness, globus, and abnormal throat sensations (25%). Incomplete measurements were obtained in three (3%) of these patients due to poor probe attachment or inadequate data retrieval from the recorder secondary to device or computer malfunction. One patient did require a repeat endoscopy for chest pain, and the capsule was knocked off into the stomach. Two patients died from progressive cancer and one from unrelated cancer.

Conclusions: EMR with or without other modality should be considered as a treatment option in all esophageal HGD or superficial adenocarcinoma patients.

81 Slimline™ vs Glass: Are Antimony Catheters Reliable for Measuring Esophageal Acid Exposure?
John E. Pandolfino, M.D., Christopher Boniquit, B.A., Qing Zhang, M.D., Sudip Ghosh, Ph.D., Peter J. Kahrilas, M.D.* Medicine/Division of Gastroenterology, Northwestern University, Chicago, IL.

Purpose: This study compared the pH recording accuracy of the Slimline™ antimony pH monitoring system and a conventional glass electrode catheter pH monitoring system during ambulatory conditions.

Methods: 18 asymptomatic subjects (13 males, 23–45 y/o) underwent simultaneous pH monitoring using the Slimline™ antimony pH electrode and MIC M3 glass pH electrode pH monitoring systems for 12 hours. The catheters were attached with tape and placed 5 cm above the LES. The subjects consumed 100 cc of orange juice and 100 cc of cranberry juice at 37°C to synchronize the data and measure pH electrode accuracy. After 11 hours the subjects returned to the lab and the catheter was advanced 10 cm into the stomach for 1 hour. Differences in% time the pH < 4 and number of reflux events were analyzed and compared by manual extraction of the data onto an excel spreadsheet. Agreement between the two systems in recording reflux events was analyzed by observing the point-by-point discrepancy of +0.5 pH units and also by performing a Kappa analysis for pH above and below 4.

Results: The correlation between Slimline™ and the Glass MIC M3 catheter was excellent for the total time pH < 4 (r = 0.84) and there was no statistical difference in the median value measured by the two systems (Slimline™: 2.5%, Glass 1.9%, P = 0.77). The difference in recorded reflux events was also not significantly different between the two systems, with the absolute difference being 23 events (SD, 26.0). Although the point-by-point discrepancy was 28.2% (SD, 17.5%) when using a 0.5 pH unit threshold, the agreement in terms of pH events above and below 4 was excellent (Kappa value, 0.89, SD, 0.09). In addition, the in-vivo pH measurement identified two Slimline™ catheters and one glass catheter that were malfunctioning.

Conclusions: The antimony Slimline™ pH catheter compares favorably to the Glass MIC M3 pH catheter in terms of measuring standard pH parameters. Although there is substantial point-by-point disagreement, it is typically less than 0.5 pH units and does not substantially alter diagnosis based on a threshold pH value of 4.

82 “Silent” Gastroesophageal Reflux in Patients with Unexplained Sleep Complaints
William C. Orr, Ph.D.,* Suzanne Goodrich, Ph.D., Robert Sturgeon, B.S., Russell Rosenberg, Ph.D., Paula Fernstrom, M.S. Sleep Laboratory, Lynn Health Science Institute, Oklahoma City, OK; Lynn Institute of the Rockies, Colorado Springs, CO; Atlanta Sleep Medicine Institute, Atlanta, GA and AstraZeneca, Molndal, Sweden.

Purpose: Patients with gastroesophageal reflux (GER) commonly report poor sleep, and it has been established that the arousals from sleep are frequently associated with acid mucosal contact via GER. It has also been shown that individuals with significant GER exacerbating respiratory symptoms may frequently be without complaints of heartburn. We posed the question of whether a substantial portion of individuals with sleep complaints, without significant heartburn, experience “silent” reflux during sleep.

Methods: 104 individuals with documented sleep complaints at least three nights per week were randomized after a two-week run in period with recorded sleep diaries. 81 subjects completed two polysomnographic sleep evaluations including distal esophageal pH separated by 10–21 days.
Results: Of the 81 subjects studied, 26% had reflux (pH < 4 for more than 30 sec) on at least one night. Of the participants with reflux, 21% had more than 4% acid contact time (ACT), 25% had at least one event that lasted more than five minutes and the average ACT was 28%. The average duration of each reflux episode was 34.4 minutes. Almost all (94%) of the recorded reflux events were associated with an arousal or awakening. An historical comparison group of symptomatic GERD patients with concomitant sleep complaints had an average ACT of only 12% (p < .05).

Conclusions: 1. A substantial portion of individuals with sleep complaints, and without significant heartburn symptoms, revealed “silent reflux” during sleep. 2. “Silent reflux” may be the cause of sleep disturbances in individuals with unexplained sleep disorders.

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Relationship Between the Position of the Esophageal Sphincters and Body Height in Healthy Subjects

A. Ruiz de Leon, M.D.,∗ M. Cascales, M.D., on behalf of the Spanish Digestive Motility Group (GEM.D.). Hospital Clinico San Carlos, Madrid, Spain and Novartis Farmaceutica, Barcelona, Spain.

Purpose: Establishing the position of the esophageal sphincters is of particular interest when performing certain functional studies, especially in those situations in which manometry and endoscopy are not available and a pH-metry study is required. Objectives: To establish whether a relationship exists between body height and the position of the esophageal sphincters as determined by manometry in a group of healthy subjects without gastroesophageal reflux symptoms and with a normal pH-metry.

Methods: A multicentre study involving a group of 91 non-obese, healthy subjects (37 men and 54 women) with a mean age of 29 years (range, 18–72 years) and with non-gastrointestinal symptoms, with a low esophageal sphincter pressure >6mmHg and without pathological reflux measured by pH-metry. Esophageal manometry was performed in all subjects using the continuous perfusion and stationary pull-through technique. The distance was measured from the anterior nares to the upper border of the Lower Esophageal Sphincter (LES) and to the lower border of the Upper Esophageal Sphincter (UES). The correlation was studied between individual height and the nares–sphincter distances. An ambulatory pH-metry of long duration (24 h) was performed with the customary technique.

Results: The mean height was 169.5 cm (range 148–193). The lower border of the LES was situated at 41.5 cm (range 35–49.5). The results showed a clear relationship between height and the position of the two sphincters (p < 0.0001), allowing the following equations to be established: LES = 1.3663 + (0.1098 × height); UES = 6.1774 + (0.2093 × height)

Conclusions: There is a direct correlation between height and the position of the esophageal sphincters; this may be determined by means of simple equations.

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Esophageal Perforation after Placement of Wireless Bravo pH Probe

Noel R. Fajardo, M.D., James L. Wise, M.D., G. Richard Locke III, M.D., Nicholas J. Talley, M.D., Ph.D.∗ Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN.

Purpose: Esophageal pH monitoring is important in patients with atypical or refractory gastroesophageal reflux disease (GERD). The technology of esophageal acid exposure monitoring with the use of a catheter-free radiotelemetric pH capsule, called the BRAVO™ pH monitoring system (Medtronic Inc., Shoreview, MN) is a recent new technique demonstrated to be comparable to the conventional catheter system for quantifying esophageal pH. Its use is more comfortable and allows the patient to be more active during the test period with minimal complications. We describe a case of esophageal perforation during that occurred during the placement of the catheter delivery system.

A 67/F with recurrent reflux underwent EGD and placement of a BRAVO™ pH probe. EGD was normal. During advancement of the BRAVO™ catheter probe, resistance was met at the proximal esophagus. Immediate withdrawal of the catheter and endoscopy revealed a large mucosal tear and the procedure was immediately aborted.

After the procedure, the patient had chest discomfort, was afibrile and hemodynamically stable. Cardiac, pulmonary and abdominal examinations were normal. CBC and electrolytes are all normal other than mild leukocytosis (WBC 13.6) which normalized the next day.

Pharyngoesophagram with gastroganin contrast demonstrated extraluminal extravasation of gastroganin in the upper esophagus along the anterior left aspect. The CT scan of the chest demonstrated air in the posterior mediastinum consistent with esophageal perforation.

The patient was admitted for observation and managed conservatively, i.e. NPO, pain control, IV hydration, and coverage with broad spectrum antibiotics. The patient remained stable over the next few days, and a clear liquid diet was started on the 4th hospital day was eventually discharged on the 6th hospital day without developing further complications, with the advice of advancing to a regular diet after within one week, and to continue a one-week course of oral antibiotics. After several weeks after the incident, the patient was eventually able to resume her normal diet and activities without developing further complications.

The BRAVO™ pH system is well tolerated and its use in several institutions is becoming more widespread. Recognition that esophageal perforation may be a complication is important. The physician should consider such risks in the consideration of determining the appropriateness of testing in patients with GERD.

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Gram-Negative Bacteremia: Rare Sequelae of Black Esophagus

Robin Forman, DO, AnnMarie Huyseman, M.D., Seth Cohen, M.D.∗ Division of Digestive Diseases, Beth Israel Medical Center, New York, NY and Internal Medicine, Mount Sinai Medical Center, New York, NY.

Purpose: A 43-year-old woman presented with hypertension, chest pain, and shortness of breath. Her past medical history included hypertension, diabetes mellitus, coronary artery disease, myocardial infarction (MI), cerebrovascular accident, chronic renal insufficiency, and antiphospholipid antibody syndrome.

The patient was admitted to the ICU for hypertensive emergency. On hospital day #2 she had an episode of hematemesis with epigastric pain and dysphagia. She was hemodynamically stable and afibrile. Physical exam revealed mid-epigastric tenderness and brown guiac positive stool. White count was 15.2 k/mm³, hemoglobin was 11.1 g/dL, creatinine was 1.8 mg/dL, platelets and coagulation studies were normal. Esophagagogastroduodenoscopy (EGD) revealed markedly abnormal mucosa, covered with confluent black exudates with a “burnt marshmallow appearance” in the distal third of the esophagus. Biopsies showed pseudomembranes with polymorphonuclear cells (PMNs) and squamous epithelium with numerous clusters of PMNs, consistent with acute necrotizing esophagitis.

Oral cefazolin and bid pantoprazole were initiated. On hospital day #5, the patient was discharged. One week following the initial EGD she was complaining of continued dysphagia and odynophagia. EGD at that time revealed marked improvement of the mucosa, but still showed severe erythema with overlying yellowish exudate. Repeat biopsies showed histological improvement of acute inflammation by resolution of PMNs. However, the presence of gram negative bacilli was noted. Silver stains of the tissue revealed yeast and pseudohyphae depicting superinfection with candida species.

Three days following the second EGD, the patient was admitted to the hospital for fever and gram (-) bacteremia, Proteus species. This correlated with the GNR seen on the biopsy from the second endoscopy. The patient was treated with oral ciprofloxacin and discharged.

Black esophagus is a rare endoscopic finding. Although the pathogenesis remains unknown, an ischemic origin appears likely. It seems to occur in patients with overall poor general health and treatment consists of conservative
therapy. The natural history of the disease is that of spontaneous resolution. Our patient was admitted a few days after her second EGD for gram (-) bacteremia, an unreported sequelae of acute necrotizing esophagitis. We postulate that the bacteremia was a result of the manipulation of the mucosa from endoscopy and biopsy.

STOMACH

Clinical Approach for 30 Patients with Gastric Cancer on First Biopsy but Negative Results on Re-Biopsy at Referred Hospital

Jeong Kim, Jun Haeng Lee, Professor,* Jae J. Kim, Professor, Jong Chul Rhee, Professor, Sung Kim, Professor. Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea and Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

Purpose: After referral of the patients with pathologically confirmed gastric cancers, re-examination is frequently performed to determine further management plans. However, biopsy results at referred hospital may be different from the original pathology report. Some patients may have persistently negative results on repeated biopsies. In this study, we analyzed the clinical results of 30 patients with this challenging problem (gastric cancer in first biopsy but no evidence of malignancy in the re-biopsy after referral).

Methods: From January 2003 to March 2005, we analyzed 30 patients with gastric cancer diagnosed on outside biopsy (28 adenocarcinomas and 2 signet cell carcinomas) and negative results on first biopsy at Samsung Medical Center, a tertiary hospital in Seoul, Korea. We recommended surgery or endoscopic mucosal resection depending on the characteristics of the lesions. Medical records, endoscopic images, and pathology reports were retrospectively reviewed.

Results: On our first biopsy, 7 patients had adenoma, 2 patients had atypical gland, and the remaining 21 patients had nonspecific findings. Without evidence of cancer at first biopsy, endoscopic mucosal resection (EMR) was performed in 8 patients, and the results were EGC in 4 patients, adenoma in 3 patients, gastritis in 1 patient. In the second or third biopsies of 20 patients, gastric cancer was confirmed in 5 patients (40%), and surgery (n = 7) and EMR (n = 1) was done. In 8 patients with no evidence of cancer in at least 2 repeated biopsies, surgery was performed, and the results were gastric cancer in 6 patients, MALT lymphoma in 1 patient, no residual cancer in 1 patient. In summary, the final results of 30 patients were early gastric cancer in 17 patients (56.7%), MALT lymphoma in 1 patient, adenoma with high grade dysplasia in 5 patients, no evidence of residual cancer in 2 patients, and unconfirmed in 5 patients (follow up loss in 4 patients, and waiting for 4th biopsy in 1 patient).

Conclusions: When patients are referred with biopsy-proven gastric cancer, one negative result on the re-biopsy is not enough to exclude malignancy. In a majority of patients with this discrepancy, the final diagnosis is early gastric cancer. Endoscopic mucosal resection can be a good option for both diagnostic and therapeutic purpose.

The Prevalence of Peptic Ulcer Disease and Helicobacter Pylori Infection in Sickle Cell Disease Patients

Adewunike O. Laiyemo, M.D., Samuyika Chava, M.D., Duane T. Smoot, M.D.* Medicine, Howard University Hospital, Washington, DC.

Purpose: There have been case reports suggesting Helicobacter pylori infection, and peptic ulcer disease as causes of abdominal pain in sickle cell disease patients. The common practice is to treat sickle cell patients with narcotics and hydration and endoscopic evaluation is seldom performed. Our aim was to determine the prevalence of peptic ulcer disease and helicobacter pylori infection in patients with sickle cell trait, and sickle cell disease as compared to those without the genetic abnormality.

Methods: We conducted a retrospective case controlled study of African American patients with sickle cell disease and sickle cell trait who had upper endoscopy, and compared them to age and sex matched African American controls.

Results: Fifty-one patients were identified. There were 16 (26.2%), 7 (11.5%), and 38 (62.3%) patients with genotype AS (trait), SC and SS, respectively. Fifty-nine patients (96.7%) were in-patients at the time of the upper endoscopy with 30 of the patients (50.8%) being hospitalized for vaso-occlusive crises. Fifty-six patients (91.8%) were born in the USA. The procedure was generally performed after pancreatitis, and gall bladder disease had been excluded. In fact, 18 patients (29.5%) already had had a cholescctomy. There was no significant difference in endoscopic findings between sickle cell patients and controls, with normal endoscopy found in 21.3% vs 9.8% (p < 0.05). Peptic ulcer disease was found in 19.7% vs 16.4% (p = 0.29). H. pylori infection was found in 30.6% vs 20% (p = 0.11) when all the sickle cell patients (including traits) were considered, and 32% vs 20% (p = 0.105) in patients with sickle cell disease (SS and SC genotype only) as compared to the controls.

Conclusions: Our study did not show any significant difference in the prevalence of H. pylori infection, nor in the occurrence of peptic ulcer disease between sickle cell disease patients and African American controls. We advocate evaluating sickle cell disease patients with abdominal pain as one would for any patient without the genetic abnormality, including endoscopic evaluation, rather than the common practice which is to administer narcotics and hydrate patients with sickle cell disease who present with abdominal pain with the assumption that the etiology is probably just due to sickle cell abdominal crises.

Is Gallbladder Ultrasound Necessary in Patients Undergoing Laparoscopic Roux-en-Y Gastric Bypass?

Gintaras Antanavicius, M.D., Cornelia Savopoulou-Kralios, M.D., Daniel J. Gagne, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

Purpose: We reviewed our patients with biliary disease undergoing laparoscopic Roux-en-Y gastric bypass (RYGBP).

Methods: From 7/1999–10/2004, 647 patients underwent RYGGBP in our institution and preoperative ultrasound (US) was available in 557. Preoperative US were routinely obtained early in our series and selectively thereafter, in patients with symptoms suspicious for biliary disease. Cholecystectomy was at the time of RYGGBP was performed in symptomatic patients with positive US.

Results: 137 of 557 patients who had cholecystectomy prior to RYGGBP. Ninety-seven of the remaining 424 patients had preoperative US. Thirty-five US patients had undergone biliary exploration. Of these patients, 324/424 (76%) underwent cholecystectomy during exploration; 9/324 (2.8%) underwent sphincterotomy or common bile duct exploration. Our study did not show any significant difference in the prevalence of H. pylori infection, nor in the occurrence of peptic ulcer disease.

Conclusions: Omission of preoperative US is associated with an acceptable rate of postoperative biliary disease, which can be treated laparoscopically safely.
Endocrine Cell Carcinoma of the Stomach

Young Sik Chung, M.D., Kanji Nishiguchi, M.D., Nobuhiko Tanigawa, M.D.*, Yuko Takahashi, M.D., Kazuhiro Sumiyoshi, M.D. General and Gastrointestinal Surgery, Hokusetsu General Hospital, 16–23 Kitayamagawa-cho Takatsuki-City, Osaka, Japan; General and Gastrointestinal Surgery, Osaka Medical College, 2–7 Daigaku-cho Takatsuki-City, Osaka, Japan and Pathology, Osaka Medical College, 2–7 Daigaku-cho Takatsuki-City, Osaka, Japan.

Purpose: Endocrine cell carcinoma of the stomach has been reported rarely in the literature. A series of two such cases is described in this article.

Methods: Clinical and pathologic data were recorded and the literature was reviewed.

Results: One case was a 53-year-old male who had a type 2 like mass (Japanese classification) in the lesser curvature of the body of the stomach, as viewed by enhanced-magnification endoscopy with acetic acid, which has not been investigated thoroughly. Using this technology, this study investigated the presence of the gastric surface pattern of neoplastic and surrounding non-neoplastic mucosa.

Surface patterns of gastric tumors and the surrounding mucosa were classified into 5 types: type I, small round pits of uniform size and shape; type II, slit-like pits; type III, gyrus and villous patterns; type IV, irregular arrangement and size of types I, II and III; type V, destructive pattern of types I, II and III. The predominant pattern of the surrounding mucosa was type III, and most type III mucosa had characteristics of intestinal metaplasia. Although all elevated adenomas showed type II or type III surface patterns, both depressed adenomas showed type IV. Elevated carcinomas showed type III (42.9%), or type IV (57.1%) surface patterns; while depressed carcinomas showed type IV (70%) or type V (30%). Although differentiated tubular adenocarcinomas showed type III (10.3%), type IV (86.2%) or type V (3.5%) surface patterns, all of the signet-ring cell carcinomas and poorly-differentiated tubular adenocarcinoma showed type V.

Conclusions: Enhanced-magnification endoscopy may be useful for identifying gastric tumors and determining the extent of horizontal spread, especially in tumors of the depressed type.
Role of Endoscopic Ultrasound in the Evaluation of Gastric Fold Thickening Identified on Abdominal CT Scan

Brian P. Bosworth, M.D., Felice Schnoll-Sussman, M.D.,* Mark B. Puchglin, M.D. Gastroenterology and Hepatology, New York Presbyterian Hospital; Weill Cornell Center, New York, NY and Jay Monahan Center for Gastrointestinal Health, Weill Medical College of Cornell University, New York, NY.

Purpose: With the increasing number of abdominal CT scans performed for various reasons, more incidental abnormal findings, such as esophageal or gastric wall thickening, are evident. A standard upper endoscopy is frequently performed to evaluate the abnormalities. However, endoscopic ultrasonography (EUS) is a diagnostic modality that can better clarify these reported lesions.

Methods: We retrospectively reviewed all the gastric or gastroesophageal junction EUS examinations performed from January 2000 to August 2004 and identified those whose primary indication was an abnormal gastric wall or gastroesophageal wall thickening on CT scan. All biopsy and fine needle aspiration (FNA) specimens from these procedures were also reviewed and correlated with operative histopathology.

Results: Of the 82 gastric or gastroesophageal junction EUS examinations performed at our institution during the study period, 13 were prompted by an abnormal CT scan. EUS studies were completely normal in 46.1% (6/13) of cases, with no biopsy deemed necessary. Of the remaining 7 patients, 71.4% (5/7) had an abnormal thickening of 1 or multiple gastroesophageal wall layers, but FNA or well-biopsy revealed only chronic inflammation or reactive gastropathy. There were 2 patients with positive histopathology: the first had a well defined mass arising from the 4th gastric layer (muscularis propria) and had a c-kit positive gastrointestinal stromal tumor confirmed at surgical resection; the second had a mass extrinsic to the stomach but pressing on the gastric wall with FNA positive for neuroendocrine tumor. In both cases of malignancy, a pre-EUS upper endoscopy revealed only a slight bulge in the body of the stomach and prominent antral folds respectively.

Conclusions: Endoscopic ultrasonography with fine needle aspiration is an effective modality to evaluate abnormal gastric and gastroesophageal thickening incidentally identified on abdominal CT scan, and standard upper endoscopy may not be sufficiently sensitive to determine which patients have an underlying malignancy.

The Dopamine-3 Receptor and Gastric Motility

Purna C. Kashyap, M.D., Maria-Adelade Micci, Ph.D., Pankaj Jay Pusrricha, M.D.* Internal Medicine, University of Texas Medical Branch, Galveston, TX.

Purpose: Dopamine (DA) is a neurotransmitter present in large amounts in the gut. According to current concepts, DA inhibits acetylcholine release and gastrointestinal (GI) motility via neuronal D2 receptors (D2R). However, antagonists of this receptor have proven only partially useful in the relief of symptoms associated with various GI motility disorders. We hypothesized that other newly discovered dopamine receptors such as D3 (D3R) may also participate in dopaminergic control of gastric motility. The aim of this study was to investigate the effect of selective activation of the D3R on gastric motility in the rat.

Methods: Adult male Sprague-Dawley rats were used in the study. D3R expression was measured in rat pylorus protein extracts using a commercially available antibody (Zymed Lab, San Francisco, CA). The pyloric function was assessed by measuring the relaxation of pyloric strips in an organ bath in response to electrical field stimulation (EFS) in the presence of varying concentrations of D3R agonist (0.1, 1 and 10 mM). Gastric emptying was assessed by the phenol red method 20 minutes after feeding a non-nutrient methylcellulose meal to rats treated with varying doses of a selective D3R agonist (PD 128907 hydrochloride, 0.2, 0.5 or 1 mg/kg i.p.) or vehicle (PBS).

Results: Western blot analysis showed that the D3R is expressed in the rat pylorus. The D3R agonist significantly reduced EFS-induced relaxation of pyloric strips in an organ bath (P = 0.011 by two-way ANOVA). This effect was dose dependent, showing a greater decrease in relaxation with increasing doses of D3R agonist (1 μM vs control, P < 0.05; 10 μM vs control, P = 0.001). Gastric emptying was significantly delayed in rats injected with the D3R agonist in a dose-dependent fashion as compared to vehicle (see figure). [figure1]

Conclusions: Our data show for the first time that activation of D3R impairs pyloric relaxation and delays gastric emptying in the rat. These findings suggest a novel potential target for new pharmacological treatments for disorders of motility such as gastroparesis.

Prolonged Exposure to H. pylori (Hp) in Developing Countries: Is There an Increased Risk of Infection?

Mae F. Go,* Holly Clark, Bona Bona Shell Christison, Stephanie Hatton-Ward, Amnon Sonnenberg. Medicine / Gastroenterology, VA SLC Health Care System, Salt Lake City, UT and Medicine / Gastroenterology, Portland VA Medical Center, Portland, OR.

Purpose: It has been speculated that prolonged exposure to Hp infection increases risk for infection, especially in developing countries with a high prevalence of the infection.
We asked whether Hp seropositivity was more frequent among young men from the Church of Latter Day Saints who had recently returned from two-year missions in developing countries compared with the seropositivity among missionaries to areas in the US and developed countries.

**Methods:** 456 subjects were recruited into the study: 149 who served in developing countries, 177 who served in the US or developed countries; 130 male subjects who had not yet done their mission served as controls. Age range was 19–27 years of age. Women were excluded because of a variable duration of their missionary service, which may have confounded the analyses. Hp QuickVue test was used to determine presence of Hp antibodies in serum. Each subject completed the validated GSRS questionnaire on GI symptoms. Statistical analyses included chi-square tests for comparison of categorical variables, t-tests and ANOVA for comparison of continuous variables, and multivariate logistic regression for overall prediction of Hp seropositivity. The study was approved by the University of Utah IRB Committee.

**Results:** Hp antibodies were detected in 5.4% (95% CI, 3.9–11.9%) of missionaries to developing countries, 7.9% (95% CI, 3.9–11.9%) of missionaries to developed countries, and 8.5% (95% CI, 3.7–13.2%) of those prior to their missions. The average birth order was later among subjects who tested positive vs. those who tested negative for Hp antibodies: 3.9 vs. 3.0, p = 0.01. Subjects who served in developing countries had higher GSRS scores (more severe symptoms) than missionaries who had served in a developed country or those who had not yet completed a mission: 22.9 vs. 21.8 and 19.8, respectively. F-ratio = 15.2437, p < 0.0001. In a multivariate logistic regression analysis, only birth order was a significant predictive factor for a positive Hp test.

**Conclusions:** The similar rates of Hp seropositivity in the three groups suggests that risk of Hp infection in young healthy adults is low even after prolonged exposure in developing countries with high frequencies of Hp infection. Our study detected an increased likelihood of Hp infection in children of later birth order while family size was not a predictor of Hp seropositivity.

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**Low Prevalence of H. pylori Associated Gastric Carcinoma in a Community Based Population; a 15 Year Review**

Douglas J. Sprung, M.D., F.A.C.G., Gregory M. Sprung.* Medicine, Gastroenterology Group, Maithland, FL.

**Purpose:** To examine the prevalence of H. Pylori (HP) in gastric carcinoma (GC) in our community practice.

**Methods:** We retrospectively reviewed 49 patients found to have a diagnosis of GC between 1/90–12/04 in our private practice in Orlando, FL. All tumors were contained within the stomach, without extension into the esophagus. Endoscopic biopsies and surgical pathology specimens were examined for HP presence.

**Results:** Of 49 patients with GC, 6/49 (12%) were HP positive. 50% were female, 50% male, mean age 63 years. 74% were causacian, 76% (37/49) had adenocarcinoma, (13/37) were signet ring type), 16% (8/49) had lymphoma, and one person each had sarcoma, malignant carcinoid, melanoma and leiomyosarcoma. 39% were located in the cardia, 20% in the body of the stomach and 41% in the antrum. Mean size of GC was 5 cm, the median was 3 cm. The most common clinical signs and symptoms were epigastric pain, anemia, weight loss and heartburn.

**Conclusions:** 1. Only 12% of patients had demonstrable HP at the time of endoscopic diagnosis of GC or surgical resection. 2. The prevalence of GC was almost twice as high between 1990–1995, as it was between 1995–2005. 3. Country of origin (for those born outside the United States) did not predict HP presence. 4. Further community studies in the United States would help to assess the distribution of HP related GC geographically, enabling us to compare prevalence data with other countries and within our own diverse country.

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**An Unusual Case of Gastric Cryptococcosis Presenting as Ulcerations in an AIDS Patient**

Marie L. Borum, M.D., Ed.D., M.P.H.,* M. Aamir Ali, M.D., Christopher Cirino, D.O., David Parenti, M.D. Division of Gastroenterology, Dept of Medicine, George Washington University, Washington, DC and Division of Infectious Diseases, Department of Medicine, George Washington University, Washington, DC.

**Purpose:** Cryptococcus neoformans is the most common systemic mycosis in AIDS. While this organism is known to cause disseminated disease, gastric involvement has rarely been reported. There presently are only 4 published cases of gastric cryptococcosis. We report the first case of gastric cryptococcosis presenting as ulcerations in an AIDS patient.

**Case:** The patient is a 36 year old man with a history of AIDS (CD4 count 34) who was referred for evaluation of a 2 week history of progressive nausea, vomiting and an inability to maintain oral intake. He also reported several days of odyophagia and diarrhea. Past medical history was significant for a diagnosis of HIV one year prior to admission following a 40 pound unintentional weight loss. He had no prior opportunistic infections. The patient’s medications included antiretroviral therapy and prophylactic Bactrim and Zithromax. The examination was significant for a temperature of 38.8°C, scant oral thrush, mild abdominal distention and guaiac negative stool.

While hospitalized the patient developed right arm and leg paresthesias and weakness. Blood cultures, stool cultures and a lumbar puncture were performed. A head CT was negative. An abdominal CT revealed colonic dilatation. An EGD demonstrated diffuse esophageal and gastric erythema with multiple, irregular nonbleeding ulcerations. Biopsies demonstrated Cryptococcus neoformans. Blood, stool and CSF cultures were also positive for Cryptococcus neoformans. The patient was treated with intravenous amphotericin B with rapid resolution of the gastrointestinal and neurologic symptoms.

**Conclusion:** Cryptococcal infections most commonly cause pulmonary or CNS disease. In severely immunocompromised patients, Cryptococcus neoformans can become disseminated. However, gastric involvement has rarely been reported antemortem and the endoscopic description has been variable. This is the first case of gastric cryptococcosis presenting as ulcerations. It is important to recognize this gastric manifestation of cryptococcosis in effort to increase our understanding of the disease and enhance our management of infected patients.

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**Lactobacillus reuteri Tablets Can Suppress Helicobacter pylori Infection: A Double-Blind, Randomised, Placebo-Controlled Cross-Over Clinical Study**

Kyoto Imase, Akitumi Tanaka, Kengo Tokunaga, Hajime Sugano, Shin’ichi Takahashi.* Third Department of Internal Medicine, Kyorin University School of Medicine, Tokyo, Japan.

**Purpose:** The aim was to investigate the effect of Lactobacillus reuteri strain SD2112 Tablets (Reuterina®), in suppressing on H. pylori urease activity and to use the urea breath test (UBT) as a marker for burden of infection.

**Methods:** Assessment of UBT and H. pylori density, 33 H. pylori-positive patients were obtained gastric biopsy specimens by upper gastrointestinal endoscopy. The correlation between UBT and H. pylori density was investigated. The individual UBT values were established for each patient. The patients were divided into three groups according to H. pylori density: Group I (low density group), Group II (moderate density group), and Group III (high density group). The individual UBT values were then correlated to the established H. pylori quantity.

**Method:** 2 Assessment of suppressive effect of L. reuteri on H. pylori urease activity asymptomatic 40 volunteers with an UBT value higher than 15%
were randomly allocated to four groups, as follows. Subjects in Group A received active treatment for 4 weeks (period 1) and placebo treatment for the following 4 weeks (period 2), in Group B received the study treatment in the reverse order. In Group C received placebo and in Group D consisted of volunteers that had a negative UBT received active treatment, for the full 8 weeks.

**Results:**
1. UBT values were 11.6 ± 2.0%, 22.1 ± 2.6% and 35.4 ± 7.6% in Groups I, II and III, respectively, showing the UBT value to increase significantly (I vs. II: \(p < 0.01\) and I vs. III: \(p < 0.05\)) according to *H. pylori* density.

2. There were significant differences in the decrease in UBT value before versus after medication in Group A and Group B. Moreover, in Group A, lower UBT value was maintained until the end of the full 8-week period. The overall rate of decrease in the UBT value due to medication with *L. reuteri* Tablets was 69.7 ± 4.0% (\(p < 0.05\)).

**Conclusions:** Administration of *L. reuteri* Tablets significantly decreased UBT values in *H. pylori*-positive subjects, demonstrating that *L. reuteri* suppresses *H. pylori* urease activity and *H. pylori* density.

### 99 Central Neuronal Mechanisms of Implantable Gastric Electrical Stimulation Therapy for Obesity

**Jing Zhang, M.D., Ming Tang, M.D., Xiangrong Sun, M.D., Jiande Chen, Ph.D.** Physiology, Qingdao University Medical College, Qingdao, China and Internal Medicine, University of Texas Medical Branch, Galveston, TX.

**Purpose:** Implantable gastric stimulation (IGS) has been shown to reduce appetite, increase satiety and induce weight loss in obese patients. However, possible central mechanisms of hypothalamus involved with the IGS treatment of obesity are still unclear.

**Aim:** The purpose of this study was to investigate the effects of IGS with different parameters on the neuronal activity of gastric related neurons in the PVN and VMH.

**Methods:** Electrophysiological potentials of single neurons in the PVN and VMH were recorded in 58, 52 anesthetized rats, respectively. Gastric distension (GD) was produced by air inflation of a latex balloon surgically placed in the stomach to identify as GD- excitatory (GD-E) neurons or GD-inhibitory (GD-I) neurons. One pair of platinum electrodes (0.3 cm apart) was sutured onto the serosal surface of the lesser curvature of the stomach. IGS with four sets of parameters was applied for one minute on GD-Responsive (GD-R, both GD-E and GD-I) neurons: IGS-A (the parameters currently used in clinical trials for the treatment of obesity): 6 mA, 0.3 ms, 40 Hz, 2s-on, 3s-off; IGS-B: same as IGS-A but decreased train on-time of 0.1s; IGS-C: same as IGS-A but increased pulse width; IGS-D: same as IGS-A but decreased pulse frequency of 20 Hz.

**Results:**
1. Of 115 PVN and 96 VMH neurons tested by GD, 104 and 82 neurons were responsive to GD, respectively. (2) Among these GD-responsive neurons 79%, 63.2%, 91.4% and 69.8% of them in the PVN and 55.0%, 17.6%, 77.8%, and 14.3% of them in the VMH were activated by IGS-A, B, C and D respectively. (3) In the PVN, neuronal activity was affected more frequently with IGS-C than IGS-B (\(P < 0.001\)) or IGS-D (\(P < 0.01\)); however, no significant difference was noted between IGS-C and IGS-A; IGS-A was significantly more effective than IGS-B (\(P < 0.05\)). In the VMH, more GD-E neurons were excited by IGS-C (\(P < 0.001\), vs. IGS-B; \(P = 0.02, vs. IGS-D\)) and by IGS-A (\(P = 0.002, vs. IGS-B; P = 0.016 vs. IGS-D\)); in addition, 63.6%, 73.3%, 37.9% and 51.8% of GD-I neurons were excited by IGS-A, B, C, D respectively (\(P < 0.05\), IGS-B vs. IGS-A/IGS-C).

**Conclusions:** IGS with appropriate parameters can activate gastric-related neurons in both PVN and VMH and the effect seems related to stimulation strength (pulse frequency, pulse width as well pulse train on-time). The activation of neurons in the hypothalamus of the PVN and the VMH indicates the central mechanism of IGS in the treatment of obesity.

### 100 Extended Octreotide Suppression Test To Determine Hormone Responsiveness in a Patient with Multiple Gastric Carcinoid Tumors

**Mohammad Fayyaz, M.D., Shahid Mehboob, M.D., Valerie Andersen, Michael D. Sitrin, M.D.*** Division of Gastroenterology, State University of New York at Buffalo, Buffalo, NY.

**Purpose:** Type 1 gastric carcinoid tumors arise from enterochromaffin-like (ECL) cells of gastric fundus under the trophic effect of hypergastrinemia. Histidine decarboxylase (HDC), the enzyme responsible for histamine production in these cells, is regulated by gastrin. Lesions less than 1 cm and fewer than 3 – 5 in number are typically managed by endoscopic resection. Management of tumors that are larger than 1 cm or more than 5 in number is controversial. Antrectomy has been reported to result in complete regression of tumors. However, in some cases the tumors may become autonomous and no longer gastrin dependent. This has led some authorities to recommend total gastrectomy for tumors that are large or multiple.

**Methods:** A 62 year old asymptomatic male referred for mild anemia, was found to have at least 12 gastric carcinoids 3–10 mm in size in the setting of chronic atrophic gastritis. Biopsies of the intervening mucosa revealed microcarcinoidiosis. There was no evidence of local extension or metastasis. We decided to do an extended octreotide suppression test to determine if the tumors are still gastrin dependent and would likely regress after antrectomy. The patient was started on octreotide infusion at 12.5–25 mcg/hr for 86 hours after obtaining an informed consent and then started on octreotide depot injections every 4 weeks for five months. Serum fasting gastrin levels and chromogranin A (CGA) levels were measured and an endoscopy with biopsies was performed immediately before and after the infusion and at five months. RNA was extracted from the biopsy specimens and comparative quantitation of HDC mRNA was performed using real-time PCR with FAM-labeled LUX primers after generation of cDNA.

**Results:** Serum fasting gastrin levels decreased from 306 pg/ml pre-treatment to 31 pg/ml at the end of infusion and 112 pg/ml at 5 months. CGA levels decreased from 4–6 times the upper limit of normal to within the normal range at the end of infusion and stayed normal at 5 months. Tissue HDC mRNA decreased 54 fold at the end of infusion and decreased further at five months. There was a decrease in size and number of tumors at five months.

**Conclusions:** Long term octreotide treatment resulted in effective suppression of serum gastrin, serum CGA, and tissue HDC mRNA associated with partial tumor regression. These results demonstrate that the carcinoid tumors in this patient are still gastrin dependent and expected to regress after antrectomy.

### 101 Pantoprazole QD Is Superior to BID Ranitidine in Control of Nighttime and Daytime Heartburn Symptoms in GERD Patients: A Sub-Analysis from 2 One-Year Maintenance Studies

**Gail M. Comer, M.D.,* David C. Metz, M.D., Brian Field, M.S., Richard Lynn, M.D.** Clinical Research, Wyeth Pharmaceuticals, Collegeville, PA and University of Pennsylvania Medical Center, Philadelphia, PA.

**Purpose:** The results of two well controlled 12-month, randomized, multicenter trials comparing pantoprazole (PAN) 40mg QD to ranitidine (RAN) 150mg BID for maintenance of healing in patients with healed erosive esophagitis (EE), reported that >90% of nights and days were heartburn free in patients receiving PAN (1, 2). The results were reported as mean symptom-free days. A sub-analysis was performed to determine the percentage of patients heartburn free (nighttime or daytime) for 70, 80 and 90% of days.

**Methods:** Patients with healed EE received 12 months of therapy. Patients recorded heartburn episodes using daily diary cards. Patients without heartburn for at least 70%, 80% or 90% of the nights or days were compared among treatment groups by Fisher’s exact test.
Results: A total of 351 patients were included in this sub-analysis (Study 1: PAN (n = 82); RAN (n = 83); Study 2: PAN (n = 93); RAN (n = 93). The results are shown in Table 1.

Percentage of Patients Heartburn Free Over 12 Months

<table>
<thead>
<tr>
<th>Period (Study)</th>
<th>70% of Days PAN</th>
<th>80% of Days PAN</th>
<th>90% of Days PAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nighttime (Study 1)</td>
<td>93.9%</td>
<td>91.5%</td>
<td>79.3%</td>
</tr>
<tr>
<td>Nighttime (Study 2)</td>
<td>89.2%</td>
<td>87.1%</td>
<td>71.0%</td>
</tr>
<tr>
<td>Daytime (Study 1)</td>
<td>93.9%</td>
<td>92.7%</td>
<td>85.4%</td>
</tr>
<tr>
<td>Daytime (Study 2)</td>
<td>91.4%</td>
<td>87.1%</td>
<td>69.9%</td>
</tr>
</tbody>
</table>

Conclusions: PAN 40 mg QD controlled nighttime and daytime heartburn in patients with healed EE. Approximately 90% of patients treated with PAN 40 mg QD were free of nighttime and daytime heartburn for at least 70% of the time and about 75% were symptom free 90% of the time. For each degree of symptom control, PAN 40 mg QD was superior to RAN 150 mg BID.

1. Metz, APT 17:155, 2003
2. Richter, APT 20:567, 2004

The Efficacy and Tolerability of Rifaximin, Doxycycline and Lansoprazole in the Treatment of H. Pylori Gastritis: An Open Label Pilot Study

Raouf E. Hilal, M.D., Talal Hilal, M.D. Gastroenterology, Center for Advanced Gastroenterology, Orlando, FL.

Purpose: Given the recent availability of newer antibiotic therapy such as rifaximin (Xifaxan) with its in-vitro activity against H. Pylori and an excellent side effect profile, this pilot study examined the efficacy and side effect profile of a novel drug combination using rifaximin, doxycycline and lansoprazole in the treatment of H. Pylori.

Methods: Twenty-five patients who present for evaluation of upper GI symptoms and undergo an EGD with biopsy confirmed H. Pylori gastritis will be recruited for the study. By open label design and intention to treat, all patients will be treated with lansoprazole 30 mg BID, doxycycline 100 mg BID and rifaximin 400 mg TID for a 14-day course regimen. Patients that complete the treatment regimen will then get a follow-up Urea Breath Test (UBT) at 4 weeks post treatment to document eradication. Patients will be also be monitored for side effects and adverse reactions.

Results: Preliminary results of the initial 5 patients that completed the treatment regimen and had a follow-up UBT show an H. Pylori eradication rate of 70% when using rifaximin, doxycycline and lansoprazole for 14 days. Side effects of treatment were minimal and none of the patients stopped the treatment.

Conclusions: Rifaximin, doxycycline and lansoprazole treatment regimen for H. Pylori appears to be tolerable but so far show a low eradication rate against H. Pylori. Further studies are needed to establish the efficacy and optimal dosage of rifaximin in the treatment of H. Pylori.

Is the Medical Management of Patients with Suspected Acute Upper Gastrointestinal Hemorrhage Influenced by the Assessment of the Nasogastric Aspirate?

Andres J. Rivero, M.D., Steven Sivak, M.D., Gilberto Torres, M.D., Sadia Benzaken, M.D., Carolina L. Ramirez, M.D. Medicine, Albert Einstein Medical Center, Philadelphia, PA.

Purpose: Evaluate the information gained by assessment of the appearance of the nasogastric aspirate and determine if this influenced the management of patients with suspected active upper gastrointestinal bleeding.

Methods: 178 patients, clinically thought to have acute upper gastrointestinal tract bleeding (defined as the presence of hematemesis or melena) were recruited at presentation at Albert Einstein Medical Center, Philadelphia, PA. A nasogastric aspirate was obtained and described. Subsequently, each patient underwent esophagogastroduodenoscopy by a fellow under the supervision of attending physicians.

Association Between Undergoing Nasogastric Aspiration and the Need for Transfusions

<table>
<thead>
<tr>
<th>Transfused</th>
<th>No Transfused</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Gastric Aspirate</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>Negative Gastric Aspirate</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>61</td>
</tr>
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</table>

Chi2 = 2.32 P = 0.12

Results: A statistically significant correlation was found between the physician’s assessment of the presence of acute upper gastrointestinal bleeding based on the appearance of the nasogastric aspirate and the endoscopic findings. The sensitivity and specificity of the physician assessment of the nasogastric aspirate for the presence of upper gastrointestinal tract bleeding were 53% and 65%, respectively. The PPV was 60%, and the NPV 58%; the positive likelihood ratio was 1.51 while the negative likelihood ratio was 0.72. Although, there was a correlation between the presence of blood in a nasogastric aspirate and need for pharmacologic treatment; a relationship between a positive aspirate and the facts of being admitted, transfused or undergoing colonoscopy could not be established.

Association Between Undergoing Nasogastric Aspiration and Treatment Wit Proton Pump Inhibitor

<table>
<thead>
<tr>
<th>Proton pump inhibitor</th>
<th>No Proton pump inhibitor</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Gastric Aspirate</td>
<td>34</td>
<td>44</td>
</tr>
<tr>
<td>Negative Gastric Aspirate</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>63</td>
</tr>
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</table>

Chi2 = 0.72 P = 0.39

Conclusions: These results suggest that a nasogastric aspirate is not sufficient to accurately predict active bleeding and does not seem to change some aspects of their hospital course or medical management.

Effects of Esomeprazole on Acid Output in Patients with Zollinger-Ellison Syndrome (ZES) and Idiopathic Gastric Acid Hypersecretion (IGH): 6-Month Results

Joseph R. Piseuga, M.D., Mark B. Sostek, M.D., EA. C.G., Philippe Ruszniewski, M.D., Christopher E. Forsmark, M.D., M.A., C.G., John Monyak, Ph.D., David C. Metz, M.D.* David Geffen School of Medicine, UCLA, Los Angeles, CA; AstraZeneca LP, Wilmington, DE; Beaujon Hospital, Clichy, France; U of Florida, Gainesville, FL and U of Pennsylvania, Philadelphia, PA.

Purpose: To evaluate if appropriate dose titration of esomeprazole could control basal acid output (AO) in patients with documented ZES or IGH.

Methods: This ongoing, 12-month, open-label, multicenter study (D9612C00025) included 19 patients with ZES and 2 patients with IGH. Patients were changed from their prior proton pump inhibitor therapy to esomeprazole 40 mg twice daily or 80 mg twice daily. At baseline and after 7–10 days, AO was evaluated by nasogastric aspiration and pH titration. Adequate control of AO was defined as AO < 5 mmol/L and <10 mmol/L for patients who had and who had not had prior gastric-acid reducing surgery, respectively. Patients with controlled AO were maintained on the same dose, and AO was measured again at 3 and 6 months. If AO was not controlled, doses were uptitrated (to a maximum dose of 240 mg/d) until control was
attained. At any time, doses could be increased at the investigator’s discretion in patients reporting symptoms.

**Results:** Of the 15 men and 6 women (mean age, 55 years; range, 42–72 years), 3 had multiple endocrine neoplasia type 1 (MEN-1) syndrome and 8 had metastatic ZE disease. None withdrew. AO was not controlled in 2 patients at some time during the study. At 6 months, AO was adequately controlled in 14 of 15 patients who received esomeprazole 40 mg twice daily. The AO of the other 6 patients was controlled with esomeprazole 80 mg twice daily (n = 5) or 80 mg 3 times daily (n = 1).

**Acid Output (mmol/h)**

<table>
<thead>
<tr>
<th></th>
<th>Baseline visit</th>
<th>3 months</th>
<th>6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (range)</td>
<td>2.16 (0–20.30)</td>
<td>0.30 (0–2.07)</td>
<td>0.66 (0–5.93)</td>
</tr>
</tbody>
</table>

Esomeprazole was generally well tolerated at all doses. Of the 4 serious adverse events reported, 1 (hypomagnesemia) was assessed as possibly drug-related but resolved without drug cessation.

**Conclusions:** After the first 6 months in this ongoing study, maintenance esomeprazole treatment has effectively controlled AO in 95% of enrolled patients with ZES or IGH. Esomeprazole 40-mg, twice-daily is effective in 67% of these patients. These results suggest that esomeprazole is an effective medical therapy for patients with ZES. Supported by AstraZeneca LP.

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**105 Cardiac Safety and Phase I Clinical Data for ATI-7505, a Selective 5-HT4 Receptor Agonist**

**Monica Palme, Agnes Choppin, Donn Dennis,* Ian Irwin, Tonya Green, Peter Milner, Pascal Druzgala. Research and Development, ARYx Therapeutics, Fremont, CA; Pharmacology, Product Safety Labs, Dayton, OH and Gen. Surgery, Medical College of Wisconsin, Milwaukee, WI.**

**Purpose:** The clinical utility of 5-HT4 receptor agonists with gastrointestinal (GI) prokinetic activity has been limited due to cardiac effects. A GI prokinetic agent of this class that lacks these liabilities may have important application in several therapeutic areas. ATI-7505, a potent and selective 5-HT4 receptor agonist, is being developed for GERD and diabetic gastroparesis. Results from pre-clinical cardiac safety pharmacology studies, and Phase I single- and multi-dose ATI-7505 studies in healthy volunteers are reported.

**Methods:** Preclinical studies: Standard electrophysiological (EP) techniques were used to assess the cardiac effects of ATI-7505 on: a) Single cell: HEK-293 cells expressing hERG -I Kr; single guinea pig (GP) ventricular myocytes expressing native non-IKr currents (I_{Kr, early}, I_{Kr, L}, I_{Kr, K1}), b) Tissue/organ: isolated GP hearts-conduction times and ventricular repolarization; rabbit Purkinje fibers-amplitude, dV/dt, APD, RMP; and c) Anesthetized animals: rabbit methoxamine model and in vivo EP (surface ECG) studies in dog and guinea pig.

Clinical studies: Six single doses of ATI-7505 ranging from 0.3 to 60 mg were tested in a double-blind, randomized, placebo-controlled Phase I study. Six doses of ATI-7505 ranging from 3 to 50 mg were given QID in a double-blind, randomized, placebo-controlled multi-dose Phase I study.

**Results:** Cardiac findings: (1) low activity at human I_{Kr} channel (IC_{50} = 24,500 nM), particularly compared to its binding affinity to the 5-HT4 receptor (Ki = 1.4 nM); (2) negligible activity at non-IKr cardiac currents (NOEL >1000 nM), (3) negligible effect in GP hearts (NOEL = 1000 nM) and rabbit Purkinje fibers (NOEL>1000 nM), (4) safe in vivo cardiac profile: in the rabbit methoxamine model (NOEL>3 mg/kg IV; no QT effect or torsades), in anesthetized dogs (no EP effects at cumulative dose = 3.4 mg/kg IV) and GPs (NOEL = 1 mg/kg IV).

No serious adverse events and no clinically significant adverse events were seen in Phase I studies, but mild GI and non-GI events were reported. No ECG changes were seen. PK parameters for both ATI-7505 and its primary metabolite are reported.

**Conclusions:** ATI-7505 was safe and well tolerated in Phase I human clinical trials. No serious adverse events occurred and intensive cardiac monitoring using ambulatory Holter recordings has demonstrated no significant cardiac effects. ATI-7505 is being further investigated in pharmacodynamic and Phase II efficacy studies for treatment of various GI disorders.

**106 Effect of ATI-7505, a Selective 5-HT4 Receptor Agonist, on Gastric Emptying**

**Agnes Choppin, Monica Palme,* Mary Otterson, Donn Dennis, Henry Jacoby, Pascal Druzgala, Pharmacology, ARYx Therapeutics, Fremont, CA; Pharmacology, Product Safety Labs, Dayton, OH and Gen. Surgery, Medical College of Wisconsin, Milwaukee, WI.**

**Purpose:** ATI-7505, a highly potent 5-HT4 receptor agonist, is being developed to treat diabetic gastroparesis and GERD. Preclinical studies and Phase 1 human trials indicate that ATI-7505 has a safe cardiac profile. ATI-7505 (IV) was previously found to increase upper gut motility in fasting dogs. We tested whether ATI-7505 accelerates gastric emptying in fed normal dogs, and fasting normal and diabetic rats.

**Methods:** Dog Model: In 6 fasting dogs with strain gauge transducers located on the upper gut, after completion of a migrating motor contraction (MMC), test drugs (vehicle, ATI-7505, cisapride) were given IV over 20 mins, then the dogs were fed a solid meal. Dogs with control MMC values <25% of before and after drug (5/6 dogs) were used in the analysis. The MMC return time was used as an index of gastric emptying.

**Rat Model:** Hyperglycemia was induced with streptozotocin (STZ, IV). After IP injection of the test drugs (5 rats/grp), 10 glass beads (1 mm diam), were inserted in the stomach. After 15 min (norm) or 30 min (STZ), the rats were euthanized and the number of remaining gastric beads was counted.

**Results:** Dog Model: ATI-7505 (0.05 mg/kg) significantly shortened the time of MMC return, indicating acceleration of gastric emptying and was more potent than cisapride.

**Rat Model:** In both normal and hyperglycemic rats, ATI-7505 was more potent than cisapride at accelerating gastric emptying. A dose of 0.01 mg/kg IP ATI-7505 was optimal to enhance gastrokinesis.
Conclusions: ATI-7505 improves gastrokinetic function in normal fed dogs, and fasting normal and diabetic rats, and warrants further clinical investigation.

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Intragastric Acid Control with Oral Esomeprazole or Pantoprazole after Intravenous Pantoprazole Administration in Healthy Adults
Philip B. Miner, Jr., M.D., F.A.C.G., Radu Tutuian, M.D., Donald O. Castell, M.D., M.A.C.G., Sherry Liu, Ph.D., Mark Sostek, M.D., F.A.C.G.*
Oklahoma Foundation for Digestive Research, Oklahoma City, OK; Division of Gastroenterology-Hepatology, Medical University of South Carolina, Charleston, SC and AstraZeneca LP, Wilmington, DE.

Purpose: After a prescribed course of intravenous proton pump inhibitor therapy, patients may require continued oral antisecretory therapy. The objective of this study was to compare intragastric acid control with oral esomeprazole 40 mg once daily with that of oral pantoprazole 40 mg once daily after 5 days of intravenous pantoprazole 40 mg once daily.

Methods: In this randomized, open-label, comparative, 2-way crossover study (D9612L00066), healthy adults were randomized to 1 of 2 dosing sequences. Each 10-day dosing period included 5 days of daily injections over 2 minutes of intravenous pantoprazole followed by 5 days of once-daily oral doses of esomeprazole 40 mg or pantoprazole 40 mg. There was a 10–21-day washout period between dosing periods. All doses were administered, under observation at the investigator’s site, 30 minutes before breakfast. Non–high-fat, non–high-calorie meals were provided to study subjects. On days 1 and 5 of oral dosing (before receiving the daily dose), a calibrated electrode was positioned 10 cm below the lower esophageal sphincter for 24-hour pH monitoring. The pH technicians and readers were blinded to subject treatment sequence. Only data from patients who had evaluable tracings from both day-5 tests were included.

Results: All 38 subjects with evaluable data were H. pylori-negative and white, 63% were men, and the mean age was 25 years (range, 19 to 57 years). The mean number of evaluable hours of pH data for both treatment sequences was 24.

Conclusions: There was no difference between the 2 treatment groups regarding the primary end point of intragastric acid control with oral esomeprazole or pantoprazole.

Leslie W. Calvert, M.D., M.P.H., Susan Roh, Ph.D., Scott Halpern, M.D., F.A.C.G., Barry Derose, M.D., M.P.H., Board of Directors of the American College of Gastroenterology, Chicago, IL and AstraZeneca LP, Wilmington, DE.

Purpose: In NSAID users, two strategies, PPI co-therapy or coxibs, are associated with reducing clinically significant upper GI events. Many osteoarthritis (OA) patients taking NSAIDs require low-dose aspirin (ASA) for cardiovascular prophylaxis. However, ASA use with nonselective (ns) NSAIDs or coxibs further increases risks of GI events. No prospective study has compared GI risks of coxibs alone compared to ns-ASA + PPI in patients taking low-dose ASA. This study compared the 12-wk GD ulcer rates among subjects taking low-dose ASA with either the combination of lansoprazole 30mg QD and naproxen 500mg BID (LAN+NAP) or celecoxib 200mg QD (CEL).

Methods: 1045 OA subjects requiring chronic NSAIDs and daily ASA (81 mg or 325 mg QD) were enrolled in a randomized, prospective, double-blind, active-control study. H pylori negative subjects with <10 GD erosions at baseline endoscopy, no prior history of ulcer or GI bleed within the past year, and using stable NSAID doses prior to screening were randomized to LAN+NAP or CEL in addition to open-label ASA. 1014 met admission criteria and received ≥1 dose of study drug; 854 completed the end of study endoscopy (35 endoscoped for cause prior; 819 endoscoped as scheduled at wk 12). An ulcer was defined as a GD mucosal break ≥3 mm with depth.

Results: Baseline characteristics of the two treatment arms did not significantly differ. Results are shown in the Table. The overall proportion of subjects reporting AEs was not significantly different between the treatment groups. Among the most common AEs were diarrhea (7% vs 4%; p = 0.02) and dyspeptic signs/symptoms (7% vs 10%; p = 0.03), for LAN+NAP compared to CEL, respectively.

Gastroduodenal Ulcer Rates

<table>
<thead>
<tr>
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<th>LAN + NAP</th>
<th>CEL</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Overall*</td>
<td>8.9% (38/428)</td>
<td>9.9% (42/426)</td>
<td>0.64</td>
</tr>
<tr>
<td>ASA 81 mg</td>
<td>7.8% (30/383)</td>
<td>9.6% (36/376)</td>
<td>0.44</td>
</tr>
<tr>
<td>ASA 325 mg</td>
<td>17.8% (8/45)</td>
<td>12.0% (6/50)</td>
<td>0.56</td>
</tr>
<tr>
<td>Prior NSAID/Coxib#</td>
<td>11.0% (31/283)</td>
<td>8.2% (22/268)</td>
<td>0.31</td>
</tr>
<tr>
<td>No Prior NSAID/Coxib#</td>
<td>4.8% (7/145)</td>
<td>12.7% (20/158)</td>
<td>0.02</td>
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*p Primary endpoint; #NSAID/Coxib use at least 14 d prior to start of study drug.

Conclusions: In patients taking low-dose ASA, the two pain relief strategies, LAN + NAP and CEL have similar GD ulcer rates. However, in ASA patients who have not recently taken NSAIDS nor coxibs, LAN + NAP has significantly lower GD ulcer rates.

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Helicobacter pylori and Gastric Cancer: A Clinico-Pathological Study
Ratha-korn Vilaichone, M.D., Ph.D.*, Yarooha Mahachai, M.D., F.A.C.G., Medicine-Gastroenterology, Thammasat University Hospital, Pathumthai, Thailand and Medicine-Gastroenterology, Chulalongkorn University Hospital, Bangkok, Thailand.

Purpose: Gastric cancer is a major cause of cancer death worldwide with variable incidence and multifactorial etiologies. Helicobacter pylori (H. pylori) infection is considered to be one of the major causes of this cancer. This cross-sectional study was design to evaluate the clinico-pathological features and prevalence of H. pylori infection in gastric cancer of Thai patients.

Methods: Clinical information, endoscopic findings, histological features and H. pylori status were collected from gastric cancer patients between January 2000 and May 2002. H. pylori infection assessed by the combination of rapid urease test, histology, culture and serology. Patients were regarded as H. pylori-positive if at least one of the tests gave a positive result.

Results: Total of 59 gastric cancer patients was enrolled in this study (31 men and 28 women, mean age of 59.8 years (range 33–86 years). The common presenting symptoms were dyspepsia (71.2%) followed by weight loss (69.5%) and anorexia (42.4%). The mean duration of symptoms prior to diagnosis was 104.9 days. Overall prevalence of H. pylori infection was 83.1% and there was no different between male and female (87.1% vs. 78.6%; p > 0.05). The histological staging was not statistical significant between H. pylori positive and negative group. There was also no different between prevalence of H. pylori infection in diffuse type and intestinal type gastric
cancer (82% vs. 85%; p > 0.05). However, the prevalence of H. pylori infection was significantly higher in non-proximal gastric cancer than those with proximal gastric cancer (89% vs. 6%; p < 0.01).

**Conclusions:** H. pylori infection was commonly found in gastric cancer patients and was significantly higher in non-proximal gastric cancer than proximal gastric cancer. There was no difference of clinical symptoms, histology type and staging between H. pylori positive and H. pylori negative gastric cancer patients.

### 110 Gastrointestinal Complications of Over-the-Counter Non-Steroidal Anti-Inflammatory Drugs

J. Biskupiak, Ph.D., ∗D. Brixner, Ph.D., G. Oderda, PharmD, K. Howard, PharmD Department of Pharmacotherapy, Univ of Utah, SLC, UT and Outcomes Research, Pfizer, Inc., NYC, NY.

**Purpose:** This study assessed the risk for perforations, ulcers and bleeds (PUBs) in a US representative population using OTC dosage strengths of naproxen or ibuprofen with or without concomitant aspirin in a real world setting.

**Methods:** A retrospective review of an electronic medical record (EMR) database containing the ambulatory health record data for over 3.2 million individuals was conducted. Subjects were eligible for inclusion in the study if they received naproxen (220 mg) or ibuprofen (200 mg). An index date for each subject was defined as the first mention of an OTC NSAID in the dataset. Exclusion criteria: concomitant oral steroid usage, concomitant co-morbid conditions: infectious diseases, GI cancers, enteritis, colitis and diverticula of the intestines. The dataset was analyzed for concomitant aspirin use and PUBs. A pre-/post analysis was conducted using a case-crossover design with subjects as their own controls. The index date was the defining event, in order to determine the odds ratio associated with OTC NSAID usage. Two different pre-index time periods were evaluated for PUBs, 180 and 365 days. For the post-index time period, only PUBs that occurred within 90 days of the OTC NSAID entry in the EMR dataset were considered.

**Results:** The dataset contained 11,957 subjects on naproxen and 38,507 subjects on ibuprofen. In all cases, OTC NSAID usage was associated with a statistically significant increase in the odds ratio for PUBs.

<table>
<thead>
<tr>
<th>OTC NSAID</th>
<th>Odds Ratio (95% CI, p value)</th>
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<tr>
<td>Ibuprofen</td>
<td>2.51 (1.84 – 3.44, p &lt; 0.00001)</td>
</tr>
<tr>
<td>Naproxen</td>
<td>2.74 (1.70 – 4.41, p &lt; 0.00001)</td>
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</table>

The concomitant aspirin population consisted of 2,328 naproxen subjects and 4,843 ibuprofen subjects. In both cases, concomitant aspirin usage was associated with a significantly higher risk for PUBs than the corresponding monotherapy. Subjects taking both ibuprofen and aspirin had an odds ratio of 3.36 (2.36 – 4.80, p < 0.00001), while those on naproxen and aspirin had an odds ratio of 2.07 (1.21 – 3.49, p = 0.005) relative to those subjects on ibuprofen and naproxen monotherapy, respectively.

**Conclusions:** Even at OTC doses, ibuprofen and naproxen are associated with increased risk of serious GI events. Concomitant aspirin use can significantly increase such risk.

### 111 Molecular Study on Frequency of Single Nucleotide Polymorphism of TP53 Gene among Iranian Patients with Gastric Cancer

Ala Melatt-Rad, M.D., Minoosh Vosoughi, M.D., Shahab Akhoundi, M.D., Mahmood Jedditehrani, Ph.D., Mohammad Reza Zali, M.D., F.A.C.G., Babak Noorinayer, M.D. ∗ Research Center for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran and Monoclonal Antibody Research Center, Avesina Research Institute, Tehran, Islamic Republic of Iran.

**Purpose:** We have hypothesized that the two non-synonymous single nucleotide polymorphisms (SNPs) on exon 4 of the p53 gene may be associated with sporadic gastric cancer and also survival and prognosis of the patients.

**Methods:** One hundred cases with sporadic gastric cancer and one hundred and fifty matched healthy controls were enrolled in a case-control study adjusting for potential confounding factors of age, sex and ethnicity. We used PCR-RFLP to distinguish between the alleles at the SNPs 1042522 and 1800371 on exon 4 of the TP53 gene. Both loci were amplified by a single PCR reaction which resulted in 240 base pair (bp) amplicons. For the SNP 1042522, homozygous GG cases were digested to 100 and 140 fragments. The heterozygous cases had three bands at 240, 140 and 100 bp. For the SNP 1800371 homozygous cases for the TT allele were digested to 25 and 215 segments. The heterozygous cases had three bands at 240, 215 and 25 bp. Selected characteristics of cases such as demographic factors, major risk factors, site (topography), Tumor Grade, General Summary Stage, clinical staging and survival were obtained from the cancer registry database of the research center for Gastroenterology and Liver Diseases (RCGLD).

**Results:** The frequency of CC, CG and GG genotypes among the cases and controls for the SNP 1042522 were as follows: 22.7% vs. 14.6%, 77.3% vs. 85.4%, 0% vs. 0% respectively. For the SNP 1800371 all the genotypes were CC among the cases and controls. No significant difference was observed between the cases and controls for either of the SNPs. In the SNP: 1042522 mutant genotype were more frequent in females compared with males (p = .007). Poorly differentiated tumors displayed no difference in the levels of mutation in compare with moderately or well differentiated tumors. Mutant genotypes show no association with the survival and other clinicopathological characteristics of the patients.

**Conclusions:** Our preliminary result shows that the SNPs: 1042522 and 1800371 in the TP53 gene has no apparent association with gastric cancer and its clinicopathological characteristics among a sample of Iranian patients.

### 112 Predictors of Endoscopic Findings after Roux-en-Y Gastric Bypass for Obesity

Jason A. Wilson, M.D., Joseph Romagnuolo, M.D., Karl T. Byrne, M.D., Katherine Morgan, M.D., Frederick A. Wilson, M.D. ∗ Internal Medicine, Medical University of South Carolina (MUSC), Charleston, SC; Division of Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, SC and General and Gastrointestinal Surgery, Medical University of South Carolina, Charleston, SC.

**Purpose:** To evaluate the spectrum and predictors of endoscopic findings in symptomatic patients after Roux-en-Y Gastric Bypass (RYGBP).

**Methods:** Retrospective chart review of 226 patients referred for upper endoscopy following RYGBP surgery performed by one surgeon at the Medical University of South Carolina from January 1993 to January 2005. Multiple logistic regression analysis was used to calculate adjusted odds ratios (AOR) with 95% confidence intervals (CI) for predictors of normal endoscopy, marginal ulcers, stomal stenosis, and staple-line dehiscence.

**Results:** The most common endoscopic findings were: 99 (44%) normal post-surgical anatomy, 81 (36%) marginal ulcer, 29 (13%) stomal stenosis, and 8 (4%) staple-line dehiscence. Factors that significantly increase the risk of marginal ulcers following RYGBP surgery include smoking (AOR = 41.5; 95%CI [11 to 159]) and NSAID use (AOR = 11.2; [5.3 to 24.1]). A significant interaction term suggested that the risks of NSAID use and smoking together were less than additive. PPI therapy following surgery was protective against marginal ulcers (AOR = 0.32; [0.13 to 0.86]). There were non-significant trends towards nausea/vomiting predicting stenosis, and smoking increasing the risk of dehiscence (both p = 0.06). The other exposures were not predictive for marginal ulcers, stomal stenosis, or staple-line dehiscence.

**Mean time to diagnosis for marginal ulcers following surgery was 6.9 months, 77 of 81 (95%) presented within 12 months. Stenosis tended to present earlier at
a mean of 3.4 months, and dehiscence later at a mean of 28 months. Trends regarding time to presentation, because of overlap, were not significantly predictive of findings at endoscopy.

Conclusions: Following RYGBP surgery for obesity, smoking and NSAID use significantly increase the risk of marginal ulceration, and PPI therapy is protective but does not eliminate this increased risk. Because a significant majority of marginal ulcers present within 12 months of surgery, prophylactic PPI therapy should be considered during this time period, especially for high risk patients (i.e. smokers and/or NSAID users).

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Differential Host Chemokine Response to Helicobacter pylori: Inhibition of IL-8 Expression in a Mixed Infection

Dharmalingam Subramanian, Ph.D., Vincet Ahuja, M.D., Usha A. Rao, Ph.D., Douglas E. Berg, Ph.D., Brian K. Dieckgraefe, M.D., Ph.D., Shrikant Anant, Ph.D.* Internal Medicine/Gastroenterology, Washington University School of Medicine, Saint Louis, MO and Microbiology, University of Madras, Chennai, India.

Purpose: Helicobacter pylori infection is one of the most common infections worldwide. Although most of the cases are asymptomatic, some induce a vigorous immune response. Hp is a genetically diverse bacteria, and infection generally occurs with multiple strains. Hence, we hypothesized that some Hp strains may suppress robust host response induced by virulent strains. The gastric epithelium secretes chemokines in response to Hp infection. Strains that encode cag pathogenicity island activate transcription factor NF-κB, resulting in induction of IL-8 gene expression. The objectives of this study was to determine whether strain SS1, a weak inducer of host chemokine response had a suppressive effect on more virulent clinical strains.

Methods: 489 patients in Chennai, South India were screened by endoscopy. Multiple gastric biopsies were obtained for rapid urease test, histopathology and culturing Hp. CagA and VacA (s1/s2, m1/m2) status were determined by RT-PCR. For Hp-mediated host chemokine response, IL-8 mRNA expression was determined in AGS cells, a human gastric epithelial cell line by Real Time RT-PCR. For NF-κB activation, EMSA assays were performed with nuclear extracts.

Results: Rapid urease test was positive in 205 patients, of which 110 had positive cultures for Hp. While 89% of the isolates were resistant to metronidazole, only 11% were resistant to both metronidazole and clarithromycin, and <1% had quadruple resistance to metronidazole, amoxicillin, clarithromycin and ciprofloxacin. We next determined the status of Cag A and VacA by PCR. 35/43 of strains encoded CagA, 35/43 strains were vacA s1, and 38/43 were m1. To determine host IL-8 response, we chose two of these strains (CH1 and CH8), both being CagA+, VacA s1m1. AGS cells were either infected with strains CH1, CH8, and SS1 (CagA+, VacA s2m2), individually or together. Both, CH1 and CH8 robustly induced, while SS1 only modestly induced IL-8 mRNA expression. Furthermore, SS1 significantly suppressed the CH1- or CH8-mediated induction of IL-8 expression. Moreover, SS1 inhibited the CH1- and CH8-mediated activation of NF-κB.

Conclusions: The ability of strain SS1 to suppress the vigorous IL-8 induction mediated by the other strains suggests that a critical balance in strain-specific infection may determine the degree of chemokine response from the gastric epithelium.

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The Development of Gastric Cancer Associated with Okadaella gastrococcus (Og) Infection Following Helicobacter pylori (Hp)

Eradication: A Case Report

Takuyuki Okada, M.B.B.S., Hiroto Miwa, M.D., F.A.C.G.* Graham Adkins, F.R.C.P.A, Medicine, Okada Medical Clinic, Brisbane, Queensland, Australia; Internal Medicine, Hyogo College of Medicine, Nishinomiya, Hyogo, Japan and Pathology, Sullivan Nicolaides Pathology, Taringa, Queensland, Australia.

Purpose: We have reported the intracellular presence of Og in erosive gastric ulcer, gastritis, intestinal metaplasia, dysplasia, and adenocarcinoma of GEJ. The presence of Og in these gastric mucosal lesions raises the possibility that Og might be associated with the development of gastric cancer. We present a case of a small gastric adenocarcinoma following Hp eradication.

Results: Case report: a 69 years old, non-smoker, Japanese male with the family history of colon cancer and diabetes mellitus. His past history included duodenal ulcer, asthma, and type II DM, cardiac arhythmia, and hibakush Hiroshima 1945. He had active chronic gastritis with focal epithelial atypia associated with Hp and Og infection when he had the first EGD in May 1998. He underwent Hp eradication consisted of Ranitidine 300mg, Tetracycline 1.5g, and Metronidazole 600mg daily for 2 weeks. EGD one year later revealed multiple gastric erosions in the prepyloric antrum and dysplastic areas in the border of corpus and antrum. Successful Hp eradication was confirmed by UCBT, urease test on gastric aspirates and biopsy specimens, histology including Hp immunoperoxidase test, transmission electron microscopy (TEM), and by culture. The histology was chronic gastritis with atrophy, intestinal metaplasia, and low grade dysplasia. Persistent intracellular Og infection was identified in these areas by TEM. He was offered an Og eradication. He refused the treatment, but he did agree to have annual EGD. EGD in November 2003 identified a small nodular lesion (about 5mm in diameter) in the antrum of lesser curvature. The histology was well differentiated adenocarcinoma. He underwent ESD, and the histology confirmed the complete excision of the gastric cancer. His post-operative course was complicated with a small bleed from the ulcer created by ESD, AF, myocardial infarction, and right CVA. He recovered quite well with minimal residual disability.

Conclusions: This is the case of a small gastric adenocarcinoma developed 5.5 years after Hp eradication, which was associated with chronic intracellular Og infection. This case suggests the importance of follow-up EGD for the patient who has the higher risk of developing gastric cancer, even after the successful Hp eradication. This case also illustrated the post-operative complication of ESD.

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Upper Gastrointestinal Bleeding Due to Gastric Necrosis Following Cardiovascular Surgery

Ashish P. Shah, M.D., Thomas Kowalski, M.D.* Gastroenterology and Hepatology, Thomas Jefferson University Hospital, Philadelphia, PA.

Purpose: A 36 year-old African American male presented with acute onset of chest pain. He had no past medical history and took no medications. Physical examination revealed a blood pressure of 180/100 mm Hg, heart rate 90 beats per minute and temperature 98.7°F. His abdomen was soft and non-tender. Laboratory testing revealed hemoglobin of 11.5 gm/dL (hematocrit 32%), white blood cell count 6,500/mm3, international normalized ratio 1.0 and serum creatinine 1.1 mg/dL. Computerized tomography showed a thoraco-abdominal aortic dissection from the aortic arch to the iliac arteries without involvement of the celiac axis, superior mesenteric artery or inferior mesentric artery. He was urgently brought to the operating room and underwent repair of the aortic dissection. There were no periods of hypotension. Postoperatively, the patient was brought to the intensive care unit. A nasogastric tube was placed. Soon thereafter, copious amounts of bright red blood emerged from the suction tubing. On examination, blood pressure was 160/75 mm Hg and heart rate was 110 beats per minute. His abdomen was non-distended with hypoactive bowel sounds. Rectal exam revealed brown guaiac negative stool. Laboratory studies were significant for a hemoglobin of 10mg/dL (hematocrit 30%) and lactate 39 mg/dL (normal 0–20mg/dL). An esophagastroduodenoscopy revealed bright and dark blood throughout the stomach. The mucosa of the body and fundus appeared blackened and necrotic with multiple linear tears (Figures 1–2). The patient was given 2 units of packed red blood cells, intravenous pantoprazole and fluids. Bleeding stopped and the remainder of his postoperative
Late Stage Diabetes Mellitus May Be the Most Common Cause of Rapid Gastric Emptying (RGE) and Early Dumping Syndrome (EDS)

Amolak Singh, M.D.* Nuclear Medicine, University of Missouri Health Care, Columbia, MO.

Purpose: In-spite of our recent work and publication (CNM 2003, 28: 658–662) many clinicians in our experience do not seem to recognize diabetes mellitus (DM) as a common cause of RGE and EDS. Many associate gastroparesis with late-stage DM and EDS with prior gastric surgery or early-stage DM. The purpose of this paper is to emphasize late-stage DM as the most common cause of EDS and describe its association with other complications of DM.

Methods: Thirty-one (31) diabetic patients (pts) with RGE, selected out of 750 pts who had undergone gastric emptying studies over about 10-year period were included in this retrospective analysis. The gastric emptying studies were performed with a dual head gamma camera using an egg meal labeled with 2 mCi of Tc-99m sulfur colloid. The rapid gastric emptying half time (GEHT) was calculated from decay corrected mean geometric gastric counts, using linear regression analysis. EDS was defined as GEHT less than 35 minutes.

Results: Of 31 pts with DM and EDS, 16 were type-1, 15 were type-2 diabetics. There were 22 females, 9 were males with mean age of 54.7 ± 18.34 years (range 18–89). The mean duration of DM was 17.36 ± 9.25 years (range 5–38). The mean duration of DM in type-1 and type-2 diabetics was 18.38 ± 9.9 and 16 ± 8.4 years. The mean GEHT of 27 ± 6 and 26 ± 6 minutes were similar in type-1 and type-2 diabetics. Peripheral neuropathy was present in 15 of 31 (48%) pts. Twenty-seven pts (87%) were taking variable dose and types of insulin, 4 were being treated with diet control and/or oral hypoglycemic agent (glyburide). Almost all pts with RGE presented with nonspecific symptoms such as nausea, vomiting, and post-prandial abdominal discomfort. The gastric emptying studies were ordered to rule out gastroparesis and many referring physicians failed to comprehend phenomenon of RGE and EDS.

Conclusions: In our experience DM is the most common causes of RGE and EDS. This phenomenon is most often seen with late-stage DM and is frequently associated with other neuropathic complications such as diabetic peripheral neuropathy.

Gastrointestinal Bleeding Following Ingestion of Low-Dose Ibuprofen


Purpose: Chronic utilization of non-steroidal anti-inflammatory drugs (NSAIDS) is known to cause gastrointestinal ulcers and bleeding. This phenomenon has generally been thought to be dose-dependent; however we report the occurrence of significant gastrointestinal bleeding resulting in hematemesis in 4 pediatric patients taking low-dose ibuprofen.

Methods: All 4 patients were evaluated following initial examination in the Emergency Room for hematemesis. These evaluations included physical examination, routine bloodwork, coagulation studies, esophagogastroduodenoscopy, endoscopic biopsies and cultures.

Results: The mean age of these patients was 23.5 ± 9.0 months, 3 of the 4 were female and all exhibited symptoms of fever; 50% had a cough and 50% had rhinitis. Three of the 4 children received a single, age-appropriate dose of ibuprofen while the 4th child received 2 successive age-dependent doses at the recommended dosing intervals. All four children developed hematemesis at home within 24 hours of initial ibuprofen ingestion and were sent by their pediatricians to the Emergency Room. The history obtained showed that all 4 children had no previous underlying medical problems and no other medications were being taken at the time. The hemoglobin values for these patients ranged from 6.4 to 10.9 g/dl; all other laboratory testing, including coagulation studies, were normal. All patients had an isolated ulcer in the gastric antrum that was seen during esophagogastroduodenoscopy. Proton pump inhibitors were then administered intravenously and no patient required transfusions. Cultures and histology of gastric biopsies were negative for Helicobacter pylori. Upon hospital discharge, all patients were instructed against the use of NSAIDS and were treated for 2 months with oral proton pump inhibitors. There was no recurrence of gastrointestinal bleeding during follow-up that lasted for 1 year.

Conclusions: NSAID therapy is commonly used to treat fever in young children without regard to its effects on the gastrointestinal tract. Our experience indicates that even a single dose of NSAIDS can result in significant gastrointestinal bleeding and ulcer formation.

An Unusual Cause of Shortness of Breath: Krukenberg Tumors: A Case Report and Review of Literature

Theodore M. Perlman, M.D., Kaleem M. Rizvon, M.D., Steven S. Yang, M.D., Paul J. Mustacchia, M.D.* Gastroenterology, Nassau University Medical Center; East Meadow, NY.

Purpose: A 33 year old hispanic female without any pmhx. was admitted to the hospital complaining of worsening shortness of breath, pleuritic chest pain, 20 pound weight loss with vague epigastric and suprapubic discomfort over a four week period. She denied hematemesis, heartburn, dysphagia, melena, fever/chills, asa/nsaid usage or diarrhea. Socially she denied tobacco, alcohol and narcotics. On admission she was afebrile, bp 116/87, hr 116, rr 22. Physical exam revealed an alert and oriented female who appeared ill. Neck was negative for adenopathy, lung: decreased breath sounds bilaterally, tachycardic. Her abdomen was soft, mildly distended, positive for suprapubic discomfort, positive for bowel sounds, dme: no masses, no gross blood, brown stool. Abnormal labs included ALP-161, WBC-22.2, HB-8.5 TRANS.SAT-6%, CA125-771. CT of the chest, abdomen and pelvis revealed mediastinal, b/l hilar, para cardiac, and diffuse abdominal adenopathy, fundal wall thickening with infiltration of adjacent fat and masses, large lower abdominal masses, ascites, ill defined lung densities and lytic osseous metastases. EGD revealed a single ulcerated mass at the incisura, biopsies were positive for poorly differentiated adenocarcinoma with features of signet ring cell carcinoma.

Discussion: A Krukenberg tumor is a metastatic adenocarcinoma to the ovaries, usually from the stomach but may be from any part of the gastrointestinal tract or the breast. It is rare in the U.S.A. accounting for 4% of ovarian tumors. 90% of ovarian cancers are adenocarcinomas which are divided into Intestinal and Diffuse(Infibrillarative) types. The prototype of diffuse adenocarcinomas is the signet ring cell. These cells lack cohesion resulting in scattered individual cells infiltrating the lamina propria causing a diffuse thickening the gastric wall. Discrete masses are uncommon. They may be easily missed unless mucin stains or immunohistochemical staining are used. The diffuse type have similar incidences in most countries. They are not associated with environmental factors but may have a familial predilection. They predominate in women and younger patients and have a
worse prognosis. Krukenberg tumors have no known histological precursor and commonly spread to the peritoneum. Prognosis is extremely poor with a mean survival of 7–11 months. Treatments include chemotherapy, debulk- ing procedures and metастasectomies in patients with tumors confined to the pelvis.

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Effect of Lying on Gastric Electrical Rhythm
Trisha Parsicha, Hansa Salam, M.D., Jiande Chen, Ph.D., Pankaj J. Parsicha, M.D.* Internal Medicine, University of Texas Medical Branch, Galveston, TX.

Purpose: The gastrointestinal tract is uniquely sensitive to mental stress, reflecting the communication between the central nervous system and the enteric nervous system. We hypothesized that this relationship could be exploited to provide insight into the psychological state of an individual when lying by analyzing changes in gastric physiology. Current lie detection methods (using standard polygraph) rely on non- GI physiological changes (ie. heart rate and sweating), but are only about 90% accurate and often unreliable.

Methods: Sixteen healthy volunteers (13F, 3M) were recruited. Simultaneous electrogastrogram “EGG” and electrocardiogram “EKG” recordings were done for 3 periods, Baseline “BsL”, “Lying” and “Truth”; the later 2 being randomized. Autonomic activity was assessed via spectral analysis of heart rate variability (HRV) data derived from EKG. Gastric slow waves were assessed via spectral analysis of EGG signal. Statistical analysis was done using Student t-test and ANOVA as appropriate.

Results: The 2nd channel of EGG, located on stomach proximal antral area, showed a significant decrease in% normal slow wave in Lying vs. BsL (75.39 ± 5.5 vs. 82.29 ± 4.47; P = 0.04). This may be attributed to significant increase in% arrhythmia in Lying vs. BsL (11.13 ± 3.87 vs. 6.35 ± 2.86; P = 0.02). HRV analysis showed a significant increase in average heart rate in Lying and Truth vs. BsL (75.76 ± 1.73; 74.4 ± 1.69 vs. 72.19 ± 1.43); (p = 0.05, 0.002, 0.001 respectively). There was a significant increase in sympathovagal balance in Lying vs. BsL (1.67 ± 0.33 vs. 1.35 ± 0.32; P = 0.045), which might be attributed to significant decrease in vagal activity in both Lying and Truth periods vs. BsL (0.32 ± 0.04 and 0.33 ± 0.04 vs. 0.4 ± 0.04; P = 0.026 and 0.003 respectively).

Conclusions: Lying and truth telling are both associated with an increase in heart rate and sympathovagal balance. However, the act of lying is associated with a significant increase in gastric arrhythmia. Thus standard polygraph methods to assess heart rate variability may not perform as well as the EGG in distinguishing between lying and telling the truth. The addition of the EGG to standard polygraph methods has clear value in improving the accuracy of current lie detectors. In addition to a new, potentially breakthrough method for a variety of security applications, the results also provide understanding of the complex communication between the big brain and the little brain in the stomach. Further research in real-life situations and using larger numbers is necessary to validate these results.

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Seven-Day Triple Rabeprazole-Containing H. pylori Eradication Therapy on the Texas-Mexican Border
David T. Graham, M.D.*, Antoine R. Opekun, P.A-C., Armando Campos, M.D., Leoncio Guerrero, M.D., Hala El-Zimatty, M.D., Alfredo Chavez, M.D., Zhannat Z. Nurgalieva, M.D., Victorq Cardenas, M.D., Medicine, Michael E. DeBakey VAMC, Houston, TX; Medicine, Baylor College of Medicine, Houston, TX and University of Texas School of Public Health, El Paso, TX.

Purpose: Antibiotic resistance is the main reason of failure of triple H. pylori eradication therapy with PPI-amoxicillin-clarithromycin triple therapy. Aims: To test a triple therapy in a population along the US-Mexico border in relation to clarithromycin resistance.

Methods: A random sample of adults from Ciudad Juarez with H. pylori infections identified by culture, histology or both received rabeprazole 20 mg, clarithromycin 0.5 g and amoxicillin 1 g, each b.i.d. for seven days. Efficacy was assessed by 13-C urea breath test (UBT) done 4 or more weeks after therapy.

Results: 122 patients were enrolled, and 111 were evaluated by UBT at 4 or more weeks after receiving therapy. A total of 102 completed the protocol, 2 deviated from protocol, and five stopped because of adverse events. The cure rate (ITT) was 93/111 [83.8% (95% CI = 76–89.8%)]; the PP cure rate was 91/102 [89.2% (95% CI = 79.9–95.2%)]. Side effects were not serious and only 6.0% (5/75) of those with AE stopped medication because of side effects. In the group of patients completing therapy, only 2.2% of isolates had clarithromycin resistant H. pylori (MIC ≥ 0.5); none of them had their infection cured. Resistance was not responsible for most of the treatment failures in this population.

Conclusions: In Ciudad Juarez, Mexico a 7 day rabeprazole containing triple eradication therapy was both effective and well-tolerated. Clarithromycin resistance was uncommon the low resistance rate may be responsible for the better outcome compared to recent studies in US populations (Vakil et al., Aliment Pharm Ther 2004; 20:99–107).

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High Missed Rate of H. Pylori Infection and Detection by C-13 Urea Breath Testing in Patients Referred for Evaluation of Iron Deficiency Anemia /Obscure Gastrointestinal Bleeding by Capsule Endoscopy in a Large Community Practice
Sriniivas S. Fasirdredi, M.D., FA.C.P.* Gastroenterology, Bayshore Community Hospital, Holmdel, NJ and Gastroenterology, JFK Medical Center, Edison, NJ.

Purpose: To assess the percentage of missed patients with H. Pylori gastritis in all the patients referred to the office for the evaluation of obscure gastrointestinal bleeding and iron deficiency anemia by capsule endoscopy, after a thorough prior conventional endoscopic evaluation by other gastroenterologists in the community setting, and to discuss any clinical/practice implications.

Methods: Seventy five(75) out of a total of one hundred and twenty five(125) patients referred to the office between January 2003 and June 2005 for the evaluation of iron deficiency anemia or obscure gastrointestinal bleeding and iron deficiency anemia by capsule endoscopy, were administered a C-13 urea Breath test for H. Pylori(using UBT/Breathek by Mereteck). All patients were instructed to be off any antibiotics and Proton Pump Inhibitors, if any, for at least 1 week prior to the test. All these patients were confirmed to have had either a negative giemsa stain for H. Pylori like organisms on the gastric biopsy specimens or a negative CLO(Campylobacter like organism) test from the review of reports of the referring gastroenterologists. Patients referred to the office between January 2003 and June 2005 for the evaluation of iron deficiency anemia or obscure gastrointestinal bleeding and iron deficiency anemia.

Results: Fifteen(15) of the seventy five(75) patients tested for H. Pylori by the C-13 Urea Breath test were positive (20% incidence rate). Subsequent analysis of the findings of capsule endoscopy in all these positive patients revealed erythema and few antral erosions, indicative of gastritis.

Conclusions: A significant percentage (20%) of patients referred for work up of obscure gastrointestinal bleeding or iron deficiency anemia by capsule endoscopy in the community practice setting had missed diagnosis of H. Pylori infection by conventional upper endoscopy done by referring gastroenterologists. Such decreased detection rates could have been secondary to concomitant use of antibiotics and Proton Pump Inhibitors at the time of the original endoscopy, inadequate ‘non-standardized tissue sampling techniques or decreased detection rates associated with any hemorrhagic states. In all such instances the conventional “gold standard” methodology of endoscopic detection may very well become a “brass” standard, with significant miss rates. Routine incorporation of C-13 Urea breath testing into the diagnostic and treatment algorithms of capsule endoscopy may thus be warranted, based on the evidence that currently exists supporting an association between H. Pylori infection and iron deficiency anemia.
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Frequency of Helicobacter pylori and CagA Antibody in Patients with Gastric Neoplasms and Controls: The Indian Enigma

Uday Chand Ghoshal, DM,∗ Shridhar Tiwari, M.Sc., Rakesh Pandey, M.D., Sadhana Dhiingra, M.D., Ujajda Ghoshal, M.D., Himani Singh, M.Sc., A. K. Nagpal, D.M., V. K. Gupta, D.M., Sita Naik, M.D., Archana Ayyagari, M.D. Gastroenterology, SGPGI, Lucknow, UP; Pathology, SGPGI, Lucknow, UP; India; Microbiology, SGPGI, Lucknow, UP; India; Gastroenterology, Central Command, Lucknow, UP; India and Immunology, SGPGI, Lucknow, UP; India.

Purpose: Despite an association between H. pylori and gastric neoplasm (GN) from developed world, studies from India, where infection is commoner and is acquired early in life, are scanty, contradictory and had small sample size.

Methods: 279 patients with histologically confirmed GN from two centers in northern and one from eastern India during December 1997 to January 2005, 355 healthy volunteers (HV) and 101 non-ulcer dyspepsia (NUD) were evaluated for H. pylori using RUT, histology and serology for IgG anti-H. pylori and CagA antibody (Genesis Diagnostics, Cambridge shire, UK).

Results: Patients with GN (263 gastric carcinoma and 16 [5.7%] primary gastric lymphoma, 208 male) were older than HV (n = 355, 188 male) and NUD (n = 101, 54 male) (53.4 ± 12.3 vs. 43.7 ± 17.4 and 42.8 ± 13.2, respectively; p < 0.0001) though age of HV and NUD was comparable (one-way ANOVA with post-hoc Scheffe test). Eastern Indian patients with GN (n = 145) were younger than northern Indian patients (n = 134) (51.5 ± 11.9 vs. 55.4 ± 12.3, respectively; p = 0.007, ‘t’ test). Among patients with GN and NUD, positive RUT (86/225, 38% vs. 46/101, 45.5%), serum IgG anti-H. pylori antibody (154/198, 77.8% vs. 85/101, 84.1%) and H. pylori on histology (136/213, 63.8% vs. 55/101 54%) were comparable (p = ns for all; X² test). Serum IgG anti-H. pylori antibody was commoner among HV than patients with GN (300/355, 84.5% vs. 154/198, 77.8%; p = 0.04, X² test). Intestinal metaplasia was detected in 101/252 (40%) patients with GN and in 2/101 (2%) with NUD (p < 0.00001, X² test). 124/163 (76%) GN, 87/98 (87.7%) HV and 64/101 (63.4%) NUD had serum CagA antibody (p < 0.05, X² test).

Conclusions: Frequency of H. pylori as detected using endoscopy and serology-based tests is not higher among patients with GN as compared with HV and NUD in India. Further studies to explain this Indian enigma are needed.

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Molecular Study on Frequency of Single Nucleotide Polymorphism of DNMT1 among Iranian Patients with Gastric Cancer


Purpose: We have hypothesized that SNPs within the DNMT1 may be associated with sporadic gastric cancer.

Methods: In this case-control study, we enrolled 80 sporadic gastric cancer and 80 age, sex and ethnicity matched healthy controls. Genomic DNA was extracted and the locus for the SNP: 721186 on exon 20 and SNP: 13784 on 3’ untranslated region and SNP: 4804123 of the DNMT1 gene was amplified. We used RFLP reaction by the AcylI enzyme for snp 721186 and BstAPI for snp 13784 and Alw26I for snp 4804123. The undigested amplicons in snp 721186 and 13784 were of 210 bp. In case of homozygotes state for the CC allele the amplicons were digested to 27 and 183 segments. The heterozygotes had three bands at 210, 27 and 183 bp. The undigested amplicons in SNP 4804123 were of 280 bp. In case of homozygotes state for the AA allele the amplicons were digested to 28 and 232bp segments and homozygotes state for the GG allele the amplicons were digested to 28 and 108 and 124bp segments. The heterozygotes had four bands 232, 124,108 and 280bp.

Results: The frequency of the GG, GA and AA genotypes among the cases and controls were: 98% vs. 98%, 0% vs. 0%, 2% vs. 2% respectively. The G and the A allele frequencies among the cases and controls were 98% vs. 98% and 2% vs. 2% respectively. The frequency of the CC, CT and TT genotypes among the cases and controls were: 100% vs. 100%, 0% vs. 0%, 0% vs. 0% respectively. The C and the T allele frequencies among the cases and controls were 56% vs. 44% and 61% vs. 39% respectively. There was no significant difference between the cases and controls.

Conclusions: The SNP: 721186, 13784 and 4804123 polymorphisms of the DNMT1 gene has no apparent association with gastric cancer among a sample of Iranian patients.

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An Audit of Incidence of Gastric Adenocarcinoma in Northern Western Region of Pakistan


Purpose: A Retrospective/Observational study.

Place: Department of Gastroenterology & Hepatology, PGMI, HMC, Peshawar.

Methods: A retrospective analysis of the endoscopy record of patients under-going upper GI endoscopies was made during the last 5 years from data entered in record books. The data was recorded on a properly structured proforma and findings, including physical examination, endoscopic findings and histopathological findings, were noted and analyzed using SPSS version 10.

Results: Of the 8600 patients studied, 380 (4.4%) had adenocarcinoma. 277 (72.8%) patients were male and 103 (27.1%) were females. The age range was 18 – 70 years with a mean of 52 ± 7. 8 Endoscopically the type of lesion most commonly found was fungating/polyoidal in 40%, excavating ulcers type in 26%, nodular and circumferencil in 25% and diffuse infiltrating type (scirrhous) in 7.3% of the cases. The antrum was the main site of involvement (42%). The fundus & greater curvature were involved in 23.6% of the cases followed by cardia and lesser curvature in 16.3% and 10.5% of the cases respectively.

Pathologically the tumors were classified according to the Lauren’s and Japanese Classification. 34.7% were undifferentiated type, 30% moderately differentiated type, 16.8% signet ring cell type and well-differentiated type in 18.40% of the cases. 94.2% were diffuse infiltrative type and 5.7% were intestinal type according to the Japanese classification.

Conclusions: Gastric Adenocarcinoma was more common in the adult male patients. The most common endoscopic type was polyoidal/fungating mass. The commonest site involved was antrum, and the most common histopathological type was undifferentiated.

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CyclinD1 Single Nucleotide Polymorphisms and Risk of Gastric Cancer among Iranian Patients, A Pilot Genetic Association Study

Minoosh Vossoughi, M.D., Ala Melati-Rad, M.D., Elham Sharif Panah, M.Sc., Mohammad Reza Zali, M.D., F.A.C.G., Babak Noorinayer, M.D.,∗
Purpose: Our aim in this study was to investigate the association of cyclin D1 (G870A and G30T) single nucleotide polymorphisms with susceptibility to gastric cancer among a sample of Iranian patients and compares the results with normal group.

Methods: We investigated the association between G870A and G30T polymorphisms of the CCND1 gene and gastric cancer. 100 patients and corresponding control matched for their age, sex and ethnicity were enrolled. Genomic DNA was extracted and specific primers designed for the target regions were used. RFLP was used to detect the presence or the absence of the polymorphisms.

Results: For the G870A SNP, 18% of cases were of wild type genotype while 50% were heterozygous and 32% were of AA (polymorphic) genotype. The respective numbers for our controls were 19%, 41% and 38%. For the G30T SNP, 100% of cases and controls were of wild type (GG).

Conclusions: Our preliminary result shows that the G870A and G30T polymorphisms of the cyclin D1 gene have no apparent association with gastric cancer among a sample of Iranian patients. Further investigation involving more patients and investigating other polymorphisms of this gene are required to delineate the true role of CCND1 polymorphisms in pathogenesis of gastric cancer.

The Importance of Candida albicans Infection of the Duodenal Ulcer Perforation – Clinical and Experimental Analysis

Tetsuya Nakamura, M.D., Masashi Yoshida, M.D.* Hideki Ishikawa, M.D., Go Wakabayashi, M.D., Motohide Shima, M.D., Minoru Tanabe, M.D., Shigeyuki Kawachi, M.D., Koichiro Kamai, M.D., Tetsuro Kubota, M.D., Yoshihide Otani, M.D., Yoshitomo Saikawa, M.D., Masaki Kitajima, M.D.
Surgery, Keio University School of Medicine, Shinjuku, Tokyo, Japan; Emergency and Critical Care Medicine, Keio University School of Medicine, Shinjuku, Tokyo, Japan; Center for Diagnostic and Therapeutic Endoscopy, Keio University School of Medicine, Shinjuku, Tokyo, Japan.

Purpose: The process of ulcer perforation has not yet been clearly elucidated, and the incidence of ulcer perforation remains unchanged. This study was performed to examine whether Candida infection is involved in the process of ulcer perforation.

Methods: Clinically, we reviewed the clinical records from 1993 to May 2004 a total 57 patients underwent surgery for stomach or duodenal perforation at the Keio University Hospital. In experimental analysis, male Wistar rats weighing 220–240 g were anesthetized with diethyl ether, and administered cysteamine at the dose of 31 mg/100 g three times at 4-hourly intervals on Day 1. Candida albicans at a density of 10^6 in 0.5 ml saline (n = 17) or only saline (n = 15) was administered 1 hour before 12 hours and 24 hours after the cysteamine administration. The animal experiments were conducted in accordance with the guidelines of the Keio University School of Medicine.

Results: In the clinical examination, Candida was most frequently (40%) observed microorganisms in ascites of the patients with perforated peptic ulcers. Candida infection was observed in 6 out of 8 patients with postoperative subcutaneous or intra abdominal abscess. In the experimental examination, perforations of duodenal ulcers were observed in 94.1% in the Candida group, but only 26.7% in the saline group. Statistical analysis revealed the significant difference between the control group and the Candida group (p < 0.01). The area of the duodenal ulcers in the Candida group was 40.8 ± 33.07 mm^2 and that in the saline group was 16.53 ± 20.4 mm^2, the difference being significant (p < 0.05). The survival rate was found to be significantly worse in the Candida group than in the saline group (p < 0.05).

Staining of the specimens with H&E., PAS reagent and Grocott’s silver revealed that the ulcer base was found to be colonized by C. albicans in the Candida group.

Conclusions: It was demonstrated that Candida albicans aggravates duodenal ulcer perforation in the experimental model of cysteamine-induced duodenal ulcer perforation. Clinically, Candida infection may have a role in the process of ulcer perforation.

A Novel Implant for the Treatment of Obesity: Early Safety and Tolerability Results in a Porcine Model

Raman Muthusamy, M.D., Daniel R. Burnett, M.D.,* George Triadafilopoulos, M.D., Jordan T. Bajor, B.S.
Department of Medicine, University of California, San Francisco, San Francisco, CA; Polymorfix Inc., Hayward, CA; Department of Medicine, Stanford University, Stanford, CA and Polymorfix Inc., Hayward, CA.

Purpose: Obesity and its medical complications are at epidemic proportions and affect almost 60 million Americans. Because of poor compliance, treatment of obesity with dietary, behavioral or pharmacologic therapies has yielded disappointing results. Surgical approaches to obesity may be associated with significant morbidity and even mortality. As an endoscopic treatment of obesity, we have developed a temporary, transpyloric implant that would reduce the rate of gastric emptying and facilitate weight loss. In this study, we evaluated the safety of this novel endoscopically-delivered and removable implant in a porcine model.

Methods: Eighteen adult Yucatan pigs initially weighing between 50–60 kg underwent endoscopic insertion of two different implants intended to result in two distinct degrees of pyloric obstruction (n = 7 each) or a sham procedure (n = 4). Specific endpoints included successful implant placement across the pylorus, symptomatic tolerance, lack of distal implant migration, and a lack of endoscopic or histopathologic ulceration, fibrosis, or pyloric stenosis. Efficacy was assessed by weekly pig weights. Fluorescent images were obtained at 1 week, 1 month, and 2 months post-implantation to verify device location. Endoscopic evaluation for evidence of gastroduodenal injury was performed at 3 months. Four pigs from each group will be euthanized at 6 months and full histopathology of the gastroduodenal region will be performed (these results will be available at the meeting). Two pigs from each device group will be survived an additional 3 months post device removal to evaluate potential latent implant effects.

Results: Endoscopic transpyloric implant delivery was successful over a guide wire in all cases. Mean procedure time was 24 minutes. All implants have been seen to be transpyloric in at least one followup fluorescent image. With the exception of a single pig that regurgitated the device, all pigs have remained asymptomatic. No instances of device migration distally into the duodenum have been observed.

Conclusions: Based on our initial experience, this novel implant appears to be easily delivered, tolerable, and safe in a porcine model. Additional porcine efficacy studies and human tolerance and efficacy trials are planned.

Helicobacter pylori Treatment in a Community-Based Setting: “Cost-Conscious” Therapy (Amoxicillin, Metronidazole, Esomeprazole) Versus “Expensive Pre-Packaged” Therapy (PrevPac)?

Betty J. White, AR.N.P, Michael F. Lyons, M.D.* Division of Gastroenterology, Tacoma Digestive Disease Center, Tacoma, WA.

Purpose: The United States has the highest per capita cost of health care in the world. Therapy for H. pylori infection can dramatically add to that expense. The purpose of this study was to determine whether a “cost-conscious” treatment regimen is as effective as an “expensive pre-packaged” treatment regimen for the eradication of H. pylori-subjects in a community-based Gastroenterology practice.

Methods: Patients identified with H. pylori infection were treated with the “cost-conscious” treatment regimen (amoxicillin 1 gram po bid × 10 days plus metronidazole 250 mg po tid × 10 days plus esomeprazole 40 mg po qd × 10 days) or with the “expensive pre-packaged” treatment regimen (amoxicillin and clarithromycin 1 gram po bid × 10 days plus metronidazole 250 mg po tid × 10 days plus esomeprazole 40 mg po qd × 10 days)
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**Association of Gastroduodenal Disease Phenotype with ABO Blood Group and Helicobacter pylori Virulence-Specific Immunoserotypes**

Ala I. Sharara, M.D.*, Heitham Abdul-Baki, M.D., Ihab ElHajj, M.D., Nabeela Kreidieh, Elizabeth M. Kfoury Baz, M.D. Internal Medicine, AUBMC, Beirut, Lebanon and Pathology and Laboratory Medicine, AUBMC, Beirut, Lebanon.

**Purpose:** The aim was to investigate the prevalence of *H. pylori* infection in Lebanon and the association between recognized virulence factors (CagA and VacA), ABO blood groups, and disease phenotype in symptomatic *H. pylori* infection.

**Methods:** The study population consisted of symptomatic patients with *H. pylori*-associated endoscopic findings and healthy blood donors. ABO typing and Western blot (HelicoBlot 2.0) for CagA and VacA was performed on all participants. The sensitivity of the immunoblot and rapid urease assay was determined from the symptomatic cohort.

**Results:** 130 patients and 104 healthy donors were evaluated. Based on the Western blot results, the prevalence of *H. pylori* infection in healthy Lebanese males (age range 18–55) was 68.3%. The sensitivity of the immunoblot and rapid urease assay was 94.6% and 91.8% respectively. *H. pylori* isolates were categorized into two major types: Type I (expressing both CagA and VacA) and Type II (expressing neither). Type I *H. pylori* was the predominant phenotype in both groups and was more common in the symptomatic population (71.5% vs. 46.5%, p < 0.01). By contrast, Type II and VacA-only strains were more common in the asymptomatic cohort (p < 0.05 for both). Overall, CagA-negative strains were present in 35.2% of asymptomatic individuals and in only 8.9% of symptomatic patients (p < 0.01). There was no significant association between any of the *H. pylori* serotypes and ABO blood groups or benign gastroduodenal disease. Notably, all patients with gastric malignancy were CagA-positive but this was not significantly different from the prevalence of Cag-A positive strains in benign disease (100% vs. 82.9%, p = 0.12). However, we found a higher prevalence of blood group A in patients with gastric malignancy compared to the general population (47.6% vs. 25%; p = 0.04).

**Conclusions:** The seroprevalence of *H. pylori* is moderately high in Lebanon. Phenotypic classification based on CagA and VacA identifies a higher prevalence of Type I *H. pylori* in patients with symptomatic disease. Although we found no direct association between virulence factors and ABO or disease phenotype, there was a significant relationship between infection with a CagA-positive strain in blood type A patients and the risk of gastric malignancy.

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**The Role of Metallothionein in Helicobacter pylori Positive Gastric Mucosa with or without Early Gastric Cancer and the Effect on Its Expression after Eradication Therapy**

Toshifumi Mitani, Daisuke Shirasaka,* Haya Miki, Nobuo Aoyama.

Department of Clinical Molecular Medicine, Division of Diabetes, Digestive and Kidney Disease, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan and Department of Endoscopy, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan.

**Purpose:** Metallothionein (MT), a low-molecular-weight, cysteine-rich, metal-binding ligand, has proven to sequester reactive oxygen species and reduce tissue damage. Helicobacter pylori (*H. pylori*) infection is associated with increased production of reactive oxygen species within the gastric mucosa. This study investigates the role of MT in *H. pylori*-induced gastritis with or without gastric cancer and evaluates the effect on MT expression after its eradication therapy.

**Methods:** Biopsy samples in the corpus and antrum were immunohistochemically examined for MT expression in 36 *H. pylori*-negative subjects without gastric cancer, and 89 positive ones with or without early gastric cancer. Gastritis was also evaluated according to an updated Sydney System. In 30 successfully eradicated subjects, the assessment described above was repeated every year for 2 years.

**Results:** The rate of MT expression was higher in *H. pylori* negative subjects than in positive ones (p < 0.01). Analyzing *H. pylori* positive subjects, its rate was higher in those without cancer compared to cancer patients (p < 0.05). A negative correlation was found between MT expression and atrophic change (r² = 0.356, p < 0.01). MT expression in *H. pylori* positive subjects was gradually recovered after eradication, and increased to the same degree in *H. pylori* negative ones after two years.

**Conclusions:** *H. pylori* infection was associated with the enhancement of MT expression in the gastric mucosa, which may indicate that MT expression plays a negative role in the initiation of gastric carcinogenesis. *H. pylori* eradication may reduce the risk of gastric cancer by leading the increase of MT expression.

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**Hydrogen Peroxide (H₂O₂), *H. pylori*, NSAIDs, and Clot Stability: Do They Matter?**

Subbaramiah Sridhar, MB, B.S.*, Sherman Chamberlain, M.D., Sankar Sethuraman, Ph.D., Robert Schade, M.D. Section of Gastroenterology, Dept. of Medicine, Medical College of Georgia, Augusta, GA and Statistics, Augusta State University, Augusta, GA.

**Purpose:** Adherent clots obscure visualization of ulcer bases, prevent endoscopic therapy in patients with acute upper gastrointestinal bleeding (AUGIB). Endoscopic use of 3% H₂O₂ spray oxidizes hemoglobin, removing overlying ulcer clots. *H. pylori* (HP) status and use of non-steroidal anti-inflammatory agents (NSAIDs) in patients with AUGIB may impact on the stability of the overlying clot. We prospectively evaluated patients to determine whether their HP status and NSAID usage would impact on the volumes of H₂O₂ required in the removal of overlying clots.

**Methods:** 56 patients (43 male & 22 female) between 22 and 85 who presented to the Medical College of Georgia with AUGIB with adherent clot on the ulcer base were studied. Emergency upper GI endoscopy was performed within 6 hours on all patients by a single endoscopist (S.S). The potential bleeding sites were vigorously washed with aliquots of water mixed with simethicone followed by 3% H₂O₂. The amount of H₂O₂ used to clean the ulcer bases to achieve grade 3 visualization (described by Kalloo) was
recorded. Biopsies for rapid urease (CLO) were obtained from the antrum and high body in all subjects.

**Results:** 41 DU, 14 GU and 2 Mallory Weiss tears noted. Excellent visualization of the ulcer bases was achieved after H$_2$O$_2$ spray, however, volume used differed significantly (significance at 1% level) between the CLO- and NSAID+ group when compared to the group –ve for both. There were no significant differences between CLO+ and NSAID− and CLO+ & NSAID+ groups, however, significant differences were noted between CLO+, NSAID- and CLO-, NSAID+ group when compared with – for both. No adverse effects of H$_2$O$_2$ were noted.

**Conclusions:** HP (+) status and NSAID use determined the volume of H$_2$O$_2$ required to remove ulcer clots. The stability of the overlying clot is likely to be inversely proportional to the amount of H$_2$O$_2$ used. This is the first study to determine that patient’s HP status and NSAID usage may affect the amount of H$_2$O$_2$ required to remove ulcer clot, due to its underlying instability. [figure 1]

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**Hydrogen Peroxide (H$_2$O$_2$) Spray Effectively Facilitates Endoscopic Visualization of Bleeding Lesions in Patients with Acute Upper Gastrointestinal Bleeding (AUGIB) – A Single Center Prospective Study**

Subburamiah Sridhar, MB, B.S.,* Sherman Chamberlain, M.D., Sankar Sethuraman, Ph.D., Robert Schade, M.D. Medicine, Section of Gastroenterology, Medical College of Georgia, Augusta, GA and Statistics, Augusta State University, Augusta, GA.

**Purpose:** Endoscopic management of AUGIB can be challenging and technically difficult owing to the presence of blood and clots, which may obscure the bleeding sites. Animal experiments and a few small-number studies have noticed improved visualization of the ulcer base using 3% H$_2$O$_2$ spray via endoscope. H$_2$O$_2$ oxidizes red hemoglobin to a translucent clot. We report the largest study to date to support the usefulness of H$_2$O$_2$ spray in patients with AUGIB.

**Methods:** Fifty-six subjects (22 female & 34 male patients between ages 22–85 who presented to the Medical College of Georgia with AUGIB.

**Results:** Total of 144 family members including 71 family members of $H. pylori$ positive and 69 family member of $H. pylori$ negative were evaluated in this study. The seroprevalence of $H. pylori$ infection among Thai families. Improvement of personal and family hygiene should be emphasized for prevention of $H. pylori$ infection.

**Conclusions:** $H. pylori$ is safe and effectively improves the visual field, thus facilitates localization of bleeding sites & stigmata of bleeding during emergency therapeutic endoscopy. This may become a standard therapy for improved visualization of lesions in AUGIB. [figure 1]

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**Intrafamilial Transmission of *Helicobacter pylori* in Thailand**

Varoche Mahachat, M.D., F.A.C.G.,* Ratha-korn Vilaichone, M.D., Ph.D. Medicine-Gastroenterology, Chulalongkorn University Hospital, Bangkok, Thailand and Medicine-Gastroenterology, Thammasat University Hospital, Pathumthani, Thailand.

**Purpose:** Intrafamilial transmission is considered as a major route of *Helicobacter pylori* (H. pylori) infection. This cross sectional study was designed to evaluate the factors associated with intrafamilial H. pylori transmission and seroprevalence of H. pylori infection among Thai families.

**Methods:** Clinical information, structured questionnaires and blood samples were obtained between June 2002 and May 2003. The structured questionnaire was completed for all family members by the same researcher. H. pylori status assessed by anti-H. pylori serology (HM-CAP; Enteric Product Inc., Westbury, NY and HB 2.1; Genelabs Diagnostics, Singapore).

**Results:** Total of 140 family members including 71 family members of H. pylori positive and 69 family member of H. pylori negative were evaluated in this study. The seroprevalence of H. pylori infection in H. pylori positive family members was significantly higher than family members of H. pylori negative (74.7% vs. 39.1%; p < 0.001). The multiple logistic analysis demonstrated that age (OR = 6.3; 95% CI = 2.1–19.2, p < 0.01), share drinking cup behavior (OR = 10.5; 95% CI = 2.7–40.5, p < 0.001) and being to family member of H. pylori positive patients (OR = 10.8; 95% CI = 4.1–28.5, p < 0.001) are the independent risk factors of H. pylori infection.

**Conclusions:** This study supported the role of intrafamilial transmission of H. pylori infection among Thai families. Improvement of personal and family hygiene should be emphasized for prevention of H. pylori infection.

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**Proton Pomp Inhibitors (PPIs): A Marker of Disease Severity in Hospitalized Patients**

Nathalie Saheb, M.D., J. Pepin, M.D., G. Faust, M.D.* Gastroenterologie, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada.

**Purpose:** Proton Pomp Inhibitors (PPIs) are widely prescribed drugs in an hospital setting. Many reviews denounce an overuse of these medications. Our hypothesis is that PPI use correlates with disease severity in hospitalized patients.
Methods: We undertook a retrospective cohort study of the patients hospitalized at the Centre Hospitalier Universitaire de Sherbrooke (Quebec) between January 1st 2003, and June 30th, 2004. Sex, age, length of stay in hospital, PPI use, and death information was collected from 7420 episodes of care, corresponding to 5619 patients. Comorbidities were noted and the severity graded according to the Charlson score (18 criteria). Data was analysed using Cox regression.

Results: 3134 hospitalized patients (42.2%) received PPIs during their hospital stay, of those 43.3% were males, and 56.7% were females. Of the patients on PPIs, 852 (27.2%) were aged 18–64, while 2282 (72.8%) were 65 and over (p = 0.00). The Charlson score was analysed using 4 subgroups (group 1 = no comorbidity, group 2 = 1–3 comorbidities, group 3 = 4–6 comorbidities, group 4 = 7 or more comorbidities). 329 pts (20.9%) were taking PPIs in group 1, compared to 1457 (42.5%) in group 2, 955 (54.2%) in group 3, and 393 (59.5%) in group 4 (p = 0.00). PPIs were prescribed to 439 pts (24.6%) hospitalized for 1–3 days, while they were prescribed to 783 pts (38.4%) hospitalized for 4–7 days, to 728 pts (45.3%) staying for 8–14 days, and to 1184 pts (59.5%) hospitalized for 15 days or more (p = 0.00). Of the pts who died during the study period, 633 (54.6%) were taking PPIs, compared to a 40% use in pts still alive (p = 0.00).

Conclusions: PPI use is related to advanced age, increased comorbidities (higher Charlson score), longer hospitalizations, and higher risk of death. Perhaps our study was not meant to evaluate the misuse of PPIs, our data mostly indicates that PPI use is a reflex of the burden of disease of hospitalised patients, and thus could be a sign of poorer prognosis.

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Pilot Evaluation of a Novel Combination Tablet (PN 100) Containing a Proton Pump Inhibitor and a Nonsteroidal Anti-Inflammatory Drug in Prevention of Upper Gastrointestinal Mucosal Injury


Purpose: To compare the incidence of gastric and duodenal mucosal injury with twice-daily administration of PN100, twice-daily enteric-coated naproxen, and twice-daily naproxen with delayed-release lansoprazole once daily.

Methods: A single-center, randomized, parallel-group study enrolled 60 male and female volunteers aged 40–65 years. After normal baseline endoscopy, subjects received 14 days' treatment with either: (a) twice-daily PN100 (immediate-release lansoprazole 15mg and enteric-coated (EC) naproxen 500mg in a combination tablet), (b) twice-daily EC naproxen 500mg, or (c) delayed-release lansoprazole 15mg capsule each morning and twice-daily naproxen 500mg. The endoscopist was blinded to treatment groups. No mucosal lesions meeting criteria for Lanza Grade 4 injury were identified (p = 0.02). Kruskal-Wallis test among 3 treatment groups). No mucosal lesions meeting criteria for Lanza Grade 4 were present at day 14 in subjects receiving PN100, whereas 53% of subjects receiving EC naproxen and 30% of subjects receiving naproxen and lansoprazole met criteria for Lanza Grade 4 injury (≥25 erosions or hemorrhages or any ulcer). Gastric pH monitoring suggested the possibility of better nocturnal acid suppression with use of twice-daily PN100 than with once-daily delayed-release lansoprazole and twice-daily naproxen.

Conclusions: A combination tablet containing lansoprazole and EC naproxen administered with a morning dose of delayed-release lansoprazole. If these results are confirmed, clinical use of this novel formulation would ensure adherence with gastroprotective therapy when recommended for use with an NSAID.

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Utilization of Electrogastrography To Determine Treatment of Patients with Symptoms of Dyspepsia and Gastroparesis

Charles W. Randall, M.D.∗, Carlo M. Taboada, M.D., Cesar Garza, M.D. GI, Methodist Specialty and Transplant Hospital, San Antonio, TX and Research, Gastroenterology Clinic of San Antonio, San Antonio, TX.

Purpose: Many patients (pts) present to clinics with upper GI symptoms. Dyspeptic pts w/ negative evaluations are often diagnosed w/non-ulcer dyspepsia (NUD). Pts w/ symptoms of delayed gastric emptying (DGE) w/ or w/o collaborating imaging studies may be classified as gastroparesic (G). Empiric therapy is often initiated w/ variable results. The purpose of this study was to follow the efficacy of therapeutic decisions based upon pts' motility patterns.

Methods: Pts presenting to our clinic underwent complete evaluations that included a medical interview, endoscopy, imaging studies & laboratory analysis. The pts were placed into 2 groups based upon symptoms. Those w/symptoms suggestive of DGE were placed in the gastroparesis group (G), while those whose main complaint was epigastric discomfort or pain were put in the dyspepsia group (D). An electrogastrogram (EGG) was performed on each pt & interpreted by 2 physicians. There were 4 main patterns: tachygastria (TG), bradygastria (BG), mixed (combination of BG & TG) & normal (NUD). The TG pts were subdivided into those w/ pre- & postprandial TG & those w/ predominant postprandial TG. Treatments included tricyclics (TCAs) for prolonged TG, (often w/ a preprandial anticholinergic (ACH) added), ACHs alone for postprandial TG, prokinetics (PK) for BG & either a TCA or ACH for NUD. Efficacy was graded as E for remission, S for improved quality of life, & U for unsatisfactory results.

Results: 43 pts were followed for a mean time of 8.2 months. 20 pts w/TG were identified (10 in group D, 9 in group GP). 8 pts had prolonged hypermotility while 12 were primarily TG postprandially. 7 pts were graded E & 13 were S. 3 pts had BG. 1 treated w/erythromycin was graded E, while another was graded U. The third pt was treated w/metoclopramide & judged to be S. In the mixed group, pts were often given a combination of an ACH & PK (given at different times depending upon the predominant phase of the cycle). 3 pts were graded E & 5 were S. In the NUD pts, 7 were graded S & 5 were graded E.

Conclusions: 1. EGG is efficacious in directing therapy of pts w/dyspepsia & gastroparesis.

2. 97.7% of pts noted significant improvements in their quality of life (37.2% graded E; 60.5% were S).

3. Knowing the motility pattern of pts prior to treatment will hasten symptom relief.

4. Long-term follow-up showed symptom relief was continuous.

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Electrogastrographic Results of Outpatients Presenting with Symptoms of Dyspepsia or Gastroparesis

Charles W. Randall, M.D.∗, Carlo M. Taboada, M.D., Cesar Garza, M.D. Research, Gastroenterology Clinic of San Antonio, San Antonio, TX.

Purpose: The utilization of the electrogastrogram (EGG) to distinguish functional from motility disorders of the stomach is gaining in popularity. The purpose of this study was to determine the motility patterns of patients presenting with upper gastrointestinal symptoms.

Methods: 54 patients presented to our outpatient clinic with a variety of complaints that included epigastric discomfort, bloating, nausea or early satiety. Traditional evaluation with endoscopy, imaging studies and laboratory tests had been unrewarding. Patients were divided into 2 groups. Those with nausea, bloating, distension or early satiety (one or more symptoms) were placed in the gastroparesis group (GP). Patients whose primary complaint
was epigastric pain were labeled as having dyspepsia (D). A 3-CPM EGG unit provided the data. The EGG was performed by one dedicated nurse and interpreted by 2 physicians. Pattern analysis was determined as normal, tachygastria, bradygastria, or mixed pattern (a combination of tachygastria and bradygastria).

**Results:** 39 of the patients were female (F) and 15 were male (M). In the D group (F = 25; M = 6) 13 patients had tachygastria (42%); one with bradygastria (3.2%); 5 were mixed pattern (16.1%); and twelve showed normal motility (38.7%). In the GP group (F = 14; M = 9), 18 were tachygastric (78.3%); 2 were bradygastric (8.7%); and 3 had a mixed pattern (13%). None of the GP group had a normal pattern.

**Conclusions:** Tachygastria is the predominant motility disorder in both GP (78.3%) and D (42%) groups. Motility disorders (61.3%) were more common than non-ulcer dyspepsia (38.7%) in patients with dyspepsia. Dyspepsia is more common in females than is gastroparesis (64% vs. 36%). The small number of male patients undermines a statistical conclusion but GP was more common than D in males (60% vs. 40%). No patients with GP had a normal motility pattern.

Knowledge of patient’s motility may direct treatment; this is especially true in patients presenting with GP where empiric therapy with prokinetics is used. Knowledge of patient’s motility may direct treatment; this is especially true in patients presenting with GP where empiric therapy with prokinetics is used.

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**The Profound Stimulatory Impact of Gastrin on Gastric Mucus Production in Helicobacter pylori-Negative Asymptomatic Volunteers: Its Potential Clinical Significance**

**Tomasz Skoczyłas, M.D., Irene Sarosiek, M.D., Katherine Roessler, B.S., Grzegorz Wallner, M.D., Jerzy Sarosiek, M.D.* GI Muscle & Nerve Function Center, GI Res Lab, Kansas University Medical Center, Kansas City, KS and II Department of General Surgery, Medical University of Lublin, Lublin, Poland.**

**Purpose:** Gastrin plays the leading role in regulation of gastric acid secretion as well as mucosal cell proliferation and growth. Although circulating hypergastrinemia and gastric hyperacidity are hallmarks of Zollinger-Ellison syndrome, it is still unclear why peptic ulcers are less likely to develop within the gastric mucosa. The integrity of the gastric mucosa depends upon equilibrium between aggressive factors and protective mechanisms. Although the impact of gastrin on gastric acid and peptic secretion in humans has been a subject of numerous investigations, its impact on the major protective factor gastric mucus still remains to be explored.

**Methods:** The study approved by HSC at KUMC was conducted in 21 asymptomatic, *H. pylori*-negative, volunteers (11F & 10M; mean age of 34, 23–56 range). The gastric juice was collected in basal conditions and during stimulation with pentagastrin (6 µg/kg SC). Freshly aspirated gastric juice was dialedyzed using Multi-Dialyzer (EZ-1, Spectrum, CA), and subsequently lyophilized using freeze-drier (Free Zone; Labconco, MO). The content of gastric mucus in each sample was assessed gravimetrically. Analysis of data was implemented using Sigma-Stat (SPSS, San Rafael, CA).

**Results:** The volume of gastric mucus in basal condition was 51.7 ± 6.0 ml/h but increased 179% to 144.1 ± 8.3 ml/h after pentagastrin administration (p < 0.001), whereas its pH declined from 2.11 ± 0.22 to 1.24 ± 0.02 (p < 0.001). Gastric mucus output, however, after stimulation with pentagastrin increased profoundly by 56% (219 ± 31.3 vs. 118 ± 22.6 mg/h, p < 0.005). Therefore, the concentration of gastric mucus declined only 34% after administration of pentagastrin (1.50 ± 0.19 vs. 2.28 ± 0.24 mg/ml; NS).

**Conclusions:** (1) Presented data indicate that gastrin plays not only the major role in governing gastric acid and peptic secretion but by augmenting gastric mucus output it preserves the balance between aggressive factors and protective mechanisms within the gastric mucosal barrier. 2) Gastrin may represent the major alimatory tract hormone maintaining the integrity of the gastric mucosa, thus preventing mucosal damage by the luminal injurious milieu.

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**Evaluation of Rapid *H. pylori* Stool Antigen Test Before and after Eradication Therapy**

**Akifumi Tanaka, M.D., Kengo Tokunaga, M.D., Kyoto Imase, M.D., Hajime Sugano, M.D., Hitoshi Ishida, M.D., Shin’ichi Takahashi, M.D.* The Third Department of Internal Medicine, Kyorin University School of Medicine, Mitaka, Tokyo, Japan.**

**Purpose:** The *H. pylori* stool antigen (HpSA) test based on enzyme immunoassay is useful method for the diagnosis of *H. pylori* infection. Recent years, the rapid HpSA test based on immunochromatographic method has been developed. The aim of this study was to evaluate the diagnostic accuracy of the rapid HpSA test before and after eradication therapy.

**Methods:** 144 patients were underwent upper gastrointestinal endoscopy with biopsies for the diagnosis of *H. pylori* infection using the culture, histology and rapid urease test. 62 *H. pylori* positive patients were treated with 1-week triple therapy. 6–10 weeks after the end of therapy, the patients were underwent re-endoscopy and received the same biopsy based methods. In addition, the 13C-urea breath test was performed. Stool specimens were collected before and 6–10 weeks after the end of therapy. We evaluated diagnostic accuracy of the rapid HpSA test (Immunocard STAT! HpSA: Meridian Bioscience Europe, Italy) and the HpSA test (Premier Platinum HpSA: Meridian Bioscience, USA) compared with biopsy based methods. Patients were defined as positive for *H. pylori* if culture was positive, or if
Gastric Ulceration and Microsphere Seeding Occur after Intra-Hepatic Yttrium-90 Microsphere Therapy Despite Prophylactic Embolization of the Gastroduodenal Artery

Mary C. Raven, M.D., Shameetha Shah, M.D., James W. Smith, M.D., Moises Yoselevitz, M.D., Babak Etemad, M.D.* Greg Barre. Internal Medicine, Louisiana State University Health Sciences Center; Earl K. Long Medical Center, Baton Rouge, LA and Gastroenterology and Hepatology, Ochsner Clinic Foundation, New Orleans, LA.

**Purpose:** The purpose of this report is to present two consecutive cases of large gastric ulceration occurring after yttrium-90 microsphere infusion for hepatic tumors despite radiographically confirmed ablation of the gastroduodenal artery.

**Methods:** The medical records of two consecutive patients presenting with gastric ulceration after intrahepatic yttrium-90 microsphere therapy were reviewed. Details on the clinical history, visceral angiography, the use of antisecretory medications before and after therapy, EGD, and pathology were reviewed.

**Results:** Two patients having hepatic metastases presented to the interventional radiology department for yttrium-90 microsphere therapy. Each had preprocedural visceral angiography with ablation of the gastroduodenal artery to prevent extrahepatic seeding of microspheres. Success of ablation was confirmed with routine fluoroscopic imaging. Infusion of microspheres occurred without obvious complication via the hepatic artery by an experienced interventional radiologist. Approximately one week after therapy, each patient presented with post prandial abdominal pain, nausea, and vomiting with no hematemesis. CT demonstrated thickening of gastric wall but no other lesions. In each patient EGD demonstrated a large gastric ulcer along the lesser curvature. Ulcers were greater than 2cm and were associated with otherwise normal appearing mucosa in the rest of the stomach. Biopsies revealed ulcerated lamina propria and foreign body microspheres within the specimens. One patient was on omeprazole prior to the procedure. Both required hospitalization for parenteral nutrition and bowel rest after the ulcers were diagnosed.

**Conclusions:** Prophylactic embolization of the gastroduodenal artery prior to intrahepatic yttrium-90 therapy for liver malignancies does not adequately protect against aberrant seeding of gastric mucosa by yttrium microspheres. Severe, symptomatic gastric ulceration requiring hospital admission and parenteral nutrition was a result in both patients. In patients presenting with severe, symptomatic gastric ulceration requiring hospital admission and protect against aberrant seeding of gastric mucosa by yttrium microspheres.

**Conclusions:** The rapid HpSA test is a useful method for the diagnosis of *H. pylori* infection before and after eradication therapy.

Cyclic Vomiting Syndrome Is Associated with Rapid Early Gastric Emptying

Noel R. Fajardo, M.D., G. Richard Locke, III, Nicholas J. Talley, M.D., Ph.D.* Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN.

**Purpose:** Cyclic Vomiting Syndrome (CVS) is described as a paroxysmal, recurrent, and severe vomiting disorder, characterized by stereotypic episodes of intense nausea and vomiting lasting hours to days, which are separated by symptom-free intervals. The cause of CVS is not known. The aim of the study was to describe disturbances of gastric emptying among patients with CVS.

**Methods:** The medical records of patients diagnosed with Cyclic Vomiting Syndrome (ICD 536.2) over an 8-year period (1996–2003) at our institution were extracted and individuals who underwent scintigraphic measurement of gastric emptying were identified. Concomitant comorbidities (e.g. diabetes, liver disease, previous abdominal surgeries, medications that may affect gastric motility, etc.) were excluded from the analysis. Gastric emptying was performed by scintigraphy (131I-egg meal). Gastric Emptying at 1, 2 and 4 hours (GE1h, GE2h and GE4h) was obtained as proportion of isotope emptied (%). Subjects were considered to have an abnormal test if gastric emptying endpoints were outside reference values (GE1h 11–39%, GE 2h 40–76%, GE4h 80–94%) previously published from our institution. GE2h of CVS patients were compared to the GE2h of a consecutive cohort of 364 patients who underwent GE study at our institution. Wilcoxon test was used to compare differences between groups.

**Results:** 64 adults were diagnosed to have CVS, 50 (28M/22F, mean age 33 ± 2 years, range 18–65 years) met inclusion/exclusion criteria and 21 (42%) (15M/6F, mean age 36 ± 3 years, range 19–65 years) underwent gastric
emptying study. There was no significant difference in age (30 ± 2 vs. 36 ± 3, in years), gender (44% male [95% CI 28–62%] vs. 71% male [95% CI 50–86%]) and BMI (25 ± 1 vs. 25 ± 1, in kg/m²) between those who did and did not undergo a GE study. 62% (13/21) patients had accelerated GE1hr, 52% (11/21) patients had accelerated GE2hr and 19% (4/21) had accelerated GE4hr. There was no significant difference in age (39 ± 4 vs. 33 ± 4, in years), gender (80% male [95% CI 49–94%] vs. 64% male [95% CI 35–84%]) and BMI (25 ± 4 vs. 24 ± 4, in kg/m²) between those who had normal and accelerated GE2h. The odds ratio of a patient with CVS having a rapid GE2 as compared to controls was 13 (95% CI 5–33).

Conclusions: CVS is associated with a rapid early-phase (1 and 2 hours) gastric emptying. Likewise, patients with CVS are 13 times as likely to have accelerated GE2 as compared to controls. This provides physiologic evidence suggesting that CVS may be due to a disorder of gastric function.

Detection of H. pylori in Urease Test Negative Gastric Samples by a Novel Multiplex PCR Assay

Xiangwen Meng, Ph.D., Hongjun Zhang, Ph.D., Tat-Kin Tsang, M.D.*
Evanston Northwestern Healthcare, Northwestern University Feinberg School of Medicine, Evanston, IL.

Purpose: All patients with dyspepsia, either newly or previously diagnosed, should be tested for H. pylori infection. The CLOtest assay is widely used in clinical practice to detect the urease enzyme of H. pylori in gastric mucosal biopsies and many physicians consider it as a gold standard method. However, this is not sensitive enough to diagnose H. pylori infection. We have developed a novel one-step multiplex PCR detection system that can amplify 10 DNA fragments from 5 DNA regions in the genome of H. pylori at the same time. The objective of this study was to assess the diagnostic value of this new multiplex PCR assay to detect H. pylori infection, and further evaluated the negative results from the CLOtest.

Methods: This study was performed on the same urease test negative gastric specimen, which had been detected by CLOtest from 276 individuals with dyspepsia symptoms undergoing endoscopy at Evanston Northwestern Healthcare. The CLOtest was performed first and if the result was negative, the negative specimen was collected from the CLOtest gel. From this specimen, the DNA was isolated and was performed the one-step multiplex PCR.

Results: Positive results were achieved in 42% (116/276) with multiplex PCR from the H. pylori negative samples tested by CLOtest.

Conclusions: Our results indicate that our multiplex PCR method is a highly specific and sensitive method in the detection of H. pylori. The results of H. pylori tested by current methods should be carefully reviewed to ensure that the result is not a false-negative and to obtain the correct diagnosis it would be better that the negative samples of CLOtest were further confirmed by the multiplex PCR assay.

Eosinophilic Gastritis—A Rare Entity Masquerading as Cyclical Vomiting

Razi M. Arifiudin, M.D., Matthew M. Batchi, M.D., George Philips, Benedict J. Maliakkal, M.D.* Digestive and Liver Disease Unit, University of Rochester Medical Center, Rochester, NY.

Purpose: Primary eosinophilic gastritis (EG) is a rare condition characterized by the accumulation of eosinophils in the stomach. Presenting symptoms are non-specific and include anorexia, diarrhea, abdominal pain, nausea and vomiting. Histology reveals clustered eosinophilic infiltrates within the lamina propria and submucosa. Diagnosis is confirmed by ruling out secondary causes of eosinophilia. Here we report a rare case of EG previously misdiagnosed as cyclical vomiting syndrome. The patient is a 41-year-old female who presented with recurrent emesis. She had a history of intermittent epigastric abdominal pain, nausea, vomiting, and}

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Characteristics of Patients with Idiopathic Delayed Gastric Emptying in a Rural Clinical Practice: A High Incidence of Abnormal 3 Hour Glucose Tolerance Test (GTT), Family History of Diabetes and Reported Weight Gain

Howard P. Monsour, M.D.,* Nancy Walsh, R.N., M.S.N, C.S., A.N.P.
Gastroenterology and Hepatology, Gastrointestinal and Liver Associates, Granbury, TX.

Purpose: To explore the clinical, laboratory and endoscopic characteristics of patients with delayed gastric emptying.

Methods: We retrospectively reviewed 90 consecutive cases of delayed gastric emptying from May 2002 to May 2004. Gastric emptying was assessed by having the patient eat scrambled egg whites labeled with 1 mCi Tc-99m Sulfur Colloid on 2 slices of buttered toast. Images at 0, 20, 60, 120, and 240 minutes were obtained with the patient standing. Gastric emptying was assessed by having the patient eat scrambled egg whites labeled with 1 mCi Tc-99m Sulfur Colloid on 2 slices of buttered toast. Images at 0, 20, 60, 120, and 240 minutes were obtained with the patient standing. Images at 0, 20, 60, 120, and 240 minutes were obtained with the patient standing.

Results: Ninety consecutive patients were identified. The mean age of the patients was 50 years. Eighty three percent (75/90) were female and 17% (15/90) were male. The mean and median Body Mass Index (BMI) was 27. Three percent (3/90) had a previous viral illness before symptoms began. Nausea with or without vomiting was present in 73%. Complaints of eructation were found in 66%, and epigastric pain or persistent dyspepsia in 62%. Less common was abdominal bloating (46%), antral chest pain (14%), and sore throat (12%).

Abnormal bowel habits were present in 54 of the 90 patients, with 53% (29) having diarrhea (>6 bowel movements per day), 35% (19) reported constipation (one bowel movement >3 days) and 11% reported having alternating diarrhea with constipation. Of the remaining 75 patients 51 had a 3 hour GTT. Twenty nine percent (15/51) were positive. Sixty seven percent (10/15) of these had a positive family history for diabetes. Seventy three percent reported weight gain. The median BMI was 30 (mean 29) as compared to 27 for the entire group. Of those tested, abnormal transaminases were found in 20% (10/50). The median BMI of this subgroup was 27 with 30% (3/10) having an abnormal GTT.
An EGD was performed in 70/90 patients. The primary findings were gastritis, 56% followed by esophagitis. Fourteen percent had documented bile reflux.

**Conclusions:** The majority of patients who presented with UGI complaints, that were ultimately found to have an abnormal Gastric Emptying Study, were women. An abnormal glucose tolerance test was found in nearly one third of patients who otherwise had no previous history of diabetes. These patients were heavier (BMI 30 vs. 27), had a strong family history of diabetes, and reported weight gain (73%). Diarrhea was more common in these patients.

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**The Changing Pattern of Upper GI Bleeding over the Last 8 Years**

Sinan M. Katty, M.D., Leonardo Salese, M.D., C. S. Pitchumoni, M.D.*

**Gastroenterology, St. Peter’s University Hospital, New Brunswick, NJ.**

**Purpose:** Changes in the pattern of upper gastrointestinal bleeding over the past 8 years may have occurred given the increase in the availability of selective Cox-2 inhibitors and effective treatment of Helicobacter pylori. This study was designed to investigate the above hypothesis.

**Methods:** Four hundred and twenty nine charts from a university hospital with documented gastric and duodenal ulcers between the years 1996 and 2004 were analyzed. An Excel database was created documenting patient demographics, endoscopic findings, use of NSAIDs, results of helicobacter testing, and admission laboratory data. The data was analyzed specifically to document patterns in the presumptive ulcer etiology, in particular NSAIDs, helicobacter colonization, and other causes of upper GI ulcers.

**Results:** The number of patients with UGI bleeding admitted in 1996 (60), 1997 (45), 1998 (48), 1999 (53), 2000 (64), 2001 (37), 2002 (37), 2003 (44), 2004 (41) did not significantly change. [Figure 1]

![Percent Etiologies of Upper GI Bleeds](image)

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**UPN H. pylori Infection in Patients with Nonulcer Dyspepsia**

Tai-Kin Tsang, M.D.*, Xiangwen Meng, Ph.D., Hongjun Zhang, Ph.D.

Evanston Northwestern Healthcare Research Institute, Northwestern University Feinberg School of Medicine, Evanston, IL.

**Purpose:** Many factors may account for the controversies with regard to the link between H. Pylori infection and nonulcer dyspepsia (NUD). One important factor is the reliability of the diagnostic test for H. Pylori. One-step multiplex PCR has been developed and the higher sensitivity and specificity has been achieved. This study aimed to implore the effect of H. Pylori treatment on NUD patients based on the indication given by the novel one-step multiplex PCR assay.

**Methods:** 41 patients with dyspepsia, who underwent EGD were diagnosed by CLOtest and regular pathological examination (immunohistochemistry and H&E staining) as negative cases but diagnosed by one step multiplex PCR as positive cases, named as UPN H. pylori patients, were enrolled in this study. The group of patients was treated with Prevpac. About two to three weeks after treatment, these patients were examined with second EGD and one step multiplex PCR was performed on the biopsy. The severity of upper GI symptoms was measured on a ten-point scale. The treatment responses were evaluated in view of the proportion of patients who improved points on the initial dyspepsia summary score. Nonresponders, partial responders and total responders were designated according to less than 40%, between 40% and 80% and more than 80% symptom improvement respectively.

**Results:** Of 41 patients, 44% (18/41) had complete symptom responses, 39% (16/41) had partial responses, and 17% (7/41) had non-response. In 61% (25/41) patients, the second PCR detection on biopsy after treatment turned into negative.

**Conclusions:** This study showed that the H. Pylori – positive patients who were revealed by one-step multiplex PCR beyond CLOtest and pathological examination do respond well to the treatment with Prevpac. Further continued evaluation of the nonulcer dyspepsia and H. pylori treatments based on the more reliable test, one-step multiplex PCR, is needed to aid in the management.

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**Botulinum Toxin Injection at the Pylorus for Treatment of Severe Refractory Idiopathic Gastroparesis Guided by Electrogastrography (EGG)**

Raonof E. Hilal,* Talal E. Hilal, Sandy Atwell. Gastroenetrology, Center for Advanced Gastroenterology, Maitland, FL.

**Purpose:** To evaluate the benefit of Botulinum injection at the pylorus for idiopathic refractory gastroparesis with tachygastria and tachyduodenum as followed by serial Electrogastrography (EGG) pre and post therapy.

**Methods:** This case study report of a patient with severe refractory gastroparesis that was assessed by EGG prior to Botulinum injection (BoTox) at the Pylorus with and EGD. A total of 100 units were injected circumferentially around the pylorus (25 units in each quadrant × 4) and followed serially with EGG to document neuroelectrical changes. This was correlated with clinical symptomatology 1, 2 and 3 months post injection with BoTox.

**Results:** Post BoTox injection at the pylorus, the patient’s quality of life improved dramatically; the Electrogastrography(EGG) revealed a decrease in Tachygastria, Tachy-duodenum and relief of pyloric spasm. Amazingly, the patient experienced complete relief of symptoms and was able to discontinue all medications. The EGG correlated strongly with her clinical resolution of symptoms.

**Conclusions:** Treatment with BoTox as guided by EGG appears to be promising therapy for a subset of patients with idiopathic refractory gastroparesis with gastric and duodenal dystrythmia.
Extra-Ordinary Cases – Lives Saved, Job Restored and Problems Solved Due to Positive H. pylori Identified by Multiplex PCR

Tat-Kin Tsang, M.D.,* Xiangwen Meng, Ph.D., Hongjian Zhang, Ph.D.
Evanston Northwestern Healthcare Research Institute, Northwestern University Feinberg School of Medicine, Evanston, IL.

Purpose: Upper gastrointestinal diseases are well recognized and in majority of cases, etiologies are well recognized and treatments are successful. However, there are cases with no obvious etiologies, which make treatments difficult. In this report, we present four extra-ordinary cases, for which multiplex PCR assay is helpful in diagnosis and treatments.

Methods: A novel one-step multiplex PCR method would amplify 10 DNA fragments from five regions in the genome of H. Pylori to diagnose H. Pylori infection.

Results: Case 1: A 58 years old white female, whose father had gastric carcinoma, who has had epigastric pain for 2 years. She has been on PPI but no improvement. Her father has gastric cancer, and biopsies were performed for multiple PCR which turned positive, but negative for CLOtest and pathology. She was treated with Prevpac for 2 weeks with total resolution of symptoms, and repeat gastroscopy showed negative PCR for H. Pylori.

2. 31 years old white female who has had epigastric pain for many years. Multiple gastroscopies revealed gastritis and esophagitis. PPI's did not improve her symptoms. Recent gastroscopy clamed H. Pylori by multiplex PCR. Two weeks of Prevpac totally eradicate the old symptoms and H. Pylori.

3. 55 years old policemn who suffered from GERD with regurgitation for 6 months for the pain of suffocation. He had gastroscopy which showed positive H. Pylori by multiplex PCR. Two weeks of Prevpac eradicated the H. Pylori and 80% symptom resolution.

4. 53 years old white male salesman who has had two months history of GERD with hoarseness for the pain he had to quit his job. Gastroscopy showed H. Pylori by multiplex PCR. He was treated with Prevpac for 2 weeks with some improvement. He was then treated with PPI, tetracycline, metronidazole, peptobismol with 80% improvement. He could back to work.

Conclusions: Diagnosis of H. Pylori can be difficult. The negative CLOtest and pathology may not mean negative H. Pylori infection. The above cases demonstrate that multiplex PCR is the ultimate diagnostic test to clarify the presence of H. Pylori infection. The adequate diagnosis provides adequate treatments, which resist in extraordinary treatment results.

COPD Is a Predictor of Mortality in PEG Consult Patients

Gita A. Koshy, Indira Donnepudi, Nejat Kiwici, Edward Norkas, Hilary Hertan.* Gastroenterology, Our LADY of Mercy Medical Center, Bronx, NY.

Purpose: Patients with respiratory problems present challenges for anesthesia during PEG placement. Yet, to our knowledge, there have been no randomized studies in the US that examine respiratory conditions as an independent risk factor for death in patients undergoing PEG.

Objective: To determine if respiratory status predicts a higher risk of mortality in PEG consult patients.

Methods: A sample of 191 consecutive patients [mean age of 81 yrs (range 49–105 yrs), 58% female] referred for PEG placement between March 2003 and March 2005 were included in the study. Twenty-one percent of patients were being seen for new PEG insertion vs. 79% for replacement PEG. Correlation between Patient comorbidity, age, gender, BMI, race, community vs. NH, new PEG vs. replacement, reason for PEG, MICU vs. floor, length of stay (LOS), clinical lab values, nutritional status classification score and outcome (discharge vs. death) was assessed. Data was examined using Student t-tests, chi-square analysis and logistic regression analysis.

Results: Patients who died and were discharged had similar ages (P = .6630), gender distribution (P = .828), race (Caucasian vs. African American vs. Hispanic, P = .371) and place of residence (community vs. nursing home, P = .272). However, patients who died, more often came from the MICU (P < .0005) and had longer LOS than discharge patients (mean of 31 vs. 21 days, P = .0231). Logistic regression analysis was used to determine which, of 13 comorbid conditions (asthma, CAD, cancer, CHE, COPD, dementia, diabetes, HTN, hypothyroidism, psychiatric, renal insufficiency, stroke, deep vein thrombosis) were risk factors for death among PEG consult patients. Previously unrecognized, COPD was found to be the most powerful risk factor for death (13.3-fold increased risk, P = .001) vs. CAD (10.8-fold, P = .001), renal (6.3-fold, P = .014), HTN (6.3-fold, P = .012), stroke (1.6-fold, P = .001), and psychiatric disorders (1.5-fold, P = .026). The analysis also determined that asthma, cancer, CHE, dementia, hypothyroidism, deep vein thrombosis, in addition to patient age, gender, place of residence, PEG insertion, and PEG type (new vs. replacement) were not risk factors for death (all P > .05).

Conclusions: Comorbidities that are risk factors for death among PEG patients is important clinical information that the gastroenterologist may use during patient evaluation. Our findings identify, COPD as a strong predictor of death in patients undergoing PEG.

PANCREATIC/BILIARY

Post-Endoscopic Retrograde Cholangiopancreatography Pancreatitis: Retrospective Multicenter Survey (24 Institutions)

Koichi Fuwakawa, M.D., Yutaka Aoyagi, M.D.,* Rintaro Narisawa, M.D., Yoshishisa Tsukada, M.D., Teruo Sekine, M.D., Nobukhiro Akiyama, M.D., Takasi Tomidokoro, M.D., Tomoteru Kamimura, M.D., Toru Takahashi, M.D., Yoshikazu Yuzanigawa, M.D., Atsu Sekine, M.D. Gastroenterology, Niigata City General Hospital, Niigata, Japan; Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, Niigata, Japan; Internal Medicine, Niigata Prefectural Shibata Hospital, Shibata, Niigata, Japan; Internal Medicine, Niigata Prefectural Cancer Center Hospital, Niigata, Japan; Internal Medicine, Mokuriren Nagoa Chuo General Hospital, Nagoa, Niigata, Japan; Gastroenterology, Saiseikai Nagaoka Second Hospital, Nagaoka, Niigata, Japan; Internal Medicine, Nagaoka Red Cross Hospital, Nagaoka, Niigata, Japan; Internal Medicine, Shinnakuen Hospital, Niigata, Japan and Internal Medicine, Niigata Prefectural Yoshiwa Hospital, Yotani, Niigata, Japan.

Purpose: We conducted a retrospective study of patients hospitalized for the treatment of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) between April 1993 and March 2002, to investigate causative factors and reasons for exacerbation of PEP.

Methods: 1. Comparative study based on classification by pancreatitis severity: We divided the cases into two groups (mild versus moderate and severe), based on the Japan Ministry of Health, Labour and Welfare classification of severity of pancreatitis. 2. Comparison between institutes with high and low rates of PEP: We divided institutes into two groups depending on the rate of PEP.

Results: The rate of PEP remained constant. There were 57 cases of PEP among the total of 10717 ERCP cases, an occurrence rate of 0.532%. There were significantly more cases in which contrast media was not excreted from the minor duodenal papilla than there were cases with this excretion. The time between the completion of ERCP and onset of abdominal pain was significantly shorter in the moderate and severe group than in the mild group. In contrast, the diagnosis was significantly delayed in the moderate and severe group, even though symptoms developed earlier. Other items that differed significantly between the two groups of institutes included whether or not patients were instructed to restrict alcohol and fat intake after the operation.

Conclusions: The incidence of PEP has remained constant. To prevent the occurrence of PEP we must consider the high risk group. It is necessary to make the system of early check up PEP and patients education.
Glycemic Load, Glycemic Index and Risk of Cholecystectomy in Women
Chung-Jyi Tsai, M.D., F.A.C.G.,* Michael Leitzmann, M.D., Walter Willett, M.D., Edward Giovannucci, M.D. Division of Digestive Diseases and Nutrition, University of Kentucky Medical Center; Division of Cancer Epidemiology and Genetics, National Institutes of Health and Channing Lab., Department of Medicine, Harvard Medical School and Brigham and Women’s Hospital.

Purpose: High-carbohydrate diets with a high glycemic response may exacerbate the metabolic consequences of the insulin resistance syndrome. The effect of glycemic load and glycemic index on the incidence of gallstone disease is unclear.

Methods: We examined the associations between high-carbohydrate diets with a high glycemic response and the risk of cholecystectomy in a cohort of U.S. women who had no history of gallstone disease. As part of the Nurses’ Health Study, the women reported on validated questionnaires every two years both their carbohydrate intake and whether they had undergone cholecystectomy. A validation study of the self-reported cholecystectomy with gallstones was conducted. We calculated the average dietary glycemic index for each woman by summing the products of the carbohydrate content per serving for each food multiplied by the reported average number of servings of that food per day, times its glycemic index, and then divided this sum by the total amount of daily carbohydrate intake. We also calculated glycemic load by multiplying the carbohydrate content of each food by its glycemic index, then multiplied this value by the frequency of consumption and summed the values from all foods. Multivariate analyses were performed using Cox proportional hazards regression model.

Results: During 932,676 person-years of follow-up among 70,408 women from 1984 to 2000, we ascertained 5,771 new cases of cholecystectomy. After adjusting for known or suspected risk factors in a multivariate model, the relative risk for the highest compared with the lowest quintile of dietary carbohydrate was 1.35 (95% C.I., 1.17 to 1.55, P for trend <0.0001). The relative risks for the highest compared with the lowest quintile were 1.50 for glycemic load (95% C.I., 1.32 to 1.71, P for trend <0.0001) and 1.32 for glycemic index (95% C.I., 1.20 to 1.45, P for trend <0.0001). Independent positive associations were also seen for intakes of starch and sucrose. We repeated the multivariate analyses within subgroups of potential confounding variables to examine if the association was modified by risk factors for gallstones. The positive associations persisted and there was no effect modification.

Conclusions: Our findings suggest that a higher consumption of glycemic load and glycemic index may increase risk of cholecystectomy in women.

APACHE-II Survey Risk Scoring System

Methods: Binary logistic regression was performed to assess if obesity is a risk for SAP and to determine the clinical factors associated with severe disease. Serum levels of IL-6, MCP-1 (early markers) and CRP and Ranson’s score (later markers) were compared between obese and non-obese patients with AP.

Results: Admission APACHE-II (AUC: 0.893) and APACHE-II cut-off value of 9 showed a sensitivity of 84%, specificity 82%, positive predictive value 52%, negative predictive value 96% and accuracy 83%. BMI was identified as a significant risk for SAP (OR: 2.8, p = 0.048). CRP levels and Ranson’s score were significantly higher in obese than non-obese patients with AP (p = 0.0001 and p = 0.021 respectively). Admission IL-6 and MCP-1 levels showed a trend toward higher levels in obese patients but did not reach statistical significance (p = 0.368 and p = 0.325 respectively).

Conclusions: Obesity is an independent risk for severe acute pancreatitis. Admission APACHE-II score is not more accurate than APACHE-II. Our study results suggest that obesity increases the severity of AP by amplifying the inflammatory response to injury. [figure 1]

Activated AKT and ERK Expression May Predict Survival after Surgery in Pancreatic Carcinoma
Krishideep S. Chaudha, M.D., Jennifer Black, M.D., Thauer Khoury, M.D., John Gibbs, M.D., Jinhhee Yu, Ph.D., Charles LeVae, M.D., Milind M. Javle, M.D.* Department of Internal Medicine, State University of New York at Buffalo, Buffalo, NY; Department of Gastrointestinal Oncology, Roswell Park Cancer Institute, Buffalo, NY; Department of Pathology, Roswell Park Cancer Institute, Buffalo, NY, Department of Surgery, Roswell Park Cancer Institute, Buffalo, NY and Department of Biostatistics, Roswell Park Cancer Institute, Buffalo, NY.

Purpose: Less than 20% of patients (pts) with pancreatic cancer are alive, 5 years after surgical resection. EGFR- signaling pathway activation may lead to an aggressive disease course. Prior studies demonstrated increased EGFR protein expression in pancreatic cancer. However, there are limited data regarding downstream activation of EGFR signaling. We investigated expression of EGFR, ERK, AKT and their phosphoforms (p-) and correlated these with clinical outcome.

Methods: Thirty-nine consecutive cases of pancreatic carcinoma treated with surgical resection, from 1996–2002 were included. Immunohistochemical staining of paraffin embedded blocks was performed using monoclonal antibodies against EGFR, ERK, p-ERK, AKT and p-AKT. Standard immunoperoxidase technique was used to detect the avidin-biotin peroxidase complex. Staining in tumor tissue was visually scored using histoscore method. Two pathologists (CL, TK) independently scored the protein expression. Clinical data were obtained in accordance with IRB approved protocol.

Results: Pts characteristics were as follows: sex-17 males, 22 females; median age- 66 years (range: 38 to 84); AJCC Stage I-3 pts, Stage II/III-32 pts and Stage IV-4 pts. Tumor was grade 1 in 4, grade 2 in 17 and grade 3 in 18 cases (WHO classification). Additional therapies included chemotherapy
EGFR Related Signaling Pathway Has Prognostic Significance in Cholangiocarcinoma

Krisideep S. Chadha, M.D., Thaer Khoury, M.D., Charles LeVae, M.D., Ph.D., Jihnhee Yu, Ph.D., Milind Javle, M.D.∗ Department of Medicine, State University of New York, Buffalo, NY; Department of Pathology, Roswell Park Cancer Institute, Buffalo, NY; Department of Biostatistics, Roswell Park Cancer Institute, Buffalo, NY and Department of Gastrointestinal Oncology, Roswell Park Cancer Institute, Buffalo, NY.

Purpose: Overexpression of signaling proteins including EGFR, Akt, MAPK and COX-2 was reported in cholangiocarcinoma cell lines. However, clinical prognostic value of these markers is unknown. No prior study correlated the expression of these signaling proteins with clinical outcome. Further, co-expression of these proteins is undefined. Co-expression may reflect cross-talk between signaling pathways. In this clinicopathologic study, we report the overexpression and co-expression of EGFR and related signaling proteins in cholangiocarcinoma describe their relationship to clinical outcome.

Methods: Twenty-four consecutive cases of cholangiocarcinoma treated from 1996 – 2002 at Roswell Park Cancer Institute were included. Immunohistochemical staining of paraffin-embedded tissue sections was performed using antibodies against Akt, p-Akt, MAPK, p-MAPK, COX-2, EGFR and p-EGFR. Two pathologists (JG, TK) independently scored the protein expression and there was full concordance. Clinical data were obtained in accordance with IRB approved protocol.

Results: COX-2, Akt, and p-MAPK were commonly expressed in biliary cancers (91%, 88% and 74% of malignant cells respectively). EGFR (50%) and p-EGFR overexpression (13%) was also detected. There was a significant association between EGFR and p-EGFR (p = 0.027) as well as Akt and p-Akt (p = 0.017) expression in tumor tissue. A noteworthy association was shown between MAPK (ERK) and p-Akt (p = 0.054). Multivariate analysis using the Cox-proportional hazard model identified use of combined modality therapy [Hazard ratio (HR) = 0.185, p = 0.0008] and p-AKT [HR = 0.238, p = 0.0373] as the best predictors of overall prognosis.

Conclusions: Activation of EGFR signaling pathway is commonly seen in cholangiocarcinoma. Expression of p-Akt and use of combined modality therapy may predict favorable prognosis.

Endoscopic Ultrasound Versus Cholangiography for the Diagnosis of Biliary Disorders – Meta-Analysis of Prospective Controlled Trials (PCT)

James E. Lusby, M.D., Pankaj Singh, M.D.∗ Gastroenterology, Scott & White Memorial Hospital, Temple, TX and Gastroenterology, Central Texas VA Health Care System, Temple, TX.

Purpose: There is no consensus on the best approach (EUS versus ERCP) for diagnosing biliary disorders. Our aim was to compare the diagnostic accuracy of the EUS and ERCP for the biliary disorders using meta-analysis.

Methods: Literature was systematically searched for PCT that compared EUS and ERCP for the diagnosis of the biliary disorders (CBD stone, biliary pancreatitis and extra-hepatic biliary obstruction). The primary outcome was proportion of patients in whom correct diagnosis of biliary disorder could be established. Secondary outcome was comprised of complication rate of the diagnostic procedure. Gold standard for the diagnosis of CBD stone and biliary pancreatitis was stone extraction by endoscopic sphincterotomy or intra-operative stone extraction. Subjects who had normal EUS, and ERCP was not performed, follow up of minimum of 6 months was essential to categorize patients not having CBD stone. Malignant structure was defined as tissue diagnosis and/or evidence of mass with metastases. Stricture was defined as benign if both EUS and ERCP were non-diagnostic and subjects were followed for minimum of 12 months. For the purpose of Intention to treat analysis, subjects with unsuccessful ERCP and/or EUS were included in the study. Sensitivity, specificity and accuracy of the EUS and ERCP were determined and compared.

Results: Ten controlled trials with 861 subjects were identified for the meta-analysis. A total of 809 of these patients underwent EUS and 775 patients underwent ERCP. EUS was performed prior to ERCP in all participants. Five studies were for CBD stone, two for biliary pancreatitis and three for the evaluation of extra-hepatic biliary obstruction. There was no significant difference in the overall accuracy of the EUS and ERCP. Analysis of subgroups (biliary stone; biliary stricture) showed no significant difference in the diagnostic accuracy. Complication rate was higher with diagnostic ERCP as compared to EUS (2% versus 0.2%; p = 0.02).

Conclusions: Pooled analysis of PCT showed similar diagnostic accuracy of EUS and ERCP for biliary disorders. Since ERCP was associated with significantly higher complication rate as compared to EUS, EUS should be the preferred diagnostic tool for biliary disorders.

Initial Intravenous Hydration in Acute Pancreatitis Contributing to Unchanged Mortality 1994 and 2004

Robin Baradarian, M.D., Tejal Shah, M.D., Jian Jun Li, M.D., Scott Tenner, M.D., M.P.H.∗ Division of Gastroenterology, Maimonides Medical Center, Mount Sinai School of Medicine, Brooklyn, NY.

Purpose: Due to advances in critical care management, mortality from acute pancreatitis has substantially decreased over the last 3 decades. However, despite an initial decrease in mortality from acute pancreatitis, several investigators have found that the mortality now persists at 6–8% over the past decade.

Methods: In order to determine the reasons behind the persistent mortality over the last decade, we evaluated all patients’ records with acute pancreatitis in 1994 and 2004. Charts were reviewed to determine the underlying factors, including initial management that may have led to unnecessary morbidity and mortality.

Results: In 1994, there were 258 patients with acute pancreatitis admitted compared to 266 patients in 2004. During these two years, the mortality rate was unchanged, 7.0% in 1994 (18 deaths) vs 7.1% in 2004 (19 deaths). There was no significant difference between the groups regarding etiology, comorbidities, age, Ranson or APACHE score (p > 0.05). All patients had severe disease defined by the Atlanta Symposium. There was no difference in the number of patients who had renal insufficiency, cardiovascular insufficiency, pulmonary insufficiency, GI bleeding. There were no differences in admissions to ICU, surgical intervention, late complications, including necrosis. In both groups of patients, intravenous hydration was less than expected during the first 6 hours and 24 hours (p < 0.05). In 1994, 138 ± 80 cc/hr for the first 6 hours, 160 ± 60 for the first 24 hours was given. In 2004, 148 ± 88 cc/hr for the first 6 hours and 144 ± 77 for the first 24 hours was given. There were no differences in the HCT or change in the hematocrit between the two groups. All but one patient had presented with HCT less than 47 (admission HCT). In 1994, a change in HCT of less than 1 point over the first 24 hours was seen in 8 patients, 1–3 points, in 7 patients and greater than 3 in 3 patients. In 2004, a change in HCT of less than 1 point was seen in 6 patients, 1–3 points in 10 patients, and greater than 3 points in 3 patients. In this select population of patients, only a hematocrit at 48 hours
correlated with severity (APACHE), p = 0.03. New onset renal insufficiency was the most common cause of morbidity in both 1994 and 2004.

**Conclusions:** We conclude that the unchanged morbidity and mortality of patients with acute pancreatitis over the last decade is related to a persistent failure to adequately hydrate patients early in the course of the disease.

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**The Role of Endoscopic Ultrasound Guided Fine Needle Aspiration in Distinguishing Pancreatic Cystic Lesions. An Academic Institution’s Experience**

Bhavani Moparty, M.D., Roberto Logrono, M.D., William H. Nealon, M.D., Irving Waxman, M.D., Gottumukkala S. Raju, M.D., Pankaj J. Pasricha, M.D., Manoop S. Bhutani, M.D.* Internal Medicine, University of Texas Medical Branch, Galveston, TX; Pathology, University of Texas Medical Branch, Galveston, TX and Surgery, University of Texas Medical Branch, Galveston, TX.

**Purpose:** Distinguishing mucinous from non-mucinous cystic lesions of the pancreas often constitutes a diagnostic dilemma. Various centers have conflicting results in their ability to detect mucin and appropriately reach a diagnosis based on endoscopic ultrasound (EUS) guided fine needle aspiration (FNA). The aim of this study is to assess the ability of cytology from EUS guided FNA to reach a diagnosis to differentiate a mucinous from non-mucinous lesion.

**Methods:** We reviewed records of patients who underwent EUS of pancreatic cystic lesions. If FNA was performed and a mucinous neoplasm was suspected, aspirate was studied for presence of mucin and cytomorphology. FNA results were compared to final diagnosis if surgery was performed.

**Results:** Cytology revealed a diagnosis in 28/30 (93%). When results of EUS FNA were compared to final surgical pathology, FNA accurately made a diagnosis in 10/11 cases with a sensitivity of 100% and specificity of 89% for detection of malignancy. Accuracy was 100% for identification of mucin and mucinous cystic neoplasms on FNA.

**EUS FNA Results**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>8 (26%)</td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Mucinous cystic neoplasm</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Mucinous cystadenoma</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Intraductal papillary mucinous neoplasm</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Solid pseudopapillary neoplasm</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Non-diagnostic</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
</tr>
</tbody>
</table>

**Conclusions:** Our institution’s results indicate that in the appropriate clinical and imaging setting, EUS guided FNA with cytology and analysis for mucin is an important test in distinguishing pancreatic cystic lesions and guiding further management.

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**Isolated Elevation in Pro-Carboxypeptidase A Is Specific for Pancreatic Cancer**

Dengda Tang, M.D., John M. Davis, M.D., Arthur A. Topilow, M.D., Charles Gilvarg, Ph.D.∗ Oncology Services, Jersey Shore University Medical Center, Neptune, NJ and Department of Molecular Biology, Princeton University, Princeton, NJ.

**Purpose:** Carboxypeptidase A (CPA) is a digestive zymogen produced from its pro-form (Pro-CPA) in the pancreas. A new assay that can measure serum levels of both CPA and pro-CPA was recently developed. Both levels are significantly elevated in pancreatitis. Isolated elevation in Pro-CPA was found in patients with pancreatic cancer. Shamamian et al. found out that 22 out of 34 patients with pancreatic cancer have isolated elevation in Pro-CPA. More importantly, all 7 patients with stage I and stage II pancreatic cancer had elevated Pro-CPA. These findings made Pro-CPA a very sensitive diagnostic tool for pancreatic cancer, especially early pancreatic cancer. This study is to examine the specificity of the assay.

**Methods:** Consecutive patients with cancer other than pancreatic cancer presented to Jersey Shore Medical Center oncology service were consented for the study (n = 45). CPA and Pro-CPA levels were measured.

**Results:** Of the 45 patients, 42 (93%) had neither elevated CPA or Pro-CPA. The other 3 patients (7%) had elevated Pro-CPA, but all 3 also had elevated CPA. Likely all these patients had subclinical pancreatitis. [Figure1]

**Conclusions:** Isolated elevation in Pro-CPA is potentially a very sensitive and specific diagnostic test for pancreatic cancer, especially for early pancreatic cancer. Larger clinical trials are warranted.

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**Arterial Infusion Chemotherapy and Biliary Stenting for Unresectable Hilar Cholangiocarcinoma**

Shinichi Mezawa, M.D., Hisato Homma, M.D., Takehide Akiyama, M.D., Sho Takahashi, M.D., Kazuhiko Koike, M.D., Kenichiro Hirata, M.D., Katsuhisa Kagawa, M.D. Gastroenterology Center, Tokeidai Hospital, Sapporo, Hokkaido, Japan.

**Purpose:** Unresectable hilar cholangiocarcinoma are associated with a very poor prognosis. The feasibility and efficacy of arterial infusion chemotherapy of 5-fluorouracil and Gemcitabine with biliary drainage by tube and metal stent insertion were evaluated.

**Methods:** From January 2002 to December 2004, we treated 10 patients with unresectable hilar cholangiocarcinoma. Continuous intra-arterial chemotherapy was administered using percutaneously implantable port-catheter system with the tip fixed at the gastroduodenal artery with coils and side hole opened at the common hepatic artery. 5-fluorouracil was administered at a dose of 350 mg/m² on days 1 to 7 and 15 to 21 as a continuous arterial infusion. Gemcitabine was delivered at a dose of 700 mg/m² once weekly for 3 consecutive weeks of every 4 weeks as a 30-min arterial infusion. Metal stent placement in the right biliary duct and tube stent in the left were performed with a bilateral transhepatic approach in all patients.

**Results:** Overall, there were 3 grade III chemotoxic events related to treatment. Chemotoxic events included two hematologic events and one gastrointestinal event. Catheter obstruction occurred in one patient and the catheter replacement was performed. Biliary obstruction recurred in 5 patients (50%). Tumor overgrowth was the major cause of reobstruction. Reintervention was performed in 4 patients. 3 of the 4 patients benefited from repeated intervention. Mean and median survival were, respectively, 18.2 and 21 months.

**Conclusions:** Arterial infusion chemotherapy of 5-fluorouracil and Gemcitabine with biliary drainage by metal and tube stent appears to be an effective and safe treatment option for unresectable hilar cholangiocarcinoma.
Evaluation of Pancreatic Exocrine Function with the 13C Breath Test Using a Neutral Lipid Mixture

Tomoko Tada, M.D., Masaki Ikeda, M.D., Takeo Ukita, M.D., Iruru Maetani, M.D., Yoshihiro Sakai, M.D.* Devision of Gastroenterology, Department of Medicine, Toho University Ohashi Medical Center, Tokyo, Japan.

Purpose: Although there are examinations to evaluate pancreatic exocrine function, as measurement of fecal fat, these tests can be both cumbersome and unpleasant. Recently, the 13C breath test for lipid digestion and absorption using a neutral lipid mixture has been used as a non-invasive and simple method. However, comparisons have not been made between this breath test and other pancreatic exocrine functional tests. We evaluated pancreatic exocrine function using the 13C breath test with a neutral lipid mixture in comparison with both the bentiromide (B) and secretin(S) tests.

Methods: Eighteen healthy controls, 11 patients with chronic pancreatitis without pancreatolithiasis (Group I) and 28 patients with chronic pancreatitis and pancreatolithiasis (Group II) were studied. Group II patients were examined by a 13C breath test a total of 81 times. Fasting patients and controls were administered orally 200 mg of a capsulated 13C-neutral lipid mixture with a test meal. Expired breaths were collected every 30 minutes for 8 hours and recovery rates of cumulative 13CO2 expired were calculated. At the same time, 16 control subjects and 11 group I patients were examined once by the B test. In group II, 23 patients were examined by the 13C breath test and B test two or more times in follow up (total 67 tests.) Twenty-four group I and II patients were administered the S test as well as the 13C breath test, for a total of 41 examinations. We used the amount of pure pancreatic juice for absorption using a neutral lipid mixture has been used as a non-invasive and simple method. However, comparisons have not been made between this breath test and other pancreatic exocrine functional tests. We evaluated pancreatic exocrine function using the 13C breath test with a neutral lipid mixture in comparison with both the bentiromide (B) and secretin(S) tests.

Results: Recovery rates of cumulative 13CO2 expired in the breath were 14.5±4.1% in controls, 12.8±4.0% in group I and 10.2±6.3% in group II. In group I, all cases were within mean±2SD of healthy controls. But in group II, 16 of 28 cases (25 of 81 tests) had a lower level of mean -2SD than healthy controls. The correlation coefficients for the breath test with the B test and S test were 0.375 and 0.404, respectively, and the p-values were 0.0002 and 0.0092, respectively. The results of the breath test correlated with those of the B and S tests.

Conclusions: Many of those with calcified pancreatitis had deteriorated function for assimilated lipid compared with healthy controls. Results suggested that the breath test is comparable to the bentiromide and secretin tests.

Comprehensive Genetic Analysis of a Spontaneous Chronic Pancreatitis Model (Male WBN/Kob Rat)

Satoshi Kitajima, M.D., Naoyuki Katoh, M.D., Toshijumi Takano, M.D., Fumio Itoh, M.D.* Department of Internal Medicine, Div. of Gastroenterology and Hepatology, St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan and Dept. of Pathology, St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan.

Purpose: Although the causes of human chronic pancreatitis are quite diverse, there are many aspects of its onset that are currently unclear. WBN/Kob rat serve as a model of spontaneous chronic pancreatitis that presents with impaired internal and external pancreatic secretion in males only, and causes fibrosis and inflammatory cells infiltration consisting mainly of monocytes in the pancreas starting at age 12 weeks. In this study, a comprehensive genetic analysis was conducted using an Oligo Microarray for the purpose of determining the mechanism of pancreatitis.

Methods: The animals used in this study consisted of 8-, 10-, and 12-week-old male WBN/Kob rats and male Wistar rats (control). Total RNA was extracted from the pancreas followed by competitive hybridization using a Rat Oligo Microarray.

Results: Reg1 was highly expressed at 8 weeks, while Pap was highly expressed at 10 weeks as compared with the control. Prrs1 was highly expressed at 8 weeks, while high levels of expression of Nes were observed starting at 12 weeks. In addition, the expression of two genes (designated as A and B) of unknown protein function was prominently observed continuously starting at 8 weeks.

Conclusions: The expression of the secretory stress proteins of Reg1 and Pap was thought to be involved in the onset of chronic pancreatitis in male WBN/Kob rats. The involvement of Prrs1, Spin1 and Cfr genes was suggested with respect to the onset of human chronic pancreatitis. Since Prrs1 was also highly expressed in the study rats, studies including SNP analysis are considered to be useful in the future. Spin1 and Cfr were not significantly expressed in the study rats. The activation of pancreatic stellate cells has attracted attention in fibrosis associated with chronic pancreatitis. Pancreatic stellate cells have been reported to be stained by Nestin during pancreas damage induced by pancreatic duct ligation. Increases in expression of Nes starting at 12 weeks observed in the study rats as well is considered to constitute an interesting finding. Genes A and B were highly expressed starting at 8 weeks and their expression was continuous, thereby suggesting the possibility of their involvement in the onset of pancreatitis in these rats.
Management of Stent Migration during Endoscopic Drainage of Pancreatic Pseudocysts
Dhanasekaran Ramasamy, M.D., C.N.S.P., Mahfuzul Haque, M.D., F.R.A.C.P.* Internal Medicine / Gastroenterology, Brody School of Medicine at East Carolina University, Greenville, NC.

Purpose: To report a patient with stent migration during endoscopic drainage of pancreatic pseudocyst and its successful management.

Case Report: 61 y/o female with history of pancreatitis presented with abdominal pain, nausea and weight loss. CT scan revealed a large pancreatic pseudocyst (16 x 10 cm) with mass effect on the stomach. A suitable site in the stomach was chosen by Endoscopic Ultrasonography and a needle knife was used to puncture the pseudocyst. The tract was dilated with a 10 mm balloon. Two 0.035 inch guide wires were placed for sequential deployment of three 10Fr double pig-tail stents. During the process of deployment the first stent slipped into the pseudocyst cavity with a spring-like motion, probably because of disproportionate tensile strength of the 10Fr stent on the 0.035 guide wire and because maximum length of the stent was inadvertently advanced too far inside the cyst cavity. Because cyst cavity was still full of turbid fluid limiting visibility and stent retrieval, we proceeded with the planned placement of two more stents to allow cyst drainage. Endoscopy was repeated on the following day and the two transgastric stents were removed and then the cyst-gastrostomy tract was further dilated. An upper endoscopy was gently inserted into the pseudocyst cavity via the cyst-gastrostomy tract. Cyst fluid had almost completely emptied and the dislodged stent was easily located within the cyst cavity. It was grasped with a snare and retrieved. Subsequently, three 7Fr double pig-tail stents (narrower and less tensile than 10Fr stents) were chosen and their midpoint marked with an indelible ink. They were then deployed sequentially, making sure that the midpoint mark remained visible within the stomach during deployment.

Discussion: Stent migration can be minimized by marking the midpoint of the double pig-tail stents with an indelible ink. This gives a visual guidance during the deployment of the stents so that they are not advanced too far into the cyst cavity. Spring-like jerky motion of the stent may also be minimized by choosing a stiffer guide wire and more pliable stent.

Conclusion: Stent migration occurs rarely during endoscopic pseudocyst drainage and can be successfully managed endoscopically. Minor modifications in the stents and in their placement technique can minimize stent migration.

Elevated Serum Bioactive Ghrelin Levels in Patients with Metastatic Neuroendocrine Tumors Maintains Body Weight
Hank S. Wang, M.D., David S. Oh, M.D., Gordon V. Ohting, M.D., Ph.D., Joseph R. Pisegna, M.D.* Department of Medicine, David Geffen School of Medicine at UCLA, LA, CA and Department of Gastroenterology, VA Greater LA Healthcare System, LA, CA.

Purpose: Ghrelin is the first and only circulating gut-brain peptide shown to have orexigenic effects. In patients with neuroendocrine tumors (NETs), we have observed weight preservation despite widely disseminated disease and hypothesize that elevated ghrelin levels in these patients accounts for maintenance of BMI. In this study, we sought to establish ghrelin levels in patients with NETs and to evaluate for differences in ghrelin levels in NETs with and without hepatic metastases.

Methods: The study was conducted as a single-center, prospective trial enrolling 31 patients with NETs. Bioactive ghrelin levels were measured and analyzed for differences by two-tailed unpaired Student’s t-test (P < 0.05) between subgroups including patients with and without metastases, patients on and off concurrent octreotide therapy, patients on and off concurrent proton pump inhibitor therapy, carcinoid tumors versus pancreatic NETs, multiple endocrine neoplasia type I (MEN I) versus non-MEN I, and Zollinger-Ellison versus non-Zollinger-Ellison.

Results: Bioactive ghrelin levels in patients with NET and hepatic metastases (591±275 pg/ml) were significantly (P = .03) elevated compared to the group of NET patients without hepatic metastases (387±234 pg/ml). The former had a mean weight of 176lbs compared to a mean of 163lbs for the latter. These higher ghrelin levels correlated with serum chromogranin A levels. Bioactive ghrelin in patients on long-acting octreotide and on proton pump inhibitor therapy differed significantly (P = .04 and.05, respectively) from untreated patients. No significant differences in ghrelin levels were seen between any other subgroup analysis.

Conclusions: These data suggest that there is a correlation in the levels of ghrelin and the presence of metastatic NETs. The elevations in serum ghrelin observed correlate with the aggressive nature of the disease as determined by measurements of biochemical markers. These data support the possibility that ghrelin is co-released from NETs and exerts an orexigenic effect in patient with NETs.

Pancreatic Stenting for Prophylaxis of Post-ERCP Pancreatitis: Expanded Efficacy Data Using 5F Stents
Paul R. Tarnasky, M.D., Jeffrey D. Linder, M.D.* Digestive Health Associates of Texas, Methodist Dallas Medical Center, Dallas, TX.

Purpose: Long (>7 cm) 3F pancreatic stents without internal flaps (IF) are increasingly being used for prophylaxis against post-ERCP pancreatitis (PEP). 3F stents rarely cause ductal changes and typically do not require endoscopic removal. However, 3F stents can only be placed over more difficult to use guidewires (0.018 in dia) and long stents may be inapropriate for patients with tortuous ducts. Duration of pancreatic drainage using stents without IF is inconsistent and there are limited efficacy data for 3F stents. Randomized-controlled trials which first demonstrated protection against PEP used short (<3cm) 5F stents with IF but study groups were small. The purpose of this study was to further evaluate the efficacy of 5F pancreatic stents for prophylaxis of PEP.

Methods: From a prospective database, we identified all patients who had pancreatic stents placed for prophylaxis of PEP. Data collected included stent configuration (size, shape, ± internal flap) and incidence and severity of PEP.

Results: From 1999–2004, pancreatic stents were placed for prophylaxis of PEP during 251 of 1260 (20%) procedures. Dorsal duct stents were placed in 25 cases of which 23 had accessory papillotomy. Another 2 patients underwent stenting and sphincterotomy of both the main and minor pancreatic papillae. 224 procedures involved main pancreatic stenting alone (n = 68) or stenting plus pancreatic sphincterotomy (n = 156). Sphincter manometry was performed in 162 of 224 (72%) cases. Access (precut) biliary papillotomy was performed in 57 of 224 (25%) cases. 5F stents were placed in 205 patients: 152 straight 5F (n = 110 < cor = 3cm, n = 42 >3cm) and 53 single pigtail 5F (n = 26 < cor = 3cm, n = 27 >3cm) pancreatic stents. Post-ERCP pancreatitis occurred in 12 of 205 (5.9%) cases after placement of a 5F pancreatic stent (7 mild, 4 moderate, 1 severe). The risk of PEP for 5F pancreatic stents was similar for all stent configurations: straight (10/152, 6.6%) vs. single pigtail (2/53, 3.8%), < cor = 3cm long (8/136, 5.9%) vs. >3cm long (4/69, 5.8%), and No IF (2/38, 5.3%) vs. +IF (10/167, 6.0%); p>0.6 for all comparisons.

Conclusions: 5F pancreatic stents effectively protect against PEP. The risk of pancreatitis after treatment with 5F pancreatic stents is independent of stent configuration. Comparative studies are needed to evaluate efficacy, safety, and ease of use between 5F and 3F pancreatic stents for prophylaxis of PEP.

Early Gall Bladder Cancer

Purpose: Gall bladder cancer (GBC) is the commonest biliary tract cancer. Overall prognosis is poor because most of the cases are diagnosed in advanced stages. Resection and cure are possible in early stages of the disease.
We report our experiences with early (T1) gall bladder cancer (EGBC) – T1a confined to mucosa and T1b involving muscularis propria.

**Methods:** Between 1989 and 2004, resection was performed in a total of 231 patients with GBC in a 60-bed Surgical Gastroenterology Unit at a tertiary level referral hospital in north India. These included 29 (12%) patients with EGBC; other stages included II = 39, III = 100 and IV = 63.

**Results:** Clinical diagnosis was GBC in 2 patients and GBC was diagnosed on US/CT in 11 other patients. 16 patients were operated with a diagnosis of cholecystitis–GBC was suspected during operation in 4 and diagnosis of GBC was made on histological examination (incidental GBC) in 12.

Extended cholecystectomy was performed in 8 patients and 21 underwent simple cholecystectomy. Gall stones were present in 20 patients. Mucosal disease (T1a) was found in 7 patients and 20 had involvement of muscle (T1b); these details were not available in 2 patients. Nodal status was N0 in 16 patients (8 extended cholecystectomy and 8 simple cholecystectomy with cystic lymph node); it was NX in 13 patients who underwent simple cholecystectomy. 8 patients received adjuvant chemo-radiotherapy. 21 patients were available for follow up ranging from 4 to 107 months. Overall median survival was 63 months and 5-year survival was 52%. 10 patients (9 with T1b) died during follow up – 6 within 30 months and 4 after 60 months. No patient with T1a disease died before 60 months – 3 patients with T1a disease are alive at 11, 13 and 88 months and one died at 68 months. Of the 10 patients with T1b disease who underwent simple cholecystectomy 4 died within 24 months, 3 died at 60, 63 and 107 months and 3 are alive at 72, 87 and 100 months. Patients with T1b disease who received chemo-radiotherapy after simple cholecystectomy had better survival than those who did not. Out of 15 patients eligible for 5-year follow up 4 are alive without disease at more than 60 months.

**Conclusions:** EGBC constitutes a small proportion of patients with GBC. Majority of patients with EGBC are operated with a diagnosis of cholecistitis and are diagnosed at operation or at histology. Overall prognosis is good after resectional surgery but simple cholecystectomy is not enough for T1b (muscularis) disease.

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**Use of Prophylactic Pancreatic Duct Stenting in Case of Endoscopic Papillary Balloon Dilatation and Metallic Biliary Stenting**

Sassamu Shinoara, M.D., Yutaka Yamaguchi, M.D., Yoshiaki Shimabukuro, M.D., Kaoru Kikuchi, M.D., Yoshimizu Keida, M.D.∗

Gastroenterology–hepatology, Medicine, Okinawa Chubu Hospital, Uruna, Okinawa, Japan.

**Purpose:** To review our findings in the use of prophylactic pancreatic duct stenting in cases of endoscopic papillary balloon dilatation and metallic stent insertion.

**Methods:** We reviewed all cases between July of 2003 and May of 2005 in which patients underwent therapeutic endoscopic retrograde cholangio-pancreatogram (therapeutic ERCP). We evaluated the effects of prophylactic insertion of pancreatic duct stenting in case of endoscopic papillary balloon dilatation (EPBD) and metallic stent insertion.

**Results:** There were 280 cases of therapeutic ERCP over a period of 23 months at our institute. Of these, endoscopic sphincterotomy (ES) was performed in 113 cases, bile duct stenting in 100 cases, and pancreatic duct stenting in 108 cases. EPBD was performed in five cases and metallic stent insertion to common bile duct in 16 cases.

Etiology of EPBD were acute cholangitis (3) and cholecoldolithiasis (2). Indication for EPBD was coagulopathy, low platelet count or antplatelet use. Of the five EPBD cases, prophylactic pancreatic duct stenting was performed in four without post procedural pancreatitis. The 16 cases of metallic stent insertion to common bile duct, the etiology of metallic stenting were pancreatic head cancer (10), CBD cancer (4) and external compression of CBD by metastatic lymph nodes (2). Of these 16 cases, prophylactic pancreatic duct stenting was performed in 4 cases, all of which malignant stricture was noted at distal common bile duct requiring protrusion at the tip of metallic stent from papilla. There was no complication as post procedural pancreatitis in these four cases.

**Conclusions:** EPBD is an effective and valuable procedure in case of acute cholangitis or cholecoldolithiasis with coagulopathy, low platelet count or antplatelet use. However, lack of randomized control trials on long term effect and complications as post procedural pancreatitis prevent the procedure from becoming well used as ES. Metallic stent insertion is also a useful method for inoperable malignant stricture of CBD with occasional reports of post procedural pancreatitis caused by occlusion at the tip of main pancreatic duct with the metallic stent. Prophylactic pancreatic duct stenting is an easy and safe procedure minimizing the possible complication as post procedural pancreatitis in these cases.

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**Endoscopic Treatment of Hemobilia by Passage of an Endoscope through a Choledochoduodenal Fistula**

Gulam Khan, M.D., Isaac Moshenyat, M.D., Robin Baradarian, M.D., Kadirawel Iswara, M.D., Jian Jun Li, M.D., Scott Tenner, M.D., M. P. H. ∗

Division of Gastroenterology, Maimonides Medical Center, Mount Sinai School of Medicine, Brooklyn, NY.

**Purpose:** Hemobilia is found in less than 1 percent of all patients who present with upper gastrointestinal bleeding. The anatomic location of the site of bleeding in the biliary tree typically prevents successful endoscopic therapy. We present a case of massive upper gastrointestinal bleeding secondary to an ulcerated cholangiocarcinoma that was successfully treated with endoscopic therapy by passage of an endoscope into the biliary tree. The patient was a 73 year old woman who presented to the emergency room with melena. She had undergone a cholecystectomy 40 years prior for cholecystitis. She was otherwise healthy, no other hospitalizations or surgeries. There were no medications. On physical exam, she was in moderate distress, tachycardic (110 bpm) and hypotensive (90/60 mmHg). Other than a midline abdominal scar and melena on rectal examination, the remainder of the exam was normal. Laboratory evaluation revealed a hematocrit of 28%, Bilirubin of 3.6 mg/dl, AST 176 IU/dl, and alkaline phosphatase 192 IU/dl. Intravenous hydration and pantoprazole were given. After stabilization, an endoscopy was performed. On passage of the endoscope to the duodenal bulb, blood was seen arising from a diverticulum. In preparation of endotherapy, the diverticulum was irrigated and a fistulous tract was appreciated. The endoscope was passed 7 cm into the biliary tree and an actively bleeding ulcer was seen. After control of bleeding with injection of 3 cc (1:10,000) epinephrine, heater probe was applied. The patient remained well post-procedure with a low grade fever. Antibiotics were given. Computed tomographic scan demonstrated air in the biliary tree, a choledochoduodenal fistula and a 2 cm mass in the right hepatic duct. Repeat endoscopic evaluation revealed a 2 cm ulcer. Biopsies of the ulcer demonstrated cholangiocarcinoma. This case demonstrates that placement of an endoscope into the biliary tree through a choledochoduodenal fistula can assist in the diagnosis of cholangiocarcinoma and the treatment of hemobilia. Passage of an endoscope into the biliary tree appears to be safe when ductal dilatation allows. The risk of introducing an infection into the biliary tree must be weighed against the potential benefits.

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**Can Choledocolithiasis Be Predicted by Laboratory or Imaging Tests?**

Melchor V. Demetrius, M.D., Erick H. Chinga-Alayo, M.D., Bashar M. Attar, M.D.,∗ Gonzalo Pandolfi, M.D., Rony Ghous, M.D., Benjamin Go, M.D., Frida Abrahamian, M.D. Department of Medicine, Division of Gastroenterology, John H. Stroger Jr. Hospital of Cook County, Chicago, IL.

**Purpose:** Endoscopic retrograde cholangiopancreatography (ERCP) should be performed selectively for the patients suspected of having CBD (common bile duct) stone due to its morbidity and cost. The predictive value of non-invasive tests for the presence of CBD stone is controversial. To evaluate whether laboratory and imaging parameters could predict the presence of CBD stone on ERCP.
Methods: 264 patients were evaluated. Indications for ERCP were: suspected choledocholithiasis in patients with abdominal pain, abnormal liver function tests, biliary dilatation and gallstone pancreatitis. The following parameters were evaluated: serum albumin, serum protein, total bilirubin, direct bilirubin, AST, ALT, Alkaline phosphatase, Gamma-glutamyl-transpeptidase (GGT), lipase, amylase, US and CT scan findings.

Results: Previous cholecystectomy was seen in 12.1%(32) of the evaluated patients. CBD dilatation on imaging was present on 11.4%(29). CBD stone on imaging was observed on 28.4%(75). On ERCP CBD stone was prevalent in 48.9%(128). CBD dilatation was observed in 10.9%(14/128) of patients with CBD stone on ERCP and in 11.2%(15/136) of patients with no CBD stone on ERCP (p = 0.95). A CBD stone on ERCP was found on 57.3%(43/75) of patients with CBD stone on imaging and in 44.5%(77/173) of patients with no CBD stone on imaging (p = 0.06). In those patients with normal imaging studies (no stone or CBD dilatation), three or more laboratory abnormalities were present in 5.9%(5/84) of patients with CBD stone on ERCP compared to 34.2%(13/38) in those with no CBD stone (p = 0.64). In contrast, in those patients with abnormal imaging studies, three or more laboratory abnormalities were present in 37.7%(20/53) of patients with CBD stone on ERCP compared to 34.2%(13/38) in those with no CBD stone (p = 0.86). On multivariate analysis, the evaluated variables showed poor discrimination for the presence of CBD stone on ERCP.

Conclusions: Laboratory and imaging parameters are frequently abnormal in patients without CBD stones on ERC. ERC is still the more appropriate invasive method to diagnose CBD stones.

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Idiopathic Fibrosing Pancreatitis in Children
Gary Fanjiang, M.D., M.B.A., Leonel Rodriguez, M.D., Moises Guelrud, M.D., Jeffrey Biller, M.D., Robert Fissumyan, M.D.∗ Pediatric Gastroenterology & Nutrition, Tufts-New England Medical Center, Boston, MA.

Purpose: Idiopathic fibrosing pancreatitis is a rare entity that presents with common bile duct (CBD) obstruction. We describe two cases of idiopathic fibrosing pancreatitis in children.

Methods: Two females, ages 4 and 10, presented similarly with jaundice and pale stools. They took no medications and were otherwise asymptomatic. Their labs and imaging studies mirrored each other. One of their labs showed a total bilirubin of 7.4, a direct bilirubin of 5.6, an amylase of 125, a lipase of 419, an alkaline phosphatase of 559 and a mild transaminase elevation. A total bilirubin of 7.4, a direct bilirubin of 5.6, an amylase of 125, a lipase of 419, an alkaline phosphatase of 559 and a mild transaminase elevation. Their labs and imaging studies mirrored each other. One of their labs showed.

Results: An ultrasound showed CBD dilation of 9.2 mm but no lithiasis or pancreatic duct dilatation. CT, MRCP and ERC confirmed this and showed a large pancreatic head. Exploratory laparotomy revealed a thickened nodule at the pancreatic head and a dilated biliary tree. Pathology showed interstitial fibrosis surrounding the pancreatic ductules. Post-operatively, the patient did well with normalization of her labs over two weeks despite no surgical or endoscopic intervention to relieve the CBD obstruction. A one week postoperative MRCP showed improvement in her CBD dilation and a smaller pancreatic head suggesting resolution of a focal inflammatory process, with or without acinar atrophy, which may have relieved the obstruction. She was also started on pancreatic enzymes for suspected pancreatic insufficiency. She continues to do well with no sign of pancreatitis or CBD obstruction.

Conclusions: There have only been 44 reported cases of idiopathic fibrosing pancreatitis in children. More common in males, it has been described in patients as young as 4 months. Patients with idiopathic fibrosing pancreatitis are usually treated with surgical decompensation. Some have also suggested using temporary stents. In 3 such patients, CBD compression diminished as the pancreas atrophied. With time, normal biliary drainage returned and the stents were discontinued. Our 2 cases of spontaneous resolution suggests that the natural course of idiopathic fibrosing pancreatitis may involve pancreatic acinar atrophy which ultimately relieves the CBD obstruction. Since surgical and endoscopic interventions do not alter the clinical course, they may be unnecessary.

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Eosinophilic Gastroenteritis: Recurrent Pancreatitis Secondary to Eosinophilic Infiltration in a Patient Taking Nutritional Supplements
Sheraj Jacob, M.D.∗ John L. Gosserand, M.D.∗ Department of Gastroenterology, Ochsner Clinic Foundation, New Orleans, LA.

Purpose: First described in 1937 by R. Kajiser, eosinophilic gastroenteritis (EGE) is the infiltration of gastrointestinal mucosa by eosinophils. All segments of the gastrointestinal tract can be affected. Clinical symptoms vary depending on the depth and the site of infiltration. There have been reports of the infiltration resulting in simple gastritis to severe biliary obstruction. In 25–75% of the cases, there was a history of atopy and allergies. We report a case of eosinophilic infiltration of the duodenum with possible obstruction of the pancreaticobiliary system causing recurrent pancreatitis.

Case: A 51-year-old white male with a remote past medical history of alcohol abuse was admitted to the hospital with severe epigastric pain and vomiting for approximately ten hours in duration. Labs revealed elevated amylase and lipase, and computed tomography (CT) of the abdomen showed images consistent with acute pancreatitis. After a two day hospital stay, the patient was discharged home in good condition. Unfortunately he returned with similar complaints and was noted to have elevated enzymes once again. Careful history revealed that the patient recently started ingesting nutritional supplements, one being whey protein. CT during this episode showed a thickened bowel wall involving the antrum, pylorus and proximal duodenum. Subsequent endoscopy revealed diffuse erythematous mucosa in the gastric body, antrum, pylorus and duodenum. Biopsies showed approximately 400 eosinophils per high power field, which is consistent with eosinophilic gastroenteritis. The patient was asked to stop the nutritional supplements and was given a tapering doses of steroids. Repeat endoscopy and biopsy revealed no eosinophilic infiltration. There has not been another episode of acute pancreatitis since starting this therapy.

Discussion: Eosinophilic infiltrative symptomatology is based on the area in which it has been localized as well as the mucosal layer involved. For instance, involvement of the pylorus, might cause gastric outlet obstructive symptoms. In contrast, infiltration around the sphincter of Oddi might cause a picture consistent with cholestasis or pancreatitis. Obstruction of the instestine secondary to this infiltration seems realistic in that disruption of the muscular continuity can cause dymotyil and localized spasms. These patients can be easily treated with glucocorticosteroids and leukotriene receptor antagonist along with stopping the offending agent.

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Operator Controlled Guidewire Cannulation of the Bile Duct during ERCP Is Safe
Paul R. Tarnasky, M.D., Shahryar S. Nasi, M.D., Jeffrey D. Linder, M.D.∗ Digestive Health Associates of Texas, Methodist Dallas Medical Center, Dallas, TX.

Purpose: ERCP cannulation is traditionally accomplished using a catheter with contrast injection. Guidewire cannulation was thought to be associated with increased ERCP complications. There are limited data regarding success and safety of primary guidewire cannulation. New short-wire devices now allow operator control of the guidewire. The purpose of this study was to evaluate success and complications of operator controlled guidewire cannulation (GWC) of the bile duct during ERCP.

Methods: ERCPs during which operator controlled GWC of the bile duct was attempted were included. Patients with prior sphincterotomy and procedures where only pancreatic cannulation was intended were excluded. Prospectively collected data included: ERC indication, desired duct(s) for GWC, order of GWC, cannulation success, frequency of access papillotomy (precut), and incidence of post-ERCP pancreatitis.

Results: 168 of 399 patients that had ERCP during 1 yr were studied. 105 patients were low-risk and 63 were high-risk patients (unexplained pain or pancreatitis). Successful GWC of the bile duct without unintentional
pancreatic GWC or contrast injection was accomplished in 56/101 (55%) cases. GWC of both ducts was intended in the other 67 patients. Of these, bile duct cannulation was achieved first in 58% of low-risk patients. In contrast, the pancreatic duct was cannulated before the bile duct in 77% of high-risk patients. Overall, 42 of 168 (25%) underwent a needle-knife precut to achieve deep biliary access after attempted GWC. Cannulation success and precut requirements according to patient risk are tabulated. Five (2 mild and 3 moderate severity) of 399 patients developed post-ERCP pancreatitis of which only 1 (mild) occurred after operator controlled GWC. One retroperitoneal perforation occurred after GWC and a pancreatic spherocenteterotomy.

### Low-Risk Patients

<table>
<thead>
<tr>
<th>Intended Duct (s)</th>
<th>GWC of Bile Duct (%)</th>
<th>Required Precut (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile Duct Only</td>
<td>85/86 (99%)</td>
<td>22/86 (26%)</td>
</tr>
<tr>
<td>Both Ducts</td>
<td>18/19 (95%)</td>
<td>1/19 (5%)</td>
</tr>
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### High-Risk Patients

<table>
<thead>
<tr>
<th>Intended Duct (s)</th>
<th>GWC of Bile Duct (%)</th>
<th>Required Precut (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bile Duct Only</td>
<td>15/15 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>Both Ducts</td>
<td>45/48 (94%)</td>
<td>15/48 (31%)</td>
</tr>
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</table>

**Conclusions:** These data suggest that operator controlled GWC of the bile duct is safe and effective in both low and high-risk patients. A significant minority of patients undergo precut papillotomy after attempted GWC of the bile duct. Efforts to establish pancreatic access early when GWC attempts are either difficult and/or in high-risk patients may explain a higher incidence of precut papillotomy.

**Efficacy of Double Contrast Cholangiography**

**Yuki Nagata, Koji Yoshida,* Tomoya Kawase, Jun Uschio, Toshiyasu Iwao, Kazuhiro Sato. Gastroenterology, Aizu Central Hospital, Tsuruga, Aizuwa, Fukushima, Japan; Hepatobiliarypancreatology, Kawasaki Medical School, Matsushita, Kurashiki, Okayama, Japan; Radiology, Teikyo University Ichihara Hospital, Ichihara, Chiba, Japan and Gastroenterology, Showa University Toyoa Hospital, Kouto, Tokyo, Japan.**

**Purpose:** Currently, elevated mucosal of gallbladder have been often detected by ultrasonography (US). Most of them are benign but some cases make it difficult to diagnose accurately and need further examination. Endoscopic ultrasonography (EUS) is considered to have the intrinsic potential to becoming standard image modality for differential diagnosis gallbladder polyps. The suggestion of gallbladder malignancy on EUS is essential to the choice of surgical resection. The presence of superficial tumor without polypoid component is considered a major problem in the diagnosis gallbladder malignancies in the early stage. So using ERCP technique, we developed the double contrast cholangiography to detect superficial flat tumors of the gallbladder.

**Methods:** After endoscopic retrograde cholangiography, insert 6 Fr pig tail naso-gallbladder drainage tube to empty gallbladder and put barium sulfate and CO2 gas into the gallbladder.

**Results:** For 2 years, US revealed gallbladder disorder in 577 of 9456 cases. In 320 cases EUS was performed and in 91 cases which were suspected early gallbladder cancer double contrast study was performed. Reticular mucosa represent the normal mucosa. Granular and irregular mucosa corresponded to gallbladder carcinoma. We can diagnose 16 cases of early gallbladder carcinoma including 3 flat mucosal type.

**Conclusions:** Double contrast cholangiography is valuable in the early detection of gallbladder cancer, especially in superficial flat tumors of the gallbladder.

**Use of Endoscopic Naso-Biliary, Naso-Pancreatic and Naso-Cystic Drainage in Pancreatobiliary Diseases**

**Susumu Shinoura, M.D., Tatara Yamaguchi, M.D., Yoshiki Shimabukuro, M.D., Kazu Kikuchi, M.D., Yoshitide Keida, M.D.* Gastroenterology-Hepatology, Medicine, Okinawa Chubu Hospital, Uruma, Okinawa, Japan.**

**Purpose:** To review our findings in the use of endoscopic naso-biliary drainage (ENBD), naso-pancreatic drainage (ENPD) and naso-cystic drainage (ENCd) in management of pancreatobiliary diseases.

**Methods:** We reviewed all cases between July of 2003 and May of 2005 in which patients underwent therapeutic endoscopic retrograde cholangiopancreatogram (therapeutic ERCP). We conducted an analysis of 13 cases in which ENBD, ENPD or ENCD were employed.

**Results:** There were 280 cases of therapeutic ERCP within 23 months at our institute. Of these, endoscopic sphincterotomy (ES) was performed in 113 cases, bile duct and pancreatic duct stenting in 100 and 108 cases, and endoscopic papillary balloon dilatation (EPBD) in five cases. ENBD was performed in nine cases, ENPD in two cases, and ENCD in two cases (for a total of 13). Indication of therapeutic ERCP for these 13 cases were obstructive jaundice (4 cases), cholangiocarcinoma with cholangitis (3), malignant strictures (2) and pancreatitis with pseudocyst or ascites (4). Of nine (9) ENBD cases, the reason for ENBD insertion was to treat and evaluate obstructive jaundice (3), drainage for possible penetration during ES (2), need to closely monitor bleeding for large volumes of bleeding during ES (1), need to monitor quality of drainage in the case of severe acute cholangitis or acute cholangitis with commodity (2) and for other reasons (1). Reason...
for ENPD insertion in two cases were acute and chronic pancreatitis with pancreatic pseudocyst and ascites. Reason for ENCD insertion in two cases were chronic pancreatitis with giant pseudocyst and ascites. All cases except for one, whose clinical course complicated by deterioration of infection and intraabdominal hemorrhage, survived.

Conclusions: ENBD, ENPD, and ENCD are effective for following reasons; 1. Evaluation of stricture in detail is available along with sufficient bile drainage for each single procedure of ENBD 2. Collection of bile for cytology is available in the case with suspicion of malignant stricture along with bile drainage for each single procedure of ENBD 3. ENPD and ENCD are useful in monitoring amount of drainage 4. ENPD and ENCD are useful in early detection of bleeding or infection in the pancreatic pseudocyst.

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EUS in Evaluation of Dilated Biliary(CBD) and/or Pancreatic Duct(PD) of Unclear Etiology
Robert F. Wong, M.D., G. S. Raju, M.D., William Nealon, M.D., P. Jay Pusricha, M.D., Manoop S. Bhutani, M.D.* Internal Medicine, University of Texas Medical Branch, Galveston, TX.

Purpose: The purpose of this study was to evaluate EUS as a diagnostic method for CBD and PD dilation detected by non-invasive imaging modalities.

Methods: A database was retrospectively analyzed with IRB approval for patients who underwent EUS since June 2002 for dilation of the CBD and/or PD without obvious cause identified on prior radiographic imaging. We reviewed all available records for endoscopy (EUS, ERCP), clinic/hospital visits, surgeries, radiology studies and pathology results. EUS diagnoses were categorized as: 1) pancreatic mass; 2) chronic pancreatitis (≥ 5 EUS features of chronic pancreatitis or pancreatic calcifications); 3) CBD stones; and 4) unspecified benign disease (no apparent cause). The final diagnosis was established by: surgery, pathology, ERCP and clinical follow-up.

Results: We included 22 patients in our analysis (median age 60 years, 11 female, 15 white). Based on prior cross-sectional imaging (US, CT, MRI), 6 patients had isolated CBD dilation, 5 patients had isolated PD dilation and 11 had dilation of both the CBD and PD. Nine patients had focal enlargement of the pancreatic head. Seventeen patients were symptomatic (abdominal pain and/or weight loss). EUS diagnoses were as follows: mass (n = 5), chronic pancreatitis (n = 9), CBD stones (n = 2); and unspecified benign disease (n = 6). Final diagnoses were: pancreatic cancer (n = 6), chronic pancreatitis (n = 7), CBD stones (n = 3), papillary stenosis (n = 5) and intra-ampullary stricture (n = 1). EUS identified a pancreatic mass in 5/6 cases of pancreatic cancer. Of the pancreatic cancers, radiographic studies identified focal pancreas enlargement in 5/6 cases and double duct dilation in 2/6 cases. EUS correctly diagnosed all cases of chronic pancreatitis. All benign stenosis/strictures were labeled as unspecified benign disease on EUS. The sensitivity, specificity, PPV and NPV of EUS were as follows: for cancer = 83%, 100%, 100% and 94%; for chronic pancreatitis = 100%, 87%, 77% and 100%; for gallstones = 67%, 100%, 100% and 95%; and for benign stenoses/strictures = 100%, 100%, 100% and 100%. Overall, EUS appropriately identified the causes of duct dilation in 20/22 (91%) cases.

Conclusions: EUS can often correctly identify the etiology of CBD and/or PD dilation seen on non-invasive imaging modalities and should be considered as the next step in the diagnostic algorithm for pancreatico-biliary duct dilation of undetermined etiology before contemplating more invasive procedures, such as ERCP.
of the members of the MAP kinase pathway viz. MEK (194% of vehicle) and MAPK (434% of vehicle). The pro-angiogenic protein VEGF was increased (234% of vehicle) in the Src-activated cells as compared to control. Transfection of Mia PaCa2 cells with specific siRNA directed against Csk resulted in 28% reduction in CSK message. The transfected cells showed more proliferation as compared to control.

Conclusions: Our data indicates that activation of Src through down-regulation of its negative regulator-Csk, results in increased proliferation and increased angiogenesis in pancreatic cancer cell line Mia PaCa2. Thus, modulating the Csk/Src axis would represent a novel and important modality for pancreatic cancer treatment and possibly prevention.

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Safety of Pancreatic Sphincterotomy in Elderly Patients with Pancreatic Papillary Stenosis
Giuseppe Aliperti, M.D.∗ Midwest Therapeutic Endoscopy Consultants, St. Louis University School of Medicine, St. Louis, MO.

Purpose: Papillary stenosis in the elderly is an underreported condition often leading to reduced nutritional status and QOL. Experience with pancreatic sphincterotomy (PDES) is slowly accumulating worldwide. Though post-ERCP pancreatitis is less frequent in the elderly, common co-morbid conditions and the typical malnourished state enhance the gravity of eventual complications. We herein report our experience with PDES and the use of protective stenting in elderly patients with pancreatic papillary stenosis (PPS).

Methods: 414 pts 65 yo and older (304/414 F, 110/414 M, median age 74 y, r 65–97 y) with previous negative EGD underwent PDES for PPS between 1999 and 2005 for access or drainage. Indications for ERCP included: persistent/recurrent pancreatobiliary pain (317), acute or chronic pancreatitis (98), abnormal LFTs (66), biliary/pancreatic abnormalities on non-invasive imaging (52), nausea/vomiting/anorexia/weight loss/failure to thrive (50), pancreatic pseudocyst (7), pancreatic fistula (2) or a combination of the above. Diagnosis of PPS was based on manometric criteria in 262/414 (dual readings in 165, pancreatic alone in 97) and on radiographic criteria in 152/414 pts. PDES was performed with the arc sphinctertome in 404/414 and with the needle knife in 10/414 pts using pure cut current after access biliary sphincterotomy. Protective pancreatic stenting was performed in 414/414 pts and concurrent biliary stenting in 326/414. Stents were removed after 2–3 days and were left in place for longer if perforation occurred.

Results: PDES was successfully completed in 414/414 pts. Complications related to the procedure occurred in 22 (5.3%) pts and totally in 35 (8.4%) pts: 11 (2.6%) pancreatitis; 5 (1.2%) perforations (1 requiring delayed surgical, 1 percutaneous abscess evacuation); 4 (1%) transfusion-requiring bleeding; 13 (3.1%) other complications (CHF/pneumonia/digitalis toxicity/fall/fx/bleeding ulcer/pneumothorax/C. Difficile diarrhea, MI); 1 (0.2%) death from intractable CHF. Average hospital days were 4.2 in total, 10.2 for pts with complications, and 3.6 for pts without.

Conclusions: (1) Endoscopic pancreatic sphincterotomy after access biliary sphincterotomy is generally safe in the elderly population. (2) Utilization of short-term biliary pancreatic stenting may reduce frequency and/or severity of complications. (3) Complication rates are comparable to what is reported for biliary sphincterotomy alone. (4) Long-term follow-up after such therapy in this patients group is currently in progress.

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Community-Based Tumor Marker Testing—Are We Ordering Appropriate Tests?
Srinivas R. Pulagam, M.D., Tarun Madappa, M.D., Abul Ahsan, M.D., Loren Kirchner, M.D.* Internal Medicine, Canton Medical Education Foundation (NEOUCOM), Canton, OH.

Purpose: Carbohydrate antigen 19–9 (CA 19–9) is commonly utilized in the evaluation of patients suspected to have GI related malignancies. We previously found that a large proportion of CA 19–9 tests may be obtained in a manner inconsistent with current recommendations. The present study evaluated the use of concomitant additional tumor markers when CA19–9 was employed in a diagnostic workup.

Methods: We obtained all in-patient test results, demographic data, physician specialty, and reason for ordering for all patients who had a CA 19–9 test performed at a large community-based teaching hospital between May 1, 2002 and November 30, 2004 (30 months). In addition, we performed detailed chart reviews to determine the reason for ordering, differential diagnoses, patient outcomes, other testing related to the reason for ordering the CA 19–9 test, and concomitant ordering of additional tumor markers.

Results: Of 224 CA 19–9 tests, 88 (39.3%) were positive (normal cutoff < 37 IU/ml). Of these, 30 (34.1%) were in patients with newly diagnosed, biopsy proven, pancreatic cancer (PC). The remaining 58 (65.9%) had other diseases including pancreatitis, metastatic liver disease, cancer of unknown primary, and jaundice. Other than following patients with PC, the most commonly cited reasons for testing included abdominal pain (37%), abnormal CT scan of the pancreas or suspicion of PC(26.5%), and pancreatitis (20%). Out of 224 inpatients, 154 also had CEA levels ordered [49 (31.8%) were positive]. Only 10% had colon cancer, while the remaining had pancreatic or lung carcinoma or pancreatitis. The average number of concomitant markers was 1.36, in addition to CA 19–9. The most common additional markers were CEA (69%), CA 125 (35%), AFP (21%), and PSA (11%). [figure 1]

Conclusions: We found that there is a high probability of obtaining other additional tumor markers whenever CA 19–9 is obtained as part of a diagnostic strategy. This may be reflective of clinical uncertainty on the part of the ordering physician. We are using this data to develop a systems-based improvement process to reduce unnecessary tumor marker ordering at our institution.

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Gallbladder Carcinoma Associated with Occult Pancreatobiliary Reflux
Masayasu Chikamori, Jin Kan Sai, Masafumi Suyama,∗ Kei Kato, Hiroaki Sigoka, Hiroyuki Tadokoro, Takayoshi Kamiya, Yasushi Takahashi, Yoshihiro Kabukawa, Kouiti Inami. Gastroenterology, Juntendo University, Tokyo, Japan.

Purpose: Pancreatobiliary reflux can occur even if the patient has a normal pancreaticobiliary junction (occult pancreatobiliary reflux) and it can be associated with the occurrence of gallbladder carcinoma. The aim of the present study was to examine the mucosal changes of the gallbladder in patients with occult pancreatobiliary reflux.
Methods: The gallbladder mucosa of 15 cholecystectomized patients, who had a normal pancreaticobiliary junction and whose biliary amylase concentration was more than 10,000 IU/L, was examined histologically. The gallbladder of patients without carcinoma was further examined using immunohistochemical techniques to detect Ki-67, and the results were compared with those of normal controls.

Results: Six (40%) of the 15 patients had gallbladder carcinoma, and 9 (60%) did not. Of the 9 patients without carcinoma, 4 (44%) had dysplasia accompanied with hyperplasia, and 3 (33%) had only hyperplasia of the gallbladder. The Ki-67 labeling index was significantly higher in hyperplastic and dysplastic mucosa than in control gallbladder mucosa (p < 0.0004).

Conclusions: Occult pancreatobiliary reflux could be associated with the cancerous and pre-cancerous mucosal changes such as hyperplasia and dysplasia of the gallbladder with increased cellular proliferation, and could be a possible risk factor for gallbladder carcinoma.

Sphincter of Oddi Dysfunction Is Associated with Pancreatic Duct Anomalies
Jeffrey D. Linder, M.D., Shahryar S. Narsi, M.D., Michelle E. Moate, M.D., Paul R. Tarnasky, M.D.* Digestive Health Associates of Texas, Methodist Dallas Medical Center, Dallas, TX and Department of Radiology, Methodist Dallas Medical Center, Dallas, TX.

Purpose: Sphincter of Oddi dysfunction is known to be associated with pancreas divisum but other types of pancreatic ductal anomalies (PDA) have not been well studied. Duct tortuosity and tight angulation can make deep guidewire cannulation difficult or impossible. Recognition of ductal anomalies is important in patients with suspected SOD because of the need for deep pancreatic cannulation and stent placement for prophylaxis of post-ERCP pancreatitis.

Methods: Data form 1428 consecutive ERCP procedures performed on 1032 patients between 1999 and 2005 were collected prospectively. Two subsets of patients were then extracted from the database: those diagnosed with sphincter of Oddi dysfunction (SOD) and patients with PDA. Each PDA was independently reviewed and classified by a radiologist trained in reading ERCP studies. PDAs were classified as looping above main duct (upper ansa), looping below main duct (lower ansa), tightly angulated (switchback), dorsal dominant, or mixed PDA.

Results: Of the 1032 patients included in our study, 270 (26%) were identified as having SOD of which 27 (10%) had PDAs. There were 762 without SOD of which 7 (0.9%) had PDAs. Thus PDAs occurred more frequently in patients with SOD than without SOD (p < 0.0001). Of the 34 total patients with PDAs, there were 9 (26%) upper ansa loops, 10 (29%) lower ansa loops, 10 (29%) switchback loops, 1 (3%) dorsal dominant, and 4 (12%) mixed PDAs.

Correlation of PDAs with SOD

<table>
<thead>
<tr>
<th>SOD +</th>
<th>SOD -</th>
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<tbody>
<tr>
<td>PDA</td>
<td>27 (10%)</td>
</tr>
<tr>
<td>No PDA</td>
<td>243</td>
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</table>

p < 0.0001.

Conclusions: PDAs occur much more frequently in patients with SOD compared to patients without SOD. Recognition of PDAs is important in patients with suspected SOD because the potential difficulty to achieve deep guidewire cannulation and subsequent pancreatic stent placement. An association between SOD and PDA may imply a congenital etiology for SOD.

Mechanical Simulator for ERCP Training
Micha Rojany, M.D., Joseph Leung, M.D.* Robert Wilson. Division of Gastroenterology, UC Davis Medical Center, VANCHCS, Sacramento, CA.

Purpose: Diagnostic and therapeutic ERCP requires special technical skills and thus specific training. With a higher expectation set for competency, many training programs may not be offer GI fellows sufficient experience in advanced therapeutic procedures especially ERCP-related. There are no accepted alternatives to clinical teaching. Currently available computer simulators are unrealistic and lack tactile sensation. Animal models or ex-vivo tissue require special training settings. An economical, portable and reproducible simulator will help with training and assessing fellows’ progress in ERCP without jeopardizing patient care.

Aim: To evaluate the use of a mechanical simulator for training and teaching new ERCP techniques to GI fellows.

Methods: 13 advanced GI fellows from Western United States participated in a hands-on ERCP practice course. All completed an anonymous pre-practice and post-practice survey on their endoscopy experience. ERCP was performed using a mechanical simulator and an artificial biliary duct with a built-in stricture. A pin-hole camera is used (in place of fluoroscopy) to monitor events within the bile duct. Time taken (minutes) to negotiate the stricture with a guide wire, perform balloon dilation and brushing cytology, and insertion of a plastic biliary stent using the conventional method or the Fusion system were measured including total procedure time (TT) for stent placement and fluoroscopy time (FT) to monitor the process. Each fellow worked with an experienced assistant and performed each task two times.

Results: All participants performed more than 400 upper endoscopies and the mean number of ERCPs was 140. All participants were able to complete the four ERCP tasks using conventional accessories and the Fusion system. The mean TT and FT was 15.1 min and 12.6 min respectively. The survey revealed only 6/13 participants would have done > 200 ERCPs at graduation yet all intended to perform ERCP. 9/13 fellows were trained with long ERCP accessories but 10/13 fellows planned to use short wire accessories in future practice. 10/13 participants planned to enter a community practice.

Conclusions: The mechanical simulator provides a risk-free setting for GI fellows to learn and practice ERCP techniques. All fellows regardless of their prior training experience with different accessories were able to complete the tasks. Although the mechanical simulator does not substitute clinical ERCP experience, it serves as an adjunct to allow fellows to practice and familiarize themselves with new techniques or accessories.

Prior Experience and Use of Short Wire Technology Predicts Faster ERCP Procedure Time
Micha Rojany, M.D., Joseph Leung, M.D.* Robert Wilson. Division of Gastroenterology, UC Davis Medical Center, VANCHCS, Sacramento, CA.

Purpose: Therapeutic ERCP requires advanced training beyond regular endoscopy. ERCP utilizes side-viewing scopes and different accessories, in addition to fluoroscopy. Close coordination is required between endoscopist and assistant in manipulating accessories. Traditional teaching involves use of conventional long accessories. The short wire Fusion system minimizes exchanges, allows better control by the endoscopist and less reliance on the assistant, thus shortening the ERCP procedure.

Aim: Using a mechanical simulator, we determine 1. if use of short accessories will shorten procedure time compared to long accessories, and 2. determine the possible correlation between procedure time and actual ERCP skill (total experience).

Methods: 13 advanced GI fellows from the Western United States participated in a hands-on practice ERCP course. An anonymous survey documents the pre-practice endoscopy experience, and post-practice evaluation of simulator practice in ERCP training. ERCP was performed using a mechanical simulator and an artificial biliary duct with a built-in stricture. A pin-hole camera is used in place of fluoroscopy to monitor events within the bile duct. Time taken (minutes) to negotiate the stricture with a guide wire, perform balloon dilation and brushing cytology, and insertion of a plastic biliary stent using the conventional method or Fusion system were determined. The total procedure time (TT) and fluoroscopy time (FT) were taken. Each fellow was
paired with an experienced assistant and each set of tasks was repeated two times. Five experienced biliary attendings also performed the same tasks. T-tests were used for statistical analysis.

Results: The mean TT and FT taken by fellows (n = 13) was 15.1 min and 4.31 min for long accessories and 12.6 min and 4.88 min for the Fusion system respectively. The difference for TT between long and short accessories (p < 0.05) was significant, but not FT (p = 0.14). The mean TT for attendings using long accessories was 7.87 min and 6.43 minutes for the Fusion system (p = 0.02). The differences in both time taken for long and short accessories between fellows and attendings were significant (p < 0.005 for both).

Conclusions: The mechanical simulator allows comparison of objective data for ERCP practice with different accessories. The procedure time is inversely related to the total ERCP experience. Short wire and accessories may shorten procedure time compared to long accessories.

Utility of Endoscopic Ultrasound in Characterizing Mass Lesions in Chronic Pancreatitis
Jayaprakash Sreenarasinghiah, M.D.* Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, Dallas, TX

Purpose: Chronic pancreatitis is a well-established risk factor for the development of pancreatic cancer. CT and MRI are frequently used to detect changes of chronic pancreatitis and the presence of potential pancreatic neoplasms. However, not all lesions are malignant. Endoscopic ultrasound (EUS) is known to provide detailed images of the pancreas with characteristics often not detected by other conventional imaging modalities. The aim of this analysis is to determine the influence of EUS in characterization of lesions in the setting of chronic pancreatitis.

Methods: A retrospective analysis was conducted of 105 consecutive EUS examinations of the pancreas between January 2004 and May 2005. All procedures were performed by a single endoscopist. EUS-FNA was performed using an Olympus (GFUC30P) linear array echoendoscope and a Wilson-Cook 22-gauge biopsy needle.

Results: Of 105 examinations, 53 patients had pre-test clinical suspicion for chronic pancreatitis. 41 of 53 (77%) had confirmation of this by EUS criteria. The remainder had normal pancreatic sonographic images. In 33 patients, clinical suspicion supported by CT or MRI images suggested chronic pancreatitis with a pancreatic mass. Subsequently, all underwent EUS examination. Of these, 28 (85%) had a confirmed mass along with findings of chronic pancreatitis. EUS-FNA biopsy revealed 9 (32%) adenocarcinomas. The remaining 19 (68%) had benign lesions determined by either FNA biopsy, clinical observation for greater than 6 months, or surgical exploration. The benign lesions were regarded as manifestations of pancreatic inflammation and fibrosis. The location of all masses detected by EUS included the head of the pancreas in 23 (82%), the body in 4 (14%), and one in the uncinate process (4%). EUS also determined that the mass was solid in 26 (93%) cases and cystic in 2 cases (7%), one of which was a malignant cystic degeneration of adenocarcinoma.

Conclusions: In clinically suspected chronic pancreatitis, the diagnosis is erroneous in 23% of cases based on EUS criteria. In the background of chronic pancreatitis, an actual mass is confirmed by careful EUS examination in 85% of those with radiographic suspicion by either CT or MRI. Pancreatic masses analyzed by EUS in the setting of chronic pancreatitis are seen in the head of the pancreas in more than 80% of cases. Moreover, two-thirds are found to be benign lesions.

Efficacy of Endoscopic Ultrasound (EUS) with Fine-Needle Aspiration (FNA) Biopsy in Diagnosis of Pancreatic Neoplasms
Jayaprakash Sreenarasinghiah, M.D.* Division of Digestive and Liver Diseases, University of Texas Southwestern Medical Center, Dallas, TX

Purpose: Mass lesions of the pancreas can include a variety of malignant and benign tumors. Differentiating these tumors is essential for optimal management and outcome. The aim of this study is to determine the utility of EUS in cytopathologic diagnosis of pancreatic lesions and to understand the distribution of types of tumors that present in a tertiary referral center.

Methods: All consecutive pancreatic EUS examinations were analyzed between January 2004 and May 2005. A single endoscopist performed all examinations. A 22-gauge needle was used in EUS-FNA. Single pass biopsy of cystic lesions was performed with prophylactic antibiotics. An average of 7 FNA passes was achieved with solid tumors. A cytopathologist was present at bedside during each examination.

Results: EUS examination of the pancreas was performed in 105 patients consecutively for a variety of reasons such as tumors, pancreatitis, or abnormal imaging studies. In 59 individuals (average age 57.2 years, 33M/26F), EUS identified a mass. 45 (76%) were solid tumors and 15 (24%) were cystic in nature. Solid tumors included a total of 26 malignant lesions of which 23 (88.5%) were correctly diagnosed by EUS-FNA. The remaining 3 cases were identified by histology acquired during surgical exploration. Distribution of solid pancreatic malignancies included 13 adenocarcinomas in head of pancreas, 4 adenocarcinomas in the body/tail region, 3 neuroendocrine tumors, 3 ampullary adenocarcinomas with T3 extension into the pancreatic head, 2 metastatic lesions to pancreatic head from squamous cell carcinoma of the lung, and 1 uncinate process adenocarcinoma. EUS-FNA revealed that 3 (20%) of 15 cystic lesions were malignant and included both mucinous cystadenomas and cystic degeneration of adenocarcinoma. The remainder of the cysts included 6 pseudocysts, 5 benign serous cystadenomas, and 1 pancreatic abscess following resolution of acute pancreatitis. 2 of 15 cystic lesions (13%) had an uncertain diagnosis with EUS-FNA and resulted in surgical resection revealing histologically benign serous cystadenomas. Overall complications included one patient (1.7%) with post-FNA pancreatitis.

Conclusions: EUS and EUS-FNA accurately identified neoplastic solid tumors in 88.5% of cases. 100% of malignant cystic neoplasms and 87% of all cystic lesions in general were diagnosed by EUS-FNA. This is a safe modality for diagnosing both solid and cystic pancreatic neoplasms with high diagnostic yield.

Is the Incidence of Pancreatic Cancer Increasing in Patients with Chronic Pancreatitis?
Prasun K. Jula, M.D., Samuel Davidoff, M.D., Kostas Sideridis, M.D., Simmy Bank, M.D.* Division of Gastroenterology, Long Island Jewish Medical Center-Albert Einstein College of Medicine, New Hyde Park, NY.

Purpose: To determine if there has been any increase in the incidence of pancreatic cancer in patients with chronic pancreatitis.

Methods: (1) regional series: 162 patients with diagnosed chronic pancreatitis were followed up for a median of 12 years (10–14 yrs) from 1984 to 1996 in Long Island Jewish Medical Center and 2) International series: Data obtained from 21 published case series through a PubMed and Medline search combining MeSH terms ‘chronic pancreatitis,’ ‘complications’ and ‘mortality’; furthermore, a questionnaire was sent out to the selected pancreatologists from 15 centers worldwide with particular references to the outcome in patients with chronic pancreatitis from all causes and the length of follow up. The incidence of pancreatic cancer in the regional series was compared with age-stratified and gender-specific incidence of pancreatic cancer in the general population from SEER database to calculate the standardized incidence ratio (SIR).

Results: In the regional series, 17 patients (10.5%) had cancer and pancreatic cancer was diagnosed in 7 (4.3%). The incidence of pancreatic cancer in this cohort was significantly higher than the general population (SIR, 41, p < 0.0001). Pancreatic cancer was the cause of death in 13% of patients and all cause mortality was 33% in this group. In the international series, only 12 out of 21 studies recorded the incidence of pancreatic cancer, with median follow up of 10 yrs (5–20 yrs); the incidence of pancreatic cancer was 1–5%, except in cases of tropical pancreatitis with an incidence of 22%. The average
incidence of pancreatic cancer was 2.9% (1–5%) in patients diagnosed before 1984, compared with 4.2% (3–5%) in cases diagnosed after 1984 (did not achieve statistical significance).

Conclusions: Pancreatic cancer in patients with chronic pancreatitis is probably increasing, though enough data are not available due to poor reporting in published series. The increased incidence of pancreatic cancer may be due to chronic inflammation and in part, to an improvement in survival with therapy in patients with chronic pancreatitis.

A Higher Bilirubin Level Is Associated with Failure of Endoscopic Stent Placement in Patients with a Pancreatic Head Mass and Biliary Obstruction
Maarouf Hotet, M.D., Kamil Obideen, M.D., Aasma Shaukat, M.D., M.P.H., Naveen Narahari, M.D., Qiang Cai, M.D., Ph.D. * Division of Digestive Diseases, Emory University School of Medicine, Atlanta, GA.

Purpose: The aim of this study is to investigate the association between the bilirubin level and failure endoscopic stent placement in patients with a pancreatic head mass and biliary obstruction.

Methods: We conducted a retrospective review of a database of all patients who underwent an ERCP at a large tertiary care teaching hospital between January 2000 and October 2004. Patients with a pancreatic head mass seen on CT or MRI and an elevated bilirubin level (> 1.5 mg/dL) were included. Patients with an existing biliary stent at the time of ERCP patients in whom the visualization of the ampulla was not possible, patients with a previous failure of endoscopic stent placement at our facility, as well as patients with known chronic liver disease were excluded. The latest available laboratory values and imaging reports prior to ERCP were reviewed. For the purpose of this study, successful ERCP was defined as the ability to place a stent across the biliary stricture.

Results: A total of 950 ERCP reports were reviewed. After the inclusion and exclusion criteria were applied, 47 patients were available for analysis. The mean patient age was 67 ± 12 years. The final diagnosis was pancreatic adenocarcinoma in the great majority of patients (39 patients, 83%). Liver metastasis was found in 7 patients (15%). The ERCP was successful in 28 patients (60%) and failed in 19 patients (40%). Patients with a failed ERCP had a significantly higher mean level of bilirubin compared to patients with a successful ERCP (17.8 ± 7.4 mg/dL vs 10.5 ± 6.7 mg/dL, p = 0.0009). The association persisted after patients with liver metastasis were excluded. No statistically significant association was found between failure of ERCP and other factors (age, sex, operator, liver enzyme level, estimated mass size).

Conclusions: Endoscopic stent placement in patients with a pancreatic head mass may be particularly challenging in patients with a higher bilirubin. Patients with a high level of bilirubin elevation should have their initial ERCP done in centers where Radiology and Surgery backup is readily available.

Nocturnal Hydration — An Effective Modality To Reduce Recurrent Abdominal Pain and Recurrent Acute Pancreatitis in Patients with Adult Onset Cystic Fibrosis
Kamil Obideen, M.D., Maarouf Hotet, M.D., Qiang Cai, M.D., Ph.D. * Division of Digestive Diseases, Emory University School of Medicine, Atlanta, GA.

Purpose: The objective of this study was to determine whether nocturnal hydration (NH) prevents recurrent abdominal pain and recurrent acute pancreatitis in patients with adult onset cystic fibrosis (CF).

Methods: Patients who were referred to the GI clinic for recurrent abdominal pain and pancreatitis were enrolled in the study. Each patient was initially told to drink as much water as they could before bed and to also drink as much as they could during the night when they woke up (Maximal Nocturnal Hydration, MNH). If they felt better after MNH, they could titrate the hydration volume down by 10% every 2 weeks. They could repeat this titration up or down, based on their symptoms, to find an optimal volume of nocturnal hydration (Optimal Nocturnal Hydration, ONH). Each patient established a 6-month diary (3 months before, 3 months after NH was initiated), recording the frequency and severity of their abdominal pain, the amount of pain medication taken, and the volume of their water intake. We also reviewed the number of doctor’s clinic visits, emergency room visits and hospitalizations about one year before and one year after the initiation of the NH.

Results: The enrolled patients were 6 females and 3 males. The mean age was 52 years. They all had CF confirmed by genetic testing. The frequency of abdominal pain in this group of patients was significantly reduced (54/month vs. 16/month, P < 0.05) after the NH. The severity of the abdominal pain significantly decreased from 5.1 to 1.8 (using a 0 to 10 scale) (P < 0.001). The amount of pain medication, the number of emergency visits and hospitalizations for abdominal pain and acute pancreatitis were reduced.

Conclusions: NH significantly reduces the frequency and severity of recurrent abdominal pain in those patients. NH also reduces the amount of pain medication, the number of ER visits and hospitalizations. NH is a simple and cost-effective method to prevent recurrent abdominal pain and pancreatitis in patients with adult onset cystic fibrosis.

Annular Pancreas Causing Duodenal and Biliary Obstruction
Ryan Palmer, M.D. *, Paul Jordan, M.D., Kenneth Manas, M.D., Ankur Sheth, M.D. GI, LSUHSC, Shreveport, LA.

Purpose: The incidence of annular pancreas is about 1:20,000. It is a congenital abnormality of pancreatic tissue that circles the duodenum and is of ventral pancreas in origin. Its most common presentation is of duodenal stenosis, peptic ulceration, and pancreatitis. In this rare case we will present a patient who presents with both duodenal obstruction and biliary obstruction.

Methods: Case: A 42 y/o male with past medical history significant for diabetes and hypertension presents with a three day history of intractable nausea and vomiting. On admission patient was in acute renal failure with a creatinine of 1.7. He was also jaundiced with a total bilirubin of 12.2 mg per dL and a conjugated fraction of 9 mg per dL. Other laboratory testing revealed an AST of 149 U/L, an ALT of179 U/L, an Alkaline Phosphatase of 103 U/L, and an albumin of 2.2 mg per dL. An abdominal series revealed air fluid levels in the distal stomach and the fundus. A CT scan was then performed that revealed a 1.5 cm common bile duct, a 7 mm pancreatic duct, a dilated stomach with no filling of contrast into the duodenum. No mention was made of annular pancreas. An EGD was performed to evaluate for gastric outlet obstruction. This revealed a massively dilated duodenum with a stenotic area in the second portion of the duodenum proximal to the ampulla. This stenosis made ERCP impossible. Annular pancreas was suspected at this time and the patient was taken to surgery for a bypass operation.

Results: Discussion: Annular pancreas has a bimodal presentation, the first peak being in neonates and the second being in the fourth and fifth decades of life. Trisomy 21, duodenal atresia, tracheoesophageal fistula, and cardioenal abnormalities have an association with annular pancreas. Because the pancreatic tissue often extends into the duodenal wall and may contain a large pancreatic duct, symptomatic cases of annular pancreas are best treated by surgical bypass rather than surgical resection.

Conclusions: This case illustrates the importance of suspecting annular pancreas when patients present with either duodenal stenosis or biliary obstruction even if ct scan findings are negative.

The Appropriate Method of Pancreatic Pseudocyst Drainage Can Be Predicted with an Endoscopic Ultrasound Based Scoring System
Damien Mallat, M.D., Deri Lewis, M.D., Joseph Kuhn, M.D., Jeffrey Lamont, M.D. * Gastroenterology, Baylor University Medical Center, Dallas, TX and Surgery, Baylor University Medical Center, Dallas, TX.
Purpose: Endoscopic management of pancreatic pseudocysts (PP) is a less invasive, effective alternative to standard surgical drainage procedures. The purpose of this study was to identify characteristics elicited by endoscopic ultrasound (EUS) that would predict whether a patient with PP should be managed via endoscopy versus a surgical approach.

Methods: A retrospective review was performed on patients with suspected PP who underwent EUS by a single gastroenterologist between September, 2003 and March, 2004. Specific cyst characteristics were postulated to be potential risk factors for failure of endoscopic management: cyst size greater than or equal to 6 cm, septations within the cyst, internal debris, pancreatic ductal communication, thick cyst wall, and multiple cysts. Failure of endoscopic management was defined as cyst recurrence after two endoscopic drainage procedures or cyst recurrence requiring surgery.

Results: Twenty-six patients with a median age of 61 years (range 36–64) underwent EUS evaluation and eleven patients additionally had an ERCP. Seven patients (27%) with PP were observed while 19 (73%) underwent a drainage procedure. Seven patients had multiple endoscopic drainage procedures. Endoscopic drainage consisted of aspiration, placement of internal drainage stent, or transpapillary stenting. Eight patients (42%) failed endoscopic management and 7 patients (37%) eventually required an open surgical drainage procedure. Cyst characteristics among patients with attempted drainage included ductal communication (n = 5), cyst size greater than or equal to 6 cm (n = 14), septations present within the cyst (n = 9), thick (n = 15) or thick (n = 3) debris present within the cyst, thick cyst wall (n = 5), and the presence of multiple cysts (n = 7). No single cyst characteristic was predictive of failure. The mean number of risk factors in patients who eventually required surgery was 3.86 compared to 2.15 in patients successfully managed endoscopically (p = 0.05). The rate of success of endoscopic drainage was 100% in patients 0–2 risk factors and 11% in patients with 3 or more risk factors.

Conclusions: EUS is essential in evaluating PP and can yield detailed information regarding these lesions. EUS-defined characteristics can help predict which patients can be managed endoscopically and which patients should undergo surgical drainage. Patients with 3 or more adverse cyst characteristics should be treated surgically.

Pancreas Plays a Role in the Excretion of an Excess of Plasma Amino Acids
Keisuke Fukushima, M.D., Hideyuki Doi, M.D.,* Susumu Satomi, M.D. Advanced Surgical Science and Technology, Graduate School of Medicine, Tohoku University, Sendai, Japan.

Purpose: High uptake of amino acids in pancreas demonstrated by recent positron emission tomography (PET) studies using radiolabeled amino acids led us to the hypothesis that pancreas could regulate the level of plasma amino acids by excreting an excess of amino acids into the pancreatic juice. Purpose of this study was to find a new function of pancreas by determining the levels of amino acids of the pancreatic fluid before or after the intravenous administration of amino acids.

Methods: Sprague-Dawley male rats were anesthetized, and a polyethylene tube was inserted into the pancreatic duct at the junction between the duct and duodenal wall for collection of pure pancreatic juice. The rats received saline solution, 2% valine solution, 2% leucine solution, 2% isoleucine solution or mixed amino acids solution. The samples of pancreatic juice were collected during 1 hour before the administration of an amino acid solution (basal pancreatic juice). After each solution was administered intravenously (1 ml/100 g), the juice was continuously collected for every 1 hour during the experimental period (2 hours). In addition, blood samples were collected for every 1 hour. The samples of the juice and plasma were deproteinized with 4% sulphosalicylic acid and the supernatants were analysed using the amino acid analyzer.

Results: The amino acid analysis of the basal pancreatic juice revealed that the concentrations of almost every free amino acid were detected in juice by aminoimino without the intravenous injection of amino acids. After the administration of valine, leucine or isoleucine, the valine concentration of the pancreatic juice increased from 56.4 to 179.6 nmol/ml, leucine from 53.9 to 111.7 nmol/ml and isoleucine from 32.5 to 112.5 nmol/ml in each juice collected during first 1 hour period. After 2 hours, the increased concentration of each amino acid returned to the level of the basal juice. Similarly, the concentrations of all amino acids increased in the juice after the injection of mixed amino acids solution. Free amino acids concentrations in plasma as well as the juice increased sharply after the injection and decreased after 2 hours.

Conclusions: We first demonstrated that almost every free amino acid were excreted into the pancreatic juice and the increase of amino acids was observed in the juice as well as plasma after the injection of amino acids solution. These results raised the possibility that pancreas might control the plasma amino acids homeostasis by excreting an excess of amino acids.

The Utility of Endoscopic Ultrasound Guided Fine Needle Aspiration (EUS-FNA) in Evaluating Pancreatobiliary Masses: Experience at a New EUS Center
Rahul Verma, M.D., Kourosh Ghassemi, M.D., Janak N. Shah, M.D., V. Raman Mathusamy, M.D.* Division of Gastroenterology, University of California, San Francisco, CA.

Purpose: The indications for EUS-FNA in staging and diagnosing pancreaticobiliary malignancy continue to grow. Increasing numbers of centers are performing EUS-FNA. We aim to evaluate the performance of this technique at a newly established EUS center.

Methods: A retrospective analysis of all patients undergoing EUS-FNA from 1/2002 through 4/2005 for the evaluation of known or suspected pancreaticobiliary masses based on imaging or clinical data was performed. The following information was abstracted from the endoscopy database and medical records: EUS indications, FNA results, procedural complications, and patient clinical data. EUS-FNA results were compared to surgical findings and/or long-term clinical follow up.

Results: Ninety-two patients underwent 94 EUS-FNA procedures during the study period. All procedures were performed by an EUS fellowship-trained gastroenterologist. Indications for EUS included: suspected mass on radiologic imaging (77%) or ERCP (16%), idiopathic abdominal pain (5%), chronic pancreatitis (3%), elevated CA19–9 (3%), and jaundice (1%). All patients underwent FNA of visible masses seen on EUS. Cytologic diagnoses at EUS-FNA were: adenocarcinoma 64%, chronic pancreatitis 12%, neuroendocrine tumor 4%, benign 15%, and lymphoma, solid pseudopapillary tumor, benign papillary neoplasm, and renal cell cancer (1% each). Overall, EUS-FNA was accurate in 87 of 92 patients (92%), based on comparison to surgical findings or at least 6 month long-term clinical follow up. One major complication occurred (duodenal perforation). EUS-FNA established a cytologic diagnosis in 59 of 64 patients with adenocarcinoma. Two patients were diagnosed at a second EUS-FNA performed for high clinical suspicion of malignancy, but prior non-diagnostic EUS-FNA. Of the 5 patients with false negative EUS-FNA specimens, 4 had benign cystology and 1 had cytologic findings consistent chronic pancreatitis. This yields a sensitivity of 92%, PPV of 100%, and NPV of 80% for EUS-FNA in establishing a diagnosis of adenocarcinoma. Per annum, the accuracy of EUS-FNA for establishing correct cytological diagnoses increased: 87% in 2002, 91% in 2003, and 94% in 2004.

Conclusions: At a newly established EUS center, EUS-FNA is a useful procedure to evaluate patients with suspected pancreaticobiliary tumors. The diagnostic accuracy with this technique may improve with increased operator and center experience.

Oeacm’s Razor: Are Synchronous Primaries an Exception?
Iqbal M. Binoj, M.D., Milica S. Bogdanovic, M.D., Emilio H. Pandika, M.D., Ahmed S. Eid, M.D., Roshan J. Lewis, M.D., M. Mansour, M.D., F.A.C.G., G. Posner, M.D., F.A.C.G.* Internal Medicine, Interfaith Medical Center, Brooklyn, NY.
Purpose: A 60 year old African American lady with a history of Hypertension, presented with anorexia, weight loss of 40 pounds over 6 months and jaundice of one month duration. During this time, she noticed a progressively enlarging right breast swelling which she disregarded. Even though she had a strong family history of breast cancer, her last mammogram was over 5 years ago. She was afebrile, icteric, with a right lower outer quadrant, hard, non tender mass of 6 cm with overlying skin retraction and no nipple discharge. The liver span was 17 cm. She had a total bilirubin of 12 mg/dL, direct bilirubin of 7.4 mg/dL, ALP 490 IU/L, AST 365 IU/L and GGTP 730 IU/L. CT scan of abdomen revealed a mass in the head of pancreas with biliary duct dilatation. Tumor markers revealed CA 19-9 of 119.7(<33.0), with CEA and AFP in the normal range. Endoscopic stenting with fine needle biopsy of the pancreatic mass was done. Metastatic workup with PET scan was negative for metastasis to bone,brain and lungs. She underwent a modified radical mastectomy which showed an infiltrating ductal carcinoma. Hormone receptor status was positive for Estrogen and Progesterone. Ten days later she had a Whipple’s procedure which identified a well differentiated adenocarcinoma of the pancreas. Population studies by the German Consortium for Hereditary Breast and Ovarian Cancer1 have confirmed the association between BRCA 1/2 mutation carriers and pancreatic cancer. It is estimated that about 5 to 10% of pancreatic cancers are familial. Evidence of BRCA1/2 cancer susceptibility is verified by Wang et al2 in clusters of pancreatic and breast cancers. Given the dismal prognosis of pancreatic cancer, all patients who are found to have BRCA 1/2 mutations need to have early workup for detection of pancreatic cancer.

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Endoscopic Ultrasound Fine Needle Aspiration (EUS-FNA) of Pancreatobiliary Masses in Patients with a Previously Negative Cytologic Evaluation
Rahul Verma, M.D., Kourosh Ghassemi, M.D., Janak N. Shah, M.D., V Raman Mathusamy, M.D.* Division of Gastroenterology, University of California, San Francisco, CA.

Purpose: Establishing a diagnosis for pancreatobiliary malignancy is of paramount importance for prognostic and therapeutic purposes. Radiologic guided fine needle aspiration (RG-FNA), cytological brushings during endoscopic retrograde cholangiopancreatography (CB-ERCP), and EUS-FNA are all common techniques used for tissue acquisition. There is limited experience on the role of repeat FNA in patients with previous non-diagnostic FNA. We evaluate the yield of EUS-FNA in patients with prior non-diagnostic RG-FNA, CB-ERCP, and EUS-FNA.

Methods: A retrospective review of medical records of all patients undergoing EUS-FNA between 01/2002 through 04/2005 for suspected pancreatobiliary neoplasm was performed. Patients with previous non-diagnostic cytological or pathological evaluation and 6 months of clinical followup were included.

Results: Ninety-two patients underwent EUS-FNA for a suspected pancreatic or biliary mass during the study period. Of these, 20 patients had 23 procedures with benign cytologic findings by previous FNA: RG-FNA in 7, CB-ERCP in 13, EUS-FNA in 2, and exploratory laparoscopy with pancreatic biopsy in 1. Overall, the cytologic diagnostic accuracy was 90% for EUS-FNA in patients with a previous non-diagnostic FNA. We evaluate the yield of EUS-FNA in patients with prior non-diagnostic RG-FNA, CB-ERCP, and EUS-FNA.

Conclusions: The role of EUS-FNA continues to evolve in pancreatobiliary diseases. In patients with previous unsuccessful cytological or pathological studies, EUS-FNA provides an excellent means of tissue acquisition with a high overall diagnostic accuracy.

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The Absent or Non-Communicating Santorini’s Duct—A Possible Cause of Pancreatitis?
Erina N. Foster, M.D., Joseph W. Leung, M.D., F.A.C.G.* GI/Hepatology, UCSF Medical Center, Sacramento, CA and GI/Hepatology, Veteran Affairs Northern California Health Care System, Sacramento, CA.

Purpose: Pancreatic ductal hypertension may predispose to pancreatitis. Lack of an overflow valve via the minor papilla resulting from an absent Santorini’s duct (ASD) or a non-communicating Santorini’s duct (NCSD) with the duodenum may render patients at risk of pancreatitis if there is main duct or sphincter obstruction. We performed a retrospective review of a series of patients presenting with pancreatitis or pancreatic pain and were found to have ASD or NCSD on pancreatogram, and assessed their response to treatment.

Methods: The ERCP database (GIFrac, Akron Systems) at a single center was reviewed. 368 patients underwent ERCP between 1995 and 2005 with a diagnosis of pancreatitis. 19 patients were found to have either ASD (n = 13) or NCSD (n = 6) on pancreatogram. The main pancreatic duct (PD) appeared normal in 14 and abnormal in 5. Those with proven pancreatitis received pancreatic sphincterotomy and/or PD stenting.

Results: There were 14 females, with a mean age of 47 yrs. 18/19 presented with pancreatic-type pain and abnormal amylase/lipase, or a prior history of documented acute pancreatitis. 9 patients were managed conservatively with low fat diet, no alcohol and pancreatic enzyme supplements. 9 underwent pancreatic sphincterotomy and stenting and 1 had sphincterotomy alone. Only 1 patient reported symptomatic improvement on conservative treatment, 5 had improvement in pain after pancreatic therapy. The mean follow up period was 15 months (range 2 – 47 months). 4 patients remained asymptomatic after pancreatic therapy, 5 patients required multiple pancreatic stenting and 2 needed additional dilation of the pancreatic sphincterotomy. 1 patient developed multiple pancreatic strictures and eventually underwent a Puestow operation. Overall, 5 patients who had pancreatic therapy improved as compared to 1 who was treated conservatively.

Conclusions: Absent or non-communicating Santorini’s duct may predispose an individual to acute pancreatitis. In a selected group of patients, short term pancreatic therapy may improve the pain or pancreatitis, but the long term follow up results have been rather disappointing as 4 patients had recurrent symptoms and 1 patient eventually required surgery.

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A Comparison of Two Scoring Systems (Ranson’s Versus Sequential Organ Failure Assessment, SOFA) in Predicting Outcome in Acute Pancreatitis—A Preliminary Study
Wiesen Ari, M.D., Kostas Sideridis, D.O., Prasun K. Jalal, M.D., Simmy Bank, M.D.* Division of Gastroenterology, Long Island Jewish Medical Center-Albert Einstein College of Medicine, New Hyde Park, NY.

Purpose: To evaluate the outcome of patients admitted with acute pancreatitis and comparison of Ranson’s score with maximum sequential organ failure assessment (SOFA) score to predict the prognosis

Methods: Data from consecutive patients admitted with acute pancreatitis in a referral center in the year 2003–2004 were retrospectively collected. All charts were reviewed for Ranson’s score at admission and 48 hrs and SOFA score daily for the first 5 days. The total maximum SOFA score was calculated summing the highest scores for all six systems. Organ dysfunction was considered as SOFA score of 1 or 2 points and organ failure as a SOFA score of 3 or more. The primary outcomes were mortality and duration of hospital stay. Patients with <18 years of age, known diagnosis of chronic pancreatitis or serum amylase and lipase <3 times normal were excluded.

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**Results:** 67 patients were admitted to the hospital with a diagnosis of acute pancreatitis over the one year period (34 male, 33 female; median age 54 years, range 21–96 years). The etiology of pancreatitis was alcohol (27%), gall stone (40%), post-ERCP (7%) or other (26%). The Ranson’s score at admission was 1.26; 1.07 and at 48 hrs 1.43±1.40. The maximum SOFA score at admission was 1.64±1.76 and at 48 hrs was 1.47±1.65. Two patients (2.9%) died from complications of acute pancreatitis. The Ranson’s score was 1 in both patients at admission and at 48 hrs, but the maximum SOFA score was 4 and 5 respectively. The median hospital stay for all patients with acute pancreatitis was 7 days (range 2–49 days). High Ranson’s score at 48 hrs and the mean maximum SOFA score both predicted a longer hospital stay. 4 patients (6%) had pancreatic necrosis involving >50% of pancreas and 4 patients had pseudocyst (2 in patients with necrosis) and both Ranson’s score and SOFA scores were comparable in predicting the outcome in these patients. **Conclusions:** Both Ranson’s score and SOFA score are useful in predicting the outcome with regard to the duration of hospital stay, pancreatic necrosis and pseudocyst formation. The SOFA score was better in predicting a fatal outcome in two patients that died.

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**3D-MRCP with Stereoscopic Viewing for Preoperative Information of the Cystic Duct Prior to Laparoscopic Cholecystectomy**

Tetsuya Yamagishi, M.D.,* Takao Itoi, M.D. Diagnostic Radiology and Endoscopy, Tokyo Medical University, Tokyo, Japan and Internal Medicine 4, Tokyo Medical University, Tokyo, Japan.

**Purpose:** It is important to have, prior to a gallbladder resection, a thorough knowledge of the anatomical information of the patients’ cystic duct, especially for the laparoscopic approach. We applied Prospective Acquisition CorR-Ection (PACE), which is one of the novel techniques using navigator triggering for scanning position correction, to high-resolution MRCP. This presentation is to show that the combination of high-resolution MRCP data and stereoscopic viewing leads to a decisive improvement for obtaining the three-dimensional (3D) extent of the cystic duct.

**Methods:** Thirty-five patients prior to laparoscopic cholecystectomy with fully informed consent underwent 2D and 3D MRCPP. The 2D examination was performed by single-shot with thick slab (5–7cm) around the horizontal and vertical axis/ every 10-degree. The source image of 3D was acquired with thin section (0.8mm) by respiratory-gating with PACE (total 88–96 slices). Data sets were imported into commercial available 3D rendering software. The sequential stereoscopic maximum intensity projection (MIP) images with omni-directional rotation of 3D-MRCP were created. The resulted 3D images were viewed with Red/Green glasses for stereoscopic visualization and compared with conventional 2D images. Fourteen board certified radiologists and endoscopists independently evaluated to compare observer performance in the detection of the 3D extent of the cystic duct and the value for making surgical planning prior to cholecystectomy by a four-point questionnaire survey: 1. excellent, 2. good, 3. adequate, 4. poor.

**Results:** All observers evaluated the morphological delineation of the cystic duct was decisively improved by 3D-data acquisition with HR. Ninety-three percent of the observer evaluated the resulted images as excellent for the purpose of detecting 3D extent of the cystic duct by stereoscopic images versus 26 percent by the conventional 2D images. By stereoscopic visualization variant of the cystic duct (e.g. posterior spiral insertion to the common bile duct) could be easily grasped. Stereoscopic visualization was also helpful to get rid of the signal overlay to surrounding organ.

**Conclusions:** In conventional MRCP, difficulties may occur to obtain firm anatomical information of the cystic duct. The observer performance of MRCP was decisively increased by HR data acquisition and stereoscopic viewing. Thus presented method is useful for obtaining information prior to laparoscopic cholecystectomy.

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**The Long-Term Natural History of Pancreatitis: Pancreatic Duct Morphology Does Not Predict Development of Pancreatic Failure**

Bimaljit S. Sandhu, M.D., William A. Hackworth, Stacey Stevens, Ph.D., Doumit S. Bouhaidar, M.D., Alvin M. Zfas, M.D., Arun J. Sanjay, M.D.∗ Division of Gastroenterology, Hepatology & Nutrition, VCU Medical Center, Richmond, VA.

**Purpose:** The aim of this study was to evaluate the natural history of subjects with acute recurrent and specific stages of chronic pancreatitis (CP) with respect to development of exocrine and endocrine failure and complications. **Methods:** A retrospective analysis of CP or acute recurrent pancreatitis was performed. PD changes were categorized as: 0 = no change, 1 = side branch etiata or pancreatic atrophy, 2 = 1+ irregularity of main PD, 3 = 2+ calcifications, PD stricture or dilatation. Pain was categorized as type A (intermittent acute), B (continuous) or combined (Ammann, Gastro 1999). Exocrine failure was defined by steatorrhea and endocrine failure by diabetes. Complications were defined clinically. The risk of developing each complication was assessed by Kaplpan-Meiers method and across group differences measured by logrank analysis. Logistic regression was used to identify risk factors for each endpoint. **Results:** A total of 154 subjects (stage 0 = 59, 1 = 20, 2 = 12, 3 = 63) with pancreatitis due to alcohol = 110, idiopathic = 32, others = 12 were studied. Baseline features included: (mean) age = 48 yrs, males = 93, Caucasian = 76, diabetes = 38. 80% of subjects developed steatorrhea(mean follow up 8 yrs) and 48% developed diabetes. Baseline PD changes did not predict either endpoint. The frequency of flares of pancreatitis predicted steatorrhea (p<0.04) and weight predicted diabetes (p<0.03). Pain continued with the following patterns: A = 78, B = 45, and C = 36. The baseline stage of duct change (p<0.02) and triglyceride levels (p<0.03) significantly predicted the frequency of acute flares of pancreatitis. Pseudocyst developed in 70 subjects requiring intervention in 23. A bile duct stricture developed in 15 subjects; 2 required drainage and surgical biliary decompression. The rest were managed endoscopically and secondary biliary cirrhosis developed in none. 20% subjects developed splenic vein thrombosis but none have bled from varices. Only 2 patients developed pancreatic carcinoma during follow-up. Ongoing alcohol consumption did not correlate with any endpoint. **Conclusions:** CP is associated with a high risk of exocrine and endocrine failure. The baseline PD changes do not predict these endpoints. Baseline PD changes correlate with risk of recurrent flares of pancreatitis which correlate with risk of steatorrhea. Weight independently predicts risk of diabetes.

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**Pancreatic Duct (PD) Stenting with the Johlin Wedge Stent (JPWS) in Pancreatic Disease**

Adam Lowe, M.D., Romeo F. Esquivel, M.D., John T. Cunningham, M.D.∗ Medicine, Arizona Health Sciences Center, Tucson, AZ and Medicine, Southern Arizona VA Health Care System, Tucson, AZ.

**Purpose:** Endoscopic management in pancreatic disorders is widely accepted. PD stenting for an obstructed/disrupted duct has been described. However, these stents are often placed short-term. We describe our experience with the JPWS in a series of pts with chronic pancreatitis (CP) or pancreatic cancer (PCa).

**Methods:** All pts, between October 2002 and March 2005, with symptoms or objective data suggesting either an obstructed/disrupted PD were evaluated for stent placement. ERCP was performed and an 8.5 or 10 Fr JPWS was deployed. Pts were followed at either 12 or 24 week intervals with repeat ERCP ± stent exchange.

**Results:** A total of 21 pts, ages 26 to 83 years, underwent ERCP with placement of the JPWS. A total of 34 stents were placed; 9 pts had serial stent placements. All pts had ductography changes at ERCP consistent with CP by the Cambridge Classification or PCa with stricture. The etiology of pancreatic disease in these pts was PCa (3), alcoholism (7), idiopathic (5), gallstone (2), IPMN (1), p. divisum (1), hereditary (1) and papillary stenosis (1). Indications for stent placement were: 6 PD disruptions (3 pseudocysts,
2 pseudocyst with pancreatic ascites, 1 pancreaticopleural fistula), 8 PD strictures and 6 PD stones. 29 were placed in the main PD; 5 stents were placed in the dorsal duct. Follow-up was completed in 17 of the 21 pts (81%). 2 pts underwent stent removal within 14 days for abdominal pain and 1 pt had early stent removal for bacteremia of unknown source. Of the remaining 14 pts, 7 had resolution of both their symptoms and underlying process; 6 pts remain with a JPWS in place and continue with marked improvement in symptoms. The remaining pt went for surgery shortly after stent placement for pancreatic head malignancy. In 2 pts at interval ERCP, the stents were noted to partially migrate distal to the duodenum, but they remained asymptomatic. There were no clinical stent occlusion events. Stents remained in the PD between 95 and 252 days with a mean length of 163 days. There were no complications related to length of time the stent remained intraduodenal.

Conclusions: Placement of the JPWS is effective in the management of pts with symptoms related to pancreatic disease. Palliation of abdominal pain and resolution of leakage and strictureting occurred in the majority of pts alleviating the need for surgical intervention. In addition, these stents may be safer left in place for up to 24 weeks allowing for less frequent stent exchanges.

203 Experience Using a Therapeutic Linear Echendooscope for Pancreatic Pseudocyst Drainage

Young S. Oh, M.D., Steven A. Edmundowicz, M.D., Eileen M. Janec, M.D., Dayna S. Early, M.D., Sreenivasa S. Jonnalagadda, M.D., Riad R. Azar, M.D.* Division of Gastroenterology, Washington University School of Medicine, Saint Louis, MO.

Purpose: We report our experience in pancreatic pseudocyst drainage using a therapeutic linear echoendoscope with a 3.7 mm diameter working channel to place 10 French stents.

Methods: Consecutive pts who were considered for endoscopic ultrasound (EUS)-guided pancreatic pseudocyst drainage from 10/1/2002 to 5/24/2005 were identified retrospectively from the endoscopic database at our institution. Factors predictive of successful EUS-guided pseudocyst drainage were determined by Chi-squared testing.

Results: EUS-guided pseudocyst drainage was considered in 38 pts (39 pseudocysts) during this time period. EUS-guided cystenterostomy was technically successful for 24 pseudocysts in 23 pts. Complete pseudocyst resolution occurred in 16 out of the 24 pseudocysts (67%); 7 patients (7 pseudocysts) eventually required surgery for persistent or refractory pseudocysts and 1 patient (1 pseudocyst) was lost to follow up. Pseudocyst drainage was attempted but was technically unsuccessful in 4 patients – 2 patients had free intraperitoneal air after the procedure, 1 patient had stent migration into the peritoneum, and 1 patient had unexplained hypotension during the procedure likely the result of propofol used for sedation. No significant complications, such as death or bleeding resulting in hemodynamic instability, occurred in any patient undergoing the procedure. In 11 patients (29%), endoscopic drainage was not attempted based on the EUS findings, most commonly the presence of debris in the pseudocyst and gastric varices. Lack of pancreatic necrosis on CT scan was found to be predictive of successful EUS-guided pseudocyst drainage on statistical analysis (p = 0.008).

Conclusions: EUS-guided pseudocyst drainage was effective in achieving pseudocyst resolution in two-thirds of cases. Drainage in patients with necrotizing pancreatitis was not as successful as in those patients without necrosis. EUS is important in delineating factors that may preclude successful pseudocyst drainage, such as the presence of debris, unsuspected cystic neoplasm, and gastric varices.

204 Endoscopic Ultrasound: A Meta-Analysis of Test Performance in Suspected Biliary Disease

Donald Garrow, M.D., Scott Miller, M.B.S., Brenda J. Hoffman, M.D., Robert H. Hawes, M.D., Joseph Romagnuolo, M.D.* Division of Gastroenterology, Hepatology, Digestive Disease Center, Medical University of South Carolina, Charleston, SC.

Purpose: Endoscopic ultrasound (EUS) achieves high-resolution images of the bile duct and pancreas, and avoids the risks of endoscopic retrograde cholangiopancreatography (ERCP). While studies show performance similar to MR cholangiopancreatography (MRCP), it has not nearly been as widely disseminated. We aimed to summarize the EUS test performance in suspected biliary disease with a meta-analysis.

Methods: Relevant studies were identified via Medline search (January 1988 – December 2004) and citation indexing. Studies were selected if they permitted reconstruction of a 2 x 2 contingency table of EUS compared with a gold standard involving direct biliary opacification (ERCP, intraoperative/percutaneous cholangiography) and/or adequate clinical follow-up. Random-effects models were used to estimate the pooled sensitivity and specificity, after adjusting for sample size, prevalence of disease, publication year, and study quality. Summary receiver-operating characteristic analysis was performed. Two independent observers graded study quality (blinding, consecutive enrollment, single (versus composite) gold standard, and direct cholangiography in >90% of patients). The effects of prevalence of disease and sample size, clinical context (obstructive jaundice, pancreatitis, etc), radial vs. linear echoscopy, publication year (surrogate of “EUS era”), on diagnostic performance were assessed. Performance regarding overall presence of obstruction, cholecodolithiasis and benign vs. malignant obstruction were analyzed. Influence of FNA has not yet been analyzed.

Results: 31 eligible, non-overlapping studies met inclusion criteria (3,186 patients). EUS had a high overall pooled sensitivity (87%; [95% CI: 84% to 89%]) and specificity (92% [89% to 94%]) for biliary obstruction (92% under the curve – 0.92). The procedure was more sensitive (89%, CI = 86% to 92%) and specific (95% [91% to 96%]) for cholecodolithiasis than malignancy (sensitivity = 79% [73% to 89%], specificity = 82% [67% to 89%]). Confounding factors were not significant.

Conclusions: EUS is a highly accurate non-invasive imaging modality. Like MRCP there is excellent overall accuracy for diagnosing cholecodolithiasis, with less-impressive results for malignany when FNA is not used; the latter will improve when FNA is considered. Its lack of radiation and lower procedure-related morbidity make it an attractive option for diagnosing biliary disease.

205 Incidence Pattern and Survival for Gall Bladder Cancer over Three Decades—An Analysis of 10301 Patients

Ravi P Kiran, M.B.B.S., Stanley J. Dudrick, F.A.C.S.* Department of Surgery, St Mary’s Hospital and Yale New Haven Hospital, Waterbury, CT.

Purpose: Gall bladder cancer is associated with a poor prognosis. Little is known about its incidence and survival pattern over the last decade.

Methods: Patients included in the Surveillance, Epidemiology and End Results Program of the National Cancer Institute with a diagnosis of primary gall bladder cancer between 1973 and 2002 were studied. Incidence, patient and tumor factors, treatments and survival for patients diagnosed between 1993–2002 (Group B) were compared to the others (Group A). Five year conditional survival and factors influencing survival were evaluated. Data is presented as median (interquartile range) for nonparametric data. Fisher’s exact, chi-squared and Kruskall-Wallis tests were used to determine the significance of differences between groups. p < 0.05 was considered statistically significant.

Results: 10334 patients had a diagnosis of gall bladder cancer in the database. 33 patients with lymphoid histology were excluded. Confirmation of cancer was by positive pathology in 94.4% patients. Median age was 73 years (72.4% female). SEER histlogic stage was localized in 22.3%, regional in 35.3%, distant in 36.6% and unstaged in 5.8% patients. Tumor differentiation was moderate in 22.3%, poor in 28.1%, well in 10.6%, undifferentiated or anaplastic in 1.2% and unknown in 35.7%. 62.3% patients underwent surgery and 13% radiotherapy. Median survival was 4 months. 5-year survival was 41.6% for localized, 5.7% for regional, 1.1% for distant and 8.8% for unstaged cases. A gradual reduction in the incidence of the disease occurred over the last 3 decades in both males and females, primarily in patients > 50 years. Though significantly fewer Group B patients underwent surgery (75% vs 90%, p < 0.0001), median survival was significantly higher compared to
**Purpose:** Small bowel tumors (SBT) are uncommon, representing less than 2-3% of all tumors of the gastrointestinal tract. SBT are frequently found late in their development and often carry a poor prognosis. Wireless capsule endoscopy (WCE) (PillCam SB) is a new tool in the evaluation of the small bowel. Endoscopy (WCE) (PillCam SB) is a new tool in the evaluation of the small bowel diseases that may allow early and accurate SBT detection. In a recent series of 562 patients referred for gastrointestinal hemorrhage, Cobrin et al found SBT in 8.9% of patients receiving PillCam SB (Gastroenterology 2004;126:A-194). Adenocarcinomas were the most commonly represented tumor (22% of SBT), followed by carcinoids (14%), and GISTS (6%). The aim of our study is to provide the incidence rate of symptomatic and asymptomatic small bowel tumors in a series of 240 WCE studies.

**Methods:** 240 PillCam SB studies conducted between September 2003 and March 2005 were retrospectively reviewed for the incidence of small bowel tumors. Patients received PillCam SB for various indications, including anemia (66%), GI hemorrhage (31%), Abdominal pain (21%), and diarrhea (11%).

**Results:** We detected 4 tumors (1.6% of all studies). Of these, 2 were in patients with symptomatic gastrointestinal hemorrhage. Tumors therefore represented the etiology in 3% of all GI hemorrhage cases. The other 2 tumors were incidental findings in patients without hemorrhage or anemia (0.8% of all patients). These incidental tumors appeared as submucosal lesions, presumably gastrointestinal stromal tumors (GIST). Neither patient was recommended for resection, so a definitive diagnosis could not be made. Of the two bleeding tumors, one was found to be consistent with a primary malignant melanoma, and the second a carcinoid tumor.

**Conclusions:** SBT represented the etiology of 3% of gastrointestinal hemorrhage cases referred to our institution for WCE. SBT appeared as incidental findings in 0.8% of patients undergoing PillCam SB.

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**Purpose:** Pill cam studies are compromised by slow transit times which necessitate long reading times and by incomplete studies which fail to evaluate the terminal ileum. Transit times were compared for patients with(MET+) and without metoclopramide(MET-) premedication to see if these end points would be affected. Metoclopramide is a promotility agent which has been shown to have activity in the esophagus, stomach and small bowel.

**Methods:** Consecutive patients, without a history of stricture or surgical alteration of the gastrointestinal tract, were included. All were studied after an overnight fast; one group was given metoclopramide 20 mg one hour before the studies. All tests were performed with Givens M2A Capsule and read with Rapid Reader. Mouth to pylorus(MP), pylorus to cecum(PC), mouth to cecum(MC) times in minutes and study completion(SC) were compared. Differences were evaluated with the t-test; values are given as the mean.

**Results:** There were 28 ZEL− patients, age 69. There were 20 ZEL+ patients, age 60. There were 28 MET− patients, age 69. There were 26 MET+ patients, age 61.

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No patient reported any Zelnorm adverse reaction.

**Conclusions:** There was no difference in transit times or study completion when premedication with Zelnorm was compared to no premedication. Zelnorm does not effect more efficient M2A capsule examination of the small bowel.
Methods: Data entered in the MDACC registry from 1944 to 2003 was extracted for all microscopically proven adenocarcinomas of the small bowel excluding ampullary and periampullary cancers and non-adenocarcinomas. Codes utilized by the MDACC registry were cross-referenced for age, gender, ethnicity, anatomic site, and analyzed for differences related thereto plus epidemiological trends during the sixty year specified interval. Distribution and trends were correlated with the published literature for comparative analysis.

Results: The data base included 523 cases of SBA of which 460 were classified for specific anatomic site. Peak incidence occurred in the sixth decade (mean 54.4 ±13.2 yrs), with decreasing incidence at extremes of ages. The relative incidence at different anatomic sites remained constant over the period of 60 years whereas site-specific incidence showed an interesting trend when cross-referenced with age at diagnosis. Jejunal SBA comprised 21% of the site-specific total (SST); however, 49% of all jejunal SBA occurred in the 0–49 age group. Duodenal SBA (59% of SST) and ileal SBA (20% of SST) were more uniform in age related distribution. SBA occurred more frequently in males (58% vs. 42%), with M:F ratio unity below age 50 and increasing with advancing age. Subsite distribution was similar for both genders. Caucasian ethnicity comprised 82% of the study, which is almost identical to the NCDB (80%) and SEER (84%) distribution; however, within the African-American subset, 51% occurred before age 50. Overall M:F ratio for Caucasian was 1.5; African American 0.7 and Hispanic 0.9. Ileal SST was 22% for Caucasians, 7% for African American, and 6% for Hispanics.

Conclusions: Significant differences exist in SBA prevalence and sub-site distribution within different age, gender, and ethnic groups. These features have been relatively preserved during the last six decades. Our observations a) provide insight from which further studies can be focused on presumed etiological factors and b) site-specific / age related distribution impacts on clinical practice related to diagnosis and screening for SBA.

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Small Bowel Ulcers Are Common in Patients Not Taking NSAIDs
Eric L. Tatar, M.D., Eric H. Shen, M.D., C.S. Pitchumoni, M.D.*
Gastroenterology & Hepatology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

Purpose: To assess the incidence of small bowel ulcers in a series of 194 patients undergoing wireless capsule endoscopy, and to evaluate for association with use of non-steroidal anti-inflammatory medications (NSAIDs).

Methods: 194 sequential patients who underwent wireless capsule endoscopy (WCE) were used to evaluate the incidence of small bowel ulcer occurrence. For the purpose of this study, the definition of “ulcers” included superficial erosions. Patients with ulcers in the duodenal bulb or with suspected inflammatory bowel disease were excluded from the study. The association of ulcer occurrence with age, gender, NSAID use, proton pump inhibitor (PPI) use, and body mass index (BMI) were investigated.

Results: Patient indications for WCE were anemia (66%), gastrointestinal hemorrhage (30%), diarrhea (11%), abdominal pain (20%), and other (9%). At least one small bowel ulcer was present in 36% of all patients, and in 39% of patients with anemia. Small bowel ulcers were not found to be associated with age (p = 0.69), male gender (p = 0.36), or BMI (p = 0.84). Although occurrence of ulcers in patients on NSAIDs were 10% greater than those not on NSAIDs, this difference was not statistically significant (p = 0.37). A large proportion of patients not taking NSAIDs had small bowel ulcers (32%). Patients on both NSAIDS and proton pump inhibitor medications did not have a lower incidence of small bowel ulcers than patients on NSAIDS alone (48% vs 40% respectively, p = 0.56).

Conclusions: 1. Small bowel ulcers occur commonly in WCE patients not taking NSAIDs. This high rate occurrence may be idiopathic, due to medications, or due to unknown factors. 2). Proton pump inhibitor treatment is not associated with lower small bowel ulcer occurrence. 3). Because NSAID and PPI use are not associated with small bowel ulcer occurrence, the mechanism of ulcer formation in the small bowel is likely to be different from the gastric model, which involves prostaglandin inhibition and acid injury.

4). Given the remarkable high incidence of small bowel ulcers in this study, an examination of small bowel ulcer incidence in the asymptomatic general population would be warranted.

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Prevalence of Abnormal Liver Function Chemistry in an American Cohort of Patients with Celiac Disease
Shanti L. Erswaran, M.D., William D. Chey, M.D., Frederick Askari, M.D., Anna S. Lok, M.D., Robert J. Fontana, M.D., Jorge A. Marerro, M.D.*
Department of Internal Medicine, Division of Gastroenterology, University of Michigan, Ann Arbor, MI.

Purpose: Celiac disease (CD) is one of the most common autoimmune diseases in the United States. Even though liver chemistry abnormalities are commonly reported in European patients with CD, the prevalence, the response to gluten-free diet (GFD) and its severity in the United States is unknown.

Methods: This is a retrospective study of patients with CD diagnosed from January 2000 to December 2004. CD was based on duodenal biopsy. Laboratory and clinical data was obtained at diagnosis and after GFD.

Results: A total of 123 patients with CD were identified. The symptoms at diagnosis were abdominal pain (49%), diarrhea (63%), weight loss (49%) and iron deficiency (28%). Eighty-four patients had liver chemistries drawn before and after GFD therapy, and 57 (68%) were found to have abnormalities. Elevated aspartate aminotransferase (AST) or alanine aminotransferase (ALT) were seen in 21, both ALT and AST in 23, alkaline phosphatase only in 5, and AST, ALT and alkaline phosphatase in 8 patients. The total bilirubin and prothrombin time were normal. After GFD, 88% normalized their abnormal liver biochemistries. Liver histology was performed in 8 patients, 2 had developed cirrhosis and 1 had moderate fibrosis at the time of CD diagnosis. No patient developed hepatic failure after a median follow up of 18 months.

Conclusions: Liver abnormalities are commonly seen in CD and the majority improved after GFD. Significant histological hepatic injury can occur in patients with CD but the clinical course appears benign in our cohort. Further studies should evaluate the natural history of the hepatic involvement in CD.

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Video Capsule Endoscopy—Experience in Private Practice in Rural New Mexico
Adil M. Choudhary, M.D.,* Frederick French, M.D., Shams Tabrez, M.D. Division of Gastroenterology, Digestive Disease Institute, Roswell, NM.

Purpose: Video Capsule Endoscopy is a noninvasive diagnostic imaging procedure allowing proper visualization of entire small bowel. Currently the most common medicare approved indications include heme positive stools, unexplained iron deficiency anemia and gastrointestinal bleeding of obscure origin when upper GI endoscopy and colonoscopy fail to explain the cause.

Methods: We would like to present our experience over a one year period (November 2003 to November 2004). A total of 80 patients underwent this procedure using the Given M2A video capsule. The indications were: Ob- scure GI bleeding (41 patients), Iron deficiency anemia (32 patients), Change in bowel habit with unexplained diarrhea (4 patients), Inflammatory bowel disease (1 patient), Celiac disease (1 patient), Unexplained abdominal pain (1 patient).

Results: The findings were: Angiodysplasia (32 patients), Normal study (33 patients), Ulceration (6 patients), Mild diffuse erythema (8 patients), Tumor (1 patient). There were no complications except for one patient with a previously unknown stricture where the capsule got stuck in mid small bowel. Patient refused surgical intervention. Eventually the capsule passed on its own and the patient recovered uneventfully.

Conclusions: The diagnostic yield was highest in patients with unexplained iron deficiency anemia and obscure GI bleeding. We conclude that video capsule endoscopy is safe and the investigation of choice for GI bleeding of obscure etiology and unexplained iron deficiency anemia.
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Celiac Disease and Internal Medicine Housestaff: A Single Center Experience
Timothy B. Gardner, M.D., Jeffrey A. Oringer, M.D., Douglas J. Robertson, M.D.* Gastroenterology, Dartmouth-Hitchcock Medical Center; Lebanon, NH and Gastroenterology, White River Junction VA Medical Center, White River Junction, VT.

Purpose: Previous investigations determined that both generalists and gastroenterologists demonstrate significant knowledge deficits regarding the diagnosis and management of patients with celiac disease. No studies have examined knowledge of celiac disease among resident physicians. We aimed to determine exposure to and knowledge of celiac disease in a cohort of internal medicine residents at a tertiary care center.

Methods: A sixteen-item survey was mailed to all current internal medicine housestaff at our medical center. The survey evaluated exposure to and basic knowledge of celiac disease. Knowledge questions were based on a recent widely circulated review on celiac disease.

Results: 63 surveys were mailed and 61 were returned for a response rate of 96.8%. 45.9% of respondents were first-year residents, 27.9% were in their second year, and the remainder were in their third year. 42.6% recalled receiving a lecture mentioning celiac disease in medical school, 68.8% had ordered a blood test to diagnose celiac disease, 37.7% had cared for a patient with celiac disease, and 9.8% had diagnosed a patient with celiac disease. Less than one quarter of respondents knew the prevalence of celiac disease in North America or that the most common presenting symptom of the disease in adults is iron deficiency anemia. Most respondents did not know that the tissue transglutaminase test can be falsely negative in IgA-deficient individuals (45.9%) or that tissue transglutaminase can be followed serially to monitor dietary compliance (26.2%). Most respondents (59.1%) knew that celiac disease is associated with other autoimmune diseases. The average score on the knowledge component was 50.7%, although more time in residency was significantly associated with higher scores. Resident physicians who had cared for a patient with (66.3% vs. 51.6%, p = 0.047) and made the diagnosis of (77.6% vs. 55.3%, p < 0.01) celiac disease scored better on the knowledge exam. There was no statistically significant difference in scores between those who had received a medical school lecture and those who had not (59.6% vs. 55.4%, p = 0.11).

Conclusions: Resident physicians’ knowledge pertaining to the diagnosis and management of celiac disease is often deficient. Exposure to patients with celiac disease improves general knowledge. More efforts are needed to educate resident physicians about this common disease.

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Analysis of Classified Advertisements for Gastroenterology in NEJM over 20 Years; 1985–2004
Nirmal S. Mann, M.D.,* Rafael E. Diaz, Ph.D. Gastroenterology, University of California, Davis, Davis, CA and Statistics, University of California, Davis, Davis, CA.

Purpose: Colonoscopy is considered the preferred method for colon cancer screening. Since July 2001, medicare program reimburses for screening colonoscopy every 10 years in average-risk persons, resulting in the increase in the number of colonoscopies performed (AJG 2003; 98:194–199), causing increased demands for gastroenterologists’ services. We evaluated the no. of classified advertisements (Ads) for Gastroenterology (G) in NEJM and compared them with Ads for Cardiology (C), the other procedure-oriented subspecialty of Internal Medicine, over the 20 year period from 1985–2004.

Methods: Ads for C and G from NEJM were manually counted on a weekly basis. The C/G ratio was calculated. The smallest and largest no. of Ads for C and G in a week were noted. The total no. of Ads for C and G were added up. Statistical method used for evaluating mean monthly Ads was time series analysis. The changes in C/G ratio during different periods were evaluated by first order auto-correlation model. The Shapiro-Wilk test statistics using the lower and upper Scheffe band was utilized.

Results: During these 1042 weeks there were 76713 Ads for C; mean 73.76 (range 14–218) per week. There were 26130 Ads for G; mean 25.12 (range 1–122) per week. The C/G ratio was 2.93 (range 1.37 – 18.20) per week. The smallest no. of Ads for G (one) occurred in 6/13/85 issue; the largest no. of Ads for G (122) occurred in the 11/4/99 issue. The smallest no. of Ads for C (14) occurred in the 1/24/85 issue and the largest no. of Ads for C (218) occurred in the 11/4/99 issue. The largest no. of Ads for both C and G occurred in the months of September to November; the smallest no. of Ads for C and G occurred in April to July. Probably these Ads are targeted to Fellows in training. The C/G ratio from 1985 to 1997 was in the range of 3.10 – 5.81 (95% confidence) and it was significantly higher than the C/G ratio from 1998 to 2004 which was in the range of 1.85 – 2.79 (95% confidence). The mean C/G ratio from 1997 to 2001 was 2.40 which was not different from the one from 2002 to 2004 which was 2.48. However, C/G ratio from 2002 to 2004 did not decrease any further.

Conclusions: The no. of Ads (and presumably demand for GI services) have increased since 1997 correlating with the use of screening colonoscopy. The number of Ads for C is three times that for G. The largest no. of Ads for C and G are placed during Sept. to Nov; the lowest in April to July.

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Fructose Induced Breath Hydrogen in Patients with History of Fruit Intolerance
Nirmal S. Mann, M.D.,* Eddie C. Cheung, M.D. Gastroenterology, University of California, Davis, Davis, CA and Gastroenterology, VA Medical Center; Martinez, CA.

Purpose: Some patients complain of abd cramps and diarrhea after ingesting certain fruit e.g. mango. We evaluated the Breath Hydrogen, no. of flatus passage and bloating score after 20 gm of oral fructose and compared them with healthy controls.

Methods: There were 4 normal male volunteers (Group 1) and there were 8 men with h/o fruit intolerance (Group II) in this study. All the subjects fasted overnight. The fasting breath hydrogen was measured using an EC 60 gasanalyser (Bedfont Scientific, Medford, N.J.), which has a sealed electrochemical sensor specific for H2. They ingested fructose 20 gm in 30 ml of water. Thereafter, breath H2 was recorded every 15 min for the next 8 hours (480 minutes). Number of flatus passage over 8 hours was recorded as a bloating score (on a scale of 1–10). Cumulative H2 over 8 hours was calculated by area under the curve (AUC). The data are reported as mean ± standard error of the mean (SEM) and were compared using t-test; p value of <0.05 was considered significant.

Results: The age of Group I subjects was 48.7 ± 3.5 (range 34–63) years was not different from the Group II patients 53.8 ± 5.2 (range 24–71) years. The mean bloating score of Group II 5.7 ± 0.1 (range 4–7), the no. of flatus passage 13.8 ± 0.3 (range 6–24) and cumulative H2 1745.2 ± 7.8 (range 1065–2147) ppm in 8 hours was significantly higher compared to Group I subjects who had a bloating score of 2.7 ± 0.2 (range 2–4), no. of flatus passage 7.2 ± 0.5 (range 5–9) and cumulative H2 of 712.5 ± 5.8 (range 393–1066) ppm in 8 hours.

Conclusions: Compared to healthy controls, patients with h/o fruit intolerance, after fructose ingestion produce more breath H2, pass a larger no. of flatus and have more bloating. Such patients should avoid fruits with high fructose content.

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Aspartic Fluid Density Measured by Hounsfield Units (HU) on Computed Tomography (CT) Scan as a Predictor of Total Protein and Albumin Content of the Aspartic Fluid
Ashvini Sahni, M.D.,* Sudipta Mazumder, M.D., Matthew Tangorra, D.O., Muhammad Abdullah, M.D.* Gastroenterology, Coney Island Hospital, Brooklyn, NY.

Purpose: Direct use of attenuation values from CT in the form of Hounsfield units (HU) is yet to be established for the measure of ascitic fluid density. The aim of the study was to determine if density of ascitic fluid as measured
by HU on abdominal CT correlates with the protein and albumin content of ascitic fluid; a non-invasive approach.

**Methods:** 48 patients with ascites who had abdominal CT and paracentesis were identified and retrospectively evaluated. Patients were analyzed using ascitic fluid protein, ascitic fluid albumin and serum ascites albumin gradient (SAAG). Ascitic fluid density using HU was calculated on abdominal CT by a single radiologist as a mean of fluid density taken at five points on the CT.

**Results:** The ascitic fluid with protein > 2g/dl had a mean attenuation value density of 21HU (± 9 SD) which was significantly higher than that of the fluid with protein less than 2 g/dl 8.2HU (±6) (p < 0.05). Ascitic fluid with albumin > 2g/dl had a mean HU density of 18.8HU (± 8.6) which was significantly higher than that of the fluid with albumin less than 2 g/dl 7.6HU (± 6) (p < 0.05). 35/37 (94.6%) patients with ascitic fluid with protein less than 2g/dl, and 23/25 (92%) patients with ascitic fluid with albumin less than 2g/dl had an attenuation value lower than 20HU on CT. Attenuation values of ascitic fluid with SAAG >1.1 did not differ significantly from fluid with SAAG <1.1, 13.6 HU (± 10.7) vs. 12.5HU (± 8.0) (p = 0.68).

**Conclusions:** Attenuation values of ascitic fluid (HU) on CT abdomen correlates with the protein and albumin content of ascites, and hence can be a useful tool to estimate the protein and albumin content of ascitic fluid in the event of inability to perform paracentesis.

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**Prevalence of Celiac Disease in Patients with Hepatitis C Virus in Manhattan**


**Digestive Diseases, Beth Israel Medical Center; University of Maryland and Columbia Presbyterian Hospital.**

**Purpose:** Celiac disease (CD) is associated with various liver diseases including hepatitis C virus (HCV) and has developed in those receiving interferon-based treatments for HCV. The aims of the study are to determine the prevalence of CD in HCV patients in the New York City area and to determine if CD is precipitated by interferon treatment.

**Methods:** Cross-sectional study of 12 months duration. All HCV patients at the liver clinics at Beth Israel and Columbia Presbyterian Medical Center from May 2004 to June 2005 were offered enrollment. Celiac serologies: TTG IgA, EMA IgA, anti-gliadin(AGA)IgA/IgG, (total IgA in selected cases) were obtained and biopsies if positive. CD positivity was defined as TTG IgA +, EMA IgA +, AGA IgG + and total IgA negative. Demographics, viral load, genotype, treatment regimen and length, ethnicity were recorded. Data were analyzed by chi square analysis. Prevalence of CD in the general population is 1 in 133(0.8%), (Fasano, 2003).

**Results:** One hundred and eighty-two subjects and 78 controls were enrolled. Characteristics are in the table below. All those on treatment received pegylated interferon (PEG-IFN) plus ribavirin.

<table>
<thead>
<tr>
<th></th>
<th>HCV</th>
<th>Controls</th>
<th>Treated HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>182</td>
<td>78</td>
<td>27 (15%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47.7±14.9</td>
<td>50±15</td>
<td>48±15.3</td>
</tr>
<tr>
<td>Male</td>
<td>117 (74%)</td>
<td>24 (31%)</td>
<td>21 (78%)</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>67 (42%)</td>
<td>14 (18%)</td>
<td>12 (44%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>51 (32%)</td>
<td>57 (70%)</td>
<td>9 (33%)</td>
</tr>
<tr>
<td>Non-Hispanic Black</td>
<td>27 (17%)</td>
<td>7 (9%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (4%)</td>
<td>2 (3%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Length Tx (weeks)</td>
<td>20.4±15.9</td>
<td>19.6±15.9</td>
<td>20.4±15.9</td>
</tr>
<tr>
<td>Viral Load (IU/ml)</td>
<td>1,853,825±</td>
<td>1,930,947±</td>
<td>2,007,136</td>
</tr>
<tr>
<td>Genotype 1</td>
<td>87 (77%)</td>
<td>17 (68%)</td>
<td></td>
</tr>
<tr>
<td>TTG (p = 0.32)</td>
<td>4 (2.2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>EMA (p = 1.0)</td>
<td>1 (0.56%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AGA IgG (p = 0.32)</td>
<td>4 (2.2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AGA IgA (p &lt; 0.05)</td>
<td>81 (45%)</td>
<td>18 (23%)</td>
<td>18 (67%)</td>
</tr>
</tbody>
</table>

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**A Novel Radical Scavenger Attenuates Acute Lung Injury after Intestinal Ischemia/Reperfusion**

Koji Ito, M.D. Ph.D.,* Susumu Hiramoto, M.D., Saburo Horikawa, Ph.D. Surgery, Tsuchiura Kyodo General Hospital, Tsuchiura, Ibaraki, Japan and Pathological Biochemistry, Tokyo Medical and Dental University Medical Research Institute, Tokyo, Japan.

**Purpose:** Intestinal ischemia/reperfusion (I/R) is a critical and triggering event in the development of distal organ dysfunction, frequently involving the lungs. Respiratory failure is a common cause of death and complications after intestinal I/R. We have shown that pharmacological preconditioning with doxorubicin, an anticancer drug, protects the acute lung injury induced by intestinal I/R. This effect is due to the induction of antioxidant protein heme oxygenase-1. But the procedure of the preconditioning needs to be conducted before the intestinal ischemia. In this study we investigated the effects of edaravone (3-methyl-1-phenyl-2-pyrazoline-5-one), a newly developed hydroxyl radical scavenger which has been widely used for protection against I/R injury in patients with cerebral infarction, on the prevention of lung injury induced by intestinal I/R in rats.

**Methods:** Male Wistar rats were used. Under anesthesia, SMA was occluded with a small clamp. Following occlusion for 2 or 3 hours, reperfusion was initiated by removing the clamp. Administration of edaravone was intravenously injected into rats before reperfusion. Survival rate, histopathology, lung myeloperoxidase activity, lung malondialdehyde levels etc were analyzed.

**Results:** When rats were subjected to 3 h of intestinal ischemia, a high incidence of mortality was observed within 24 h. Under this situation, intravenous administration of edaravone just before the start of reperfusion reduced the mortality. To examine the efficacy of edaravone on the lung injury induced by intestinal I/R in more detail, we performed 2 h of intestinal ischemia followed by 2 h of reperfusion. Edaravone treatment decreased the neutrophil infiltration into the lungs and the levels of lipid membrane peroxidation in the lungs after intestinal I/R as compared to the I/R-treated rats lungs without edaravone treatment. Histopathological analysis also showed that edaravone treatment improved the lung injury induced by the intestinal I/R.

**Conclusions:** In this study, we demonstrated that administration of the novel radical scavenger, edaravone, attenuated acute lung injury induced by intestinal I/R. Application of the newly developed free radical scavenger, edaravone shows promising results in animal models of lung injury induced by intestinal I/R and may become powerful tools in the treatment of acute lung injury that occurs in intestine transplantation and intestinal surgery.
AGA IgA serologies were significantly more common in HCV patients. CD was only identified in patients with HCV. Of the four TTG IgA positive HCV patients only one had a biopsy; this was negative. The others are to be biopsied. The prevalence of CD is at least 0.6% (1 EMA positive patient), possibly 1.6% (3/182).

**Conclusions:** CD is more prevalent in our chronic HCV patients compared to the general population. IgA AGA is common in this population. The prevalence of CD in our HCV patients is not significantly increased compared to non-HCV controls. These patients will be followed while receiving PEG-IFN to determine if this treatment causes the development of CD.

**Video Capsule Endoscopy for the Evaluation of Small Bowel Polyps in Familial Adenomatous Polyposis (FAP): A Comparison with Standard Endoscopy**

Robert F. Wong, M.D., Ashok K. Tuteja, M.D., Derrick S. Haslem, M.D., Lisa Pappas, Aniko Szabo, Maydeen Ogara, James A. DiSario, M.D.*

**Internal Medicine, University of Utah, Salt Lake City, UT.**

**Purpose:** Compare video capsule endoscopy (VCE) to standard endoscopy for the diagnosis of small bowel polyps.

**Methods:** This was a single center, prospective study. Eligible patients had a clinical diagnosis of FAP. Most patients were concurrently enrolled in a NIH study and had at least 20 polyps in the duodenum and prior placement of a tattoo in the proximal small bowel (n = 28). Four FAP patients referred for routine VCE evaluation for small bowel polyps were also included. VCE was performed followed by push enteroscopy (PE) and lower endoscopy (LE). Two VCE readers independently determined the number and sizes of polyps in the following regions of small bowel: 1) defined segment of small bowel from the duodenal bulb to the tattoo; 2) quarters of small bowel determined by small bowel transit time. A single endoscopist blinded to VCE determined the number and sizes of polyps in the following regions: 1) defined segment of small bowel from the duodenal bulb to the tattoo; 2) maximum insertion length of PE; and 3) maximum insertion length of LE. The primary outcome was the number of polyps in the defined segment of small bowel, comparing VCE to the gold standard of PE. Agreement was calculated utilizing kappa coefficients.

**Results:** Thirty two patients participated in the study (median age 45 years, 41% female). On VCE, 94% of patients had polyps proximal to the tattoo compared to 100% on PE. VCE diagnosed less polyps in this region (median 10 and 9 for each reader) compared to PE (median 41) (p = 0.002). Agreement between VCE and PE was fair for polyp counts (k = 0.34, 0.36). For agreement determining the size of the largest polyp was poor to fair (k = 0.10, 0.22). VCE and PE disagreed for detecting large polyps (≥1cm) (k = −0.20, −0.27). For the entire small bowel, VCE detected significantly less polyps (median 38 and 54 for each reader) compared to combined (PE+LE) endoscopy (median 138) (p < 0.001). Agreement was fair to moderate between VCE and combined endoscopy (k = 0.21, 0.56).

On VCE, the percentage of patients with polyps in the first, second, third and last quarter of small bowel was: 100%, 35%, 15% and 46%, respectively. Polyps were more common in the first quarter than in the remaining quarters combined (p < 0.0001). Mean size of polyps was less than 5 mm in each quarter.

**Conclusions:** VCE underestimates the number of small bowel polyps in patients with FAP and does not reliably detect large polyps.

**The Capsule Identifies Obscure Primary Carcinoids in the Small Intestine**

Asma P Khapra, M.D., Richard R.P Warner, M.D.,* Blair Lewis, M.D.

**Division of Gastroenterology, The Mount Sinai Hospital, New York, NY.**

**Purpose:** Carcinoid tumors are a heterogeneous group. Midgut carcinoid accounts for approximately 50% of all carcinoid tumors in adults, the majority of which arise in the ileum. Since the clinical symptoms are often vague and unrecognized until disease becomes advanced, a majority of patients have metastatic disease at time of diagnosis. It is important to determine the location of the primary since, to a considerable degree, it directs management and predicts outcome. The aim of this study was to assess the utility of wireless video capsule endoscopy in identifying a suspected intestinal primary in patients with demonstrated metastatic carcinoid and no detectable primary on standard investigation.

**Methods:** A retrospective chart review was performed and 24 patients with metastatic carcinoid of unknown primary origin were encountered. Patients’ baseline characteristics, clinical presentations, radiological evaluations, chemistries, and therapies were all recorded. All patients underwent wireless video capsule endoscopy in search of a primary lesion after having negative localizing or nonspecific findings on EGD/Colonoscopy, Small Bowel Series, CT scan and OctreoScan®.

**Results:** Of the 24 patients, 8 (33.3%) had positive findings on capsule examination, suggesting a primary carcinoid tumor. All had previously diagnosed metastatic carcinoid on needle biopsy. 5 of these (62.5%) had an ileal primary, 1 (12.5%) had a jejunal primary, and 2 (25%) were simply classified as a mid small bowel primary. In all cases this positive finding changed management. 7 of the 8 patients (87.5%) underwent surgery and had confirmed small bowel carcinoid tumors. 1 patient who had very advanced disease and was not operated upon had an change in his chemotherapy regimen after the positive capsule finding. Of the 16 patients who had negative capsule studies, 6 had metastatic carcinoid diagnosed by liver biopsy, 1 had an orbit biopsy, 1 had a mesenteric mass biopsy, 1 had a lymph node biopsy, and 3 had significantly abnormal chemical markers (urine 5-HIAA, chromogranin A, and serotonin) strongly indicating carcinoid. No primary was found in 12 of the 16 patients, whereas in 4 patients the primary was proven by biopsy to be in the pancreas.

**Conclusions:** We conclude that wireless video capsule endoscopy is useful in detecting carcinoid tumors originating in the small bowel and not detected by any other conventional method. This localization is significantly important in directing treatment and management of these patients.

**M2A Wireless Capsule Endoscopy for Diagnosing Gastrointestinal Bleed Due to Ulcerative Jejunitis**

Sadnya Sarji, M.D., Bethany DeVito, M.D.* Department of Gastroenterology, Hepatology and Nutrition, North Shore University Hospital, Manhasset, NY.

**Purpose:** Nongranulomatous ulcerative jejunitis (NGUJ) is a rare, often fatal disorder that produces multiple nonmalignant small bowel ulcerations. The diagnosis is often missed or delayed because of the non-specific clinical features, limited usefulness of available radiologic tests, and failure to identify the lesions on endoscopy. Here, we describe a patient whose first presentation of NGUJ was massive gastrointestinal bleeding (GIB), diagnosed by wireless capsule endoscopy (WCE).

**Case Report:** A 75 year old female presented with melena, lethargy and anemia. She had a history of HIV (CD4<200) and remote history of anal cancer and breast cancer. She had been on anti-retroviral medications and did not use NSAIDs. On presentation, the patient had a blood pressure of 92/38 mmHg and pulse 104. Physical exam was significant for pallor, mild abdominal distension and melanic stool. Initial hemoglobin was 3.9 g/dL. She required transfusion of 24 units of packed red blood cells and was placed on IV proton pump inhibitor and parenteral nutrition. Multiple small bowel radiographs were normal. Serology for inflammatory bowel disease and celiac disease were negative. Upper endoscopy was normal. Colonoscopy, with terminal ileum intubation, demonstrated mild left sided colitis and ileitis. Biopsies taken during endoscopy revealed non-specific inflammation. No infectious agents were found. The patient was placed on Rowasa enemas but with continued bleeding. Bleeding scan was positive for small bowel bleed. Angiogram was normal. M2A WCE was performed, which revealed NGUJ, i.e. flattened jejunal mucosa and ulcerations. The
Seroprevalence of IgA Antibodies to Tissue Transglutaminase in a University-Based Population Study in Mexico City

Juan A. Valcarce-Leon, Student, Mariana Santiago-Lomeli, Ph.D., Max Schmulson, M.D., Aldo J. Montano-Loza, M.D., Dana Lau-Corona, Student, Guillermo B. Robles-Diaz, M.D.∗ Experimental Medicine, Faculty of Medicine, Universidad Nacional Autonoma de Mexico-UNAM, Mexico City, Mexico and Gastroenterology, Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico.

Purpose: Celiac disease (CD) is one of the most common chronic conditions worldwide. The disease develops following gluten ingestion in genetically susceptible individuals. Because of the wide clinical spectrum of a given target population ranging from silent, and atypical to classic cases with malabsorption syndrome, the overall frequency can only be determined by screening a given target population using a sensitive serological test, such as IgA tissue-transglutaminase (tTG) antibodies. Overall, the prevalence of CD in Western populations is close to 1% and may be higher in Northern European countries, whereas the disease is uncommon among people from purely African-Caribbean, Chinese, or Japanese background. Studies on CD prevalence in the Mexican population have not been reported but there seems to be a wide gap in the frequency of CD between Europe and Mexico. Therefore our aim was to determine the seroprevalence of IgA anti-tTG antibodies in a population from Mexico City.

Methods: Professors, students and workers from a public university (Universidad Autonoma Metropolitana) were invited to voluntarily participate in the study. Serum was tested for anti IgA tTG antibodies using an enzyme linked immunosorbent assay (INOVA Diagnostics, Inc). A positive result was considered when a value of more than 20 units was obtained. Positive cases were confirmed by duplicate testing.

Results: So far 553 subjects have been studied, 336 females (60.7%) and 217 males (39.3%) with an overall median age of 29 years (range: 17 – 69). Four subjects had positive serology (3 males and one female). This result provides an estimated prevalence of 0.72% (95% CI 0.31–1.13).

Conclusions: Preliminary results of this ongoing study, show a seroprevalence of CD in Mexico based on Anti-tTG to be in the range of 0.5% to 1%, affecting 1 of every 138 subjects, which is similar to the prevalence estimates in western populations. Additional tests such as duodenal biopsies are still required to ascertain the diagnosis of CD in these cases. These findings may increase the degree of awareness for this under diagnosed disease in clinical practice in Mexico.
Biopsies were characterized using Marsh criteria. PPV and 95% confidence intervals (CI) were calculated.

**Results:** Ninety-five patients had positive TTG (TTG > 20), with 59 confirmed biopsies (PPV = 0.62). Eighteen of 26 asymptomatic TTG positive patients were true positives (PPV = 0.69). Forty-one of 69 symptomatic TTG positive patients were true positives (PPV = 0.59). Forty-nine TTG positive patients had levels > 100, with 44 confirmed biopsies (PPV = 0.90). Thirty-eight TTG positive patients had levels > 150, with 37 confirmed biopsies (PPV = 0.97). Forty-one patients had a positive EMA, with 36 confirmed biopsies (PPV = 0.88). Eleven of 12 patients who screened positive with both TTG and EMA had confirmed biopsies (PPV = 0.92).

Positive Predictive Values of Pediatric Celiac Screening

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>True (+)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTG (+) (TTG &gt; 20)</td>
<td>95</td>
<td>59</td>
<td>0.62 (CI = 0.52–0.72)</td>
</tr>
<tr>
<td>Asymptomatic TTG (+)</td>
<td>26</td>
<td>18</td>
<td>0.69 (CI = 0.48–0.86)</td>
</tr>
<tr>
<td>Symptomatic TTG (+)</td>
<td>69</td>
<td>41</td>
<td>0.59 (CI = 0.47–0.71)</td>
</tr>
<tr>
<td>TTG &gt; 100</td>
<td>49</td>
<td>44</td>
<td>0.90 (CI = 0.78–0.97)</td>
</tr>
<tr>
<td>TTG &gt; 150</td>
<td>38</td>
<td>37</td>
<td>0.97 (CI = 0.87–0.99)</td>
</tr>
<tr>
<td>EMA (+)</td>
<td>41</td>
<td>36</td>
<td>0.88 (CI = 0.74–0.96)</td>
</tr>
<tr>
<td>TTG (+) and EMA (+)</td>
<td>12</td>
<td>11</td>
<td>0.92 (CI = 0.64–0.98)</td>
</tr>
</tbody>
</table>

Conclusions: EMA seems to have a greater PPV compared to TTG. Increasing the cutoff for TTG to 100 or 150 increases its PPV to a level comparable to EMA. There is little difference in the PPV of TTG for screening symptomatic patients versus those screened only because of family history or comorbid diagnoses. This data suggests using both TTG and EMA for screening celiac patients versus those screened only because of family history or comorbid conditions.

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*Is There a Threshold Dose for Nonselective (NS) NSAID-Associated Small Bowel Injury?*

**Purpose:** Aspirin (ASA) and (ns) NSAIDs are associated with the development of dose dependent gastroduodenal ulcers and ulcer complications. In a recent placebo (P) controlled trial using video capsule endoscopy (VCE), full dose naproxen (500 mg bid) was associated with an approximately 27 fold increased rate of endoscopic small bowel (SB) mucosal injury as compared to those subjects randomized to P.

**Hypothesis:** Compared to P, over-the-counter (OTC) ns NSAIDs or low dose ASA use is associated with a dose dependent increased incidence of SB mucosal injury.

**Methods:** In a single center, two independent, prospective, double blind, P controlled trials using VCE, evaluated the incidence of SB mucosal breaks (MBs) in healthy subjects treated with P or naproxen sodium (NapNa) (220 mg/day or 440 mg/day; Trial 1) or with P or ASA (81 mg/day or 325 mg/day; Trial 2). In each study, subjects underwent a 2 week run-in period followed by a baseline VCE. Subjects without MBs, and who met inclusion criteria, were randomized to blinded drug for 2 weeks and then underwent a second VCE. The primary endpoint was the mean number of MBs/subject. The secondary endpoint was the percent of subjects with at least one or more SB MBs.

**Results:** Combining the results of baseline exams in both studies, 7.9% (n = 14/177) of subjects had at ≥ 1 MBs and were excluded from randomization. Of the 56 subjects randomized in the NapNa trial, the mean number of MBs/subject was 0.16 in the P group (n = 3/19), 0.11 in the 220 mg/day group (n = 2/19), and 0.22 in the 440 mg/day group (n = 4/18). The percent of subjects with ≥ 1 MBs was 10.5% (P), 5.3% (220 mg/day), and 16.7% (440 mg/day). Of the 80 subjects randomized in the ASA trial, the mean number of MBs/subject was 0.43 in the P group (n = 12/28), 0.22 in the 81 mg/day group (n = 6/27), and 0.32 in the 325 mg/day group (n = 8/25). The percent of subjects with ≥ 1 SB MB was 28.6% (P), 11.1% (81 mg ASA), and 16% (325 mg ASA). The differences comparing either dose of ASA or NapNa to P were not statistically significant.

**Conclusions:** Our data suggest that at OTC doses, NapNa and ASA are not associated with an increased incidence of SB mucosal injury. The results of earlier studies together with our data suggest that there may be a threshold dose of NapNa and ASA that may be required in order to cause detectable SB mucosal injury using VCE.

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*Capsule Endoscopy for Obscure Gastrointestinal Bleeding: Preliminary Report of a Prospective Study from India*

**Purpose:** Obscure gastrointestinal bleed (OGIB) is difficult problem requiring extensive investigations. Capsule endoscopy, a new and potentially effective method to evaluate small bowel, may be useful for patients with OGIB.

**Methods:** 16 patients with OGIB were evaluated using capsule endoscopy (Given Imaging Ltd., Yqneam, Israel) during 19 mo period (from November 2003 to May 2005) after standard bowel preparation. Each patient was clinically evaluated. The images were downloaded to a computer after 8-h and examined by single investigator using a software (Rapid Reader). The patients with a definite diagnosis on capsule endoscopy received specific treatment and were followed-up.
Results: Of 16 patients (median age 57±y, range 25 to 76; 9 males), symptomatic for a median duration of 15 months (range: 0.5 to 240), bleed was occult, overt or combined in 4, 9 and 3, respectively requiring blood transfusions (median 11 units, range 0 to 30). One patient presented with recurrent bleed after right-hemicolecotomy and one other had negative exploratory laparotomy, both done elsewhere. Capsule endoscopy could detect the lesions potentially causing OGIB in 13 of 16 (81%) patients and these included isolated bleeding lesion in distal small bowel in one ( ulcerated Meckel’s diverticulum with bleeding at surgery), ulcerated stricture in small bowel in three patients (verified at surgery in two and one responded to anti-tubercular drugs), worms infestation (successfully treated with ivermectin), anastomotic ulcer in one, multiple angiodysplasia in two (verified by colonoscopy both), isolated bleeding spot in duodenum in one, multiple small intestinal varices in two, small intestinal tumor in two (both verified by surgery) and no specific lesion in three patient. Though one patient had delayed capsule expulsion, none developed intestinal obstruction due to retained capsule. **Conclusions:** Capsule endoscopy is effective and safe for diagnosing lesions causing OGIB.

**Trichomethoprim-Sulfamethoxazol Prophylaxis Against Isospora belli Infection in Advanced AIDS Disease. Does It Help?**
Edson Jurado da Silva, M.D.,* Dirce B. de Lima, Ph.D., Valeria R. Gomes, M.D., Marcio N. Boia, Ph.D., Gustavo Albino P. Magalhaes, M.D.
Digestive Endoscopy, Casa de Portugal, Rio de Janeiro, Brazil and Internal Medicine, State University of Rio de Janeiro, Rio de Janeiro, Brazil.

**Purpose:** The aim of this study was to evaluate the usefulness of trimethoprim-sulfamethoxazole (TMP-SMX) prophylaxis for Pneumocystis carinii pneumonia (PCP) in reducing the incidence of isosporiasis in patients with advanced AIDS and chronic diarrhea.

**Methods:** Adult AIDS patients with persistent diarrhea seen in our hospitals from 1985 to 1992 without PCP prophylaxis Group A were compared with adult AIDS patients with chronic diarrhea been followed with TMP-SMX prophylaxis for PCP from 1996 to 2004 Group B. The diagnosis of protozoa was based on identification of the organism in stool by the modified acid-fast method. Student t test was used for means and chi-square to compare frequency. A p < 0.05 was considered significant.

**Results:** Ninety four adult AIDS patients Group A, age 42 ± 8.7 and 170 Group B, age 40 ± 9 p > 0.05 were submitted to stool examination for Isospora belli, being positive in 21 (22.3%) for the first Group and 5 (2.9%) for the second one p < 0.01.

**Conclusions:** The reduced incidence of isosporiasis in advanced AIDS might be related to PCP prophylaxis with TMP-SMX. The Highly Active Antiretroviral Therapy (HAART) regimen could be another possible reason.

**Small Bowel Bacterial Overgrowth Is a Potential Mechanism for Thiamine Deficiency Identified after Roux-en-Y Gastric Bypass Surgery**
Shilen V. Lakhani, M.D., Hiral N. Shah, M.D., Kenneth Alexander, R.N., Frederick C. Finelli, M.D., J.D., John R. Kirkpatrick, M.D., Timothy R. Koch, M.D.* Section of Gastroenterology. Washington Hospital Center. Washington, DC; Department of Medicine, Washington Hospital Center. Washington, DC and Department of Surgery, Washington Hospital Center. Washington, DC.

**Purpose:** Present evidence supports a saturable, carrier-mediated exchange mechanism for thiamine transport across jejunum. It is proposed that thiamine deficiency after gastric bypass surgery results from prolonged nausea and emesis. We observed that individuals after gastric bypass surgery developed thiamine deficiency and elevation of serum folate levels, a proposed marker for small bowel bacterial overgrowth. We hypothesized that small bowel bacterial overgrowth interferes with absorption of thiamine from the small intestine.

**Methods:** We performed a retrospective review of consecutive patients who underwent Roux-en-Y gastric bypass surgery from 2002–2004 in our institution. To eliminate immediate, post-operative changes, we included patients who received evaluation at 3 months or longer after surgery. There were 75 patients with determination of serum thiamine and folate levels. This included 48 females and 27 males with an average age of 46 years (range 21 to 68). Five patients with low serum thiamine and elevated serum folate levels had undergone glucose-hydrogen breath testing.

**Results:** There were 37 patients with serum folate levels greater than the upper limit of normal; among these patients, 23 (62%) had serum thiamine levels below the lower limit of normal. There were 38 patients with serum folate levels within normal range; 11 (29%) had serum thiamine levels below the lower limit of normal (Chi-squared test comparing thiamine deficiency in the normal folate group to the elevated folate group: p < 0.01). All 5 patients who underwent glucose-hydrogen breath testing had abnormal findings supporting a diagnosis of small bowel bacterial overgrowth: 4 patients had a significant rise (> 10 ppm) in breath hydrogen within 45 minutes after glucose ingestion, while 1 had an elevated fasting breath hydrogen level of 57 ppm.

**Conclusions:** Thiamine deficiency is common after Roux-en-Y gastric bypass surgery. Small bowel bacterial overgrowth appears to be common after gastric bypass surgery, as determined by elevation of serum folate levels or the presence of abnormal glucose-hydrogen breath testing. The results support the hypothesis that small bowel bacterial overgrowth following gastric bypass surgery can interfere with thiamine absorption.

**The Effect of Patient Positioning on Complete Small Bowel Examination Rates with Wireless Capsule Endoscopy: An Interim Analysis**
Colm J. O’Loughlin, M.D.,* Nathan E. Slinde, M.D. Gastroenterology & Hepatology, Medical College of Wisconsin, Milwaukee, WI.

**Purpose:** To evaluate (1) the effect on the gastric emptying time (GET), (2) the proportion of complete SI studies and (3) the diagnostic yield of WCE in patients placed in the right lateral position (RLP) compared with the standing/sitting position post CE ingestion (SSP).

**Methods:** 67 consecutive studies in patients undergoing WCE for investigation of obscure Gastrointestinal bleeding (OGIB) from 9/03 – 9/04 were analyzed retrospectively. 9 patients were excluded; 5 (endoscopic placement of the CE), 3 (h/o gastric surgery), 1 (gastroparesis). Patients remained in the RLP or in the sitting/standing position for 30 mins post CE ingestion. Major findings were defined as ulcers, AVMs, strictures, and active bleeding.

**Results:** The 58 remaining studies (31 men, 27 women, age range 16–80), included 35 patients from the RLP group and 23 from the SSP group. The mean GET (time from the first image of the stomach to the first image of the duodenum) in the RLP grp was 27 mins compared with 52 mins in the SSP grp (P < 0.05). The mean small intestinal emptying time was similar in both groups, RLP 207 mins and SSP 203 mins. Major findings were reported in 57% of the RLP grp and 43% of the SSP grp (NS). Stricture of the SI precluding passage of the CE occurred in 4 cases and 1 case in the RLP and SSP grp respectively. 2 battery failures occurred in the SSP. Otherwise incomplete examinations of the SI were reported in 6% of the RLP grp and 9% of the SSP grp (NS).

**Conclusions:** Positioning patients to the RLP facilitated passage of the CE into the SI without need for promotility agents and should be considered an initial option in the clinical setting. Although there was a numerical trend toward increased diagnostic yield and complete examinations of the SI in the RLP grp these were not significant.

**Capsule Endoscopy and Polyposis: A Close Relationship?**
Barbara Bizzarri, M.D., Benedetta Ghidini, M.D., Francesca Vincenzi, M.D., Nicola de’ Angelis, M.D., Valentina Maffini, M.D., Fabiola Fornaroli, M.D., Francesca Guatelli, M.D., Gian Luigi de’ Angelis, Prof.* Paediatric, Gastroenterology and Endoscopic Unit. Parma, Italy.
Purpose: Aim: to evaluate the necessity to introduce capsule endoscopy (CE) in diagnosis and follow-up of polyposis.

Methods: October 2001–May 2005: 22 patients with polyposis (7–45 years; 10 females, 12 males). Six patients were affected by Peutz Jeghers syndrome (PJS), 13 by Familial Adenomatous Polyposis (FAP), 1 by SAPHO Syndrome, 1 by Familial Colic Polyposis, 1 by Neurofibromatosis (NF) type 1. Ten out of 13 PAF underwent surgery before the execution of CE. Eleven patients (50%) repeated the procedure yearly (Group A: 5 PAF, 1 Neurofibromatosis, 5 PJS), while 11 (50%) patient underwent the exam just once (Group B: 8 PAF, 1 Familial Colic Polyposis, 1 SAPHO syndrome, 1 PJS). We use the GIVEN Workstation. Older patients spontaneously swallowed the capsule. In infants unable to swallow the capsule, it can be brought in the proximal duodenum endoscopically in general anaesthesis.

Results: We performed 39 exams totally. All patients, except 2, swallowed spontaneously the capsule. Group A: a) 5 coelosmized PAF: P.M. underwent 4 CE: lasting multiple ileal polyps; B.E. underwent 3 CE: worsening results from micro to macro ileal polyps which needed surgery; M.P. underwent 2 CE: both negative; P.M. underwent 2 CE: lasting diffuse polyps; V.V. underwent 2 CE: in the first, rectal fragment polyps, in the second the capsule remained in the stomach. b) 5 PJS: D.A. underwent 2 CE: lasting duodenal-jejunal micropolyps; F.P. underwent 2 CE: lasting ileal polyps; F.E. underwent 4 CE: worsening gastric-ileal pattern; E.F. underwent 4 CE: lasting gastric-ileal micropolyps; P.M. underwent 2 CE: lasting ileal polyps; c) 1 NF: C.A. underwent 2 CE. The first showed an occult distal ileum neoformation, surgically removed with the capsule (histologically: adenocarcinoma). The second exam showed diffuse micropolyps. Group B: a) 8 PAF: 4 diffuse polyps, 1 duodenal polyps, 1 pouch polyps, 1 negative, 1 the capsule remained in the stomach; b) 1 PJS: diffuse polyps; c) 1 SAPHO: ileal and cecal polyps; d) 1 familial colic polyposis: diffuse right colic polyps, which needed total colectomy.

Conclusions: CE, in our experience, is essential, with upper and lower endoscopy, to diagnose and follow up poliposis. It permits a global visualization of the small bowel and allows the polyps’ count. Its use is, therefore, diriment to decide if continue a clinical follow-up or to address the patient to surgery. Therefore CE is, in our experience, a gold standard for polyposis.

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Difficult Encounters & Strategic Management in Routine Lap'scopic Procedures

Nayan Ranjan Nanda, M.S.* Gastroenterology Surgery, Kalinga Hospital, Sun-Apollo Hospital, Bhubaneswar/Cuttack, Orissa, India.

Purpose: Laparoscopic cholecystectomies & Appendectomies are being routinely performed around the Globe. Key to successful lap’scopic surgery is in avoiding mishaps by intuisingly apprehending it in certain susceptible, complicated cases, while doing the endo-dissection.

Methods: In these video clips I did encounter certain difficulties, due to reasons as follows—

# straying while dissecting inside the distorted & unusual anatomical plane, resulted by the disease process.
# opening up an incidental Duodenal perforation, which was already sealed by adhesions including the hanging Gallblader packed with multiple calculi.
# entering into a Pericholecystic phlegmon containing gangrenous, perforated G.B & adhesions.
# entering inside a pyoperitoneum, caused by a ruptured Appendix with peri appendicular lump.

All these cases were tried & managed laparoscopically without compromis ing on patients safety & surgical principles, as follows—

*In the 1st case, the site of biliary leak was ascertainment by metuculous dissection in a different anatomical plane & thus skelitising the calot’s triangle; a single clip solved the problem. The leak was from cystic duct_impacted calculus which initially was thought to be from C.H.D.

*The perforation was suture closed & a lap cholecyst was done as well.

*The gangrenous phlegmon was carefully dissected safeguarding the adjacent colon, duodenum etc. Gangrenous gallbladder was taken out in piece meal in an endopouch. A 32F tube drain was placed in subhepatic area after peritoneal toileting. Friable neck area of the Gallblader was managed by endosutore. A suction of the entire pus from all the gutters & pouches of peritoneal cavity was carried out first, thorough irrigation, lavage done with normal saline. Appendix was located; the surrounding adhesions were dissected safe. Meso appendix was dissected satisfactorily & root of the diseased organ was suture ligated, secured & taken out.

Results: The Cases Discussed were Successfully Operated by Laparoscopic Method. Their Post Op’ n Period was Uneventful. Post-Op’n Hospital Stay was Within 24 to 72 Hours.

Conclusions: The key to tide over such entoward encounters/disease mishaps lies in it’s timely anticipating, on the spot decision to proceed, taking each individual case as a different one & of course with incisively meticuous endodissection, thus developing a gentle rapport with the diseased tissue & one’s instruments, which eventually result in a friendly outcome.

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Manifestations of Celiac Disease Found on Pillicam SB (Wireless Capsule Endoscopy)

Eric H. Shen, M.D., Eric L. Tatar, M.D., C.S. Pitchumoni, M.D.* Gastroenterology and Hepatology, Robert Wood Johnson Medical School, New Brunswick, NJ and Gastroenterology and Hepatology, St. Peters University Hospital, New Brunswick, NJ.

Purpose: The purpose of this study was to determine and explore the various findings of celiac disease detected on capsule endoscopy (CE).

Methods: Up until the present time, the small bowel mucosa distal to the duodenum has been very difficult to evaluate. Capsule endoscopy is now a well-established means to evaluate the entire small bowel. There have been a few studies on the utility of capsule endoscopy in celiac disease. We sought to describe and examine the different findings of celiac disease detected on CE. We marked all reports where findings suggestive of celiac disease were mentioned. We also examined all reports where the indication was to evaluate previously-diagnosed celiac disease or to rule out celiac disease.

Results: Out of 280 CE tests performed at our institution, 13 had findings suggestive of celiac disease. These findings included scalloping of folds, mucosal atrophy in association with segments of normal mucosa, and intussusception in one case confirmed by CT scan. Of these patients, 6 were referred for anemia, 3 for GI bleeding, 3 for abdominal pain, and 1 for chronic diarrhea. Three patients with a known history of celiac disease underwent CE for anemia. Only 1 of these had findings suggestive of celiac disease. Three patients were referred for CE to rule out sprue. 1 of these had findings of celiac disease on examination. One patient referred for abdominal pain initially had a normal capsule endoscopy. However, on repeat examination 2 months later, she was found to have focal areas of scalloping and mucosal atrophy.

Conclusions: 1. Celiac disease is becoming increasingly recognized as a cause of anemia, abdominal pain, and diarrhea. 2. Wireless capsule endoscopy is a useful tool to aid in the evaluation of a patient with possible celiac disease. 3. In those patients who are found to have celiac disease on capsule endoscopy, anemia is the most likely indication. 4. Findings of celiac disease detected on CE include mucosal atrophy in association with normal mucosa, scalloping of folds, and rarely intussusception.

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Video Capsule Endoscopy for Evaluating Obscure Gastrointestinal Bleeding in a Tertiary Care Center; an Unexpected Finding of Small Bowel Tumors

Purpose: In recent years video-capsule endoscopy has revolutionized the investigation of obscure gastrointestinal bleeding (OGIB). Multiple studies have shown superiority over conventional modalities, including push enteroscopy and small bowel radiography. Wireless video capsule endoscopy (VCE) is a new technology that enables us to visualize the entire small bowel mucosa. It involves swallowing a video capsule endoscope, which is painless.

Aim: To investigate etiologies of obscure gastrointestinal bleeding in a large tertiary care institution.

Methods: All charts of patient who underwent VCE between 2001 and 2005 were retrospectively reviewed. There were 466 charts available with the complete VCE reports.

Results: Total of 466 patients with nondiagnostic upper and lower endoscopies underwent VCE. The mean age was 59.5 years (range 7–90). There were 265 female patients and 201 male patients. The most common indication for the procedure was OGIB in 366 patients (84.9%). A possible cause of OGIB was identified in 304/366 (76.8%) of patients. The most common cause of the bleeding was angioectasias, which were identified in 42.1% of patients. Gastritis was identified in 21% and small bowel ulcerations were visualized in 11% of the patients. Small bowel erosion and duodenitis were present in 9% and 8% of patients respectively. Active bleeding without any identifiable cause was seen in 8% of the patients. 4.9% of patients were diagnosed with a small bowel mass.

Conclusions: VCE identifies a possible etiology of OGIB in majority of the patients. Angioectasias is the most common finding. Small bowel masses are identified in nearly 5% of patients undergoing VCE for OGIB. VCE is a diagnostic modality of choice for investigating obscure gastrointestinal bleeding with a significant yield for previously unrecognized small bowel tumors.

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Microsatellite Instability and Expression of MLH1 in Mucinous Adenocarcinoma of the Distal Duodenum Associated with HNPCC

Vasu Appalaneni, M.D., Sherin John, M.D., Mark Walsh, M.D.*

Gastroenterology, Dayton Veterans Affairs Medical Center, Wright State University School of Medicine, Dayton, OH and Gastroenterology, Wright State University School of Medicine, Dayton, OH.

Purpose: Hereditary nonpolyposis colorectal cancer is an autosomal dominant disorder that accounts for 3 to 6 percent of the colorectal cancers. Here, we report a case of adenocarcinoma of the duodenum associated with microsatellite instability (MSI) in a patient with HNPCC.

Case Presentation: A 60-year-old woman presented with a one-month history of epigastric tenderness, decreased appetite, postprandial nausea, vomiting and 5 pound weight loss. The patient has history of HNPCC – MLH1 gene mutation which was diagnosed when she developed endometrial cancer and two other family members were diagnosed with colon cancer. Patient had a colonoscopy nine months ago which showed a single colorectal adenoma. The physical examination showed normal vital signs, epigastric fullness with tenderness and hyperactive bowel sounds. The computed tomographic scanning of the abdomen showed dilatation of the stomach and the proximal duodenum. An upper endoscopy revealed a circumferential friable mass lesion obstructing the lumen at the third portion of the duodenum. An exploratory laparotomy showed a hard mass involving the small bowel, pancreas and the celiac axis, encasing the major vessels to the viscera and fixing the retroperitoneum. The biopsies of this lesion revealed moderately differentiated adenocarcinoma with abundant mucin production and glandular architecture. The biopsies also showed microsatellite instability with six of nine markers tested (MSI-H), a feature associated with HNPCC. A gastrojejunal bypass procedure was done for palliative relief secondary to inability of resection for cure.

Discussion: Small bowel adenocarcinoma is quite rare, accounting for less than 5 percent of all the gastrointestinal malignancies. The incidence of small intestinal tumors is greatly increased in patients with the HNPCC due to an inherited mutation of genes (specifically MLH1 and MSH2) responsible for DNA mismatch repair function during the cell replication. The adenocarcinomas associated with HNPCC are highly mucinous and associated with microsatellite instability (MSI). This patient has no prior history of colon cancer, which is more common than small bowel malignancy in patients with HNPCC.

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Goblet Cell Carcinoid: A Review of the Literature and Experience with 16 New Cases

John C. Byrn, M.D., Ju-Lin Wang, M.D., Celia M. Divino, M.D., F.A.C.S., Richard R.P. Warner, M.D., F.A.C.G.*

Department of Surgery, Mt. Sinai Medical Center, New York, NY; Division of Gastroenterology, Department of Medicine, Mt. Sinai Medical Center, New York, NY and Chief, Division of General Surgery, Department of Surgery, Mt. Sinai Medical Center, New York, NY.

Purpose: Goblet cell carcinoid tumors of the gastrointestinal tract have attracted attention as a unique neoplastic entity since the 1970’s. While the debates over histopathologic classification have been largely resolved, knowledge of the clinical behavior of these tumors relies on case series observation. More importantly, surgical recommendations of right hemicolectomy, regarding unexpected goblet cell carcinoid tumors of the appendix, remain vague and inconsistently followed.

Methods: A review of the literature and 16 cases from a single institution/referral center was performed.

Results: Median age was 52.2 yrs with a slight female preponderance (9:7). Clinical presentation was dominated by appendicitis, however, 6 patients presented with chronic symptoms attributed to an abdominal mass or concurrent diagnosis. Two patients were known to have Crohn’s disease. Six patients had second operations for formal right hemicolectomy. In 4 patients the initial operation was a right hemicolectomy or ileo-colic resection. In these cases the diagnosis of goblet cell carcinoid was not known preoperatively and the indications for the more formal resections were 1 Crohn’s disease and 3 with abdominal mass. The mean time for follow-up after undergoing surgery in our 16 patients was 1.39 years. Two patients were metastatic at presentation and 4 patients are known to be alive with metastatic disease at last follow up. Two patients died from their disease and 1 patient died from unrelated causes. Four patients are known to be free of disease at last follow up.

Conclusions: Goblet cell carcinoid is a rare subset of carcinoid tumors largely affecting the appendix. Scarcey of cases and long-term follow up remain a consistent weakness in the goblet cell carcinoid literature. The preponderance of metastatic disease at presentation and with short term follow up indicates the appropriateness of formal right hemicolectomy in these appendiceal tumors.

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SLX-4090: A Novel, Intestinal-Specific MTP Inhibitor for Lowering Plasma Triglyceride and Cholesterol Levels in Dyslipidemia

Paul Sweetnam, Ph.D.*, Enoch Kim, Ph.D., Yingfei Yang, M.S., Stewart Campbell, Ph.D. Pharmacology, Surface Logix, Inc., Brighton, MA.

Purpose: Microsomal triglyceride transfer protein (MTP), found primarily in the small intestine and the liver, is essential for the uptake of dietary triglycerides and cholesterol, and for secretion of VLDL. Potent inhibitors that specifically target the activity of MTP in intestinal epithelial cells without affecting hepatic MTP. SLX-4090 emerged as a lead compound having the desired pharmacological properties.

Methods: Intestinal-specificity was achieved using a proprietary technology platform based on biophysical chemistry designed to limit systemic availability; compounds were optimized to retain potency to inhibit MTP and for their pharmacokinetic properties, including luminal accumulation
and no systemic distribution. MTP inhibitors were characterized *in vitro* using triglyceride transfer and ApoB secretion assays and Caco-2 permeability assays. The compounds were characterized *in vivo* for their effects on absorption of triglycerides and cholesterol, for systemic exposure, and for safety.

**Results:** Predictions from an absorption model based on differential permeability of MTP inhibitors across apical and basolateral lipid bilayers were consistent with experimental observations leading to the identification of a novel class of potent, small molecule MTP inhibitors. These inhibitors accumulated within intestinal epithelial cells, but were not absorbed into systemic circulation. A lead compound in this series, SLx-4090, displayed low nanomolar potency against MTP *in vitro* and inhibited chylomicron secretion *in vivo*. When administered orally to rats, SLx-4090 lowered plasma triglyceride and cholesterol levels, but was undetectable in plasma. In a chronic *in vivo* study, SLx-4090 did not alter liver AST or ALT, and liver triglyceride and cholesterol remained at baseline levels.

**Conclusions:** A novel class of small intestine-specific MTP inhibitors has been identified. The lead compound, SLx-4090, effectively reduced plasma triglyceride and cholesterol levels and demonstrated an excellent safety profile based upon its lack of systemic exposure. SLx-4090 may enable novel therapies for dyslipidemia, either as a monotherapy or as a combination with existing drugs.
S 102 Abstracts

241 Adult Autoimmune Enteropathy: Mayo Clinic Rochester Experience
S. Akram, M.D., J. A. Murray, M.D., P. S. Darrell, M.D., S. C. Abraham, M.D., G. L. Alexander, M.D., J. A. Schaffner, M.D. Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN and Division of Anatomic Pathology, Mayo Clinic, Rochester, MN.

Purpose: Autoimmune enteropathy (AIE) is a rare cause of intractable diarrhea associated with circulating gut autoantibodies and a predisposition to autoimmunity. It is rarely observed in adults with only nine cases reported to date. Current study is the largest series of adult cases of AIE diagnosed at a single institution.

Methods: 15 adults with AIE were identified at Mayo Clinic, Rochester, between May, 2001 to May, 2005. The demographic, clinical and treatment data were abstracted from their records.

Results: The study population was predominantly Caucasian 12/15 (80%) with median age of 46 years (range: 33 to 76 years). 8/15 (53%) were females. All patients had protracted diarrhea, weight loss and malnutrition. Celiac disease (CD) was excluded by lack of response to gluten free diet or absence of the CD susceptibility HLA genotypes. Concomitant lymphocytic colitis was present in 7/15 (46%) and chronic gastritis in 2/15 (13%). 11/15 (73%) were tested for gut epithelial cell antibodies (GECA), 9/11 (81%) were positive for anti-enterocyte and/or anti-goblet cell antibodies which were predominantly IgG type. Predisposition to autoimmune diseases was noted in 8/15 (53%), as indicated by a host of circulating autoantibodies. Various mild immunoglobulin deficiencies of either IgG subtype or IgM were noted in 5/15 (33%). Characteristic small intestinal histopathologic findings were subtotal villous atrophy and lymphocytic infiltration in the lamina propria with relatively few intraepithelial lymphocytes. Immunophenotyping of intestinal lymphocytes revealed a predominance of CD3+ and CD4+ T cells most of which were also positive for T-cell receptor αβ. T-cell receptor gene rearrangement studies were negative in all. 11/15 (73%) received immunosuppressive therapy. Clinical improvement was noted in 4/11 (36%) after 4–6 weeks of steroids therapy. Long-term clinical remission was maintained in 2/11 with low dose prednisone or budesonide. In one refractory case, Tacrolimus and in another Infliximab were successful in inducing clinical remission. Median duration of follow-up was 24 months (range: 4 to 60 months). One death occurred from complications of severe malnutrition and volume depletion.

Conclusions: AIE is a heterogeneous disease and should be considered in the differentials of refractory enteropathy. Presence of GECA can help confirm the diagnosis. No single agent is unequivocally effective in inducing remission and immunosuppressive therapy is required in most cases.

242 Cumulative Experience of 594 Capsule Endoscopy Procedures in a Single Tertiary Community Hospital Read by One Gastroenterologist
Kanwar R.S. Gill, M.D., Christine Pizzute, M.D., Shunpei K. Iwata, M.D., Margaret Allen, L.V.N., Kenneth F Binmoeller, M.D.* Interventional Endoscopy Services, California Pacific Medical Center, San Francisco, CA.

Purpose: Capsule endoscopy is a revolutionary new diagnostic tool for the detection of small bowel disease. We describe our cumulative clinical experience of 594 wireless capsule endoscopy (WCE) procedures performed in one community hospital.

Methods: Over a 4 year period (2001–2004), 594 WCE were done for suspected SB diseases [443 obscure gastrointestinal (GI) bleeding (247 overt/171 occult/25 iron deficiency anaemia), 102 abdominal pain, 12 diagnosed and 9 suspected Crohn’s disease, 14 chronic diarrhea, 14 others]. 47 patients had an incomplete examination(Non-transit, poor visualisation). WCE findings were characterized as specific or non-specific, depending on whether the patient’s signs and symptoms could be sufficiently attributed to them or not.

Results: One or more abnormal findings were detected in 393/547 (72%) of patients; these were classified as specific in 315/547 (58%). The diagnostic yield of WCE (in terms of specific findings) was significantly higher when evaluating patients with obscure GI bleeding, compared with chronic abdominal pain (62% vs. 25%, respectively, p = 0.0001) and diarrhea (62% vs. 7%, p = 0.0001). Among obscure GI bleeders, specific findings were not significantly different in the group of overt vs. occult bleeders (61% vs. 63% respectively, p = 0.76). In patients referred for diagnosed or suspected Crohn’s disease, WCE findings were compatible with the diagnosis in 8/12 cases (67%) and in 4/9 cases (44%), respectively. Among 13 patients evaluated for other findings, specific findings were identified only in 3 (21%). 18 patients (3%) underwent repeat capsule procedure (malfunction
LIVER

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Double Balloon Enteroscopy: An Initial Multicenter U.S. Experience

Purpose: To report early DBE technical experience in multiple U.S. centers.

Methods: 8 experienced endoscopists in 6 tertiary care centers were trained (May, Wiesbaden, Germany) to perform DBE. Observations were documented in detail.

Results: 129 patients had 164 DBE: 101 per-orally, 54 per-retally, 6 via stoma, 3 for ERCP. Mean age was 57 (19–94). Mode of sedation: general anesthesia-52, MAC-59 and conscious sedation-53. Maneuvers: India ink injection in most patients, biopsies-49, argon plasma coagulation-21, electrocautery-7, balloon dilation-1, and polypectomy-2. Mean procedure time was 99 min (per-oral-98, ERCP-105, per-retal-105, and per-stomal-63). Mean time of the first 47 cases was 115 min. Two methods were used to report the max distance reached per-orally: mean 389 cm numerically and distal jejunum anatomically. 30% of per-retal exams failed to pass the ileocecal valve, whereas only 1 per-oral case could not reach the jejunum. Indications: GI bleeding/iron deficiency anemia -90 patients (70%), suspected Crohn’s-12, abdominal pain-9, neuroendocrine tumor search-3, small bowel obstruction-3, facilitate ERCP in the Roux-en-Y-3, stricture dilation-1 and others. For bleeding/iron deficiency anemia, the findings were: AVM-23% (mostly treated), ulcers-8%, ulcerated masses-2%, polyps-2%, strictures-2%, and varices-1%. 88 patients had previous capsule endoscopy (CE) done, and the two tests correlated significantly (p = 0.004). 65% of CE findings were confirmed by DBE; 10% of DBE findings were missed on CE. 6 patients experienced complications: abdominal pain at 24 hours-2, aspiration pneumonia-1, presumed asymptomatic microscopic perforation-1, mucosal tear-1, and stomal perforation-1. No prolonged ileus, commonly seen after operative enteroscopy, was reported.

Conclusions: Although experience has shortened procedure time, DBE is still time-consuming. DBE usually reaches the mid small bowel but a total intestinal examination is not achieved with initial endoscopist experience. The technique or instrument for per-retal examination needs improvement for better technical success. DBE results for bleeding/anemia directed therapy in about half of patients, and its yield is comparable to that of CE.

Purpose: Severe obesity has been considered a relative contraindication to orthotopic liver transplantation (OLT) at many centers. We present a single-center experience on OLT outcomes in severely obese patients.

Methods: Retrospective analysis of primary OLT over the last two years at our institution was performed. Severe obesity was defined as a body mass index (BMI) of > 34 kg/m². Non-obese recipients with a BMI < 30 kg/m² were used as controls.

Results: Sixteen severely obese patients underwent OLT. Thirty non-obese liver recipients were used as controls. The average BMI in the obese group was 39.4 kg/m² (range 34.1–42.8 kg/m²) versus 25.3 kg/m² (15.3–29.9 kg/m²) in the controls. Patient survival was 100% in the severely obese patients (9 of whom had one-year survival data available). One-year survival was 28/30 (93.3%) in the control patients. The average operative time was 431 minutes (270–630 minutes) in the obese and 423 minutes (248–896 minutes) in the non-obese patients. The average length of hospital stay was 15 days (8–52 days) in the obese and 16.2 days (7–57 days) in the non-obese group. The average length of ICU stay was 5.19 days (3–10 days) in the obese compared to 6.6 days (2–45 days) in the non-obese patients. The average length of time until post-operative extubation was 3.81 days (2–9 days) in the obese compared to 3.17 days (1–9 days) in the control group. Biliary complications were noted in 3/16 (18.8%) obese compared to 13/30 (43%) non-obese patients. Cardiac complications occurred in 2/16 (12.5%) obese compared to 3/30 (10%) non-obese patients. Overall infections occurred in 6/16 (37.5%) obese compared to 11/30 (36.7%) non-obese patients. Wound infections were diagnosed in 4/16 (25%) obese compared to 1/30 (3.3%) non-obese patients. Only the higher incidence of wound infections in the obese patients was found to be statistically significant (p = 0.043).

Purpose: Severe obesity (defined as BMI > 34 kg/m²) did not influence one-year survival after OLT. Operative time, hospital stay, ICU stay, and period of intubation were not different between the groups. Cardiac, biliary, and overall infectious complications showed no significant difference. Post-operative wound infections were more common in the severely obese patients.

Liver Transplantation in Severly Obese Patients: A Single Center Experience
Stanley M. Cohen, M.D.,* Eva U. Sotil, M.D., Sara E. Woon, M.D., Anthony M. Savo, M.D., Nancy Reas, M.D., Donald M. Jensen, M.D., Thelma Wiley-Lucas, M.D., Forrest Dodson, M.D. Hepatology, Rush University Medical Center, Chicago, IL; Internal Medicine, Rush University Medical Center, Chicago, IL and Surgery, Rush University Medical Center, Chicago, IL.

Purpose: Hepatitis C Genotype 4 (HCV4) is prevalent among people from the Middle Eastern. At present, the recommendation is to treat with pegylated interferon plus weight based ribavirin for 48 weeks, with an expected sustained virologic response (SVR) of about 42%. The purpose of our study was to evaluate in a retrospective manner our experience with 24 weeks of therapy for HCV4, and compare the SVR from our study with that of other studies.

Methods: A retrospective case-analysis study was conducted at Brooklyn Medical Group NY, an outpatient multi-specialty clinic affiliated with NY Methodist Hospital, Brooklyn, NY.

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24 Weeks of Treatment for Hepatitis C Genotype 4 May Be Sufficient
Shahzad Iqbal, M.D.,* Mohamad Mansour, M.D., Hussein Elsisey, M.D., Gerald Posner, M.D., Maurice A. Cerulli, M.D. Gastroenterology Division, NY Methodist Hospital, Brooklyn, NY.

Purpose: Hepatitis C Genotype 4 (HCV4) is prevalent among people from the Middle Eastern. At present, the recommendation is to treat with pegylated interferon plus weight based ribavirin for 48 weeks, with an expected sustained virologic response (SVR) of about 42%. The purpose of our study was to evaluate in a retrospective manner our experience with 24 weeks of therapy for HCV4, and compare the SVR from our study with that of other studies.

Methods: A retrospective case-analysis study was conducted at Brooklyn Medical Group NY, an outpatient multi-specialty clinic affiliated with NY Methodist Hospital. We analyzed the charts of all the patients, who were treated for HCV4. Patient demographics; type, duration and complications of treatment; serum alanine transaminase (ALT) and viral load at different stages of therapy were recorded.

Results: There were 4 patients with HCV4. All were male from the Middle East. Average age at the start of treatment was 43.7 years (range 38 to 50 years). Baseline viral load averaged 764,494 IU/ml (range 17,200 to 1,955,376 IU/ml) and mean ALT was 77 U/L (range 69 to 93 U/L). One patient had failed previous therapy. Three treatment naïve patients were treated for 24 weeks or less. Viral load was undetectable in these three patients at 12 weeks, 24 weeks and 6-months post-treatment (SVR 100%). Average ALT at the end of treatment was 44 U/L. In one these 3 patients, treatment was stopped before 24 weeks due to complications at 18 weeks (depression and hypothyroidism). The treatment varied: 1 patient was treated with peginterferon alfa-2b (1.5 mcg/kg/week) and ribavirin (1200 mg/day); while the other 2 patients were given interferon alpha-2b (3 million units
three times/week) and ribavirin (1200 mg/day). Baseline liver biopsy was done in 2 of these patients. Both had grade 3/4 and stage 3/4 fibrosis. The 4th patient had previously failed interferon alfa-2b plus ribavirin therapy. He was treated for 48 weeks with peginterferon alfa-2a (180 mcg/week) and ribavirin (1200 mg/day). Despite a 2-log drop in HCV4 at 12 weeks, the virus was detectable at 48 weeks. This patient didn’t have liver biopsy.

Conclusions: In this small group of treatment-naive patients with HCV4, we found SVR of 100% after 24 weeks of combination therapy. The possibility that treatment-naive HCV4 pts can be treated for only 24 weeks should be further evaluated.

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Recurrent Hepatitis C after Living Donor Liver Transplantation Detected by Tc-99m GSA Liver Scintigraphy
Masaki Kawai, M.D.,* Sung Kil Ha-Kawa, M.D., Junko Hirohara, M.D., Yasuo Kamiyama, M.D. Surgery, Kansai Medical University, Moriguchi, Osaka, Japan; Radiation, Kansai Medical University, Moriguchi, Osaka, Japan and Internal Medicine, Kansai Medical University, Moriguchi, Osaka, Japan.

Purpose: Recurrence of hepatitis C after living donor liver transplantation was investigated using technetium-99m-diethylenetriaminepentaacetic acid-galactosyl human serum albumin (Tc-99m-GSA) liver scintigraphy.

Methods: A 55-year-old woman with cirrhosis due to chronic hepatitis C underwent liver transplantation with a graft from her husband. Scintigraphy was used to determine the hepatic uptake ratio of the tracer corrected for disappearance from the blood, as well as the maximal removal rate of the tracer by hepatocytes, as parameters of hepatic functional reserve.

Results: Conventional liver function parameters and the graft volume (computed tomography) were almost unchanged up to 18 months after transplantation. Serum HCV RNA was elevated from 3 months after transplantation, and was 2-fold higher at 12 months compared with 6 months. At 18 months postoperatively, liver biopsy showed an increase of histologic activity, and there was also evidence of recurrent hepatitis C. The corrected hepatic uptake ratio and maximal removal rate were decreased at 3 months postoperatively, and thereafter remained low.

Conclusions: The decrease of scintigraphic parameters at 3 months after transplantation suggested recurrent hepatitis C affecting the graft. Tc-99m-GSA liver scintigraphy is a useful noninvasive method for evaluating graft functional reserve.

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Comparison of Limited and Anatomical Hepatic Resections for Hepatocellular Carcinoma with Hepatitis C Virus
Masaki Kawai, M.D.,* Yoichi Matsu, M.D., A.-Hon Kwon, M.D., Yasuo Kamiyama, M.D. Surgery, Kansai Medical University, Moriguchi, Osaka, Japan.

Purpose: The long-term outcome after resection of hepatocellular carcinoma is influenced by factors related to the tumor and the underlying liver disease. The optimum extent of surgical resection, which can be limited or anatomical, is another important factor but is still controversial.

Methods: Among 247 patients with hepatitis C virus infection who underwent curative resection of hepatocellular carcinoma between 1992 and 2003, 213 patients underwent limited resection and 34 patients underwent anatomical resection of at least 1 liver segment with complete removal of the portal territory containing the tumor. The clinical characteristics, operative results, and long-term survival of these two groups were compared.

Results: The patients receiving limited resection had significantly worse preoperative liver function than the patients undergoing anatomical resection. The mortality and morbidity rates after limited and anatomical resection were not significantly different. Disease-free survival and overall survival were similar after both types of resection, as were the incidence and pattern of intrahepatic tumor recurrence.

Conclusions: In patients with hepatitis C virus infection and hepatocellular carcinoma, anatomic resection should not be routinely performed. In patients with a limited hepatic functional reserve, resection of the tumor with preservation of liver parenchyma may take priority over wide resection.

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Failure To Show for Initial Consultation in Patients Referred for Evaluation of Hepatitis C

Purpose: There are many impediments to the successful treatment of patients with chronic hepatitis C infection. These include potential factors present during each step of the referral, consultative, evaluation, treatment and follow-up segments. In the recent past, I have been impressed with a seemingly high “no-show” rate when patients are referred for initial evaluation of hepatitis C infection. This rate has seemed out of proportion to the “no-show” rate for patients referred for evaluation of other gastroenterologic/hepatologic problems. This study aimed to prospectively investigate whether this problem actually exists.

Methods: From 10/3/03 through 5/6/05, the number of new patients referred to a single gastroenterologist in an outpatient office setting were prospectively tabulated. The physician was part of a 5 member single-specialty gastroenterology group, in a semi-rural community. The practice members make themselves available to care for patients with all insurance plans commonly carried by residents in their catchment area, including Medicare and Medicaid. The number of “no-shows” were compared between patients referred for initial evaluation of hepatitis C, and those referred for “all other” gastroenterologic/hepatologic diagnoses.

Results: Over the study period, 543 new patients were scheduled for initial office consultation. Of these, 66 were referred for evaluation of hepatitis C, and 477 were referred for evaluation of “all other” diagnoses. The rate of “not-showing” for initial consultation was 12/66 = 18.2% for patients presenting for evaluation of hepatitis C versus 37/477 = 7.8% for patients referred for evaluation of “all other” diagnoses, (p = 0.01 by Fischers exact test; odds ratio = 2.65).

Conclusions: The results from this prospective investigation confirm the suspicion that patients who are referred for evaluation of hepatitis C are significantly less likely to show for their initial office consultation, than patients referred for a combination of “all other” gastroenterologic/hepatologic diagnoses. Many potential factors may be responsible for this phenomenon and in this regard, further study is ongoing.

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Detection of Hepatitis B Virus Surface Antigen in Hepatitis B Vaccine Recipients

Purpose: Some reports of HBSAg positivity soon after HBV vaccination have been mentioned in the literature. To study the duration of HBSAg persistence in blood after HBV vaccination in volunteers.

Methods: Thirty two healthy HBSAg negative volunteers were recruited in the study. A written consent was taken from all. HBSAg in blood of these volunteers was tested by a commercially available kit (Bioelisa HBSAg BIKIT, SA, Spain) on day 2, 4, 6, 9, and 12 after an intramuscular injection of 20 ug of recombinant Hepatitis B vaccination.

Results: The volunteers (19 M and 13 F) had a mean age of 26.65 ± 2.42 years. On day 2 HBSAg was positive in 18 (56.25%) volunteers. Of these 18 volunteers 6 (33.33%) remained positive on day 4. Two volunteers who were negative on day 2 were also positive on day 4 [Total HBSAg positivity on day 4 = 8 (44.4%)]. Out of these eight volunteers 4 were still positive
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on 6th day and out of these four only two were positive on day 9. None of these volunteers were positive for HBsAg on day 12.

**Conclusions:** HBsAg after 9 days of HBV Vaccination can be falsely positive in some individuals. It is therefore recommended that individuals who have been recently vaccinated with HBV vaccine should be enquired of the same if an asymptomatic patient is detected to be HBsAg positive.

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**Hepatic Venous Pressure Gradient Predicts the Severity of Cirrhosis**

Anne T. Wolf, M.D., Rie Maurer, M.S., Jonathan Glickman, M.D., Norman D. Grace, M.D.* Gastroenterology, Brigham and Women’s Hospital, Boston, MA and Pathology, Brigham and Women’s Hospital, Boston, MA.

**Purpose:** Liver biopsy is the gold standard for establishing cirrhosis, but may provide inadequate tissue in some patients. The purpose of this study was to determine whether the hepatic venous pressure gradient (HVPG) predicts the presence and severity of cirrhosis.

**Methods:** Patients with liver disease who had undergone HVPG measurements were identified at two Boston teaching hospitals. Patients were excluded if they lacked a liver biopsy or the slides could not be obtained, if there was an elapsed time between liver biopsy and HVPG measurement of >12 months, or if the patient had undergone a shunt, TIPS or liver transplantation prior to completion of both the liver biopsy and the HVPG measurement. Clinical, laboratory, and HVPG data were collected and biopsies were staged for the degree of fibrosis using the Laennec scoring system, a modification of META VIR, which sub-classes cirrhosis as mild, moderate or severe.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
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<tbody>
<tr>
<td>0</td>
<td>No definite fibrosis</td>
</tr>
<tr>
<td>1</td>
<td>Minimal fibrosis (no septa or a rare thin septum; may have portal expansion or mild sinusoidal fibrosis)</td>
</tr>
<tr>
<td>2</td>
<td>Mild fibrosis (occasional thin septa)</td>
</tr>
<tr>
<td>3</td>
<td>Moderate fibrosis (moderate thin septa; up to incomplete cirrhosis)</td>
</tr>
<tr>
<td>4A</td>
<td>Mild cirrhosis, definite or probable</td>
</tr>
<tr>
<td>4B</td>
<td>Moderate cirrhosis (at least 2 broad septa)</td>
</tr>
<tr>
<td>4C</td>
<td>Severe cirrhosis (at least one very broad septum or many minute nodules)</td>
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**Results:** A total of 32 patients met inclusion and exclusion criteria. Univariate logistic regression identified HVPG and platelet count as independent predictors of cirrhosis. When a proportional odds model was applied, the magnitude of the effect of HVPG on fibrosis score was described by the estimated OR of 1.34 (95% CI 1.12–1.61). Additionally, the model demonstrated that as the HVPG increased, so did the probability of having more histologically advanced cirrhosis. [figure 1]

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**Trends in Biopsy and Treatment Rates in Patients with Chronic Genotype 2 & 3 Hepatitis C Infection over a Five-Year Period**

Gopal Narasimhan, D.O., Timothy Johnson, M.D., Aaron Wolfish, M.D., David A. Labowitz, D.O., Henry C. Bodenheimer, Jr., M.D., Albert D. Min, M.D.* Division of Digestive Diseases, Beth Israel Medical Center, New York, NY.

**Purpose:** Patients with hepatitis C virus–genotype 2 or 3 (HCV 2/3) have a sustained virologic response (SVR) of about 80% when treated with pegylated interferon plus ribavirin and thus it is common to undergo treatment without liver biopsy. The aim of our study was to determine changes in liver biopsy and treatment patterns in patients (pts) with HCV 2/3 over the past 5 years at our institution.

**Methods:** We retrospectively reviewed the charts of patients with HCV 2/3 seen at our institution between Jan 2000 and March 2004. Data collected included pt demographics, risk factors for HCV, liver biopsy results, history of previous HCV treatment, reasons for not treating, and SVR.

**Results:** There were 129 pts seen with HCV 2/3. The mean age was 48 (range 26–82) with 61% men. 79 pts (60%) had a history of IV drug use (IVDU) and 23 (18%) had a history of transfusion before 1992. 12 (9.2%) were co-infected with HIV and 3 (2.3%) with HBV. 14 pts (11%) were previously treated for HCV without SVR. Overall, 60 pts (46%) were treated. Reasons for not treating included pt refusal (46.4%), medically not suitable for treatment (31.9%) or lost to follow-up (21.7%). Reasons for medically unsuitability included: minimal disease on biopsy (stage 0–1 fibrosis) in 12 pts, or contraindication to treatment including significant co-morbidity or psychiatric history in 6 pts, active IVDU in 1 pt and decompensated cirrhosis in 2 pts. 99 (77%) pts had a liver biopsy (Fig. 1) of which 51 pts (51.5%) underwent treatment. Of the 60 pts that began treatment, 38 (63%) completed...
the course. Overall, by an intent to treat analysis, SVR was achieved in 30 (50%) pts. Of those pts completing treatment, SVR was achieved in 50 pts (79%).

Conclusions: The majority of pts with HCV 2/3 had a liver biopsy, however the proportion of pts who had a liver biopsy has declined since 2001. Despite the advancements in available therapies, the proportion of pts with HCV 2/3 being treated has remained relatively constant. SVR was achieved in 79% of pts, similar to that achieved in pivotal trials. [figure 1]
Correlation of Histological Severity between Genotype 3 and Others in HCV Chronic Hepatitis
Kumaravel S. Perumalsamy, M.D., Amit Patel, M.D., Michael Bernstein, M.D.,* Muhammad Abdullah, M.D., Frank Steinheber, M.D. Department of Gastroenterology, Coney Island Hospital, Brooklyn, NY.

Purpose: Genome heterogeneity may be related to the wide variability of clinical and pathological features in hepatitis C virus (HCV) related chronic liver disease. The aim of this study is to see the significance of hepatitis C genotypes in relation to the severity of liver disease and to determine if the histological activity index (HAI) and fibrosis are more severe in genotype 3 than others.

Methods: Fifty-one consecutive liver biopsies of naïve patients with hepatitis C were evaluated. Serologic HCV-RNA was verified by RT-PCR and genotyping by direct sequencing. Grading of necroinflammatory and staging of fibrosis were histologically assessed by Metavir scoring system. The disease activity was graded as minimal (A1), moderate (A2) and severe (A3). The extent of fibrosis was marked as absent (F0), mild (F1), moderate (F2) and severe (F3). Results were analyzed using t-test.

Results: 28/51 (55%) were genotype 3 almost all from South Asia and 23/51 (45%) were non-genotype 3 from a mixed ethnic group mostly native born Americans. There were 23/51 (45%) males and 28/51 (55%) females. The mean age of the patients were 45.1 (age range of 26–65). There were 14/28 (50%) males and 14/28 (50%) females in genotype 3 with a mean age of 41. There were 9/23 (39%) males and 14/23 (61%) females in non-genotype 3 with a mean age of 49.2. The mean activity score was 1.178 in genotype 3 and 1.434 in non-genotype 3 (p 0.085). The mean fibrosis score was 1.964 in genotype 3 and 2.000 in non-genotype 3 with a (p 0.46)

Conclusions: There was no statistically significant difference between histological activity and fibrosis between genotype 3 and others. Genotype 3 is histologically similar to other genotypes in severity. Genotype is not useful in predicting the severity of hepatitis C related liver disease.

Preoperative Regional Maximal Removal Rate of Technetium-99m-galactosyl Human Serum Albumin (GSA-Rmax) Is Useful for Making a Final Decision on Surgical Procedure
A-Hon Kwon, M.D.,* Yoichi Matsui, M.D., Sang Kil Ha-Kawa, M.D. Department of Surgery, Kansai Medical University, Moriguchi, Osaka, Japan and Department of Radiology, Kansai Medical University, Moriguchi, Osaka, Japan.

Purpose: For safe hepatic resection, the preoperative estimation of hepatic functional reserve in the predicted remnant liver may be more important than that in the entire liver. The purpose of this study was to find the minimal GSA-Rmax in the predicted remnant liver (GSA-RL) using functional imaging that predicts postoperative hepatic failure and, by so doing, avoid this complication.

Methods: One hundred and seventy-eight patients were admitted for elective hepatectomy. Conventional liver function, and 15 min retention rate of indocyanine green (ICGR15) were carried out preoperatively. The GSA-Rmax was calculated according to a radiopharmacokinetic model and then, using the SPECT images, we calculated the regional GSA-Rmax in the predicted residual liver (GSA-RL), depending on the operative procedures. The volume of the predicted residual liver (LV-RL) was calculated on the basis of CT images.

Results: Surgical procedures consisted of 98 sub-segmentectomy cases, 41 mono-segmentectomy cases, 31 di-segmentectomy cases and 8 tri-segmentectomy cases. The preoperative LV-RL correlated well with the GSA-RL in patients with normal liver however, there was no such corre-lation in those with chronic hepatitis or cirrhosis. Postoperative major complications such as hepatic failure, hyperbilirubinemia, bleeding (requiring re-operation), ascites, liver abscess, bile leakage and pleural effusion were recorded for 45 patients after subsegmentectomy, 25 patients after monosegmentectomy and 23 patients after di- and tri-segmentectomies. Fourteen patients had more than one complication. All of 7 postoperative hyperbilirubinemia occurred in the patients with GSA-RL < 0.15. Two patients died of postoperative liver failure one to two months after the operation. These two patients GSA-RL values were 0.078 and 0.090, respectively and severe discrepancies between the GSA-Rmax in the remnant liver and ICGR15.

Conclusions: Our data suggest that GSA-RL might be a practical and reliable diagnostic method for estimating the postoperative functioning hepatocyte volume and useful for making a final decision on surgical procedure, regarding the extent of liver resection in order to avoid postoperative hyperbilirubinemia or hepatic failure.

HBV Genotype Distribution Differs in Acute Hepatitis from Chronic Hepatitis in Japan
Yasushi Takeda, M.D., Yoshiaki Katano, M.D., Kazuhiro Hayashi, M.D., Takashi Honda, M.D., Hidenori Goto, Prof. Gastroenterology, Nagoya University School of Medicine, Nagoya, Aichi Prefecture, Japan.
Purpose: Recently genotype A which is rare in the patients in chronic hepatitis B was frequently noted in patients with acute hepatitis B. To investigate their clinical and virological features, we studied the acute hepatitis B patients in the past 5 years.

Methods: 95 patients with acute hepatitis B and 80 patients with chronic hepatitis B admitted to our hospital between 1998 and 2003 were studied.

Results: Genotype A was not found in chronic hepatitis but was frequently noted in acute hepatitis (18.4%) (p < 0.001). Comparison of the clinical features of acute hepatitis between the two major genotypes, A and C, homosexual and heterosexual with multiple partners were frequently seen among genotype A patients. On the other hand, infection from steady partner showed a tendency to be more in genotype C. Acute hepatitis B caused by genotype A patients. On the other hand, infection from steady partner showed a tendency to be more in genotype C. Acute hepatitis B caused by genotype A was more likely to progress to chronic infection than genotype C, significantly. Phylogenetic analysis of genotype A revealed that almost all strains from homosexual men belonged not to the African type A’ but to the western type A.

Conclusions: Genotype A has increased recently among Japanese acute hepatitis B, and it may be related to promiscuous intercourse in high risk group. Prophylactic efforts against hepatitis B virus infection should be reconsidered from the view point of prevention from genotype A prevailing.

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Fat or Fiction: Ultrasound Diagnosis of Fatty Liver in Patients with Chronic Liver Disease

Nolan E. Perez, M.D., Nadnem Ullah, M.D., Martin Tobi, M.D., Don E. Wheeler, M.D., Faysal A. Saksouk, M.D., Murray N. Ehrinpreis, M.D.*
Gastroenterology, Wayne State University School of Medicine, Detroit, MI.

Purpose: Hepatic steatosis (or fatty liver) is common in the United States and frequent in patients with chronic hepatitis C (CHC), where it may lead to disease progression and hinder response to HCV therapy. Therefore, it is important to recognize fatty liver. Liver biopsy confirms the degree of fat, inflammation and fibrosis, but is invasive. Hepatic ultrasound is well-tolerated, non-invasive and provides good information. It is commonplace to trust the results of an ultrasound suggesting fatty liver, but there are conflicting reports on its accuracy. Therefore, we retrospectively examined liver biopsies and compared the histologic results to the ultrasound interpretations. We selected patients with chronic liver disease, primarily CHC, in order to evaluate the accuracy of ultrasound in identifying fatty liver in a typical clinical setting.

Methods: Liver biopsies were reviewed on 131 patients who had a random liver biopsy performed for evaluation of chronic liver disease (89% had CHC). The biopsies were graded for fat (grades 0–3), inflammation (grades 0–4) and fibrosis (stages 0–4). Ultrasound interpretations were grouped into 3 categories- ‘normal’, ‘fatty liver’ and ‘non-specific’, and then compared to histologic results.

Results: A ‘normal’ ultrasound interpretation was correct in excluding significant fat (grades 2–3) 95.8% of the time, but 25% had some fat (grades 1–3) on biopsy, representing false negatives. Furthermore, 37.5% had significant fibrosis (stages 2–4) and 8.3% had significant inflammation (grades 2–4). A ‘fatty liver’ interpretation was only correct in identifying some fat on biopsy in 36.4% and significant fat in 11.4%, yielding many false positives. In addition, 47.7% had significant fibrosis and 18.2% had significant inflammation. A ‘non-specific’ interpretation was associated with 25.6% significant fat, 53.8% significant fibrosis and 23.1% significant inflammation. The sensitivity of ultrasound for detecting fat ranged from 32.0–88.2% and the specificity ranged from 40.4–65.4, depending on the degree of fat on biopsy and the sonographic interpretation considered to be significant.

Conclusions: Ultrasound is inaccurate for diagnosing hepatic steatosis in patients with chronic liver disease; echogenic alterations are more likely to be the result of fibrosis or inflammation in this setting. Therefore, in patients with chronic liver disease, the ultrasound diagnosis of fatty liver is more ‘fiction’ than ‘fat’.

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Functional Significance of the Proliferating Bile Ductules in Primary Biliary Cirrhosis -Increased Expressions of Caveolin-1 and -2-
Masaya Oda, M.D., Hiroaki Tokomori, M.D. Organised Center of Clinical Medicine and Department of Internal Medicine, Sanno Hospital, International University of Health & Welfare, Tokyo, Japan and Department of Internal Medicine, Kitasato Medical Center Hospital, Kitamoto-shi, Japan.

Purpose: Bile ductular proliferation is noted in diverse human liver diseases, particularly in primary biliary cirrhosis (PBC) and obstructive jaundice. Caveolins, caveolin-1 (CAV-1) and caveolin-2 (CAV-2) are Ca++ and cholesterol-binding proteins involved in the regulation of several intracellular processes including cholesterol transport. The aim of the present study is to clarify how CAV-1 and -2 are expressed by immunohistochemical and Western blot analyses in human liver biopsy specimens from patients with PBC.

Methods: Surgical liver biopsy specimens were obtained under laparoscopy from 13 patients with PBC (12 females and 1 male, mean age 53.4 years, Scheur’s stage I–II; 6 cases, stage III; 7). As controls, wedge biopsy specimens were obtained from normal portions of the livers of 10 patients (2 females and 8 males, mean age of 57.3 years) who underwent surgical resection for metastatic liver carcinomas. Indirect immunohistochemical staining was performed on consecutive serial sections using anti-CAV-1, anti-CAV-2, and specific antibody as primary antibody and horseradish peroxidase (HRP)- conjugated anti-IgG as secondary antibody. Four-micrometer sections were cut from paraffin blocks of formalin-fixed liver tissues, deparaffinized with xylene and dehydrated by graded ethanol solutions. Bile ductules were identified by immunostaining of CK-6. Western blotting was conducted using fresh control and PBC liver tissues.

Results: In control liver, the specific immunopositive reactions for CAV-1 and -2 were hardly detected on the bile ducts and ductules. In PBC, the
immunopositive reactions for CAV-1 and -2 were increased on the proliferating bile ductules in the stage II and III of PBC, but sparsely noted on the interlobular bile ducts in the stage I of PBC. Particularly, the epithelial cells of the proliferating bile ductules at the interface between the portal tract and the lymphocytes-infiltrated parenchymal area were intensely immunostained for CAV-1 and -2. These results were confirmed by Western blot analysis.

Conclusions: The increased expressions of CAV-1 and -2 in the proliferating ductular epithelial cells of PBC may be related to the homeostatic control of cholesterol transport in the regenerating bile ductules in response to the obliterator immunodestruction of the downstream interlobular bile ducts in PBC.

### 261

**Comparison of Pegylated Interferon alfa-2a and alfa-2b in Combination with Ribavirin in Obese Patients with Chronic Hepatitis C**


**Purpose:** Obesity (body mass index (BMI) > 30) is a negative predictor of response to HCV treatment. Two pegylated interferons (PEG-IFN) are available for treatment of chronic hepatitis C (CHC). One is administered in a fixed weekly dose (PEG-IFN alfa-2a) and the other in a weight-based weekly dose (PEG-IFN alfa-2b). It is hypothesized that weight-based dosing of PEG-IFN may be superior to fixed dosing on treatment response rate in obese patients. However, no prospective, controlled efficacy data are available.

**Aim:** To determine if weight-based dosing of PEG alfa-2b is superior to fixed dose PEG alfa-2a in terms of sustained virologic response (SVR) rates in obese patients with CHC.

**Methods:** We conducted a retrospective analysis of our database of PEG treated patients at the Little Rock VA. We included 31 treatment naïve patients with BMI > 30 who received either form of PEG in combination with ribavirin. PEG alfa-2a dose was 180 μg/week and PEG alfa-2b dose was 1.5 μg/kg/week plus ribavirin 800–1200 mg/day according to weight and genotype.

**Results:** SVR data is noted in table. Age, gender, race, and baseline HCV RNA were similar between the 2 groups.

<table>
<thead>
<tr>
<th>SVR in Patients with BMI &gt; 30</th>
<th>PEG-IFN alfa-2a</th>
<th>PEG-IFN alfa-2b</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients</td>
<td>6/13 (46%)</td>
<td>8/18 (44%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HCV genotype 1</td>
<td>2/9 (22%)</td>
<td>6/14 (43%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HCV genotype 2 or 3</td>
<td>4/4 (100%)</td>
<td>2/4 (50%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

**Conclusions:** There was no difference in SVR rates between obese patients with CHC who were treated with either PEG-IFN alfa-2a or PEG-IFN alfa-2b. Further prospective studies are warranted.

### 262

**No Difference in Efficacy and Tolerability between Pegylated Interferon alfa-2a vs. alfa-2b in Combination with Ribavirin in Treatment of Naïve Patients with Chronic Hepatitis C**


**Purpose:** Two pegylated interferons (PEG-IFN) are currently available for treatment of chronic hepatitis C (CHC): PEG-IFN alfa-2a and PEG-IFN alfa-2b. No prospective, controlled efficacy data are available comparing sustained virologic response (SVR) rates between the two approved PEG-IFN.

**Aim:** To determine if there was any difference in SVR between the 2 PEG-IFN in treatment naïve CHC patients.

**Methods:** We conducted a retrospective analysis of our database of CHC patients treated with PEG-IFN at the Little Rock VA (n = 60). We included treatment naïve CHC patients who received either form of PEG-IFN + ribavirin and had follow-up of at least 18 months for genotype 1 (n = 40) and 12 months for genotype 2 or 3 (n = 20). Dose of PEG-IFN alfa-2b was 1.5 μg/kg/week and PEG-IFN alfa-2a was 180 μg/week + ribavirin 800–1200 mg/day according to weight and genotype.

**Table 1:** SVR

<table>
<thead>
<tr>
<th></th>
<th>PEG-IFN alfa-2a</th>
<th>PEG-INF alfa-2b</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>all patients</td>
<td>11/22 (50%)</td>
<td>17/38 (45%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HCV genotype 1</td>
<td>4/13 (31%)</td>
<td>9/27 (33%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HCV genotype 2/3</td>
<td>7/9 (78%)</td>
<td>8/11 (73%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

**Results:** SVR data and side-effects are noted in table. Age, gender, race, BMI and baseline HCV RNA were similar between the 2 groups.

**Table 2:** Side Effects

<table>
<thead>
<tr>
<th>Side-Effects</th>
<th>PEG-IFN alfa-2a</th>
<th>PEG-INF alfa-2b</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>5/22 (23%)</td>
<td>7/38 (18%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>3/22 (14%)</td>
<td>4/38 (11%)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

**Conclusions:** There was no difference in SVR rates between PEG alfa-2b and PEG alfa-2a in CHC naïve patients (overall and by genotype). The frequency of side-effects was similar between the two. Further prospective studies are warranted.

### 263

**Improving Sustained Response Rates in Hepatitis C Non-Responders by Combining PEG-INF alfa 2b with INF alfa 2b and RBV**

Scott M. Gioe, M.D.* Center for Pancreatic and Liver Disorders, Gastroenterology Center P.A., Gulfport, MS.

**Purpose:** PEG-interferon and Ribavirin (RBV) combination therapy is the current standard of care due to its improved sustained virologic response rate (SVR) over IFN alfa 2b and RBV combination therapy. It is felt that the improved SVR is related to sustained levels of interferon in the body. Protein pegylation does come with a price, as the viral activity of PEG-interferon-alfa 2b (PEG) is only 28% that of interferon-alfa 2b (INF) and the viral activity of PEG-interferon-alfa 2a is 7% that of Interferon-alfa 2a. It is hypothesized that a combination of the longer acting pegylated interferon with the shorter acting more virally active interferon may offer high viral activity as well as sustained pressure on the virus and improve sustain response rates particularly in previous non-responders (NR).

The aim of this study was to prospectively evaluate the use of a combination of PEG and INF, along with RBV in the treatment of Hepatitis C patients who have been non-responders to at least six months of INF ± RBV therapy.

**Methods:** Patients eligible for the study received PEG at 1.0 ug/kg SQ every Saturday and INF was dosed at 3 mil units (< 90kg) or 5 mil units (< 90 kg) SQ every Monday, Wednesday, and Friday. RBV was given at doses of 12–15 mg/kg/day. Treatment duration was for 48 weeks and NR were defined as having detectable HCV RNA at 24 weeks.

**Results:** A total of 10 patients were enrolled in the study; six had cirrhosis, seven were genotype-1, and nine were previous combo treatment NR. Initial response rates were 80% (8/10) and the SVR was 30% (3/10). Two of the five
relapsers were re-treated for 60 weeks and both of these patients became sus-
stained responders bringing the overall SVR rate up to 50%. Dose reductions of
PEG/INF were not required and only one patient had a dose reduction in
RBV. No serious adverse events were noted.

Conclusions: The combination of PEG/INF/RBV in the schedule and doses
outlined above can be given safely. Initial and sustained response rates to this
combination therapy in previous non-responders are very good particularly
if treatment extends beyond 48 weeks. Longer duration of treatment beyond
48 weeks may be needed in patients at high risk for relapse such as previous
non-responders or relapsers to therapy, cirrhotics, patients with high viral
load and genotype-1, and those who’s HCV RNA takes longer than 12 weeks
to become undetectable. If larger studies confirm these results, this could be
a method to maximize the effects of interferon in the treatment of non-
responders.

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Prophylactic Tips for Large Gastric Varices: A Pilot Study with
Four-Year Prospective Experience

Ahmad Kamal, M.D., Seth Crockett, M.D., Ronald W. Yeh, M.D., Jennifer
Roost, M.D., Emmet B. Keeffe, M.D., Aijaz Ahmed, M.D.* Division of
Gastroenterology and Hepatology, Stanford University School of Medicine,
Stanford, CA.

Purpose: Cirrhotic patients with large fundal gastric varices have high mor-
bitality and mortality. We sought to determine the role of TIPS as primary
prophylaxis for bridging such patients to liver transplantation.

Methods: Among 147 consecutive patients evaluated in the Stanford Uni-
versity pretransplant hepatology clinic, we identified 9 patients with large
fundal gastric varices (LFGV) and high-risk characteristics. Seven (78%) pa-
patients underwent TIPS, and were followed for a mean of 28 months (range,
10.7–42.8 months).

Results: At the end of the follow-up period, 2 (28.6%) patients had under-
gone liver transplantation and 2 (28.6%) had died. One patient died from
gastrointestinal bleeding and the other succumbed to severe hepatic decomp-
ensation complicated by intracranial bleeding. The other 3 patients remain
on the transplant list with no episodes of gastrointestinal hemorrhage. [figure
1]Four patients required one TIPS revision each, at a mean of 168 days from
the time of the initial procedure. These outcomes compare favorably with
published morbidity and mortality rates of patients with LFGV.

Conclusions: TIPS may be useful as a bridge to liver transplantation for pa-
ients with large gastric varices. A randomized controlled trial is warranted.

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Liver Transplantation for Hereditary Hemochromatosis—A Single
Center Experience

Kumar Desai, M.D., Elizabeth Lyden, Sandeep Mukherjee, M.D.* Internal
Medicine, Montefiore Medical Center, Bronx, NY and Gastroenterology,
University of Nebraska, Omaha, NE.

Purpose: Hereditary hemochromatosis (HH) is a systemic disease that can
lead to cardiac and liver failure requiring organ transplantation. Long-term
results of orthotopic liver transplantation (OLT) for HH have been disappoint-
ing due to an increased mortality from cardiac and infectious complications.
The aim of this study is to report the outcomes of OLT for HH from a single
transplant program.

Methods: A retrospective chart review was performed on patients trans-
planted for iron overload at the University of Nebraska Medical Center be-
tween 1985 and 2004. Patients were diagnosed with HH if three of the follow-
ning four criteria were present: iron saturation greater than 65%, C282Y mu-
tation, liver biopsy consistent with iron overload and explant histopathology
confirming excess iron deposition. The following outcomes were recorded:
prevalence of hepatocellular carcinoma (HCC), episodes of rejection, post-
transplant diabetes mellitus and sepsis, cardiac complications post-OLT,
graft and patient survival and cause of death.

Results: 16 patients were transplanted during this period. There were 13
males and 3 females. Median age was 58.8 years at OLT. HCC was present
in 3 patients, of whom two were diagnosed pre-OLT due to elevated alfa-
feto protein levels. Acute rejection occurred in 11 patients, all of whom
responded to steroid boluses and one who developed chronic rejection. Di-
abetes developed in 10 patients and 6 patients developed post-transplant
sepsis. Two patients were retransplanted for chronic rejection and hepatic
artery thrombosis. Cardiac complications occurred in 10 patients post-OLT
(cardiac arrest n = 1; arrhythmias n = 2; MI n = 5; pericarditis n = 1; aortic
stenosis n = 1) with 4 patients dying from cardiac related causes. Cumula-
tive incidence of graft failure was 0% at 1 year and 14% at 5 years (95% CI
0–45%). Overall survival at 1 year was 94% (95% CI 82–100%) and at 5
years was 75% (95% CI 61–86%).

Conclusions: Despite the encouraging one year survival for patients trans-
planted for HH, 5 year survival was disappointing compared to patients
undergoing OLT for other indications. Infections, although frequent, were
not responsible for mortality in this small series of patients. Cardiac related
causes accounted for the death in all 4 patients. Cardiac disease remains an
important cause of morbidity and mortality in patients undergoing OLT for HH.
Consideration for combined cardiac and liver transplantation may need to
be entertained for this high risk group.

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Non-Invasive Predictors of Advanced Liver Fibrosis in Patients with
Nonalcoholic Fatty Liver Disease

David H. Bruining, M.D., Bassam Arodak, M.D., Ann L. Silverman, M.D.,
Stuart C. Gordon, M.D.* Department of Internal Medicine, William
Beaumont Hospital, Royal Oak, MI and Division of Gastroenterology &
Hepatology, Henry Ford Health System, Detroit, MI.

Purpose: Patients with nonalcoholic fatty liver disease (NAFLD) require a
liver biopsy to definitively establish the presence of advanced fibrosis. The
purpose of this study was to determine whether non-invasive parameters
could accurately predict advanced fibrosis in this cohort.

Methods: We retrospectively reviewed the records of 57 consecutively biop-
sied patients with NAFLD. Data recorded included demographic features,
medical history, and clinical laboratory studies. Liver biopsy specimens were
staged and graded by an individual pathologist according to the original Brunt
system. Continuous and categorical variables were evaluated by univariate
analysis, and statistically significant variables were included in multiple lo-
gistic regression models.

Results: Of the 57 NAFLD liver biopsies, 30 (52.6%) had advanced fibrosis
(stages 3 + 4). Univariate analysis indicated that those individuals with
advanced liver fibrosis had significantly lower platelets and albumin levels
(Table 1). These patients were also more likely to have type 2 diabetes
mellitus and AST/ALT ratios greater than 1.0 (p < 0.05). Multiple logistic
regression models indicated that the Odds Ratios for advanced fibrosis were
8.9 and 10.3 for individuals with diabetes mellitus and AST/ALT ratio >
1.0, respectively. A model using the combined presence of type 2 diabetes
mellitus and AST/ALT ratio > 1.0 demonstrates an AUROC of 0.81.
Table 1. Comparisons of Study Patients with NAFLD According to Degree of Fibrosis

<table>
<thead>
<tr>
<th>Features</th>
<th>Advanced Liver Fibrosis (N = 30)</th>
<th>Non-Advanced Liver Fibrosis (N = 27)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.0 ± 9.6</td>
<td>49.6 ± 10.9</td>
<td>0.070</td>
</tr>
<tr>
<td>Gender (%M)</td>
<td>53</td>
<td>52</td>
<td>1.000</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>40.9 ± 10.14</td>
<td>37.2 ± 10.0</td>
<td>0.321</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>81.8 ± 52.1</td>
<td>118.8 ± 69.7</td>
<td>0.029</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>74.0 ± 36.8</td>
<td>61.6 ± 27.0</td>
<td>0.292</td>
</tr>
<tr>
<td>AST/ALT ratio</td>
<td>1.04</td>
<td>0.61</td>
<td>0.001</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>77.0</td>
<td>22.7</td>
<td>0.006</td>
</tr>
<tr>
<td>(% present)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets (bil/L)</td>
<td>197.0 ± 73.0</td>
<td>253.0 ± 87.5</td>
<td>0.027</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4.11 ± 0.44</td>
<td>4.32 ± 0.39</td>
<td>0.038</td>
</tr>
</tbody>
</table>

Conclusions: This data suggests that non-invasive models may allow gastroenterologists to accurately predict advanced liver fibrosis in NAFLD patients. The best model is one based on the combined presence of type 2 diabetes mellitus and an AST/ALT ratio > 1.0.

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Treatment of Hepatitis C Infected Substance Abusers within a Community-Based, Outpatient Methadone Maintenance Program

Kenneth I. Freedman, M.D.,* Paul McLaughlin, Peter Strong, M.D. Office of the Executive Director, Hartford Dispensary, Hartford, CT.

Purpose: To demonstrate the feasibility of Hepatitis C virus treatment of HCV-infected substance abusers within a community-based, outpatient methadone maintenance program.

Methods: In an effort to expand the treatment options to community-based methadone maintenance pts within a behavioral health agency, an HCV evaluation and treatment program was initiated. After HCV antibody testing and counseling, pts were screened for suitability for IFN-based tx (stable medical/psychiatric/substance abuse disease). These pts received a physician evaluation, lab (± biopsy evaluation), and IFN-based tx with lab monitoring and on-site psychiatric services.

Results: Using an intention-to-treat analysis, 15 pts on methadone maintenance therapy started a course of combination tx for chronic HCV liver disease. Demographically pts were 67% male, with mean age of 45, mean baseline ALT of 107, and 73% genotype I with a mean HCV viral load of 2,800,000 IU/ml. Mean biopsy stage was 2.4 with a mean grade of 2.4. All pts had had at least 3 months abstinence from illicit drugs prior to the initiation of tx. 8/15 (53%) had known psychiatric illness; 7 of these were diagnosed with depression.

All 15 pts were treated with PEG-IFN and RBV for 24-48 wks dependent on genotype. Only one pt withdrew from tx due to intolerance of PEG-IFN. 93% of those completing 12 wks of tx (N = 14) had an early virological response (2-log drop in HCV RNA level). Later 3 pts had a recurrence of virus, leading to discontinuation of tx prior to its intended duration. 10 pts completed a full course of tx; 9 of these had an undetectable HCV RNA (ETR 60%). 6 months post-tx, 5/15 (33%) had a sustained virological response; 2 pts had recurrence of virus, and 2 others pts remain in follow-up. 2 pts with preexisting depression experienced worsening of symptoms; temporary reduction of PEG-IFN dosage successfully reduced depressive symptoms for one of these pts. 3 other pts developed depressive symptoms. Therapy was generally well-tolerated, with side-effects similar to pts who are not on methadone. Upward titration of methadone dosage reduced side-effects in most pts. There were no serious adverse events.

Conclusions: HCV-infected pts on methadone therapy can be safely and effectively treated for HCV. Due to the enhanced ability to monitor for psychiatric decompensation and substance abuse relapse, this therapy can be effectively delivered within the setting of a community-based, outpatient methadone maintenance program.

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Is NASH Triggered by a Leaky Gut?

Sushama Gundlapalli, M.D., Farhadi Ashkan, M.D., Keshavarzian Ali, M.D.*, Gastroenterology, Rush University, Chicago, IL.

Purpose: The pathophysiology of non-alcoholic steatohepatitis (NASH) has not been clearly delineated, but there appears to be a “two hit” mechanism. Based on animal studies, one of the proposed second hit mechanisms is oxidative stress triggered by endotoxin. Increased intestinal permeability has been shown to be a source of endotoxemia and oxidative stress in alcoholics. We aim to determine whether patients with NASH have intestinal hyper-permeability and whether leaky gut can differentiate simple steatosis from NASH in obese patients.

Methods: Patients were recruited from the Bariatric surgery center or Nutrition clinic at Rush. Steatosis and NASH were diagnosed by liver biopsy using Brunt criteria. Intestinal permeability was measured using urinary excretion of poorly absorbed sugars (lactulose, sucrose, mannitol and sucralose). To determine whether patients had increased susceptibility to leakiness, the permeability test was repeated after aspirin challenge (1300mg ASA). Urinary sugars were measured by gas chromatography. Small bowel permeability was defined by the Lactulose/Mannitol (L/M) ratio and whole gut permeability was defined by sucralose excretion. Median values for sugar excretion were compared between all groups using Kruskal-Wallis and between each group using Mann-Whitney tests.

Results: There was no statistically significant difference between patients with steatosis (n = 6) and NASH (n = 10) in regards to demographics, BMI, AST, AP, bilirubin, or cholesterol. ALT levels were significantly higher in patients with NASH (98) vs. steatosis (55). (p = 0.021). Small bowel permeability (median L/M ratio) was similar between groups pre and post aspirin. Whole gut permeability (sucralose excretion) was similar between groups at baseline; control 0.0245, steatosis 0.0323 and NASH 0.0328, (p = 0.873). However, patients with NASH had a significant increase in whole gut permeability with aspirin challenge, 0.0613, compared to both controls, 0.0283 (p = 0.006) and steatosis 0.0405 (p = 0.023). In contrast, patients with steatosis had no increased susceptibility to leakiness with aspirin compared to controls.

Conclusions: Our data indicate that patients with NASH are susceptible to colonic leakiness as they have an exaggerated response to aspirin challenge. This susceptibility should result in increased endotoxemia and oxidative stress in these patients. Therefore, avoidance of factors that may deleteriously affect intestinal permeability, such as NSAIDs, is strongly suggested in those at risk for NASH.

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A Randomized Controlled Trial of Consensus Interferon with or without Zinc for Chronic Hepatitis C Patients with Genotype 2

Ken Sato, M.D., Hideyuki Suzuki, M.D., Hitoshi Takagi, M.D.,* Daisuke Kanda, M.D., Toshiyuki Otsuka, M.D., Hiroaki Nakajima, M.D., Naondo Sohara, M.D., Satoru Kakizaki, M.D., Masatomo Mori, M.D. Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, 3-39-15 Showa, Maebashi, Gunma 371-8511, Japan.

Purpose: Additive effect of zinc supplementation on the treatment of chronic hepatitis C by interferon was demonstrated in hepatitis virus genotype 1b and high viral load. This study focused on the patients with genotype 2 which is more sensitive to interferon than genotype 1b, treated by consensus interferon with or without zinc.

Methods: We randomized 83 patients with chronic hepatitis C to consensus IFN (CIFN) 18MIU 6 times/week for 4 weeks, followed by CIFN 18MIU 6 times/week for further 20 weeks given in combination with polaprezinc 300 mg/day (regimen A, n = 41) or as monotherapy (regimen B, n = 42).

Results: Thirty-one patients in regimen A and 33 patients in regimen B completed this trial; the other patients withdrew because of side effects or a transfer to another hospital. No additional side effects of polaprezinc were noted. Sustained biochemical response, defined as normal aminotransferase level at the end of the 6 months post treatment observation, was 68 and 69%,
and sustained virological response, defined as undetectable HCV-RNA at the end of the 6 months post treatment observation, was 54 and 67% for regimen A and B, respectively.

**Conclusions:** Combination of CIFN treatment with zinc did not enhance the effect of CIFN as shown by biochemical, virological criteria.

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**Risk Factors for Bacterial Infections in Cirrhotic Patients**  
Jeong Wook Kim, M.D., Jae Hyuk Do, M.D., Dae Won Kim, M.D., Hyung Joon Kim, M.D., Jae Gyu Kim, M.D., Sae Kyung Chang, M.D.,* Sill Moo Park, M.D., Jin-won Chung, M.D., Eun Jeong Kim, Ph.D. Department of Internal Medicine, Chungang University College of Medicine, Seoul, Republic of Korea and Research Planning and Management Office, Korea Food and Drug Administration, Seoul, Republic of Korea.

**Purpose:** Cirrhotic patients with bacterial infection have a significantly higher mortality than uninfected cirrhotic patients in many studies, which indicates that bacterial infection is a poor prognostic factor in cirrhotic patients. Thus, it is important to investigate and eliminate the risk factor for bacterial infection in cirrhotic patients. This study was performed to evaluate the risk factors for infections in patients with liver cirrhosis.

**Methods:** The medical records of 674 consecutive admissions with liver cirrhosis hospitalized at the Division of Gastroenterology and Hepatology of Chungang University Yongsan Hospital were retrospectively reviewed between January 2002 and December 2004. The collected data included etiology, severity and complications of cirrhosis, blood test results on admission, isolated pathogenic organism, site of infection and prognosis.

**Results:** Bacterial infections developed in 188 patients (27.9%) and 66 (35.1%) of these developed nosocomial infections. The patients with infection have a higher mortality rate than patients without infection (17.6% vs 5.8%). Gram-negative bacterial strains were the most frequently isolated pathogens, in 62 of the 81 strains isolated. Univariate analysis revealed significant differences between the groups with and without infections with regard to advanced Child-Pugh class, ascites, hepatic encephalopathy, gastrointestinal bleeding, gastroesophageal varices, decompensated liver function, total protein, albumin, total bilirubin, total cholesterol, prothrombin time and activated partial thromboplastin time. Multivariate analysis revealed advanced Child-Pugh class (p = 0.017; odds ratio, 0.566; 95% CI, 0.356–0.902), gastrointestinal bleeding (p < 0.003; odds ratio, 3.973; 95% CI, 1.577–10.011), low serum albumin (p = 0.001; odds ratio, 2.525; 95% CI, 1.440–4.427) and low serum cholesterol (p = 0.003; odds ratio, 1.008; 95% CI, 1.003–1.013) as the independent factors contributing to the development of infections.

**Conclusions:** The present study indicated to need attention should be directed to gram-negative bacterial infections in advanced cirrhotic patients with gastrointestinal bleeding and low serum albumin and cholesterol levels.

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**CD34 Expression in Hepatocellular Carcinoma and Chronic Liver Diseases**  
Katsuya Shiraki, M.D., F.A.C.G.,* Akira Hashimoto, M.D., Hiroaki Fuke, M.D., Shigeru Ohnori, M.D., Takeshi Nakano, M.D. First Department of Internal Medicine, Mie University School of Medicine, Tsu, Mie, Japan.

**Purpose:** Angiogenesis is known to be essential for the progression of hepatocellular carcinoma (HCC). However, the relationship between the occurrence of HCC and angiogenesis has been not elucidated. CD34 have been used for the detection of active angiogenesis in malignant tumors including HCC.

**Methods:** 38 specimens of liver tumor which were obtained from patients including 6 cases of HBV-associated chronic liver diseases, 30 cases of HCV-associated, 1 case of glycogen storage disease, and 1 case of liver disease with unknown etiology by US-guided fine-needle target biopsy were embedded in paraffin, and cut into 4-micrometer-thick sections. These sections were immunostained with anti-CD34 monoclonal antibodies. The standard avidin-biotin-peroxidase complex technique was applied for immunostaining. The CD34 labeling index (LI) was measured.

**Results:** CD34 staining patterns in cases without HCC were all negative or minimal. On the other hand, many of cases with HCC showed focal or diffuse staining pattern. The sensitivity and specificity of focal or diffuse CD34 staining for HCC was 76.9% and 100%. In 72% of cases, we could distinguish HCC from non-HCC area within the same specimen by CD34 staining. In a view of relationship between CD34 staining pattern of obtained tumor tissues and clinical variables of patients, platelet counts was significantly lower in cases with diffuse staining than in cases with negative and minimal staining (p < 0.005). The level of alpha-fetoprotein (AFP) tended to be correlated with the intensity of CD34 staining, and the AFP level of cases with diffuse CD34 staining was significantly higher than that with minimal CD34 staining (p < 0.05). In 34 patients with advanced stages, CD34 LI of 16 patients with progression to HCC within 5 years (HCC group) was significantly higher than that of 18 patients without HCC (non-HCC group) (P = .0199). Moreover, in the same patients, the cumulative incidence of HCC was significantly higher in the patients of CD34 LI ≥12 (n = 16) than of CD34 LI <12 (n = 18) (P = .009).

**Conclusions:** These results indicate that evaluating the CD34 expression in chronic liver disease is very useful in predicting the HCC development and diagnosis of HCC.

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**Hepatitis D Is An Important Cause of Decompensation in HBV Related Chronic Liver Disease in India**  
Kanal Das, M.D., Brijesh C. Sharma, D.M., Shiv K. Sarin, D.M.* Department of Gastroenterology, G B Pant Hospital, New Delhi, Delhi, India.

**Purpose:** To study the extrinsic causes and methods of decomposition in hepatitis B related chronic liver disease.

**Methods:** 78 patients of CLD-B; 13 compensated and 65 recently (<3 months) decompensated were included. ACLF was defined as acute deterioration in liver function over a period of 2–4 weeks in a pre-existing patient of CLD. Patients with alcohol intake ≥20 g/day, concomitant HCC, chronic liver disease due other causes, HIV positivity or severe co-morbid conditions were excluded. Serological tests including IgM anti HAV, IgM anti HEV, HB-Ag, Anti HBe, IgM anti HBe, Anti –HCV, IgM Anti –delta, HIV 1&2, HBV DNA was quantified.

**Results:** 68 patients were followed-up; 56 were ACLF and 12 were compensated liver disease patients. Patients with ACLF presented alone or in combination as jaundice, ascites or variceal bleed in 78%, 61% and 11% patients respectively. ACLF patients had higher AST, ALT, bilirubin, CPT score and lower serum albumin than compensated CLD patients. IgM anti HBe was significantly higher in ACLD (p < 0.001) but median HBV DNA was comparable to compensated CLD patients (112 (0.5–1129) vs. 1.7 (0.5–3809) pg/mL). The most common extrinsic causes of decomposition were Hepatitis E in 17.8% of patients followed by Hepatitis D in 14.2% cases. Hepatitis A in 3.5% and Hepatitis C in 1.8% were other minor causes of decomposition. Reactivation of HBV was the cause in about 63% patients.

**Conclusions:** Besides reactivation of HBV, and superinfection by Hepatitis E, Hepatitis D infection is an important cause of recent decompensation and acute on chronic liver failure in India.

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**Interferon and Ribavirin Combination Therapy in Chronic Hepatitis C: Predictors of Sustained Viral Response**  
Ayodele T. Osowo, M.B.B.S., Vinodh Jeewanantham, M.B.B.S., M.P.H., Tarun Kothari, F.A.C.P. Medicine, Unity Health System (Park Ridge Hospital), Rochester, NY and Gastroenterology, Unity Health System (Park Ridge Hospital), Rochester, NY.
Purpose: To determine the predictors of SVR in Ribavirin and Interferon alpha combination therapy.

Methods: A retrospective chart analysis was done in 228 patients treated for Hep C between (2000–2005) and 137 charts were excluded. The exclusion criteria included patients with liver transplant, HIV or other forms of hepatitis, autoimmune diseases, on immunosuppressant, poor compliance, age > 70 and any other cause of chronic liver disease. Data collected from 91 charts were analyzed. Apart from demographic variables, information was collected on initial viral count, genotype, patient type, stage and grade of liver disease, alcohol use and treatment types. The primary outcome variable, Sustained viral response was defined as viral count < 600 six months after 1 year of treatment.

Results: The mean age of total sample (N = 91) was 49.15±7.14 years. 73.3% were men, 63.7% were Caucasians, 23.1% African Americans and 13.2% were Hispanics. Distributions of Genotypes 1, 2, 3, and 4 were 70.3%, 19.8%, 3.3%, and 2.2% respectively. The distributions of patient types were 73.6% Naive, 16.5% were non-responders (NR) and 7.7% were relapsers (R). 60.4% of the patients had SVR. Univariate analysis showed that SVR was significantly correlated with patient type [χ2 5.9, p = 0.015], race [χ2 5.9, p = 0.052] and alcohol use [χ2 3.65, p = 0.056]. SVR was also significantly correlated with early viral response (EVR) [0.875, p < 0.001]. SVR did not have correlation with age, weight, smoking, stage and grade of liver disease, and treatment type. Although the genotypes differed in the initial viral count [F3.18, p < 0.01], they did not show differences in SVR. A secondary observation made in this study is that the reason for incomplete treatment (<1 year) was 30.2% non-response to treatment and 25.5% as a result of side effects.

Conclusions: In our study race, alcohol intake, patient type and early viral response showed significant correlation with sustained viral response to ribavirin and interferon alpha combination therapy. Identification of these variables might provide help in improving treatment outcomes and pretreatment counseling. Further studies are needed to confirm this findings.

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Epidemiology of Chronic Hepatitis B Infection in South Bronx Community Hospital

David Widjaja, M.D., Suresh K. Yarlagadda, M.D., Bheema S. Singu, M.D., Raghu S. Loganathan, M.D., Prospere Remy, M.D., Suresh K. Yarlagadda, M.D., Bheema S. Singu, M.D., Bronx Lebanon Hospital Center, Bronx, NY.

Purpose: Prior study reported that prevalence of hepatocellular carcinoma (HCC) and portal hypertension from chronic hepatitis B virus (HBV) infection was 44% among Hispanics and 28% among Blacks. Since our institution predominantly serves these populations therefore we retrospectively studied the epidemiology of HBV infection in our community.

Methods: We reviewed medical records all patients ≥18 years with chronic HBV infection who had been evaluated at the clinics affiliated with Bronx Lebanon Hospital Center between January 1, 2002 and December 31, 2004.

Results: 167 patients with chronic HBV infection were identified with mean age of 40 years (range 18–81). Of these, 82 (49%) patients were males. 103 (62%) were African-Americans, 60 (36%) Hispanics and 4 (2%) others. Majority of the patients were covered by health insurance (127, 76%). Co-morbidities included HIV (23, 14%), HCV (8, 5%), HIV and HCV (4, 2%). Of the 16 patients with liver cirrhosis, 9 (56%) were found to be decompensated and 1 (6%) had HCC. Among 68 patients who had HBeAg status known, 23 (34%) had positive HBeAg. Of 78 patients with alpha-fetoprotein (AFP) known, 69 (88%) had AFP level less than 10 ng/mL. Liver imaging study for HCC screening was performed in 80 (48%) patients. 12 (7%) patients underwent HBV treatment. Among 155 patients who were not treated, 107 (69%) had alanine aminotransferase (ALT) level less than upper limit of normal (ULN) without evidence of liver cirrhosis. 48 patients were not eligible for HBV treatment for the following reasons: 20 (42%) were active injection drug or heavy alcohol users, 17 (35%) were non-compliant with visits during the evaluation period and 11 (23%) did not have health insurance coverage.

Conclusions: In the South Bronx, nearly half of our patients underwent HCC screening. More than half of patients with liver cirrhosis were decompensated. Most of our patients were not considered to be candidates for treatment because of normal ALT levels and potentially modifiable social factors. Recognition and management of the identified factors may increase rate of HCC screening and HBV treatment.

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Liver Dysfunction in Patients with Inflammatory Bowel Disease

Flavia Mendes, M.D., Cynthia Levy, M.D., Felicity B. Enders, Ph.D., Edward V. Loftus, M.D., Keith D. Lindor, M.D.* Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; Gastroenterology and Hepatology, University of Florida, Gainesville, FL and Biostatistics, Mayo Clinic, Rochester, MN.

Purpose: The prevalence of liver dysfunction in inflammatory bowel disease (IBD) varies across studies. Little is known about the relationship between liver dysfunction and IBD activity. In IBD patients we sought to 1) determine the prevalence of liver dysfunction, defined by abnormal serum levels of aspartate aminotransferase, alanine aminotransferase and/or alkaline phosphatase; 2) determine the prevalence of chronic liver disease; and 3) clinically compare patients with and without liver dysfunction.

Methods: IBD patients seen for the first time at Mayo Clinic Rochester from 1/1/00 to 12/31/00 were identified. Medical records were abstracted for gender, age, IBD subtype, extent and activity, medications, history of liver disease, and liver biochemistries. Chi-square, student t-test or rank tests were used as appropriate.

Results: We identified 544 patients with available hepatic biochemistries. Abnormal liver tests were found in 159 (29%), of whom 81% had no specific diagnosis. Primary sclerosing cholangitis (PSC) was present in 4% of all patients, and in 14% of those with liver dysfunction. Other liver diseases were autoimmune hepatitis (n = 2), fatty liver (n = 1), hepatitis C (n = 1), portal or hepatic vein thrombosis (n = 2) and metastatic cancer (n = 1). The prevalence of liver dysfunction was 27% for those with active IBD and 36% for those in remission (p = 0.06). Patients with and without liver dysfunction did not differ with regards to gender, age or subtype of IBD, but were less likely to be on oral 5-aminosalicylate (5-ASA) agents (35% vs. 51%, p < 0.001). 5-ASA did not modify or confound the effect of IBD activity in liver dysfunction. The use of other medications did not differ between groups. Follow-up liver tests were obtained in 118 patients (74%) with liver dysfunction. Abnormalities persisted in 39 (32%), with PSC being diagnosed in 15 (38%).

Conclusions: Liver dysfunction was detected in 29% of IBD patients. Surprisingly, we found no association between liver dysfunction and IBD activity. Patients with liver dysfunction were less likely to be on 5-ASA. One-third of those with abnormal liver tests had persistent abnormalities, and PSC was present in a significant proportion of them. Abnormal liver tests should not be attributed to active IBD. Rather, they should be monitored and work-up should be undertaken if liver dysfunction persists, even if IBD is active.

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Mild-Moderate Alcohol Consumption Does Not Enhance Liver Fibrosis Progression in Patients with Chronic Hepatitis C Virus (HCV)

Opan Cheung, Jennifer Salvatore, Sarah Hubbard, Richard K. Sterling, Velimir J. Luketic, Todd R. Strauvitz, Arun J. Sanyal, Scott A. Mills, Melissa J. Contos, Mitchell L. Shiffman. Hepatology Section & Division of Surgical Pathology, Virginia Commonwealth University Medical Center, Richmond, VA.

Purpose: Previous studies have suggested that regular ETOH use may lead to more rapid progression of chronic HCV. These studies focused on patients who consumed excessive amounts of ETOH (>6gms/day) and implied that any amount of ETOH may be deleterious to patients with chronic HCV. The present study is a retrospective, although detailed analysis assessing the impact of ETOH consumption on liver fibrosis in patients with chronic HCV.
Methods: 474 patients with well characterized chronic HCV followed at our center were enrolled. All patients underwent a baseline liver biopsy, serum HCV RNA level (Roche Amplicor) and genotype. Liver biopsy was staged according to the criteria of Knodell. Questions regarding a range of risk factors to estimate the date of infection as accurately as possible along with detailed history of ETOH use according to the Skinner Alchohol Examination Questionnaire were obtained during a one-on-one interview. Patients were grouped according to mean lifetime daily ETOH use (<1 drink, 1–3 drinks, 3–8 drinks, >8 drinks) and HCV duration (<10yrs, 10–29yrs, 30–39yrs, > or = 40yrs). A one-way ANOVA statistical analysis and linear regression were used to compare mean fibrosis with daily ETOH intake among each HCV group.

Results: The mean age of the group was 50 years, 58% were male and 71% Caucasian. The median duration of HCV infection was 27 years. Mean ETOH use was 3.2 drinks ± 8.8/day; mean fibrosis score 2 ± 1.5 and this increased stepwise with the duration of infection. For every level of ETOH consumption a broad range of fibrosis was observed. For each fibrosis stage (no fibrosis through cirrhosis), no relationship to ETOH use was observed. At least 40% of patients in each fibrosis group consumed <1 drink/day. An increase in fibrosis was observed in patients who consumed 5–6 drinks/day, more likely to affect fibrosis progression than ETOH consumption. It appears unnecessary. These data suggest that other factors, likely genetic, are required for cirrhosis therefore appear unnecessary. These data suggest that other factors, likely genetic, are more likely to affect fibrosis progression than ETOH consumption.

Conclusions: Results from these two studies (N = 99) suggest that IFN-induced depression may be a predictor of a positive response to antiviral therapy and may be an indication of optimal dosing. Patients who developed MDD were treated with SSRIs, which alleviated IFN-induced MDD and allowed continuation of therapy. Antidepressants may have permitted patients to remain on optimal antiviral therapy dosing and increase their chances of viral clearance. More research regarding the effects of depression and antidepressant use on antiviral responsiveness is needed. However, our results show that with regular monitoring, early symptom detection, and appropriate treatment intervention, patients who develop depression during HCV treatment can successfully complete a course of IFN therapy and achieve SVR.

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Predictive Factors for the Distant Recurrence of Hepatocellular Carcinoma after Radiofrequency Ablation of Hepatocellular Carcinoma

Hiroaki Fuku, M.D., Yutaka Yamanaka, M.D., Norihiko Yamamoto, M.D., Takeshi Nakano, M.D., Katsuya Shiraki, M.D., F.A.C.G.* First Department of Internal Medicine, Mie University School of Medicine, Tsu, Mie, Japan.

Purpose: Radiofrequency ablation (RFA) therapy for hepatocellular carcinoma (HCC) has made good local control possible. After the local control, however, distant recurrences are frequently observed in remnant liver. In this study the efficacy of RFA is evaluated and predictive factors for the distant recurrence are revealed.

Methods: 135 patients with initial HCC who underwent RFA in our hospital (Male/Female = 100/35) were selected for this study. After transcatheter arterial embolization, RFA was performed under the real-time CT guided. Safety margins of more than 5mm around tumors were confirmed by dynamic CT after the RFA with all those patients. The mean age is 66.9 years old, HBV/HCV/HBV+HCV/NBN= 10/109/1/15, Child-Pugh A/B/C = 96/35/4, the average follow-up period is 21.8 months (3–54months). We studied local and distant recurrence rates, predictive factors for the distant recurrence of HCC, and treatment performed for the recurrence.

Results: After RFA for the initial HCC, survival rates are 84.5%, 82.4% and 62.8% for two, three and four years respectively. The recurrence rates after RFA are 5% and 12% in two and four years respectively for local, and 41.4% and 67.7% in two and four years respectively for distant. RFA could be performed again for 76% of the patients with distant recurrence. The study of predictive factors for cumulative distant recurrence rates by Kaplan-Meier method shows significant high recurrence rates in cases of initial multi-occurrence, low albumin level, high AST level, low platelet count and low prothrombin time (PT). The predictive factors for cumulative distant recurrence after RFA by Cox proportional hazard regression model are low albumin level and high AST level.

Conclusions: While RFA enables good local control for the initial HCC without remarkably worsening liver functions, distant recurrences in remnant liver are observed at high rates in the cases with low albumin, platelet and PT level. Low albumin and high AST level are predictive factors for the distant recurrence, and it is possible to control distant recurrence by caring nutrition and lowering AST after RFA.

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Association between Antioxidant Use and the Prevalence and Severity of Steatosis and Fibrosis in Patients with Chronic Hepatitis C Virus Infection


Purpose: Oxidative stress is increased in patients with chronic hepatitis C virus (HCV) infection and may be involved in the pathogenesis of this
Impact of Ethnicity and Antioxidant Use on the Prevalence and Severity of Steatosis in Patients with Chronic Hepatitis C Virus Infection

Irphan Gaslightwalla, M.D., Edmund J. Bini, M.D., M.P.H.* VA New York Harbor Healthcare System and NYU School of Medicine, New York, NY.

Purpose: Both ethnicity and antioxidant use may affect the prevalence of steatosis among patients with nonalcoholic steatohepatitis. Although steatosis is a common histologic finding in patients with chronic hepatitis C virus (HCV) infection, it is unclear if ethnicity or antioxidant use influence steatosis formation. The aim of the present study was to determine the impact of ethnicity and antioxidant use on the prevalence and severity of steatosis in patients with chronic HCV infection.

Methods: Prior to liver biopsy, patients were interviewed by a research assistant who obtained detailed demographic and clinical data, as well as information on the use of antioxidants (vitamin C and E). Steatosis was scored according to the percent of hepatocytes involved as none (no steatosis), mild (<33%), moderate (33%–66%), or severe (>66%) using the Brunt system; fibrosis was scored on a scale from 0–4.

Results: Of the 577 patients enrolled, current antioxidant use was reported by 241 subjects (41.8%). Overall, 336 (58.2%) were not taking any antioxidants, 99 (17.2%) used vitamin C only, 62 (10.7%) used vitamin E only, and 80 (13.9%) were taking both vitamin C and E. The prevalence of steatosis of any grade (42.3% vs 60.1%, p < 0.001), moderate/severe steatosis (15.8% vs 24.7%, p = 0.009), and stage 3/4 fibrosis (23.7% vs 34.5%, p = 0.005) were significantly lower in patients who were taking antioxidants as compared to those who were not taking these supplements. The lower odds of steatosis (OR = 0.46; 95% CI, 0.31–0.69) and stage 3/4 fibrosis (OR = 0.68; 95% CI, 0.42–0.94) among patients who were taking antioxidants remained significant even after adjusting for age, gender, race, alcohol use, diabetes, BMI, triglycerides, and HCV genotype. However, the prevalence of steatosis of any grade (42.3% vs 60.1%, p < 0.001), moderate/severe steatosis (15.8% vs 24.7%, p = 0.009), and stage 3/4 fibrosis (23.7% vs 34.5%, p = 0.005) were significantly lower in patients who were taking antioxidants as compared to those who were not taking these supplements. The lower odds of steatosis (OR = 0.46; 95% CI, 0.31–0.69) and stage 3/4 fibrosis (OR = 0.68; 95% CI, 0.42–0.94) among patients who were taking antioxidants remained significant even after adjusting for age, gender, race, alcohol use, diabetes, BMI, triglycerides, and HCV genotype. However, the prevalence of steatosis of any grade (42.3% vs 60.1%, p < 0.001), moderate/severe steatosis (15.8% vs 24.7%, p = 0.009), and stage 3/4 fibrosis (23.7% vs 34.5%, p = 0.005) were significantly lower in patients who were taking antioxidants as compared to those who were not taking these supplements. Randomized controlled trials to evaluate the beneficial effect of antioxidants are warranted in patients with chronic HCV infection.

Fulminant Hepatic Failure Secondary to Low Dose Amiodarone

Saadia Shenzri, M.D., Ganapathi Parameswaram, M.D. Internal Medicine, Unity Health System, Rochester, NY.

Purpose: Amiodarone is a commonly used antiarrhythmic medication. Abnormal liver function are frequently reported with its use, however clinically symptomatic disease is rare. Toxic effects are well described with high dosages, there have only been a few case reports of low dose amiodarone and fulminant liver failure. We report a rare case of a patient who developed fatal fulminant hepatic failure with low dose oral amiodarone.

Case Report: 70 years old male admitted to the hospital with symptoms of anorexia, nausea, and generalized weakness for several days. He had history of coronary artery disease, ischemic cardiomyopathy with ejection fraction of 25% and Diabetes Mellitus. Amiodarone 200 mg was started 11 months ago for nonsustain ventricular tachycardia. Medications included atenolol, enalapril, atrovastatin, and Metformin. No history of recent alcohol, recreational or herbal drug use. Exam revealed a somnolent, normotensive, afibrile, non icteric patient, in no distress. Cardiopulmonary exam revealed bibasilar crackles. Abdominal exam was normal. Lab data showed, ALT 1821 U/L, AST 1424 U/L, total bilirubin of 5 mg/dl, direct bilirubin of 3.4 mg/dl, and ALP 269 U/L, HB 6g/dl, WBC of 17.9(81% neutrophils) BUN 90 mg/dl and creatinine 5.7 mg/dl. Blood cultures were negative. Hepatitis A, B and C profiles were negative. Chest X-ray showed pleural effusions bilaterally with cardiomegaly. Despite discontinuing the amiodarone patient’s condition worsened rapidly. He developed multiple organ failure, and died on the third hospital day. Autopsy showed centrlobulbar hemorrhagic necrosis with cholestasis and ductal inflammation consistent with drug induced hepatitis.

Discussion: Amiodarone is widely used for treatment of ventricular and supraventricular arrhythmia. When long term amiodarone therapy is used potential drug toxicity must be considered. Acute hepatic failure is a rare complication of Amiodarone therapy. Our patient had acute hepatic failure without any identifiable cause and the autopsy was consistent with drug toxicity. An exclusive ischemic cause of acute hepatitis seemed to be unlikely as there was no documented precipitating event. Whether additional factors contributed to the hepatitis cannot be ruled out. The patient did have ischemic cardiomyopathy and the literature shows amiodarone toxicity is more common in patients with congestive heart failure with a low ejection fraction.

Interferon alfa/ Ribavirin Combination Therapy in Mixed Hepatitis C Virus (HCV) Genotype Infection

Arif Q. Khan, M.D., F.A.C.P., F.A.C.G.* Faisal Q. Khan, MD, Qamar Iqbal, M.B.B.S., Asadullah Ijaz, M.B.B.S., Atif Imran, M.B.B.S. Department

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Is C Reactive Protein (CRP) a Useful Test in Distinguishing Steatosis from Steatohepatitis in Patients with Non Alcoholic Fatty Liver Disease (NAFLD)?

Wilma Cotto, M.D., Hill Hinkle, M.D., Michelle Abadie, R.N., Satheesh Nair, M.D.∗ Department of Gastroenterology and Hepatology, Ochsner Clinic Foundation, New Orleans, LA.

Purpose: NAFLD encompasses a spectrum of liver diseases ranging from fat accumulation in the liver (steatosis), inflammation, cell necrosis (steatohepatitis) and cirrhosis. Steatohepatitis is a progressive disease leading to cirrhosis, whereas steatosis has a benign course. There are no clinical or biochemical markers to distinguish steatosis from steatohepatitis. CRP is a widely available blood test that has been used as a marker of systemic inflammation. The aim of our study is to determine if CRP can be used to distinguish steatosis from steatohepatitis.

Methods: CRP values (ultraquant, normal < 0.3 mg/dl) were measured in 44 patients with NAFLD and 8 controls with chronic hepatitis C virus (HCV) infection who underwent liver biopsy in the same period. Liver function tests, fasting insulin levels, glucose and lipid profile were also obtained. The liver biopsies in patients with NAFLD were graded based on percentage of steatosis, inflammation and fibrosis as per published guidelines. Biopsies of 8 HCV patients were graded and staged by Knodell scoring system. Insulin resistance was calculated by QUICKI.

Results: Results are shown in table 1 and figure 1. CRP values were higher in patients with steatohepatitis compared to patients with simple steatosis. The values were highest in patients with severe inflammation. There were no differences in transaminases, insulin resistance, and lipid levels between the groups of patients.

Conclusions: Lower SVR to interferon alfa/ribavirin combination therapy was noted in mixed HCV genotype infections.

Clinical and Biochemical Profile

<table>
<thead>
<tr>
<th></th>
<th>Steatosis (n = 8)</th>
<th>Steatohepatitis (n = 36)</th>
<th>HCV (n = 8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48.5 ± 12</td>
<td>47.8 ± 12</td>
<td>46.6 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>31.9 ± 4.2</td>
<td>31.3 ± 7.9</td>
<td>32.1 ± 9.7</td>
<td>NS</td>
</tr>
<tr>
<td>AST</td>
<td>36.3 ± 16</td>
<td>48.7 ± 21</td>
<td>42.3 ± 14</td>
<td>NS</td>
</tr>
<tr>
<td>ALT</td>
<td>65.8 ± 30</td>
<td>73.3 ± 36</td>
<td>59.5 ± 31</td>
<td>NS</td>
</tr>
<tr>
<td>CRP</td>
<td>0.86 ± 1.5</td>
<td>2.19 ± 3.0</td>
<td>0.52 ± 0.4</td>
<td>0.08</td>
</tr>
<tr>
<td>QUICKI</td>
<td>0.322</td>
<td>0.311</td>
<td>0.318</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusions: C reactive protein appears to be a useful marker to distinguish steatohepatitis from steatosis. Studies with a larger number of patients are needed to clarify whether it can be used as a substitute for liver biopsy.

Profile of Liver Involvement among Adult Patients in Dengue Virus Infection

Srivenu Itha, M.D., Rakesh Aggarwal, M.D.∗ Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India.

Purpose: Little data are available on liver involvement in adult patients with dengue virus infection.

Methods: During a recent outbreak in India, we looked for evidence of liver dysfunction among adult patients with dengue fever, dengue hemorrhagic fever and dengue shock syndrome. Diagnosis of dengue infection was based on presentation, during the outbreak, with fever of short duration and thrombocytopenia.

Results: Forty five patients [median age 33 (range 7–65) years; 29 male; 39 adult; 23 dengue fever, 15 dengue hemorrhagic fever and 7 dengue shock syndrome] were studied. Median platelet count was 34 × 10^9/L (9.99 × 10^9). Seven patients (15%) had jaundice, 11 (24%) hepatomegaly and nine clinically-detectable ascites; none had splenomegaly. Twelve (27%) patients had hyperbilirubinemia. Serum alanine and aspartate aminotransferase activities were elevated in 43 (96%) patients each; 5-fold elevated levels were more frequent in severe disease. Hypoalbuminemia was found in 31/41 (76%) patients. Seven patients died, including two with acute liver failure.

Conclusions: Our data show that liver injury is common in adult patients with dengue virus infection. Further studies are needed to determine the mechanism of liver injury in this disease.

Effect of BMI on Survival after Liver Transplant: A Single Center Experience

Sohail Asifandyar, M.D., Mary Ann Sherbundy, M.D.,∗ Dilip Moonka, MD Internal Medicine, Henry Ford Hospital, Detroit, MI.

Purpose: Orthotopic liver transplant has become an accepted modality for the treatment of end stage liver disease. The increase prevalence of obesity in the United States has resulted in an increased number of obese recipients as well as obese donors. Questions have emerged on whether these recipients with less than ideal body weights have increased morbidity and mortality.
Aims: 1. To determine whether BMI affects patient survival and post-surgical complication rate. 
2. To assess the effect of BMI on renal function after liver transplant. 
3. To determine whether survival rate changes in patients who develop co-morbid conditions (i.e. diabetes, hypertension) after transplant.

Methods: A retrospective database of all adult patients undergoing first time liver transplant at our center from 1995 to 2002 was established. The database was divided into patients with BMI < 30 kg/m² (low) and patients with BMI > 30 kg/m² (high). The groups were evaluated for survival, post surgical complications, and worsening renal function which was defined as renal transplant, dialysis or 3 consecutive creatinines over 1.8 mg/dL.

Results: From 1995 to 2002, 309 adult patients underwent first time liver transplant, of which 264 patients had BMI measurements. The mean BMI of the patients was 27.9 kg/m². In comparing patients with low and high BMI, the post-surgical complication rate was not significantly different between the two groups. Additionally, worsening renal function was not significantly different between the two BMI groups. On univariate analysis, development of diabetes adversely affected post-transplant survival (p = 0.02). However, on multivariate analysis, which included the development of hypertension, diabetes, and the presence of obesity, no conditions significantly affected post-transplant survival. Finally, when looking at survival rates between the two BMI groups, there is worse 3 year survival for the high BMI group (p = 0.03) while after 3 years post-transplant, there was a better survival for the high BMI group (p = 0.09).

Conclusions: In our experience with liver transplant, obesity did not affect the post-surgical complication rate. This was different than previously published reports from other single center studies. The development of diabetes post-transplant adversely affects patient survival. Patients who are obese have poorer short term survival, but appear to have better long term survival although continued follow-up of these patients is necessary to confirm this conclusion.

Anemia during Ribavirin Treatment for Hepatitis C: Can Creatinine Clearance Predict the Risk of Anemia and Response to Erythropoietin Treatment

Satheesh Nair,* Sreekala Satheesh. Gastroenterology and Hepatology, Ochsner Clinic Foundation, New Orleans, LA.

Purpose: There is paucity of data on the incidence of ribavirin induced anemia and effectiveness of erythropoietin in patients with pre-existing renal insufficiency (RI). The aim of this study is to determine whether pre-treatment creatinine clearance can predict the occurrence of anemia and response to erythropoietin.

Methods: 46 patients (15 females, mean age 53.8 yr (range 44–71) with HCV infection after liver transplant were enrolled in the study. The antiviral regime comprised of pegylated interferon alpha 2b (1 microgram/kg/week) and 800 mg ribavirin. Weekly monitoring of hemoglobin and hematocrit was done. Erythropoietin alpha (procrit™) 40,000 units was given for a decrease in hemoglobin level of < 10 gm/dl or a drop in hemoglobin > 3 gms if patients had prior heart disease or are symptomatic. The erythropoietin was continued in weekly doses till an improvement in hemoglobin was noted or continued throughout treatment if hemoglobin remained stable. Creatinine clearance (CCR) was calculated by using modified diet in renal disease formula (MDRD1).

Results: Occurrence for anemia in each CCR group is shown in the table. Twenty patients (45%) required erythropoietin alpha and of these 9 patients had dose reduction in ribavirin. There were 11 (55%) patients who have improvement in hemoglobin by at least 1 gm/dL on erythropoietin, five (25%) remained stable and four (20%) patients had further drop in hemoglobin. The response to erythropoietin was similar in all groups of patients.

<table>
<thead>
<tr>
<th>CCR</th>
<th>Drop HB &lt;1gms</th>
<th>Drop HB 1–3 gms</th>
<th>Drop HB 3–5 gms</th>
<th>Drop HB HB&gt;5</th>
<th>P value</th>
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<tr>
<td>≥70</td>
<td>17%</td>
<td>26%</td>
<td>48%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>50–69</td>
<td>0%</td>
<td>58%</td>
<td>56%</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>29%</td>
<td>14%</td>
<td>14%</td>
<td>49%</td>
<td>0.05*</td>
</tr>
</tbody>
</table>

P value indicates difference in Drop > 5 gms.

Conclusions: Severe RI (CCR <50 ml/mt) is associated with marked decrease (> 5 gms) in hemoglobin levels. Erythropoietin (40000 units weekly) stabilizes the hemoglobin levels in majority of patients even in those with severe RI.

Hepatitis C Treatment Eligibility and Outcomes in Patients with Psychiatric Illness

Douha Sabouni, M.D., Muhamad Aly Rifai, M.D., James K. Moles, M.D., Brian J. Van Der Linden, M.D.* Veterans Affairs Medical Center, University of Virginia, School of Medicine, Roanoke-Salem Program, VA and Office of the Clinical Director, National Institute of Mental Health / NIH, Bethesda, MD.

Purpose: This report describes the existing status of Hepatitis C Virus (HCV) treatment eligibility, utilization and outcomes in a large sample of patients with HCV and co-morbid psychiatric illness. This would serve as a first step toward the facilitation of HCV treatment in psychiatric populations.

Methods: Our sample was derived from the sequential screening of all admissions (N = 3470) to an inpatient psychiatric service at a VA medical center from 1998 to 2002. HCV treatment evaluation and outcomes were tracked in 360 HCV (+) patients. The patient’s primary psychiatric admission diagnoses included one of the following: substance use disorders (alcohol, cocaine, marijuana); anxiety disorders; affective disorders (depression, bipolar) or psychotic disorder (schizophrenia).

Results: As illustrated in Figure 1, more than 2/3 of patients did not receive HCV treatment due to: non-adherence, active psychiatric symptoms and active substance use. Eleven percent died from HCV complications. Sustained virologic response (SVR) was achieved in 31% of those treated with interferon-α (IFN) and ribavirin (RBV). Patients with psychotic or anxiety disorders were less likely to achieve SVR (p<0.002)
more likely to have neuropsychiatric adverse effects from IFN treatment (p < 0.004) when compared with patients with affective or substance use disorders.

Conclusions: HCV infection in patients with psychiatric illness was associated with significant mortality. IFN-based therapy combined with RBV can be safely administered to patients with HCV and psychiatric illness. However, many patients with HCV and psychiatric illness were found ineligible for HCV treatment due to their psychiatric illness, and non-adherence to the evaluation process leading to HCV treatment was substantial. Our results highlight the need to develop better management and therapeutic approaches to engage, manage and successfully administer HCV treatments to patients with psychiatric illness. [figure 1]

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Outcomes of Gastric Variceal Bleed: Results of Sclerotherapy with N-Butyl 2 Cyanoacrylate

Purpose: To study the incidence and outcomes following NBC sclerotherapy of GV bleed.

Methods: Retrospective analysis of case records of 1436 patients who underwent endoscopy for PHTN from March 2000 to March 2005. GV were classified according to Sarin’s classification. Outcomes with respect to primary hemostasis i.e., bleeding control within first 24 hrs of endoscopy, rebleed ie., bleed after the first 24 hrs of endoscopy & in-hospital mortality were analyzed.

Results: The incidence of GV in patients with PHTN was 220/1436 (15%) and of these, 50 (22.7%) had bled. Mean age of patients with bleeding GV was 50 ±11 years, and 30/50 (60%) were males. The main etiology of PHTN in bleeders was hepatitis C in 34 (68%), followed by HBV and NBNC in 6 (12%) patients respectively; IGV-I were observed in 22 (44%), GOV-I in 16 (32%) and GOV-II in 15 (30%). A comparison of bleeding and non bleeding GV revealed that IGV-I was seen in 22/50 (44%) patients who bled as compared to 39/170 (23%) who never bled (p < 0.005).

Primary hemostasis was achieved with NBC in all patients. Rebleed occurred in 7 (14%) patients. Secondary hemostasis with repeat NBC sclerotherapy was achieved in 3 (43%); 2 (28.5%) patients died after repeat sclerotherapy and one each during TIPSS and surgery. Treatment failure related mortality rate was 4/50 (8%).

Conclusions: GV were observed in 15% patients presenting with portal hypertension and bleed occurred in 22.7%. There was an increased risk of bleed from IGV-I. NBC was effective in controlling GV bleed. In hospital mortality in patients with bleeding GV was 8%.

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Predictors of Early Rebleeding Following Endoscopic Control of Variceal Bleeding
Eman Abdel Sameea, Nabil Omar, Ashraf Abu Gabal, Imam Waked,∗ Saleh M. Saleh. Hepatology, National Liver Institute, Shebeen El Kom, Egypt.

Purpose: Early rebleeding is a major complication of variceal hemorrhage. Factors associated with early rebleeding after endoscopic control of the initial bleeding episode are not fully clarified. The aim of this study was to examine the frequency of early rebleeding, and to investigate factors related to its occurrence.

Methods: Acute variceal bleeding was controlled in by endoscopic intervention in 846 patients (662 males, 184 females, mean age 52.6 years). All patients received antibiotic prophylaxis, and were followed for the occurrence of early rebleeding for 5 days or till discharge.

Results: Early rebleeding occurred within the first 5 days in 82 patients (9.7%). Rebleeding was successfully re-controlled endoscopically in 37 (45.1%) (significantly less than in 764 of 918 patients (83.2%) with initial bleed (OR 6.03, 95%CI 3.7, 9.64). Rebleeding was related to severity of liver disease (none of Child A patients rebled, vs. 4.6% of Child B and 13.5% of Child C patients, OR < 0.05, Child C vs Child B OR 3.2 [1.77,6.01]). Rebleeding mortality occurred more in rebleeding Child C patients compared to Child B (62.3% vs 15.4% respectively, OR 9.1, [1.87, 44.3]). Earlier endoscopic intervention for managing the initial bleed was associated with significantly less re-bleeding (rebleeding occurred in 20 of 363 patients (5.5%) in whom endoscopy was done within 3 hours of admission, vs 26 of 264 (9.8%) with endoscopy between 3 and 6 hours, and 36 of 219 (16.4%) with endoscopy > 6 hours, p < 0.05). Patients with gastric varices injected with tissue adhesive had more rebleeding than patients with esophageal varices managed with either sclerotherapy or band ligation (25 of 161 patients (15.5%) vs. 57 of 685 patients (8.3%); OR 2.03, [1.22, 3.36]). Rebleeding was significantly related to the presence of encephalopathy, ascites, initial diagnosis of SBP in ascitic patients, renal impairment on admission, the presence of HCC, and the number of blood units needed to achieve hemodynamic stability before the initial endoscopic intervention. It was not related to method of initial management of esophageal varices, (banding vs. sclerotherapy), and was not related to age, sex, whether first or recurrent attack, and endoscopic description of varices.

Conclusions: Early rebleeding is a serious risk following control of bleeding from varices, and carries high mortality. Further preventive measures are needed for high risk patients to ensure prevention of early rebleeding.

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Non-Alcoholic Fatty Liver Disease in an Area of Northern Italy: Incidence and Main Clinical and Histological Aspects
Giancarlo Spinzi, M.D., Mariaantonietta Casiraghi, M.D., Marco Andreoletti, M.D., Elaria Arena, M.D., Roberto Ceriani, M.D., Giorgio Minoli, M.D.∗ Gastroenterology, H Valduce, Como, Italy; Gastroenterology, H Legnano, Legnano, Italy; Internal Medicine, H Lecco, Lecco, Italy; Gastroenterology, H Varese, Varese, Italy and Gastroenterology, Humanitas, Milan, Italy.

Purpose: The incidence of NASH in pts with abnormal transaminases has not been clearly defined. The purpose of this prospective study was to determine the incidence of NASH in asymptomatic pts with abnormal ALT referred for evaluation to five Hepatology Units in northern Italy.

Methods: In the period from January to December 2003, pts (18–60 years old) with persistently abnormal ALT levels, normal US and alkaline phos- phatase were studied. The diagnosis of NASH was based on: (1) a weekly intake of less than 40 g of ethanol (evaluated using coded questionnaires and modalities) (2) exclusion of all other liver diseases such as drug induced and autoimmune hepatitis, hemochromatosis, Wilson’s disease, PBC, PSC 3) exclusion of hepatitis B or C infection 4) abnormally high plasma aminotransferase levels for at least 6 months 5) no exposure to known toxins such as pesticides or other xenobiotics. All pts with NASH underwent a liver
biopsy (scored according to Brunt EM et al Am J Gastroenterol 1999; 94: 2476–84).

**Results:** We evaluated 553 with abnormal ALT. NASH was found in 33 pts (6%). This population included 27 males with a median age of 40.2 years (range 27–60), BMI of 26.8 ± 1.9 (range 24–30) and 6 females with a median age of 40.7 (range 34–57), BMI 25.8 ± 1.7 (range 23–29). Four pts had hypertension, two hyperlipidemia, one patient had hyperlipidemia and hypertension. In 26 pts we found no co-morbidity. Clear obesity was found only in two pts, while none claimed to have recent weight loss. Grade of necroinflammation (grade1/grade2/grade3) was found in 8/4/4 pts respectively. Fibrosis score (1/2/3/4) was reported in 8/4/2/2 pts respectively. Liver histology was normal or near normal in 12 pts. Liver biopsy specimens were insufficient for histology in 5 pts.

**Conclusions:** In the setting of unexplained chronic liver transaminase abnormalities, NASH is found in 6% of our patients. A great proportion of pts with NASH present a normal or near normal liver histology. Cirrhosis was found in 6% of our population with NASH. Non alcoholic steatohepatitis can also occur in lean male and female pts without associated conditions.

**Purpose:** T-cells play a critical role in the immunological surveillance network against cancer formation. Activation of T-cells is initiated by binding of T-cell receptors (TCR) with antigen epitopes. Polymorphism of TCR-γ microsatellite (short tandem repeats, STR) marker has been found to be associated with early-onset colorectal cancer. The aim of this study was to elucidate the relationship of TCR-γ STR genetic polymorphism and hepatocellular carcinoma (HCC).

**Methods:** A total of 192 chronic hepatitis B or C carriers with HCC and liver cirrhosis were enrolled in this study. The other 192 sex-matched cirrhotic patients without HCC were recruited as controls. Their TCR-γ STR polymorphisms at loci D7S1818 and D7S2206 were detected by polymerase chain reaction. Dietary habits and other possible risk factors for HCC were also assessed by a structured questionnaire.

**Results:** Neither genotype nor allele of TCR-γ STR was found to be related to the susceptibility of HCC. However, after grouping the 20 genotypes of TCR-γ STR of D7S1818 into a high TCR-γ STR group (one or both alleles 3 or 3 in repeated number, GATA) and a low TCR-γ STR group (both alleles < 3 of repeated number), we demonstrated the former had a higher risk of HCC than the latter, in subjects younger than 60 years old (67.5% vs 42.8%, p = 0.006). This finding remains true after adjustment for dietary habits (OR: 2.72, 95% CI: 1.29–5.75).

**Conclusions:** TCR-γ STR polymorphism may be associated with the susceptibility of early-onset HCC. The viral hepatitis-associated cirrhotics with high TCR-γ STR may have T-cell dysfunction and increase the risk of HCC at a younger age.

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**Detection of Precore Mutants of Hepatitis B Virus by Ligase Chain Reaction (LCR) in the Patients of Chronic Liver Diseases**

Premashis Kar, M.D.,* Tarun Bansal, Abdul Malik, Ph.D., Bhudev C. Das, Ph.D., Syed A. Husain, Ph.D, Medicine, Maulana Azad Medical College, New Delhi, India; Molecular Oncology, Institute of Cytology and Preventive Oncology, New Delhi, India and Biosciences, Jamia Millia Islamia, New Delhi, India.

**Purpose:** Hepatitis B is one the most important cause of chronic hepatitis. Several recent studies have been shown that mutants of hepatitis B virus have important clinical and therapeutic implications of the many mutants described, mutations involving the precore region which suppresses expression of HBeAg have substantial clinical significance. The most sensitive and specific method of detecting these mutants is nucleotide sequencing. Ligase chain reaction is an alternative, simple and reliable method of detecting precore mutants. The study was designed with the following.

**Objectives:** To detect the precore mutant with a point mutation from G to A at nucleotide 83 in the precore region using Ligase chain reaction (LCR), and to study the clinical and biochemical profile of patients harboring HBV precore mutations and their comparison with those infected by wild type HBV and finally to compare the course of illness and clinical outcome due to precore mutation with that of wild type HBV.

**Methods:** 104 patients of serologically proven HBV chronic liver disease, which included cases of chronic hepatitis (90), Cirrhosis of liver (8) and HCC (6), were inducted in the study.

**Results:** The cases were evaluated on the basis of history, clinical examination, liver function profile and serological test of HBV infection (HBsAg, anti HBe (Total), HBeAg using commercially available Elisa Test. Those cases, which were HBsAg +ve, HBeAg –ve & HBV DNA +ve were subjected to LCR. 18 cases out of the total 104 cases were serologically suspected as precore mutants. These serologically suspected cases were subjected to LCR. 15 out of total 18 (83.3%) were positive for LCR confirming the presence of precore mutants, which were also confirmed by direct sequencing. The sequencing data analyzed showed that 7/15, (46.6%) of the cases were infected predominantly by the mutant form of the virus while the remaining 8/15, (53.3%) of the cases showed the presence of mixed infection with the wild and the mutant form of the virus.

**Conclusions:** The present data suggests that precore mutations is seen in 14.4% of the patients of Asian Indian origin suffering from chronic liver disease and the disease is more symptomatic and aggressive in patients with the mutant form of the virus as compared with the wild form of the virus.
No Association between Mannose-Binding Lectin Gene Polymorphisms in Patients with Chronic Hepatitis B and Spontaneously Recovered among Iranian Population

Leila Alidoust, M.S., Mohammadreza Agah, M.D., Leila Najafi, M.S., Zahra Hajebrahimi, Ph.D., Maryam Zafarghandi, M.D., Mohammad Hossein Somi, M.D., Mohammad Reza Zali, M.D., E.A.C.G.* Liver, Research Center for Gastroenterology and Liver Disease, (RCGLD), Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran.

Purpose: To determine the frequency of codon +57 (G to A) and position +4 (C to T) of non-translated region mannose-binding lectin (MBL) gene polymorphisms in chronic hepatitis B subjects, spontaneously recovered subjects and healthy controls.

Methods: In a case-control study, we examined 100 (27female and 73 male) unrelated patients with Chronic hepatitis B and 100 (24female and 76 male) spontaneously recovered patients referred to RCGLD, and 100 healthy controls (70 female and 30 male) which all had been matched by sex and age.

DNA extraction with salting-out method was performed on blood samples. MBL gene polymorphisms were determined by PCR-RFLP and SSP-PCR methods.

Results: Considering codon +57 the A/A genotype was not detected in either chronic hepatitis B patients or the spontaneously recovered ones. The frequency of A allele was estimated as 0.5% in chronic hepatitis B and 0.5% in spontaneously recovered patients. In the meanwhile the frequency of T allele at position +4 (C to T) of non-translated region was measured as 13.5% and 17.5% in chronic hepatitis B and spontaneously recovered patients, respectively. The occurrence of the codon +57 and position +4(C to T) of non-translated region polymorphisms in patients with chronic hepatitis B infection did not differ significantly from that in patients with spontaneously recovered infection or controls. (p value > 0.05).

Table. Distribution of MBL Genotypes in the Studied Population

<table>
<thead>
<tr>
<th>Polymorphisms</th>
<th>Healthy Controls N (%)</th>
<th>Spontaneous recovered HBV N (%)</th>
<th>Chronic HBV N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C/C</td>
<td>75 (75)</td>
<td>68 (68)</td>
<td>74 (74)</td>
</tr>
<tr>
<td>C/T</td>
<td>24 (24)</td>
<td>29 (29)</td>
<td>25 (25)</td>
</tr>
<tr>
<td>T/T</td>
<td>1 (1)</td>
<td>3 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Codon +57 G/G</td>
<td>90 (90)</td>
<td>99 (99)</td>
<td>99 (99)</td>
</tr>
<tr>
<td>G/A</td>
<td>9 (9)</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>A/A</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Conclusions: Our findings do not show any association between codon +57 and position +4 promoter polymorphisms of the MBL gene with persistent HBV infection in Iranian population which may be because of the variation in ethnicity.

TNF-alpha Promoter Polymorphisms in Patients with Chronic HBV and Spontaneously Recovered among Iranian Population

Zahra Hajebrahimi, Ph.D., Leila Najafi, M.Sc., Leila Alidoust, M.Sc., Mohammadreza Agah, M.D., Maryam Zafarghandi, M.D., Mohammad Hossein Somi, M.D., Mohammad Reza Zali, M.D., E.A.C.G.* Liver, Research Center for Gastroenterology and Liver Disease (RCGLD), Taleghani Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran and Genetic Department, Faculty of Basic Science, Tarbiat Modares University, Tehran, Islamic Republic of Iran.

Purpose: The aim of present study was to examine whether TNF-alpha gene promoter polymorphisms (−308G/A, −857C/T, −863C/A, −1031T/C) are associated with the clearance of HBV infection in chronic HBV patients and spontaneously recovered subjects.

Methods: We investigated 308, −857, −863, −1031 TNF-alpha polymorphisms in 100 patients with chronic HBV infection, 100 subjects who had spontaneously recovered from acute HBV infection, and 100 healthy controls. Genomic DNA was obtained from peripheral blood leukocytes by standard phenol-chloroform extraction. The −308G/A, −857C/T, −863C/A and −1031T/C polymorphisms in the promoter region of TNF-a gene were detected by PCR-RFLP.

Results: Our finding have shown that the frequency of −308A, −857C, −863A and −1031C alleles were 0.12, 0.835, 0.21 and 0.245 in chronic HBV patients, respectively; 0.13, 0.7, 0.185 and 0.25 in spontaneous recovered subjects and 0.105, 0.84, 0.13 and 0.16 in healthy controls. As shown in the table below our data suggest no significant difference among chronic HBV patients, spontaneously recovered subjects, and healthy controls considering the four evaluated TNF-alpha promoter polymorphisms (p value > 0.05).

Distribution of TNF-Alpha Genotypes in Chronic HBV Patients, Spontaneously Recovered Subjects and Healthy Controls

<table>
<thead>
<tr>
<th>Polymorphisms</th>
<th>Chronic HBV patients N (%)</th>
<th>Spontaneously recovered subjects N (%)</th>
<th>healthy controls N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>−308 A/A</td>
<td>2 (2)</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>−308 A/G</td>
<td>20 (20)</td>
<td>22 (22)</td>
<td>19 (19)</td>
</tr>
<tr>
<td>−308 G/G</td>
<td>78 (78)</td>
<td>76 (76)</td>
<td>80 (80)</td>
</tr>
<tr>
<td>−857 C/C</td>
<td>70 (70)</td>
<td>60 (60)</td>
<td>71 (71)</td>
</tr>
<tr>
<td>−857 C/T</td>
<td>27 (27)</td>
<td>35 (35)</td>
<td>26 (26)</td>
</tr>
<tr>
<td>−857 T/T</td>
<td>3 (3)</td>
<td>5 (5)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>−863 A/A</td>
<td>4 (4)</td>
<td>4 (4)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>−863 A/C</td>
<td>34 (34)</td>
<td>29 (29)</td>
<td>16 (16)</td>
</tr>
<tr>
<td>−863 C/C</td>
<td>62 (62)</td>
<td>67 (67)</td>
<td>79 (79)</td>
</tr>
<tr>
<td>−1031 C/C</td>
<td>5 (5)</td>
<td>5 (5)</td>
<td>6 (6)</td>
</tr>
<tr>
<td>−1031 C/T</td>
<td>39 (39)</td>
<td>40 (40)</td>
<td>20 (20)</td>
</tr>
<tr>
<td>−1031 T/T</td>
<td>56 (56)</td>
<td>55 (55)</td>
<td>74 (74)</td>
</tr>
</tbody>
</table>

Conclusions: In contrast to other studies, these findings suggest no association between the TNF-alpha promoter polymorphisms and the development of chronic HBV infection in Iranian population, which probably ethnic differences could lead to different results.

Postresectional Adjuvant Intraportal Chemotherapy Improves Survival of Patients with TNM Stage I and II Hepatocellular Carcinoma

Gar-Yang Chau, M.D., Shyh-Haw Tsay, M.D., Wing-Yiu Lui, M.D.* Surgery, Taipei Veterans General Hospital, Taipei, Taiwan.

Purpose: Hepatic resection for hepatocellular carcinoma (HCC) carries a high postresectional recurrence rate. Tumor portal vein invasion is considered the major cause of recurrence. Adjuvant intraportal infusion chemotherapy (IPIC) was initiated in an effort to improve postresectional survival.

Methods: During June 1998 to May 1999, 28 HCC patients who underwent curative hepatic resection (study group) were placed on a protocol of postoperative IPIC daily for 2 days with 5-fluorouracil (650 mg/m²), leucovorin (45 mg/m²), doxorubicin (10 mg/m²), and cisplatin (20 mg/m²). Treatment was repeated every 3 weeks for a total of six cycles. Patient outcomes were compared with those of 66 matched HCC patients (control group) who underwent resection with no adjuvant therapy. The two groups were matched for age, gender, liver function status and tumor TNM stage.

Results: Adjuvant chemotherapy started 5–24 days after operation. The study group patients received an average of 5.2 cycles of chemotherapy.
Twenty patients (71%) experienced adverse events related with IPIC treatment, mainly upper abdominal pain, vomiting and myelosuppression. The median follow-up in the study group was 74 months. The 5-year disease-free and overall survivals of the study group were 44.6% and 60.7%, respectively. In subgroup analysis of patients with TNM stage I and II disease, the tumor recurrence rates were significantly lower in the study group (33.3%) than those in the control group (65.0%) (P = 0.025); the 5-year disease-free and overall survivals of the study group (70.6% and 83.3%, respectively) were significantly better than those of the control group (33.4% and 46.9%, respectively) (P < 0.05).

Conclusions: This study indicates that early postoperative IPIC is feasible in HCC patients with good liver functional reserve. Comparing to those of matched controls, adjuvant IPIC decreased the tumor recurrent rate and improved survival in patients with TNM stage I and II disease. The survival advantages demonstrated in this study justifies a selection of patients for future trials. [figure 1]

Clinical Features of Hepatocellular Carcinoma in Patients with Mutant p53 and/or Mismatch Repair Genes
Masatsugu Iano, M.D., Keizo Sagino, M.D., Toshiyuki Ianno, M.D., Toshimasa Asahara, M.D.* Department of Surgery, Akane Foundation Tsuchiya General Hospital, Hiroshima, Japan and Department of Surgery II, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan.

Purpose: There have been great advanced made in hepatic surgery, but the prognosis of the hepatocellular carcinoma (HCC) patients after curative resection remains poor. One of the most important reasons is the high recurrence rate. There are two types of intrahepatic recurrences. One is intrahepatic metastasis and the other is multicentric occurrence. If analysis of the molecular aspect of HCC could be used as a prognostic indicator of recurrence and the type of recurrence, it could greatly improve the prognosis of patients. In molecular biology, recent advances also have identified various genetic abnormalities important in hepatocarcinogenesis. In this respect, one of the best studied genes is the p53 tumor suppressor gene. And several studies have demonstrated that there may be a causal role for microsatellite instability in hepatocarcinogenesis. We report on a close correlation in mutations in either the p53 or mismatch repair gene (hMSH2 gene) and clinical features such as survival and recurrences.

Methods: We obtained tissue samples from 79 HCC patients by surgically curative resection. After extraction of DNA, SSCP was performed to screen the hMSH2 and p53 genes for variant sequences. Then we identified the mutations by the direct sequencing method.

Results: hMSH2 gene mutations were detected in 12 patients (15.2%) and p53 gene mutations in 14 patients (17.7%). There was a significant reduction in the percentage of cases with HCC metastasized in the group with mutations of p53 and/or hMSH2 (mutation-positive group) (34 months) in comparison with the value for the group with mutations neither gene (mutation-negative group) (98 months) (p < 0.05). In the mutation-positive group, a high portion of the patients (88.0%) showed recurrence; of these only 13.6% experienced multicentric recurrence, but there were 59.1% that experienced intranshepatic metastasis. In the mutation-negative group, 42.6% experienced intrahepatic recurrences; only 13.6% experienced intranshepatic metastasis and almost one half of the others that experienced multicentric occurrence.

Conclusions: We found that the presence of either a p53 or an hMSH2 gene mutation in HCC patients could lead to the poor outcome. And we also obtained the convincing evidence that mutation of either gene could be value in the prediction of HCC recurrent patterns.

Liver Biopsy Is Necessary To Accurately Diagnose the Severity of Chronic Hepatitis B
Ramesh Koka, M.D., Kenneth D. Rothstein, M.D., Victor Araya, M.D.* Division of Hepatology, Albert Einstein Medical Center, Philadelphia, PA.

Purpose: Hepatitis B (HBV) practice guidelines include viral load, HBsAg (eAg) status, Alanine aminotransferase (ALT) and histology for patient management. Little histological data exists for those with low viral load (LVL), normal ALT, and negative HBsAg since disease progression is felt to be rare.

AIM: Compare histological disease in HBV patients.

Methods: A cross sectional study of sequential HBV infected patients referred to our center was performed. Inclusion criteria: (1) measurable HBV DNA (Taqmam Real Time PCR); (2) no co-infections; (3) immune competent; (4) no prior antiviral treatment; (5) liver biopsy. Low viral load (LVL) was defined as <10⁴ copies/ml and high viral load (HVL) as >10⁵ copies/ml. METAVIR scores were categorized using the following combined histological severity definitions: Normal (grade 0/stage 0); Mild (grade 1 ± stage 1); Moderate (grade 2 ± stage 2); and Severe (grade 3–4 ± stage 3–4). Patients were then categorised into 3 groups based on ALT and Viral load. Group A: normal ALT/LVL; Group B: normal ALT/HVL; Group C: abnormal ALT/HVL. Demographics, Body mass index (BMI), ethanol use and eAg status were determined.

Results: 23 patients met inclusion criteria of which 11 were women and 12 men. Race: 18 Asians (Vietnamese 13, Korean 1, Cambodian 1, Chinese 2, Taiwanese1), Hispanic 2, African descent 3. Age range 30–71 (mean 50). Groups: A: N = 11 (all HBsAg negative); B: N = 8; C: N = 4. Group histology results by eAg status: B: eAg− (n = 2) 1 mild, 1 moderate, eAg neg. (n = 2) both severe; C: eAg+ (n = 4), 2 severe, 1/3 moderate, eAg neg. 2/3 severe, 1/3 moderate.

Significant alcohol intake in 1 Group C patient with cirrhosis, all others denied significant alcohol use. All patients below 40 years (n = 6) had mild to moderate disease.

Histology vs Viral Load

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>HISTOLOGY</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Normal</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>45</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>27</td>
<td>28</td>
<td>20</td>
</tr>
<tr>
<td>Severe</td>
<td>18</td>
<td>58</td>
<td>80</td>
</tr>
</tbody>
</table>

Conclusions: ALT, viral load and eAg status can be unreliable in predicting HBV disease progression. High rates of histologically worrisome disease was observed in our patients with LVL or HVL and normal ALT regardless of eAg status. Therefore, a liver biopsy should be considered in all HBV infected patients with detectable viremia, even low level viremia. These results need to be confirmed in a larger cohort.
High Dose Daily Consensus Interferon and Ribavirin Is an Effective Option in Chronic Hepatitis C Patients Who Are Nonresponders to Peg-Interferon and Ribavirin

Kenneth D. Rothstein, M.D., Ramesh Koka, M.D., Holly Hargrove, P.A.-C., Angel Fernandez, M.D., Shailender Singh, M.D., Victor Araya, M.D., Santiago J. Munoz, M.D.* Division of Hepatology, Albert Einstein Medical Center, Philadelphia, PA.

Purpose: The majority of nonresponder and relapper patients with chronic hepatitis C are unable to achieve a sustained virologic response (SVR) with the combination of Peg-Interferon (PEG-IFN) and ribavirin (RBV), especially those who have genotype 1 and advanced disease. Consensus interferon (Interferon alfacon-1, CIFN) is a bio-optimized alfa interferon that exhibits increased in-vitro antiviral activity than the naturally occurring alfa interferons 2a and 2b. Improved response rates have been reported with high-dose CIFN therapy and RBV for patients who have failed to respond to PEG-IFN/ RBV.

Aim: Evaluate efficacy and safety of high-dose daily CIFN and RBV in HCV patients who failed therapy with PEG-IFN/RBV.

Methods: Patients who had been treated with PEG-IFN/ RBV for HCV but did not obtain a SVR were eligible for treatment if they: 1) tolerated treatment with PEG-IFN / RBV, and 2) had advanced liver disease. Patients were given 27 ug of CIFN daily and RBV 400 mg BID during the first four weeks, followed by 18 ug daily and ribavirin 400 mg BID daily for the next eight weeks. At 12 weeks, CIFN was decreased to 15 ug daily while RBV was increased to 1,000–1,200 mg daily for 36 weeks.

Results: Thirty-two patients have been enrolled in the study, 76% male with a mean age of 52 years old. 94% had genotype 1. 22% of patients had stage 2 fibrosis. 78% had stage 3–4 fibrosis of which 39% of patients who have completed 72 weeks of treatment, 7 patients discontinued Treatment response (EOT). In an Intention to treat analysis, (ITT) of the 12 patients who were undetectable at 24 weeks and 8 patients (43%) achieved an End-of-Treatment response (EOT). In an Intention to treat analysis, (ITT) of the 12 patients who have completed 72 weeks of treatment, 7 patients discontinued therapy, 5 patients achieved an EOT (41%), 3 of these patients (25%) have achieved a Sustained Virological Response (SVR). 6 patients were dose reduced and 3 patients stopped therapy due to adverse effects.

Conclusions: For HCV patients with advanced histologic disease who had previously failed therapy with Peg-IFN and RBV, the combination of high-dose CIFN and RBV is a well-tolerated and effective option. Although our numbers are small, 25% of patients achieved a SVR.

Clinical Utility of AFP-L3% in Early Detection of Hepatocellular Carcinoma

Young Y. Wang, M.D., Shinji Satomura, Ph.D.,* Margaret Wise, Fatosi Kanke, Tonya Mallory, Myron E. Schwarz, M.D., Richard K. Sterling, M.D., Lemnos Jeffers, M.D., Fredric Gordon, M.D., Rajender K. Reddy, M.D., Alan P. Venook, M.D., Morris Sherman, M.D. New Diagnostic Business & Technology Development Department, Wako Pure Chemical Industries, Ltd, Richmond, VA; Wako Diagnostics, Wako Chemicals USA, Inc., Richmond, VA; Transplant Surgery, Mount Sinai School of Medicine, New York, NY; Hepatology, Virginia Commonwealth University, Richmond, VA; Hepatology, University of Miami School of Medicine/Miami VA Medical Center, Miami, FL; Hepatology, Lahey Clinic Medical Center, Miami, FL; Hepatology, University of Pennsylvania Health, Philadelphia, PA; Hepatology, University of California-San Francisco Medical Center, San Francisco, CA and Hepatology, Toronto General Hospital, Toronto, VA, Canada.

Purpose: AFP-L3 is an isof orm of alpha-fetoprotein (AFP) from malignant liver cell, which is the Lens culinaris agglutinin (LCA)-reactive fraction. To determine the clinical utility of AFP-L3% as an early cancer biomarker of HCC in a high risk population, a prospective and double-blinded study was conducted in North America.

Methods: AFP-L3% is the ratio of AFP-L3 against total AFP. AFP-L3% can be measured by using an automated analyzer, the LiBASys (Liquid-phase Binding Assay System), manufactured by Wako Pure Chemical Industries.

Results: A total of 440 patients with chronic hepatitis or liver cirrhosis related to hepatitis B or hepatitis C infection were enrolled in this study. Thirty-nine subjects had developed clinically verifiable HCC during the study. AFP-L3% was significantly associated with the development of HCC on multiple logistic regression analysis (p = 0.001). The risk of HCC, given an AFP-L3% elevation, was 40.0% (95%CI: 26.4%–53.6%). The risk of HCC, given an AFP-L3% below the cutoff, was 4.9% (95%CI: 2.7%–7.0%). The relative risk for developing HCC within the next 21 months after an initial AFP-L3% elevation was 8.2 (95%CI 4.7–14.3). The average and median lead times between the first elevated AFP-L3% and radiological demonstration of cancer were 205 and 130 days, respectively (ranging from 0–619 days). HCC patients exhibiting a tumor doubling time of less than 90 days had significantly higher AFP-L3% values (p = 0.0066).

Conclusions: The AFP-L3% is a useful cancer biomarker in early detection of HCC. An early elevation of AFP-L3% in patients blood offers a unique early warning for HCC in high risk patients.
an increased rate of breakthrough infection during the course of treatment. Overall, Hispanic veterans with genotype 1 have a lower sustained virological response to the standard combination therapy. This SVR is comparable to that observed in AA’s, but lower than reported for white American descendants. It appears that ethnicity may affect the treatment outcome of this subpopulation.

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Is Low Serum HDL the First Marker for Insulin Resistance in Early Stage Hepatitis C?

Rehan Rafiq, M.D., Amit Sohagia, M.D., Adnan Muhammad, M.D., Anna Pankratov, M.D., Hilyar Herten, M.D., Nejat Kiyici, M.D., Edward Norkus, Ph.D. Medicine/Div of Gastroenterology, Our Lady of Mercy Medical Center, Bronx, NY.

Purpose: Hepatitis C (HCV) is believed to cause insulin resistance and non-insulin dependent diabetes (NIDDM) through expression of TNF-α. This association is observed regardless of the stage of liver disease. It is also known that advanced cirrhosis causes impaired glucose tolerance regardless of etiology. Insulin resistance has been implicated in the progression of liver fibrosis and decreased sustained virologic response to interferon therapy. Insulin resistance is also known to be a risk factor for metabolic syndrome. We examined the relationship between insulin resistance in early HCV patients and the appearance of risk factors for metabolic syndrome.

Methods: A prospective sample of 42 HCV patients [mean MELD score of 7.5 ± 4.2 (sd)] was examined at our University teaching hospital. Patients had no history of NIDDM. Data were collected on patient’s age, gender, waist circumference, BP, BMI, race, clinical labs including fasting HDL, triglycerides, glucose and insulin, HCV risk factors and drug treatment for HCV. Data were analyzed by normal BMI vs. elevated BMI, by Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) and by fasting insulin using student t-tests, chi-square analysis, multiple linear and logistic regression analysis.

Results: Patient age ranged from 30–87 years [mean = 5 ± 13 (sd) yrs]; 71% were male. Insulin resistance was found in 76% (33/42) of patients (HOMA-IR used). Eleven patients (26%) had impaired glucose tolerance and 21 (50%) had NIDDM. Patients with insulin resistance had a 61-fold increased risk of low HDL (P = .025) and the effect was greatest in males (116-fold increase likelihood). No association between insulin resistance and other parameters of metabolic syndrome was observed. These findings were independent of patient’s BMI.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>ROC Area</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High glucose</td>
<td>96%</td>
<td>0%</td>
<td>.8698</td>
<td>&gt;.50</td>
</tr>
<tr>
<td>High waist</td>
<td>50%</td>
<td>50%</td>
<td>.5000</td>
<td>&gt;.050</td>
</tr>
<tr>
<td>High TG</td>
<td>83%</td>
<td>60%</td>
<td>.7722</td>
<td>&gt;.050</td>
</tr>
<tr>
<td>High BP</td>
<td>93%</td>
<td>50%</td>
<td>.7238</td>
<td>&gt;.050</td>
</tr>
<tr>
<td>Low HDL</td>
<td>73%</td>
<td>93%</td>
<td>.9075</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusions: Low HDL is the earliest marker for insulin resistance in patients with early HCV. HCV causes insulin resistance regardless of patient’s BMI. The identification of low HDL in early HCV suggests that an accurate and simple clinical marker for insulin resistance may be available so that intervention with insulin sensitizing therapies is initiated at the earliest.

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Efficacy and Safety of Selective Internal Radiation Spheres (SIR-spheres) To Treat Patients with Unresectable Hepatocellular Carcinoma (HCC) and Liver Cirrhosis

Mariam Mouli, M.D., Cheryl Levine, Ph.D., Travis Vannmeter, M.D., Jeff Weinstein, M.D., Stephen Cheng, M.D., Alejandro Mejia, M.D., Bo Husbug, M.D., Reem Ghalib, M.D.* The Liver Institute, Methodist Dallas Medical Center, Dallas, TX. and Radiology, Methodist Dallas Medical Center, Dallas, TX.

Purpose: Selective internal radiation spheres (SIR-spheres) is currently FDA approved for treatment of inoperable tumors from primary colorectal cancer that have spread to the liver. The purpose of this study was to evaluate the efficacy and safety of the SIR-spheres to treat patients with unresectable hepatocellular carcinoma (HCC) and liver cirrhosis.

Methods: This is a case series of 10 patients (8 males, 2 females) with HCC and liver cirrhosis who have been treated with at least one session of SIR-spheres. Baseline lab tests along with abdominal CT or MRI 3–12 weeks prior to the first treatment with SIR-spheres. Follow-up CT or MRI was done within 12 weeks after treatment and repeated as indicated.

Results: Patients age range was 51–80 years (mean 68±11.1) with Child–Pugh scores between 5 to 8 (Child’s class A). Two patients had small multifocal lesions and a total of 13 hepatic lesions were present in the other 8 patients. All patients were treated with at least 1 session of SIR-spheres with 4 patients having 2 sessions. Additional tumor therapy following SIR-spheres included chemoembolization in 3, radiofrequency ablation in 2, and surgical resection in 1 patient. Based upon follow-up imaging, tumor shrinkage occurred in 6/10 with tumor burden reduction between 20–52% in 4/10 patients. Liver failure with subsequent death occurred in 4/10 patients of which 3 had experienced progression of liver tumor prior to liver failure. One other patient died from extra hepatic carcinomatosis despite hepatic response. One patient had had surgical resection of the tumor and 4 patients continue to be monitored.

Conclusions: Treatment with SIR-spheres is safe in patients with extensive HCC and liver cirrhosis. Tumor shrinkage occurred in 60% of patients. In some patients tumor burden can be decreased substantially to enable curative resection to be performed. Further data need to be collected on safety and efficacy of SIR-spheres in treating patients with HCC.

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Change of Serum Ghrelin Concentration According to Severity of Hepatosteatosis

Yong Kyun Cho, M.D., Byung Ik Kim, M.D.,∗ Won Young Lee, M.D., Tae Woo Yoo, M.D., Woo Kyu Jeon, M.D., Hong Joo Kim, M.D., Ki Won Oh, M.D. Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea and Internal Medicine, Hallym University, College of Medicine, Pyungchon, Korea.

Purpose: Recently, ghrelin was reported to be associated with insulin resistance. Nonalcoholic fatty liver disease (NAFLD) is a condition in which insulin resistance relatively plays a pivotal role. The aim of this study was to evaluate change of serum ghrelin concentration according to severity of hepatosteatosis.

Methods: Sixty five apparently normal male adults who underwent health screen examinations were classified into three groups, Group I: normal liver (27 subjects), Group II: mild fatty liver (24 subjects) and Group III: moderate to severe fatty liver (14 subjects), according to ultrasonographic findings of liver. We analyzed the association between serum ghrelin concentration and severity of hepatosteatosis by ANOVA test. And the independent correlation between serum ghrelin concentration and insulin resistance related factors, HOMA (homeostatic model assessment), BMI (body mass index), WC (waist circumference), HC (hip circumference), WHR (waist to hip circumference ratio) were analyzed by multiple linear regression analysis.

Results: Serum ghrelin concentration tended to decrease according to severity of hepatosteatosis (Group I: 230.9±94.3, Group II: 195.2±97.2, Group III: 164.3±71.4 pmol/L). But this was statistically insignificant (p = 0.081). The independent correlation between serum ghrelin concentration and insulin resistance related factors were not observed.

Conclusions: Our study did not prove the correlation between insulin resistance related factors and serum ghrelin concentration in NAFLD according to severity of hepatosteatosis. However, we found tendency to decrease of
Thyroid Dysfunction in Patients with Chronic Hepatitis C Treated with Pegylated Interferon alpha Therapy
Ashwini Sahni, M.D., Mai Le, M.D., Syvia Bercovici, M.D., Michael Bernstein, M.D.* Department of Gastroenterology, Coney Island Hospital, Brooklyn, NY.

Purpose: Thyroid dysfunction has been reported in patients with chronic hepatitis C treated with interferon therapy. We prospectively studied this hypothesis in our patients with chronic hepatitis C on pegylated interferon alpha therapy and attempted to determine if autoimmune mechanisms play a role in the etiology of the thyroid dysfunction in these patients.

Methods: 39 patients (18 males and 21 females) aged 18–55 years with chronic hepatitis C were treated with pegylated interferon alpha. Thyroid stimulating hormone (TSH) and free thyroxine (free T4) levels were obtained on all patients prior to therapy. Antibodies to the microsomal and thyroglobulin receptor were obtained for baseline evaluation in all patients. All patients were euthyroid prior to beginning interferon therapy. TSH and free T4 levels were monitored on a monthly basis for the duration of the therapy. If the TSH or free T4 increased above or reduced below the normal range of the laboratory values during treatment, microsomal and thyroglobulin receptor antibodies were obtained to evaluate for development of autoimmune thyroid dysfunction.

Results: Of the 39 patients in our study, 4 patients (3 females, 1 male) had past history of hypothyroidism and one in this group had preexisting anti-thyroglobulin and anti-microsomal antibodies, 2 patients (both females) had past history of hyperthyroidism and one had preexisting anti-thyroid antibodies. 9 out of 39 patients (8 females and 1 male, 23%) showed changes in their thyroid function activity during treatment. Of these 8 patients became clinically hypothyroid and 1 patient became thyrotoxic and later became hypothyroid. Of the hypothyroid group 1 patient developed new anti-thyroglobulin antibody while the other showed increase in the level of pre-existing anti-thyroglobulin and anti-microsomal antibodies. The patient that became hyperthyroid following a thyrotoxic course also developed new thyroglobulin and microsomal antibodies. Therefore, 2 of 9 patients (22%) with thyroid dysfunction during the interferon therapy developed microsomal or thyroglobulin receptor autoimmune antibodies.

Conclusions: Patients on pegylated interferon therapy for treatment of chronic hepatitis C develop thyroid dysfunction. There appears to be a female predominance to this phenomenon. All patients become hypothyroid with or without preceding hyperthyroidism. This may be associated, but not entirely explained by the development of thyroglobulin and microsomal antibodies.

Human Telomerase Reverse Transcriptase (h-TERT) as Regulator of Telomerase Activity in Indian Hepatocellular Carcinoma
Shoket Chowdry, M.D., Nitin Saini, M.Sc., Sanjeev Sharma, M.Sc., Radhika Das, Ph.D., Arvind Rajvanshi, F.R.C.P., Yogesh Chawla, D.M.* Hepatology, Postgraduate Institute of Medical Education & Research and Cytology, Postgraduate Institute of Medical Education & Research, Chandigarh, India.

Purpose: Telomerase is a ribonucleoprotein that acts as reverse transcriptase. The protein adds the hexanucleotide repeats (TTAGGG)n on the ends of telomeres and is essential for cellular immortality. It is a multimeric enzyme and composed of three subunits: (1) h-TERC, (2) h-TEP1, and (3) h-TERT. h-TERT is essential for in vivo activity of telomerase and has been identified as the catalytic subunit of human telomerase.

Objective: To investigate whether telomerase activity is related to h-TERT mRNA expression in hepatocellular carcinoma (HCC) and non-HCC tissues.

Methods: Patients of hepatocellular carcinoma (HCC) coming to the Liver Clinic of our Institute were included in the study. Clinical history and examination were done in all patients. Diagnosis of HCC was made by USG/CECT/MRI/AFP and confirmed by imaging guided FNAC. FNAC samples of 17 HCC patients (Group 1) and liver biopsy samples of 15 chronic hepatitis patients (Group 2) without HCC were taken. Total RNA extracted by using acid guanidinium thiocyanate phenol-chloroform extraction method. cDNA generated and h-TERT was amplified using cDNA as template. Telomerase activity was measured using a telomeric repeat amplification protocol (TRAP assay).

Results: There were 14 (82.3%) males and 3 (17.7%) females (mean age 57.63 ± 9.68 yrs; 32–72 yrs) in group I, 13 patients (76.47%) were positive for HBsAg, 1 (5.88%) for anti-HCV and 3 patients (17.65%) negative for both HBsAg and anti-HCV. In group 2, 11 (73.33%) were males and 4 (26.67%) females (mean age 41.2 ± 9.57 yrs; 27–58 yrs), 8 patients (53.33%) were positive for anti-HCV and 7 (46.67%) for HBsAg. h-TERT mRNA was expressed in 15 (88.24%) of 17 HCC samples (12 HBsAg –ve and 3 –ve for both the viral markers). These 15 (88.24%) h-TERT positive patients were also positive for telomerase, showing high level of positive correlation between the two. Telomerase and h-TERT mRNA were not present in any of the chronic hepatitis tissue samples.

Conclusions: Telomerase is strongly expressed in HCC but not in chronic hepatitis liver biopsy samples. Also, the h-TERT mRNA was detected in all tissues that were telomerase positive and it was undetected in all tissues that were telomerase negative. Thus, h-TERT may be used as an important target for cancer drug development.

The Increased Risk for Non-Alcoholic Fatty Liver Disease (NAFLD) in Indian Immigrants with Type 2 Diabetes Mellitus
Praveen G. Murthy, C. S. Pitchumoni, M.D.* Department of Medicine, St. Peter’s University Hospital, New Brunswick, NJ.

Purpose: NAFLD, the most prevalent liver disease in the US, is associated with obesity, type 2 diabetes mellitus, insulin resistance, and hyperlipidemia. The aim of this study is to assess the prevalence of biochemical NAFLD in immigrants from the Indian subcontinent, where the incidence of type 2 diabetes and dysmetabolic syndrome is rapidly increasing (Chitturi and George. NAFLD/NASH is not just a western problem: some perspectives on NAFLD/NASH from the east. Fatty Liver Disease: NASH and Related Disorders. Blackwell Publishing, Massachusetts, 2005. Pp. 218).

Methods: In this retrospective study, we reviewed data from the initial visits of 200 patients with type 2 diabetes to assess the prevalence of NAFLD (ALT>40 u/L) and its relation to BMI and hemoglobin A1c in Caucasians (n = 104), African Americans (n = 34), and Indians (immigrants from the Indian subcontinent; n = 31). In addition, we used the ratio of aspartate to alanine aminotransferases (AST/ALT) to evaluate the severity of fibrosis across the three ethnic groups. Patients with history of hepatitis or alcohol use (>20 g/day) were excluded.

Table 1: Prevalence of NAFLD (% with ALT>40 u/L)

<table>
<thead>
<tr>
<th></th>
<th>African Americans</th>
<th>Caucasians</th>
<th>Indians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Prevalence</td>
<td>5.9%</td>
<td>23.1%</td>
<td>29.0%</td>
</tr>
<tr>
<td>BMI: &lt;25</td>
<td>14.3%</td>
<td>16.7%</td>
<td></td>
</tr>
<tr>
<td>25–30</td>
<td>2.3%</td>
<td>15.6%</td>
<td>30.1%</td>
</tr>
<tr>
<td>&gt;30</td>
<td>8.7%</td>
<td>33.3%</td>
<td>N/A*</td>
</tr>
<tr>
<td>HbA1c: &lt;6.0</td>
<td>2.0%</td>
<td>13.3%</td>
<td>1.7%</td>
</tr>
<tr>
<td>6.0–8.0</td>
<td>3.3%</td>
<td>19.6%</td>
<td>36.8%</td>
</tr>
<tr>
<td>&gt;8.0</td>
<td>12.5%</td>
<td>32.6%</td>
<td>11.1%</td>
</tr>
</tbody>
</table>

*No patients in this category displayed abnormal ALT

Results: See Tables 1 and 2.
Table 2: Prevalence of Increased Fibrosis

<table>
<thead>
<tr>
<th></th>
<th>African Americans</th>
<th>Caucasians</th>
<th>Indians</th>
</tr>
</thead>
<tbody>
<tr>
<td>% with AST/ALT &gt; 1.0</td>
<td>38.2</td>
<td>34.6</td>
<td>22.6</td>
</tr>
</tbody>
</table>

Conclusions: In Indian immigrants with type 2 diabetes, the prevalence of NAFLD:

1. is greater than in Caucasians or African Americans.
2. is greater at lower BMI levels. A BMI of 25–30 in Indians poses nearly the same risk for NAFLD as a BMI >30 in Caucasians.
3. increases dramatically as HbA1c rises above 6.0, while a similar increase in Caucasians occurs only with HbA1c >8.0.

Therefore, BMI alone may not be a good risk indicator for NAFLD in Indians; the waist-hip ratio may be preferable. Conversely, an AST/ALT ratio greater than 1.0, which may indicate an increased level of fibrosis, is less prevalent in Indians than in the other ethnic groups. Overall, higher standards for control of diabetes are necessary to reduce the risk for NAFLD. These observations are based on a small number of patients, and our studies are in progress.

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A Pilot Study of Hepatitis C Non-Responders Treated with a Combination of Parental Vitamin B-12 along with Pegylated Interferon α2b and Ribavirin
Junaid Siddiqui, M.D., Harjot Gill, M.D., Dimple Raina, M.D., Amir Mohammad, M.D., George Y. Wu, M.D.∗ Gastroenterology and Hepatology, University of Connecticut Health Center, Farmington, CT.

Purpose: The current treatment of naïve Hepatitis C patients has a response rate that results in a large number of non responders. Recent experiments have shown that vitamin B12 (cyanocobalamin) inhibited HCV internal ribosomal entry site (IRES)-dependent translation of a reporter gene in vitro. This inhibition is selective for the HCV IRES in the presence of cap-dependent RNA, and is specific for HCV IRES relative to other viral IRES. At high cobalamin (B12) concentrations, reduced viral translation may result in concentrations of viral proteins that are inadequate for replication and packaging, and may effect the virologic response in vivo. We conducted a pilot study to assess the efficacy of treatment with pegylated interferon α2b, ribavirin and vitamin B12 in patients with hepatitis-C, prior non-responders to standard therapy not limited to pegylated interferon and ribavirin.

Methods: Thirty one patients with normal baseline vitamin B-12 levels were enrolled at the University of Connecticut Health Center liver diseases clinic. Patients received vitamin B-12 (1000 µg subcutaneous) at baseline and at week 24, along with weekly pegylated interferon α2b and daily weight-based Ribavirin (800–1400 mg daily). The primary end point was a sustained virologic response (SVR).

Response Ratio with Reference to Prior Treatment

<table>
<thead>
<tr>
<th></th>
<th>Interferon only</th>
<th>Interferon + Ribavirin</th>
<th>Pegylated Interferon + Ribavirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responders/ Treatment, SVR pending 2 patients.</td>
<td>0/2</td>
<td>4/16</td>
<td>2/11</td>
</tr>
</tbody>
</table>

Results: The median age was 50 years, 74% were men, 74% were genotype 1 and 38% were previous pegylated interferon and ribavirin non responders. Twenty six (83%) completed at least 24 weeks of treatment, and twenty five (80%) went on to complete 48 weeks of treatment. Eighteen patients (58%) had an early virological response (EVR) at week 24. Fourteen patients (45%) showed an end of treatment response (EOT), while six patients (21%) had a sustained virological response (SVR). Four of the six patients (66%) were genotype 1. SVR for two patients is pending.

Conclusions: Our results show that Vitamin B-12 along with current standard treatment induced an SVR of 21% in previous Hepatitis-C non responders. In pegylated interferon with ribavirin non responder subgroup the SVR was 18% compared to 25% in interferon and ribavirin non responders subgroup.

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Cholangitis Complicating Percutaneous Radio-Frequency Ablation [RFA] of Liver Metastases
Nadia Trigg, M.D., Manish Patel, M.D., Amar Hamad, M.D., C. Feria, M.D., Charles Berkelhammer, M.D., F.A.C.G.∗ Gastroenterology, Oncology and, Internal Medicine, University of Illinois, Oak Lawn, IL.

Purpose: RFA is becoming increasingly popular as a non surgical method for ablating primary or metastatic liver tumors. The reported complication rate for RFA varies between 2% and 10%. We report an unusual complication following RFA.

Case: A 75 year old female with colon cancer metastatic to the liver, underwent RFA of three hepatic lesions in one session. Her baseline liver biochemistries prior to RFA were normal. The RFA treatment was itself uneventful. However, four weeks later the patient presented with jaundice and biliary colic. Her bilirubin increased to 4.2 mg/dl (normal <1.0), alkaline phosphatase 326 U/L (normal <126), AST 223 U/L (normal <39) and, ALT 247 U/L (normal <59). CT scan showed markedly dilated bile ducts. One metastatic lesion was in contiguity to one of the dilated bile ducts. Whereas the baseline CT scan showed three liver metastases but no dilation of the bile ducts. ERCP revealed a dilated bile duct containing debris. A sphincterotomy was performed and the bile duct was cleared off necrotic debris and blood clots. Patient liver enzymes returned to baseline post-ERCP.

Discussion: Since one metastatic lesion was adjacent to a bile duct, we hypothesize that the RFA caused necrosis of both the tumor and the biliary duct. This allowed subsequent sloughing of necrotic debris and blood clots into the biliary duct resulting in obstructive cholangitis. Obstructive cholangitis is an unusual complication following RFA.

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Relationships of Hepatic Histology to Metabolic, Inflammatory and Viral Parameters in Chronic HCV Infection
Safak Reka, M.D., Irina Kaplaunov, M.D., Ellen S. Engelson, Ed.D., Antonella Zanchi, M.D., Neil Theise, M.D., Donald P. Kotler, M.D.∗ Medicine, SUNY-Downstate Medical Center, Brooklyn, NY; Medicine, St. Luke’s-Roosevelt Hospital Center, Columbia P&S, New York, NY and Pathology, Beth Israel Medical Center, New York, NY.

Purpose: Hepatic steatosis is commonly associated with chronic hepatitis C infection (HCV). The purpose of this study was to determine the associations between hepatic histology, and metabolic, inflammatory and viral parameters.

Methods: This was a cross-sectional study of 31 hepatitis C infected subjects prior to HCV treatment, 21 male and 10 female, of whom 21 were HCV/HIV co-infected and 9 were HCV mono-infected. The infection was genotype 1 in 22 cases. Serum HCV RNA, soluble TNF receptors I and II (sTNFRI, II), fasting triglycerides, HDL-cholesterol, glucose and insulin levels were measured. Insulin resistance (IR) was calculated by HOMA. Body composition measures included BMI, body fat and fat free mass by bio-impedance analysis (BIA), and anthropometric measures of fat distribution. Liver biopsies were evaluated using a 4-point scale for disease activity (grade), and a 6-point scale for fibrosis (stage). Steatosis was measured using NIDDK 4-point scale plus a quantitative percent area estimate of macro and microvesicular fat. Data was analyzed by the general linear model method and by multiple regression, using steatosis, steatohepatitis, disease activity...
and fibrosis as dependent variables; and metabolic, inflammatory, HCV viral parameters and HIV as independent variables.

**Results:** HIV infection was associated with greater area of steatosis \( (p = 0.07) \), greater waist:hip ratio \( (p = 0.04) \), thinner thigh skinfolds \( (p = 0.006) \). Steatosis was directly associated with serum insulin level \( (p = 0.04), \) HOMA \( (p = 0.03) \), sTNFR II \( (p = 0.02) \). Grade was related to HCV RNA \( (p = 0.04) \), AST \( (p = 0.004) \), total body fat \( (p = 0.07) \). Disease stage was associated directly with sTNFR II \( (p = 0.0001) \), and AST \( (p = 0.07) \), and inversely with HDL. By multiple regression steatosis was associated with increased sTNFR I and II, grade was related to IVDU, HCV viral load, gender, and stage was related to sTNFR II, HCV viral load, and glucose.

**Conclusions:** Multiple factors affect hepatocyte histology in subjects with chronic HCV infection. While HCV viral load affects disease activity, the metabolic syndrome and TNF may be related to steatosis and fibrosis.

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**African-Americans with Genotype-1 with Chronic Hepatitis C Respond Poorly to Pegylated-Interferon and Ribavirin Combination Treatment as Compared to Caucasians**

Afreen A. Khan, M.D., Milton G. Matchnick, M.D., Murray N. Ehrinpreis, M.D., Ravi Dhar, M.D., Firdous A. Siddiqui, M.D.* Gastroenterology, Wayne State University School of Medicine, Detroit, MI.

**Purpose:** African-Americans (AA) with chronic hepatitis C (CHC) have a lower response to interferon (IFN) monotherapy as well as standard IFN and ribavirin combination therapy than Caucasians (Cau). Recent data suggests AA patients with CHC demonstrate a lower response to pegylated-interferon (PEG-IFN) and ribavirin combination therapy as well. Our aim was to determine and compare the sustained virologic response (SVR) rates in AA and Cau patients treated with PEG-IFN and ribavirin therapy for CHC.

**Methods:** This is a retrospective study consisting of consecutive patients seen and treated for CHC between March 2001 and February 2003. All patients included had measurable HCV RNA by polymerase chain reaction (PCR) assay and were treatment naïve. We treated 139 patients with PEG-IFN and ribavirin for 24 to 48 weeks. Treatment was discontinued in those with less than a 2 log drop in HCV RNA at week 24; however those with a greater than 2 log drop or negative HCV RNA were treated for 48 weeks. The primary end point was an SVR defined as a negative PCR for HCV RNA six months after completion of therapy. Variables affecting the treatment outcome such as ethnicity, gender, viral load, genotype, stage of fibrosis, pre- treatment ALT and 12 week PCR results were analyzed.

**Results:** Of the 139 patients (AA = 95, Cau = 44) treated, genotype was available for 130 patients. Genotype 1 was seen in a significantly higher proportion of AA \( (n = 78, 86\%) \) compared to Cau \( (n = 27, 69\%), p = <0.008) \). Mean age in both groups was 49–50 years. There were no statistically significant differences between the viral load and stage of fibrosis between AA and Cau. However, ALT values were found to be lower in AA \( (p = <0.02) \). Overall, SVR was higher in Cau \( (30\%) \) as compared to AA \( (19\%) \). Only 14% of AA compared to 32% of Cau with genotype 1 achieved an SVR \( (p = <0.001) \). However, the SVR in both AA and Cau with genotype 2 and 3 was 50%. In addition to genotype, stage of fibrosis \( (p = <0.001) \), baseline viral load \( (p=0.003) \) and a negative PCR at week 12 \( (p = <0.0001) \) significantly influenced the SVR in AA and Cau.

**Conclusions:** African-American patients with genotype 1 CHC have a lower treatment response to PEG-IFN and ribavirin combination therapy compared to Caucasian patients. In addition, we noted that a lower baseline viral load, lower stage of fibrosis and negative 12 week PCR are associated with an improved SVR in AA patients with CHC.

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**Fulminant Hepatic Failure Secondary to Lamotrigine**

Shashin Shah, M.D.∗, Weizheng Wang, M.D. Gastroenterology, University of Medicine and Dentistry New Jersey, Newark, NJ.

**Purpose:** Lamotrigine is a triazine derivative which inhibits release of glutamate (an excitatory amino acid) and inhibits voltage-sensitive sodium channels, which stabilizes neuronal membranes. It is often used in the treatment of primary seizure disorders. Lamotrigine metabolism occurs primarily in the liver by glucuronic acid conjugation. We report a case of lamotrigine induced hepatic necrosis, and fulminant liver failure one month after initiation of this drug.

33-year-old Jamaican male with history of Hepatitis C, HIV with CD4 count of 250 c/UL and alcohol abuse presented to our hospital with seizures after a drinking binge. After being treated in the intensive care unit for delirium tremens with benzodiazepines, he was discharged on lamotrigine and multi-vitamins with minerals which he took daily leading up to our hospitalization. While home, he began developing jaundice over the next three weeks. He denied illicit drug or resumption of alcohol use, drinking bush tea, eating mushrooms, anti-retroviral therapy, travel, exposure to animals, sick contacts, or new rash.

On presentation to our hospital three weeks after the recent discharge, he was encephalopathic and jaundiced. He had leukocytosis \( (wbc of 38,000 u/l) \) with mild eosinophilia \( (3\%) \). The patient had a total bilirubin of 18 mg/dl, rising to 35 mg/dl \( (18 mg/dl direct bilirubin) \) over the next two weeks. Records from the outlying hospital show total bilirubin at time of discharge to be less than 3 mg/dl. During this hospitalization, the aspartate aminotransferase and alanine aminotransferase were in a 4:1 ratio \( (120:29) u/l \). Prothrombin time was elevated at 19.2 seconds which did not correct with vitamin K therapy.

**M.D.∗ Medicine, University of Illinois at Chicago, Chicago, IL and Biostatistics, University of Illinois at Chicago, Chicago, IL.**
Sericologic workup for acute decomposition of chronic liver diseases such as Hepatitis A, B, and C was negative. Liver biopsy showed acute hepatitis with lobular disarray, hepatocyte dropout minimal steatosis, consistent with drug or toxin exposure. Special stains for herpes virus and cytomegaloviruses were negative.

During the hospital course the patient developed renal failure requiring dialysis. Following a three week intensive care unit course, the patient improved and was discharged home.

**Conclusions:** This patient developed fulminant liver failure manifested as severe, acute cholestasis which was temporally related to lamotrigine use. Our case reveals a rare adverse effect of a commonly used neuro-psychiatric medication.

### Abstracts

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**Hepatocellular Carcinoma (HCC): Outcome of Patients Treated Surgically at the University of Illinois at Chicago (UIC)**

Moushmi Shah, M.D., Chinmammal Kandaswamy, M.D., Chris Cho, M.S., Tom Weichle, B.S., Divyesh G. Mehta, M.D., Diely A. Pichardo, M.D.*

Medicine, University of Illinois at Chicago, Chicago, IL and Biostatistics, University of Illinois at Chicago, Chicago, IL.

**Purpose:** Surgical approaches remain the only curative option for HCC. The two main procedures available are resection and liver transplantation.

The purpose of this study was to analyze the outcome of 36 patients treated surgically with curative intent at the UIC.

**Methods:** Information about all patients with HCC treated at UIC since 1998 was retrospectively collected by electronic chart review. Statistical Analysis was performed utilizing the SAS Biostatistical software.

**Results:** A Total of 194 patients were identified. The distribution of the stages was: 18 (9.2%) were Stage I, 65 (33.5%) stage II, 44 (22.7%) stage III, 60 (30.9%) stage IV and 7 (3.6%) had unclear stage. Of these, 36 (18.6%) underwent surgical therapies with curative intent. Eleven (5.7% of the total), underwent resection and 25 (12.9%), transplant. Using the Wilcoxon statistical test, the median survival time for these patients was 37 months with 95% confidence interval (CI 95%) 30–42 months. In patients treated with non surgical therapies the median survival was 12 months (CI 95% 8–17 months). There was no significant difference in the recurrence time between transplant and resection groups. Recurrence was treated with a second surgical procedure, ethanol ablation, chemoembolization or systemic chemotherapy. Even though the percentage of patients potentially eligible for surgery (stages I and II combined) was 44.1%, less than half of these received either one. The inferior median survival of the patients treated with palliative modalities is probably explained at least in part by a more advanced median stage as well as other comorbidities that precluded surgery. Survival seemed better in patients treated with transplant than in those treated with resection; however these results should be taken with caution because of the wide confidence interval.

**Conclusions:** HCC continues to carry a very poor prognosis. Patients who are able to undergo surgical resection or transplant have the longest survival but most patients are not eligible for these interventions.

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**Neutropenia Associated with Pegylated Interferon Treatment for Chronic Hepatitis C: A Single Center Experience**

Tran T. Tran, M.D.; Tatin Patel, M.D.; Joshua S. Benner, Allison A. Petrilla, Fred Poordad, M.D.* Department of Medicine, Cedars Sinai Medical Center, Los Angeles, CA and ValueMedics Research, Arlington, VA.

**Purpose:** Pegylated interferon (p-IFN) and ribavirin (RBV) are currently the standard of care for the treatment of chronic hepatitis C. Bone marrow suppression is a side effect of interferon and the degree of neutropenia may differ based on the type of p-IFN used.

**Methods:** 63 patients with HCV treated between Jan 2003 and Apr 2004 were analyzed. Patients were treated with p-IFN 2a (180 mcg/wk)+ RBV(1000 mg/day <75kg, or 1200 mg if >75kg) (Group 1, n = 36) or p-IFN 2b (1.5 mcg/kg/week) +RBV (13 mg/kg/day) (Group 2, n = 27). Complete blood counts (CBC) with absolute neutrophil count (ANC) were measured at baseline, weeks 2, 4, 6, 12, 18, and 24 and as clinically indicated thereafter. Grade 3 neutropenia was defined as ANC <750 cells/ mm³, grade 4 neutropenia was defined as ANC <500 cells/ mm³. Statistical analysis was performed using the one-tailed Chi square with Yates correction.

**Results:** Baseline white blood cell counts were equivalent between the two groups (6.10 vs. 6.26/UL), and initial ANC prior to therapy was 3235 cells/ mm³ in group 1 and 3148 cells/ mm³ in Group 2. Neutropenia at week 4 in Group 1 was 6% vs 0% in Group 2 (NS). Treatment with granulocyte colony stimulating factor (G-CSF) was started in 12 patients (19%): 7 patients in the p-IFN alpha 2a group and 5 patients in the p-IFN alfa 2b group. Grade 3 and 4 neutropenia was noted in both groups (Table 1).

**Table 1.** Baseline Characteristics (N = 63)

<table>
<thead>
<tr>
<th>Patients,%</th>
<th>Gp 1 (n = 36)</th>
<th>Peg 2a</th>
<th>Peg 2b</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48</td>
<td>48.5</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Gender (female)</td>
<td>52.9</td>
<td>44.8</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Race (non-white)</td>
<td>20.6</td>
<td>17.2</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Genotype-1</td>
<td>67.7</td>
<td>51.7</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Weight lbs (kg)</td>
<td>164.1 (74.5kg)</td>
<td>187.0 (85 kg)</td>
<td>0.026</td>
<td></td>
</tr>
<tr>
<td>Baseline hemoglobin (g/dl)</td>
<td>14.1</td>
<td>14.7</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Pts treated with G-CSF</td>
<td>7</td>
<td>5</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Ave nadir ANC (cells/mm3)</td>
<td>882</td>
<td>1010</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Grade 3 neutropenia (ANC &lt;750)</td>
<td>8 (22%)</td>
<td>10 (37%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Grade 4 neutropenia (ANC &lt;500)</td>
<td>8 (22%)</td>
<td>1 (4%)</td>
<td>P = 0.043</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Neutropenia is commonly seen in patients treated with p-IFN.

Grade 4 neutropenia was observed more often in patients treated with p-IFN alpha 2a vs. p-IFN alfa 2b. This may be attributable to differences in bone marrow toxicity between interferons however the effect of weight on bone marrow toxicity needs to be further assessed.

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**Hepatocellular Carcinoma Occurring in a Patient with Crohn’s Disease Treated with Both Azathioprine and Infliximab**

Shawn C. Chen, M.D., Oscar W. Cummings, M.D., Michael P. Hartley, M.D., Carol A. Filomena, M.D., Won Kyoo Cho, M.D.* Department of Medicine, Division of Gastroenterology/Hepatology, Indiana University Medical Center, Indianapolis, IN; Department of Medicine, Division of Gastroenterology/Hepatology, Roudebush VA Medical Center, Indianapolis, IN and Department of Pathology, Indiana University Medical Center, Indianapolis, IN.

**Purpose:** In this report, we describe a case of hepatocellular carcinoma and focal hepatic glycogenosis (FHG) occurring in a non-cirrhotic Crohn’s disease patient who has been treated with both azathioprine and infliximab.

**Case Report:** A 28-year-old, non-cirrhotic female with history of fistulizing Crohn’s disease was hospitalized for further evaluation of fever prior to undergoing routine maintenance infusion of infliximab. She had been experiencing rectal pain for two weeks prior to admission. Admission labs were significant for anemia with a hemoglobin level of 8.8 g/dL, thrombocytosis, and a positive leukocyte esterase on her urinalysis. Chemistry was unremarkable with normal hepatic panels, amylase, and lipase. Because there was a concern for perianal abscess, a CT of abdomen and pelvis with oral and IV contrast was performed, that revealed a perianal fluid collection, moderate
thickening of the sigmoid colon, and an incidental finding of a 2-cm hypo-
density in the right lobe of the liver. A fine needle aspiration of the liver mass
revealed hepatocellular carcinoma and focal hepatic glycogenosis without
cirrhosis. Viral serologies were negative. Surgery service was consulted and
the patient underwent a total proctocolectomy with permanent end ileostomy
followed by segmentectomy of the liver lesion as an outpatient.

Conclusion: To the best of our knowledge, this is the first case of hepatocel-
lar carcinoma occurring in the absence of hepatic cirrhosis in a Crohn’s
disease patient who has been treated with both azathioprine and infliximab.
Although a direct causal relationship cannot be established, it is possible
that infliximab may have been a contributing factor in its pathogenesis in
addition to azathioprine. Further studies will be needed to better understand
the role of various immunosuppressants on the development of FHG and
hepatocellular carcinoma in non-cirrhotic patients.

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Immune Response to Influenza Vaccine in Adult HCV Patients Receiving Peginterferon and Ribavirin Therapy
Cristian R. Vallejos, M.D., Lisa Nyberg, M.D., Robert L. Atmar, M.D.,
Heather Patton, M.D., Scott Moon, PA, Andrea Duchini, M.D., Paul J.
Pockros, M.D.* Department of Gastroenterology/Hepatology, Scripps
Clinic, La Jolla, CA; Department of Microbiology & Virology, Baylor
College of Medicine, Houston, TX; Department of Gastroenterology/Hepatology, Baylor College of Medicine, Houston, TX
and Department of Gastroenterology, UCSD Medical Center, San Diego,
CA.

Purpose: Influenza virus infection may cause significant complications in
patients with chronic liver disease from hepatitis C virus infection (HCV)
(1). Patients with advanced liver disease due to HCV and those who are
post-liver transplantation have an impaired response to influenza vaccination
(2). Whether influenza vaccination is effective in patients with HCV who
are undergoing therapy with peginterferon and ribavirin is unknown. We
performed a pilot study to assess the immune response to influenza vaccine in
patients with HCV infection on interferon (HCV/IFN) therapy in comparison
to HCV controls not on therapy.

Methods: HCV/IFN pts (n = 22) and HCV controls (n = 9) were ad-
ministered the standard dose of the 2004–05 inactivated trivalent vac-
cine (A/MOSCOW/10/99[H3N2]; A/NEW CALEDONIA/20/99[H1N1];
B/HONG KONG/330/2001). Antibody responses to each of 3 components of
the vaccine were measured at baseline and after 6 weeks by hemagglutination
inhibition.

Results: Vaccination was tolerated with no side effects observed. Initial
results show the rate of seroconversion to ≥ 2 of the 3 vaccine antigens to
be greater in HCV controls than in HCV/IFN patients, 78% vs 41%, p =
0.085.

Conclusions: This trend toward statistical significance suggests that patients
with HCV on interferon treatment could have an impaired immune response
to the influenza vaccine and merits further investigation. We are currently
in the process of completing serologic analysis of the final 10 control cases
not included in this abstract.

1. Duchini A, Viernes E, Nyberg L et al. Hepatic decompensation in pa-
tients with cirrhosis during infection with Influenza A. Arch Intern Med

2. Duchini A, Hendry M, Nyberg L, et al. Immune response to in-
fluenza vaccine in adult liver transplant recipients. Liver Transplantation

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Correction of Both Hepatic and Brain Lysosomal Glycosaminoglycan
Storage Using a Single Gene Transfer Vector in a Murine Model of
Mucopolysaccharidosis VII
Yang Lu, M.D., Yujo Kawashita, M.D., David S. Strayer, M.D., Chandan
Guha, M.D., Jayanta Roy-Chowdhury, M.D., Namita Roy-Chowdhury,
Ph.D.* Liver Research Center, Albert Einstein College of Medicine, Bronx,
NY and Pathology, Jefferson Medical College, Philadelphia, PA.

Purpose: Lysosomal storage disorders (LSDs) are characterized by cellular
accumulation of glycosaminoglycans (GAGs), due to the deficiency of GAG-
degrading enzymes. Mucopolysaccharidosis type VII (MPS-VII) is caused by
β-glucuronidase (GUSB) deficiency, inherited as autosomal recessive trait.
GAG accumulation affects the liver, spleen, cornea and bones, as well as
the brain. GUSB is secreted into plasma and endocytosed by cells via the
mannose-6-phosphate receptor. Thus, hepatic GUSB expression following
gene therapy results in “cross-correction” of all abdominal viscera. However,
brain lesions are not ameliorated, because GUSB does not cross the blood-
brain barrier. Our purpose was to test if recombinant simian virus 40 (SV40)
 vectors would not only transduce the abdominal viscera, but also cross the
blood-brain barrier to transduce neural cells.

Methods: The T-antigen gene of the SV40 genome was replaced with human
GUSB encoding sequences. The recombinant viral genome was transfected
into COS-7 cells for packaging the vector (SV-GUSB). Viral titer was deter-
mined by infecting primary MPS VII mouse skin fibroblasts and staining for
GUSB activity. MPS-VII micewere injected with SV-GUSB (10⁷ rfu). Serial
serum GUSB levels were measured. Mice were sacrificed at intervals after
the injection. GUSB expression, GUSB activity and histological clearance
of GAG deposits was examined in various tissues.

Results: Two weeks after SV-GUSB injection, serum GUSB activity in-
creased from undetectable levels to 40–150% of normal. Southern blot anal-
ysis showed transduction of multiple organs (liver > spleen > kidney >
lung > brain), but not spermatozoa. All abdominal viscera were repleted with
GUSB in two weeks. In addition, a significant number of brain cells,
including neural cells and microglia exhibited GUSB activity and clearance
of the GAG deposits in two months. Molecular analysis showed integration
of the transgene into the host genome along with life-long expression.

Conclusions: rSV40 vectors are the first gene transfer vehicles that permit
efficient correction of LSD lesions in both abdominal organs and the brain
after intravenous administration. This integrating, non-immunogenic vector
can be administered repeatedly and is an attractive vehicle for comprehensive
gene therapy of MPS-VII.

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Seroprevalence of Hepatitis A: a Community Clinic Experience
Andrew Batey, M.D.,* Mian K. Khalid, M.D., Eric Alcaraz, M.D.
Gastroenterology, Carle Clinic, Urbana, IL and Medicine, University of
Illinois, Urbana-Champaign, IL.

Purpose: The Center of Disease Control (CDC) Third National Health and
Nutrition Examination Survey (NHANES III) between 1988 and 1994 found
serological evidence of prior exposure to Hepatitis A virus (HAV) of 37.4%
in the US general population. Some studies from urban settings have shown
higher seroprevalence rates. The seroprevalence of anti-HAV antibodies in a
community is important in assessing the need for vaccination against HAV
in high-risk individuals. This study was designed to determine the incidence
of HAV seropositivity in a typical midwestern community clinic setting.

Methods: In a prospective study, 399 patients were screened for evidence
of prior exposure to HAV with anti-hepatitis A antibody (IgG), over a 3year
period from July 2002 to June 2005. Patients with prior immunization his-
tory were excluded. There were 252 (63%) males and 147(37%) females
comprising 283 (71%) Caucasians, 56(14%) African Americans, 44(11%)
Asians and 16(4%) people of other races. Their ages ranged from 20 years
to 79 years with a mean of 47 years. The main reason for testing was to
to determine the need for vaccination in high-risk individuals, which included
healthy travelers 20 (5%), patients with chronic viral hepatitis 291(73%),
other chronic liver diseases 48(12%) and HIV 40 (10%).

Results: Of the 399 subjects studied, 127(31.8%) were positive (* vs.
NHANES III 37.4%). The127 seropositive subjects included 53(42%)
Caucasians, 26(20%) African Americans, 34(27%) Asians and 14(11%)
people of other races. Subset analysis of each ethnic group revealed the
lowest incidence of seropositivity in Caucasians of 53/283 (18%) compared
to 29% (p < 0.001) in NHANES III. In the African American group 26/56
(46%) were positive and for the Asian group 34/44 (77%), while the highest
incidence was among people of other races who were mainly immigrants
from developing countries with 14/18 (88%) testing positive.
Conclusions: The incidence of HAV seropositivity in a midwestern community clinic is comparable to NHANES III although with different population demographics. The seropositivity rates varied widely among different ethnic groups, thus one’s ethnic background may be important when individualizing vaccination strategies for hepatitis A in our community.

MELD Score vs Child Score in Predicting the Outcome of Elective Abdominal Surgical Procedures in Patients with Cirrhosis

Mauroof Hotel, M.D., Ammar Ghazale, M.D., Andrew Bain, M.D., Frank A. Anania, M.D.* Division of Digestive Diseases, Emory University School of Medicine, Atlanta, GA and Department of Internal Medicine, Emory University School of Medicine, Atlanta, GA.

Purpose: The aim of this study is to evaluate the outcome of patients with cirrhosis undergoing elective abdominal surgery and to compare the capacity of the Child-Turcotte-Pugh (CTP) and Model for End Stage Liver Disease (MELD) scores to predict that outcome.

Methods: We conducted a chart review of patients with cirrhosis who underwent general anesthesia between January 1999 and December 2004 at Emory University Hospital and Emory Crawford Long Hospital. Patients with documented cirrhosis undergoing elective abdominal surgery were included. Patients undergoing liver transplantation or other surgical procedures involving the liver were excluded. Patients with evident extrahepatic cholestasis were excluded as well.

Results: A total of 617 charts were screened. After the inclusion and exclusion criteria were applied, 66 procedures performed on 62 patients were identified. The mean MELD score was 9.4 ± 3.3, the mean CTP score was 7.3 ± 1.5. Twenty (30.3%) patients were classified as CTP class A, 40 (66.6%) as class B and 6 (9.1%) as class C. The most common procedures were hernia repair (21, 31.8%), cholecystectomy (17, 25.7%), and diagnostic laparoscopy/laparotomy (15, 22.8%). One patient (1.5%) died of pneumonia in the postoperative period. Signs of decompensated liver disease (hepatic encephalopathy, new ascites, variceal hemorrhage) in the postoperative period were noted in 5 patients (7.6%). There was no statistically significant difference in the CTP or MELD scores between patients who developed signs of decompensation and those who did not. Nine patients (13.6%) developed postoperative transaminase elevation (at least twice the baseline value). The patients with postoperative transaminase elevation had a higher baseline MELD (12.3 ± 3.9 vs 9.1 ± 2.6, p = 0.004), but not a higher CTP score (7.7 ± 2.2 vs 7.4 ± 1.5, p = 0.68).

Conclusions: Our data suggests that elective abdominal procedures in patients with cirrhosis appear to be relatively safe, with a low risk of liver-related complications. The MELD score correlates better than the CTP score with postoperative transaminase elevation. This may reflect an acute injury to the liver in the perioperative period. More studies are needed to better define the roles of the CTP and MELD scores in predicting the outcome of elective surgical procedures in patients with cirrhosis.

Symptoms of Sjögren’s Syndrome in Patients with Primary Biliary Cirrhosis Improve after Liver Transplantation

Harry J. Rodriguez, M.D., John P. Roberts, M.D., Nathan M. Bass, M.D.* Gastroenterology Division(1), Department of Surgery(2), UCSF, San Francisco, CA.

Purpose: PBC is a slowly progressive cholestatic liver disease that predominantly affects middle-age women. Sjögren’s syndrome (SS) is a chronic autoimmune inflammatory disorder frequently associated with PBC with a high prevalence in the United States. Characteristic symptoms of SS include dry eyes, dry mouth, dry cough, arthralgias, fatigue and Raynaud’s phenomenon. To date, no studies have evaluated the outcome of these symptoms after transplantation.

Aim: The aim of this study was to determine the outcome of SS symptoms in patients with PBC after liver transplantation.

Methods: This is a retrospective cohort study in 57 patients with PBC who underwent OLT at UCSF between August 1988 and September 2003. Questionnaires were administered to 40 patients who consented to participate in this study. The subjects ranked symptoms of dry eyes, dry mouth, dry skin, dry cough, Raynaud’s phenomenon, GERD, pruritus and fatigue before and after transplantation according to a simple objective severity scale (0–1, 2–3 and 4–5). Data were expressed as mean difference score (DS) and compared using the Wilcoxon signed-rank test.

Results: The group consisted of 5 men and 35 women. A high prevalence of SS symptoms were present in this group of patients before OLT. The most commonly reported SS symptoms were Raynaud’s (20/40 = 50%), dry eyes (19/40 = 48%), arthralgias (19/40 = 48%), dry mouth (15/40 = 38%), and dry cough (8/40 = 20%). 63% of patients reported dry skin, which may occur in either PBC or SS. The most commonly reported PBC symptoms were pruritus (36/40 = 90%) and fatigue (33/40 = 83%). Most patients reported improvement in their symptoms after liver transplantation with the exception of GERD, which did not change (pre-32.5% vs post-32.5%, DS = 0). The most clinically significant findings were the improvement after transplantation of dry eyes (DS = −2; p = 0.0254), dry skin (DS = −1; p = 0.0366) and Raynaud’s (DS = −2; p = 0.0055). As anticipated, there was significant improvement after transplantation in the major PBC-related symptoms of pruritus (DS = −4; p < 0.0001) and fatigue (DS = −2; p < 0.0001).

Conclusions: SS symptoms are very common in patients with PBC and may have a significant negative impact on quality of life. These symptoms may improve after liver transplantation, although the mechanism for improvement is unclear. These results, which require confirmation by prospective study, suggest an important positive impact of liver transplantation on SS symptoms in PBC.

Frequency and Biochemical Expression of Hemochromatosis (HFE) Gene Mutations in 1029 Blood Donors in Iran

Mohammadreza Agah, M.D., Maryam Zafarghandi, M.D., Zahra Motahari, PharmD, Hanieh Alsadat Jazaeri, B.S., Bashir Hajibi-egi, M.D., Zohreh Attarchy, M.D., Tajbakhsh Rajabi, B.S., Mohammad Reza Zali, M.D., F.A.C.G.* Liver, Research Center for Gastroenterology and Liver Diseases, Tehran, Islamic Republic of Iran and Research Center of Iranian Blood Transfusion Organization, Tehran, Islamic Republic of Iran.

Purpose: To determine the frequency and biochemical expression of the hemochromatosis associated mutations, C282Y and H63D, in Iranian adult population

Methods: We investigated the frequency of the C282Y/H63D HFE gene mutations in a group of 1029 randomly selected Iranian blood donors as well as transferrin saturation (TS), serum iron and serum ferritin (SF) levels. DNA extraction with salting-out method was performed on blood samples and the analysis of HFE gene mutations was performed by PCR amplification followed by digestion with Rsal and BclII restriction enzymes.

Results: No homozygote for the C282Y mutation was found. Heterozygosity for the C282Y mutation was 0.2%, while homozygosity and heterozygosity for the H63D mutation were 1.6% and 19.6%, respectively. There was no compound heterozygote for the C282Y/H63D mutation. These data resulted in allele frequencies of 0.1% and 11.3% for C282Y and H63D mutations, respectively. Serum iron and TS were not affected from the type of C282Y and H63D mutations. However, there was a trend toward higher SF levels in men with H63D heterozygotes and homozygotes genotypes in comparison with wild type (P = 0.06).

Conclusions: This study shows low allele frequency for C282Y and H63D mutations in Iran. These results also suggest that there is not any strong association between HFE gene mutations and iron, TS and ferritin level among Iranian population. The genetic screening for the HFE gene mutations in Iran is not recommended until the true prevalence of other mutations in all hemochromatosis genes will be established.
Heme Oxygenase-1 mRNA Expression in Chronic Hepatitis B

J.Y. Lee, M.D., M.K. Jong, M.D., *J.H. Lee, M.D., H.Y. Kim, M.D., J.Y. Yoo, M.D. Internal Medicine, Hallym University Medical Center, Seoul, Korea.

Purpose: Heme oxygenase (HO)-1, a stress-responsive enzyme, has previously been shown to prevent inflammation-related apoptotic liver damage as well as protect grafts from ischemia/reperfusion injury. In addition, recent studies showed HO-1 had anti-fibrogenic effect and had close relation with pathogenesis of NASH. The aim of this study was to investigate the HO-1 mRNA expression in chronic hepatitis B and evaluate the relation between the apoptosis and/or fibrosis and HO-1 expression.

Methods: Reverse transcriptase-polymerase chain reaction was used to identify intrahepatic expression of HO-1 in liver biopsy specimens from twenty four patients with chronic hepatitis B (CHB). In addition, TUNEL method was used to determine the degree of apoptosis and histologic activity index (HAI) and ALT were measured.

Results: Intrahepatic mRNA expression of HO-1 was demonstrated in 5 cases, all of those cases were stage 4 histologically (Figure). There were no associations between HO-1 expression and apoptosis index. Moreover, there were no associations between HO-1 mRNA expression and serologic activity including ALT.

Conclusions: This study suggests HO-1 is an anti-fibrogenic protein indirectly as showing that HO-1 mRNA is expressed in chronic hepatitis B, for the most part, in cirrhotic stage. However, studies on the association between the HO-1 expression and apoptotic liver injury in CHB will be warranted.

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Hemochromatosis and Transferrin Receptor-2 Gene Mutations in Iranian Patients with Chronic Hepatitis C

Mohammadreza Agah, M.D., Zahra Motahari, PharmD, Maryam Zafarghandi, M.D., Hossein Sendi, M.D., Samad Amini, M.S., Maryam Firoozi, B.S., Seyed Moayed Alavian, M.D., Mohammad Reza Zali, M.D., F.A.C.G.* Liver, Research Center for Gastroenterology and Liver Diseases, Tehran, Islamic Republic of Iran and Tehran Hepatitis Center, Baqiyatallah University of Medical Sciences, Tehran, Islamic Republic of Iran.

Purpose: to determine frequency of hemochromatosis gene mutations (C282Y, H63D and S65C) and transferring receptor-2 (TfR2) gene mutation (Y250X) in patients with chronic hepatitis C and healthy controls and to evaluate the effect of these mutations on ferritin level.

Methods: we investigated the frequency of these mutations in 149 patients and 149 age- and sex-matched healthy controls. DNA extraction with salting-out method was performed on blood samples and afterwards, mutation detection was done by PCR-RFLP method.

Results: Reverse transcriptase-polymerase chain reaction was used to identify intrahepatic expression of HO-1 in liver biopsy specimens from twenty four patients with chronic hepatitis B (CHB). In addition, TUNEL method was used to determine the degree of apoptosis and histologic activity index (HAI) and ALT were measured.

Results: Intrahepatic mRNA expression of HO-1 was demonstrated in 5 cases, all of those cases were stage 4 histologically (Figure). There were no associations between HO-1 expression and apoptosis index. Moreover, there were no associations between HO-1 mRNA expression and serologic activity including ALT.

Conclusions: This study suggests HO-1 is an anti-fibrogenic protein indirectly as showing that HO-1 mRNA is expressed in chronic hepatitis B, for the most part, in cirrhotic stage. However, studies on the association between the HO-1 expression and apoptotic liver injury in CHB will be warranted.

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A Comparison of Sustained Viral Response in Patients with Chronic Hepatitis C Virus (HCV) Treated with Peginterferon Alfa-2a (Peg2a) Versus Peginterferon Alfa-2b (Peg2b) and Ribavirin

Fred Poordad, M.D., *Tram T. Tran, M.D., Wald Ayoub, M.D., Yatin Patel, M.D. Department of Medicine, Cedars Sinai Medical Center, Los Angeles, CA.

Purpose: Pegylated interferon (pIFN) is superior to non-pegylated interferon across all genotypes. There are two available pIFNs available, but there is little head to head data comparing efficacy of these two treatment regimens.

Aim: To evaluate treatment efficacy of the two available pIFNs and ribavirin (RBV) regimens.

Methods: Interferon-naive patients with chronic HCV treated consecutively at a single center between 2001 and 2003 formed this retrospectively and prospectively collected data set. Patients received either Peg2a 180 µg/wk or Peg2b 15 µg/kg/wk, combined with ribavirin (RBV), per preference of the treating physician. RBV was administered either as a standard 800 mg dose in 20% of patients, or a weight-based (WB) dose in 80% (Peg2a: 1000 mg for patients <75 kg and 1200 mg for ≥75 kg; Peg2b: 13 mg/kg). Genotype 1 or 4 (G1,4) patients were treated 48 weeks, while genotypes 2 or 3 (G2,3) were treated 24 weeks. The treatment protocols for dose reduction or discontinuation were identical across patients treated, regardless of regimen used. The primary endpoint was sustained virologic response (SVR), defined as undetectable serum HCV RNA (<50 IU/mL) 24 weeks post treatment.

Results: Eighty-five patients with G1,4 (n = 51) and G2,3 (n = 34) were included in the analysis; 38 received Peg2a (WB RBV n = 32, flat RBV n = 6) and 47 received Peg2b (WB RBV n = 36, flat RBV n = 11). Early discontinuation for any reason occurred in 9/38 (24%) Peg2a and 8/47 (17%) Peg2b recipients (NS). Groups were well matched for age, weight, race, fibrosis, genotype and baseline viral load. SVR rates were greater in Peg2b compared with Peg2a (77% vs 47%; p = 0.007). See Table.

Table 1: Virologic Response Rates

<table>
<thead>
<tr>
<th>Time point</th>
<th>G1,4</th>
<th>G2,3</th>
<th>G1,4</th>
<th>G2,3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 24</td>
<td>19/28 (67%)</td>
<td>9/10 (90%)</td>
<td>19/23 (83%)</td>
<td>22/24 (92%)</td>
</tr>
<tr>
<td>Wk 48</td>
<td>17/23 (74%)</td>
<td>5/10 (50%)</td>
<td>16/19 (84%)</td>
<td>22/24 (92%)</td>
</tr>
<tr>
<td>Wk 72</td>
<td>13/28 (46%)</td>
<td>#</td>
<td>14/23 (61%)</td>
<td>#</td>
</tr>
<tr>
<td>Relapse rate</td>
<td>28%</td>
<td>40%</td>
<td>23%</td>
<td>40%</td>
</tr>
</tbody>
</table>

* p = 0.014; # p = 0.40.

Conclusions: Sustained virologic response was higher in Peg2b treated patients compared with Peg2a. While both regimens suppressed virus well, relapse rates were higher with the Peg2a regimen. These results require confirmation in other studies.

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Antigenic Variations of Core Protein among Different Genotypes of Hepatitis C Virus

Chandra Madhavi, Mohammed Nanne Khaja, Ph.D., Thippavazhu Rkha, Ph.D., Mohammed Ajeaz Habeeb, M.D., D.M., Chittoor Mohammed Habibullah, M.D., DM* Centre for Liver Research and Diagnostics, Deccan College of Medical Sciences, Hyderabad, Andhra Pradesh, India.

Purpose: Antibodies against core antigen are reliable markers of virus replication, since their presence is found to be closely associated with the presence of specific mRNA. Hence the aim of the present study was to evaluate antigenic variations of 120 amino acids of core gene among 1a, 1b, 3a and 3b genotypes.

Methods: Serum samples of 120 patients who were anti HCV positive by 3rd EIA, 50 subjects were negative for all hepatitis markers.
Use of Erythropoietin Increases the Likelihood of Achieving Viral Clearance in HCV Infected Patients Treated with Pegylated Interferon and Ribavirin

Fred Poordad, M.D.,† Tran T. Tran, M.D., Yatin Patel, M.D., Walid Ayoub, M.D., Kerstin Newland, R.N. Department of Medicine, Cedars Sinai Medical Center, Los Angeles, CA.

Purpose: The current standard of treatment for hepatitis C (HCV) is pegylated interferon (pegIFN) and ribavirin (RBV). The latter causes hemolytic anemia. Dose reduction of RBV has been reported to have a negative impact on sustained virologic response (SVR). Erythropoietin (EPO) is used for the treatment of RBV induced anemia in an estimated 8–10% of cases. While several studies have suggested that the use of EPO allows for maintenance of the appropriate dose of RBV, no study has shown that it is correlation to SVR.

Aim: To assess the use of EPO in a clinical hepatology practice and its effect on treatment outcomes in HCV pts.

Methods: A data base of 87 treatment naïve HCV pts between 2001–2004 were evaluated for this study. Of these, 48 were genotype 1 (G-1), while the remainder were genotype 2 and 3 (G-2,3). Of the pts, 54% were male and 84% were Caucasian. SVR was defined as viral clearance 24 wks beyond the end of therapy by a negative qualitative PCR (<50 IU/mL). Pts were treated with either pegIFN alpha 2a or 2b, for either 24 (G-2,3) or 48 wks (G-1). The mean RBV dose in the EPO group was 1062 mg and 1017 mg in the non-EPO group. The decision to use EPO was based upon either hemoglobin (Hb) <10 mg/dL or Hb <12 mg/dL associated fatigue or dyspnea. Dose given was 40,000 units SQ weekly. Dose reduction of RBV by 200–400mg was the standard for individuals not receiving EPO if Hb fell below 10 mg/dL, followed by dose escalation once stable.

Results: Baseline Hb was 14.3 mg/dL. The mean weight in the EPO group was 77.65 kg, vs 79.42 kg in the others. A total of 26% required EPO. Of those in the EPO group, 65% were female. RBV dose reductions in G1 were required in 8% of pts receiving EPO vs. 40% in those not (p = 0.04). A total of 26% of pts in the EPO group discontinued early vs 16% in the non-EPO group either for side effects or for non response (NR). See TABLE 1.

Conclusions: The use of EPO was associated with fewer dose reductions of RBV in HCV patients undergoing therapy. EPO was associated with higher SVR rates in all genotypes, including G-1 patients. The use of EPO appears to be justified as adjuvant therapy for anemia in HCV patients undergoing treatment with pegIFN and RBV.

Complications from Transjugular Liver Biopsy: An Analysis of 1000 Procedures


Purpose: Transjugular liver biopsy (TLB) is an invasive diagnostic procedure extremely useful in assessing liver disease in all kinds of coagulopathy patients. We have analysed the type of complications from this technique, considering all the steps involved, including jugular, cardiac and liver catheterization.

Methods: We analysed retrospectively 1000 TLB, performed in 14 years. 350 were achieved with TJ Henriksen aspiration needle, and 650 with TruCut needle.

Results: The complications that we observed were: carotid puncture in 28 patients (2.8%), that did not preclude the liver biopsy; cerebral haemotoma in 12 patients (1.2%), without arterial puncture; transitory auricular arrhythmia in 15 patients (1.5%), that did not need pharmacological intervention or suspending the procedure; lumbar pain in inferior vena cava catheterization (without dissection) in 3 patients (0.3%); right hipocondrial pain in distal catheterization of hepatic veins, pre biopsy, in 5 patients (0.5%); ascitic fluid recovery in aspirative biopsy in 2 patients (0.2%); hemobilia in 1 patient.
Results: Among patients completing the study, the following NASH histologic variables: macrovesicular steatosis, balloon-ling, and disarray, lobular inflammation, portal tract inflammation, Mallory’s hyaline, acidophil bodies, glycogenated nuclei, lipogranulomas, and hepato-cellular iron; overall necroinflammatory grade and fibrosis stage were also recorded. Results: 8 subjects were enrolled; 1 withdrew because of breast cancer and 1 removed due to recurrent irritable bowel symptoms. In 8 patients, the access was from left jugular vein. We did not have any complications related to the usual premedication (25–50 mg, iv, meperidine), to contrast allergy or to inadvertent puncture of any cardiac afferent. 

Conclusions: Even in serious and delicate conditions that the candidates for this procedure present, the complication rate, 6.7%, is exceptionally low, and generally quite benign and of minor importance. This suggests TLB as an extremely useful and safe tool in assisting acute or chronic severe liver disease patients.

330 Histologic and Liver Biochemistry Improvement in Patients with Non-Alcoholic Steatohepatitis (NASH) after 12 Months of Treatment with S-Adenosyl Methionine (SAMe)

Terecsc E, Angtuaco, M.D.* David McElreath, D.O., Laura Lamps, M.D. Gastroenterology, University of Arkansas and Central Arkansas Veterans Healthcare, Little Rock, AR and Pathology, University of Arkansas, Little Rock, AR.

Purpose: Hepatic steatosis and oxidative stress are key factors in the pathogenesis of NASH. SAMe prevents fat deposition and glutathione depletion in the liver. Oral SAMe restored hepatic glutathione content in humans with chronic liver disease. The aim is to determine the efficacy of SAMe in reducing histologic inflammation and fibrosis, and improving liver biochemistry in patients with biopsy-proven NASH.

Methods: Patients with biopsy-proven NASH who did not have other known liver diseases, and did not consume >20 gm of alcohol per week, or take vitamin E, betaine, or ursodeoxycholic acid, were given SAMe (Nature Made, Pharmavite Corporation) 1,600 mg daily for 12 months (mos). Their liver enzymes and weight were recorded every 3 mos until end of treatment; liver biopsy was done at month 12 and compared with their pre-treatment biopsy.

A single pathologist, who was blinded, reviewed the liver biopsies and graded the following NASH histologic variables: macrovesicular steatosis, ballooning and disarray, lobular inflammation, portal tract inflammation, Mallory’s hyaline, acidophil bodies, glycogenated nuclei, lipogranulomas, and hepatocellular iron; overall necroinflammatory grade and fibrosis stage were also recorded.

Results: 8 subjects were enrolled; 1 withdrew because of breast cancer and 1 removed due to recurrent irritable bowel symptoms. 6 completed.

Purpose: Radiofrequency ablation (RFA) is a new percutaneous tissue ablative therapy. We present our experience of RFA in liver secondaries.

Methods: Using Berchtold (Tuttlingen, Germany) RF generator (35–50 watt output); 1500–2000 watts energy/cc tumour was delivered according to the size of liver secondaries.

Between February 2001 and December 2004, 49 patients (32 men) aged 44 to 72 years (mean 59 years) had RFA of 177 liver secondaries from: Gall bladder = 12; colorectal = 22; Breast = 10; carcinoid/neuroendocrine = 3 and stomach = 2 cancers. Lesions were sized < 3 cm in 44; 3–4 cm in 89 and >4 cm in 44. RF needle was placed US guided in 46, CT guided in 1 and at an open Surgery in 2 patients.

Follow up was by contrast enhanced CT scan.

Results: There was no procedure related mortality. All patients were discharged within 24 hours except two. There was no major morbidity. There were 6/49 (12%) minor morbidity (self limiting ascites = 2, self limiting pleural effusion = 4).

Efficacy: Complete necrosis was seen in all (100%); 44/44 of lesions up to 3 cm size and 34.8% (31/89) of lesions 3–4 cm in size. Recurrence at completely treated site, at mean follow up of 12 months was 7/75 (9.3%). On more than 6 months follow up, 31/43 (72%) patients developed new hepatic metastases and 23/43 (53%) patients also had systemic metastases.

Survival: 26 patients (53%) are alive and being followed. One year survival was 49% and 2 year survival was 12%

Conclusions: RFA is safe and effective local tissue ablative method for liver secondaries. More randomized controlled trials are required to ascertain efficacy of RFA in improving quality of life and/or survival in patients with liver secondaries.

332 Critical Analysis of Radiofrequency Assisted Liver Resection

Subodh Varshney, M.S.* Sandesh Sharma, M.S., Sorabh Kapoor, MCh, Ajit Sewkani, M.S., Saleem Naik, M.S., Krishna Kant Maudar, Ph.D., Gaurav Jain, M.S. GI Surgery, Bhopal Memorial Hospital and Research Centre, Bhopal, MP, India.

Purpose: Radiofrequency (RF) tumor ablation is a well established local ablative procedure. Recently newer applications of RF have been suggested. RF can be used for performing hepatotomies safely. We analysed our 8 cases of segmental liver resection, using radiofrequency energy.

Methods: We performed RF aided liver resection using Berchtold (Germany) RF generator in eight cases of: Carcinoma of the Gallbladder (Segment IVb and V or wedge resection); Gastrocarcinoma (Segment III); n = 5.

Liver metastasis from Gastric carcinoma (Segment IVb); n = 1.

Liver metastasis from colonic malignancy (Segment V); n = 1.

Suspected carcinoma of gallbladder, Xanthogranulomatous cholecystitis (Segment IVb and V); n = 1.

RF energy was used to coagulate 1 cm columns of liver parenchyma in a continuous row. Subsequent liver transaction was bloodless and it also coagulated the small bile ducts. Any additional bleeding point was directly treated with RF needle.

Results: There was no procedure related mortality. Blood loss varied between 5–20 ml except 100 ml in one case of bleeding from segment 3 artery. No patient required blood transfusion. There was no procedure related early morbidity. 3/8 (37%) patients had liver or sub diaphragmatic abscess in the late postoperative period (>2 weeks post op).

Three patients had post procedure abscess formation. Two patients had developed liver abscess in segment 8, far away from operated site. Both these patients had bactobilia due to biliary stent or bilioenteric anastomosis. Third patient of Carcinoma Gall bladder had associated pyocele.

At median, follow up of 1 year (6–24 months) all patients are alive with no locoregional recurrence, except one patient who had died of unrelated cause.

Conclusions: RF energy can be safely used for liver resection. It should be avoided in patients with overt local sepsis due to bactobilia (due to biliary stent or bilioenteric anastomosis) or pyocele.
Frequency of Nonalcoholic Fatty Liver Disease, Nonalcoholic Steatohepatitis and Degree of Hepatic Steatosis in African American Patients

Samuel A. Giday, M.D., Zaleema Ashiny, M.D., Tammy Naab, M.D., Alpha T. Banks, M.D.* Division of Gastroenterology and Hepatology, Howard University College of Medicine, Washington, DC and Pathology, Howard University College of Medicine, Washington, DC.

Purpose: To evaluate degree and distribution of hepatic steatosis in African American (AA) patients who had liver biopsies over a period of five years

Methods: A search in the pathology registry was performed for the presence of fat in liver biopsies. Of 320 liver biopsies performed from 1999 to 2003, 61 had fatty infiltration. Each biopsy was assessed by an expert pathologist. Patient records, imaging studies and laboratory tests were analyzed. The severity of steatosis was graded based on the percent of hepatocytes demonstrating fat as follows: Grade 1: <5%, Grade 2: 5–33%, Grade 3: 33–66%, Grade 4: >66%. Steatohepatitis was assessed by using guidelines by brunt et al. Fisher’s exact test and ANOVA were used.

Results: There were 320 liver biopsies that were reviewed. A total of 61 biopsies were found to have steatosis. The mean age was 49 years and 55% of the patients were male. Fifty six of the 61 patients were African American. The mean Body Mass Index (BMI) in those AA patients was found to be 30. Majority had chronic hepatitis C (78%). Grade 1 steatosis was found in 16 patients, grade 2 in 22 patients, grade 3 in 14 patients and 9 patients had grade 4 steatosis. Alcoholic Steatohepatitis was present in 2 (4%) patients. The degrees of fat infiltration in the two patients with alcoholic steatohepatitis were 50% and 80%. Four patients fulfilled the criteria for the diagnosis of NAFLD (No history of alcohol use and had normal workup for causes of abnormal liver function test). All four patients had simple steatosis without any inflammation. The frequency of NAFLD in our study population was found to be less than 2%. Non alcoholic steatohepatitis (NASH) wasn’t found in any of our study population. Dyslipidemia was found in all four patients with steatosis. Two of the patients were Diabetic. The mean values of AST, ALT, INR, Platelet count and BMI were compared amongst the four groups by using ANOVA test. There was no statistically significant difference when those variables were compared by the degree of steatosis.

Conclusions: NAFLD has a low prevalence in African Americans. NASH was not found in any of the AA patients seen at our institution. The severity of fatty infiltration didn’t appear to have an impact on the severity of hepatic inflammation. BMI had no direct correlation to the degree of fatty infiltration in our study.

Ophthalmic Findings in Chronic Hepatitis C (CHC) Patients Treated with Pegylated-Interferon (PIFN) and Ribavirin (RBV)

Nilesh Mehta, M.D., Uma K. Murthy, M.D.,* Vivek Kaul, M.D., Gerald P Abruzzese, OD, Vijay Vadrevu, M.D., John B. Sweeney, M.D., Charles Teitelbaum, M.D. GI/Hepatology, VA Medical Center, Syracuse, NY and Ophthalmology, VA Medical Center, Syracuse, NY.

Purpose: Retinal changes have been described in 18–86% of CHC patients receiving interferon alfa2a/2b. There is paucity of data on ophthalmic changes in CHC patients on PIFN+RBV.

Methods: Baseline eye exams were performed in 108 CHC patients treated with PIFN+RBV for 24–48 weeks. In a subcohort of 57 patients, visual acuity, tonometry, slit lamp and fundus examinations were done before, during and after therapy. Visual field testing, gonioscopy, color vision testing and fundus photography ± angiography were done, if indicated. Statistical comparisons between patients who developed retinopathy, Group A (GpA) versus those that did not, Group B (GpB) were performed (Student t test, p < 0.05).

Results: Patient Characteristics: mean age 49.7y (26–68), male 53/57, Caucasian 86%, African American 12.5%, smoking status–50% active smokers, 25% ex-smokers; hypertension 37%, diabetes 14%, hypercholes-

terolemia 14%, thrombo-embolic events–0%, vasculitis–1.7%, epogen use–26%, advanced fibrosis/ cirrhosis 37%, genotype 1–82% and high viral load—65%. GpA and GpB were statistically similar. Laboratory data: Hgb, Platelets, WBC, ALT, Albumin, Bilirubin and INR were similar in the two groups.

Retinopathy, cotton wool spots (CWS) and/or intraretinal hemorrhage (IRH) developed in 16 of 57 (28%) patients 1 to 9 months after start of therapy and in the majority (11) within 3 months. 12 patients had CWS, 3 had CWS+IRH and 1 had IRH. Treatment was continued in 15 of 16 patients with resolution in 9 (all had CWS only) during or shortly after completion of therapy. 3/4 patients with IRH continued to have stable eye changes (normal visual acuity) after completion of therapy; eye exam in the fourth patient is pending. Therapy was stopped in only 1 patient with complete resolution within 2 months. Visual and ocular symptoms: GpA: 9/16 (itching, blurring, floaters, diplopia). GpB: 15/41 (blurring, diplopia, eye pain, redness, grittiness). Dry eye syndrome was noted in 6 GpB patients, 2 at baseline and 4 during therapy.

Conclusions: (1) Retinopathy developed in 28% of patients treated with PIFN+RBV (2) 44% patients with retinopathy were asymptomatic. (3) Conversely, 62.5% of patients with visual and ocular symptoms had no retinopa-

thy. (4) CWS remained stable or resolved despite continued therapy. (5) IRH persisted after completion of therapy, however did not affect vision. (6) Retinal changes developed early during PIFN+RBV therapy.

Treatment of Hepatitis C: Clinical Experience at a VA Medical Center

Hector Rodriguez-Luna, M.D., Erin Tharaldson, NP, Elizabeth Ewanch, NP, David A. Johnson, M.D., Francisco C. Ramírez, M.D.* Gastroenterology, Carl T Hayden VA Medical Center, Phoenix, AZ.

Purpose: Chronic HCV infection is highly prevalent in the VA population but its treatment may be compromised by ETOH/drug use, psychiatric con-

traindications, and co-morbid conditions. Response rates and adherence to treatment have been reported to be lower in this population.

AIMS: To describe the clinical experience of treating patients infected with hepatitis C at a single VAMC.

Methods: Retrospective review of naive veteran pts with HCV infection treated with combination Pegylated interferon + (either 2b or 2a) + Ribavirin (Riba). All patients had their genotype determined at entry. Initiation of treatment was decided by a gastroenterologist but the administration and follow-up was closely monitored by a nurse practitioner under his/her direct supervision. Sustained virological response (SVR) was assessed 6-months after discontinuation of therapy in those with end of treatment response on an ITT and completion of therapy analysis.

Results: A total of 186 pts (115 Peg-Inf 2b; 71 Peg-Inf 2a) had completed therapy, were 6-mo beyond discontinuation of treatment, and could be evaluated for SVR. The average age was 51.

The overall SVR for all genotypes was 43.5% with a discontinuation rate of 26.9%. The discontinuation rate was independent of Interferon type.

SVR Rates on ITT & (Completed Treatment)

<table>
<thead>
<tr>
<th></th>
<th>PEG IFN 2b</th>
<th>PEG IFN 2a</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVR all Genotypes</td>
<td>38.3% (53.7%)</td>
<td>52.1% (68.5%)</td>
<td>43.5% (59.6%)</td>
</tr>
<tr>
<td>SVR Genotype 1</td>
<td>30.1% (44.4%)</td>
<td>36.6% (51.7%)</td>
<td>32.1% (46.7%)</td>
</tr>
<tr>
<td>SVR non-Genotype 1</td>
<td>72.7% (84.2%)</td>
<td>73.3% (88.0%)</td>
<td>73.1% (86.4%)</td>
</tr>
<tr>
<td>Discontinuation Rate</td>
<td>28.7%</td>
<td>23.9%</td>
<td>26.9%</td>
</tr>
</tbody>
</table>

There were no significant overall differences between the two forms of Peg-Inf regarding SVR. Analysis of weight showed a slightly higher BMI for non-SVR in the Peg-Inf 2a group (29.3) vs. Peg-Inf 2b group (28.6). (p = NS) Side effects were the cause of discontinuation in 62% of cases whereas other causes (non-compliance, financial/work-related issues, etc) represented 32%. Three patients discontinued therapy due to liver decompensation.
Conclusions: 1. Even in a tightly monitored environment the SVR for all genotypes was lower than those reported in the literature but higher than previously reported in other VA populations. Side effects or reasons other than no-response accounts for a 27% discontinuation rate.
2. There is a trend for slightly lower SVR in higher BMI patients treated with Peg-Inf 2a vs. Peg-Inf 2b.
3. Intense monitoring results in higher SVR than previously reported in this population.

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MELD Score as a Predictor of Esophageal Varices Re-Bleeding Risk
Hector Rodriguez-Luna, M.D., David A. Johnson, M.D., Francisco C. Ramirez, M.D.∗ Gastroenterology, Carl T Hayden VA Medical Center, Phoenix, AZ.

Purpose: Upper gastrointestinal bleeding secondary to esophageal varices in patients with end-stage liver disease (ESLD) is unpredictable with approxi- mately 30% of these having at least one event. The 1-year risk of re-bleeding could be as high as 70%. The severity of underlying liver disease has been previously identified as a risk factor for re-bleeding, therefore we conducted an analysis of MELD score among patients with history of variceal bleeding and no bleeding in an effort to identify those at highest risk of re-bleeding based on this new parameter.

Aim: To establish an association between the severity of MELD score and the risk of re-bleeding in patients with ESLD.

Methods: Retrospective data analysis of patients with ESLD that presented to our institution with at least one episode of UGI bleed (UGIB) from 1997 to 2002. There were 94 patients with complete database which we matched to 71 patients with ESLD and no history of bleeding (NUGIB).

Results: A total of 166 patients with ESLD were evaluated. Of those, 94 had at least one episode of variceal bleeding. The mean age was 55.7 years. Etiologies of liver disease included ETOH: 100, ETOH/HCV: 34, HCV: 13, Co-Infection: 4, and Other: 15. The MELD score among patients with history of UGIB and NUGIB was 11.5 vs. 14.8 (p = 0.08) and CTP score of 7.93 vs. 8.4 (p = 0.13). There was no age difference among groups. (p = NS) Subgroup analysis of patients with history of UGIB who had further episodes of UGIB vs. those with only one episode of UGIB showed a MELD score of 14.9 in the rebleeding vs. 11.9 in the non-rebleeding groups (p = 0.04) and a CTP score of 8.59 vs. 7.52 (p = 0.013). The likelihood ratio for a repeat bleeding episode in the MELD >14 group was 1.54.

MELD Score and Rebleeding

<table>
<thead>
<tr>
<th>MELD Score</th>
<th>Bleeding &lt; 1</th>
<th>Bleeding &gt; 2</th>
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</thead>
<tbody>
<tr>
<td>MELD &gt; 14</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>MELD &lt; 14</td>
<td>40</td>
<td>16</td>
</tr>
<tr>
<td>TOTAL</td>
<td>60</td>
<td>33</td>
</tr>
</tbody>
</table>

Sensitivity: 52%; Specificity: 67%; Likelihood ratio: 1.54.

Conclusions: 1. Analysis of ESLD patients with history of variceal bleed vs. re-bleed showed a statistically significant higher MELD score in the re-bleeding group when compared to patients with only one episode of bleeding. However, it appears that MELD score is not a good overall predictor of index variceal bleeding in patients with ESLD as previously shown for CTP score.
2. Patients with a MELD score over 14 were 50% more likely of having two episodes of bleeding.
3. We propose that history of variceal bleeding and a MELD score >14 might identify those patients at risk of variceal re-bleeding.

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A Crossover Retrospective Chart Review Evaluating Hospitalizations Associated with the Use of Rifaximin vs Lactulose in the Management of Patients with Hepatic Encephalopathy
Carroll B. Leevy, M.D.,∗ James A. Phillips, Dr.P.H. Pathology, University of Medicine & Dentistry of NJ, Newark, NJ and Biostatistician, Self Employed, Elfland, NC.

Purpose: Hepatic encephalopathy (HE) is a common condition among patients with liver disease, leading to repeated hospitalizations at an average daily cost of $6,230. This chart review compared the number and duration of hospitalizations associated with a discharge diagnosis of HE among patients treated first with lactulose and then rifaximin.

Methods: This study was a single-center, crossover, retrospective chart review of 145 patients diagnosed with HE. All patients received lactulose (30 cc bid) for ≥ 6 months then rifaximin (400 mg tid) for ≥ 6 months. Charts were reviewed to compare patients’ last 6 months on lactulose therapy and first 6 months on rifaximin therapy. The primary endpoint was the number of hospitalizations a patient had during each 6-month therapy period. Hospitalizations were assigned 2005 dollar value based on inflation-adjusted Healthcare Cost Utilization Project (H-CUP) 2002 data for HE. Secondary endpoints were length of hospitalization, HE grade, presence of asterixis, patient reported medication compliance, and side effects severity during each therapy period.

Results: The number of hospitalizations was significantly lower during the period of rifaximin therapy compared with lactulose (mean 0.5 vs 1.6, respectively, P < 0.001). During the rifaximin therapy period, patients spent significantly less time in the hospital (mean time 3.14 days) than during the lactulose period (mean time 12.52 days, P < 0.001). Compared with the lactulose therapy period, HE grade was significantly lowered following rifaximin therapy (P < 0.001). Significantly fewer patients had asterixis at the end of the rifaximin therapy period compared with the end of the lactulose period (P < 0.001), as well as fewer diarrhea, flatulence, and abdominal pain side effects (P < 0.001). Medication compliance was significantly higher with rifaximin therapy compared with lactulose (P < 0.001). Using H-CUP data, the reductions in occurrences and duration of hospitalizations realized with rifaximin therapy resulted in an average cost savings of $67,559 per patient.

Conclusions: After 6 months of rifaximin therapy, HE grade was significantly lowered compared with the prior 6 months of lactulose therapy. Subse- quently, hospitalizations were fewer and shorter during the rifaximin therapy period compared lactulose, resulting in substantially lower costs. Based on these results rifaximin should be considered as first-line therapy for HE.

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Retrospective Analysis of Chronic Hepatitis C and Autoimmunity
Umavathy Manoharan, M.D., Vijaya R. Chalamalasetty, M.D., Michael D. Bernstein, M.D.∗ Internal Medicine, Coney Island Hospital, Brooklyn, NY.

Purpose: To assess the influence of age, sex, genotype and histological profile of liver in patients with autoimmune chronic Hepatitis C (HCV) and to demonstrate the variation of effectiveness of anti-viral therapy in autoimmune positive and negative patients in respect to sex, genotype and histological profile

Methods: This retrospective study was conducted in fifty biopsy proven chronic hepatitis C patients in the hepatology clinic at Coney Island Hospital, Brooklyn, New York. Designated pathologist scored the biopsy results using META VIR scoring system. Thirty patients received the antiviral treatment. Sustained viral response is defined as viral load less than 50 IU/ml on Roche Amplicor method after six months of treatment. Results were analyzed by using Chi-Square and independent t-test.

Results: The overall prevalence of auto-immunity was 42%. Mean age of autoimmune positive and negative patients was 44.57 and 46.62 years respectively (P = 0.47). 38% of male and 62% of female were found to have autoimmune positive HCV (P = 0.79). Majority of patients had genotype 3a and 50% were found to have autoimmune antibody positive. However presence of autoimmunity is not significantly influenced by genotype (P = 0.44). Presence of autoimmunity did not affect the severity of the histological profile both in activity score (P = 0.86) and in fibrosis score (P = 0.99).

Genotype was significantly related to treatment response in the autoimmune positive patients (P = 0.02) but lacks significant response in negative patients (P = 0.31). On the other hand, gender difference showed little variation in treatment response but failed to demonstrate statistically significant difference in outcome whether autoimmune positive (P = 0.15) or negative (P = 0.36).
Autoimmunity played no role in histological profile of the liver and the treatment response. The $p$ value of activity scores in the autoimmune positive and negative groups are 0.35 and 0.36 while the $p$ value of fibrosis score are 0.16 and 0.42 respectively.

**Conclusions:** Increasing prevalence of autoimmunity is observed in HCV patients. The autoimmune positive and negative groups are not different by age, sex, genotype and histological profile. The outcome of treatment in autoimmune positive and negative groups is independent of sex and histological profile. However, the presence of genotype 3a and autoimmunity revealed a better prognosis. Further study in large population is needed for clinical application of this conclusion.

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**Advanced Hepatoma—Role of Transarterial Chemoembolization (TRCE)**

Kovil Ramasamy, M.D., Anaka Prakash, M.D., Baburao Koneru, M.D.,∗ Kanara Wignarajan, M.D. Medicine -Gastroenterology, Bayonne Medical Center, Bayonne, NJ; Surgery- Liver Transplant, UMDNJ University Hospital, Newark, NJ and Medicine, Bayonne Medical Center, Bayonne, NJ.

**Purpose:** Hepatocellular carcinoma is an aggressive tumor that frequently occurs in the setting of chronic liver disease and cirrhosis. It is typically diagnosed late in the course of patients with chronic liver disease, with the median survival following diagnosis of approximately 6 to 20 months. Hepatocellular carcinoma generally occurs in patients with cirrhosis. Curative options, such as liver transplantation, hepatic resection, and percutaneous alcohol injection, are applicable to a minority of cases. Because systemic chemotherapy and radiation therapy provide dismal results, transarterial chemoembolization (TACE) remains an approach to antagonizing the cancer growth in most patients. Although most tumors show an extensive necrosis after TACE, the beneficial effect on survival has not been properly substantiated, so that its application still remains a matter of debate. Although the mainstay of therapy is surgical resection, several other treatment modalities may also have a role.

**Methods:** 81 year lady was hospitalised 18 months ago with anemia, weakness and abdominal distention. She was diagnosed to have cirrhosis, Hepatitis C and hepatic mass. She was found to have both esophageal and gastric varices. Biopsy of the hepatic mass was reported as hepatocellular carcinoma-pseudoglandular variant. There were two hepatic lesions measuring 6cm and 5cm in the right lobe. She was referred to hepatic surgical unit. She had transarterial chemoembolization. With adriamycin and 5FU twice with good results. Patient tolerated well. She is being followed at primary physician’s office on regular basis. She is taking propranonol and diuretics. She lives alone with only limited assistance.

**Results:** The above case illustrates the effective role TRCE in her case with advanced liver disease with large hepatomas.

**Conclusions:** TACE is an effective palliative treatment which should be considered in patients who are not candidates for surgical treatment. It can offer good palliation in selected patients.

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**A Placebo Controlled Double Blind Clinical Trial of the Efficacy of Hepavirin in Viral Hepatitis B**

Sarabjeet Singh, M.D.,∗ Vishwajee Bembi, M.D., Vijay K. Goel, M.D., Tungvir S. Arya, M.D., D.M., Skand Shukla, M.D. Medicine, L.L.R.M. Medical College, Meerut, Uttar Pradesh, India.

**Purpose:** The drug hepavirin is a new polyherbal formulation consisting of phyllanthus amarus. Treatment of hepatitis B carriers is expensive. The study was conducted (a) to study the natural profile of hepatitis B in initial 4 weeks of the disease and (b) to evaluate the efficacy of Hepavirin in hepatitis B viral infection and in liver functions.

**Methods:** 200 patients of serologically proven acute hepatitis B (100 patients in each group A and B) of all the age groups were included in the study. Detailed history, physical examination and investigations like Hb, TLC, DLC, ESR, Platelet count, Serum bilirubin, SGPT, SGOT, Serum Proteins, HBSAg, HBeAg, IgM-Anti HBeAb were recorded. All patients received 1 tablet of hepavirin 500 mg thrice a day; in group A and of the placebo in group B for a total of 4 weeks. All patients were clinically monitored weekly at 0, 16 and 24 weeks.

**Results:** At the end of 24 weeks 82 patients (82%) in the drug group and 80 (80%) in the placebo group completed the trial. Clinical symptomatic improvement and return of SGPT and SGOT to normal was significantly faster with the drug than with the placebo. 79 (96.3%) patients receiving the drug and 65 (81.2%) receiving placebo cleared HBSAg from their sera ($p < 0.001$). HBeAg was cleared from 79 (96.3%) patients receiving drug and 71 (88.7%) patients receiving placebo ($p < 0.001$). Liver enzymes were raised in 8 patients in the placebo group as compared to 0 patients in the Hepavirin group which is significant.

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**Predicting Relapse to Pegylated Interferon and Ribavirin Therapy According to First HCV RNA Negativity**

Jeffrey P. McMahon, P.A-C.,∗ Ann L. Silverman, M.D., Stuart C. Gordon, M.D. Gastroenterology, Henry Ford Hospital, Detroit, MI.

**Purpose:** Although current HCV antiviral treatment algorithms reliably predict virologic nonresponders at TW12, a method to identify potential relapsers remains unclear. We sought to determine whether available clinical data could predict those patients likely to experience relapse.

**Methods:** 52 consecutive treatment naïve chronic HCV genotype 1 patients received PEG/ribavirin therapy (weight based) for 48 weeks. Therapy was stopped in those patients who did not achieve EVR (greater than 2 log decline) at TW 12 or viral negativity at TW 24. Liver biopsies were performed within one year of therapy and were scored by an individual pathologist (Ishak). We assessed HCV RNA levels (Bayer Versant quantitative with reflex TMA qualitative) at TW 4, 8, 12, 16, 20, 24, 48 and at week 24 follow-up. We examined factors (BMI, baseline viral load, and fibrosis stage) that might affect relapse rate. We also assessed whether late virologic response (HCV RNA positive at TW 12 and negative at TW 24) or duration of viral negativity were associated with subsequent relapse. We used two sample t-tests and the Wilcoxon rank sum tests to assess significance. All data were expressed according to ITT analysis.

**Results:** The mean age was 49 yrs (range, 33–71), 57% men; 81% Caucasian, 13% AA, 6% Asian. The SVR rate was 44% (23/52) and relapse rate was 13% (7/52). 6/52 discontinued treatment prematurely. The median baseline viral level for SVR was 1,275,000 IU and 1,490,000 IU for relapsers.
(p = 0.90). The mean time to viral negativity was 15.5 weeks for those patients who achieved SVR and 22.3 weeks in those who relapsed (p < 0.001). No relaper became viral negative before TW 20. There was a trend toward higher mean BMI and among relapsed compared to SVR patients. The mean BMI in patients with an SVR was 25.5 (range, 21.3–32.5), and 27.7 (range 23.7–32.7) for relapers (p = 0.096). 7/23 (30%) of SVR patients and 2/7 (28%) of relapers had advanced fibrosis or cirrhosis (p = 0.89). 16/52 (30%) genotype 1 patients failed to achieve EVR or viral negativity at TW 24.

Conclusions: (1) The rate of virologic relapse is directly related to time to first HCV RNA negativity. (2) Relapers have a shorter duration of viral negativity during therapy than do sustained responders on a 48-week treatment regimen. (3) These findings corroborate recent reports suggesting that extending HCV antiviral therapy from 48 to 72 weeks lowers relapse rates.

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Radiofrequency Ablation (RFA) in Patients with Non-Resectable Hepatocellular Carcinoma

Stanley J. Rogers, M.D., John P. Cello, M.D.,* Rytaruo Hirose, M.D., Francis Yao, M.D. Surgery and Medicine, University of California, San Francisco, San Francisco, CA.

Purpose: Primary hepatocellular carcinoma is the seventh most common cause of cancer in men and ninth most common in women. Nearly 500,000 patients per year worldwide are diagnosed with hepatocellular carcinoma. While surgery is the only chance for cure, the tumor grows rapidly and the diagnosis is usually made late in the disease. It is estimated that less than 10% of patients with hepatocellular carcinoma are candidates for curative resective surgery. In addition, the minority of patients with hepatocellular carcinoma are candidates for liver transplantation given the large size and/or the multiplicity of tumors noted on presentation. Laparoscopic RFA provides a minimally invasive means of thermally debulking hepatomas as adjunctive therapy to chemotherapy and/or as a “bridge” to hepatic transplantation.

Methods: From 3/99 to 5/05, we treated 48 patients (30 men, 18 women) with non-resectable hepatocellular carcinoma using laparoscopic RFA. All procedures were done under general anesthesia using laparoscopic ultrasound assistance employing the RITA laparoscopic RFA probes. The 48 patients with a mean age (± SD) of 63.0 ± 11.3 years were from varied ethnic backgrounds: 19 Asian/Pacific Islanders, 16 Caucasians, 2 African-Americans and 11 others. Twenty-three patients had HCV while 4 patients had HBV.

Results: Forty-one patients received one laparoscopic RFA treatment session and 7 patients received 2 treatment sessions. A total of 94 individual lesions were treated by laparoscopic RFA (mean 2.0 lesions per patient, range 1 to 5 lesions per patient). The largest lesion mean diameter per patient was 3.5 ± 1.7 cms (range 1.4 to 10 cms); while the aggregate tumor mean diameter per patient was 5.8 ± 3.6 cms (range 1.4 to 16 cms). The vast majority of patients was hospitalized for only 2 days and experienced symptomatic improvement and computed tomographic documented palliation of tumor size. Given the marked improvement and in some virtually complete CT resolution of tumor mass, 11 of 48 patients (24%) underwent subsequent successful liver transplantation, two of whom had no evidence of residual hepatoma in the explanted liver.

Conclusions: Laparoscopic RFA is a substantial addition to our armamentarium for palliation of hepatocellular carcinoma. In some patients, RFA can substantially debulk and in some patients eradicate hepatoma such that patients can either be bridged or downstaged to become acceptable candidates for hepatic transplantation.

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Hepatitis C Genotype 1 Treatment Picture in the Real World: Where Are Our Patients Failing?

Razi M. Arifuddin, M.D., Matthew M. Baichi, M.D., Benedict J. Mallikah, M.D., Purvez S. Mantry, M.D.* Digestive and Liver Diseases Unit, University of Rochester Medical Center, Rochester, NY.

Purpose: Clinicians treating patients with genotype 1 Chronic Hepatitis C (CHC) using pegylated interferon and ribavirin are faced with several challenges. Despite advances in therapy and use of growth factors, a majority of these patients do not achieve a sustained virologic response (SVR). We postulated that side effects play an important role in the discontinuation of therapy especially during the early weeks of treatment in clinical practice. Our aim was to explore the nature and frequency of adverse events that led to premature termination of combination therapy at our tertiary referral center.

Methods: Medical records were reviewed on consecutive CHC genotype 1 patients who initiated 48 weeks of standard pegylated interferon (alpha 2a or alpha 2b) in combination with weight based ribavirin therapy. Data on the reasons for therapy discontinuation (constitutional, organic, psychiatric side effects) and response (early virologic, end of treatment, or sustained) was recorded and treatment was discontinued if early virologic response (EVR) was not obtained.

Results: Overall on 100 patients with genotype 1 EVR was 60%, end of treatment response was 40%, and SVR was 28%. In the first 12 weeks 33 patients did not achieve an EVR and 7 patients discontinued therapy due to side effects. Of the 60 patients with EVR, in the next 36 weeks 8 patients did not achieve an end of treatment response and 12 patients discontinued therapy due to side effects. Overall, of the 19 patients who discontinued therapy 6 patients had psychiatric side effects (major depression, suicidal ideations, or psychosis), 4 patients had organic side effects (recalcitrant cytopenias or retinopathy) and 9 patients had various constitutional symptoms as the prominent reason for discontinuing therapy.
Conclusions: In our clinical practice 19% of genotype 1 patients discontinued treatment during a planned 48-week course of standard combination therapy. Among those who discontinued therapy 7/19 (37%) patients did so prior to achieving an EVR versus an unexpected 12/19 (63%) patients post-EVR. Constitutional and psychiatric side effects prompted discontinuation in 5/7 (71%) patients pre-EVR versus 10/12 (83%) patients post-EVR. Our study shows that constitutional and psychiatric side effects are the major cause of discontinuation of therapy even after EVR. Continued post-EVR vigilance and proactive management of side effects may significantly reduce patient drop-out and improve SVR.

Combination Therapy for Genotype 1 Hepatitis C—Can We Accurately Identify Predictors of Response?
Razi M. Arifuddin, M.D., Matthew M. Baichi, M.D., Arun Laing, M.D., Arun Srivatsa, M.D., Parvez S. Mantry, M.D.* Digestive and Liver Disease Unit, University of Rochester Medical Center, Rochester, NY.

Purpose: Current evidence suggests that more than 50% of patients with genotype 1 chronic hepatitis C (CHC) who undergo combination treatment with pegylated interferon (PIN) and ribavirin do not achieve sustained virologic response (SVR). Our aim was to retrospectively identify patient-related and biochemical factors that predict improved outcomes for genotype 1 CHC patients outside of registration trials.

Methods: Medical records were reviewed on consecutive genotype 1 patients who initiated PIN (alpha 2a or 2b) in combination with weight based ribavirin therapy. Treatment was discontinued on patients who did not have a 2 log drop after 12 weeks. Patient demographics, alcohol use, diabetes history, prior therapy (non-PIN and ribavirin), and antidepresant use was recorded. Baseline biohistochemical data on HAI and fibrosis score, viral load, hematocrit, platelet count, liver enzymes, and transferrin saturation was recorded.

Results: Complete data was available on 102 patients with genotype 1 with an overall SVR of 28%. The factors that positively influenced SVR on multivariate analysis were: no prior therapy (p = 0.005, OR 21.04), Ishak fibrosis score <3 (p = 0.027, OR 4.48), pre-treatment viral load <50,000 IU/ml (p = 0.011, OR 4.31), and none/minimal alcohol use (p = 0.042, OR 3.82). Age <40 (p = 0.04) and total bilirubin <1.0 (p = 0.0001) reached statistical significance in univariate analysis. The remaining variables showed a favorable trend that did not meet statistical significance (Table 1).

Table 1. Factors With a Favorable SVR Trend

<table>
<thead>
<tr>
<th>Factor</th>
<th>SVR (%)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transferrin Sat &lt; 35% / = 35%</td>
<td>35.6 / 15.6</td>
<td>0.200</td>
</tr>
<tr>
<td>Normal AST, ALT / Abnormal</td>
<td>33.3 / 21.8</td>
<td>0.395</td>
</tr>
<tr>
<td>Hematocrit &gt; 40 / &lt; 40</td>
<td>30.5 / 22.7</td>
<td>0.665</td>
</tr>
<tr>
<td>No Prior Antidepressants / Prior Use</td>
<td>31.7 / 16.7</td>
<td>0.316</td>
</tr>
<tr>
<td>Caucasian / Non-Caucasian</td>
<td>32.4 / 20.6</td>
<td>0.496</td>
</tr>
<tr>
<td>No Diabetes / Diabetes-II</td>
<td>31.3 / 16.7</td>
<td>0.405</td>
</tr>
<tr>
<td>Modifying Antidepressants / Not</td>
<td>48.3 / 20.0</td>
<td>0.067</td>
</tr>
</tbody>
</table>

Conclusions: Patients with low hepatic fibrosis, viral load, alcohol use and those with no prior therapy had an improved SVR with combination therapy in a multivariate analysis of our CHC genotype 1 cohort. Age <40 and total bilirubin <1.0 made a significant positive impact on SVR in univariate analysis. We suggest that treatment-naive younger genotype 1 CHC patients with a low viral load and fibrosis score may have the highest response rates and should be considered for therapy earlier in their disease presentation.

Restless Legs Syndrome Diminishes Quality of Life in Chronic Liver Disease
Ramesh Ashwathmarayan, M.D., Kia Saetian, M.D., Jose Franco, M.D., Arthi Sanjeevi, M.D., Jack Daniel, R.N., Archana Deshpande, M.D., Rose Franco, M.D.* Division of Hepatology and Gastroenterology, Medical College of Wisconsin, Milwaukee, WI and Division of Pulmonary and Critical Care, Medical College of Wisconsin, Milwaukee, WI.

Purpose: Restless Legs Syndrome (RLS) is a clinical syndrome that affects approximately 10% of the general population. RLS can be debilitating and lead to reduced quality of life. We have previously shown that RLS is more prevalent in patients with chronic liver disease (CLD). The impact of RLS on quality of life (QoL) of CLD patients has not previously been assessed. We prospectively evaluated the impact of: 1. RLS on the QoL in CLD patients; 2. The severity of liver disease on the presence of RLS.

Methods: CLD patients presenting to an outpatient Hepatology clinic were queried for presence of RLS using validated RLS survey tools. Patients found to have RLS were then contacted by telephone and the Johns Hopkins RLS Quality of Life Questionnaire was administered. The main outcome measure was the score on the RLSQoL questionnaire, a validated instrument that measures quality of life on a scale of 0 (poor quality) to 100 (good quality). This scale includes daytime somnolence, ability to concentrate, social activity impairment, sexual health and work productivity. MELD and Child’s score were determined in patients based on chart review. Mann-Whitney rank sum test was used to compare MELD scores and Chi square to compare Child’s class in RLS and non-RLS groups.

Results: Of 141 CLD patients surveyed, 86 were found positive for RLS. Of those positive for RLS, 34 (40%) self-reported risk factors including kidney disease (9), iron deficiency (19), and/or neuropathy (22). We were able to contact 76/86 RLS positive CLD patients for RLSQoL questionnaire and 74 CLD patients responded (2 refused). Average calculated RLSQoL score was 68, which reflects moderate diminished QoL and RLS severity. MELD score was available in 64/86 RLS positive patients and 37/55 RLS negative patients. Mann-Whitney rank sum test showed no significant difference (p = 0.90) in MELD score between RLS positive (Median 6) and RLS negative patients (Median 7). Further, there was no significant difference in the Child’s class between the RLS and non-RLS groups (see table).

Child’s Class–RLS

<table>
<thead>
<tr>
<th>Child's class with RLS (%)</th>
<th>without RLS (%)</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>73.25</td>
<td>70.91</td>
</tr>
<tr>
<td>B</td>
<td>13.95</td>
<td>16.36</td>
</tr>
<tr>
<td>C</td>
<td>5.81</td>
<td>3.64</td>
</tr>
</tbody>
</table>

Conclusions: RLS occurs with a surprisingly high prevalence in patients with liver disease and results in significantly diminished quality of life, with an average QoL score of 68 on a 0–100 scale. Presence of RLS in CLD patients is not directly related to the severity of their underlying liver disease. The cause for increased prevalence of RLS in liver patients is unknown and warrants further investigation.

Can Use of Growth Factors Enhance SVR to Combination Antiviral Therapy for Hepatitis C amongst Veterans?
Prashant K. Pandya, DO,* Karen K. Luken, AR.N.P, Ruth J. Corbett, AR.N.P, Dean Reker, Ph.D. Gastroenterology and Hepatology, Kansas City VA Medical Center, Kansas City, MO; Research, Kansas City VA Medical Center; Kansas City, MO and Gastroenterology and Hepatology, University of Kansas Medical Center, Kansas City, KS.

Purpose: Previous studies have suggested that sustained virologic response (SVR) to interferon alpha and ribavirin antiviral therapy in the VA population is less than half of that achieved in randomized controlled trials using similar therapies. Most of these studies attribute this lack of response to high drop out rates and comorbidities. The use of growth factors to enhance outcomes and minimize drop out rates in the veteran population has not been examined. Our aim was to assess the SVR to pegylated alfa (PEG) interferon combined...
with weight adjusted ribavirin in veterans who received adjunctive therapy with erythropoietin as needed for anemia.

**Methods:** A retrospective review of a cohort receiving combination antiviral therapy with either PEG interferon 2a or 2b and weight based ribavirin was performed. Eighty consecutive patients who met the approved guidelines for treatment with PEG interferon and ribavirin were offered therapy. During therapy erythropoietin support was initiated if the hemoglobin value dropped to 11 gm and if patient was symptomatic. Demographics, laboratory, and histologic parameters were compared to determine predictors of SVR using Chi square and logistic regression analysis.

**Results:** The mean age of the cohort was 49.9 ± 5.02. The average BMI was 28.9 ± 4.78. 84.8% (67/79) of patients were Caucasian, 11.4% (9/79) were African Americans, and 3.8% (3/79) were Hispanic. Genotype 1 comprised 69.6% of the cohort, whereas 27.8% were genotype 2 or 3 and one patient was genotype 4. 32.4% of the cohort had advanced fibrosis (stage 3 or 4). The SVR in the 71 veterans who had completed therapy was 63.4%. The SVR for Genotype 2 and 3 (87.5% and 83.3%) was significantly higher than the SVR for genotype 1 (52.1%) (p = 0.04). SVR was not significantly associated with Age, BMI, race, presence of DM, advanced fibrosis, and erythropoietin use by chi square or logistic regression analysis. 46.8% of the cohort received adjunctive support with erythropoietin.

**Conclusions:** Higher than expected response rates can be achieved with combination antiviral therapy using PEG interferon and Ribavirin in a veteran population when erythropoietin is used to mitigate the dose reduction or discontinuation.

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**Ethnic Differences in Cryptogenic Cirrhosis in Patients Undergoing Liver Transplantation**

Julia Gore Thornton, M.D., Virginia R. Mugford, Kris V. Kowdle, M.D.*
Department of Medicine, University of Washington, Seattle, WA.

**Purpose:** Studies suggest a substantial number of patients with cryptogenic cirrhosis have nonalcoholic steatohepatitis, and that it is more frequent among minorities. We used the Scientific Registry of Transplant Recipients (SRTR) to determine the ethnic distribution of patients listed and transplanted for cryptogenic cirrhosis (CC) compared to alcoholic cirrhosis (AC) or alcoholic cirrhosis with Hepatitis C (AHC), which represent common disorders for which minorities are listed for transplant.

**Methods:** The SRTR was used to determine the proportion of patients of different ethnicities added to the registry or transplanted from 1/1/1990 to 12/31/2004 with CC, AC, or AHC. Chi square analysis tested whether there were differences in the ratio of various ethnic groups listed or transplanted for CC compared to AC or AHC.

**Results:** 9,560 patients were added to the registry with a diagnosis of CC, of which 77% were White, 14% Latino, 5% Black, 3% Other. Patients with AC or AHC (n = 23,767) included 79% White, 14% Latino, 5% Black, 2% Other. Chi square analysis revealed a greater percentage of Latinos listed on the registry with CC compared to Whites (p = 0.009). There was no difference in the percentage of Blacks vs. Whites (p = 0.49) or Blacks vs. Latinos (p = 0.38) listed with CC.

6,597 patients were transplanted for CC. The ethnic distribution included 79% White, 12% Latino, 6% Black, 3% Other. Patients transplanted with AC or AHC (n = 12,382) included 82% White, 11% Latino, 5% Black, 2% Other. A greater percentage of Blacks (p < 0.001) and Latinos (p = 0.009) were transplanted for CC compared to Whites who were more frequently transplanted for AC or AHC. There was no statistically significant difference between Blacks and Latinos (p = 0.08) transplanted for cryptogenic cirrhosis.

Chi square analysis also suggested a greater percentage of Latinos with CC were listed for transplant compared to Whites but were less likely transplanted for CC than Whites (p < 0.001). There was no statistically significant difference between Blacks and Whites (p = 0.687).

**Conclusions:** In the SRTR, there was an increased prevalence of CC in Latinos compared to Whites which may reflect differences in advanced liver disease and NASH in this ethnic group. Additionally, although Latinos were more likely to be added to the registry with a primary diagnosis of CC, they were less likely to be transplanted for CC than Whites. A better understanding of these differences is necessary, with future studies exploring the potential reasons for this disparity.

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**Effect of Needle Biopsy in the Outcome of Hepatocellular Carcinoma (HCC)**

Chinnammal C. Kandaswamy, M.D., Moushmi Shah, M.D., Tom Weichle, B.S., Chris Cho, M.S., Divyesh G. Mehta, M.D.* Diely A. Pichardo, M.D., Medicine, University of Illinois at Chicago, Chicago, IL and Biostatistics, University of Illinois at Chicago, Chicago, IL.

**Purpose:** Diagnosis of HCC can usually be made by a combination of radiographic appearance and Alpha Fetoprotein levels. However, many patients still require a needle biopsy for pathological diagnosis. There have been several anecdotal reports of needle track tumor seeding after a biopsy but not enough evidence to document a connection. In this study we have attempted to answer the question about whether needle biopsy has an impact in HCC survival or risk of recurrence.

**Methods:** Information about all patients with HCC treated at UIC since 1998 was retrospectively collected by electronic chart review. Statistical analysis of the data was done to correlate the clinical and pathological size of the tumor, nodal involvement and presence of metastasis. SAS Biostatistical software was used.

**Results:** The database included a total of 194 patients, from these, 61 patients had documentation of having had a needle biopsy. Multivariate analysis was done. The variables most strongly correlated with survival were clinical stage, receiving surgical treatment (resection or transplant) and having a recurrence. The unadjusted survival analysis showed that the hazard ratio of death for patients whom had had a needle biopsy was 1.381 (Chi square 2.864. p = 0.0906). The adjusted survival analysis, controlling for clinical stage and surgical treatment, revealed a hazard ratio of death of 1.057 (Chi-square 0.0809; p = 0.776). However, controlling for whether a patient experienced a recurrence, patients who received a needle biopsy had a hazard ratio of death of 1.89 (chi-square 6.2116; p = 0.0127). All other covariates (diagnosis age, stage and type of treatment) were found to be not significant after controlling for biopsy status and recurrence status. The non-significant trend of correlation between having had a needle biopsy and increased probability of death disappears after adjustment by stage and treatment type, and may suggest a confounding effect. The significant effect of biopsy on survival after adjusting for recurrence may be due to a tendency to take smaller tumors directly to surgical resection and reserve biopsy for larger tumors. However, it raises the question of whether the detrimental effect of biopsy is related to systemic dissemination of disease as opposed to a local recurrence.

**Conclusions:** In this multivariate analysis, needle biopsy seems to predict survival when controlling by recurrence.

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**Detection of Focal Hepatic Lesions in Patients with Liver Cirrhosis Undergoing Transplant Evaluation: Ultrasound Versus Magnetic Resonance Imaging**

Mariam Mouri, M.D., Cheryl Levine, Ph.D., Travis Vannmeter, M.D., Jeff Weinstein, M.D., Stephen Cheng, M.D., Alejandro Mejia, M.D., Bo Husberg, M.D., Reem Ghahib, M.D.* The Liver Institute, Methodist Dallas Medical Center, Dallas, TX.

**Purpose:** Ultrasound imaging (US) and magnetic resonance imaging (MRI) are used extensively in the clinical practice to detect focal lesions in the liver. The purpose of this study is to determine the sensitivity of MRI compared to US in detecting focal hepatic lesions in patients with end stage liver disease undergoing liver transplant evaluation.

**METHODS:**Included were patients with liver cirrhosis undergoing transplant evaluation. All patients had undergone ultrasound (U/S) and magnetic resonance imaging (MRI) of the liver within two months of each other. The MRIs were done with a 1.5 Tesla Trilogy system using conventional T1, T2, and CT measurement sequences. Ultrasound images were obtained using Tengor US6000. The MRIs were evaluated by a radiologist blinded to the previous imaging. Lesions were subdivided into solid and cystic. Sensitivity of MRI was determined by the number of lesions found on MRI which was not found on ultrasound. Statistical analysis was done using Fisher’s exact test.

**RESULTS:**Forty patients were enrolled in the study. MRI found a total of 47 lesions which were not found on ultrasound. Ultrasound had a sensitivity of 0.77 compared to MRI which had a sensitivity of 0.99. Statistical analysis revealed a significant difference in sensitivities (p = 0.0001).

**CONCLUSIONS:** MRI is more sensitive then ultrasound in detecting liver lesions. This should be considered when evaluating patients with liver cirrhosis undergoing transplant evaluation.
Methods: This was a retrospective study of patients with decompensated cirrhosis undergoing liver transplant evaluation. As part of the routine liver transplant evaluation at our institution, patients undergo imaging of the liver with both US and MRI. Identified lesions are then managed as appropriate based on clinical relevance. Patients were selected who had imaging with both US and MRI within the same month and identified lesions were evaluated for clinical significance requiring further management.

Results: From March, 2003 to May, 2005, a total of 268 patients underwent liver transplant evaluation. A total of 147 patients (93 males; 54 females) met the inclusion criteria for the study including imaging using both US and MRI with one month time period. There were 34 (23%) patients with focal lesions identified on imaging. Of these, 16 (47%) patients were identified by both US and MRI, 17 (50%) were identified by only MRI, and 1 (3%) was identified by only US (McNemar’s p < .0002). Sensitivity was 50% and 97% with a NPV of 87% and 99% on US and MRI, respectively. Two lesions identified as cysts not requiring further follow-up. The other 32 (94%) lesions were all clinically significant that resulted in a change in management of the patient.

Conclusions: Prevalence of focal liver lesions in patients with end stage disease was 23% with 94% of these having clinical significance requiring a change in management. Imaging with MRI was significantly superior to US in identification of focal liver lesions including clinically relevant lesions. In this population with end stage liver disease undergoing liver transplant evaluation, recognizing potentially malignant liver lesions is critical in the management of these patients. Further studies to correlate lesions identified on imaging with pathology are needed.

Ophthalmologic Complications Occurring during Treatment of Chronic Hepatitis C Infection with Pegylated Interferon

James D. Panetta, DO, Nooman Gilani, M.D., Junaid Syed, M.D., Erin Ophthamologist. Veterans Affairs Medical Center, Phoenix, AZ.

Purpose: Ophthalmologic disorders are among the reported complications of pegylated interferon (IFN); however, there is little data on the frequency, associated symptoms, duration of onset, or whether either of the available forms of IFN put patients at higher risk for these complications. The aim of this study is to assess the incidence and nature of ophthalmologic complications from the use of IFN in the treatment of chronic HCV.

Methods: Charts for patients treated for chronic HCV between December 2002 and May 2005 were retrospectively reviewed. Patients were treated with ribavirin in combination with either IFN alfa-2a or alfa-2b. Ophthalmologic complications were defined as either vision changes reported by the patient or findings on dilated eye examination including cotton wool spots, retinal hemorrhages, or optic neuropathy. Any visual symptom prompted immediate treatment cessation until the patient could be evaluated by an ophthalmologist.

Results: A total of 294 patients, including 285 men and 9 women, were treated with IFN. Of these, 173 were treated with IFN alfa-2b while 121 received alfa-2a. In 23 of these patients ophthalmologic complications occurred and treatment was discontinued. Twelve patients complained of visual changes, 5 of which had observable ophthalmologic lesions. Of the remaining 7 without findings, treatment was resumed in 4 without sequelae, while it was not resumed in the other 3. Fifteen patients had findings on eye examination. Cotton wool spots were the most frequently observed lesion (n = 11), followed by optic neuropathy (n = 4). Among those with cotton wool spots only one reported symptoms, while all those with optic neuropathy were symptomatic. The earliest visible changes on eye exam were observed in a patient with a previously normal eye exam who began treatment 4 weeks prior. Of the patients receiving IFN alfa-2a, 7 (5.7%) had findings on exam; whereas 8 (4.6%) of those treated with IFN alfa-2b had detectable lesions.

Conclusions: Ophthalmologic complications were observed in 7% of patients receiving IFN. Five percent had lesions on exam. These complications can lead to blindness, are often asymptomatic, and can occur as soon as one month after treatment initiation, thus supporting the need for baseline and follow-up eye examinations. Vision changes alone do not preclude treatment continuation. There does not appear to be a significant difference between IFN alfa-2a and alfa 2b with regards to these complications.

Spectrum of Advanced Liver Disease in a Tertiary Care Institution

Kuntal M. Thaker, M.D., Kaldip S. Banwait, M.D., Maya Spodik, M.D., Steven K. Herrine, M.D., Victor Navarro, M.D.* Division of Gastroenterology and Hepatology, Thomas Jefferson University Hospital, Philadelphia, PA.

Purpose: In population based studies, the rise of HCV infection has surpassed alcoholic liver disease (ALD) as the most common cause of chronic liver disease. However, it is unknown if HCV is becoming the dominant cause of advanced liver disease. The aim of this study was to determine the distribution of etiologies in a cohort of patients presenting with advanced liver disease.

Methods: A retrospective review of patients presenting with advanced liver disease defined as the presence of endoscopically identified esophageal or gastric varices for the period between January 1999 and December 2002. Etiologies of hepatic injury were identified from the clinical record and laboratory database. Patients were excluded if their disease could be attributed to more than one cause (i.e. alcohol & HCV) or had a non-hepatic cause of portal hypertension. Patients were grouped according to etiology: (1) HCV (2) ALD (3) hepatitis B (HBV) and (4) other (cryptogenic cirrhosis, non-alcoholic fatty liver disease, autoimmune hepatitis, portal vein thrombosis).

Results: A total of 411 patients were identified as having either esophageal and/or gastric varices. The mean age was 56.1 years (range 19–89). There were 275 males (66.9%) and 136 females (33.1%). The proportions of females in those with HCV and ALD were similar although women were predominant in non-viral, non-alcohol related disease group compared to other diagnoses (59.4% vs. 24.3%, p < 0.0001). Etiology of liver disease differed in those older than 65 years of age compared to younger patients for all diagnostic categories (p < 0.0001) with ALD being more prevalent than HCV in older patients (p = 0.0120). Race was evenly distributed amongst groups. Hepatitis C represented the single most common etiology (42.1%) followed by alcohol (29.9%), other predominantly non-viral, non-alcohol diagnoses (20.0%), and hepatitis B (8.0%).

Conclusions: Etiology of liver disease drastically differs in those older than 65 years of age compared to younger patients. Higher prevalence of ALD rather than HCV in elderly population alludes to different risk behavior pattern between the two groups (i.e., intravenous drug use more common in younger patients). For patients younger than 65 years of age, HCV is the major cause of cirrhosis and burden of complications of cirrhosis attributable to HCV infection should be expected to rise as this population ages.

Plasma Factor VII May Increase the Sensitivity and Specificity of the APRI Score in Separating Mild and Significant Fibrosis in Patients with Hepatitis C

Rami Hawari, M.D., Ned Snyder, M.D.,∗ Shu-Yuan Xiao, M.D., John Peterson, Ph.D. Internal Medicine- Gastroenterology Division, University of Texas Medical Branch, Galveston, TX.

Purpose: Separating mild from significant fibrosis is an important step in the decision making process in treating and evaluating the prognosis of HCV patients. Liver biopsy remains the gold standard. The APRI. is a recently proposed index (Wai et al. Hepatology; 38:518–526) that we have found to be accurate in both a retrospective and prospective study of patients with HCV undergoing liver biopsy at our institution. Cutoffs of ≤0.42 and ≥1.2 accurately identified patients with mild and significant fibrosis (Snyder et al...
Gastroenterol 126:A-304, Snyder et al Am J Gastroenterol 99 $100–101$. Rodriguez-Hilgo et al, found that the percentage of hepatocytes expressing Factor VII was significantly lower in stage 4 liver fibrosis patients than in stage 3, stage 2, stage 1 and stage 0 patients (P < .001). (Blood Coagulation & Fibrinolysis, 12:193). We hypothesized that addition of Factor VII measurement might enhance the sensitivity of the APRI. 

*APRI = AST/ULN × 100/platelets(109/L)

Methods: The patients studied were 19 patients with chronic HCV undergoing pretreatment liver biopsies. Patients were excluded if they had received anti-viral treatment within the last year, if they were co-infected with HBV or HIV, or had an organ transplants. All patients had blood drawn on the day of the biopsy. The Factor VII assay was run on the STA-R instrument (Diagnostic Stago Parsippany, NJ). The APIR was calculated. The liver biopsies were read blindly by one pathologist using the Ludwig Batt’s criteria for staging of fibrosis. Analysis was performed using Insightful Miner 2 software (Insightful Corporation Seattle, WA.).

Results: One patient had an inadequate biopsy and two other patients did not have Factor VII measured because of inadequate specimen. Based on the biopsy results, there were 13 patients with significant fibrosis (F2–F4) and 5 patients with mild fibrosis (F0–F1). By logistic regression, the APIR had a sensitivity of 84.6% and a specificity of 60%. The combination of the APIR and Factor VII resulted in an improved sensitivity of 100% and a specificity of 100% in separating patients with significant fibrosis from patients with mild fibrosis.

Conclusions: Factor VII measurement may improve the sensitivity and the specificity of the APRI score in separating mild and significant fibrosis in patients with HCV. A larger number of patients is needed to evaluate this further.

Post-Transplant Lymphoproliferative Disorder (PTLD): The Great Mimic in Liver Transplantation (LTx)

David Koch, M.D., Ira Willner, M.D., Prabhakar Baliga, M.D., Chavin Kenneth, M.D., Lin Angelo, M.D., Adrian Reuben, M.D.* Liver Transplant Program, Medical University of South Carolina, Charleston, SC.

Purpose: PTLD complicates all organ transplantation but the diversity of clinical presentation is often unappreciated, and may delay diagnosis. Therefore the current aim is to chronicle the clinical spectrum, histopathology and outcome of PTLD in LTx, and to relate these variables to the prior level of immunosuppression.

Methods: Retrospective analysis of LTx database at the Medical University of South Carolina 1–1990 through 5–2005. Results: PTLD occurred in 23/621 (3.7%) LTx patients, 13m + 11f, mean age 43y (7mo-61y), interval 3 wks to 11y (mean 33mo) post-LTx. Clinical Presentation: Common (n ≥ 1)

1. Lymphadenopathy 5 (diffuse 3, focal 2)
2. Necrotic liver mass 5 (biliary stricture 1)
3. Lymphomatous ascites 3 (chylous 1)
4. Monoclonal gammopathy 2
5. Uncommon (1 each)

Skin nodules, biloma, hemolysis, breast mass, tonsillar lymphoma, malignant hydrenephrosis, gastrointestinal ulceration, multiorgan failure

Of these: 1 patient had sequential Hodgkin and non-Hodgkin lymphoma, 1 diffuse Hodgkin lymphoma with persistent amyloidosis, 2 Burkitt’s lymphoma, 1 large cell T cell lymphoma.

EBV infection was implicated in 13 (57%); 6 (26%) patients had steroid-resistant rejection and received antilymphocyte therapy. PTLD responded to treatment in 13 (57%) patients but led to death in 7 (30%) patients who did not respond; 3 patients are still under treatment.

Conclusions: PTLD, which is relatively common in LTx, has a diverse spectrum of clinical and histopathologic presentations that mimic other diseases. A low threshold of suspicion is needed to diagnose PTLD. Remission can occur with treatment in more than half the patients but there is also a high rate of fatality. Whereas EBV and antilymphocyte therapy may predispose to PTLD, these risk factors are not invariable.

Differences in the Evaluation and Management of Hepatitis C Patients Seen by Gastroenterologists Compared to Hepatologists

Hariprabhjit Singh, M.D., Faisal Khan, M.D., Dilip Moonka, M.D.* Division of Gastroenterology, Henry Ford Hospital, Detroit, MI.

Purpose: The current study is a retrospective analysis of patients with HCV seen at an integrated health care system to determine differences in the management of patients seen by a gastroenterologist vs. a hepatologist.

Methods: The database of an integrated health care system was queried to identify hepatitis C patients. Between 1977 to present, 7588 patients over the age of 18 were identified who were hepatitis C antibody positive. Of these, 1793 patients were seen by 1 of 5 hepatologists and 1696 were seen by 1 of 7 gastroenterologists. 150 patients seen by a hepatologist were randomly chosen and compared to 150 randomly chosen patients seen by a gastroenterologist. Chart reviews were performed on all 300 patients and data was collected on demographics including age, gender, alcohol use, route of transmission, HCV genotype and rates of liver biopsy. Data was collected on therapy including whether treatment was offered or accepted, rates of completion and dose adjustment, use of antidepressants and growth factors and rates of sustained virologic response (SVR). Differences were assessed using Fisher’s exact test.

Results: Patients did not differ between the 2 groups by demographics including age, gender, social practices (alcohol and drugs), and genotype. Hepatologists were more likely to perform liver biopsy (55% v. 30%; p < 0.001) and hepatologists were more likely to perform the liver biopsy themselves (83% v. 40%; p < 0.001). Rates of bridging and fibrosis were comparable between the two groups (15% v. 17%). Gastroenterologists were at least as likely to offer therapy to their patients as hepatologists (72% v. 59%; p = 0.091). However, patients offered therapy by hepatologists were more likely to accept than patients offered therapy by gastroenterologists (80% v. 51%; p < 0.001) and more patients seen by hepatologists ended up receiving treatment (47% v. 37%; p = 0.08). There was no difference in the use of growth factors (3% v. 8%) and anti-depressants (20% v. 17%) between the groups. There were no difference in SVR between patients treated by hepatologists (41%) and those treated by gastroenterologists (38%; p = 0.760).

Conclusions: Hepatitis C patients seen by hepatologists were more likely to undergo a liver biopsy than those seen by gastroenterologists. Both gastroenterologists and hepatologists offered therapy at comparable rates but patients seen by a hepatologist were more likely to accept treatment. The rates of SVR were no different between the two groups.

Endoscopic Argon Plasma Coagulation for the Treatment of Portal Hypertensive Gastrophy: Short Term Effects on Chronic Blood Loss

Talaat Zakareya, Nabil Omar, Ashraf Abu Gabal, Mohsen Salama, Imam Waked.* Hepatology, National Liver Institute, Shebeen El Kom, Egypt.

Purpose: Argon plasma coagulation (APC) has been used to treat chronic blood loss from gastric antral vascular ectasia. Its role in the management of chronic blood loss and anemia in patients with portal hypertensive gastrophy (PHG) is not settled. The purpose of this study was to evaluate the use of APC for the treatment of chronic blood loss and iron deficiency in patients with PHG.

Methods: The study included 30 patients (17 post-menopausal females and 13 males, mean age 50.7 years) with liver cirrhosis, iron deficiency anemia and severe PHG diagnosed endoscopically. All had hemoglobin <10 gm/dl, with no active bleeding from varices within the previous 6 months. 18 patients had obliterated varices following endoscopic therapy, with the last session more than 6 months before inclusion, and 12 patients had varices that had not bled previously (7 grade 1 and 5 grade 2). Patients had APC sessions with multiple brief pulses delivered to all areas of visible angioectasias or red spots. Endoscopy was repeated after 3 weeks, and further sessions were performed as needed. Patients receiving blood transfusion or iron therapy
within the preceding 3 months were not included in the study. Response was assessed by change in hemoglobin and serum iron parameters over the following 2 months after completion of the sessions.

**Results:** APC was delivered in 1 session to 24 patients (16 fundal, 5 body, and 3 antral). Six patients had diffuse PHG with ectasia, 5 requiring 3 sessions and 1 patient requiring 4 sessions of APC. Hemoglobin, MCV, serum iron, and tranferrin saturation increased significantly over the following 2 months in all patients.

**Conclusions:** APC is a safe procedure for the management of PHG. Short term result show favorable response in controlling chronic blood loss and iron deficiency. Whether these results are sustained over longer periods is to be evaluated.

<table>
<thead>
<tr>
<th>Mean Hemoglobin &amp; Iron Profile</th>
<th>Pre APC</th>
<th>1 Month</th>
<th>2 Months</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (gm/dL)</td>
<td>8.10 ± 0.95</td>
<td>8.86 ± 0.93</td>
<td>9.68 ± 1.07</td>
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<tr>
<td>MCV</td>
<td>75.93 ± 3.45</td>
<td>78.06 ± 3.39</td>
<td>80.33 ± 3.95</td>
<td>&lt;0.05</td>
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<tr>
<td>Serum Iron (mcg/dL)</td>
<td>45.83 ± 6.18</td>
<td>58.56 ± 7.62</td>
<td>71.46 ± 12.3</td>
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<tr>
<td>Total Iron Binding Capacity (mcg/ dL)</td>
<td>496.4 ± 21.1</td>
<td>482.4 ± 94.8</td>
<td>441.6 ± 31.2</td>
<td>ns</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>9.29 ± 1.66</td>
<td>12.66 ± 1.98</td>
<td>16.4 ± 3.41</td>
<td>&lt;0.05</td>
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</tbody>
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**Methionine Breath Test and Serum Clearance as a Diagnostic Tool in Chronic Liver Disease**

Rehan Khan, M.D., Jonathan Goldstein, M.D., Jennifer Lanter, B.S.N., Theresa Chen, Ph.D., Craig McClain, M.D., Daniell B. Hill, M.D.* Medicine-Gastroenterology, University of Louisville, Louisville, KY and Pharmacology and Toxicology, University of Louisville, Louisville, KY.

**Purpose:** It is well known that there is impaired methionine metabolism in patients with alcoholic and non-alcoholic liver disease (at a lesser level) due to defective hepatic mitochondrial oxidation. Patients with these liver disorders have hypermethionemia, prolonged methionine half life, and decreased plasma methionine clearance. The evaluation of hepatic mitochondrial function normally involves time consuming and composite testing. Despite extensive investigational efforts, there is no widely accepted investigational or diagnostic test to directly assess liver function. **Aims:** To assess the efficacy of methionine breath testing and serum clearance testing as tools for the diagnosis of liver disease in humans.

**Methods:** The non-radioactive 13C-Methionine Breath Test was performed in healthy subjects (n = 10), patients with documented non-alcoholic steatohepatitis (n = 8), and alcoholic hepatitis (n = 5). Study subjects were recruited from General Clinical research Center at University of Louisville, and informed consent was obtained with IRB approved forms. After an overnight fast of 8hrs, vitals were obtained and initial evaluation was performed by one of the principal investigators, then baseline breath sample was obtained in commercially available sealed packed kit supplied by Metabolic Solution Inc. Later, subjects were asked to drink 200 mg of non-radioactive 13C-Methionine dissolved in water, and 40 minutes later another breath sample was obtained. Both samples were sent to Metabolic Solutions Inc for analysis.

**Results:** Preliminary data from patients with severe alcoholic hepatitis/cirrhosis and non-alcoholic steatohepatitis with advanced disease showed reduced exhalation of non-radioactive 13C as compared to normal control, but data for compensated liver disease have indeterminate findings.

**Conclusions:** It appears that the Methionine Breath Test may be useful in diagnosing and assessing improvement in progression of different stages of liver impairment. Further large scale studies are required to prove the efficacy of this non-invasive test in evaluation of hepatic mitochondrial function.

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**N-2-butyl-cyanoacrylate for Gastric Varices—A Study To Determine Its Optimal Technique, Immediate and Long-Term Efficacy and Complication Rates**


**Purpose:** Fundal and isolated gastric varices are at high risk of bleeding and are a life-threatening complication of portal hypertension. Management of bleeding gastric varices has not been standardized but it has recently it has been shown that Cyanoacrylate injection therapy is safe with results comparable to patients treated with TIPS. Cyanoacrylate injection therapy becomes particularly relevant in Pakistan as TIPS or Liver transplant is not easily available. Our study was done to (1) evaluate the immediate and long-term efficacy of cyanoacrylate injection therapy (2) to evaluate the efficacy of injection of smaller amounts of cyanoacrylate at the time of initial endoscopic examination with reinjection on an as needed basis only. This was expected to decrease the cost of the procedure significantly.

**Methods:** A prospective study conducted at the endoscopy unit of two tertiary care centers from January 2002 to December 2004. The data was collected by a formal questionnaire from the medical records and follow-up was done by outpatient visits, surveillance endoscopy, telephone calls and interviews of the patients. The data was analyzed using the SPSS 10.0 software.

**Results:** 38 patients underwent cyanoacrylate injection therapy for isolated gastric varices. 27 patients had bleeding gastric varices or signs of recent bleeding while 8 patients had elective Cyanoacrylate injection therapy. In 15 patients a 2:1 ratio of lipoidal and cyanoacrylate was used. In 6 patients 1:1, 3 patients a 3:1 and in 2 patients a 4:1 ratio of the two agents was used. 1 patient had no lipoidal injected with 2 cc of cyanoacrylate being used. There was one mortality during the therapy session but all others were noted to have excellent post-procedure hemostasis. Amongst the 18 patients followed long-term, the cumulative rebleeding rates at 3, 6, 12 and 24 months were 6%, 12%, 18% and 24%. All the patients who rebled were controlled with repeat cyanoacrylate injection. 2 patients expired during the follow-up period due to unrelated causes.

**Conclusions:** (1) Cyanoacrylate injection remains an effective modality for control of bleeding from isolated gastric varices. (2) Smaller amounts of cyanoacrylate can also be effective in achieving good results with significant cost savings and lower risk of complications. (3) The overall complication rate is low and acceptable in a setting where TIPS or Liver Transplant is not a viable option.

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**Demographics of Hepatocellular Carcinoma and Association with Alcohol Intake and Presence of Diabetes Mellitus among US Veterans. A Cross Sectional Analysis**

Yuryr Tsrilin, M.D., Gul Batliyar, M.D., Samy I. McFarlane, M.D., Ayse Ayteman, M.D.* Gastroenterology, VA New York Harbor HCS, Brooklyn, NY and Endocrinology, Diabetes and Hypertention, SUNY Health Science Center at Brooklyn, Brooklyn, NY.

**Purpose:** Incidence of hepatocellular carcinoma (HCC) is on the rise in the US and around the world. In the US population rate of occurrence has doubled in the past two decades. The most common etiologies for HCC include viral hepatitis C and B, alcohol (ASH), non alcoholic steatohepatitis (NASH) and hemochromatosis (HC). Alcohol doubles the risk of HCC in chronic hepatitis C patients. The impact of NASH and ASH on HCC is largely unclear.

**Methods:** A database has been created to prospectively evaluate the interactions of HCV and DM/ metabolic syndrome in a population of male US veterans. Here we present the demographic data for a consecutive case series
HBV-DNA was positive among 53 of 100 patients with liver cirrhosis (14% with liver cirrhosis and 39 HCV negative, 14 with liver cirrhosis and 39 HCV negative). All procedures were performed in duplicate. Patients were 185 HCV geno- type 4. Several reports indicated the higher prevalence of occult hepatitis B in chronic hepatitis C infection due to HCV genotype 4. Disease and Patients with Hepatitis C

Control 227 2 (0.8%)
HCV -ve cirrhosis 14 57 (30.8%)
HCV -ve CAH 25 6 (42.9%)
HCV -ve Total 39 1 (4%)
Liver Disease Total 224 7 (17.9%)
Control 227 2 (0.8%)

Purpose: Several reports indicated the higher prevalence of occult hepatitis B infection in patients with chronic hepatitis C, and that occult HBV might influence the clinical and biochemical features, and the severity of disease. This has not been studied among Egyptian patients with chronic HCV infection due to HCV genotype 4.

Methods: 224 HBsAg negative patients with liver disease and 227 HBsAg negative and HCV negative individuals without liver disease had serum HBV-DNA tested using nested PCR by specific primers of surface antigen. All procedures were performed in duplicate. Patients were 185 HCV genotype 4 positive (86 with liver cirrhosis, 58 with chronic hepatitis, 41 with consistently normal ALT and 39 HCV negative (14 with liver cirrhosis and 25 with chronic active hepatitis).

Results: HBV-DNA was positive among 53 of 100 patients with liver cirrhosis (54% in HCV+ve vs 43% in HCV-ve, ns). Of these, 5 were seronegative for all HBV markers. Similarly, in CAH, the prevalence of HBV-DNA did not differ among patients with and without HCV infection. HBV was more prevalent among patients with liver disease than controls (p < 0.001, OR45, 95%CI: 11.59–382), among patients with HCV infection than controls (P < 0.001, OR50, 95%CI: 12.8–427), and among patients with advanced than mild liver disease (cirrhosis vs CAH p < 0.005, OR878, 95%CI: 3.4–25.2). No significant biochemical differences were observed among HBV-DNA positive or negative patients with similar stages of liver disease, and the Child-Pugh score and clinical indications of severity were similar among HBV-DNA positive and negative patients with cirrhosis.

Conclusions: Occult hepatitis B is highly prevalent among patients with hepatitis C and with liver disease compared to control, and the prevalence increases with advanced liver disease. Among patients with similar degree of liver disease the presence of HBV-DNA is not associated with increased markers of disease severity. The role of occult hepatitis B in the progression of liver disease remains to be identified in future studies.

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Pegylated Interferon alpha-2a (Pegasys) Versus Pegylated Interferon alpha-2b (Pegintron) in the Treatment of Chronic Hepatitis C Infection

M. Raza Anees, M.D.*, Savio Reddyman, M.D., Hannamah R. Beijani, M.D., Gloria Caldito, Ph.D. Medicine, Overton Brooks VAMC, Shreveport, LA; Medicine, LSUHSC-Shreveport, Shreveport, LA and Statistics, LSUHSC, Shreveport, LA.

Purpose: Hepatitis C infection is a major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma. Highest overall end of treatment response (ETR) and sustained viral response (SVR) in chronic hepatitis C infection have been achieved with weekly sub-cutaneous injections of pegylated interferon alpha and ribavirin. However there have been no trials comparing Pegasis versus Pegintron in the treatment of chronic hepatitis C infection, when combined with standard doses of ribavirin. We conducted a retrospective study comparing the two drugs for the treatment of chronic hepatitis C infection.

Methods: 42 naïve hepatitis C patients from the Overton Brooks VAMC were divided into two groups, based on treatment with weekly subcutaneous injections of Pegintron (weight based regimen) or Pegasis (180 mcg). There were 32 patients in the Pegentin group and 10 patients in the Pegasis group. Both groups were treated with standard dose of ribavirin. Duration of treatment was 48 weeks for genotype 1 and 24 weeks for genotype 2 or 3. Both groups were matched for age, sex, weight, body mass index (BMI) race, and genotype. Outcomes were compared for ETR and SVR.

Results: There was no significant difference in ETR (70% vs. 71.9%, P > 0.99), or in SVR (40% vs. 53.1%, P = 0.47) in both the groups. P values for covariates; weight, BMI, race, genotype, were tested by linear and logistic regression methods based on drug used and outcomes (ETR and SVR), and were not significant. P value for age was only significant (0.03) for ETR (Irrespective of drug used, greater the age, better the response) but not for SVR (0.5).

Conclusions: In naïve patient with chronic hepatitis C infection, combination of Pegasis and ribavirin is no different than combination of Pegentin and ribavirin in achieving ETR and SVR.

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A Case of Multiple Bile Duct Hamartomas (Von Meyenburg Complexes) with Suspicion for Malignant Transformation

Scott Merkley, M.D., Joey Sum, M.D., Ilana Boneyeva, M.D.* Digestive Disease and Nutrition, University of Kentucky, Lexington, KY and Digestive Diseases and Nutrition, Veterans Affairs Medical Center, Lexington, KY.

Purpose: Multiple bile duct hamartomas (Von Meyenburg complexes–VMC) are benign malformations of the bile ducts due to absence of persistent remodeling of the embryonic bile duct network. It presents as diffuse, small, cystic lesions consisting of deformed bile ducts. VMC can be confused with metastatic disease on imaging studies and histologic examination
is usually required for diagnosis. Although VMC is thought to be innocuous, malignant transformation has been reported.

Methods: A 71 year old female with a 5-year history of right upper quadrant abdominal pain was found on abdominal CT scan to have multiple hypodense liver lesions. Routine labs were normal and the work up for chronic liver disease was negative. There was no evidence of primary malignancy elsewhere on imaging and endoscopic studies as well. A CT-guided biopsy was obtained from one of the lesions and it showed bile duct hamartomas. The patient presented to our clinic 3 years later with recurrent abdominal pain. A MRI of abdomen showed multiple small cysts throughout the liver and a 1.0 × 1.5 cm focus in the left lobe concerning for dysplastic nodule. The repeat liver function tests were normal, tumor markers CEA and AFP were normal, but CA 19–9 was elevated at 38 U/ml. A follow up MRI 2 months later showed unchanged size of the dysplastic nodule but another one 6 months later was much less suspicious for a dysplastic nodule. The absence of malignant transformation was also confirmed on a total body PET scan which did not show any abnormal focus of hypermetabolism, including in the liver. The follow up CA 19–9 showed levels of 119 U/ml and later 83.7 U/ml but since this tumor marker can be elevated in a wide variety of benign biliary lesions, we did not feel that this was due to malignant transformation of the bile duct hamartomas in the absence of any other clinical, laboratory, and imaging data to support this.

Conclusions: Von Meyenburg complexes are seen frequently in the liver and are generally benign lesions. Although neoplastic transformation has been reported, a causative relationship has never been proven. We present our case to increase the awareness for possibility of malignant transformation and to emphasize the importance of following disease progression. In addition, VMC should be considered in the differential diagnosis of metastatic liver disease where histologic evaluation can help to avoid misdiagnosis.

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**Increased S-Adenosylhomocysteine (SAH) May Predispose to TNF Liver Injury in Human Alcoholic Liver Disease (ALD)**

**Jonathan W. Goldstein, M.D., Theresa Chen, Ph.D., Rehan Khan, M.D., Jennifer Lanter, B.S.N, Shirish Barve, Ph.D., Craig McClain, M.D., Daniell B. Hill, M.D.**

**Purpose:** There are several potential mechanisms by which chronic alcohol may sensitize the liver to tumor necrosis factor (TNF) liver injury. SAH is a product of methionine in the transmethylation pathway, and is a competitive inhibitor of most methyltransferases. In vitro studies and in vivo animal studies have shown that elevated SAH decreases S-adenosylmethionine (SAMe), and a low SAMe/SAH ratio are key elements sensitizing hepatocytes to damage from TNF in the setting of chronic alcohol exposure. There has not yet been an in vivo study documenting abnormal SAH metabolism in human subjects with chronic ALD.

**Aim:** Demonstrate any differences in SAH, SAMe, and SAMe/SAH ratios in stable ALD patients compared with non-alcoholic subjects.

**Methods:** Blood samples were collected in EDTA vacutainers from stable cirrhotic ALD subjects (n = 5) who had been abstinent from alcohol for at least one year, as well as from non-alcoholic volunteers (n = 10). Plasma concentrations of SAH and SAMe were assayed by reverse-phase HPLC by a modified method of Merali et al. (2000). SAMe and SAH were detected using a Waters 2487 absorbance detector at 254 nm. Standard solutions of SAMe and SAH were prepared in 4% MPA. An internal standard, S-adenosylhomocysteine (SAE), was added to all samples and standard solutions to a concentration of 100 nmol/mL.

**Results:** Averaged values for cirrhotic patients, versus non-alcoholic volunteers, indicate elevated plasma levels of SAH in cirrhotics (3.54 nmol/mL, SD ± 1.31 versus 2.20 nmol/mL SD ± 0.46; p < 0.05), decreased levels of SAMe (0.12 nmol/mL, SD ± 0.05 versus 0.17 SD ± 0.01; p < 0.05), and a decreased SAMe/SAH ratio (0.048 ± SD 0.032 versus 0.079 ± 0.017; p < 0.05).

**Conclusions:** These data document significantly elevated SAH, as well as significantly decreased SAMe levels and SAMe/SAH ratios, in human subjects with chronic ALD. This supports previous in vitro human cell line studies and in vivo animal studies implicating elevated SAH and depleted SAMe as mechanisms leading to TNF sensitization in hepatocytes in the setting of alcoholism. Although there are studies demonstrating that blocking TNFa can prevent alcohol-induced hepatocellular damage, future studies may examine whether liver damage can be prevented by reducing SAH levels or blocking hepatocyte exposure to SAH in the clinical setting of alcoholism.

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**Histopathologic Features of Hepatic Steatosis in Patients with Hepatitis C Virus Genotype 3 Infection**

**Steven A. Gonzalez, M.D., Lydia M. Petrovic, M.D., Ira M. Jacobson, M.D.**

**Purpose:** To determine the histopathologic features of hepatic steatosis in patients with chronic hepatitis C virus genotype 3 infection (HCV 3).

**Methods:** A total of 43 patients with chronic hepatitis C were evaluated. Histopathologic features were assessed in liver biopsies stained with hematoxylin and eosin.

**Results:** The most common histopathologic feature was steatosis, which was present in all patients. Other features included inflammation, fibrosis, and necrosis. There was no significant correlation between the degree of steatosis and the genotype or the stage of fibrosis. However, there was a trend towards more severe steatosis in patients with higher stages of fibrosis.

**Conclusions:** The histopathologic features of hepatic steatosis in patients with HCV 3 infection are similar to those in patients with HCV 1 infection. Further studies are needed to determine the significance of these findings.
Purpose: Steatosis is frequently associated with chronic hepatitis C virus (HCV) infection. Studies have suggested steatosis associated with HCV genotype 3 infection may result from a viral etiology, evidenced by regression of steatosis following successful antiviral therapy. Histopathologic features that may distinguish viral from metabolic steatosis in this setting have not been well characterized. The aim of this study was to identify histopathologic features associated with HCV genotype 3 infection that may be attributable to viral steatosis in contrast to metabolic steatosis.

Methods: Liver biopsies from 26 treatment-naive patients with chronic HCV infection were evaluated, including patients infected with genotypes 1 (n = 8), 2 (n = 10), and 3 (n = 8). Histopathologic features including the type, severity, and zonal distribution of steatosis, lobular inflammation, portal inflammation, and fibrosis in all biopsies were evaluated by a single pathologist who was blind to the clinical status of each patient. Clinical and demographic information was obtained from the medical record.

Results: Patient age, gender, race, weight, mean ALT levels, fibrosis stage, and necroinflammatory grade did not differ between genotypes. Genotype 1 patients had higher HCV RNA levels compared with genotypes 2 and 3 (p = 0.003). Overall, 13 patients (genotype 1, n = 4; genotype 2, n = 3; and genotype 3, n = 6) had significant macrovesicular steatosis (grades 2/3 and 3/3). The distribution of steatosis in genotype 3 patients was predominantly centrilobular, involving zones 2 and 3 (5/6, 83%), while steatosis occurring in genotype 1 and 2 patients was nonzonal (7/7, 100%; p = 0.005). Genotype 1 and 2 patients tended to have increased portal inflammation compared with genotype 3 patients (56% vs. 25%, p = 0.06). Increasing ALT levels correlated with lobular inflammation in genotype 3 patients (r = 0.76, p = 0.03) and with portal inflammation in both genotype 2 (r = 0.78, p = 0.01) and genotype 3 patients (r = 0.76, p = 0.03).

Conclusions: Patients infected with HCV genotype 3 have a predominantly centrilobular (zones 2 and 3) distribution of steatosis, while steatosis in genotypes 1 and 2 appeared nonzonal. Histopathologic differences in patterns and distribution of steatosis among different HCV genotypes may help in identifying features associated with viral versus metabolic hepatic steatosis.

Hepatitis B and C Viral Markers among Family Members of Patients with Advanced Liver Disease and Occult Hepatitis B


Purpose: The risk of infectivity of HBV is high among unvaccinated family members of HBsAg+ve patients. The risk among family members of patients with occult HBV remains unknown. The aim of this study was to examine the HCV and HBV serological markers and viral status of immediate family members of HBsAg−ve patients with liver cirrhosis.

Methods: 100 HBsAg−ve patients with Child C cirrhosis agreed to provide 4 consenting unvaccinated family members each for testing for markers of HBV and HCV infection, and biochemical and clinical parameters of liver disease. Patients and family members were tested for HBsAg, anti-HBs, anti-HBc, anti-HCV, HCV-RNA by PCR, and had serum HBV-DNA tested using nested PCR by specific primers of surface antigen.

Results: Family members were 25 spouses, 268 offspring and 107 siblings. 86 Patients were −ve for HCV, 53 were HBV-DNA−ve (48 sero−ve and 5 sero−ve) and 17 were anti-HBC−ve and HBV-DNA−ve. Among the 400 family members tested, 122 had antibodies to HCV (30.5%), 49 were HBsAg+ve HBV-DNA+ve (12.25%), 13 (3.25%) had occult hepatitis B (all anti-HBC+ve). HCV−ve patients had 32% of their relatives+ve for HCV vs 21.4% of the relatives of HCV−ve patients (p = 0.05). Patients with occult hepatitis B had 18.4% of their relatives HBV-DNA+ve vs 11.7% of the relatives of HBV-DNA−ve patients. Patients−ve for HBV and HCV markers had none of their relatives+ve for any HBV markers. HBV markers were not different among siblings, spouses and offsprings (HBsAg+ve in 16.8%, 10.1% and 16% respectively; ns; occult HBV in 6.5%, 1.9% and 4% respectively, ns). Spouses had significantly higher prevalence of HCV (56%) compared to siblings and offsprings (28% and 28.7% respectively). 58 Of 99 relatives+ve for HCV (58.6%) had biochemical and clinical indications of asymptomatic liver disease, vs 25 of 252 HCV negatives (10%) and 12 of 49 with HBsAg+ve(25%).

Conclusions: Family members of patients with HBsAg−ve chronic liver disease are at higher risk of being +ve for HCV than HBV. This risk is higher if the patient is HCV+ve than occult hepatitis B+ve, and is highest if both are positive. The routes of infection need be further studied. The high prevalence of HBsAg positivity in relatives vs occult infection is indicative that occult HBV is a stage in the disease progress of HBV infection.

Improved SVR Rates in Southeast Asians with Chronic Hepatitis C Treated with PEG-Interferon and Ribavirin

Toan T. Nguyen, M.D., Kenneth D. Rothstein, M.D., Victor Araya, M.D.* Gastroenterology, Albert Einstein Medical Center, Philadelphia, PA.

Purpose: To describe our HCV treatment experience with Southeast Asian (SEA) patients.

Methods: Retrospective cross sectional study of all SEA patients seen at a single center between 2001–2004. Inclusion criteria: 1. patients self identified as SEA (Vietnam, Cambodia, Laos, and Thailand) 2. Detectable quantitative HCV RNA (IU/ml) 3. Treatment naive 4. No coinfections. Genotype (GT) was done using the INNO-Lipa assay. High viral load (HVL) was defined as >600,000 IU/ml. All patients in cohort received standard PEG/RBV dosing. Patients were categorized as non-responders (NR), early virologic response (EVR), end of treatment response (ETR), relapse, and sustained virologic response (SVR). Standard patient pre-treatment demographics were collected. META VIR histologic scoring was utilized.

Results: 25 SEA patients were identified; 11 were not treated (8 are still being evaluated; 2 were lost to follow up; 1 refused treatment) 1 is in the midst of therapy. The study cohort consisted of 13 patients that completed management. Age range was 19–67(mean 52). BMI range was19–31 (mean 24). EVR, ETR, relapse, and SVR rates are seen in the table. 6 patients with HVL achieved 83% SVR. 7 patients with a low viral load achieved 86% SVR. 3 of 13 patients discontinued treatment. 2 of whom still achieved SVR (1 stopped after 20 weeks due to psychosis had GT6, LVL., and stage 2 histology. 1 stopped after 5 weeks had GT1b, LVL, and refused biopsy). The patient that relapsed stopped at 24 weeks after developing influenza had GT6, HVL, and stage 3 histology. 5 patients required dose reductions (1 NR, 1 relapse, 3 SVR). Growth factors were used in 2 patients (1 relapse, 1 SVR). 1 patient with cirrhosis relapsed (GT1b,HVL).

Virologic Response

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>EVR</th>
<th>ETR</th>
<th>Relapse</th>
<th>SVR</th>
</tr>
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<tr>
<td>Total</td>
<td>13</td>
<td>100%</td>
<td>92%</td>
<td>15%</td>
<td>85%</td>
</tr>
<tr>
<td>GT 1</td>
<td>6</td>
<td>100%</td>
<td>100%</td>
<td>17%</td>
<td>83%</td>
</tr>
<tr>
<td>GT 2</td>
<td>4</td>
<td>100%</td>
<td>100%</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>GT 6</td>
<td>3</td>
<td>100%</td>
<td>67%</td>
<td>33%</td>
<td>67%</td>
</tr>
</tbody>
</table>

Conclusions: SEA patients have high rates of response to PEG/RBV treatment independent of genotype and viral load. Larger prospective studies are needed to confirm these findings.

Dramatic Rise in the Incidence of Ischemic Codramatic Rise in the Incidence of Ischemic Collitis in Two Metropolitan Hospitals over a 10 Year Period

Michael E. Elmore, M.D.*, Robert N. Elliott, M.D. Gastroenterology & Hepatology, Indianapolis Gastroenterology Research Foundation, Indianapolis, IN.

Purpose: The incidence of ischemic colitis as determined by colonoscopy was evaluated retrospectively from 1992 though 2001 at two large metropolitan hospitals in Indianapolis, Indiana.
Is IBS among PTSD Patients Under Diagnosed in the VA Healthcare System?
Oswald L. Haye, M.D.* Gastroenterology, Orlando VA Healthcare Center, Orlando, FL.

Purpose: The VA has been task with the health care of all veterans, including GI health issues. During the month of March’95, 19 patients with the diagnosis of Post Traumatic Stress Syndrome (PTSD) were evaluate for screening colonoscopy. None had a history of weight loss, rectal bleeding or anemia, however, 12 gave a history of recurrent abdominal pain, gas, bloating, and altered bowel pattern. Based on this history, it was decided to evaluate them for Irritable Bowel Syndrome (IBS).

Methods: All patients were evaluated by a staff gastroenterologist. Each had a complete history and physical, all available lab data was reviewed and patients had screening colonoscopy to the cecum. In addition all patients were subjected to the ROME II criteria for IBS.

Results: Of the 19 patients seen for routine colorectal screening colonoscopy who carried the established diagnosis of PTSD, 12 (~60%) met the ROME II criteria for IBS. None of these patients had previously been diagnosed with this disorder even though numerous studies of IBS patients have shown a psychosocial component to this disorder as well as other functional bowel disorder.

Conclusions: This study though small in number (19 patients) and limited over time (4 weeks), would suggest that IBS is under diagnosed in the PTSD population in the VA system, and warrants further study.

Potential Role of Differentiation and Vascular Invasion Together as Independent Prognostic Marker of Colorectal Cancer
Rajesh K. Choudhary, F.R.C.S., Debasish Debnath, F.R.C.S., Keith A. Gunning, F.R.C.S.* Surgery, Bishop Auckland General Hospital, Bishop Auckland, Co Durham, United Kingdom; Surgery, King George Hospital, Ilford, Essex, United Kingdom and Surgery, Darlington Memorial Hospital, Darlington, Co Durham, United Kingdom.

Purpose: Vascular invasion and differentiation can influence staging of certain cancers. However little is known of such an impact on the staging of colorectal cancer (CRC). We aimed to assess any correlation between the states of vascular invasion, differentiation and Dukes’ stages of colorectal cancer.

Methods: All valid cases of CRC that took place at Bishop Auckland General and Darlington Memorial Hospitals, United Kingdom, between August 2001 and July 2003 were studied. Differentiation was described as ‘well’, ‘moderate’ and ‘poor’. Vascular invasion was classified as ‘present’ or ‘absent’. Stages of CRC was categorised as ‘early’ (Dukes’ A and B) and ‘late’ (Dukes’ C and D). Pearson Chi-Square test was used for statistical analysis.

Results: A total of 100 CRC were studied where relevant information were available. ‘Well’ and ‘poor’ differentiation were associated with ‘early’ and ‘late’ stages (p = 0.001) respectively. Moderate differentiation (n = 46) did not bear any significant correlation. ‘Absence’ and ‘presence’ of vascular invasion was associated with ‘early’ and ‘late’ stages respectively (p < 0.0001). However, when considered in combination, ‘early’ stage was significantly associated with ‘absence’ of vascular invasion, irrespective of the state of differentiation (p < 0.0001). Similarly, ‘late’ stage was significantly associated with ‘presence’ of vascular invasion, irrespective of the state of differentiation (p < 0.00001).

Summary of Results

<table>
<thead>
<tr>
<th>Vascular Invasion</th>
<th>Vascular Invasion</th>
</tr>
</thead>
<tbody>
<tr>
<td>‘Absent’ (‘Well’)</td>
<td>‘Present’ (‘Poor’)</td>
</tr>
<tr>
<td>‘Early’ stage (Dukes’ A &amp; B)</td>
<td>30 2 0 0 32</td>
</tr>
<tr>
<td>‘Late’ stage (Dukes’ C &amp; D)</td>
<td>8 5 4 5 22</td>
</tr>
</tbody>
</table>

Conclusions: The combination of differentiation and vascular invasion, by virtue of strong correlation with the stage, can potentially act as an independent prognostic marker of colorectal cancer. The association of vascular invasion is stronger than differentiation.

Truth behind Male Stoicism: A Colorectal Cancer Perspective
Debasish Debnath, F.R.C.S., Rajesh K. Choudhary, F.R.C.S., Keith A. Gunning, F.R.C.S.* Surgery, King George Hospital, Ilford, Essex, United Kingdom; Surgery, Bishop Auckland General Hospital, Bishop Auckland, Co Durham, United Kingdom and Surgery, Darlington Memorial Hospital, Darlington, United Kingdom.

Purpose: Males are traditionally depicted as stoic and reluctant to present themselves to their general practitioners (GP). A natural hypothesis follows, therefore, that males are likely to have a longer natural history, advanced disease on presentation and would merit more urgent referral. We aimed to corroborate this hypothesis by comparing any association between the presentation and outcome of the colorectal cancer (CRC) in both sexes.

Methods: All valid referrals made by GPs to specialist rapid access colorectal cancer clinics of Bishop Auckland General and Darlington Memorial hospitals, UK, between August 2001 and 2003, were derived. Duration of illness on presentation to the GP was measured in weeks (mean ± 1 standard error). Distribution of quality of referral letters, both in terms of compliance to guidelines and completeness, was also assessed. Stage of CRC was categorised as ‘early’ (Dukes’ A and B) and ‘late’ (Dukes’ C and D).

Results: A total of 516 cases were studied. The mean age of the male (63.9 ± 8.0; n = 254) was not significantly different than the female (63.6 ± 8.0; n = 262) [p = 0.77]. There was no significant difference of duration of history on presentation to GP amongst the male (11.0 ± 0.8), compared to
the female (9.7 ± 0.7) [p = 0.23]. Adherence to guidelines of referral was comparable in both males (n = 179; 76.5% of 234) and females (n = 219; 77.7% of 282) [p = 0.75]. Completeness of the referral letters were alike in the male (n = 40; 17.1% of 234) and female (n = 48; 17% of 282) [p = 0.98]. There was no significant difference of ‘late’ CRC amongst the male (n = 10; 58.8% of 17), compared to the female (n = 15, 55.6% of 27) [p = 0.83].

Summary of Results

<table>
<thead>
<tr>
<th>Guidelines followed</th>
<th>Referral letter</th>
<th>Stage of CRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
<td>Complete</td>
</tr>
<tr>
<td>Male</td>
<td>179</td>
<td>55</td>
</tr>
<tr>
<td>Female</td>
<td>219</td>
<td>63</td>
</tr>
</tbody>
</table>

Conclusions: There is no significant difference in the presentation, referral pattern and outcome of the colorectal cancer amongst males and females. This should help dispel the traditional myth about ‘stoicism and lateness’ associated with the ‘male’.

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Neurofibroma in the Colon
Samuel Davidoff, M.D., Ari Wiesen, M.D., Kostas Sideridis, DO, Ronald Greenberg, M.D.*; Olga Falkowski, MD. Gastroenterology, Long Island Jewish Medical Center, New Hyde Park, NY.

Purpose: Neurofibromatosis type I (von Recklinghausen’s disease), is a common disorder occurring in 1 per 3,000 live births. As many as 25% of the cases involve the gastrointestinal system, most cases involve the stomach or small bowel. Colonic involvement in Neurofibromatosis is uncommon. When it occurs, it usually presents in the advanced stages of the disease.

Case: A 56 year old asymptomatic male with Neurofibromatosis (NF) Type I presented for a screening colonoscopy. His family history was noncontributory and he was average risk for colon cancer. On physical examination, significant findings were limited to multiple cutaneous neurofibromas primarily over the face and arms. The patient was heme-occult negative. On colonoscopic examination a single polyp was located in the transverse colon (Figure 1) and removed (Figure 2). Pathological examination of the polyp showed diffuse proliferation of benign spindle cells in the lamina propria (Figure 3). The immunostaining of the cells for the S-100 protein revealed their neural origin (Figure 4). These findings were consistent with mucosal neurofibroma.

Conclusions: Colonic involvement in Neurofibromatosis is rare. We have described a case of a patient with a diagnosis of Neurofibromatosis who was found to have an isolated neurofibromatous polyp during a screening colonoscopy. This is the second reported case of neurofibromatous polyp of the colon, and the first case of single colonic polyp in a patient with generalized NF. [Figure 1]

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Morphogenesis of Colorectal Neoplasm from the Viewpoints of Isolated Crypts and Pit Pattern
Satoru Tamura, M.D., Ph.D.,* Takayoshi Yamada, M.D., Tomoko Onishi, M.D., Hiroshi Mizuta, M.D., Toshiki Ichimori, M.D., Saburo Onishi, M.D., Ph.D. Department of Endoscopy, Kochi Medical School, Nankoku, Kochi, Japan.

Purpose: Three morphogenetic theories for colorectal neoplasms have been proposed: the first: budding in the proliferative zone, the second: crypt fusion, and the third: top-down morphogenesis. Causes of the differences among these three theories are still not clarified. We evaluated these morphogenetic theories from the viewpoints of isolated crypts and pit patterns in the lesions of depressed, protruded, and laterally spreading type (LST) tumors.

Methods: Depressed type (n = 25), protruded type (n = 19) and LST (n = 39) lesions were examined endoscopically, stereomicroscopically, and histopathologically from 1997 to October 2004. Pit patterns were classified into 6 types. For the crypt isolation, the HCl-digestion method was used.

Results: 1. Features of the lesions: Of the 83 lesions (adenomas: 64, carcinomas: 19), the gender ratio (M/F) and mean age were: 2.3:1 (58/25); 66.2 years (43 to 84). Lesions were located in the rectum (n = 12), sigmoid colon (n = 23), descending colon (n = 11), transverse colon (n = 29), ascending colon (n = 7) and cecum (n = 1). The dominant pit pattern of adenomas in the depressed, protruded, and LST tumors were type 3S, 3L, and 3L respectively. 2. Features of isolated crypts with type 3L pit pattern: The average lengths of the isolated crypts of LST and protruded types were 311 ± 123 micron, 434 ± 163 micron, respectively (p < 0.001), and the average widths of LST and protruded types were 140 ± 68 micron, 172 ± 73 micron, respectively (p = 0.02). The average score of the degree of nodules of the LST and protruded types were 1.18 ± 0.44, 1.57 ± 0.53 respectively (p < 0.0001). As for the features of the isolated crypts, the LST type exhibited a two-layer structure and the protruded type had the shape of a spindle with protuberances. 3. Features of isolated crypts with type 3S pit pattern: The isolated crypts of depressed type lesions were classified into two types: one was a single columnar crypt without bifurcation, and the other was a bifurcated columnar crypt. The bifurcation occurred in the base of tumor crypt. The shape of both isolated crypts was tapered and curved and had an uneven surface without protuberances. Conclusions: It is proposed from our results that depressed type tumor enlarges by the “crypt fission theory” in which a single crypt divides into two crypts, whereas the LST develops by “top-down morphogenesis theory”, and the protruded type tumor develops by the “budding theory”.

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Laparoscopic Right Colectomy Versus Open Right Colectomy for Neoplasia

William Harb, M.D., Michelle M. Olson, M.D., Thomas E. Read, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

Purpose: The purpose of this paper is to determine if there is short-term benefit to laparoscopic versus open right hemicolectomy.

Methods: Records for patients undergoing right hemicolectomy for neoplasia from 8/2000 to 8/2004 were reviewed to determine length of postoperative hospital stay and assess development of wound infection.
Delayed Presentation of Splenic Rupture after Colonoscopy
Richard A. Fortunato, DO, Daniel Gagne, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

Purpose: A review of delayed presentation of splenic rupture after colonoscopy.

Methods: Splenic rupture after a colonoscopy is a rare but potentially fatal complication. Patients typically present with signs of abdominal pain and hemorrhagic shock within minutes to days after the procedure.

Results: We present a case of a 59 year-old woman with a past history of Hodgkin’s disease and gastric bypass who developed increasing abdominal pain three weeks after a routine colonoscopy and polypectomy. The patient presented with hypotension and underwent aggressive resuscitation with IVF and IV pressors. CT scan demonstrated a large subcapsular hematoma of the spleen. Angiography did not reveal active bleeding. Due to the patient’s continued clinical deterioration, she was taken emergently to the operating room for an exploratory laparotomy, which demonstrated a full splenic capsular avulsion and hemorrhage. The patient underwent splenectomy and had an uneventful recovery.

Conclusions: Though usually presenting hours to a few days after colonoscopy, severe splenic injury can have an insidious onset weeks from the original insult. This is the most delayed presentation of such an injury after colonoscopy to date.

Avoiding Conversion in Laparoscopic Colectomy: A Novel Approach
David N. Ferraro, M.D., Thomas E. Read, M.D., Richard A. Fortunato, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Pittsburgh, PA.

Purpose: To evaluate the efficacy of a novel approach to avoid conversion to laparotomy during laparoscopic colectomy.

Methods: Data from a consecutive single surgeon series of 104 patients (56 men/48 women, mean age 63 years) with the intention of proceeding with lap colectomy were reviewed. Patients deemed high risk for conversion were favored, a hand assist device was placed and the procedure performed laparoscopically. If unfavorable, the midline incision was simply extended.

Results: Operative procedures included right colectomy/ileocelecsection, anterior resection/left/sigmoid colectomy, APR, subtotal or total abdominal colectomy. 74 initially approached laparoscopically, 4 required conversion to laparotomy secondary to dense adhesions or ureteral injury. 30 who underwent initial mini-laparotomy, 5 underwent extension of the incision to formal laparotomy because of unfavorable intraperitoneal conditions. 25/30 underwent hand-assisted laparoscopic colectomy, with one conversion to formal laparotomy to secondary to severe diverticulitis with enterocolic fistula. 5/99 in whom laparoscopic access was established by either method underwent conversion to formal laparotomy.

Conclusions: This novel approach to a potentially hostile abdomen allows for rapid assessment of intraperitoneal conditions that would preclude successful laparoscopic colectomy. This strategy is associated with a low rate of conversion from laparoscopy to laparotomy.

Risk Factor Assessment of Submucosal Invading Colorectal Cancers
Satoru Tamura, M.D., Ph.D.,* Takayoshi Yamada, M.D., Tomoko Onishi, M.D., Hiroshi Mizuta, M.D., Toshiki Ichimori, M.D., Yuichi Yokoyama, M.D., Ph.D., Saburo Onishi, M.D., Ph.D. Department of Endoscopy, Kochi Medical School, Kohasu, Okoh-cho, Nankoku, Kochi, Japan.

Purpose: Colorectal submucosal invading cancer is a boundary lesion between endoscopic mucosal resection (EMR) and conventional surgery with regional lymph-node (LN) resection. Because the frequency of LN metastasis is about 10% in the lesion of submucosal invading cancer, a large number of cases with this lesion can be cured by EMR. In the present study, we assess the correlation between LN metastasis and parameters, and extract significant factors by multivariate statistical analysis from these parameters and clarify the indication of EMR.

Methods: During the period from July 1985 to September 2005, a total of 407 lesions of submucosal invading cancers were detected. We classified the submucosal extension according to the vertical level of invasion as sm1, sm2 or sm3. The patterns of infiltrating growth into the submucosal layer were further divided into two groups: expanding growth with a distinct border, and infiltrating growth with an indistinct border.

Results: 1. We treated 142 carcinomas endoscopically and 265 carcinomas surgically. Lymph node metastasis occurred in sm2 and extension cancer in more advanced stages. The frequencies of LN metastasis in each invasion level were as follows (p = 0.0269): sm1, 0/59(0%); sm2, 10/116(8.6%); sm3, 11/91(12.1%).
2. As for patterns of invasion, the frequencies of LN metastasis in the groups of expanding growth and infiltrating growth were 0.9% (1/109) and 13% (20/154), respectively (p = 0.0004).
3. The frequencies of LN metastasis in the lesions of lymphatic permeation positive and venous invasion positive were 14/81(17.3%, p = 0.0002) and 7/66(10.6%, p = 0.358) respectively.
4. As for the location of cancer, LN metastasis is statistically significant high rate in the sigmoid colon (Odds ratio 2.963, 95%CI 1.181–7.433).
5. The results of multivariate statistical analysis form these significant parameters were as follows: infiltrating growth pattern (Odds ratio 11.343, 95%CI 5.564–23.137, p = 0.001); lymphatic permeation positive (Odds ratio 4.21, 95%CI 1.544–11.481, p = 0.005); sigmoid colon (Odds ratio 3.553, 95%CI 1.31–9.636, p = 0.013).

Conclusions: The significant factors which extracted by multivariate statistical analysis were infiltrating growth pattern, lymphatic permeation positive and tumor location of sigmoid colon. The frequencies of LN metastasis were 8/22 (36.4%) in the cancers with all these three factors on the one hand and 0/56(0%) in the cancers with none of these three factors on the other hand (p = 0.0001).

The Correlation of Colonoscopy Preparation Grading Scales
Donald J. Denby, M.D., Jack D. Bragg, DO, Clint G. Wallis, M.D., Bin Ge, M.D., Greg F. Petroski, Ph.D., John B. Marshall, M.D.* Division of Gastroenterology, University of Missouri, Columbia, MO and Office of Medical Research and Biostatistics, University of Missouri, Columbia, MO.

Purpose: The purpose of this study was to identify a simplified means of scoring bowel preparation quality by way of comparing four different bowel preparation grading scales.

Methods: 310 patients were prospectively enrolled in a study to determine the adequacy of colonoscopy preparation using 4 different grading scales/questionnaires. The first questionnaire (Q1) evaluated the prep in relation to the remnant stool in the colon. The second (Q2) evaluated the prep in relation to potential lesions missed on colonoscopy. The third (Q3) evaluated the aspiration ability of the remnant stool. The fourth (Q4) evaluated the colon in relation to the visualization of the underlying colonic mucosa. Each questionnaire could be answered on a four point ordinal scale with a short phrase anchoring each response option. Pairwise correlations between the items were estimated and Cronbach's Coefficient Alpha was calculated to judge the internal consistency of the items when combined into a single summated scale.

Results: A Coefficient Alpha of 0.70 has traditionally been regarded as a minimally acceptable value for significance. In this study, alpha for the four items was 0.97 indicating a high degree in internal consistency. The inter-item correlations were all statistically significant (p < 0.001) and all greater than 0.88 in magnitude.

Conclusions: The four items comprise a highly reliable scale, but the inter-item correlations are sufficiently high as to suggest that the four questionnaires are redundant rather than individually informative. Thus, it may be the case that a single questionnaire is sufficient for judging the quality of the prep. If such scales can be compared in a similar manner to a reliable and validated colonoscopy preparation grading scale, the task of grading colonoscopy preparation could be simplified. This will be the subject of future research.

Conclusions: This study found that diabetes and Medicaid insurance status predisposed patients to a less than adequate colonoscopy preparation. Two other factors (history of arthritis and indication of hematochezia) were also associated with a statistically increased risk of poor colonoscopy preparation but to a lesser degree. Ideally, using this information, certain pre-procedural questions could be utilized to modify standard preparation instructions for high risk patients.

380 Oral Mesalamine (Asacol) in Treating Diverticulitis
Bertram T. Chinn, M.D.* Colon and Rectal Surgery, UMDNJ-RW Johnson University Hospital, New Brunswick, NJ.

Purpose: Diverticulitis is an inflammatory process generally involving the sigmoid colon. Like Crohn's Disease, the inflammation is usually segmental in nature and may result in recurrent attacks of pain and alterations to bowel habits. In more complicated cases, sepsis with abscess formation or strictures and fistulas may occur. There is little in the literature comparing the similarities of these two entities and even less describing the treatment of diverticulitis with mesalamine (Asacol). The purpose of this is to evaluate the potential benefit of mesalamine in select cases of diverticulitis.

Methods: Two patients with ongoing symptoms of pain and bloating from diverticulitis were evaluated for alternative management prior to surgery. Symptoms were present for over 1.5 years despite various non-operative managements including antibiotics and anti-spasmodics. Prior colonoscopies and CT scans were consistent with diverticulitis. Endoscopic biopsies demonstrated mucosal inflammation but no histologic evidence of Crohn's Disease. After excluding complications of diverticulitis, treatment with oral mesalamine (2.4 grams daily) was implemented.

Results: A 64 year old female and a 55 year old male were treated with oral mesalamine. In each case, symptoms of pain resolved within 6 weeks. Mucosal inflammation improved or resolved as well. Both patients remained asymptomatic while taking mesalamine. The female patient ultimately developed symptoms of bloating and constipation secondary to stricture formation 6 years later and required an elective sigmoid resection. She however had no recurrence of the symptoms which led to her initial presentation. The male patient continues to remain without problems 4 years after beginning mesalamine. The average dose and duration of mesalamine was 2.4 grams daily for 6 years (female patient) and 2.4 grams daily for 4 years (male patient). No side effects were encountered with mesalamine therapy.
Purpose: Visicol® Tablets, an effective colonoscopy prep, contains a MCC tablet binder, that may appear as white residue in the ascending colon (AC). A new MCC-free NaP formulation (INKP-102) was developed. In a multicenter, investigator-blinded study, INKP-102 at 40 (60g) and 32 (48g) tabs, taken po as 20 tabs the night before and 20 or 12 tabs 3–5 hrs prior to procedure, was compared to V at the recommended 40 (60g) tabs dose.

Methods: Prior to colonoscopy eligible adult pts were randomly assigned to 40 tabs V, taken 3 at a time, 40 tabs or 32 tabs INKP-102, 4 at a time; each increment was to be taken with 8 oz of clear fluid. OCC efficacy was assessed using a 4-point scale based on retained “colonic contents.” The primary endpoint was the OCC response rate to treatment (score of excellent/good) using a 4-point scale based on retained “colonic contents.” The primary endpoint was the OCC response rate to treatment (score of excellent/good) vs. non-response (fair/inadequate). OCC response rate was also obtained.

Results: 816 pts were randomized; 110 (103 before study med, per-protocol) were discontinued; 2 excluded for investigator error; 704 pts were included

Summary of OCC & ACC Response Rates

<table>
<thead>
<tr>
<th>Visicol</th>
<th>INKP-102 40g</th>
<th>INKP-102 32g</th>
</tr>
</thead>
<tbody>
<tr>
<td>60g (40 tab)</td>
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<td>N = 236</td>
</tr>
<tr>
<td>60g (40 tab)</td>
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</tr>
<tr>
<td>48g (32 tab)</td>
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<tr>
<td>Responder n (%) OCC</td>
<td>222 (94.5%)</td>
<td>226 (97.0%)</td>
</tr>
<tr>
<td>ACC</td>
<td>208 (88.5%)</td>
<td>220 (95.7%)</td>
</tr>
<tr>
<td>P-value for diff.</td>
<td>0.1554a</td>
<td>0.6198a</td>
</tr>
<tr>
<td></td>
<td>0.0019b</td>
<td>0.0272b</td>
</tr>
<tr>
<td>Lower limit of one-sided</td>
<td>–1.0a</td>
<td>–2.8%a</td>
</tr>
<tr>
<td>97.5% CI of diff.**</td>
<td>2.8%b</td>
<td>0.6%b</td>
</tr>
<tr>
<td>P-value for noninferiority</td>
<td>&lt;0.0001*</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

*Significant at the 0.05 level; **OCC, b ACC; 1 comparison with Visicol; ** If the lower limit of the one-sided 97.5% confidence interval is ≥–10%, then the data support non-inferiority over Visicol.

Conclusions: Pts taking new 32 tab MCC-free NaP tablet (INKP-102) had comparable OCC and were statistically superior for ACC. INKP-102 pts had fewer AE’s, and excellent compliance. The preferred dosing regimen for bowel purgation is 32 tabs of INKP-102.

Purpose: The aim of our study was to evaluate the incidence of adenomatous colon polyps in patients referred for colorectal cancer screening. Our secondary aim was to evaluate the incidence of diverticulosis as well as the success rate of complete colonoscopy with usual preparation and conscious sedation.

Methods: We retrospectively evaluated all the colonoscopies performed as outpatient using conscious sedation at our Virginia Ambulatory Surgical Center in consecutive fashion from August 2002 to March 2005. All the colonoscopies were performed by a single attending gastroenterologist (KA) using Fujinon video colonoscopes. Inclusion criteria included patients 50 years old and above referred for routine screening colonoscopies. Exclusion criteria included anyone with family history of colon cancer or polyps, personal history of colon cancer or polyps, diarrhea, constipation, change in bowel habits, anemia, or rectal bleeding.

Results: Of 1031 colonoscopies performed by KA, 222 procedures were excluded. Of 809 procedures evaluated, 544 (67.4%) were noted to have one or more polyps, including 2 (2.5%) adenocarcinomas, 274 (33.9%) patients with tubular adenomas, 14 (1.7%) with tubulovillous adenoma, and 264 (32.6%) with hyperplastic polyps. When polyps were further categorized based on the largest size, 159 of 371 diminutive polyps (4mm or less) were identified as adenomas. 94 of the 129 intermediate polyps (5–9mm) were adenomas, and 29 of the 45 large polyps (>1cm) were adenomas. Cecal intubation was successful in 99.8% and terminal ileum intubation in 95 percent. Diverticulosis was present in 52.8 percent of patients.

Conclusions: The incidence of colonic adenomas discovered during screening of average risk individuals was 35.6%, which is significantly higher than previously reported. Of polyps found, 53% were adenomatous or villous lesions. Surprisingly 42.8% of polyps <5mm were also adenomas. In experienced hands complete endoscopic screening of the colon is almost always possible and removal of all polyps regardless of size is important.

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bleeding. Further studies are necessary to better define ethnic variations in lower gastrointestinal bleeding.

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Relationship of Ischemic Colitis, Irritable Bowel Syndrome and Hysterectomies: A Community Study
Douglas J. Sprung, M.D., F.A.C.G.* Medicine, Gastrology Group, Maitland, FL.

Purpose: To search for an association between ischemic colitis (IC) and irritable bowel syndrome (IBS) as has been suggested in the literature.

Methods: A retrospective review was undertaken of all patients with IC over the past 10 years in our community based private practice.

Results: 32 patients had a diagnosis of IC. 28 (87.5%) female, 4 (12.5%) male, mean age 65 (for both males and females). 11/32 (34%) had a prior diagnosis of IBS (all were female) and 14/32 (44%) had a prior hysterectomy. Of the 32 patients, 26 (81%) had 1 episode of IC, 5 (16%) had 2 episodes and 1 (3%) had 3 episodes. Location of IC was sigmoid (33%) and descending colon (67%). Surgery was performed in 2 patients. Pathological findings were consistent with IC only 84% of the time, although endoscopic findings were present 100% of the time. 5 patients were age 41–49 and only 1 was under 40 years old.

Conclusions: 1. Ischemic colitis is not common, occurring in 32/19,682 (0.16%) of colonoscopies performed over the past decade.
2. 34% of the IC patients had a prior diagnosis of IBS, and all were female.
3. 44% of the IC patients had prior hysterectomy. This observation is of unknown significance.
4. Of 7928 IBS patients seen over the past decade, 11 had IC (0.13%), which is about the same prevalence as IC in the cohort of all patients undergoing colonoscopy (0.16%).
5. Our IBS patients with IC were older (mean age 65), with only 1 patient under age 50.
6. It is difficult to ascertain any definitive relationship between IBS and IC from the above data.

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Gastrointestinal Manifestations of Cowden Syndrome
Scott H. Mackenzie, M.D., Robert F. Wong, M.D., Scott Kawada, M.D.,* Randall W. Burt, M.D. Gastroenterology, University of Utah, Salt Lake City, UT and Gastroenterology, VAMC, Salt Lake City, UT.

Purpose: Cowden syndrome (CS) is an under diagnosed, under recognized, autosomal dominant inherited syndrome. CD is associated with germline mutations in the PTEN gene and exhibits an increase risk of breast, thyroid, and possibly other malignancies. Although various benign gastrointestinal lesions, including esophageal glycogenic acanthosis and hamartomatous polyps have been described, the colorectal cancer (CRC) risk remains poorly characterized.

Methods: Nine patients (7 female, 2 males with a median age of 52.3) with a previous diagnosis of CS based on clinical criteria (International Cowden Consortium version 2000) and/or presence of a PTEN mutation were studied. All patients underwent colonoscopy, and four patients also underwent upper endoscopy.

Results: One case was diagnosed with CRC at age 42. Four patients had a family history of CRC, three with affected first degree relatives (FDR). Two cases had a family history of colon polyps and CRC before age 45 years of age. One case had two FDR with CRC and a second degree relative with CRC at age 12. Two cases had FDR with CRC after age 45. Multiple colon polyps were observed in seven patients (78%). The polyps were mostly sessile, 1 to 4mm in size and universally distributed throughout the colon. Hamartomatous polyps were present in all cases with polyps. Three patients had adenomatous polyps. Inflammatory and hyperplastic polyps were also seen. Upper GI manifestations included esophageal acanthosis, and, multiple gastric and duodenal non-adenomatous polyps were seen.

Conclusions: We found CRC in 1/9 (11%) patients with CS and three cases with first degree relatives with CRC. This study suggests further investigation of CS registries for prevalence of CRC and the potential contribution of CS to familial CRC. Endoscopic surveillance may be indicated in patients with CS.

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Randomized Controlled Trial of Long Term Outcome of Biofeedback Therapy (BT) for Dysynergic Defecation
Satish C.S. Rao,† K. J. Kinkade, M. J. Miller, K. Brown, P. E. Stumbo, B. M. Zimmerman, K. S. Schulze. Internal Medicine, University of Iowa, Iowa City, IA.

Purpose: Recent controlled trials have shown that BT is more effective than sham feedback or standard therapy or diapazem in the short term treatment of dysynergia (Gastroenterology 2005; 128: A266; A269). But, there has been no controlled long term study. Our aim was to compare 1 year outcome of BT (manometric- assisted pelvic relaxation, coordination and simulated defecation training), with standard therapy (ST; diet, exercise, laxatives).

Methods: 52 patients (*m = 47;5) with dysynergic defecation were randomized. Stool diaries, visual analog scales (VAS), colon transit, anorectal manometry&balloon expulsion tests were assessed before, after therapy&1 year.

Results: Table = mean ± sem. Repeated-measures ANOVAs,* = Fisher’s exact. Bold = p < 0.05 (Table). 44/52 patients completed 3 months treatment (end active); 21 randomized to BT, 23 to ST and 8 dropped out. Subsequently, in the BT group, 13/21 completed 1 year follow up and 7 declined. In the ST group, 7/23 completed 1 year, 6 failed treatment (1 had surgery &5 Biofeedback) but were included in ITT analysis&10 declined. Dysynergia pattern normalized, defecation index increased, balloon expulsion and colonic transit improved and bowel satisfaction improved in the BT group but not in the ST group.

Conclusions: Anorectal and colonic function and bowel satisfaction improved significantly in patients receiving biofeedback and was maintained at one year. In contrast, 46% patients failed standard therapy and there was little change in bowel function. Biofeedback is more effective than standard therapy in the long term treatment of dysynergia. Supported by NIH[RO[DK57100–0141] and NIH [HD41248–03].

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Sensitivity of Colon Cancer Cells to NSAIDS–Role of Survivin
Sarathy Mandayam, M.D., Andrzej Tarnawski, M.D., F.A.C.G.,* Shiv-Kwei Chiou, Ph.D. Division of Gastroenterology, University of California–Irvine, Orange, CA and Division of Gastroenterology, Long Beach VA Medical Center, Long Beach, CA.

Purpose: To determine whether NSAIDS can affect the sensitivity of cancer cells to chemotherapy.

Methods: Colon cancer cells were cultured in the presence or absence of NSAIDS. The cell survival was determined using the MTT assay.

Results: The sensitivity of colon cancer cells to NSAIDS was significantly increased in the presence of NSAIDS.

Conclusions: NSAIDS can increase the sensitivity of colon cancer cells to chemotherapy.
Purpose: Survivin regulates cell division and inhibits apoptosis. NSAIDS decrease survivin expression, increase apoptosis, and reduce growth of colon polyps and cancers. Three isoforms of survivin, with differing effects on apoptosis, have been identified. Expression of survivin isoforms in colon cancer cells and the effect of NSAIDS on the individual isoforms has not yet been studied. Our goals were: (1) to determine survivin isomform expression in different colon cancer cell lines and (2) to test the effects of NSAIDS on survivin isoforms in colon cancer cells.

Methods: Two colon cancer cell lines–HT-29 and RKO–were treated with indomethacin at 0.5 mM concentration. Cells were harvested at 0 hours (untreated, control), 30 minutes, 1 hour, 3 hours, and 5 hours. The presence of survivin isoforms was determined using RT-PCR and expression level of survivin isoforms was determined using real-time PCR. Western blot was used to examine survivin protein expression and LDH assay was performed to evaluate cell death after cells had been treated with 0.5 mM indomethacin for 0, 3, 6, 24 and 48 hours.

Results: 1. All 3 survivin isoforms–wild-type, 2b, and ∆Ex3–were present in both cell lines.
2. Indomethacin significantly downregulated levels of wild-type survivin and survivin ∆Ex3 mRNA but not survivin 2b mRNA in RKO cells.
3. Indomethacin did not affect survivin isoform mRNA levels in HT-29 cells.
4. Consistent with the mRNA data, treatment with indomethacin downregulated wild-type survivin protein expression in RKO cells but not in HT-29 cells.
5. LDH assay showed that RKO cells (75.7 ± 1.1% cell death at 48h) were more susceptible than HT-29 cells (25.4 ± 3.7% cell death at 48h) to cytotoxicity induced by indomethacin.

Conclusions: 1. All three isoforms of survivin are present in both colon cancer cell lines.
2. Survivin downregulation likely plays a role in indomethacin-induced cytotoxicity in colon cancer cells.
3. The abundance of the pro-apoptotic survivin isoform, 2b, relative to the anti-apoptotic isoforms, wild-type and ∆Ex3, in response to indomethacin may be a mechanism that determines sensitivity of cells to NSAID induced cytotoxicity.
4. Our data showed a difference in the response of two similarly undifferentiated colon cancer cell lines to indomethacin. This has implications in the use of NSAIDS in colon cancer chemoprevention.

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Isolated Langerhans Cell Histiocytosis [LCH] of the Colon Occurring in a Diminutive Poly

Nadia A. Trigg, M.D., J. Walloch, M.D., C. Torres, M.D., Robert Stein, M.D.,* Charles Berkelhammer, M.D., F.A.C.G. Gastroenterology, University of Illinois, Oak Lawn, IL and Pathology, University of Illinois, Oak Lawn, IL.

Purpose: LCH is a clonal proliferative disorder that results in the accumulation of tissue histiocytes in one or multiple organs. Colonic involvement is rare. Diminutive polyps are usually benign but rarely have significant pathology including invasive cancer. We describe to our knowledge the first reported case of isolated LCH of the colon occurring in a diminutive submucosal polyp in an adult.

case: A 48 year old asymptomatic female with a family history of colon cancer, underwent a screening colonoscopy. In the sigmoid colon a 5 mm submucosal polyp was seen and snared. Pathology showed a focal infiltrate of Langerhans cells extending from the lower lamina propria through the muscularis mucosa into the superficial mucosa. The origin of the infiltrate was confirmed by reactivity of the cells by CD1a (Langerhans cells), S-100, CD68 (macrophages) were weakly positive, and CD45 (leukocyte common antigen) was weakly positive. The infiltrate was negative for cytokeratin AE1/AE3, cytokeratin CAM 5.2, CD-3 (T cell), CD-20 (B cell), myeloperoxidase, and muramidase. The polyp was endoscopically completely excised, and microscopic resection margins were clear. Multiple biopsies throughout the colon, stomach, duodenum, failed to reveal any additional sites, CT scan of the abdomen, and chest, and bone scan, were unremarkable. The patient was diagnosed as having an isolated LCH of the colon. There was no recurrence after one year of follow-up.

Conclusion: We reported to our knowledge the first case of an isolated LCH of the colon occurring in a diminutive submucosal polyp in an adult. This also, illustrates that diminutive polyps can rarely have unusual findings.

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Colonscopic Screening in Asymptomatic Patients in a Non-Profit HMO Open Access GI Practice

David Geier, M.D., Alex Hower, M.D., Roy Libel, M.D., Donald Mangum, M.D., Donald Nelson, Jesse Taylor, M.D., Donald Thompson, M.D., Allan P. Weston, M.D.,* Gastroenterology, St. John’s Clinic, Springfield, MO.

Purpose: Colorectal cancer and polyp screening has been accepted as the optimal screening test for average risk, asymptomatic subjects beginning at age 50. Published studies concerning the results of screening colonoscopy are predominantly from VA/ University programs. However, given socioeconomic, racial and gender biases inherent to these studies, generalization of these results to general population remains unclear. The purpose of these study was to examine the endoscopic results of colorectal screening in an open access endoscopy facility dedicated to serve a large, non-profit, HMO in Southern Missouri.

Methods: Consecutive colonoscopy screening examinations between 3/04 and 3/05 for asymptomatic subjects referred by their PCP were prospectively entered into database. Information captured at time of endoscopy included age, gender, family history of colon cancer/polyps, quality of preparation, success at reaching cecum, polyp size and location, coincident lesions detected, and immediate complications. Post procedure data captured included polyp histology, colorectal cancer stage, & polypectomy complications. All procedures were performed by 8 experienced GI’s with Olympus Colonoscopes (PCF-160AL, CF-Q160L). Polyps were considered advanced if TA ≥ 1 cm, with villous component, with HGD, or invasive cancer.

Results: 2138 colonoscopies fulfilled criteria for asymptomatic screening for CRC (1037 M; 1101 F). Average age ± SD of 62.2 ± 9.2. 6% of cases were in subjects with one or more family members with CRC or polyps. Quality of colonoscopy prep was considered very good to excellent in 99.2%. The cecum was reached in 98.7%. No major complications (perforations, polypectomy bleeding, etc.) occurred. Non-advanced adenomatous polyp(s) were removed in 399 (18.7%). Advanced polyps were noted in 195 (9.1%) including 0.61% (13) with colon cancers (Ce/R/ HF 4, Tr 1, Left 3, Sig 3, Re 2). 3 patients had large sessile adenomatous polyps that required surgical resection. Additional significant findings included 2 small rectal carcinoids, 2 anal canal CIS lesions (surgically excised), 4 muscularis mucosa leiomyomas, 2 silent colonic IBD, and 1 pinworm infestation.

Conclusions: Screening performed by GI’s in an open access community setting is characterized by high quality preps, cecal intubation rates > 98% and no major complications. Yields of non-advanced and advanced colonic polyps are significant and mirror that in VA/University settings.

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VOTE (Visicol Observational Tolerability & Experience) Registry Demonstrates Few Physician Calls, Good Patient (pt) Tolerance, and pt Preference for Visicol® Tablets (V) in Private Practice


Purpose: V: a colonoscopy tablet bowel preparation, demonstrated excellent cleansing and pt tolerance in clinical trials. Pts tolerated V better than the 4L polyethylene glycol (PEG) solution. (Kastenberg, GIE, 2001). The most common V side effects were nausea (36%), vomiting (6%), bloating (45%) and abdominal pain (30%). With the exception of abdominal pain, which was similar for the two treatments, GI side effects occurred significantly less frequently in the V group compared to PEG. An open registry with a pt
survey was performed to assess if pt tolerance was similar and to assess pt preference when V was used by practicing gastroenterologists.

Methods: Participating practitioners selected 5 pts, scheduled for colonoscopy. These pts were prescribed V, according to the physician’s usual practice. After taking the preparation but before the colonoscopy, pts completed a patient questionnaire. Data were collected from each office and entered centrally into the Registry. Physicians reviewed their pts’ responses.

Results: A total of 163 physicians participated; 741 questionnaires were completed but not all respondents answered all questions. Of the 725 pts who recorded age, 30% were ≥ 65 yrs. There were 448 F and 273 M. Weight ranged from 85 to ≥ 250 lbs. Prior bowel cleansing preps were identified by 372 pts. Pts were asked to rate GI side effects as none, mild, moderate, or severe. Mean (± SD) total dose prescribed was 29.0 ± 5.0 tabs.

Summary of VOTE Questionnaire

<table>
<thead>
<tr>
<th>Question</th>
<th>N/# Responders</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completed prep</td>
<td>688/713</td>
<td>96.5%</td>
</tr>
<tr>
<td>Overall Nausea</td>
<td>191/683</td>
<td>27.9%</td>
</tr>
<tr>
<td>Severe nausea</td>
<td>16/663</td>
<td>2.3%</td>
</tr>
<tr>
<td>Overall Vomiting</td>
<td>45/666</td>
<td>6.8%</td>
</tr>
<tr>
<td>Severe vomiting</td>
<td>13/666</td>
<td>2.0%</td>
</tr>
<tr>
<td>Overall Bloating</td>
<td>178/681</td>
<td>26.1%</td>
</tr>
<tr>
<td>Severe bloating</td>
<td>14/681</td>
<td>2.1%</td>
</tr>
<tr>
<td>Overall Abdominal pain</td>
<td>137/677</td>
<td>20.2%</td>
</tr>
<tr>
<td>Severe abdominal pain</td>
<td>6/677</td>
<td>0.9%</td>
</tr>
<tr>
<td>Call MD during prep ingestion for a side effect</td>
<td>26/724</td>
<td>3.6%</td>
</tr>
<tr>
<td>Would take V in future</td>
<td>658/717</td>
<td>91.8%</td>
</tr>
<tr>
<td>Would take V over previous prep</td>
<td>372/400</td>
<td>93%</td>
</tr>
<tr>
<td>Would like physicians to offer choice of prep</td>
<td>586/709</td>
<td>82.7%</td>
</tr>
</tbody>
</table>

Conclusions: These data are consistent with data from previous V clinical trials, demonstrating excellent tolerability for V. Per the questionnaire, severe GI side effects were uncommon; physicians were rarely called by patients for safety issues. Most pts favored taking V over a previous prep as well as having a choice of bowel prep. V is an excellent purgative choice for community GI practitioners.

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Sigmoid Endometriosis Presenting with Colonic Obstruction after Seat Belt Trauma: A Case Report
Mohammad A. Al-Haddad, M.D., *Ernest P. Boukas, M.D., John R. Cangemi, M.D. Gastroenterology and Hepatology, Mayo Clinic Jacksonville, Jacksonville, FL.

Purpose: Extra-pelvic endometriosis is a rare disorder affecting premenopausal females. Gastrointestinal manifestations of this disease have been well characterized. However, colonic involvement with strictures has been rarely reported. A 26-year-old previously healthy female patient presented with constipation and abdominal pain after being involved in motor vehicle accident where she sustained seat belt trauma. Over the course of few months she developed symptoms of abdominal pain and bleeding per rectum along with peri-umbilical bluish discoloration at the time of her menstrual period. She was initially treated for Crohn’s disease with little response. She was hospitalized later for partial colonic obstruction. A barium enema showed sigmoid stricture with proximal colonic dilatation. Colonoscopy revealed a 6-cm sigmoid stricture with no mucosal abnormalities proximal to it (Fig. 1). Biopsies from the site were normal. The patient underwent exploratory laparotomy with segmental colonic resection and had an uneventful post-operative course. Histological examination confirmed the presence of endometrial-type glands extending circumferentially around the sigmoid and invading the submucosa, thus casing the stricture. The role of pelvic seat-belt trauma in triggering the endometriosis is unclear but could have well caused the spread of the disease outside the uterine cavity and into adjacent pelvic structures. The patient had no recurrence of her symptoms after the surgery on subsequent follow up. [figure 1]

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Portal Hypertensive Colopathy in Patients with Liver Cirrhosis
Katsuya Shiraki, M.D., F.A.C.G., *Keichi Ito, M.D., Hitoshi Yoshimura, M.D., Hirohiko Fuke, M.D., Akira Hashimoto, M.D., Takeshi Nakano, M.D. First Department of Internal Medicine, Mie University School of Medicine, Tsu, Mie, Japan.

Purpose: Portal hypertensive colopathy is found and is thought to be an important cause of lower gastrointestinal hemorrhage in patients with cirrhosis. In this study, we evaluated the prevalence of colonic mucosal changes in patients with liver cirrhosis and its clinical importance.

Methods: We evaluated the colonoscopy findings and liver function of 55 patients with liver cirrhosis over a 6-year period. The main cause of liver cirrhosis was post-viral hepatitis (68%) related to hepatitis B (6%) or C (62%) infection. All patients underwent upper gastrointestinal endoscopy to evaluate the presence of esophageal varices, cardiac varices, and congestive gastropathy, as well as a full colonoscopy to observe changes in colonic mucosa. Portal hypertensive colopathy was defined endoscopically in patients with vascular ectasia, redness, and blue vein. Vascular ectasia was classified into two types: type1, solitary vascular ectasia; and type2, diffuse vascular ectasia. Data are expressed as mean ± SD. Statistical comparisons were made with the chi-square test. A p < 0.05 was considered statistically significant.

Results: Overall portal hypertensive colopathy was present in 32 patients (66%), including solitary vascular ectasia in 18 patients (36%), diffuse vascular ectasia in 20 patients (42%), redness in 10 patients (21%) and blue vein in 6 patients (12%). As the Child-Pugh class increased in severity, the prevalence of portal hypertensive colopathy increased. Child-Pugh class B and C were significantly associated with portal hypertensive colopathy. Portal hypertensive gastropathy, esophageal varices, ascites and hepatocellular carcinoma were not related to occurrence of portal hypertensive colopathy. The platelet count was significantly associated with portal hypertensive colopathy, but the prothrombin time, serum albumin level, total bilirubin level and serum ALT level were not related to occurrence of portal hypertensive colopathy.

Conclusions: As the Child-Pugh class worsened, the prevalence of portal hypertensive colopathy increased in patients with liver cirrhosis. A colonoscopy examination in the patients with liver cirrhosis is indicated, especially those with worsening Child-Pugh class, to prevent complications, as lower gastrointestinal bleeding.
Defecography and the Diagnosis of Clinically Significant Rectoceles

Amar Bansal, M.D., Cynthia Lau, M.D., Claire Smith, M.D., Mary Morrissey, Sc.D, Keith Bruninga, M.D.* University Gastroenterology, Rush University Medical Center, Chicago, IL.

Purpose: A rectocele is any bulge outside the line of the rectal wall that can be identified on defecography. Surgical criteria for repair is largely symptom-based. However, the literature implies size can be clinically significant. The aim of our study is threefold: (1) Assess the incidence of rectoceles among patients who present for defecography. (2) Specifically identify those patients with clinically significant rectoceles. (3) Determine if specific patient complaints are associated with clinically significant rectoceles.

Methods: Between May 1993 and May 2002, 659 consecutive patients with various gastrointestinal (GI), genitourinary (GU), and gynecologic (GYNE) symptoms had a defecography examination at a single, tertiary care center. Almost all were performed and reviewed by a single gastrointestinal radiologist. All exams were reviewed for the presence of a rectocele. Furthermore, clinically significant rectoceles, as defined in the literature, were contrast-retaining rectoceles greater than or equal to four centimeters.

Results: A rectocele was seen in 482/659 patients (73%). Incidence of rectoceles by patient indications: GI complaints 145/218 (67%), GU complaints 43/54 (80%), and GYNE complaints 148/203 (73%). Patients with a combination or unknown complaints: 146/184 (79%). Overall, 166 of the 482 rectocele patients had contrast-retaining rectoceles greater than or equal to 4 cm (34%). Thus, 166 of the total 659 patients had clinically significant rectoceles (25%). For GI, GU, and GYNE specific complaints the incidence of significant rectoceles was 57/218 (26%), 15/54 (28%), and 42/203 (21%) respectively. There was no statistical difference (p = 0.34).

When looking at specific GI complaints of constipation, fecal incontinence, and rectal pain, the incidence of rectoceles was 79/110 (72%), 17/31 (55%), and 5/11 (45%) respectively. The incidence of significant rectoceles was 35/110 (32%), 4/31 (13%), and 1/11 (9%), respectively, which was statistically significant (p = 0.043).

Conclusions: There is a high incidence of rectoceles (73%) among patients who have had defecography. Overall, 25% of patients had clinically significant rectoceles as defined by the literature. There was no statistical difference in clinically significant rectoceles when comparing patients with various GI, GU, or GYNE indications. However, when reviewing specific GI complaints, constipation had a statistically higher likelihood of having a significant rectocele as compared to fecal incontinence and rectal pain.

Expression of Cell Adhesion Molecules on Vascular Endothelial Cells in Human Rectal Cancer

Yunhai Fang, M.D., Zhiyu Liu, M.D.,∗ Yao Chen, M.D., Niannning Gong, M.D., Yanli Liu, M.D. Department of Anatomy, Shandong University School of Medicine, Jinan, Shandong, China and Department of Anatomy, West China Center of Medical Sciences Sichuan University, Chengdu, Sichuan, China.

Purpose: In order to probe the relationship between expression of cell adhesion molecules and diffusion of cancer cells, our researches investigated the expression of cell adhesion molecules in peritumoral tissues and peritumoral lymph nodes.

Methods: 16 specimens of rectal cancer were obtained from peritumoral rectal tissues and peritumoral lymph nodes of rectal cancer patients and 6 specimens of health adults were taken as control. Immunohistochemical SP method was used to study the expression of intercellular adhesion molecule-1 (ICAM-1), carcinoembryonic antigen (CEA) and platelet-endothelial cell adhesion molecule-1 (CD31). The reactions were revealed using diaminobenzidine (DAB) substrate.

Results: ICAM-1 and CEA were expressed on the vascular endothelial cells of peritumoral rectal tissues and peritumoral lymph nodes. Reaction products were brown yellow and located in the cell membrane and cytoplasm. ICAM-1 and CEA were expressed on vascular endothelial cells of metastasized lymph nodes inferior to peritumoral rectal tissues and peritumoral lymph nodes. However, there was negative expression on vascular endothelial cells of specimens taken from health adults. CD31 was expressed on the vascular endothelial cells of peritumoral rectal tissues and peritumoral lymph nodes. Reaction products were also brown yellow and located in the cell membrane and cytoplasm. But different from ICAM-1 and CEA, CD31 was also expressed on vascular endothelial cells of rectal tissues and lymph nodes taken from health adults with the same intensity.

Conclusions: Our researches showed that ICAM-1 and CEA seem to play a stable adhesion effect between cancer cells and endothelial cells. However, whether CD31 plays a role in the interaction between cancer cells and endothelial cells still need further study.

Frequency of Gastrointestinal Lesions in HIV-Infected Patients with Positive Fecal Occult Blood Tests: A Prospective Colonoscopy Study


Purpose: The widespread use of highly active antiretroviral therapy (HAART) has significantly increased the life expectancy of HIV(+) patients, and many are living well beyond 50 years of age. Although fecal occult blood testing (FOBT) is recommended for all patients starting at age 50, there are no published data on the utility of FOBT in HIV(+ ) patients. The aim of this study was to determine the frequency of colonic lesions in asymptomatic HIV (+) patients with a positive FOBT.

Methods: Consecutive patients ≥ 50 years of age who were referred for evaluation of a positive FOBT were prospectively identified. Prior to colonoscopy, all patients were interviewed by a trained research assistant who obtained detailed clinical data. Colonic lesions which were considered clinically important included cancer, adenomatous polyps ≥ 1 cm, active colitis, colonic ulcers ≥ 1 cm, and vascular ectasias that numbered ≥ 5 or ≥ 8 mm in diameter.

Results: 1,232 patients were enrolled, of whom 91 (7.4%) were HIV(.). Although there was no difference in gender (p = 0.80), HIV(+) patients were younger (63.3 vs 69.1 years, p < 0.001) and differed according to race (p = 0.01), with more blacks in the HIV(+) group (48.4% vs 32.3%). Among HIV(+) patients, 56.0% had a CD4 count < 350 cells/mm3, 53.8% had undetectable HIV RNA, and 81.3% were on HAART. Colonoscopy was complete to the cecum in 95.6% of HIV(+) and 97.0% of HIV(-) subjects (p = 0.45). Clinically important lesions were not more common in HIV(+) patients (30.8% vs 26.3%, p = 0.35) and did not differ after adjusting for age, gender, and race (OR = 1.49; 95% CI, 0.92–2.44). The proportion of colon adenomas ≥1 cm (17.6% vs 15.0%, p = 0.51) and cancers (8.8% vs 7.3%, p = 0.59) were similar in the 2 groups. Only 1 HIV(+) patient had an opportunistic infection (CMV ulcers). Among HIV(+) patients, there was no difference in the frequency of clinically important lesions between subjects with a CD4 count < 350 cells/mm3 and those with higher CD4 counts (35.3% vs 25.0%, p = 0.29), patients with and without undetectable HIV RNA (32.7% vs 28.6%, p = 0.67), or between those who were and were not taking HAART (33.8% vs 17.6%, p = 0.19).

Conclusions: Screening for colorectal cancer with FOBT in HIV(+) patients ≥ 50 years of age is beneficial. Complete colonoscopy should be offered to all individuals with a positive FOBT, regardless of HIV status.

Race Based Differences in Colonoscopic Findings in Individuals Less Than Age 50

Kaleem M. Rizvon, M.D., Duane Moise, D.O. Theodore Perlman, M.D., Steven Yang, M.D., Paul J. Mustacchio, M.D.* Gastroenterology, Nassau University Medical Center, East Meadow, NY.
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**Purpose:** To identify the results of colonoscopy performed in patients less than 50 years of age and to study any differences in colonoscopy findings based on race

**Methods:** A retrospective study of colonoscopic examination results, in individuals less than age fifty, was carried out for a three year interval between January 01, 2001 and December 31, 2003, at our tertiary care teaching hospital. During this time, regardless of indication, 218 such examinations were performed. Patients with preexisting diagnosis of Inflammatory Bowel Disease (29) were excluded. In addition, 12 examinations were not included due to unclear patient information regarding race or completion of procedure. The results of the remaining 177 patients were carefully reviewed.

**Results:** There were 81 men (46%) and 96 women (54%) included in the final analysis. The breakdown according to race was 72 Caucasians (41%), 50 African Americans (28%) and 55 Hispanics (31%). 75 examinations were normal (42%). Among the 102 abnormal results (58%), the most common abnormal finding was polyps- 60 out of 102 patients with 39 of them distal to splenic flexure and 21 proximal to the splenic flexure.

The abnormal findings (102) were then reviewed for any racial differences. Among the Caucasians, the most common abnormal result was hemorroids (10 out of 17 patients). Diverticulosis was the most common finding in Hispanics (9 out of 20) and colon polyps were more common in African Americans (24 out of 60 patients with polyps)

24 out of 50 African American patients in the study had colon polyps with a prevalence of 48%. The prevalence in other races were sharply lower- 29% in Caucasians (21 out of 72 patients) and 27% in Hispanics (15 out of 55 Hispanic patients in the study). Proximal colonic polyps were also identified more commonly in African American patients with a prevalence of 14% (7 out of 50 patients). In Caucasians, it was 1% (9 out of 72 patients) and in Hispanics the prevalence of proximal colonic polyps was 9% (5 out of 55 patients)

**Conclusions:** Colorectal cancer incidence in the United States has the highest rates in African American patients. There is a paucity in the literature of racial differences in colonoscopic examination results in patients less than 50. This retrospective study showed a much higher prevalence of colonic polyps and a relatively higher prevalence of proximal lesions in black patients in this age group. Further studies are needed to gain more insight into racial disparities in colonic lesions.

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**Polyethylene Glycol (PEG) Mediated Chemoprevention of Colorectal Cancer (CRC) Involves Downregulation of Epidermal Growth Factor Receptor (EGFR)**

Jonathan C. Huang, D.O., Hemant K. Roy, M.D.,∗ Jennifer Koetsier, B.S., Dhanajay P. Kante, Ph.D., Ramesh K. Wali, Ph.D. Department of Gastroenterology, Evanston Northwestern Healthcare, Evanston, IL.

**Purpose:** Both epidemiological and experimental studies demonstrate that PEG may be a markedly superior at preventing CRC than conventional agents (NSAIDS, aspirin, statins etc) (Corpet & Pierre CEBP 2003). However, the diarrhea associated with PEG limits wide-spread applicability. Our group has been interested in elucidating the mechanisms of action of this potent chemopreventive agent. We have previously demonstrated that induction of colonic apoptosis appears to be critical (Roy et al., Can Lett 2004). Epithelial Growth Factor (EGFR) is commonly overexpressed in CRC that deregulates certain cellular functions such as apoptosis. Moreover, inhibition of EGFR caused a >80% reduction in experimental intestinal tumorigenesis (Torrance et al. Nat Med 2000) which was strikingly similar to the PEG-induced chemopreventive data. Thus, we conducted this study to test the hypothesis that PEG chemopreventive activity is related to EGFR downregulation using the azoxymethane (AOM)-treated rat model of CRC.

**Methods:** 20 Fisher 344 rats were treated with two weekly doses of AOM (15 mg/kg). Seven weeks post treatment (pre-malignant time-point), animals were randomized to receive daily gavage of PEG-3350 (10%) or vehicle for one week and then sacrificed. Colonos were isolated and subjected to immunohistochemical analysis (IHC) for both total EGFR and its activated (phosphorylated) form. IHC was graded by an observer blinded to treatment group on a 5 point scale.

**Results:** AOM treatment resulted in a marked overexpression of EGFR at this premalignant timepoint compared to saline-treated controls. This was predominantly located in the membrane. PEG supplementation caused a marked reduction in EGFR staining (60%, p < 0.05). Moreover, there was a concomitant decrease in its activated form (tyr 1045 phosphorylation).

**Conclusions:** We demonstrate, for the first time, that short term treatment with the potent chemopreventive dose PEG resulted in a dramatic downregulation of EGFR expression and activity. This suggests that EGFR may be an important target in PEG-mediated suppression of CRC. Future studies will be to designed to identify PEG regimens that maximize its chemopreventive effect via EGFR downregulation while minimizing diarrhea.

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**Multi-Ethnic Variations in Colorectal Cancer. A Five Year Study in a Community Hospital**

Emmanuel Akinyemi, M.D., Suriya Jayawardena, M.D., Shalaka Indulka, M.D., Archana Maini, M.D., Muhammad Abdullah, M.D.*

Gastroenterology, Coney Island Hospital, Brooklyn, NY; Hematology and Oncology, Coney Island Hospital, Brooklyn, NY and Pediatrics, Maimonides Medical Center, Brooklyn, NY.

**Purpose:** The aim of this study was to identify the racial distribution and anatomical profile of colorectal cancer in an urban multi-ethnic community.

**Methods:** Complete data including the age, sex, race, location of cancer, and type of cancer, degree of differentiation from patients who had biopsy proven colorectal cancer from the year 2000–2004 was recorded.

**Results:** The male-female ratio in our study was 52.5% to 47.5%. The mean age of diagnosis of colorectal cancer was 67.4 years and it did not differ according to type of cancer (p = 0.98). Caucasian patients had a significantly higher mean age of diagnosis (69.7 yr) than African Americans (63.3 yr, p = 0.02) and Asians (61.8 yr, p = 0.04), but not more than Hispanics (65.5 yr, p = 0.18). Adenocarcinoma was the most common type of colorectal cancer, and almost 60% of the patients were Caucasians >65 years. All patients including African Americans showed more left sided cancers. Hispanics showed higher proportion of adenocarcinomas in the sigmoid colon than other races (p 0.03). 73% of all moderately differentiated adenocarcinomas were seen among Hispanics. However, the incidence of colorectal cancer and its types did not differ by sex (p = 0.33), race (p = 0.08) or age group (p = 0.92).

**Conclusions:** 41% of the patients were less than 65 years and most of these patients had moderate to well differentiated adenocarcinomas. African Americans had a significantly lower mean age of presentation, making early screening important. 25% of the cancers were in the right colon and these patients are more likely to present with non specific symptoms making colonoscopy a better screening test than sigmoidoscopy. Colorectal cancer is a treatable disease with significant morbidity and mortality if diagnosed at a later stage. Knowledge of presentation of colorectal cancer among the ethnic minorities can have a significant impact on its outcome.

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**Changes of Epidemiologic Characteristics of Colorectal Cancer in Korea**

Kissung Lee, M.D., Hakyang Kim, M.D.* Gastrointestinal Depratment, Kang-dong Sacred Heart Hospital, Seould, Republic of Korea.

**Purpose:** The incidence of colorectal cancer has increased recently in Korea, with change of its clinical characteristics. This study was designed to delineate the changes of epidemiologic characteristics of colorectal cancer...
and the influence of epidemiologic characteristics on the observed changes in Korea.

Methods: We analyzed the data of colorectal cancer patients from 1993 through 2002 at Kang-Dong sacred Heart Hospital to elucidate the characteristics of colorectal cancer according to age, sex, primary location, stage, and degree of differentiation. Six-hundred forty-seven patients who were diagnosed as colorectal cancer by endoscopic biopsy were divided into the early 5-year group and the late 5-year group. Right colon cancer was defined as that from cecum to transverse colon and left colon cancer was defined as that from descending colon to rectum.

Results: The mean age of early and late period group were 53.8 ± 13.6 year and 62.2 ± 13.2 year, respectively. The mean age of late period group was significantly older than that of early period group (p = 0.000). The sex ratio was similar within each group (p = 0.189). Totally, the incidence of rectal cancer was highest, and the incidence of right colon cancer was 22.5% in the early period group and 26.7% in the late period group. Colon cancer showed the tendency to develop on right side more frequently in the late period group than the early period group. However, no statistically significant difference of subsite distribution of colon cancer between the two groups was observed (p = 0.059). Duke’s B cancers were most common (43.1%). Duke’s C patients decreased by 8.6% (p = 0.022), and Duke’s D patients increased by 11.1% in the late period group compared with the early period group (p = 0.000). The incidence of well-differentiated carcinoma in histologic study decreased by 20.5% (p = 0.000), and that of moderately- and poorly-differentiated carcinoma increased by 15.5%, and 4.8% in the late period group compared with the early period group, respectively (p = 0.000, p = 0.021, respectively).

Conclusions: Recently, the incidence of colorectal cancer in elderly has increased notably, and the incidence of right colon cancer tends to increase and the proportion of advanced colorectal cancer and poorly-differentiated carcinoma in histologic study increased in Korea. Also, we expect that this phenomenon will be further accelerated considering a recent change of Korean dietary life style.

**Efficacy and Safety Profile of Older Patients Using Oral INKP-102 as a Bowel Purgative Prior to Colonoscopy Compared to Visicol**

S. Katz, M.D., * J. Novick, M.D., R. Hardi, M.D., M. Rose, M.D., R. Karlstad, M.D., S. Lotte, M.D., N. Ettinger. GI, LI Clinical Research Assoc., Great Neck, NY; GI, Charm City Research, Towson, MD; GI, Metropolitan GI Grp, Chevy Chase, MD and CR&D, InKine Pharmaceutical Co., Blue Bell, PA.

**Purpose:** Colonoscopy is a frequent procedure in persons over the age of 50; procedures in patients over the age of 80 are not rare. To determine if age affected the clinical outcome, data from two trials were collected from 931 adults scheduled for a colonoscopy who took either Visicol® Tablets (V) or INKP-102, a new NaP tablet formulation w/o the microcrystalline cellulose binder. The main efficacy and safety results of these multicenter, investigator-blinded studies have been reported.

**Methods:** Patients were randomly assigned to either 60g V or 3 doses of INKP-102: 60g, 48g or 42g.

**Results:** Overall, 24% of the patients were ≥65 yrs; 29% in the V group and 23% in INKP-102. For V patients the median age was 56 yrs (range 20–89) and for INKP-102 the median age was 55 yrs (range 21–84). The primary analyses demonstrated no appreciable differences in the proportion of patients (≥65 yrs) who responded (cleansing scores of excellent/good) for Overall Colon cleansing (96% V; 99% INKP-102) and cleansing of the Ascending Colon (91% V patients; 97% for INKP-102) compared to patients ≤64yrs; 93% V; 93% INKP-102 for OC and 87% V; 91% INKP-102 for AC. The most common AEs experienced by ≥5% of patients irrespective of age were abdominal distension (bloating), nausea, abdominal pain and vomiting. There were no appreciable differences between treatment groups in AEs or in the frequency of AEs experienced based upon age.

**Conclusions:** Elderly patients demonstrate excellent colon cleansing with both Visicol and INKP-102, and experience no increased incidence of adverse events.

**Chemotherapy-Induced Colitis after Docetaxel**

Nadia A. Trigg, M.D., Manish Patel, M.D., Thomas Hoeltgen, M.D., Charles Berkelhammer, M.D., F.A.C.G.* Gastroenterology and Oncology, University of Illinois, Christ Hospital, Oak Lawn, IL.

**Purpose:** Docetaxel (Taxotere) has been associated with drug induced ischemic colitis as well as neutropenic enteroctitis (typhlitis). The most common side effect of this medication is mucositis/stomatitis seen in up to 42% of the patients. We describe a patient who developed colitis and typhlitis following docetaxel.

**Case:** A 66 year old female with metastatic breast cancer presented with right lower quadrant pain, profuse diarrhea and fever three days after she received docetaxel for the first time. CT scan of the abdomen showed inflammatory changes and thickening of the cecum. Her white count decreased transiently to an absolute neutrophil count of 0.6 and quickly resolved with filgrastim. Colonoscopy revealed diffuse edema and submucosal petechiae consistent with chemotherapy-induced colitis. There were ulcerations in the cecum consistent with typhlitis. Biopsies for CMV, and stool microbiology were negative. Patient had diarrhea that lasted for several days.

**Conclusion:** Our patient developed both typhlitis and chemotherapy induced pancolitis following docetaxel. This colonic complication should be kept in mind in patients receiving docetaxel.

**Mucosal Neuromas Diagnosed in an Ambulatory Endoscopy Setting: A Clinicopathologic and Immunohistologic Study of 23 Patients**

Richard Lash, M.D., * Robert Petras, M.D. Department of Pathology, AmeriPath’s Institute of Gastrointestinal Pathology and Digestive Disease, Oakwood Village, OH.

**Purpose:** Mucosal ganglioneuromas of the gastrointestinal tract have been well studied, occurring most often as isolated lesions and composed of a spindle cell proliferation (neuroma) with scattered ganglion cells. They can be associated with syndromes including neurofibromatosis, MEN type 2b, Cowden’s syndrome, Familial Adenomatosis Coli and Tuberous Sclerosis. Much less is known about pure mucosal neuromas lacking ganglion cells. The purpose of the study was to determine the clinical significance of mucosal neuromas detected in an ambulatory endoscopy setting.

**Methods:** Review of the archives of a high volume outpatient subspecialty gastrointestinal pathology laboratory, 2001–2004, yielded 31 mucosal neuromas detected in 23 patients (ages 25–77, mean = 58 years).
Results: All tumors were detected at endoscopy as small mucosal polyps or irregularities ranging in size from <1 mm to 4 mm (mean = 1.3 mm). Three neuromas were found in the esophagus/stomach, 3 in the cecum/ascending colon, 1 at the hepatic flexure, 3 in the transverse colon, 2 at the splenic flexure, 3 in the descending colon, and 13 in the rectosigmoid colon. Three neuromas were from undesignated sites in the colon. One patient also had separate colonic ganglion neuromas. Histologically, all tumors were composed of a localized proliferation of bland spindle cells with pale eosinophilic cytoplasm containing wavy small nuclei, some with intranuclear cytoplasmic invaginations and some with a schwannoma-like architecture. Immunohistochemistry performed in 25 tumors showed immunoreactivity for S100 protein. All tumors were negative for c-kit (CD117) and smooth muscle actin. At follow up, all tumors were clinically benign and unassociated with a clinical syndrome, with the exception of a 25 year old man with a 4 mm colonic polyp who was known to have neurofibromatosis.

Conclusions: We conclude that mucosal neuromas typically present as tiny mucosal polyps or and are only rarely associated with a clinical syndrome.

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Anorectal Manometric Study of Patients with Type II Diabetes
Abdalla I. Kelani, M.D., Fatema A. Baker, M.D.* Department of Medicine, Assiut University Hospital, Assiut, Egypt.

Purpose: Assessment of anorectal function in typeII diabetes.

Methods: 28 typeII diabetes randomly selected aged 40–70 years includes 18 patients with duration of diabetes <10 years and 10 patients with duration >10 years as well as 20 healthy persons subjected to anorectal manometric study by sandhill apparatus.

Results: 1-patients with diabetes showed increased lower G.I.T symptoms than the control 2-no correlation between lower G.I.T symptoms and the duration of diabetes 3-significantly reduction in resting anal canal pressure, highest mean resting pressure, maximum squeeze pressure, duration of squeeze and strain pressure in type II diabetes compared to the control 4-significantly higher threshold of rectoanal of reflex and rectal sensation in patients compared to control.

Conclusions: assessment of anorectal motility is highly needed in typeII diabetes as early as possible in order to began the treatment.

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Smoking History, Alcohol History, and Age Are Associated with Stage of Presentation in Colorectal Cancer
Anna L. Zisman, M.D., Hemant K. Roy, M.D.*, Angel Nickolov, MA, Addi Gorchow, M.S., Randall E. Brand, M.D. Department of Internal Medicine, Evanston Northwestern Healthcare, Evanston, IL; Cancer Registry, Evanston Northwestern Healthcare, Evanston, IL and Center for Outcomes Research, Evanston Northwestern Healthcare, Evanston, IL.

Purpose: While eminently curable if detected at a localized stage, colorectal cancer (CRC) remains the second leading cause of cancer mortality. Eluciating the factors associated with advanced malignancy is of paramount importance in decreasing CRC deaths. The literature on this, however, remains limited. We, therefore, investigated the role of several established demographic and environmental CRC risk factors in predicting advanced disease at presentation.

Methods: We utilized the IMPAC Medical Registry Services Cancer Information Resource File (CIRF) 1993–2003, drawing data from more than 350 teaching and community hospitals nationwide. A logistic regression model was used, with stage of colorectal cancer as the outcome variable. CRC was grouped into early (Stage 0, 1 and 2) or advanced (Stage 3 or 4). Potential explanatory variables analyzed were gender, tobacco history, alcohol history, and the interaction between alcohol and tobacco history. A p-value of less than 0.05 was considered statistically significant. Data were analyzed with SAS.

Results: Our analysis dataset consisted of 166,172 patients. The mean age was 69.6 ± 12.8 years with males and females equally represented. Tobacco and alcohol use was associated with an increased risk of advanced CRC at presentation. Younger patients appeared to present with more advanced cancers. Females were as likely as males to present with advanced cancers. There was no multivariate model as gender, alcohol and tobacco history were confounded.

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A Retrospective Analysis of Large Polypectomies Using a Methylene Blue/Epinephrine/Saline Lift Technique: A Single Center Experience

Purpose: To retrospectively evaluate the technical success and complication rates of endoscopic polypectomy of large polyps using a methylene blue/epinephrine/saline lift technique.

Background: Large colonic polyps may present a management challenge. A small but significant risk of colonic perforation, hemorrhage or incomplete polypectomy must be weighed against the inherent risks of surgery. Endoscopic snare resection of large polyps using a methylene blue/epinephrine lift technique may present a minimally invasive alternative to surgery. This may improve identification of polyp margins making assessment of complete excision easier.

Methods: A retrospective series of 32 patients was analyzed. All patients underwent endoscopic resection of large polyps (>20mm) using the above technique. Polypectomies were performed by two experienced endoscopists (JML, GB and KB) at our institution (2003 to present). Backup by an experienced laparoscopic surgeon (DEML) was available for all cases.

Results: Thirty-one large polyps were endoscopically removed from 30 patients. The remaining two patients were sent directly for laparoscopic resection after the polyp failed to lift. The mean age of the patients was 65 years with 47% being male. Nineteen polyps were found on the right side of the colon (7 in the cecum). Thirty-one percent of the polyps revealed either high-grade dysplasia or adenocarcinoma with average size being 33.8mm as deemed endoscopically. Six patients underwent surgery (4 laparoscopically). In 2 patients, whose polyps failed to lift, surgical pathology revealed invasive adenocarcinoma. Of the remaining 4 patients, 3 had no residual adenomatous tissue in the resected specimen. There were 2 complications. One patient had a post-polypectomy bleed which was endoscopically managed, and the other patient presented with abdominal pain with portal-venous air which resolved with conservative management.

Conclusions: Large polypectomies were safely performed with a methylene blue/epinephrine/saline lift technique in this retrospective series. This technique allows for improved endoscopic delineation of polyp margins. Methylen Blue/Epinephrine/Saline Lift Technique with laparoscopic surgical
back-up may, therefore, present a minimally invasive alternative to surgical resection of large polyps.

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Risk Factors of Lymph Node Metastasis in Early Colorectal Cancer Invading to Submucosa
Ichiro Takemasa, M.D.,* Naganori Kyo, M.D., Yujiro Fujie, M.D., Yo sake Seki, M.D., Tatsusi Singai, M.D., Masayosi Yasui, M.D., Masataka Ikeda, M.D., Hirofumi Yamamoto, M.D., Mitsugu Sekimoto, M.D., Morito Monden, M.D., Surgery, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan.

Purpose: To evaluate the risk factors of the locally existed early colorectal cancers for clinical decision making by the examination of detailed clinicopathological findings and clinical outcomes.

Methods: A total of 128 resected samples (9 node positive samples: 7.0%) of early colorectal cancers invading to submucosa were investigated about potential parameters for lymph node metastasis. The values of submucosal invasive depth and degree, dominant histological differentiation and that at invasive front, macroscopic configuration, lymphatic or venous invasion, existence of tumor budding, growth pattern, and co-existence of adenomatous component were examined by two accomplished pathologists. Relations between each valuable and nodal status were estimated by univariate analysis and relative risk ratios were examined by multivariate analysis.

Results: Our analysis revealed distinct three factors significantly related with nodal status. There was difference in a tumor between dominant histological type and that at invasive front, and the latter was significantly related nodal status (HR: 7.2, p = 0.044). The deeper submucosal invasion was, the more frequent node metastasis was, and submucosal invasive depth by actual survey was more significant than their relative degree (HR: 30.9, p = 0.006). Macroscopic configuration (HR: 15.3, p = 0.078) was also significantly independent lymph node metastasis-related factors.

Conclusions: Most important factor of nodal metastasis in early colorectal cancers invading to submucosal was properly the depth of invasion, which was quantitative factor. Additionally, qualitative factors such as histological type at invasive front and configuration, which were macroscopic and macroscopic findings, reflected a malignant degree and a characteristic of early invasive colorectal cancers. Such general judgment with a careful approach taking above factors into consideration for the patients with early invasive colorectal cancers was very important for keeping them safe.

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Prevalence of Microscopic Colitis in Patients with Chronic Non-Bloody Diarrhea
Monjur Ahmed, M.D., F.A.C.G.,* Aymen Elkady, M.D., Chadi Kaba, M.D., Afroza Sultana, M.D. Internal Medicine, Marshall University, Huntington, WV.

Purpose: Microscopic colitis is occasionally recognized in our clinical practice. Because of the increased awareness of this entity, colonoscopy with biopsy is done early in the investigation of chronic non-bloody diarrhea. The aim of this study is to find out the prevalence of microscopic colitis in patients with chronic non-bloody diarrhea referred for colonoscopy to a university medical center.

Methods: A case-control study was performed by reviewing charts at the medical record of a university medical center. All cases of chronic (duration >4 weeks) non-bloody diarrhea irrespective of sex, race and age above 18 who had colonoscopy with biopsy during the period of December, 2002 to December, 2004 were eligible for participation in the study. Patients with acute diarrhea and those patients who did not have colonic biopsy during colonoscopy did not fulfill the criteria.

Results: A total of 128 resected samples (9 node positive samples: 7.0%) of early colorectal cancers invading to submucosa were investigated about potential parameters for lymph node metastasis. The values of submucosal invasive depth and degree, dominant histological differentiation and that at invasive front, macroscopic configuration, lymphatic or venous invasion, existence of tumor budding, growth pattern, and co-existence of adenomatous component were examined by two accomplished pathologists. Relations between each valuable and nodal status were estimated by univariate analysis and relative risk ratios were examined by multivariate analysis.

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Conclusions: Most important factor of nodal metastasis in early colorectal cancers invading to submucosal was properly the depth of invasion, which was quantitative factor. Additionally, qualitative factors such as histological type at invasive front and configuration, which were macroscopic and macroscopic findings, reflected a malignant degree and a characteristic of early invasive colorectal cancers. Such general judgment with a careful approach taking above factors into consideration for the patients with early invasive colorectal cancers was very important for keeping them safe.

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BRAF Mutation Was Associated with Dysregulation of Apoptosis in Human Colorectal Carcinomas
Nobuo Ikehara,* Shocho Semb, Shi-ei Yoshida, Hiroshi Yokozaki, Nobuo Aoyama. Division of Diabetes, Digestive and Kidney Diseases Department of Clinical Molecular Medicine, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan and Division of Surgical Pathology, Department of Biomedical Informatics, Kobe University Graduate School of Medicine, Kobe, Hyogo, Japan.

Purpose: To understand the role of BRAF dysfunction in the carcinogenesis and progression/development of colorectal tumors, the authors investigated genetic alterations in the BRAF gene in human early colorectal carcinomas.

Methods: A total of 7 colon cancer cell lines and 197 colorectal tumors (36 adenomas and 161 adenocarcinomas) were analyzed. Genetic alterations in the BRAF (exon11 and 15) and K-ras (exon 2) genes were examined using polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) and direct sequencing analyses. In addition to the growth-inhibitory and apoptosis-inducing effects of FTI-277 in colon cancer cell lines (WiDr, TCO and LoVo) the levels of phosphorylated MEK and ERK expression were also analyzed. An immunohistochemical study was also performed to investigate the correlations between the clinicopathologic parameters involved in the Ki-67 labeling index and the number of apoptotic bodies (single stranded-DNA [ssDNA]) in tumor cells.

Results: Genetic changes in the BRAF and K-ras genes were found in 2 (28%) and 4 (57%) of colon cancer cell lines, respectively. FTI-277 did not suppress proliferation of BRAF-mutant cell lines (WiDr and TCO), whereas growth of K-ras-mutant cell line (LoVo) was remarkably inhibited by this agent. In addition, LoVo cells underwent apoptosis when the cells were treated with FTI-277, while WiDr cells did not show increase of apoptotic bodies by this agent. In tumor samples, BRAF mutations were found in 1 (2.9%) of 36 adenomas and 10 (6.2%) of 161 adenocarcinomas. No tumor exhibited mutations in both the BRAF and K-ras genes. Furthermore, we analyzed alterations in the BRAF and K-ras genes in flat-typed colorectal cancer without an adenomatous component, and found alterations in BRAF and K-ras genes were in 15% and 0% of the tumors, respectively. Neither BRAF nor K-ras mutations correlated with the Ki-67 labeling index immuno-histochemically. However, the number of apoptotic bodies was significantly decreased in the BRAF-mutant tumors.

Conclusions: Mutation in the BRAF gene may contribute to colorectal carcinogenesis by up-regulating the anti-apoptotic role of the RAS/RAF/MEK/ERK pathway.

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Predisposing Factors for Ischemic Colitis

Purpose: Ischemic colitis (IC) is usually caused by vascular insufficiency to the colon. It is important to identify the risk factors in improving the suspicion and the motivation of clinicians to make the diagnosis of IC earlier. This study was to find the clinical predisposing factors for IC.

Methods: All 80 patients with IC were consecutively enrolled from 2000 to 2004, who underwent colonoscopy because of abdominal pain with bloody
The presence of hypertension, diabetes and a 17-month increase of 17 months.

Purpose:
Chronic radiation proctopathy (CRP) is a complication of radiation therapy to the pelvis. The KTP (potassium titanyl phosphate) laser is a Nd:YAG-driven device that uses light with a wavelength of 532nm. The purpose of this study was to study the therapeutic outcomes of the KTP laser. We also evaluated whether the presence of certain co-morbidities that would predispose patients undergoing external beam radiotherapy (EBRT) to develop CRP and metastases from endoscopically proven CRP.

Methods:
All the patients treated with the KTP laser for chronic bleeding secondary to EBRT were treated at the BC Cancer Agency, British Columbia, Canada. In addition to the previously known risk factors, hypertension, smoking, constipating medication, and cancer were clinically significant predisposing factors for IC.

Conclusions:
The KTP laser is a safe and effective treatment for rectal bleeding from CRP.88.4% of patients either had complete resolution or a significant decrease in bleeding. There was an increased odds ratio for developing CRP after EBRT with the presence of these factors but it did not reach statistical significance. This is the largest study to evaluate the KTP laser in the management of CRP.

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Outcomes of Colonoscopic Evaluation for Rectal Bleeding in Asian Americans
Long H. Nguyen, Khoa D. Lam, B.A., Mindie H. Nguyen, M.D., M.A.S., Hue N. Trinh, M.D., Khanh K. Nguyen, M.D., Hue A. Nguyen, M.D., Ruel T. Garcia, M.D.* Gastroenterology, San Jose Gastroenterology, San Jose, CA; Biology, University of California, Los Angeles, Los Angeles, CA; Human Biology, Stanford University, Stanford, CA; Medicine, Stanford University, Palo Alto, CA and Research and Education, Pacific Health Foundation, San Jose, CA.

Purpose: The complaint of visible, non-acute rectal bleeding is a common reason for referral to a gastroenterologist. There may be differences in the etiology of rectal bleeding among different ethnic groups. There are no studies describing the results of colonoscopy for rectal bleeding in Asian Americans. The purpose is to determine the yield of colonoscopy for Asian Americans with non-acute rectal bleeding.

Methods: We performed a retrospective study of 2083 consecutive elective colonoscopies performed by 5 endoscopists from June 6, 2003 to September 1, 2004 at a community-based practice serving a large Asian population in the United States. We reviewed patients’ medical, endoscopy and pathology records and determined the prevalence of advanced colonic neoplasia (adenoma ≥10 mm, villous histology, or cancer). Logistic regression was used to determine predictors for advanced neoplasia.

Results: A total of 406 cases of rectal bleeding were identified. Of these, 342 were in Asians. Among Asian patients with rectal bleeding, the mean age was 57 ± 11 and 59% were male. Results of colonoscopic evaluation are summarized in the following table.

<table>
<thead>
<tr>
<th>Outcomes (N = 342)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced neoplasia</td>
<td>34 (10%)</td>
</tr>
<tr>
<td>*Cancer (all were distal)</td>
<td>*4 (1.2%)</td>
</tr>
<tr>
<td>*Isolated proximal advanced neoplasia</td>
<td>*4 (1.2%)</td>
</tr>
<tr>
<td>Small polyp (&lt;10 mm)</td>
<td>59 (17%)</td>
</tr>
<tr>
<td>Hyperplastic/normal polyp</td>
<td>44 (13%)</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>237 (69%)</td>
</tr>
</tbody>
</table>

Asian males had a significantly higher prevalence of advanced neoplasia (Figure). On multivariate analysis inclusive of age, gender, family history of colon cancer, only male gender was an independent predictor for advanced neoplasia (OR 2.3, p = 0.037).
Conclusions: Advanced colonic neoplasms are commonly found in Asian American patients with non-acute rectal bleeding. Asian males presenting with rectal bleeding are more likely to have advanced neoplasms compared to females.

412 Determination of 5-ASA in Whole or Partial Mesalamine Delayed-Release Tablets Recovered from Fecal Samples of Healthy Volunteers Alan V. Safdi, M.D.* Gastroenterology, Deaconess Hospital, Cincinnati, OH.

Purpose: Mesalamine delayed-release tablets (Asacol®, Procter & Gamble Pharmaceuticals) have a coating of methacrylic acid polymer B (EUDRAGIT-S) that allows release of mesalamine to the proximal colon with low systemic absorption (approx. 28%). This coating is pH sensitive and is released at a sustained pH level above 7. Fragments of Asacol tablets have been seen in fecal specimens, but the fragments were believed to be shells left after the 5-ASA had been released. The current study was to determine the amount of 5-ASA in whole and partial mesalamine tablets recovered from the fecal samples of healthy volunteers who received mesalamine therapy.

Methods: 30 healthy volunteers received two 400mg mesalamine tablets per bid for 4 days. After observing the presence of whole and partial mesalamine tablets in fecal specimens, the investigators recovered the tablets and fragments for further analysis. The tablets and fragments recovered from fecal specimens were photographed, crushed and added to 20mL 0.1M NaPO4 (pH 6.0) and 80mL absolute methanol. After resting at room temperature for 4 hours, 40mL of the solution was placed in a centrifuge for 10 minutes. Three 10mL aliquots of supernatant were removed, frozen and sent to a laboratory to be assayed for 5-ASA with a lower limit of quantification of 200mg/mL.

Results: Of 30 volunteers, 27(90%) provided fecal samples. Of these, 15 volunteers (55%) presented with at least 1 mesalamine tablet or fragment in at least 1 fecal sample.

Table 1.

<table>
<thead>
<tr>
<th>No. Volunteers (%)</th>
<th>No. Specimens Containing Mesalamine Tablets or Fragments (Total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 (40)</td>
<td>1 (11)</td>
</tr>
<tr>
<td>3 (11)</td>
<td>2 (6)</td>
</tr>
<tr>
<td>1 (4)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Volunteers 15 (55)</td>
<td>Specimens 21</td>
</tr>
</tbody>
</table>

All tablets and fragments recovered had detectable 5-ASA. Mean recovery was 97.2 ± 47.1 mg per tablet/fragment—approximately 24% of an intact tablet.

Conclusions: 55% of healthy volunteers who received oral mesalamine delayed-release tablets over 4 days of treatment excreted whole or partial tablets in at least 1 fecal specimen. Because all tablets and fragments recovered had detectable 5-ASA, the recovered tablets were not just physical matrices, inert shells or other excipients. Mean recovery was 97.2 ± 47.1 mg per tablet/fragment—approximately 24% of an intact mesalamine tablet. Only visually detectable fragments were measured in this study; additional undetectable fragments could have been present. The actual percentage of unreleased mesalamine may be higher than reported here and represents an important fraction of the daily mesalamine dose.

414 Population Pharmacokinetic Models for Predicting Sedation with GPI 15715 Prodrug of Propofol (AQUAVAN® Injection) for Colonoscopy Ekaterina Ghibansky, Ph.D.*, Leonard Ghibansky, Ph.D. Clinical, Guilford Pharmaceuticals Inc., Baltimore, MD and Research, Metrum Research Group, Tariffville, CT.

Purpose: GPI 15715 (AQUAVAN Injection), a novel sedative/hypnotic water-soluble prodrug of propofol with pharmacokinetics (PK) that differ significantly from those of propofol emulsion, provides rapid onset and recovery of anesthesia during colonoscopy. Models relating propofol concentrations to sedation (using Modified Observers Assessment of Alertness/Sedation [MOAA/S] scores) and predicting concentrations of GPI 15715 in plasma were developed and compared with observed sedation data from a randomized dose-ranging study of AQUAVAN in patients undergoing colonoscopy.

Methods: Patients received premedication (fentanyl 11201 g by IV bolus) and initial IV bolus dose of AQUAVAN and up to 4 supplemental doses (total dose = 4951675 mg). Proportions of patients with gastrointestinal 15715-derived propofol collected at: 1 and 9 min after initial dose; return to MOAA/S score = 5; and discharge. MOAA/S taken every 2 min until patients were fully alert. Data analyzed from 158 patients (approximately 10% >65 years old). Models developed using nonlinear repeated-measures statistical methodology (utilizing NONMEM software). Simulations tested predictive capabilities.

Results: Linear 5-compartment model described PK of GPI 15715, propofol, and GPI 15715/propofol concentration delay. Proportional odds model

M.D.* Division of Gastroenterology, University of California San Francisco, San Francisco, CA.

Purpose: Although colonoscopy is routinely used in the diagnostic evaluation of patients with suspected diverticular hemorrhage, data are limited concerning colonoscopic treatment of acute diverticular hemorrhage. Previous reports of colonoscopic hemostasis for diverticular hemorrhage have mostly consisted of hemocapulation and/or epinephrine injection. We report our experience using a relatively newer technique: endoclips.

Methods: We reviewed colonoscopy records of all inpatients from March 2004-March 2005 who underwent colonoscopy for evaluation of overt lower GI bleeding within the University of California San Francisco Hospital system. We identified those with the colonoscopic diagnosis of acute diverticular hemorrhage, defined as findings of active bleeding or nonbleeding visible vessel from within a diverticulum. The following data were retrospectively collected: patient demographics, procedural findings, endoscopic treatment techniques and success, and hospital course.

Results: Ten patients (9M/1F) had acute diverticular hemorrhage at colonoscopy. Their mean age was 71.7 years and the majority (70%) had comorbid cardiopulmonary, liver, and/or renal diseases. Patients underwent urgent colonoscopy at a median time of 20 hours after presentation and required a mean of 5 units packed red cell transfusion prior to procedure. At colonoscopy, all diverticula were vigorously irrigated, diverticular clots were removed (using irrigation, mechanical instruments, or suction), and all were meticulously examined. Active diverticular bleeding was identified in six patients, and a visible vessel was identified in four patients. Bleeding sites were located in the ascending colon (4), transverse colon (3), descending colon (1), and sigmoid colon (2). All diverticular bleeding sites were successfully treated with endoclips or without dilute epinephrine injection (used in 70%). There were no procedure-related complications. All patients were discharged within three days without further clinical evidence of bleeding, transfusion requirements, or need for additional endoscopic, angiographic, or surgical therapy.

Conclusions: Colonoscopic treatment of patients with acute diverticular hemorrhage using endoclips appears to be effective and safe. Urgent colonoscopy should be considered in patients with suspected diverticular hemorrhage, as it may enable treatment without need for more invasive therapeutic measures.

413 Colonoscopic Treatment of Acute Diverticular Hemorrhage Eugene F. Yen, M.D., Uri Ladabaum, M.D., M.S., V Raman Mathusamy, M.D., John P. Cello, M.D., Kenneth R. McQuaid, M.D., Janak N. Shah,
described probabilities of achieving specific MOAA/S scores at different concentrations. Maximum propofol concentration from GPI 15715 predicted at 45 min. Lean body weight was the best predictor of GPI 15715 and propofol concentrations for all body sizes/compositions. Patients >65 years attained same levels of sedation with 25% to 33% lower propofol concentrations compared with younger patients. Premedication had no additive effect on MOAA/S. Simulations demonstrated the models predict sedation levels and time course of sedation for different dosing regimens.

Conclusions: Fentanyl premedication did not influence GPI 15715-derived propofol-induced sedation. Older patients may require less AQUAVAN to attain sedation than younger patients. PK and sedation models allow optimization of GPI 15715 dose and dosing regimens for sedation. Safety and efficacy of optimized regimens for GPI 15715-induced sedation with premedication will be tested in a randomized, double-blind, dose-response study in patients undergoing mild-to-moderate (procedural) sedation for colonoscopy. Supported by Guilford Pharmaceuticals Inc.

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Clostridium difficile Is the Most Common Cause of Infectious Colitis
Mihaela Dascal, M.D., Marcus Zervos, M.D., Barbara Robinson-Dunn, Ph.D., Ann L. Silverman, M.D.∗ Gastroenterology, William Beaumont Hospital, Royal Oak, MI; Gastroenterology, Henry Ford Health System, Detroit, MI and Gastroenterology, Henry Ford Health System, West Bloomfield, MI.

Purpose: Clostridium difficile is a significant cause of nosocomial diarrhea but it is thought to play a secondary role in outpatient bacterial colitis. Enteric organisms such as Campylobacter, Salmonella and Shigella are thought to be the most common infectious causes of outpatient bacterial colitis. We sought to determine the relative role of bacterial pathogens in patients with diarrhea who were undergoing testing for C. difficile toxin and bacterial culture at a tertiary community hospital laboratory.

Methods: We reviewed the hospital records of patients who tested positive for C. difficile toxin A and B by ELISA, or positive culture for bacterial pathogens over a 12-month period ending December 2003. We examined the records for demographic data, microbiology, re-infection, or death.

Results: 1372 patients had positive C. difficile toxin assays, 36, 20, and 9 patients (total 65 including 12 inpatients and 53 outpatients) had positive cultures for Salmonella, Campylobacter, and Shigella, respectively. Of the patients with C. difficile, 568 were diagnosed as outpatients (OP), while 804 were diagnosed as inpatients (IP). Of the OP, 488 (83%) were nursing home residents (NH) and 80 (14%) were residents in the community. The females: male ratio was 1.5:1 in the OP. In the OP group, NH patients were significantly older (mean age 77.8 years) than the community residents (mean age 52.8 years) p < 0.001. Detection of C. difficile toxin was preceded within two months by a urine culture in 32.6% of the OP, but only 17.2% actually had a positive urine culture; women had 2.5 times more urinary tract infections than men. 17% of all OP patients had at least one relapsed or recurrent C. difficile as defined by toxin detection more than 10 days from the initial positive toxin. 26 patients died within one month after the detection of C. difficile toxin, 33 at 1–3 months and 26 at more than 6 months.

Conclusions: Our data show that C. difficile is the most common bacterial pathogen among IP and OP with colitis. Patients with C. difficile toxin detection were likely to have had a suspected diagnosis of a urinary tract infection. We propose that empiric antibiotic treatment for urinary tract infections in women may contribute to the higher C. difficile toxin detection in this cohort of patients.

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Colonic Wall Thickening Presenting as a Recto-Sigmoid Mass
Deepak Thomas, M.D., Abdulla Ghoury, M.D., Roshan J. Lewis, M.D., Ojim Ajah, M.D.∗ Medicine, Interfaith Medical Center, Brooklyn, NY.

Purpose: We present a 55 year old African American male with a history of passing blood streaked stools for one year, that have been worsening for the past 2 months and associated with anorexia and weight loss. He also complained of constipation and left lower quadrant pain of a few days duration. His past medical history is significant for hypertension and had a 3 pack year history of smoking which he quit about 2 years ago. CT scan revealed sigmoid mural thickening with no lymphadenopathy. A colonoscopy was performed which revealed a circumferential sigmoid mass. Serum tumor markers and biopsy of the specimen obtained were reported as negative for malignancy. Anterior resection of the mass was performed with an end to end anastomosis was performed. Pathology was reported as chronic diverticulosis with muscular thickening and luminal narrowing. Patient recuperated well and was discharged with instructions on healthy dietary habits and regular follow up.

Chronic diverticular disease is the likely underlying cause for this patient's colonic wall abnormality. Diverticular disease of the sigmoid colon is an increasingly common clinical problem in the ageing population of western industrialised countries. Ultrastructural study of human colonic muscle shows that, the muscular thickening in diverticular disease can be explained in terms of elastosis and contracture of the taenial coli, in the presence of normal muscle cells. Colonic wall thickening presenting as an obstructing mass is unusual. Sigmoid colon is one of the most common sites for colon cancer. The history and the characteristic colonoscopic findings in our patient makes recto-sigmoid cancer a distinct possibility. Surgical resection of the mass despite a negative initial pathology report is justified on the basis of relief of symptoms and prevention of impending obstruction, and should be considered in all patients with similar presentation.
Is DCBE an Adequate Diagnostic Test for Patient with Positive FOBT?
Carlos P. Ramos, M.D., Doris H. Toro, M.D.,∗ Algia Ojeda, M.D., Joel De Jesus, M.D., Maria I. Dueno, M.D., Jaime Martinez, M.D. Gastroenterology, San Juan Veterans Affairs Medical Center, San Juan, PR, Puerto Rico.

Purpose: Colorectal cancer is the second leading cause of cancer death in the United States. The importance of screening has been established, but the decision about which test to use seems less clear. Fecal occult blood (FOB) testing as the screening strategy has reduced mortality. The large volume of reported FOBT positive overwhelms the capacity to perform colonoscopy, therefore DCBE (Double Contrast Barium Enema) might be a reasonable alternative diagnostic test.

This study aims to compare the diagnostic yield of DCBE with colonoscopy in the evaluation of FOBT positive patients. As secondary objective we determined location, number, size and pathologic characteristics of the lesions found in colonoscopy and DCBE.

Methods: FOBT positive patients were randomly selected between October 2003 and March 2005. A complete clinical history and physical examination was obtained. DCBE and colonoscopy were performed in all patients. Both results were compared. Findings in DCBE and colonoscopy were tabulated according to location of the lesions, size, shape, histology and quality of preparation. All polyps detected in colonoscopy were removed and classified histologically.

At the end of the protocol, patients were asked about tolerability and satisfaction. This study was approved by the Institutional Review Board. All patients signed an informed consent. Results were compared using a Chi square test and Z test.

Results: Fifty (50) patients were enrolled. Most were men (49/50). The average age was 63.8 years; range 49–84. Polyps were found on colonoscopy in 40/50 patients (80%), as compared to 19/50 (38%) for DCBE. DCBE sensitivity was 45% with a specificity of 90%. 84% of polyps were missed by DCBE, most of them adenomatus, of which 17% were > 1 cm. Sensitivity of DCBE increased from the right to left colon as specificity decreased. Four colorectal carcinomas were detected in both studies. Most polyps were sessile, adenomatus, less than 0.5 cm and located in the left colon. Patients preferred colonoscopy over DCBE.

Conclusions: DCBE has a limited diagnostic yield in colon cancer screening, detecting 100% of colon cancers, but missing a significant number of polyps > 1 cm, and most of the polyps < 0.5 cm. 8% of the FOBT positive patients had colon cancer, while 80% had adenomatus polyps. This study supports the use of colonoscopy as the gold standard test for the evaluation of positive FOBT. In addition, patients preferred colonoscopy over DCBE, rendering it as a more attractive test.

New Approach for Acute Lower GI Bleeding -Using CT Scan as a Primary Tool for Diagnosis
Yutaka Yamaguchi, M.D., Susumu Shinoara, M.D., Yoshihide Keida, M.D.,∗ Hiroaki Takara, M.D. Gastroenterology, Okinawa Chubu Hospital, Uruma, Okinawa, Japan and Radiology, Okinawa Chubu Hospital, Uruma, Okinawa, Japan.

Purpose: For acute lower GI bleeding (ALGIB), colonoscopy is believed to be a valuable and important tool for diagnosis. However, especially in case of massive bleeding with circulatory insufficiency or with comorbidity, colonoscopy is not always an effective tool given its characteristics that it is required relatively long time for completion and that its usefulness in treatment is limited. We set a new algorithm putting CT scan with “bleeding protocol” ahead of colonoscopy which is different from reported guidelines. Aim of this study is to evaluate our new algorithm of management of ALGIB featuring diagnostic CT scan with “bleeding protocol” ahead of colonoscopy.

Methods: We reviewed a total of 203 consecutive patients with ALGIB presenting and admitted to our emergency department between 2003 and 2004. 30 patients (15%) were excluded for their presentation with hematemesis. Clinical features as (1) vital signs (2)characteristics of stool (3) past medical history (4)medication (5)CT scan findings are evaluated.

Inclusion criteria for CT scanning was defined as the case satisfying one of the following: (1) systolic BP < 80mmHg at any time (2) HR>systolic BP at any time (3) positive tilt test result.

Outcome was recurrent bleeding requiring surgery or angiogram after admission.

Results: Of 173 patients with ALGIB, 21(12%) were upper GI tract origin and excluded from further workup. Of 152(88%) of lower GI tract origin ALGIB, most cases are due to colon diverticuli. Of 173, CT scan was performed in 86 (50%), of which all of 50 (29%) with circulatory insufficiency were included. CT scan findings clarified location of ALGIB in almost all cases. 11 of 50 patients with circulatory insufficiency underwent angiogram. Of the 11 patients, nine had a finding of extravasation per CT scan. Recurrent bleeding after admission occurred in two cases.

Conclusions: Our approach to ALGIB ordering CT scan with “bleeding protocol” ahead of colonoscopy is effective and valuable from therapeutic standpoint especially for patients with vital unstability or comorbidity.

Figure 1

Colonic MALT Lymphoma in a Patient with Ulcerative Colitis
Joey Sum, M.D., Talal Adhami, M.D., Scott Merkley, M.D.,∗ Iliana Bouneva, M.D. Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY and Digestive Diseases and Nutrition, Veterans Affairs Medical Center, Lexington, KY.

Purpose: It is well known that patients with ulcerative colitis (UC) of more than 8 years duration are at an increased risk of developing colon cancer. We present a rare case of mucosa associated lymphoid tissue (MALT) lymphoma in a patient with an 8 year history of UC.

Methods: A 66 year old man with mild-to-moderate ulcerative pancolitis diagnosed in 1998 presented with iron deficiency anemia in 2004. His UC
was clinically well controlled on oral Mesalamine. He never required therapy with steroids or any immunomodulators. A repeat colonoscopy at that time revealed friable erythematous mucosa in the ascending colon. Biopsies of this area demonstrated a Kappa monoclonal lymphoplasmocytic proliferative disorder consistent with MALT lymphoma. Serum protein electrophoresis revealed a mild beta-chain spike of 1.3 g/dl (ref: < 1.2 g/dl). Abdominal CT scan showed only moderate wall thickening of the ascending colon but no lymphadenopathy or any other abnormalities. The patient underwent right hemicolectomy which showed a 10.3 × 3.5 cm near-obstructing lesion proximal to the hepatic flexure. The specimen was positive for Kappa. CD 19, CD 20, and CD 23, while negative for CD 5 and CD 10 cell markers—findings consistent with MALT lymphoma, stage II E. Chemotherapy was not recommended by Oncology. The subsequent colonoscopy and abdominal CT scans have been negative for lymphoma.

**Conclusions:** Immunocompromised states and certain systemic conditions (i.e. Hepatitis C, Systemic lupus erythematosus) are well recognized risk factors for non-Hodgkins lymphoma. It has long been thought that inflammatory bowel disease (IBD) may also be such a risk factor. Moreover, since many patients with IBD are on immunomodulators, there is a concern that this may result in an even greater risk for developing this condition. Different studies have shown an increased risk for developing lymphoma in patients with IBD, although very small. This perhaps is acceptable when quality of life issues are raised. As newer therapies are developed, a longer track record may demonstrate their safety or lack thereof in terms of increased lymphoma risk.

**421 Predictors of Stage of Colorectal Cancer in Patients Presenting for Outpatient Colonoscopy**

Joseph C. Anderson, M.D.,* Michael Yadegari, Bernard Lane, M.D. Department of Gastroenterology, Stony Brook University, Stony Brook, NY and Department of Pathology, Stony Brook University, Stony Brook, NY.

**Purpose:** There are no randomized controlled studies to examine the effectiveness of screening colonoscopy to detect colorectal cancer (CRC) at an early stage. Little data exists regarding the predictive factors of late stage CRC in patients diagnosed by colonoscopy. Our novel retrospective study examines the stages of CRC diagnosed by outpatient colonoscopy.

**Methods:** Our University hospital has 501 beds and serves 1.5 million people in Suffolk County. We searched our endoscopy database for patients who had a colonoscopy 1/1/99 to 9/30/04 (13,524 pts) and were diagnosed with CRC.

We excluded inpatients (eliminating pts with many co-morbid illnesses), pts with a family history of searched our pathology dept’s database to confirm diagnosis of CRC. We

**Results:** 232 CRC were detected and 110 (m = 68, f = 42) were outpatient. Screening pts (no FOBT (++) (n = 20) were more likely to have an early stage (20/20; I = 16, II = 4) than the 90 symptomatic pts (30/90; I = 8, II = 22, III = 28, IV = 32) (p < 0.001). Univariate analysis of the symptomatic pts showed that lower age (p = 0.05), having insurance (p < 0.01), not smoking (p < 0.001), NSAID use (p < 0.001) and statin use (p = 0.001) were associated with an early stage. Exam indication other than screening was not predictive. Multivariate analysis is shown in the table. Multivariate analysis of the screening pts showed that smoking (OR = 2.095%CI 1.1–3.0) was associated with a higher stage (I vs II,III or IV).

**Conclusions:** Screening colonoscopy diagnosed early stage CRC more often than those exams performed for symptoms. Smoking was associated with a higher stage in both groups. NSAID and statin use were associated with lower stages.

**422 Localization of Dendritic Cells within the Lamina Propria of Ulcerative Colitis and Irritable Bowel Syndrome**

Fabio R. Tavora, M.D., Kymberly Gyare, M.D., Frank D. Koldoge, Ph.D., Allen P. Burke, M.D.* Department of Pathology, University of Maryland, Baltimore, MD and CVPath, International Registry of Pathology, Gaithersburg, MD.

**Purpose:** Dendritic cells (DCs) are antigen presenting macrophages and have been described in the inflammatory infiltrates of ulcerative colitis. Characterization of DCs in ulcerative colitis (UC) with a comparison to irritable bowel syndrome (IBS) has not been performed.

**Methods:** We studied mucosal biopsies from 14 patients with UC (51 ± 10 years, 11 men, 3 women), 8 patients with presumed IBS (34 ± 16 years, 4 men, 4 women) and 6 trauma controls (31 ± 26 years, 4 men, 2 women). DCs were immunolocalized using antibodies to CD1a (immature dendritic cells), DC-SIGN (mature dendritic cells), and S-100 protein (pan-dendritic marker). Morphology of DCs was characterized as immature (short processes) and mature (long, delicate processes). DCs were quantitated in the lamina propria (number / mm²). Activity of UC was graded as mild, moderate or severe, based on the degree of crypt abscess formation. Results: Mean DCs were 24.4 ± 17.5 in UC vs. 16.4 ± 17.2 in IBS (p = .31), as determined by counting S-100 + DCs. Mean DCs in controls was 2.4 ± 1.5 (p = .007 vs. UC). There was no correlation between degree of activity and DC density in cases of UC. IBS cases could be separated into two groups based on DC density; those with < 3 / mm² (DC–IBS), and those with > 3 / mm² (DC + IBS). Mean DC density in DC + IBS was 25.7 ± 15 (p = .004 vs. controls, p = .8 vs. UC). Dendritic morphology in cases of DC + IBS was predominantly mature, with long delicate processes, as compared to UC, although the difference could not be statistically validated. There were no immature CD1a + positive DCs in the mucosa of any of the groups, and DC SIGN + mature DCs were similar in number to S-100 + cells.

**Conclusions:** DCs are increased in the lamina propria of UC. In regards to DC infiltrates, IBS is a heterogeneous process, with a DC-rich groups characterized by mature DCs with long processes and immunophenotype. The role of DC differentiation in the mucosa of colitic patients needs further study.

**423 Fecal Leukocyte Testing as a Predictor of Clostridium difficile Associated Diarrhea**

Savio Reddyramus, M.D., Ankur Sheth, M.D., M.P.H., Gloria Caldito, Ph.D., Daniel Banks, M.D.* Internal Medicine, Louisiana State University Health Sciences Center, Shreveport, LA.

**Purpose:** Willmore and Shearn first described the fecal leukocyte stain in 1918 followed by its clinical use for diagnosis of bacterial diarrhea in 1972 by Harris et al. Today fecal leukocyte testing (FLT) is widely used to screen for inflammatory diarrhea including C. difficile diarrhea, which account for more than 25% of all antibiotic associated diarrhea. Laboratory diagnosis of C. difficile associated diarrhea (CDAD) is based on the detection of C. difficile toxins in stool samples by a cell culture cytopathicity assay or enzyme immunoassay. We evaluated FLT within an inpatient cohort, defining the test’s sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for patients with CDAD.
Methods: A retrospective review of the INVISION database at the Louisiana State University Health Sciences Center, Shreveport, identified 263 patients with stool samples tested for FLT and C. difficile toxins for suspected C. difficile diarrhea. FLT was performed on fresh stool specimens using Geimsa stain and C. difficile toxins were tested using Enzyme Immunoassay (EIA). C. difficile associated diarrhea (CDAD) was defined as diarrhea with stool exam positive for C. difficile toxins by EIA.

Results: Of the 263 stool samples, 68 were positive for FLT and 30 were positive for C. difficile toxin (Table 1). The sensitivity and specificity of FLT as compared to C. difficile toxin assay was 30% and 74.9% respectively. The positive and negative predictive value of FLT was 13.2% and 89.3% respectively. The lower prevalence of positive C. difficile toxin assay (11.4%) may explain in part the low PPV and high NPV of FLT.

Table 1: Comparison of Results from FLT and EIA for C. Difficile Toxins.

<table>
<thead>
<tr>
<th>Test</th>
<th>EIA for C. difficile toxins</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Fecal leukocyte</td>
<td>9</td>
<td>59</td>
</tr>
<tr>
<td>Testing</td>
<td>21</td>
<td>174</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>233</td>
</tr>
</tbody>
</table>

Conclusion: In conclusion, the study presented here reinforces the fact that FLT is a poor predictor of C. difficile infection; because 70% of stool specimens positive for C. difficile toxin are negative for fecal leukocyte; however it has negative predictive value in ruling out CDAD in inpatients. Considering the poor sensitivity and comparable cost and promptness with C. difficile toxins assay in our institution, we conclude that FLT is not a good screening test for CDAD in inpatients.

Back to Back Colonoscopies To Assess the Efficacy of a Tapered Colonoscope in Female Patients

Joseph C. Anderson, M.D.,* John W. Birk, M.D., Zvi A. Alpern, M.D., Isabelle Von Allen. Department of Gastroenterology, Stony Brook University, Stony Brook, NY.

Purpose: Colonoscopy has been shown to be difficult in female patients. The pediatric colonoscope has been used to navigate the difficult left side of the colon but the thinner diameter may lead to looping on the right side. Olympus has developed a prototype colonoscope which has an adult width but tapers to a pediatric width at the distal end. This tapering occurs at 25 cm. We performed tandem colonoscopies in female patients to examine the efficacy of the prototype colonoscope.

Methods: We examined the following endpoints: (1) Need for abdominal pressure (2) Stiffening scope (3) Changing position of patient (4) Ease of cecal intubation (one could reflex). We also examined completion rate. The colonoscopies were performed in tandem fashion on consecutive patients who consented. The initial scope used was alternated between the pediatric variable stiffness colonoscope (PVSC) and the prototype (P25). Based on previous studies we estimated a sample size of 25 in each group. Data collected included age, BMI, bowel habit history, surgical history and colonoscopic findings.

Results: We performed tandem colonoscopies on 49 female patients (89% enrollment). There was no difference in age, BMI or other variables between the group who had the PVSC scope or the group who had the P25 scope. The results are shown in the table below.

<table>
<thead>
<tr>
<th>Variable</th>
<th>P25 Mean (SD)</th>
<th>PVSC Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exam complete</td>
<td>98.0%</td>
<td>94.0%</td>
<td>NS</td>
</tr>
<tr>
<td>Time to cecum</td>
<td>7.1 min</td>
<td>9.12 min</td>
<td>0.048</td>
</tr>
<tr>
<td>Ease of cecal intubation</td>
<td>96.0%</td>
<td>80.0%</td>
<td>0.05</td>
</tr>
<tr>
<td>Abdominal pressure</td>
<td>16.0%</td>
<td>44.0%</td>
<td>0.001</td>
</tr>
<tr>
<td>Change of position</td>
<td>8.0%</td>
<td>18.0%</td>
<td>0.058</td>
</tr>
<tr>
<td>Scope stiffened</td>
<td>10.0%</td>
<td>28.0%</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Conclusions: The P25 needed fewer maneuvers to complete the exam than the PVSC. Ease of cecal intubation was higher using the P25. In addition, the P25 was also faster to the cecum.
**Colonic Ischemia Secondary to Bisacodyl (Ducolax) Use — A Report of 6 Cases**

**Purpose:** To report 6 cases of colon ischemia after colon preparation with bisacodyl over a 6 month period.

**Methods:** We report a case series of 6 patients who presented for colonoscopy using a preparation of bisacodyl ± phosphosoda. None of the patients had significant comorbidities. All but one of the patients scheduled the procedure for routine colorectal cancer screening. Patients were instructed to take 10 mg of bisacodyl on the day prior to taking phosphosoda and 10 mg of bisacodyl after taking the second dose of phosphosoda. All of the patients developed abdominal pain after taking the first dose of bisacodyl. 5 of 6 patients developed rectal bleeding prior to taking phosphosoda. 2 patients did not take phosphosoda after taking bisacodyl second to abdominal pain.

**Results:** All patients developed erythema, ulceration, and biopsy proven ischemia. Affected areas were sigmoid (2) and descending (4) colon. One of the patients who did not take phosphosoda developed a 4 cm sigmoid perforation requiring operative resection.

**Conclusions:** We report 6 cases of colon ischemia associated with preparation for a colonoscopy. While it is possible that 4 of the cases could have been due to dehydration associated with phosphosoda, at least 2 of the cases were secondary to bisacodyl use. This represents the first report of ischemia secondary to bisacodyl.

**Polyflex Coated Esophageal Stents To Assist in the Closure of Colonic Anastomotic Leaks: Report of Two Cases**

**Purpose:** Enteral stents are being used increasingly as a non-surgical alternative for the treatment of benign and malignant diseases of the GI tract. A self expandable plastic stent (Polyflex, Microvasive, Boston Scientific) is commonly used to the treatment of malignant esophageal disease. The Polyflex Esophageal Stent has potential advantages compared with metallic stents as it causes less trauma to surrounding tissues and is removable. We present a novel approach to assist in the closure of colonic anastomotic leaks using this stent in two patients. The first patient is a 52 year old gentleman admitted with lower abdominal pain, fever and nausea two weeks s/p surgical resection for recurrent colon cancer. On physical examination, he was febrile with abdominal tenderness. A CT scan of the abdomen showed extravasation of luminal contrast from the recto-sigmoid region. There was associated free air in the peritoneum. Urgent surgical intervention was recommended. Despite careful explanation of the risks and benefits of surgical intervention, the patient refused. A sigmoidoscopy revealed the anastomotic site at 15 cm from the anal verge. A 1 cm colo-peritoneal fistula at the site of the anastomosis was identified. In order to close the fistula and allow adequate drainage of the pelvic collection, a 15 cm long, 21 mm diameter (25 mm flare) Polyflex Coated Esophageal Stent was placed across the site of the leak. After the procedure, the pain gradually decreased. Within 10 days, the stent passed spontaneously with a bowel movement. The patient remains well. The second patient is a 40 year old gentleman with complicated diverticulitis who had undergone a diverting colostomy. Later he presented with persistent symptoms due to an anastomotic leak. Although recommended, the patient refused surgery. Similar to our first patient, a sigmoidoscopy was performed and again a 15 cm long, 21 mm diameter (25 mm flare) Polyflex Coated Esophageal Stent was placed across the site of the leak. In both patients, resolution of the anastomotic leaks were achieved in the absence of surgical intervention. These two cases contribute to the growing evidence that plastic stents are effective in the treatment of benign disease of the colon. The use of a Polyflex Coated Esophageal Stent may be useful in similar patients who wish to avoid surgery, or who are poor surgical candidates.
Ascariasis, most common helminthic infection worldwide, affects almost a quarter of the world population. Identification of characteristic eggs in the stool is diagnostic but eggs may be absent if only the male worms infest the intestinal tract. Furthermore, limited experience of most US laboratories also makes the identification of the eggs difficult. Capsule endoscopy is a low-risk procedure and is extremely valuable in the diagnostic work-up of unexplained gastrointestinal pathology.

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Drug Interaction Presenting as an Acute Abdomen
Aravind Sugumar, M.D., Umamahesh Rangashetty, M.D.* Internal Medicine, Univ of Texas Medical Branch, Galveston, TX.

Drug interaction is a significant problem in patients who are on multiple medications especially in the geriatric population. We report an interesting case of drug interaction, presenting as an acute abdomen necessitating surgery. A 72 yr old Hispanic female with a history of mechanical mitral valve replacement on warfarin since 1986 presented with severe abdominal pain, for the past five days. She had multiple medical illnesses and her medication included levothyroxine, candesartan, digoxin, furosemide, metoprolol, alendronate and sertraline. Prior to presentation, anticoagulation was optimal with monthly follow-up and dietary restrictions. Miconazole 1% topical cream for vaginal candidiasis was started a week ago by her primary care physician. She described the abdominal pain as severe, initially periumbilical and intermittent which subsequently became continuous and diffuse, associated with nausea and diarrhea. Physical examination was notable for tachycardia and mild diffuse abdominal tenderness. Laboratory investigations were remarkable for international normalized ratio (INR) >13, hemoglobin (Hgb) of 12.2 gm/dl and heme-occult positive brown stool. An acute abdomen series revealed a normal bowel gas pattern. She was admitted, managed conservatively with intravenous fluids, NPO and pain control with morphine. Six units of fresh frozen plasma (FFP) and vitamin K (10 mg SC) were given. 18 hrs after admission abdominal pain worsened along with multiple episodes of vomiting and melena. Repeat physical examination was notable for diffuse rebound tenderness and orthostatic hypotension. Labs revealed an INR of 6 and Hgb of 8.2 gm/dl. She was transfused two units of packed RBC and CT abdomen was done which revealed numerous fluid filled loops of small bowel, which were edematous and thickened. Surgery was consulted and the patient underwent emergent exploratory laparoscopy. Intra-operatively a 20 cm length of jejunum was hemorrhagic and devitalized requiring resection. Postoperative period was uneventful. Histopathology revealed an intramural bowel hematoma. She was discharged on enoxaparin and warfarin. 

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Closure of Entero-Vesical Fistula in Crohn’s Disease with Infliximab: Two Years Follow up of Two Cases
Flavio Steinwurz, M.D., F.A.C.G.* Gastroenterology, Hospital Israelita Albert Einstein, Sao Paulo, Brazil.

Fistula is one of the most common and unpleasant complications of Crohn’s disease. Infliximab showed efficacy in healing perianal and abdominal wall fistula. We treated 2 patients with enterovesical fistula, both females, with infliximab and after they achieved the healing of the lesion they were followed for 2 years in order to evaluate the maintenance of the fistula closure. Two patients with Crohn’s disease complicated with enterovesical fistula, verified by urinary tract infection, abdominal CT and ultrasound, were treated with infliximab 5 mg/kg every 8 weeks. At the beginning they were on antibiotic (ciprofloxacin 500mg bid). They had clinical evaluation every month on the first 6 months, and every 3 months afterwards. Both had blood and urine tests done every month for the first 6 months, and every 3 months afterwards. Ultrasound every 3 months, and abdominal CT every 6 months were also done. The 2 patients achieve healing of the enterovesical fistula right after the second infusion of infliximab and remained with no symptoms for the 2 years of follow up. After 3 months they could take the antibiotic off, and had no recurrence of the urinary tract infection. Blood tests showed remission of the disease and urine tests were normal. Ultrasound showed no more evidence of thickness on the bladder wall, and no signs of possible fistula. They completed 2 years of follow up, remained with no symptoms and all the tests were absolutely normal. The treatment of enterovesical fistula in Crohn’s disease with infliximab showed good results, with sustained healing for 2 years of follow up. Despite few reports in the literature and very restricted experience, the use of infliximab in the treatment of enterovesical fistulas in Crohn’s disease seems to be a valid option.

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Dietary Fructose Intolerance Mimicking Irritable Bowel Syndrome
Jigna N. Thakore, M.D., Christopher J. Barde, M.D., Adam G. Mezoff, M.D.* Gastroenterology, Veterans Administration Medical Center, Dayton, OH and Gastroenterology, Children’s Medical Center, Dayton, OH.

Introduction: Fructose malabsorption is not commonly assessed, but its symptoms of abdominal pain, bloating, and diarrhea may be indistinguishable from irritable bowel syndrome (IBS). We report a patient with a diagnosis of IBS who had a positive fructose breath hydrogen test and her symptoms completely resolved with dietary fructose restriction.

Patient: A 16-year-old Caucasian female presented with acute dysphagia. She also complained of several years of intermittent abdominal pain and bloating, and several months of intermittent diarrhea. EGD showed a large esophageal ulcer, but the stomach and duodenum were unremarkable. Further evaluation showed that the complete blood count, comprehensive metabolic panel, and erythrocyte sedimentation rate were within normal limits. Stool studies were negative for ova, parasites, and enteric pathogens. An upper GI showed moderate gastroesophageal reflux and a small bowel follow through was normal. Tissue transglutaminase, anti-gliadin antibodies, and anti-endomysial antibodies were negative. Perinuclear-staining antineutrophil cytoplasmatic antibodies and anti-Saccharomyces cerevisiae antibodies were negative. A fructose breath hydrogen test (FBHT) was done because the dietary history revealed a high intake of fresh fruits and vegetables. Breath hydrogen analysis after fructose load of 57.5 grams showed an increase by greater than 20 parts per million of expired hydrogen above baseline within 2 hours. Patient’s symptoms resolved after eliminating all forms of fructose from her diet.

Discussion: There is an increase in the use of low-cost corn syrup and high-fructose containing syrups as sucrose substitutes by many North American food companies which has resulted in an increase in fructose in the American diet. It is possible that many patients with dietary fructose intolerance (DFI) may be misdiagnosed with IBS. Fructose malabsorption has been reported in 36% of the European population and in up to 80% of Americans. Seventy-one percent of American children aged 1 month to 17 years have been found to have incomplete absorption of fructose. Bloating, abdominal cramps, and osmotic diarrhea occur in these patients when the unabsorbed monosaccharides reach the colon where they are broken down into short chain fatty acids, CO2 and H2. Although not all children and adults with DFI have GI distress, up to 50% percent may be symptomatic. Evaluation by FBHT in this population should be considered.

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Interferon α Induced Ischemic Colitis
Sujeeth R. Panam, M.D.,* Aparna Panum, M.D., Venkateshan Ranganathan, M.D. Internal Medicine, Nacogdoches Medical Specialties, Nacogdoches, TX.
Introduction: Interferon α is a widely used treatment for chronic hepatitis B and C. Complications of interferon therapy include systemic flu like symptoms, marrow suppression, emotional liability, auto immune reactions and miscellaneous side effects. We report a case of a 51-yr old man, who developed ischemic colitis after interferon α therapy for chronic hepatitis C.

Case Report: A 51 yr old Caucasian male with history of chronic hepatitis C presented to the emergency room with bright red bleeding per rectum. Other history is unremarkable. The patient was undergoing combination therapy with pegylated interferon α and ribavirin as an outpatient for chronic active Hepatitis C for the last three months. The patient underwent colonoscopy four months prior to this hospitalization as part of routine colorectal cancer screening which was fairly unremarkable. Physical examination and routine blood work were grossly normal. Abdominal x-ray and abdominal CT were normal. Colonoscopy to the cecum revealed acute focal segmental colitis involving mid transverse to proximal descending colon. Biopsy of the colon showed acute colitis with ulceration primarily compatible with ischemic colitis. Stool analysis revealed only red cells and white cells. Further hypercoagulable workup was negative. Upper endoscopy failed to show any stigmata of active bleeding. The hepatitis C therapy with interferon α and ribavirin was discontinued. A follow up colonoscopy three months later showed complete resolution of ischemic colitis, which was proved by biopsy.

Discussion: Treatment of chronic active hepatitis C with pegylated Interferon α plus Ribavirin is a very effective treatment option. We report the first case of ischemic colitis associated with use of pegylated interferon α in the USA. There are only two histo-pathologically confirmed cases of ischemic colitis reported in Japan until now. Our patient had no risk factors for ischemic colitis. The temporal association and relief of symptoms on cessation of therapy, normalization of the colon seen on colonoscopy and repeat biopsy at 3 months clinches the diagnosis of interferon α induced ischemic colitis.

Cryptococcal Meningitis Presenting as a Fever of Unknown Origin Following Immunosuppressive Therapy for Autoimmune Hepatitis
Sadiya Sarij, M.D., David Eskreis, M.D.* Internal Medicine, North Shore University Hospital – NYU School of Medicine, Manhasset, NY.

Introduction: Cryptococcus neoformans (C.N) is an opportunistic pathogen causing chronic meningitis in immunocompromised patients. The diagnosis is often missed or delayed in these patients because of the non-specific clinical features, limited usefulness of available serological tests, and failure to isolate CN in blood cultures, positive in less than one third of patients.

Case Report: A 20-year-old female with congenital arthrogryposis presented with ascites, lower extremity edema, jaundice, coagulopathy and an autoantibody profile of autoimmune hepatitis. Diagnostic liver biopsy was followed by asymptomatic temp. to 103 F and the patient admitted for observation. An extensive fever workup during a 10 ten hospitalization was negative. She was readmitted one week with lethargy, confusion, bradycardia and recurrent fever. Medications included: Prednisone 7.5 mg daily and Immuran 100 mg daily for treatment of autoimmune hepatitis. P.E. revealed a febrile somnolent cushingoid female without focal neurologic or abdominal findings. Labs revealed coagulopathy secondary to liver dysfunction. On the second day of hospitalization, blood cultures were notable for a fungal species. She rapidly developed severe headache, vomiting, disconjugate gaze and meningismus. A lumbar puncture showed increased ICP and India ink staining of the CSF and spinal fluid and blood cultures confirmed the diagnosis of Cryptococcal meningitis. The patient was treated with Amphotericin B and 5-Flucytosine. Multiple lumbar drainages were required to control increased ICP. She made a complete neurological recovery.

Discussion: Patients on immunosuppressive therapy are at increased risk for cryptococcal diseases. Cirrhosis may be an additional predisposing factor by impairment of host defenses including complement deficiency, defects in neutrophil chemotaxis, and lymphocyte hyporesponsiveness.

To our knowledge, the diagnosis of disseminated Cryptococcosis by blood cultures in a patient with Autoimmune Hepatitis has not been described previously. This case demonstrates that prolonged fever and therapy with corticosteroids and immunomodulators should raise concern for emerging disseminated Cryptococcal disease. The acute and atypical clinical manifestations in our patient indicate the importance of early consideration of this disease as clinical deterioration and death may be precipitous.

Case Report: Multiple Myeloma Arising in the Setting of Infliximab Treatment of Crohn’s Disease
G. Joel Reynolds, M.D., Kim Annis, PA., Aruna Arekapudi, M.D., Willem J.S. deVilliers, M.D.* Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY.

The use of the chimeric monoclonal antibody against tumor necrosis factor (TNF) known as infliximab has been scrutinized for its possible association with malignancy. The National Institutes of Health Surveillance Epidemiology and End Result (SEER) database cites 6 patients who developed lymphoma out of 2,427 patients treated in clinical trials with infliximab. The three major studies of the safety and efficacy of infliximab, the ACCENT I trial, the Mayo Clinic experience in 500 patients, and the ACCENT II trial, all found a less than 1% rate of lymphoma development which could have been related to infliximab therapy.

Our case represents the only reported case of multiple myeloma arising in the setting of infliximab treatment for Crohn’s disease. A 50 year old white female had been on escalating doses of infliximab for 4.5 years when she was diagnosed with stage III multiple myeloma. It is highly probable, but difficult to be certain that infliximab therapy had a causal role in our patient developing multiple myeloma. The pathogenesis may be related to decreased apoptosis of plasma cell lines. Since it is possible
that a causal association exists between infliximab therapy and multiple myeloma, perhaps additional screening measures such as urine protein and/or urinalysis with sulfosalicylic acid should be done in patients with Crohn’s disease on infliximab.

Metastatic Melanoma Presenting as a Massive Abdominal Mass with Lower Extremity Radiculopathy: A Very Rare Presentation
Gavin F. Chico, M.D., Michelle A. Chico, M.D., Be Muslow, M.D.*
Internal Medicine, David Raines Health Center, Shreveport, LA and Internal Medicine, Overton Brooks VA Medical Center, Shreveport, LA.

Purpose: The purpose of this case report is to highlight the unusual and often vague presentations of melanoma metastatic to the abdomen.
Case: A 63-year-old male with past history of prostate cancer and surgically resected left arm melanoma, presents with left lower extremity pain and weakness, one month after finishing brachytherapy for prostate cancer. In the following months patient was evaluated for sciatica, claudication and DVT with normal doppler studies and x-rays of the lumbar spine and pelvis. The lower extremity paraskeiæs and paresis progressively worsened in this 8-month period requiring the patient to use a cane for ambulation. Patient also had 40-lb weight loss with anorexia but no other gastrointestinal complaints. At admission the abdominal exam revealed a large palpable mass extending from the midline to the left flank. Catscan of abdomen/pelvis revealed a massive 11 x 14 left abdominal mass with multiple nodular masses in the mesentery. FNA biopsy showed a poorly differentiated non-small cell carcinoma with following immunohistochemistry:
HMB-45: positive
Vimentin: strongly positive
S-100: focal weak positive
PSA: negative
CK7: negative
Cytokeratin: negative

The above findings were consistent with metastatic melanoma. An MRI of the spine done for worsening paraparesis showed cauda equina compression requiring radiation therapy. However the patient was unable to undergo further treatment due to his deteriorating clinical status and succumbed to complications of the malignancy.

Discussion: Malignant melanoma metastatic to the abdomen has a clinical diagnostic rate of just 2%, in contrast to 60% of autopsies that are found to have gastrointestinal involvement in patients that died with disseminated disease. Most cases of metastatic melanoma to the gastrointestinal tract present with vague symptoms of weakness, fatigue, abdominal pain and anemia. Our case report is very unusual in that it presented as a huge abdominal mass with mesenteric involvement and lower limb radiculopathy. It also highlights the need for early imaging which is effective in ascertaining the extent of disease and the potential benefit of surgery as complete resection of metastasis is associated with prolonged survival.

Conclusion: The presentation of melanoma metastatic to the gastrointestinal tract is vague and requires early investigation of symptoms as curative surgery can prolong survival.

Severe Colitis Caused by Staphylococcus aureus Associated with Antibiotic Use: 2 Cases
R. Erick Pecha, M.D., * Thomas Prindiville, M.D., Eliot R. Drell, M.D., Mark W. Redor, M.D. Gastroenterology Medical Clinic, Folsom, CA and Gastroenterology, UC Davis Medical Center, Sacramento, CA.

Introduction: Staphylococcus aureus (S. aureus) was believed to be the likely cause of antibiotic associated enterocolitis in the 1950’s and 1960’s. Since the 1970’s however, Clostridium difficile (C. diff.) has been the prime suspect in antibiotic induced colitis. We describe two cases of C. diff. negative colitis cause by S. aureus:
Case 1: 54 yo w with ulcerative colitis was treated with Asacol for diarrhea and improved. Two weeks after ciprofloxacin for a UTI, she developed sudden worsening with bloody diarrhea and fever. Flagyl was begun but stools tested negative for C. diff. and usual enteric pathogens. High dose steroids were begun. Colonoscopy revealed pANCELStis with intense inflammation and deep ulcerations in the ascending colon and ileocecal valve. Bloody diarrhea worsened and repeat stool cultures revealed a pure culture of methicillin-resistant S. aureus (MRSA). Marked improvement occurred after IV and oral vancomycin and steroids were rapidly tapered. Oral vancomycin and probiotics alone were continued for 2 weeks, with no relapse of symptoms over the next year.
Case 2: 55 yo w with history of rectsigmoid cancer treated with resection and radiation complicated by mild radiation proctitis and mild stricture presented one month after a course of clariíthromycin with sudden abdominal pain, watery diarrhea, and fever to 102°F. Colonoscopy revealed a mild rectal stenosis, severe pancelitis, and massive colonic dilation. Stool C. diff. was negative but stool culture revealed S. aureus, sensitive to multiple antibiotics. He was treated with oral vancomycin and probiotics and recovered rapidly.

Discussion: The temporal association of antibiotic use in these patients, the lack of stool antigen for C. diff., the pure stool culture for S. aureus, and the rapid improvement with oral vancomycin strongly suggests an etiologic role for S. aureus as the cause of severe colitis in these two cases. The background of inflammatory bowel disease in Case 1 and the radiation proctitis in Case 2 suggests that colonic mucosal immunocompromise may have predisposed both patients to the S. aureus overgrowth after antibiotic use.

Conclusion: S. aureus can cause severe antibiotic associated colitis. Stool cultures testing for S. aureus should be performed in addition to C. diff. toxin in patients with suspected antibiotic induced diarrhea. Oral vancomycin and probiotics are effective for S. aureus colitis.

Cap Polyposis: A Rare Clinical Syndrome
Warren Finkelstein, M.D., F.A.C.G.∗ The Gastroenterology Group of New Jersey, Glen Ridge, NJ.

Background: Cap polyposis is a rare disorder consisting of multiple rectal and sigmoid colon polyps covered with a cap of fibropurulent exudate and mucus. Clinically, it presents with diarrhea, rectal bleeding, and/or tenesmus. The histological findings suggest a mucosal prolapse syndrome. Treatment includes metronidazole, antibiotics for H. pylori, and anti-inflammatory medications which are often unsuccessful. A recent case report described the successful use of infliximab in a patient with cap polyposis. Surgery has most often been required to treat this condition. I document a case of cap polyposis in which medical therapy (including infiximab) was ineffective but which was successfully treated with proctosigmoidectomy.

Case Report: A 62-year-old man presented with a 3-month history of severe diarrhea, severe rectal urgency, and constant rectal discharge of mucus. Colonoscopy showed multiple polyps of the rectum and sigmoid colon with mucoid secretions (Figure 1). Pathology of the polyposis indicated hyperplastic and regenerative changes with granulation tissue and features suggesting mucosal prolapse. A trial of metronidazole was unsuccessful. A breath test for H. pylori was negative. Infliximab 5 mg/kg was given. Although the patient was markedly improved after one week, severe symptoms recurred and the patient was referred for surgery. A proctosigmoidectomy (Figure 2) with coloanal anastomosis and temporary loop ileostomy was done. The patient did well post-operatively and currently is asymptomatic. Figure 1. Figure 2. Cap polyposis is a rare clinical syndrome. Although medical therapy (including infliximab) may be attempted, proctosigmoidectomy is often required to treat this severely symptomatic disorder.
CFTR Mutations: Predisposition to Acute Pancreatitis with Intercurrent C. jejuni Infection
Leena Kandula, M.D., Mark E. Lowe, Ph.D., Seema Khan, M.D.*

Acute pancreatitis (AP) is a rare association with Campylobacter jejuni enteritis. AP in association with another infectious illness like enteritis, may be related to an underlying genetic mutation. We report a patient with C. jejuni and AP, who was later found to have cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations.

A 15 yr old girl presented with abdominal pain and non bloody diarrhea for 8 days. She had a 5 lb weight loss, bilateral knee pain, 103.8°C fever and had used acetaminophen and ibuprofen. Past history was significant for poor growth, recurrent abdominal pain, and serum lipase elevated two fold normal on two occasions. Other tests in the past were a normal ultrasound and CT of abdomen, upper gastrointestinal and small bowel series, HIDA scan, celiac disease serology and duodenal biopsies. Sweat chloride test showed Na of 69 and Cl of 60 (N 0–40 mEq/L); pulmonary function tests, 72-h fecal fat, and fat soluble vitamin levels were normal. Family history revealed celiac disease in a cousin. She had unpasteurized milk 1 week prior to the acute illness. On admission her weight was <3% ile and exam revealed epigastric tenderness. Pertinent investigations were serum amylase of 103 (N < 90 IU/L) and lipase of 3,663 (N < 200 IU/L). Pain was managed with meperidine, feedings were held and intravenous fluids were started. Fasting lipid panel, repeat abdominal ultrasound and CT were normal. C. jejuni was detected on stool culture and she was treated with azithromycin for 7 days. She was pain free while she received nasojejunal nutrition with Ensure but notably serum amylase and lipase peaked to 554 & 21,047 respectively. Magnetic resonance cholangiopancreatography at this stage was normal. Furthermore, a buccal swab was performed for CF genetic mutation analysis; she was a compound heterozygote for R117H, ∆F508 mutations. At 1 month follow-up, she remained asymptomatic on a regular diet and, serum amylase & lipase decreased to 308 & 650 respectively. CFTR mutations predispose to recurrent acute & chronic pancreatitis. In our patient with genetic predisposition to AP due to CFTR mutations, C. jejuni was thought to be an environmental modifier in initiating the acute episode.

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Celiac Sprue Presenting as Chronic, Calcific Pancreatitis in an Elderly Male
Lisbeth A. Selby, M.D., Steven Shedlofsky, M.D.* Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY.

Celiac sprue (CS) often presents with malabsorption due to immune destruction of intestinal villi. Diagnosis is not limited to children but presentation in the elderly is rare.

We report an atypical case of CS in a 75 year old. He presented with loose stools, weight loss and 6 months of leg edema. Preliminary labs revealed transaminases 1.5x the upper limit of normal. A CT revealed a large liver with extensive fatty change, pancreatic parenchymal calcifications and dilation and enlargement of the pancreatic duct. The history was remarkable for a MI at age 72. Additional labs showed hypoalbuminemia and an INR 2.3. A 72 hr stool specimen showed 30 gm of fat. He had total resolution of his loose stools after a 2–3 month phase of learning to titrate his pancreatic enzymes. The coagulopathy corrected with parenteral vitamin K and did not recur in 3 years follow up. The edema and hypalbuminemia corrected slowly over 10 months. The persistence of transaminase elevations prompted further work up. Serologic work up revealed only positive tissue transglutaminase Ab, anti-endomysial IgA, and anti-gliadin IgG and IgA. The small bowel biopsy revealed blunting of the villi, crypt hyperplasia, increased intraepithelial lymphocytes, and marked chronic inflammation within the lamina propria. CS was diagnosed. A gluten free diet (GFD) was recommended. The patient was reluctant to change his diet at his age since he felt well. The loose stools remain well controlled after 3 years with pancreatic enzyme therapy and a regular gluten-containing diet.

Our case highlights a rare presentation of CS. The patient did indeed have malabsorption which was seemingly unrelated to mucosal disease as it corrected with pancreatic enzymes. After resolution of symptoms, the sole remaining clue of CS was transaminase elevations.

Although manifestations of CS are protean and the hepatic findings are well known, calcific pancreatitis has only rarely been associated with the disease. In 2001 a pediatric group reported pancreatic failure which reversed with GFD. Chronic malnutrition has been associated with pancreas exocrine dysfunction and may play a role in this case. However, the patient did not have long-standing symptoms to suggest this. Moreover, he has no history to suggest other etiologies of chronic pancreatitis such as alcohol abuse. In summary, we propose this elderly patient’s painless, chronic pancreatitis with exocrine insufficiency is plausibly a manifestation of CS.
Esophageal Squamous Papilloma—An Unusual Cause of Chest Pain and Odynophagia

Sherman M. Chamberlain, M.D.* Division of Gastroenterology BBR-2538, Medical College of Georgia, Augusta, GA.

A 54-year-old male presented with several months of worsening chest pain and odynophagia, described as a spasmodic, searing discomfort with swallowing. The symptoms initially occurred when he ate solid food, however progressed both in frequency and severity, eventually occurring daily with ingestion of both solid food and liquids. He was treated empirically for one month with a standard dose oral proton pump inhibitor with no improvement in his symptoms, thus he discontinued the medication. A barium swallow demonstrated a 3 cm elongated filling defect in the mid-distal esophagus tethered to the esophageal wall, but which moved freely, consistent with an esophageal polyp. There was no evidence of esophageal reflux in the study. An upper gastrointestinal endoscopy revealed a smooth, consistent with an esophageal polyp. There was no evidence of esophageal distal esophagus tethered to the esophageal wall, but which moved freely, symptoms, thus he discontinued the medication.

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Chest pain is a common esophageal symptom, caused by esophageal motility disorders. Odynophagia is a frequent presenting symptom of disorders of the esophagus which cause breaches in the esophageal mucosa. This is the first case reported of an esophageal squamous papilloma causing chest pain and odynophagia. Squamous papillomas of the esophagus are rare benign tumors, composed of finger-like projections of the lamina propria covered by hyperplastic squamous epithelium, usually less than 1 cm in size. They are frequently associated with gastroesophageal reflux and HPV, neither of which appears to be associated with this case. Presumably, the length of the squamous papilloma created a pulling effect which was responsible for this patient’s symptoms of chest pain and odynophagia associated with food and liquid ingestion, since his symptoms resolved after its removal. Elongated esophageal polyps, as described in this case, should be considered in the differential diagnosis of chest pain and odynophagia.[figure1]

Background: Fecal and urinary incontinence may be caused by infiltration of abdominal or pelvic masses into nearby nerve roots. Typically abdominal imaging such as CT or MRI are used to evaluate such tumors. Herein we report a case of pelvic lipoma causing neurological symptoms diagnosed with endoscopic ultrasound (EUS) guided fine needle aspiration (FNA).

Case Report: A 55-year-old man presented with a chief complaint of a new onset of bowel and bladder incontinence, bloating, and back pain. He denied weight loss or pain radiating down his lower extremity but did admit to increasing fatigue. He had benign polyps found on colonoscopy four years earlier. Magnetic resonance imaging (MRI) and Computed Axial Tomography scan (CT) indicated a 7.7 × 5.8 cm left pelvic mass anterior to the sacrum deviating his rectum to the right, concerning for a liposarcoma. No obstruction or abdomino-pelvic lymphadenopathy was present.

EUS was performed and demonstrated a heterogeneous, encapsulated mass adjacent to the rectum approximately 10 to 15 cm from the anal verge. The mass did not appear to be invading into the surrounding structures. EUS guided FNA of the mass revealed several large clusters of non-atypical adipocytes concerning for a low-grade neoplasm. The patient underwent exploratory laparotomy with removal of the tumor. Intra-operative findings showed a lipomatous tumor posterior to the left ureter infiltrating into the third sacral foramen. The tumor was dissected off the sacral nerve root and pre-sacral attachments. Frozen sections revealed a well-differentiated adipocytic lesion.

The patient discharged home on post-op day four with full bowel and bladder function. Immediately post-operatively, there was some residual numbness along his left lateral thigh which resolved over the ensuing 4 to 6 weeks. Final pathology revealed a 9.9 cm intramuscular lipoma with focal fat necrosis.

Conclusion: This is the first documented case of a pelvic lipoma causing neurological symptoms diagnosed by EUS. It illustrates the broadening diagnostic and therapeutic utility of EUS.

A Case of Diagnosing Parasitic Infestation during Capsule Endoscopy

Manuel Martinez, M.D., Oleg Katcher, M.D., Susan Williams, M.D.* Gastroenterology and Hepatology, Metropolitan Hospital/New York Medical College, New York, NY.

44-year-old Hispanic immigrant male presented with eosinophilia and non-specific abdominal pain. He underwent a colonoscopy and upper endoscopy. The results of these procedures were normal except for mild gastritis and a positive urease test. He was subsequently treated with a triple antibiotic regimen for 2 weeks but symptoms persisted. He had an abnormal small bowel series that reported small bowel wall irregularity and thickening. Laboratory results were as follows: hemoglobin of 15–16 g/dl and an ESR of 2 mm/hr, WBC of 4.0 (10^9/L) with 8.6% eosinophils. Capsule endoscopy (CE) was performed to rule-out occult IBD. The CE study found an incidental white translucent helminthic parasite attached to the mucosa approximately at the mid-jejunum. Red blood was visible within the gut of the parasite. Multiple images demonstrated extravasation of blood oozing from the helminthic point of attachment with the mucosa. No ulcers or erosions were appreciated in the rest of the small bowel. The patient underwent stool analysis for ova and parasites in attempt to identify the parasite. On three separate stool specimen, the results were positive only for the presence of the protozoans Blastocystis hominis and Endolimax nana. Based on the morphological characteristics of the helminth such as “S-shaped, double hook” appearance, the likely diagnosis is Hookworm (picture or clip available). The patient was treated with mebendazole and his symptoms resolved after completion of the medical regimen. Hookworm infection is difficult to diagnose by using stool sampling or serologies. Its diagnosis is based on clinical suspicion, frequently based on the presence of otherwise unexplained iron deficiency anemia with associated abdominal pain. Our patient presented atypically, with a normal hemoglobin concentration, obscuring the potential diagnosis of intestinal parasitosis. We propose that capsule endoscopy is an invaluable diagnostic modality in the work-up of unexplained abdominal pain, particularly in the immigrant population.
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Spontaneous Pneumothorax and Pneumoperitoneum Complicating an Endoscopic Retrograde Cholangiopancreatography with Stent Exchange
Young Lee, M.D., Franklin E. Kasmin, M.D., Seth A. Cohen, M.D., Jerome H. Siegel, M.D.* Division of Digestive Disease, Beth Israel Medical Center, New York, NY.

A 51 year old male, heavy smoker, presented for biliary stent removal. Two months earlier, he developed abdominal pain, weight loss and abnormal biochemical profile. A magnetic resonance cholangiopancreatography (MRCP) demonstrated a common hepatic duct stricture. He underwent an ERCP with sphincterotomy, stricture brushings and biliary stent placement. The follow-up ERCP was performed in the same fashion with intravenous propofol, meperidine and midazolam sedation. The patient was maintained in sedation in the prone position while breathing spontaneously using supplemental nasal cannula. The previously placed biliary stent was removed without complication. No sphincterotomy or other therapy was performed. Well into the procedure, the patient developed hypoxia with his O2 saturation decreasing to 60% on 3L/min of oxygen via nasal cannula. The oxygen flow rate was increased to 10L/min, the propofol infusion stopped and the patient's hypoxia improved with a rise in O2 saturation to 93%. The procedure was completed. The patient was found to have a markedly distended abdomen with diffuse tenderness and crepitus extending from his chest to his neck. X-rays revealed extensive subcutaneous emphysema, a large left sided pneumothorax and free air in the abdomen. A chest tube was placed into the patient's left hemithorax, and an upper gastrointestinal series, and computer assisted tomography scan was performed using gastrografin contrast. Despite the findings of a large amount of pneumoperitoneum, pneumoretroperitoneum, pneumothorax and pneumomediastinum, there was no extravasation of contrast material. An emergency laparotomy was performed. Despite the presence of retroperitoneal air, there was no perforation and no evidence of intestinal content leakage. Examination of the lesser sac and the esophagogastric junction was negative. His post-operative course was unremarkable and he was discharged home in the fifth post operative day. Since the laparotomy failed to demonstrate perforation and the patient improved with chest tube insertion, we hypothesize that this heavy smoker developed a pneumothorax during the ERCP as a result of a ruptured sub-pleural bleb. A large amount of air dissected through the mediastinum into the retroperitoneal and peritoneal spaces during endoscopy. Although the risk of pneumothorax is very small and it is a rare cause of pneumoperitoneum, recognizing it may save patients unnecessary surgery.

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Sclerosing Hepatic Carcinoma in a Hepatitis B Carrier
Catherine T. Frenette, M.D.*, Paul J. Pockros, M.D., F.A.C.G.
Gastroenterology and Hepatology, Scripps Green Hospital/Scripps Clinic, La Jolla, CA.

A 34 year old Afghan man presented with complaints of weight loss of 20 pounds in 6 months and abdominal pain. Past medical history was significant only for the patient being a known carrier of hepatitis B since age 15. Abdominal exam revealed a palpable mass in the right upper quadrant. Initial laboratory tests showed a normal CBC, normal liver enzymes, elevated AFP of 72 ng/mL, and elevated calcium level of 11.0 mg/dl (normal range 8.1–10.5). Hepatitis B surface antigen was positive, and HBV DNA PCR was 3700 copies/mL. The HCV antibody and HCV RNA were negative. CT scan revealed a 12 cm multilobular mass in the right lobe of the liver, as well as multiple small pulmonary nodules. Core biopsy of the liver lesion revealed tissue consistent with sclerosing hepatic carcinoma. Biopsies of lung lesions confirmed metastatic disease. The patient is currently being treated with doxorubicin. His latest CT scan revealed advancement of his disease. Sclerosing hepatic carcinoma is a rare variant of hepatocellular carcinoma in which cords and nests of neoplastic cells are surrounded by dense fibrous tissue. It represents 3.5% of all hepatocellular carcinomas, and is frequently misdiagnosed as metastatic adenocarcinoma. It is associated with hypercalcemia as a paraneoplastic manifestation of the disease in 70% of cases. In contrast to typical hepatocellular carcinoma, the majority of cases do not have chronic liver disease with cirrhosis. Average age of diagnosis is 62 years, and it is found equally in men and women. Unfortunately, 80% of patients have metastases at time of diagnosis, and average survival from time of diagnosis is 4.5 months. Despite the known risk for hepatocellular carcinoma in hepatitis B carriers, this type of tumor has never been reported in the English literature in association with a positive Hepatitis B surface antigen.

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Clostridium Difficile Colitis Causing Rhabdomyolysis

We report the first case of rhabdomyolysis associated with clostridium difficile colitis.

A 57 year old man with a prior history of irritable bowel syndrome was admitted to the hospital with a 7 day history of fevers, chills, and 8–10 watery, non-bloody stools every day. Stool ELISA was positive for clostridium difficile toxins A and B. Other stool studies were negative. An abdominal radiograph revealed extensive thumb printing of the colon. CT scan of the abdomen showed ascites and severe colitis involving the entire colon. He was diagnosed with rhabdomyolysis based on Creatine Phosphokinase level of >25,300 IU/L and urinary myoglobin of 434120 ng/ml. The patient was treated with intravenous normal saline, intravenous flagyl 500mg every 8 hours and oral vancomycin 500mg four times a day. The patient maintained a brisk urine output and his CPK decreased to the normal range. His symptoms resolved completely and he was discharged home a week after admission. Clostridium difficile is a spore forming, toxin producing gram negative bacillus that has been implicated as a major cause of antibiotic associated colitis in humans.
There are numerous case reports of rhabdomyolysis associated with salmonella, pneumococcal and streptococcal infections. Clostridium perfringens infections with muscle involvement and necrosis causing rhabdomyolysis have also been reported.

We report the first case of rhabdomyolysis associated with clostridium difficile colitis. The mechanism is uncertain. There was no ischemia or direct muscle involvement. A direct cytotoxic effect of the Clostridium difficile toxins remains the most likely possibility.[figure1][figure2]

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**Diverticulitis of the Esophagus: An Uncommon Etiology of Non-Cardiac Chest Pain**

Scott D. Pollack, M.D., David R. Silvers, M.D., F.A.C.G.* Internal Medicine, Tulane University Health Sciences Center, New Orleans, LA and Metairie, LA.

A fifty-three year old male presented to the gastroenterology clinic for evaluation of chest and mid-epigastric pain after an evaluation had excluded a cardiac etiology. He also reported the sensation of abdominal bloating, occasional nausea and vomiting after large meals, and chronic constipation. He denied dysphagia and blood in his stool. The patient had a past medical history significant for coronary artery disease with previous coronary artery bypass grafting of five vessels. The patient underwent esophagogastroduodenoscopy (EGD) that showed a large distal esophageal diverticulum. Subsequently, a double contrast esophagram re-confirmed the presence of a 3.6 × 2.4 cm diverticulum in the distal esophagus. The following month the patient required hospitalization and intravenous antibiotics for the acute onset of chest pain, nausea, vomiting, and fever. Due to these continued difficulties with the esophageal diverticulum, the patient was referred to a thoracic surgeon. The patient then underwent a right posterolateral thoracotomy with surgical resection of the diverticulum plus an associated esophagomyotomy. No post-operative complications occurred and there was complete relief of the symptoms of chest pain, nausea, vomiting, and fever. On pathological review of the resected specimen, it was found that the esophageal diverticulum had scattered intraepithelial and subepithelial chronic inflammatory cells, thus acquiring the diagnosis of esophageal diverticulitis.

Diverticula of the gastrointestinal tract are a common finding among patients, most notably within the large intestine, but diverticula of the esophagus are only a small percentage of the total cases. It is rare to discover inflammation of an esophageal diverticulum as a cause of chest pain. Chest pain of esophageal origin has numerous etiologies most often from either motility disorders or inflammation of the mucosa. In this patient, the infection and inflammation of the large esophageal diverticulum resulted in acute chest pain that responded to treatment with systemic antibiotics. Surgical resection of the diverticulum, although uncommon, provides definitive treatment.

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**Extramedullary Plasmacytoma of the Rectum Diagnosed by Endoscopy: Case Study and Review of the Literature**

Scott D. Pollack, M.D., David R. Silvers, M.D., F.A.C.G.* Internal Medicine, Tulane University Health Sciences Center, New Orleans, LA and Metairie, LA.

A sixty-four year old male presented to the gastroenterology clinic with a chief complaint of bright red blood per rectum. The patient had a past medical history significant for monoclonal gammopathy of undetermined significance (MGUS) and a previous finding of esophageal leiomyoma by esophagogastroduodenoscopy (EGD). He underwent colonoscopy with the pertinent findings of a protruding submucosal and non-blooding mass in the rectum, along with internal hemorrhoids. A biopsy of the mass was performed with pathological findings consistent with extramduillary plasmacytoma. Further imaging and pathological work-up was performed and a diagnosis was made of solitary extramduillary plasmacytoma of the rectum.

Extramduillary plasmacytommas are a rare type of plasma cell neoplasms that originate outside of the bone marrow. These tumors are usually found within the upper respiratory and gastrointestinal tracts, with only approximately six percent within the lower gastrointestinal tract. Upon review of the literature there have only been twenty-three reports of extramduillary plasmacytommas of the large intestine. Additionally, diagnosis of plasmacytoma by colonoscopy is a rare finding. A definitive diagnosis of solitary extramduillary plasmacytoma in this patient was made by successfully excluding other myeloma lesions by imaging, performing a bone marrow biopsy, and analyzing the serum for Bence-Jones proteins. The current method of treatment for these rare tumors is radiotherapy due to the high sensitivity associated with them. Reports have shown that prognosis is relatively good compared to plasmacytoma of the bone and multiple myeloma, with recurrence being rare. Prognostic indicators have not been elucidated due to the overall small incidence of occurrence. Neither surgery nor adjuvant chemotherapy is currently recommended as part of the standard treatment for solitary extramduillary plasmacytommas.

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**Anisakiasis Associated to Raw Fish Ingestion**

Carlos E. Jimenez-Hiyeke, M.D., Silvette Rivera, M.D., Federico Rodriguez, M.D., Manuel Marcial, M.D.* Medicine, Gastroenterology Section, University of Puerto Rico School of Medicine, San Juan, PR, Puerto Rico and Gastroontestinal Pathology, University Pathologists, San Juan, PR, Puerto Rico.

To present two cases of Anisakiasis observed in two Puerto Rican patients. We intend to create awareness of this entity and encourage its consideration as part of the differential diagnosis in patients with particular symptoms and an appropriate history.

**Clinical Presentation:** Two female Puerto Rican patients presented with epigastric pain, nausea, and general malaise. Both had recent history of raw fish (sushi) consumption. Case 1 presented to a gastroenterologist for evaluation of these symptoms. Diagnostic upper gastrointestinal endoscopy revealed the presence of worm-like structures that were pathologically identified as *Anisakis* larvae. Case 2 was evaluated initially at the emergency room for her symptoms. Radiological evaluation suggested the possibility of a pancreatic inflammatory process although a definite diagnosis was not made. She was discharged from the hospital with no major sequelae. Persistance of symptoms led to an outpatient evaluation that confirmed the presence of *Anisakis* larvae by upper gastrointestinal endoscopy. Both patients underwent endoscopic extraction of the larvae with full and uneventful recovery.

*Anisakis* is an infection of larval nematodes acquired through the ingestion of infected squid and fish. Human infection is found wherever raw, poorly cooked, salted, or pickled fish are consumed. Popularity for raw fish consumption has spread worldwide. Common areas include Japan (sushi and sashimi), Netherlands (green herring) and Latin America (ceviche). In turn,
incidence of Anisakiasis has also increased, particularly in areas where consumption and popularity of such delicacies has increased. Clinical features depend on whether the Anisakid larvae attach or invade tissues. These vary from mild epigastric pain to signs of peritoneal irritation. No anthelminthic medications are available. Nevertheless, early removal of the larvae is curative and prevents development of complications secondary to chronic infection. Knowledge of this medical entity and its associated risk factors including raw fish consumption contributes to early endoscopic diagnosis and intervention and possibly prevents complications of late diagnosis.

Acute Pseudomembranous Appendicitis


Clostridium difficile colitis (CDC) and acute appendicitis are common conditions in the U.S. annually affecting 3,000,000 and 250,000 patients, respectively. It is exceedingly uncommon for CDC to be associated with appendicitis. A review of the literature identified only two prior case reports, we report the third.

Case: A 72 year old man was hospitalized for a COPD exacerbation and treated with IV prednisone and 7 days of IV and oral moxifloxacin. Five days after completing the antibiotic course he developed watery diarrhea and diffuse, crampy abdominal pain. On readmission he was afebrile and abdominal examination revealed diffuse tenderness without distension, guarding, or rebound tenderness. Stool tested positive for C. difficile toxin A by ELISA assay. Leukocytosis 20,500/mm³ was noted. Despite starting oral metronidazole, the patient developed a fever of 101.2 °F thirty-six hours after his initial episode of diarrhea. His abdominal pain intensified and became localized to the right and left lower quadrants. CT scan revealed both a thickened cecal wall and an edematous appendix with ileocecal stranding consistent with appendicitis. Appendectomy was performed and discovered the appendix to be suppurative in appearance and not perforated. The cecum had mild edema and erythema while the remaining colon and rectum were grossly unaffected. Pathology examination revealed pseudomembranes in the appendiceal lumen with diffuse, transmural inflammatory cell infiltrate. Anaerobic cultures and gram stain of the appendix were negative for organisms. The patient had an uneventful postoperative recovery and was discharged 3 days later with oral metronidazole 500 mg t.i.d. for 10 days total.

Discussion: We report the third known case of acute pseudomembranous appendicitis. Although appendicitis and CDC are each common disorders, acute appendicitis in the setting of CDC is extremely rare. We speculate that this association is underdiagnosed, as milder cases may respond to antibiotic therapy alone and severe cases may involve the entire colon and require total colectomy. In each scenario, the involvement of the appendix may be overlooked. [Figure 1] Figure 1: CT showing appendicitis (arrow) abutting thickened cecal wall. Appendiceal pathology showing liminal pseudomembranes and transmural inflammatory cell infiltrate.

The Colon That Would Not Decompress: A Case of a Cecal Bascule

Amy S. Oxentenko, M.D., Mark V. Larson, M.D.∗ Gastroenterology/Hepatology, Mayo Clinic College of Medicine, Rochester, MN.

Introduction: Case: A 69-year old male with a prior cardiac transplantation had onset of abdominal distension and pain six days after knee arthroplasty. Radiographs revealed significant colonic dilation, more marked in the cecum. Gastrografin imaging demonstrated abrupt cut-off in the proximal colon. Emergent endoscopic decompression was necessary, as the cecum measured 16 cm in diameter. Follow-up radiographs revealed persistent cecal dilation. Despite parenteral neostigmine and repeat endoscopic decompression, the cecum remained dilated at greater than 20 cm diameter, with resolution of colonic distension elsewhere. The patient was taken to surgery, where a massively dilated and anterosuperiorly-oriented cecum was discovered, consistent with a cecal bascule. Although early ischemic changes and small serosal tears were noted, there was no perforation. The patient underwent a laparoscopically-assisted eccectomy with ileocolonostomy. He did well post-operatively, and was dismissed five days later.

Discussion: The term bascule is French for “seesaw,” used to describe a common type of drawbridge where raised and lowered ends are counterbalanced. Cecal bascule is a form of colonic obstruction first described in 1899 by Treves, and although clinically similar to cecal volvulus, classic rotation of the colon is absent. A cecal bascule results when the cecum folds anterior to the ascending colon and adheres to it’s surface. A deep crease is formed where the colon bends on itself, occluding the lumen. This “flap valve” mechanism prevents cecal emptying, and in the presence of a competent ileocecal valve, may lead to marked cecal dilatation given the inability to decompress in retrograde fashion. Signs and symptoms of a cecal bascule are similar to those of a cecal volvulus, with abdominal pain and distention. Radiographs reveal a markedly dilated cecum located anterior to the right colon, with cecal distention out of proportion to that in the remainder of the colon. The treatment of choice is surgical intervention with decompression and fixation, and is optimally performed prior to complications such as gangrene, perforation, bacteremia or bleeding. The utility of colonoscopic decompression may be limited by an inability to advance the decompression tube into the aberrantly located cecum, as was the situation with this
patient. When ecel bascule is not considered pre-operatively, it can lead to misinterpretation of imaging studies, a delay in definitive management, and increased morbidity and mortality.

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Liposarcoma Presenting as an Enterocele: A Case Report
James Kasievez, M.D., Thomas E. Read, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

This case report is a presentation of a pelvic liposarcoma as an enterocele. The typical work up, treatment and prognosis of retroperitoneal liposarcomas were reviewed. A 63-year-old female presented with the complaint of proplapse of tissue through her vaginal wall. A large complex mass was seen on the CT scan. A laparotomy revealed a giant tumor centered in the rectovaginal septum. The tumor was resected and end colostomy was performed. A liposarcoma presenting as an enterocele is a unique presentation. Presenting symptoms are due to the tumor’s location and its compression of the localized structures. Most patients with retroperitoneal liposarcomas have complaints of abdominal discomfort, fullness, or weight loss. Total resection is the goal. Prognosis is based on grade of the tumor.

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Percutaneous CT–Guided Gastric Remnant Access after Laparoscopic Roux-en-Y Gastric Bypass
David Goitein, M.D., David J. Gagne, M.D., Scott Beasley, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

We report our experience with percutaneous, computed tomography (CT) guided gastrostomy placement into the gastric remnant after laparoscopic RYGBP (LYRGBP). Of 431 consecutive LRYGBP performed, 7 patients underwent percutaneous, CT-guided gastrostomy placement (1.6%). One additional patient was referred from another facility. Gastrostomy tubes were placed following a uniform approach. We reviewed the indications, interval between surgery to intervention, the time to removal, complications and success-outcome of the procedure in our patient population. Eight patients underwent percutaneous, CT-guided gastric remnant gastrostomy placement. Indications were: Distended gastric remnant (n = 4), nutritional access (n = 5) and remnant drainage after leak (n = 1). Of the 8 patients, two (22%) had previous gastric operations. The gastrostomies were placed 2-337 days after surgery (median = 9 days) and were removed after a median of 22 days (range 18 – 676). Attempt at percutaneous gastrostomy was unsuccessful in one additional patient, subsequently requiring laparoscopic gastrostomy (success rate 89%). No complications were encountered in this small patient group. In selected patients following LRYGBP, CT-guided gastrostomy tube placement is safe and efficient. It may be used to manage complications of LRYGBP, serve as a bridge to definitive surgery, or offer a convenient route for enteral nutritional support.

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Epidemiology of Clostridium difficile Colitis: An Institutional Review
Anton S. Dias-Pereira, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

To identify the incidence and the risk factors associated with the severe, fulminant CDC or complicated C. difficile colitis. A retrospective chart review was performed to identify the incidence and the risk factors associated with the severe, fulminant CDC or complicated C. difficile colitis. Data presented in this paper are an interim analysis of the ongoing study. Retrospective case-control study of 161 patients diagnosed with C. difficile were identified from 1/2003 to 9/2004. 107 charts were reviewed. A case was considered complicated for one of the following: toxic megacolon, perforation, colectomy or emergency abdominal surgery, shock requiring vasopressors or fluid resuscitation or death within 30 days of diagnosis. Cases were reviewed for the following risk factors: age, co-morbidities, antibiotics use, presence of tube feedings, use of PPIs, WBC > 20,000, creatinine level, chronic steroid use, albumin level 15/107 cases were complicated. There were 6 deaths and 2 patients underwent colectomy with one death. Our study shows that incidence of CDC is increasing. CDC is common in older age, however, age is not predictive of severe disease. High WBC (>20k) and elevated serum creatinine (>2.0) were predictive of severe disease. Low serum albumin level was seen in the majority of patients with severe disease. Therefore it may predict severity of disease.

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Late Recurrence of Adenocarcinoma after Endoscopic Polypectomy
Maria C. Crisanti, M.D., Michelle M. Olson, M.D., Thomas E. Read, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

The presence of invasive cancer is observed in up to 9% of polyps removed at colonoscopy. Certain histopathological features of the tumor are utilized to determine if further treatment is necessary. We present a case of an asymptomatic 70 year old woman with a mesenteric recurrence 10 years following endoscopic polypectomy of a cancer within a pedunculated sigmoid colon polyp. Her initial tumor did not display any of the adverse pathologic features which might have prompted a colectomy. The patient’s subsequent endoscopic surveillance did not reveal further mucosal abnormalities. Her recurrence was discovered during the work-up of an isolated elevated CEA level. Here we review current surveillance strategies for follow-up of colorectal adenocarcinoma, as well as the histopathological features of a cancerous polyp which would prompt colectomy. This is the first case of late mesenteric recurrence following endoscopic polypectomy of a cancerous polyp.

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Laparoscopic Transgastric Endoscopy: A Novel Approach
Frederico Ceppa, M.D., Papasavas K. Pavlos, M.D., Gagne Daniel, M.D., Caushaj F. Philip, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

We propose a minimally invasive technique to easily access the remnant stomach, after RYGBP for endoscopic diagnosis and treatment. CO2 pneumoperitoneum is established to a pressure of 12–15 mmHg. A 12-mm umbilical Visiport, 5-mm RUQ, 5-mm LLQ, and 15-mm LUQ trocars are placed. A purse string suture is placed at the anterior wall of the stomach. The endoscope is than inserted through the 15-mm trocar and the pneumoperitoneum is decrease to 7–8 mmHg. Once the evaluation is complete, the gastrotomy is closed with either a running suture or linear stapler.

Seven patients at our institution have undergone laparoscopic transgastric endoscopy. 4 had biliary pathology. Three of these patients underwent successful ERCP and papillotomy; the fourth was unsuccessful due to stone impaction at the ampulla. Two patients evaluated for GI bleeding revealed a gastrointestinal stromal tumor (GIST) in one patient and a negative endoscopy.
in the other. One patient evaluated for chronic abdominal pain had a negative endoscopy.

Laparoscopic transgastric endoscopy is a safe and minimally invasive approach for the evaluation of the gastric remnant and biliary tree in patients with a RYGBP.

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Metastasis of a Head and Neck Cancer to a Percutaneous Gastrostomy Site: A Case Report and Review of Literature
Majed Maalouf, M.D., Apostolos A. Costa, M.D., Papasavas K. Pavlos, M.D., Caushaj F. Philip, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

To examine metastasis of head and neck cancer to a percutaneous gastrostomy site.
Chart review.
A case report of a 51 y/o male with a history of recurrent squamous cell carcinoma of the right tongue base.
The patient was diagnosed in 11/1998 with a T1N0 basaloid squamous cell carcinoma. A local resection with negative margins on frozen section and radiation therapy was performed.
Patient presented:
8/2002 with a lesion on left floor of his mouth. Biopsy: moderately differentiated squamous cell carcinoma. A local excision and biopsy of additional abnormal tissue was performed, which revealed negative margins.
10/2003 with bleeding around PEG tube site. Debridement and replacement of gastrostomy tube completed.
1/2004 with increased pain and bleeding around PEG tube site. Biopsy: squamous cell carcinoma, similar to resected laryngeal type.
The implantation of head and neck cancer cells to a PEG site is considered an uncommon complication with an incidence of 1%.

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Unique Macroscopic Appearance of Sodium Phosphate-Induced Colopathy

To describe unique colonoscopic findings related to sodium phosphate bowel preparation.
A 42 yo asymptomatic female presented for screening colonoscopy. The family history was significant for her father having been diagnosed with colorectal cancer at age 52. She had no underlying medical problems, and was taking no medications. The patient underwent colonoscopy after sodium phosphate preparation.
Upon intubating the rectum, multiple aphthoid lesions with a pale central area and erythematous halo were visualized.[figure] In the distal sigmoid, several prominent, nonbleeding linear “stripes” of subepithelial hemorrhage were seen. Within the “stripes,” groups of nearly confluent aphthoid lesions were noted.[figure] The colon was otherwise normal to the cecum, as was the ileum upon intubation. The aphthoid lesions in the rectum were biopsied, as were the areas of linear “stripe” in the distal sigmoid. Only non-specific changes were seen (no chronic inflammatory infiltrate or goblet cell depletion was detected and crypt architecture was preserved) and subepithelial hemorrhage was microscopically confirmed in biopsies from the distal sigmoid lesions. No changes to suggest IBD or “watermelon” colon were detected. None of the biopsy sites bled excessively. The lesions noted were presumptively related to the sodium phosphate preparation.

A

B

This case describes a unique colonoscopic appearance of sodium phosphate-induced colorectal lesions. The unique “stripes” of subepithelial hemorrhage were seen against a background of typical aphthoid lesions. This patient had no underlying medical condition or medication use which could have precipitated or predisposed to this unusual endoscopic finding. With continued widespread use, there will likely be other variations of sodium phosphate colopathy described in the future.

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Midascending Colon Skip Lesion in Ulcerative Proctitis
Nirmal S. Mann, M.D., Suk Seo, M.D. Gastroenterology, University of California, Davis, Davis, CA.

Skip lesions are supposed to be characteristic of Crohn’s Disease whereas ulcerative colitis shows continuous superficial mucosal inflammation. However, skip lesions involving the cecum and the ostium of the appendix have been reported in ulcerative proctitis and proctosigmoiditis (Am J Gastro 1998; 93:2307; 93:2405, Mod Path 1994; 7:322–325). Recently we saw a
An Unusual Cause of Peritonitis in a Patient with Cirrhosis

Rajeshekar R. Mamadi, M.B.B.S., M.D.; Parantap Gupta, M.B.B.S.
Internal Medicine, University of Texas Medical Branch, Galveston, TX.

Cryptococcal peritonitis is a rare but well recognized complication of cirrhosis with or without any other immunosuppressive condition. Less than 50 individual cases have been reported in literature and the mortality reported was uniformly high. We report a case of cryptococcal peritonitis in a patient with cirrhosis and no other immunosuppressive condition.

A 43 year old Hispanic Male who recently immigrated from Mexico presented to Emergency Room of a teaching hospital with a 3 day history of abdominal distension, fever, chills and rigors. The patient had a past medical history of Hepatitis C cirrhosis diagnosed 6 months prior to this presentation. Examination revealed a diffusely tender abdomen without guarding or peritonitis. The terminal ileum was normal. Biopsies of the rectum and midascending colon showed cryptitis and crypt abscesses; no granulomata were seen. Biopsy of terminal ileum showed normal mucosa. PANCA, PASCA and amebic serology were negative. CAT abdomen and SBFT showed normal small bowel.

In ulcerative proctitis skip lesions not involving the cecum and appendix are rare but do not negate a diagnosis of ulcerative colitis.

First Reported Case of Adenocarcinoma of the Esophagus in Patient with Cystic Fibrosis Following Lung Transplant

Yaser Al-Solaiman, M.D.; Samah Bassas, M.D.; Mohammad M. Alsolaiman, M.D.* Internal Medicine, Albany Medical College, Albany, NY and Gastroenterology, Central Utah Clinic, Provo, UT.

Adenocarcinoma of the esophagus in association with cystic fibrosis has not been reported previously. We describe a patient with cystic fibrosis who developed an esophageal carcinoma 5 years after lung transplant. Considering the longevity of these patients, unusual diseases in this category of patients are expected to be seen.

A 45 year old female with history of cystic fibrosis underwent bilateral lung transplant 5 years ago. Her current medication included arathioprine, steroid, Pancreatic enzymes, Insulin, PPI and tacrolimus. She denied any history of smoking or drinking alcohol. She presented to the gastroenterologist attention with increasing heartburn and epigastric tenderness. Her physical exam was unremarkable. The blood test was also unremarkable except for evidence of chronic renal insufficiency and mild normocytic anemia. The patient underwent Upper Endoscopy which revealed one cm polypoid lesion at the GE junction. The biopsy showed evidence of adenosarcinoma. The patient underwent uneventful distal esophagectomy. Patient continues to do well one year after the surgery without any recurrence of the disease. Cystic fibrosis is an autosomal recessive genetic disease caused by mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR). It is relatively common, with an incidence of 1 in 2000 to 3000 whites; approximately 30,000 persons in the United States are affected. About 1 in 20 to 25 whites carry mutations in the CFTR gene. The disease affects several different organs, but most current morbidity and 90 to 95% of mortality result from chronic pulmonary infections.

Therapeutic regimens for cystic fibrosis have continued to improve. Nearly half of patients with cystic fibrosis are now adults. The gene therapy will carry a dramatic change in the life and prognosis of these patients. As survival improves, the problems facing these patients will become different and will begin to spill over into the domain of caregivers predominantly focused on the issues of adults.

The current case has not been reported before. This could reflect the longevity of the patient and her current immunosuppressive status. Increasingly, these patients will require evaluation for potential malignancies of the digestive tract. All the above will necessitate the specialized attention of gastroenterologist.
calcium was 1.41 mmol/L (1.13–1.32 mmol/L). Parathyroid hormone (PTH) was 82 pg/ml (6–40 pg/ml). Therapy with intravenous fluids, magnesium infusion, diuretics, and calcium binders failed to improve the hypercalcemia. Therefore, she underwent parathyroidectomy. During surgery, rapid PTH monitoring revealed a rapid drop in the PTH from 258 to 87 picograms/mL after removal of a 1.4 cm parathyroid adenoma. The patient did well post op with resolution of her pancreatitis. Her ionized calcium decreased to 1.0 mmol/L. The patient recently delivered a healthy baby boy and has not had any further episodes of pancreatitis.

Pancreatitis in pregnancy secondary to hyperparathyroidism and hypercalcemia is a rare phenomenon often amendable to medical therapy. In one reported case, delivery of the infant at 36 weeks resulted in a successful outcome for both mother and infant. In our case, fetal viability and maturity precluded early delivery. This case illustrates the difficult clinical situation faced when conventional therapies for pancreatitis in pregnancy are unsuccessful. When medical therapies are exhausted, surgical therapy should be considered to improve maternal and fetal outcomes.

The Successful Use of Adalimumab (Humira®) To Treat Active Crohn’s Disease of an Ileoanal Pouch during Pregnancy
Lori A. Coburn, M.D., David A. Schwartz, M.D.*, Department of Gastroenterology, Vanderbilt University Medical Center, Nashville, TN.

Background: Patients with active Crohn’s disease (CD) during pregnancy are at increased risk for poor outcomes including preterm delivery and fetal malformation. Therefore, maintenance of remission during pregnancy is a high priority. Previously because of a safety concerns during pregnancy, anti-tumor necrosis factor alpha (TNF-α) antibodies such as infliximab were avoided. However, recent reports suggest it is safe to use during pregnancy. Adalimumab is a fully humanized anti-TNF-α antibody approved for Rheumatoid Arthritis. Herein, we present the 1st report of Adalimumab (ADA) being used during pregnancy in a patient with Crohn’s disease.

Case Report: A 34-year-old female with CD who had previously undergone a proctocolectomy with ileoanal pouch for presumed ulcerative colitis seven years prior to presentation. She was subsequently found to have Crohn’s disease of her ileoanal pouch. Her course prior to presentation was complicated by multiple episodes of pouchitis treated with various agents including antibiotics, azathioprine (AZA) and infliximab. With the 2nd infusion of infliximab, she experienced an anaphylactic reaction precluding its further use. During her initial evaluation for severe Crohn’s pouchitis (20-30 stools/day) she was found to be 6 weeks pregnant. She was not on any medication for her CD at this time. Initial treatment with budesonide and antibiotics resulted in only minimal improvement. She continued to have anorexia, abdominal pain and 10-15 stools per day.

At 17 weeks gestation, her symptoms intensified. There was concern for the fetus because she had not gained significant weight thus far during her pregnancy. She did not improve with a course of high dose prednisone (60mg/d). After a lengthy discussion with the family, the pt was started on AZA 100mg/day and Adalimumab 80mg subcutaneously x 1 then 40mg every other week. After 2 weeks, she was beginning to feel better with increasing appetite and energy. She was also able to decrease her prednisone to 30mg a day. At 21 weeks, she was down to 10 stools/day and started to gain weight. By her 32nd week of gestation, she had tapered off of prednisone and was in remission. She presented for induction of labor at 38 weeks and delivered a healthy baby boy.

Conclusion: Adalimumab may be a safe and effective option during pregnancy for refractory Crohn’s disease.

Collagenous Pouchitis Following Total Proctocolectomy and Ileal Pouch-Anal Anastomosis for Collagenous Colitis
Kerry Sherman, R.N., B.S.N., Bo Shen, M.D.*, Ana Bennett, M.D., Reza Remzi, M.D., Bret Lashner, M.D., M.PHI. Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH; Department of Anatomic Pathology, Cleveland Clinic Foundation, Cleveland, OH and Department of Colorectal Surgery, Cleveland Clinic Foundation, Cleveland, OH.

Collagenous colitis is characterized by the disease limited to the colon. Some patients can develop refractory disease. The role and clinical outcome of proctocolectomy and ileal pouch-anal Anastomosis (IPAA) in collagenous colitis has not been established.

A 58-year-old Caucasian female with chronic diarrhea was diagnosed with collagenous pancolitis in 1991 based on characteristic histologic features on colon biopsy. Despite therapy including corticosteroids, 6-mercaptopurine, and infliximab, her symptoms and histologic features of collagenous colitis persisted. In 2001, she underwent total proctocolectomy with end ileostomy. The initial terminal ileum of the proctocolectomy specimen showed no evidence of an abnormality. The post-operative course was complicated by increased ileostomy output, which resulted in hospitalizations. In 2002, a J-type IPAA and ileostomy take-down were performed. Postoperatively she experienced persistent diarrhea and incontinence. In 2005, she was referred for chronic refractory, debilitating diarrhea (stool frequency of 20-25 x/day) and incontinence. She never smoked and did not use non-steroidal anti-inflammatory drugs. CBC, liver function tests, electrolytes, and celiac serology all were normal. Pouch endoscopy revealed a normal afferent limb (neo-terminal ileum), pouch, and cuff. Biopsy of the afferent limb was normal. However, mucosal biopsy of pouch showed typical histologic features consistent with collagenous pouchitis with thickened subepithelial eosinophilic band, entrapped capillaries and inflammatory cells within the collagen layer, and separation of strips in the surface epithelium from the collagen layer. She was treated with combined ciprofloxacin and rifaximin, somatostatin, and tincture of opium. At a 3 month follow-up, biopsies from repeat pouch endoscopy and EGD showed normal small bowel, pouch, and cuff, although she had persistent diarrhea with firmer stools. This is the first reported case of collagenous pouchitis. The fact that the collagen band was present in the ileal pouch and absent in the neo-terminal ileum and that histologic improvement with therapy including antibiotics would suggest that fecal stasis and bacterial load in the ileal pouch may play an important role in the pathogenesis.

Primary Gastric Melanoma Presenting as a Rare Cause of Gastrointestinal Bleed
Anupama Ravi, M.D., Robert Osborne, M.D.*, Internal Medicine, Atlanta Medical Center, Atlanta, GA.

A 50-year-old white male presented from a correctional facility with a nine month history of hematemesis, a twenty pound weight loss over the past one month and several months history of epigastric pain. Past medical history was significant for peptic ulcer disease. Physical exam showed pallor of the conjunctiva and mild epigastric tenderness. NG tube aspirate was positive for coffee colored material. EGD revealed a large necrotic ulcerated gastric mass extending from the antrum to the body of the stomach. Biopsy of the mass was reported as a poorly differentiated tumor of an unknown type. CT of the abdomen and pelvis showed thickening of the posterior wall of the body of the stomach with extension of the mass into the gastric lumen and into the adjacent fat, with two enlarged lymph nodes. Surgery revealed a mass measuring $10.5 \times 2.5$ cm involving 50% of the stomach including the gastro–colic ligaments and extending into the pancreas. Palliative resection was performed. The final pathology of the tumor showed neoplastic cells in a sheet-like growth pattern without glandular differentiation. S100, HMB45 and melan A staining were strongly positive, thus confirming a diagnosis of gastric melanoma. Patient denied any history of previous cancerous lesions of the skin. A complete examination of his skin, including oral and anal mucosa showed no suspicious lesions. Fundoscopic exam was likewise normal. Therefore, a diagnosis of primary gastric melanoma was made. The patient was discharged back to the correctional facility and was subsequently lost to follow-up.

Primary gastric melanoma is an extremely rare clinical entity. Criteria for the diagnosis of a primary melanoma include absence of concurrent lesions and...
no history of removal of a melanoma or atypical melanocytic lesion from skin or other organs. Barium radiography and endoscopy with tissue sampling usually provide the diagnosis. Immunohistochemical stains S-100, melan-A and HMB-45 have increased the diagnostic sensitivity of the biopsy and cytology. Diagnosis of malignant melanoma can be missed in poorly differentiated tumors unless appropriate staining tests are performed. So, primary malignant melanoma of the stomach could be an under-diagnosed entity. Chemotherapy options include interferon, interleukin-2 and other agents. The overall prognosis is very poor.

Ulcereative Colitis Presenting as Colonic Perforation in a Patient with Autoimmune Hepatitis
Kevin B. Mercure, M.D., John B. Rodgers, M.D., David M. Jones, M.D., Richard P. MacDermott, M.D.* Gastroenterology, Albany Medical Center, Albany, NY.

We report a 22 yo female who presented with jaundice at the age of 14. Liver biopsy done at that time was felt to be consistent with autoimmune hepatitis. Serologic testing revealed a positive ANA, a negative AMA and a negative anti-smooth muscle antibody. Initially her autoimmune hepatitis was managed with prednisone and 6-MP. She presented to our hospital with fever and lower abdominal pain. She reported a seven day history of vomiting and five, loose, maroon stools each day. Abdominal CT scan revealed no abnormalities. She underwent an EGD which revealed grade III esophageal varices that were band ed. Frank blood was present in the duodenum at the time of endoscopy. She responded well to treatment and was discharged on a prednisone taper.

Three weeks later she presented again to our hospital with increased lethargy, low grade fever, WBC of 23,000/cu.mm, and had blood cultures positive for E. coli. Her abdomen was distended and tender to palpation. A CT scan of the abdomen revealed free intraperitoneal air due to a bowel perforation. She was brought emergently to the operating room for an exploratory laparotomy. Intraoperatively a perforation of her descending colon was detected and she underwent an EGD which revealed grade III esophageal varices that were band ed. Frank blood was present in the duodenum at the time of endoscopy. She responded well to treatment and was discharged on a prednisone taper.

Ileocolonic Lymphoma Presenting as Intussusception: A Case Requiring Modification of the Current Classification System
Matthew Tangorra, D.O., Muhammad Abdullah, M.D., Pratap Gadangi, M.D., Scott Tenner, M.D., M.P.H.* Division of Gastroenterology, Mount Sinai School of Medicine, Brooklyn, NY; Division of Gastroenterology, Coney Island Hospital, Brooklyn, NY and Department of Surgery, Coney Island Hospital, Brooklyn, NY.

Primary ileocolonic lymphomas have recently been endoscopically classified according to colonoscopic findings (Gastrointest Endosc. 2003 Mar;57(3):343–7). The current classification system describes 5 groups: fungating, ulcerofungating, infiltrative, ulceroinfiltrative, and ulcerative. We report a case in which a patient presented with ileocolonic lymphoma that could not be classified endoscopically by the current classification system. The patient is a 56 year-old female who presented to the emergency room with a 4 week history of lower abdominal crampy pain. An abdominal CT scan revealed a 4 cm soft tissue mass in the cecum with extension to the terminal ileum. A colonoscopy was performed. There was a 4 cm ulcerated mass extending from the cecum to the proximal ascending colon. Multiple biopsies revealed fragments of benign colonic mucosa with inflammatory changes but without malignant cells. Due to persistent pain and the fear of an underlying submucosal malignancy, a laparoscopy was performed. Operative findings revealed that the colonic mass was originating from intussusception of a mass in the terminal ileum. Following resection and primary anastomosis, the patient did well. Pathology revealed a diffuse large B-cell lymphoma. The patient experienced an uncomplicated post-operative course and was discharged with plans for outpatient chemotherapy. This represents a rare case of adult ileocolonic intussusception caused by diffuse large B-cell lymphoma of the terminal ileum. Although there was an ulceration, this was related to ischemia to the normal mucosa from the intussusception. The ileocolonic lymphoma was entirely submucosal. Based on this case report, we suggest modification to the current classification system to include a “submucosal” presentation. Ileocolonic lymphoma can present as a submucosal mass in the cecum related to intussusception.

Real Time Capsule Endoscopy in the Evaluation of Acute Unstable Gastrointestinal Bleeding
Matthew Tangorra, D.O., Robert Kodsi, M.D., Gulam Khan, M.D., Ira Mayer, M.D., Jian Jun Li, M.D.,* Scott Tenner, M.D. Division of Gastroenterology, Maimonides Medical Center, Mount Sinai School of Medicine, Brooklyn, NY.

Endoscopic evaluation of the small bowel has traditionally been an area of difficulty, particularly in the patient with active gastrointestinal (GI) bleeding of obscure origin. Capsule endoscopy allows inspection of the small bowel to rule out pathology when upper endoscopy and colonoscopy fail to identify a source. Patients who undergo capsule endoscopy are typically having chronic GI bleeding of unknown origin. We report a case of a patient with a history of obscure GI bleeding who presented with acute upper GI bleeding. The source of bleeding was identified with a novel technique, real time capsule endoscopy. The patient is an 83 year-old with a history of recurrent gastrointestinal bleeding. Three prior upper endoscopies as well as a colonoscopy were negative for a source. He presented with melena and became unstable immediately upon arrival to the emergency room. During the resuscitation, a capsule endoscopy was performed in “real time” utilizing two recording devices. The goal was to obtain an early diagnosis by analyzing the capsule images urgently rather than waiting the typical 6–8 hours for a “down-load.” Each recording device was exchanged every 15–30 minutes to download and view the images. Images revealed a bleeding arteriovenous malformation (AVM) in the proximal jejunum. This allowed a targeted therapeutic enteroscopy when the patient’s hemodynamic status improved. The bleeding AVM was successfully ablated. This case demonstrates a role of real time capsule endoscopy in an unstable patient with active GI bleeding of unknown origin. Rather than waiting the usual 8-hour transit time before downloading images from the recording device, the two-device exchange technique allows for a “real-time” diagnostic evaluation in patients who are currently unstable for endoscopy.
Primary Hepatic Vipoma Presenting as a Colonic Pseudo-Obstruction

Kamlesh M. Shah, M.D., Xiaoli Ma, M.D.∗ Gastroenterology, Graduate Hospital, Philadelphia, PA.

Pancreatic endocrine tumors that secrete vasoactive intestinal polypeptide (VIP) are extremely rare. They are detected in approximately 1 in 10 million people per year. The vast majority have been reported to arise within the pancreas and often have metastatic spread on presentation. Other VIP-secreting tumors have been reported including colon carcinoma, hepatoma, bronchogenic carcinoma, pheochromocytoma, ganglioneuroblastoma, and adrenal tumors. Only four cases of a solitary primary hepatic VIPoma without evidence of extra-hepatic lesions have been reported. VIP-secreting tumors have been reported as presenting typically with dehydration, weakness, hypokalemia, and acid-base imbalance secondary to profound secretory diarrhea. Our aim is to report a case of a primary hepatic VIPoma presenting as a colonic pseudo-obstruction.

Our patient is a 78-year-old gentleman with a past medical history significant for hypertension, diabetes mellitus, and seizure disorder who complained of weakness on admission and presented with an acute colonic pseudo-obstruction. Review of systems revealed a history of chronic watery diarrhea at least a year in duration. On further evaluation, he was noted to have chronic, secretory diarrhea associated with profound hypokalemia. The hospital course included exclusion of other causes of colonic obstruction and exclusion of other causes of secretory diarrhea. Investigations included stool studies including assays for Clostridium difficile, blood work including a TSH, EGD, enteroscopy with bile aspirate and small bowel biopsy, colonoscopy with random biopsies, anal manometry, measure of stool osmolality, 24-hour fecal lipid analysis, urine for 5-HIAA, and bloodwork for VIP and gastrin. All of the work-up was unrevealing except a VIP level of 86.7 pg/ml (nl 6 - 30). Further investigations included somatostatin-receptor scintigraphy, which revealed a small focus of radiotracer uptake in the liver. An extensive work-up did not show any other extra-hepatic primary lesion or metastatic lesion. Medical therapy with Octreotide and selective hepatic artery embolization ameliorated all of his signs and symptoms, including the colonic pseudo-obstruction, accompanied by a decrease in the VIP level.

This patient represents the first reported case of a primary hepatic VIP-secreting tumor presenting as an acute colonic pseudo-obstruction. The recognition of bizarre presentations of rare diseases is important as outlined in this case report.

Hemosuccus Pancreaticus and Embolization of a Gastroduodenal Artery Pseudoaneurysm

C. Julian Billings, M.D.∗ Division of Gastroenterology, University of South Alabama, Mobile, AL.

Hemorrhagic complications of pancreatitis, although rare, are almost universally lethal if untreated. A patient with chronic pancreatitis and a gastro-duodenal artery pseudoaneurysm who was successfully managed with embolization is presented. A 61 year old male with chronic pancreatitis and a known 4cm pseudocyst presented to the ED describing epigastric pain, nausea, and melena for the past 24 hours. Exam revealed a tender epigastrium and melena in the rectal vault. The hemoglobin was 8.6 g/dL. CT revealed a large pseudoaneurysm adjacent to the pancreatic pseudocyst. Contrast could be seen extravasating into the pancreatic pseudocyst. Emergent angiography confirmed a saccular, bilobed pseudoaneurysm arising from the gastroduodenal artery. The pseudoaneurysm was successfully embolized, and the patient was discharged 2 days later. Major hemorrhagic complications of pancreatitis are rare, but lethal in >90% of cases if unrecognized. They are usually late sequelae in patients with chronic pancreatitis and/or pseudocysts, and likely result from persistent pancreatic ductal disruption, which leads to erosion of major vessels. Although hemorrhage can occur into the peritoneum or a hollow viscus, the most common presentation is rupture into a pseudocyst, with resultant bleeding into the GI tract via the pancreatic duct, termed hemosuccus pancreaticus or wirsun-gorrhagia. Selective mesenteric angiography is emerging as an important modality in the management of these patients, both to localize the bleeding site, as well as to achieve hemostasis. The durability of angiographic hemostasis is controversial, and in some cases it may be only a bridge to surgery.

Mesenteric angiography plays an important role in the management of acute hemorrhagic complications of pancreatitis.
Severe Antiphospholipid Antibody Syndrome Causing Abdominal Pain and HELLP-Like Syndrome of the Liver

Timothy B. Gardner, M.D., Matthew M. Walton, M.D., Brian J. Kravitt, M.D., Arief A. Suriawinata, M.D., Brian S. Berk, M.D., Dirk J. van Leeuwen, M.D., Ph.D.* Gastroenterology, Dartmouth-Hitchcock Medical Center, Lebanon, NH; Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH and Pathology, Dartmouth-Hitchcock Medical Center, Lebanon, NH.

A 31 year-old man with antiphospholipid antibody syndrome (APLAS) and a history of venous thromboembolism on chronic warfarin therapy presented with two weeks of worsening severe abdominal pain, new ascites and peripheral edema. Laboratory studies revealed a hemoglobin of 9.7 g/dL, platelet count of $3.1 \times 10^9$, total bilirubin of 6.4 mg/dL, alkaline phosphatase of 90 u/L, ALT 47 u/L, AST 62 u/L, albumin 2.4 g/dL, and INR of 2.1. Computed tomography and angiography showed no evidence of vena caval, hepatic or portal vein thrombosis but did reveal moderate ascites and cirrhosis. Ascitic fluid was consistent with portal hypertension without bacteria. ANA, AMA, ASMA, ceruloplasmin, heavy metals, urinary copper, iron studies, A1AT, and viral hepatitis serologies all returned negative. He was treated empirically with corticosteroids for the possibility of autoimmune hepatitis. Because his liver tests continuously fluctuated between normal and dramatically elevated, reaching a peak total bilirubin of 32.3 mg/dL, alkaline phosphatase of 141 u/L, AST of 916 u/L, and ALT of 207 u/L, a liver biopsy was performed. This showed multiple fibrin thrombi in the small portal veins and perportal sinusoids with focal portal-to-portal bridging fibrosis, suggesting both acute and chronic processes. Low molecular weight heparin was initiated in light of intrahepatic microthrombosis and suspected low-grade bowel ischemia, developing while therapeutic on warfarin. His ascites and peripheral edema improved with diuretic therapy, his liver tests stabilized in the normal range and he was discharged home after 15 days. In the six months since his discharge, his liver tests have remained normal. However, despite treatment with cyclophosphamide, corticosteroids, low-molecular weight heparin, rituximab and weekly plasmapheresis, he continues to suffer stigmata of APLAS featuring recurrent DVT and a myocardial infarction.

A number of case reports have documented hepatic involvement in patients with APLAS, but these have most often implicated obstruction of large hepatic veins and less frequently small vessel disease. Hepatic infarction has also been reported in association with APLAS, but small-vessel disease/HELLP-like syndrome should be listed among the liver manifestations of APLAS.
ventral pancreatic duct. Following sphincterotomy and sweeping of the CBD with balloon and 4-wire basket, during which cholecodocholithiasis nor biliary sludge was identified, he was admitted to the hospital for intravenous antibiotics. Inpatient MRCP revealed fusiform dilation of the extrahaepatic CBD extending to the ampulla without obstruction, a finding consistent with a Type I choledochal cyst. The patient's pain, which was thought most likely due to a ruptured hepatic cyst, resolved and he was discharged to home on hospital day #3. His post-hospitalization course has been unremarkable and surgical resection of the cyst has not been considered secondary to his end-stage renal disease.

Choledochal cysts represent congenital biliary tract abnormalities of unknown origin that typically present in childhood. Classification is based on cyst location, with 70–80% being Type I (confined to the extrahepatic bile duct without diverticular appearance). In the elderly, abdominal pain, usually from resultant pancreatitis or cholangitis, is the typical presenting symptom. Cystectomy with cholecystojejunostomy is the preferred treatment as approximately 50% of cysts discovered in the elderly are associated with cholangiocarcinoma. One case of choledochal cyst associated with polycystic kidney disease has been described previously, although choledochal cysts have never previously been reported in the setting of polycystic liver disease.

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Primary Amyloidosis in a Patient Presenting with a Massive Gastrointestinal Bleed from a Fungating Colonic Mass
Sadiya Sarij, M.D., Perwais Meraj, M.D., David Rosenberg, M.D., David Bernstein, M.D.* Department of Gastroenterology, Hepatology and Nutrition, North Shore University Hospital, Manhasset, NY.

Amyloidosis is due to a spectrum of diseases sharing the characteristic of extracellular deposition of fibrillar proteins. Clinical presentations vary depending on the organs involved. Primary systemic amyloidosis has an age adjusted incidence of 5.1 cases per million person years. Gastrointestinal (GI) AL amyloidosis has been described, but is generally a mild disorder. Here, we describe a patient whose first presentation of amyloidosis was massive GI hemorrhage from a fungating colonic mass.

This 72-year-old male presented with shortness of breath, abdominal fullness, loss of appetite, hematuria and hematochezia. He had a history of hypertension, dyslipidemia, rheumatic fever, and a mechanical aortic valve replacement requiring anticoagulation. On presentation, the patient was had a blood pressure of 98/60mmHg and pulse 81. Physical exam was significant for a holosystolic ejection murmur, gross hematuria, and guaiac positive stool. Hemoglobin was 8.8 g/dl, with an INR of 10. The coagulation parameters normalized with fresh frozen plasma. He required transfusions of packed red blood cells. The hematuria resolved, but hematochezia persisted. Upper endoscopy revealed diffuse inflammation, friable gastric mucosa with small ulcerations, but no active bleeding. Colonoscopy demonstrated a large fungating hemorrhagic mass with focal ulcerations and an indurated base, partially obstructing the lumen. Biopsies of the mass were consistent with AL amyloidosis. CT scans and skeletal bone surveys did not show any further lesions. A partial colectomy was performed which confirmed the diagnosis of primary systemic AL amyloidosis. The post-operative course was complicated by pseudo-obstruction, ileus, and sepsis and the patient expired several months post-op.

Amyloidosis commonly affects the gastrointestinal tract yet it rarely presents as a hemorrhagic gastrointestinal mass. This case is one of the only documented cases of large bowel amyloidosis presenting with acute, massive GI bleeding. The diagnosis was made by histopathological study of the colonoscopy biopsy specimen. Neither a predisposing condition nor any other sites of deposition were found. This rare form of amyloid deposition should be recognized so that an early diagnosis and intervention can be made. Additionally, amyloidosis should be added to the list of uncommon causes of GI bleeding.

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Metastatic Gastric Remnant Cancer Occuring Six Years after Partial Gastrectomy for Gastric Ulcer: A Case Report and Review of the Literature
Adeyinka O. Laiyemo, M.D., Duane T. Smoot, M.D.* Medicine, Howard University Hospital, Washington, DC.

To describe an early development of metastatic gastric cancer following a partial gastrectomy for a benign condition
A case report
Gastric stump cancer is known to occur following partial gastrectomy for benign diseases. However, the risk is believed to increase four to fivefold, 20 to 25 years after gastrectomy. We report a 41-year-old man with history of tobacco and alcohol abuse who presented with abdominal pain and constipation. He underwent partial gastrectomy six years previously for gastric ulcer. There was no evidence of malignancy in the surgical specimen and sampled lymph nodes at that time. He was admitted for acute pancreatitis. CT abdomen revealed multiple liver lesions, and biopsy revealed poorly differentiated metastatic adenocarcinoma. EGD revealed mild esophagitis, and duodenal erosion but colonoscopy was normal. CEA and B-HCG were elevated, but AFP was normal. The patient’s condition deteriorated and he died before palliative chemotherapy could be started for cancer of unknown primary. At autopsy, there was no gross stomach lesion, but the histopathology at the anastomotic site revealed adenocarcinoma with signet ring features. We reviewed the literature to highlight the need for identification of patients at risk of developing gastric stump cancer especially as it is now being described even in patients who underwent gastric bypass surgery for obesity, a population that continues to increase.

More studies are needed to better define any predisposition to cancer following gastric surgery

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Successful Laparoscopic Treatment of Duodenal Stenosis in Crohn’s Disease
Hiroaki Omori, M.D., Akira Sasaki, M.D., Hiroshi Asahi, M.D.*, Koki Otsuka, M.D., Hidenobu Kawamura, M.D., Jun Nakajima, M.D., Toru Obuchi, M.D., Eiji Meguro, M.D., Yoshio Hayakawa, M.D., Takashi Irinoda, M.D., Kazuyoshi Saito, M.D. Department of Surgery I, Iwate Medical University, Morioka, Iwate, Japan and Department of Surgery, Hakodate Goryokaku Hospital, Hakodate, Hokkaido, Japan.

Introduction: Duodenal Crohn’s disease (CD) is relatively rare and has an estimated incidence of 1% to 2% among patients with CD. Duodenal CD requiring surgery has traditionally been managed with an open bypass procedure. However, more recently, a laparoscopic treatment has become an acceptable surgical option. We report a case of severe duodenal stenosis in CD, successfully treated with laparoscopic gastroduodenal anastomosis (Jabouley’s pyloroplasty).

Case Presentation: A 30-year old man was diagnosed with CD at age 22 and had been treated medically, including the use of ASA and enteral diet. His disease was refractory to medical therapy, resulting in eventual laparoscopic subtotal colectomy at age 27. He subsequently complained postprandial vomiting and poor oral intake. He was admitted because of gastric outlet obstruction and a weight loss. Endoscopy and upper gastrointestinal (GI) tract X-ray showed a severe deformity and circular inflammatory stenosis of the proximal duodenum extending over 3 cm. A laparoscopic gastroduodenal anastomosis was indicated for duodenal stenosis. At laparoscopy, the duodenal wall was found to be thickened. A duodenal maneuver was fully made, while Jabouley-type pyloroplasty (gastroduodenal side by side anastomosis) was also performed by Endo GIA. A postoperative upper GI X-ray showed an improvement in the gastroduodenal passage. His postoperative course was uneventful and he has remained asymptomatic during follow-up period of 6 months.
Discussion: Duodenal CD with severe stenosis has been treated by various modalities including endoscopic dilation, surgical bypass and strictureplasty. However, surgical interventions have been widely adopted because an endoscopic dilation has a high recurrence rate. More recently, a laparoscopic treatment has become an acceptable surgical option in the surgical management of CD. Laparoscopic intervention should be considered in surgical options, since CD is an unremitting condition in which operations are frequently multiple.

Conclusion: Laparoscopic gastroduodenal anastomosis for duodenal CD is a useful and safe procedure.

Eosinophilic Gastroenteritis Presenting as Obstructive Jaundice
Ankur R. Sheth, M.D., M.P.H., Ryan Palmer, M.D., Paul A. Jordan, M.D., F.A.C.G., *Kenneth Manas, M.D. Department of Gastroenterology, LSU Health Sciences Center, Shreveport, LA.

Introduction: Eosinophilic gastroenteritis was first described by Kajiser in 1937, and is manifest by eosinophilic infiltration of any area of gastrointestinal tract, most frequently stomach and small intestine. We present a case of eosinophilic gastroenteritis presenting with inflammatory biliary obstruction; which is extremely rare.

Case: A 47-year-old male with past medical history of chronic pancreatitis and pseudocyst presented with one-week history of epigastric pain, nausea, anorexia and dark colored urine. He denied alcohol use for the six months prior to presentation. Physical examination was significant for temperature of 99.4 °F, icteric sclera, and mild epigastric tenderness without guarding or rebound. Laboratory test revealed a total white cell count of 16,900 per cmm of which 46 percent were eosinophils, a total bilirubin of 7.1 mg/dL, a conjugated bilirubin of 5.7 mg/dL, an alkaline phosphatase of 516 U/L, an AST of 144 U/L, and an ALT of 180 U/L. The amylase, lipase and prothrombin time were within normal limits. Stool studies were negative for parasites. CT scan of the abdomen showed dilatation of the common bile duct and intrahepatic biliary system with a pseudocyst in pancreatic head. Esophago-gastrodeodenoscopy revealed an abnormally thickened gastric mucosa with multifocal and superficial aggregates of eosinophils found on biopsy. ERCP revealed a dilated common bile duct with a tapered, inflammatory appearing stricture, which on biopsy revealed chronic inflammation with aggregates of eosinophils. The patient underwent an elective Roux-en-Y operation to provide permanent biliary drainage. Intra-operatively an inflammatory mass was found in the head of pancreas with evidence of chronic inflammation and marked eosinophilic infiltration on pathological analysis.

Discussion: Eosinophilic gastroenteritis is a rare gastrointestinal disorder of undetermined etiology. Talley et al identified three main diagnostic criteria; the presence of gastrointestinal symptoms, biopsy demonstrating eosinophilic infiltration, and absence of parasitic or extra intestinal disease. Peripheral eosinophilia is present in about 80% of patients and about 50% of patients are found to have allergic disorders. Steroids are the mainstay of treatment. Surgery is reserved for obstruction or perforation. This unusual case illustrates the wide variety of gastrointestinal manifestations caused by eosinophilic gastroenteritis and emphasizes the importance of clinical suspicion and endoscopic mucosal biopsies.

Do All Adult Patients with Small Bowel Intussusception Need Surgery?
Ankur R. Sheth, M.D., M.P.H., *Paul A. Jordan, M.D., F.A.C.G. Internal Medicine, Louisiana State University Health Sciences Center, Shreveport, LA.

Introduction: Intussusception of the small bowel accounts for less than 1% of cases of small bowel obstruction in adults. It has traditionally been regarded as a condition requiring surgery, because up to 90% of cases are said to be associated with a lead point disease. We present a case of small bowel intussusception in an adult, which was transient and managed conservatively without surgical intervention.

Case: A 23-year-old man presented to the Emergency Department with a three-day history of right-sided abdominal pain, nausea and bilious vomiting. On arrival, his temperature was 97.7 °F and his pulse rate was 79 beats per minute. Examination revealed a non-distended abdomen with right lower quadrant tenderness without guarding or rebound tenderness. His white cell count was 13,000 per cmm and hematocrit was 50 percent. Plain-film radiograph of the abdomen revealed a non-obstructive bowel gas pattern. Computed tomographic scanning of the abdomen showed a “target lesion”, suggestive of small bowel intussusception (Figure 1). However, no abnormality was demonstrated on barium small bowel follow-through performed the next day. The patient’s general condition improved with bowel rest.

Discussion: The reported frequency of lead point disease with adult small bowel intussusception is based on surgical series in which patients had obstructive symptoms and the diagnosis was made intraoperatively. However recent series using CT or MRI diagnosis of intussusception found increased rate of idiopathic transient intussusception approaching 50%, especially in small bowel. Features suggestive of transient intussusception are incidental presentation, proximal small bowel location, absence of peristaltic obstruction, absence of any apparent cause, target like lesion on CT scan and intussusception length less than 3.5 centimeter.

Many cases of adult small bowel intussusception that are detected with computerized tomography are self-limiting. This highlights the need for considering conservative approach in management of small bowel intussusception in adults.

Mycobacterium Tuberculosis (TB): A Cause of Severe Abdominal Pain in a Patient with Acquired Immunodeficiency Syndrome (AIDS)
Christopher Sofianos, M.D., Hala Fatima, M.D., Hong Shen, M.D., Omar Nehme, M.D.* Medicine, Indiana University, Indianapolis, IN.

Case Report: A 36 year old woman presented with a one day history of fever, severe right lower quadrant abdominal pain, nausea and vomiting. Her vital signs were significant for a heart rate of 110 and a temperature of 104 F. Abdominal exam revealed severe right lower quadrant tenderness with localized guarding. The patient’s CD4 count was 74 and the remainder of her labs including blood and urine cultures were negative. A CT scan showed circumferential thickening of the ileum. On colonoscopy the terminal ileum appeared edematous, with erythema and friability. Ileal biopsies revealed necrotizing granulomas and rare bacilli were seen on acid fast
staining. Cultures of the biopsy specimen grew Mycobacterium tuberculosis. Bronchial lavage specimen during bronchoscopy were negative for TB and a skin PPD test was non-reactive. The patient was started on isoniazid, ethambutol, pyrazinamide and rifampin and was discharged home when her fever and abdominal pain resolved. A follow up CT scan performed 8 months later demonstrated complete resolution of the ileal wall thickening.

**Discussion:** Extrapulmonary TB is a well reported disease. Its incidence in the US is on the rise particularly among immunosuppressed patients and immigrants from endemic countries. Skin testing (PPD) may not be reliable. Cultures and acid fast staining of specimen obtained from affected sites may be diagnostic. Because of its rich lymphatic content, the ileum is a site commonly affected by extrapulmonary TB however the entire GI tract may be affected. A strong index of suspicion needs to be maintained when evaluating patients at high risk.

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**Stercoral Ulcer. An Uncommon Cause of Lower GI Bleeding: Case Report and Review of Literature**

Mateen M. Hotiana, M.D., Rafael Amaryl, M.D., F.A.C.G.,∗ Muhammad N. Athar, M.D., Syed N. Hussain, M.D., Mujeeb Altaf, M.D. Internal Medicine, Mercy Hospital of Philadelphia, Philadelphia, PA.

Stercoral ulcer is a rare cause of lower GI bleeding. It means loss of mucosal integrity in the colorectal region due to the pressure effect of hardened fecal masses. It is an under diagnosed cause of GI bleeding and is not mentioned in detail in most of the medicine and surgery texts. Insufficient data exists as to what percentage of lower GI bleeding can be attributed to this cause. Clinically, it presents as a sudden onset of massive lower GI bleeding typically in hospitalized bedridden patients. Severe prolonged constipation due to any etiology is invariably present in these patients. The impacted fecal material then hardens over time and applies pressure effect on the bowel mucosa and leads to its ulceration. Stercoral ulcer should be considered as a possible cause of lower GI bleeding and abdominal pain especially in old, bed ridden patients or those with long standing constipation. GI bleeding stops spontaneously with hemodynamic support in most cases. Complications are rare and include perforation and peritonitis with mortality reaching up to 50%. Early surgical intervention is indicated in complicated cases.

This condition mainly affects people of more than 70 years of age and as the number of people living in the older age group increases in the US, this condition would be encountered more often by the physicians. We present a case report of a relatively younger; 57 yr old, African American male who developed sever constipation followed by massive lower GI bleeding after a month of stay in the hospital. On flexible sigmoidoscopy a stercoral ulcer of the rectum was diagnosed to be the cause. More research is needed to further explain the pathophysiology of this disease thus increasing our understanding of the gastrointestinal system. [figure1]

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**Infarction of the Central Nervous System (Stroke) Complicating Acute Pancreatitis: Report of Two Cases**

Ilan Aharoni, M.D., Tejal Shah, M.D., Joel Albert, M.D., Jian Jun Li, M.D., Scott Tenner, M.D., M.P.H.,∗ Division of Gastroenterology, Maimonides Medical Center, Mount Sinai School of Medicine, Brooklyn, NY.

Central Nervous System (CNS) complications following acute pancreatitis are rare and include pancreatic encephalopathy, acute axonal sensorimotor polyneuropathy, and Purtscher’s retinopathy. We describe 2 cases of CNS infarction (stroke) presenting as early complications of acute pancreatitis. A 36 yo gentleman presented with a 1 day history of epigastric pain. Although he regularly used tobacco, there was no significant past medical history, medications or family history. On initial examination, he was febrile, tachycardic, with epigastric tenderness. Neurologic exam was normal. Laboratory analysis showed a leukocytosis, amylase of 850 IU/l, lipase 1800 IU/ml. The triglyceride level was 1300 mg/dl. CT scan revealed Balthazar Grade C pancreatitis. Intravenous hydration and pain control were begun. Within 24 hours of admission for acute pancreatitis, he developed right hemiplegia and aphasia. MRI revealed a 2 cm non-hemorrhagic infarct of the left parietal lobe. Carotid duplex and echocardiogram showed insignificant disease. Hematologic evaluation was negative for abnormalities in the coagulation profile.

The second case is a 79 yo woman who presented with several days of epigastic pain, episodic vomiting & fever. PMHx was significant for non-insulin dependent diabetes, hypertension and peripheral vascular disease. On initial examination, she was febrile, tachycardic, with marked tenderness in epigastrium. Neurologic exam was unremarkable. Admission laboratory analysis revealed an amylase of 2456 IU/dl, lipase of 2700 IU/dl. Computed tomographic scan revealed Balthazar Grade B pancreatitis. Intravenous hydration and pain control were begun. On the 5th day of hospitalization, she developed left hemiplegia. MRI of the brain demonstrated an acute non-hemorrhagic infarct in the right pons. Carotid duplex and echocardiogram showed insignificant disease. Hematologic evaluation was negative for underlying disease.

The temporal association of these acute cerebral events early in the course of acute pancreatitis suggests that the pathogenesis of CNS disease is directly related to the acute pancreatitis. This is further supported by the absence of significant abnormalities on imaging and laboratory evaluation in both patients. Although further research is needed, we hypothesize that either fat embolization or a temporary activation of the clotting cascade from serum proteases likely led to the observed CNS effects.

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**Aripiprazole Causes Cholelithiasis and Hepatitis: A Rare Finding**

Gavin Chico, M.D., Aneez Raza, M.D., F.A.C.G.∗ Internal Medicine, DRCHC, Shreveport, LA and Gastroenterology, Overton Brooks VA Medical Center, Shreveport, LA.

**Introduction:** Aripiprazole is an effective antipsychotic with a favorable side effect profile. The purpose of this case report is to indicate that rare and potentially fatal side effects can occur on aripiprazole therapy.

**Case:** A 54 year old male with a history of schizophrenia, cholecystectomy, on warfarin, presents with 8-day history of vomiting, diarrhea and light
colored stools. He has no history of hepatitis B and C; recent travel, alcohol
or acetaminophen use. Patient was started on aripiprazole for schizophrenia,
two weeks prior to admission. At admission the patient was icteric with mild
hepatomegaly. Aripiprazole was discontinued and coumadin held.

Labs in Hospital

<table>
<thead>
<tr>
<th>Lab test</th>
<th>At Admission</th>
<th>4 Days Later</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.2 g/dl</td>
<td>2.9 g/dl</td>
<td>3.4–5 g/dl</td>
</tr>
<tr>
<td>Conjugated bilirubin</td>
<td>5.6 mg/dl</td>
<td>8.5 mg/dl</td>
<td>&lt; 0.3 mg/dl</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>300 IU/L</td>
<td>266 IU/L</td>
<td>38–126 IU/L</td>
</tr>
<tr>
<td>ALT</td>
<td>790 IU/L</td>
<td>1107 IU/L</td>
<td>14–63 IU/L</td>
</tr>
<tr>
<td>AST</td>
<td>971 IU/L</td>
<td>1600 IU/L</td>
<td>15–40 IU/L</td>
</tr>
<tr>
<td>INR</td>
<td>17.6</td>
<td></td>
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</table>

Normal labs included ferritin, anti-smooth muscle antibody, ANA, anti-LKM1, CA 19–9 and viral hepatitis panel.

In hospital after a dose of vitamin K the INR reversed to 1.7. Endoscopic ultrasounds showed moderate pancreatitis without ductal dilatation or stone. CT scan showed minimal hepatomegaly with normal tissue density. The patient improved significantly after discontinuing aripiprazole and was subsequently discharged.

On outpatient visit, 18 days later, the labs were: albumin 3.5 g/dl, alkaline phosphatase 95 IU/L, ALT 80 IU/L, AST 68 IU/L and INR 1.1. The patient had fully recovered.

**Discussion:** Aripiprazole is a novel atypical antipsychotic with a favorable side effect profile. The incidence of cholestasis and hepatitis is less than 1%. In the absence of a biopsy, the hepatic injury could be due to an ischemic event or aripiprazole. However, the obstructive pattern of injury does not favor ischemic hepatitis. Instead the 2-week delay of adverse hepatobiliary effects is consistent with the pharmacokinetics of aripiprazole which achieves a steady state at 2 weeks. This cumulative phase is associated with a 4-fold increase in mean peak plasma concentration; which is possibly hepatotoxic, given that the metabolism of aripiprazole is hepatic. Considering the above temporal profile and pattern of hepatic injury, the likely culprit appears to be aripiprazole and not an ischemic event.

**Conclusion:** This case report demonstrates that rare and potentially fatal side effects can occur on aripiprazole therapy, requiring close monitoring when initiating therapy.

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**Gastric Sarcoidosis Presenting with Acute Gastrointestinal Bleeding**

Upinder Rohewal, M.D., Matthew Tangorra, D.O., Emmanuel Akinyemi, M.D., Abu Matin, M.D., Muhammad Abdullah, M.D.* Gastroenterology, Coney Island Hospital, Brooklyn, NY and Gastroenterology, Maimonides Medical Center, Brooklyn, NY.

Sarcoidosis is a multisystem granulomatous disorder of unknown etiology characterized by the presence of noncaseating granulomas. Gastrointestinal involvement occurs in approximately 0.9 to 1% of patients affected. Over 60 cases of symptomatic gastric sarcoidosis have been reported in the world literature, 25 of which had documented histologic evidence of noncaseating granulomas consistent with sarcoidosis.

We present a case of a patient with upper Gl bleeding due to multiple gastric and duodenal ulcers. Gastric biopsies revealed noncaseating granulomas with negative stains for fungi and acid fast bacilli, consistent with sarcoidosis. A 58-year-old Jamaican male presented to the ER with acute-onset right-sided facial droop and slurred speech that was determined to be Bell’s palsy. The patient initially denied any medical history and did not take any chronic medications. While being evaluated for a possible stroke, the patient received one dose of aspirin and underwent urgent CT imaging of the brain, which was normal. The patient later received one dose of ketorolac (toradol) for headache, and was subsequently given prednisone 60 mg for the facial nerve palsy.

Several hours later the patient experienced one episode of hematemesis which spontaneously resolved. The following day an upper endoscopy revealed multiple gastric antral ulcers and a duodenal ulcer without stigmata of bleeding. A biopsy taken from the antrum revealed noncaseating granuloma. The patient experienced no further bleeding and remained well on PPI therapy, and the facial palsy gradually improved. Further information from the patient revealed a history of sarcoidosis diagnosed 15 years prior after an evaluation for chronic cough, which did not require steroid therapy.

**Discussion:** To our knowledge, there are no case reports of a pancreatic tail adenocarcinoma masquerading as a large bowel obstruction. Moreover, the...
stent-induced gastrocolic fistula is an infrequent complication. This underscores the importance of considering this organ as a primary source of an indeterminant adenocarcinoma.

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An Unusual Case of Metastatic Gastric Adenocarcinoma in a 19-yr-Old with Gastric Outlet Obstruction Safely Managed by Tandem Enteral Wallstents with Excellent Outcome

Kapil Gupta, M.D., Stephen Nanton, M.D., Kaumudi Somnay, M.D.*
Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY.

A 19-year-old girl was referred by her pediatrician for post prandial vomiting and a weight loss of 11lbs over one month. On examination a 10 cm X 10 cm firm mass was felt in the epigastrium which was very tender. Laboratory data showed hematocrit of 29 and CA 125 of 65.4 (normal 35). CT abdomen had shown thickening of mid to distal stomach, with surrounding fat infiltration, peri-gastric lymph nodes, thickening of transverse colon and pelvic ascites. On EGD a thickened, nodular and infiltrated appearing stomach with narrowed antrum and near complete obstruction of the pylorus was seen. Endoscopic biopsies were inconclusive. An upper GI series revealed a 13 cm long stricture extending from the distal stomach to the duodenum. EUS showed thickening of stomach wall consistent with lininits plastica, but FNA samples were inconclusive. On surgical exploration a large intramural mass in the distal stomach was noted along with omental lesions above the transverse colon, peritoneal implants on the fallopian tubes, and ascites. Pathology revealed a poorly differentiated gastric adenocarcinoma with abundant mucin or signet ring cell carcinoma. As the tumor was unresectable, a decision was made to bypass the gastric outlet obstruction with enteral stents. Two Wallstents (Microvasive) enteral endoprostheses measuring 90mm and 60mm in length were placed, in a tandem fashion with partial internal overlap to bypass the stricture. Patient was discharged home on a liquid and puree diet. Chemotherapy with 5-Flourouracil, Cisplatin and Tamoxifen was given as an outpatient. At a 20 week follow up, patient has good oral intake with weight gain. Outpatient follow up barium studies and CT scans have shown patent stents with good flow of dye. (figure1)

Gastric adenocarcinoma in young patients can present as advanced disease with metastasis and gastric outlet obstruction. Here we report one of the first cases of gastric outlet obstruction from metastatic gastric adenocarcinoma in a young patient managed with Wallstent showing feasibility, safety, and good long term patency.[figure1]

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Boerhaave’s Syndrome: A Rare Cause of Acute Chest Pain and Dyspnea

A. Shahem Kawji, M.D., Douglas G. Adler, M.D.* Internal Medicine, The University of Texas Medical School at Houston, Houston, TX.

Introduction: Spontaneous esophageal rupture (Boerhaave’s syndrome) is a rare clinical entity with a tendency to masquerade as a variety of more common intrathoracic conditions. It should be considered in the presence of vomiting followed by chest pain with or without subcutaneous emphysema. Early diagnosis is essential to permit early intervention.

Case Presentation: A 55-year-old man with no significant medical history presented with a sudden onset of epigastric pain, retrosternal chest pain, and dyspnea preceded by two episodes of retching and vomiting of food particles mixed with blood. He admitted heavy alcohol drinking the night before. On physical examination he was slightly tachycardic and in mild respiratory distress. Subcutaneous emphysema was noted in the neck and upper chest. Lung auscultation revealed diminished breath sound in the lung bases. Abdominal exam showed mild epigastric tenderness with normal bowel sounds. Laboratory studies revealed a WBC count of 11,700/mm3, ALT 117 U/L,
A 53-year-old patient with no PMHx presents with constipation and massive lower GI bleeding. Nine days after surgery, a Gastrografin esophagram showed no leakage of contrast. The patient underwent an emergent left thoracotomy and primary closure of the esophageal perforation. The patient tolerated the operation well. Nine days after surgery, a Gastrografin esophagram showed no leakage of contrast.

**Conclusion:** Spontaneous esophageal rupture is an uncommon condition associated with a catastrophic and almost always fatal course unless promptly diagnosed and treated with aggressive surgical measures.

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**Massive Lower GI Bleeding from an Uncommon Source**

*Atif Shahzad, M.D., Hulya Levendoglu, M.D.*

Brookdale Hospital Medical Center, Brooklyn, NY and Gastroenterology, Health Science Center, Brooklyn, NY.

A 53-year-old patient with no PMHx presents with constipation and massive lower GI bleeding. Initial endoscopic evaluation revealed gastric varices with no evidence of recent bleeding, and a normal colonoscopy. The patient was transfused 5 Units of PRBC and signed out AMA before further workup. Three weeks after initial admission, the patient again presents with massive lower GI bleed per rectum, weakness, HCT of 19, normal platelets and normal coag. Emergent endoscopy was done again and revealed non-bleeding gastric varices and blood through the colon without any evidence of active bleeding. A CT was performed and demonstrated a normal liver, splenomegaly, gastric varices, no esophageal varices and a normal pancreas. A tagged red blood cell scan was performed and revealed splenomegaly with tracer activity at or below the splenic flexure. A stat angiogram revealed splenomegaly with complete splenic vein thrombosis, normal portal vein, gastric varices, and a single large varix from the lower pole of the spleen going to the left colon around the splenic flexure. The splenic artery was then embolized and the patient underwent splenectomy the next day. During this admission the patient received a total of 11 units of PRBC.

Colonic varices were first described in 1954 and in 1992 there were a total of only 70 reports of bleeding colonic varices. Portal HTN and cirrhosis were the most common causes. However, isolated splenic vein thrombosis can be found among the extra-hepatic etiologies of colonic varices. More than half the patients with complete splenic vein thrombosis and varices present with GI bleeding. Surgical splenectomy is definitive and curative treatment. Pre-op splenic artery embolization is utilized to decrease the peri-op blood loss. The etiology of splenic vein thrombosis in our patient is still being evaluated.

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**Relapsing Cholestatic Acute Hepatitis A: A Case Report**

*Kaleem M. Rizvon, M.D., Theodore M. Perlman, M.D., Paul J. Mustacchia, M.D.*

Gastroenterology, Nassau University Medical Center, East Meadow, NY.

A young white female was hospitalized with one week history of malaise, abdominal pain, vomiting and low grade fever. The patient’s daughter had developed hepatitis A after a recent trip to Pakistan. On examination, the patient was icteric with mild right upper quadrant tenderness. Laboratory investigations were significant for an elevated Aspartate Aminotransferase (AST) of 570 U/L and Alanine Aminotransferase (ALT) of 525 U/L with an elevated Alkaline phosphatase and normal bilirubin level. The patient soon became icteric with peak AST level of 4837 U/L and ALT of 4461 U/L on day 3 of hospitalization. Acute viral hepatitis A was diagnosed with positive IgM antibody. Serological tests for viral hepatitis B and C and acute cytomegalovirus and Epstein-Barr infections were negative. Autoimmune and metabolic causes were also ruled out. Imaging studies were negative except for a small lesion likely a hemangioma. The patient was followed closely after her discharge from the hospital. She became progressively more icteric with peak bilirubin levels of 14.7 mg/dL and alkaline phosphatase of 917 U/L at 3 weeks of illness. An abdominal ultrasound was repeated at this time with no new findings. The patient had complained of mild pruritus which responded to antihistamines. Renal function was normal and no coagulopathy was evident. During week 4, her ALT level had reached its lowest point and subsequently increased indicating a possible relapse with a continued cholestatic picture. At week 9, bilirubin levels and alkaline phosphatase remained elevated. Even after 24 weeks of acquiring the illness, though she was asymptomatic, her alkaline phosphatase was mildly elevated at 163 U/L with normal bilirubin.

**Discussion:** Acute viral hepatitis A though uncommon in United States poses a significant risk for American travelers. Nearly 30 million Americans travel to Hepatitis A endemic areas every year. This case illustrates a transmission of the disease to an adult who did not travel out of the country. Hepatitis A follows a benign course in majority of the affected individuals but in 3–20% of cases can follow an atypical pattern with relapses and cholestasis. Extra hepatic manifestations are infrequent unlike Hepatitis B. Though healthy...
adults tolerate this atypical phase, it could be dangerous in patients with chronic liver disease. With the availability of a highly effective vaccine, this presentation could be avoided.

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Recurrent DVT Associated with Heterozygous MS-Type alpha(1)-Antitrypsin Deficiency
Larissa S. Buccolo, M.D., * Chris B. Hyun, M.D., Michael E. Herman, D.O. Family Medicine, Naval Hospital, Jacksonville, FL; Internal Medicine, Division of Gastroenterology, Naval Hospital, Jacksonville, FL and Internal Medicine, Naval Hospital, Jacksonville, FL.

Heterozygous forms of alpha(1)-antitrypsin (α1 AT) deficiency are common, occurring in up to ten percent of the United States population. However, the clinical significance of these heterozygous states is unclear. Presented is a case of heterozygous protease inhibitor MS (PiMS) α1 AT deficiency associated with recurrent deep venous thrombosis (DVT).

A 29-year-old Latino male presenting to the Gastroenterology clinic was incidentally noted to have elevated transaminases. His evaluation revealed mildly decreased α1 AT levels. Subsequent liver biopsy demonstrated periodic acid-Schiff (PAS) positive, diastase resistant granules within the hepatocytes, consistent with α1 AT deficiency. Phenotyping revealed the α1 AT phenotype PiMS. The patient's past medical history was notable for two episodes of DVT. Previous evaluation for underlying causes of hypercoagulability was unrevealing.

α1 AT is one of several serine proteinase inhibitors that regulate physiologic pathways responsible for processes such as fibrinolysis, coagulation, and complement activation. α1 AT deficiency is classically associated with emphysema and cirrhosis of the liver, although recent evidence suggests that dysfunctional forms of these proteinase inhibitors can pathologically alter a number of other physiologic pathways.

While our review of the literature showed no other causes of recurrent deep venous thromboses associated with PiMS phenotypes, there were rare reports of other thrombotic diseases associated with PiMZ. As further research identifies more pathologic states associated with this common mutation, screening of asymptomatic individuals may one day be warranted.

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Noncirrhotic Portal Hypertension in a Young Alcoholic Male
Nada Al-Skaf, M.D., John J. O'Brien, M.D., * Rhonda S. Purdy, N.P. Division of Gastroenterology & Hepatology, Creighton University School of Medicine, Omaha, NE.

A 19 year old Hispanic male (AG) presented to the emergency department with a one week history of multiple episodes of coffee ground emesis combined with bright red blood. Past medical history included a four years history of heavy alcohol abuse, otherwise unremarkable. In the emergency department, AG had evidence of ongoing upper GI bleeding with unstable vital signs. Physical exam failed to demonstrate stigmata of chronic liver disease or splenomegaly. Lab results were consistent with iron deficiency anemia (Hgb 4.7, low iron, high TIBC, low ferritin). Additional lab work revealed an INR of 1.36, otherwise, normal hepatic function tests. An urgent upper endoscopy demonstrated portal hypertensive gastropathy with Grade II-III esophageal varices. The patient underwent esophageal variceal ligation without difficulty. Abdominal ultrasound revealed a coarse echotexture throughout the liver, mild splenomegaly and pelvic ascites. Lab evaluation for chronic liver disease including viral hepatitis panel (hepatitis A, B, C), alpha 1 antitrypsin, ceruloplasmin, liver- kidney microsomal antibody, ANA, smooth muscle antibody, ANCA, and alpha-fetoprotein were unremarkable.

In addition, screening for schistosomiasis and other ova and parasites were negative. Serum drug and alcohol screening were negative. An ultrasound guided-paracentesis demonstrated a transudative ascites without evidence of malignancy. Liver biopsy showed noncirrhotic portal hypertension, mildly dilated sinusoids without significant fibrosis.

Doppler ultrasound disclosed no evidence of thrombosis. Protein C and S were marginally low. Anti-thrombin III was normal. Factor V leiden, serum arsenic, and copper are still pending.

This patient presented with variceal bleeding, anemia, splenomegaly with no clinical or pathological evidence of liver cirrhosis or schistosomiasis. He has no family or personal history suggestive of hypercoagulable state. The prothrombin screen has been unremarkable. In addition, there is no history of hepatotoxic medication use. Therefore, most likely AG had a form of Idiopathic Portal Hypertension (IPH). IPH, characterized by gastroesophageal variceal bleeding, is not uncommon in young adults, who otherwise have little or no evidence of hepatic dysfunction.

Treatments of variceal hemorrhage in patients with IPH are similar to those in patients who bleed from other causes. Although there have been no controlled trials in this setting, primary prophylaxis with a non-selective beta-blocker is reasonable.
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Endoscopic Sphincterotomy as Non-Surgical Treatment Option for Cholangitis Caused by Hepatic Hydatid Disease
Juergen M. Gschossmann, M.D.,* Peter Netzer, M.D., Frank Seibold, M.D., Herbert Dusch, M.D., Martin Anderau, M.D., Hans-Rudolf Baur, M.D., Ulrich Scheurer, M.D. Department of Gastroenterology, Inselspital / University of Berne, Bern, Switzerland; Department of Laboratory Medicine, Spital Bern Tiefenau, Bern, Switzerland and Department of Medicine, Spital Bern Tiefenau, Bern, Switzerland.

Parasitosis-associated obstruction of the biliary system is a rare cause for acute cholangitis. We report the case of a North African patient presenting with right upper abdominal pain radiating into the right shoulder. An initial abdominal ultrasound scan showed several cystic lesions in the liver which were suspicious for hydatid cysts, however no dilatation of the extra- and intrahepatic bile ducts. Positive serology for Echinococcus granulosus antigens and antibodies confirmed the diagnosis. Within one week, obstructive jaundice and cholangitis developed. Given the working hypothesis of biliary compression by hydatid cysts, a non-invasive therapy with antibiotics and antihelmintics was initiated. Following a further rise of cholestasis parameters under treatment with ceftriaxon and albendazole, an ERCP was performed. The papilla vateri was occluded by a whitish-greenish hard structure (demonstration). The injection of contrast medium showed a wide dilatation of the common bile duct and multiple contrast-free areas (demonstration). After papillotomy, a worm-like whitish-greenish structure (demonstration) followed by black bile fluid, pus and whitish debris poured into the duodenum. An endoscopic collection of the mass failed because of direct drainage of the structure into the distal duodenum. Thus, stool examinations were performed during the following days resulting in detection of the worm-like mass. Both histological and microbiological examinations revealed that the structure represented membrane parts of the known echinococcosis (demonstration). The further post-interventional follow-up was uneventful. After a stepwise normalization of the cholestasis and inflammation parameters, the patient could be discharged under continuous therapy with albendazole.

Conclusion: Beside an outside compression of the biliary system caused by echinococcal cysts, an biliary obstruction caused by echinococcal elements has to be excluded in circumstances when increased cholestasis parameters and dilated bile ducts are observed in association with positive echinococcosis serology. In our case, this obstruction could be corrected by endoscopic papillotomy without further need for surgical intervention.

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Hepatic Sarcoidosis Mimicking Klatskin Cholangiocarcinoma
S. Pungpapong, M.D., M. B. Wallace, M.D., J. Steers, M.D., A. P. Keaveny, M.D.* Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL and Transplantation, Mayo Clinic, Jacksonville, FL.

A 57-year-old African-American man presented with progressive obstructive jaundice, pruritus, and weight loss. Investigations were notable for elevated liver canalicular enzymes with negative serologies for viral hepatitis, autoimmune, and metabolic liver diseases. Serum CA 19-9, CEA, and AFP were within normal limits. ERCP demonstrated a complex stricture of common hepatic duct (CHD) at the confluence with proximal extension into both intrahepatic ducts (Bismuth-Corlette classification IV) (Figure 1). Intraductal brushings across the stricture were negative for malignancy. MRI revealed a lesion measuring $2.5 \times 2.5 \times 2.8$ cm encasing the CHD (Figure 2). At EUS, a 2.4-cm lesion was identified surrounding the CHD (Figure 3). Cytology from FNA of the lesion was negative for malignancy. Liver biopsy revealed mild lobular hepatitis without granuloma or fibrosis. CT scan of the chest showed a normal lung parenchyma without mediastinal lymphadenopathy. Given a lesion that was highly suspicious for Klatskin cholangiocarcinoma without evidence of metastasis, he underwent an exploratory laparotomy with right hepatic lobe resection and Roux-en-Y left hepaticojejunostomy. Final pathology revealed non-caseating granulomatous inflammation forming a 3.5 cm mass in the hilar soft tissue adjacent to CHD without any evidence of malignancy or infection, consistent with sarcoidosis.

In this report, we describe a unique case of hepatic sarcoidosis presenting as obstructive jaundice due to the isolated involvement of CHD and bilateral intrahepatic ducts, mimicking Klatskin cholangiocarcinoma. No involvement
of other organs was identified. To our knowledge, this is the first such case report in the literature. It highlights the great difficulty in establishing a definitive diagnosis for the etiology of a biliary stricture without performing an exploratory laparotomy despite the application of multiple pre-operative radiographic modalities and tissue sampling techniques. If hepatic actinomycosis had been diagnosed pre-operatively, a therapeutic trial of corticosteroids might have been attempted initially.[figure1]

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Intrauterine Device Related Hepatic Abscess
Steve Keilin, M.D., Frida Abrahamian, M.D.*, Bashar M. Attar, M.D.,
F.A.C.G. Gastroenterology, John H Stroger Hospital of Cook County and Rush Medical College, Chicago, IL.

Hepatic Actinomycosis is a rare, but well documented cause of liver abscess. Recent literature has demonstrated the relationship of intrauterine devices (IUD) and infection with Actinomyces species. Infections caused by Capnocytophaga species occur infrequently but usually present in patients that are immunocompromised. A 42 year old Polish female with no significant past medical history, presented with a month of upper abdominal fullness, loss of appetite, nausea, and weight loss of 30 lbs. On exam she was cachectic with right upper quadrant tenderness and hepatomegaly. Lab values were notable for WBC's of 12.1 with 27% bands, an alkaline phosphatase of 493 U/L, AST of 48 U/L, ALT of 45 U/L and albumin of 2.5 g/dL. A CT of the abdomen showed dilatation of the intrahepatic ducts, 2 large subcapsular fluid collections in the right lobe of the liver, a large fluid collection in the pelvis and the presence of an IUD. An ERCP demonstrated multiple saccular dilatations of the intrahepatic ducts and two cystic areas in the liver communicating with the biliary tree. Papillotomy was performed with drainage of purulent fluid. The patient underwent CT-guided drainage of the fluid collections in the right lobe of the liver and the pelvis, with removal of 700 ml of pus. The patient was started on piperacillin/tazobactam and the IUD was removed. The patient improved and cultures of the hepatic abscess eventually grew A. israelii and C. ochracea and the pelvic abscess grew A. israelii also. However the patient had a seizure 7 days into antibiotic therapy and CT of the head revealed 3 ring-enhancing lesions, consistent with metastatic abscesses. The patient was started on phenytoin and the antibiotics changed to ceftriaxone and metronidazole. Repeat CT of the abdomen showed resolution of the abscesses. The patient subsequently did well and eventually went home on long-term antibiotic therapy.

Actinomyces and Capnocytophaga species are both endogenous to the oral flora and occasionally can be found in the gastrointestinal and vaginal tracts. Hepatic Actinomycosis accounts for 5% of all infections with Actinomyces species. Risk factors include poor dentition, appendicitis, prior abdominal surgery, immunosuppression and IUD use. Most infections with Capnocytophaga occur in immunocompromised patients with poor dentition and clinically manifest as bacteremia, endocarditis, osteomyelitis or empyema. An extensive literature review revealed only one case report of liver abscesses due to Capnocytophaga.

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Primary Amyloidosis Presenting as Recurrent Ischemic Colitis
Jian Zhang, M.D., John McCracken, M.D.* Gastroenterology, Loma Linda University Medical Center, Loma Linda, CA.

Ischemic colitis has a myriad of causes. Primary amyloidosis is a rare cause of ischemic colitis with only a few cases reported in the literature. We present an unusual case of ischemic colitis due to primary amyloidosis. A 69 year old woman, with history of activated protein C resistance and lower extremity deep vein thrombosis on chronic warfarin treatment, presented with 1-day history of bloody diarrhea and crampy abdominal pain. Three weeks before, she was hospitalized with similar symptoms at another medical facility and diagnosed with ischemic colitis by colonoscopy. After a week of bowel rest, total parental nutrition, and intravenous antibiotics, her symptoms had resolved. She remained asymptomatic until the night prior to her current admission. She was afibrile with a blood pressure of 108/66 mm Hg and a pulse of 109 beats per minute. Physical examination was significant for mild tenderness to palpation in the lower abdomen, without peritoneal signs. Laboratory evaluation revealed normal white blood cell count, hemoglobin of 11.9 g/dL, and an International Normalized Ratio of 0.5. Abdominal computed topography showed nonspecific thickening of the colonic mucosa from the splenic flexure to the descending colon. Sigmoidoscopy revealed multiple large ulcers with areas of mucosal necrosis in the proximal sigmoid colon. Biopsies showed focal ulceration with necroinflammatory exudate. Mesenteric angiogram was unremarkable. On hospital day 7, she underwent a total colectomy with end ileostomy after ischemic changes were observed from mid transverse colon to rectosigmoid junction on intraoperative colonoscopy. Histology revealed extensive amyloidosis involving the omentum and entire colon with deposition in the muscularis mucosa, submucosa, and subserosa. Perivascular deposition of amyloid with luminal narrowing was also present. Serum electrophoresis and immunofixation revealed an IgG lambda monoclonal band, while a bone marrow biopsy showed 5–10% lambda restricted plasma cells. Our case illustrates that primary amyloidosis presenting as recurrent ischemic colitis may be missed despite thorough history, laboratory evaluation, radiographic studies and endoscopic biopsies.

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Extensive Gastrointestinal Tract Involvement with Wegener’s Granulomatosis
Raja Shekhar R. Sappati Byyani, M.D., Privi Pauskar, M.D., Smitha Battula, M.B.B.S., Eeleen Liu, M.D., Jehad Y. Asfouri, M.D., William P. Blocker, M.D., Loren M. Kirchner, M.D., Nabil M. Fahmy, M.D., F.A.C.G.*, James F. King, M.D., M.A.C.G., F.A.C.P. Department of Internal Medicine, Canton Medical Education Foundation-NEOUCOM, Canton, OH and Department of Gastroenterology, Mercy Medical Center, Canton, OH.

Introduction: Wegener’s granulomatosis (WG) is a pauci-immune systemic vasculitis mainly involving small to medium sized blood vessels of the upper and lower respiratory tract and kidneys. Here we report a rare case of WG with extensive GI tract involvement.

Case: A 34-year-old white female presented with sinusitis, bloody nasal discharge and painful sores in her mouth and on her tongue and palate. Small erythematous papules developed on her legs, which evolved into target-like lesions with central necrosis. Digital ischemia resulted in necrosis of fingers and toes. Radiography revealed diffuse bilateral pulmonary infiltrates and pan-sinusitis on CT scan of the sinuses. Infective endocarditis was ruled out with a negative TEE and negative blood cultures. Serum tests revealed C-ANCA titer of 1: 320, anti-PR3 antibody 9.1 U/mL, negative myeloperoxidase (MPO) Ab, RF of 115.9 IU/mL, positive lupus anticoagulant, negative ANA, ds-DNA Ab and anti-Smith Ab. Punch biopsy of the skin lesions was consistent with necrotizing vasculitis involving small vessels. The diagnosis of WG was confirmed and treatment was initiated with steroids and cytotoxic. Because of abdominal pain, odynophagia and dysphagia, an EGD was performed. EGD showed circumferential punched out ulcerations of esophagus at 21–36 cm from the incisors with stricture formation necessitating PEG tube placement. biopsy showed acute ulcerative esophagitis with no evidence of dysplasia or malignancy.

Discussion: Esophageal involvement with WG is a very rare but ominous sign. Vasculitis, ischemia and ulcerations are major histological findings within the GI tract. Even though endoscopic examination is the best method to determine extent of the disease, it is to be noted that the biopsies performed are superficial and might not reveal vasculitis. Endoscopic literature pertaining to the GI manifestations in WG is very limited. The findings of ulcerative lesions of the esophagus has been noted with WG, however
The Natural History of Barrett’s Dysplasia and Adenocarcinoma
Raja Shekhar R. Sappati Biyyani, M.D., Smitha Battula, M.B.B.S., Linda Chestler, Loren M. Kirchner, M.D., M.S., James F. King, M.D., M.A.C.G., F.A.C.P.* Department of Internal Medicine, Canton Medical Education Foundation-NEOUCOM, Canton, OH and Department of Gastroenterology, Mercy Medical Center, Canton, OH.

Introduction: The natural history of Barrett’s esophagus (BE) is a matter of debate in the GI literature. We report two unique presentations of BE, which demonstrates highly variable biologic behavior. This poses a management dilemma when faced with options of surveillance, ablation modalities or surgery.

Case 1: A 79-year-old diabetic, hypertensive male had long-segment BE (LSBE) with 3 years of high-grade dysplasia (HGD). He then developed a small-elevated plaque at 36–37 cm from the incisors confirmed as Barrett’s adenocarcinoma (BEAC). Because of age and comorbidities, endoscopic mucosal resection (EMR) and photodynamic therapy (PDT) were offered. The patient was resolute and refused treatments. EGD two and one-half years later revealed a 3 cm fungating, exophytic, non-obstructing poorly differentiated BEAC at 35–38 cm from incisors. A CT scan showed only a right paratracheal node less than 1 cm in size. He eventually died 5 years after diagnosis of BEAC from CHF but remained asymptomatic from the cancer.

Case 2: A 83-year-old male with CAD, hyperlipidemia, CHF, and HTN was under surveillance for 14 years because of LSBE with variable grades of dysplasia. Initial biopsy showed low-grade dysplasia (LGD), however, 3 years later HGD approaching BEAC was noted. Proton pump inhibitor dose was doubled and a repeat biopsy 3 months later showed no dysplasia. He was lost to the follow-up but 4 years later was found to have LGD and HGD. Remarkably he demonstrated HGD intermittently over a total of 14 years and died of pulmonary embolus but never developed BEAC.

Discussion: Lifetime risk to develop BEAC in patients with BE is about 5%. Patients with BE rarely die of BE or BEAC but often from unrelated illness. Whether ablation or surveillance is the best management for LSBE remains to be determined. Management often depends on the co-morbidity, biologic tumor behavior, local resources and patient preferences. Although both cases had multiple endoscopic biopsies, the procedures made very little difference in the quality of their lives.

Atypical Presentation of Portal Vein Thrombosis in the Absence of Cirrhosis
Ilina Bouneva, M.D.,* Cox Thadis, M.D., Siford Michael, M.D. Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY and Digestive Diseases and Nutrition, Veterans Affairs Medical Center, Lexington, KY.

The diagnosis of portal vein thrombosis (PVT) in the absence of cirrhosis is based on typical Doppler ultrasound findings in patients presenting with esophageal/gastric varices with or without bleeding but usually no ascites, who also frequently have an underlying hypercoagulable state. We describe a difficult to diagnose case of PVT with negative Doppler study and atypical clinical presentation and liver histology. 60 year old man without history of liver disease, was admitted with pulmonary embolism and bleeding esophageal varices. After volume resuscitation he underwent endoscopic variceal band ligation (EBL). He had Vena-Tech filters placed in the iliac veins since IVC was found to be dilated (3.4 cm). He was also diagnosed with large ascites with SAAG > 1.1 and SBP for which he was treated. All the routine lab tests (CBC, biochemistry, coagulation), were normal (except albumin 2.4 g/d); the work up for the most common causes of chronic liver disease was negative. An ultrasound with Doppler showed normal liver, gallbladder hydrops, moderate ascites, and patent hepatic vasculature with normal flow. Because the possibility of cryptogenic cirrhosis still existed, a liver biopsy was done which revealed marked sinusoidal dilatation but no fibrosis or cirrhosis. Since now there was a suspicion for hepatic venous outflow obstruction, the patient underwent an echocardiogram which was normal; and MRI/MRA, which showed normal IVC and hepatic veins but attenuated portal vein. Subsequent venogram demonstrated portal vein thrombosis. The patient was found to be heterozygous for G20210A prothrombin mutation. He underwent several sesions of EBL’s until obliteration of the varices, and then Coumadin was started for prophylaxis of further thrombotic events.

The diagnosis of PVT is usually readily established with a Doppler ultrasound (sensitivity 89%, specificity 92%). While esophageal varices with bleeding are very common, only 10% of patients have ascites caused by acute dilutional hypoalbuminemia due to fluid resuscitation. Severe sinusoidal dilatation on liver biopsy is seen typically in patients with hepatic venous outflow impairment; however, about 5.9% of such patients may have PVT. Helpful clues for diagnosis of PVT may be found in patient’s history (e.g. pulmonary embolism) and presence of hypercoagulable state (e.g. prothrombin mutation).
Hemorrhage is uncommon but serious complication of pancreatitis. It may develop by different mechanisms, involve different vascular structures, and require different therapeutic approaches. We present a patient with severe pancreatitis who developed recurrent bleeding by several different mechanisms eventually controlled by a single therapeutic intervention.

A 37 year old man with recurrent acute alcoholic pancreatitis was admitted with hematemesis. An EGD revealed bleeding gastric varices and sclerotherapy was performed with good hemostasis. Serial abdominal CT scans (incl. CT angiogram) showed pancreatic pseudocyst, splenic artery pseudoaneurym, peripancreatic hematoma, and thrombosed splenic vein. Shortly after that the patient had another episode of hematemesis. The repeat EGD did not show bleeding gastric varices but a fresh blood leaking from the duodenal wall. An angiogram was done which confirmed splenic vein thrombosis and demonstrated a leakage of the splenic artery pseudoaneurysm into the retroperitoneal space and into the pancreatic pseudocyst which had eroded into the duodenal wall. Embolization with polyvinyl alcohol particles was performed with complete occlusion of the splenic artery pseudoaneurysm and cessation of bleeding. No side effects of treatment were observed. On further 5 months follow up the patient has not had further episodes of bleeding. The follow up abdominal CT scans showed gradual resolution of pancreatitis, pancreatic pseudocyst, and splenic artery pseudoaneurysm after its occlusion.

GI bleeding by different mechanisms was observed in this patient with severe pancreatitis: bleeding gastric varices secondary to left-sided portal hypertension due to splenic vein thrombosis; and splenic artery pseudoaneurysm complicated by rupture into the retroperitoneal space and into pancreatic pseudocyst which eroded into the duodenum. The bleeding was controlled with an angiographic embolization of the splenic artery. Mesenteric angiography is not only the gold standard for localization of bleeding pseudoaneurysms but, if combined with embolization, it achieves control of bleeding in 75%. In addition, even though splenectomy is a treatment of choice for symptomatic patients with splenic vein thrombosis, the percutaneous splenic artery embolization, is an good alternative for a “non-surgical splenectomy”.

Management of Hyperemesis Gravidarum with Nasogastric Tube Feeding
Arun Srivatsa, M.D., Linda Lord, R.N.P, C.N.S.N., Arthur DeCross, M.D.*
Department of Internal Medicine, University of Rochester, Rochester, NY; Nutrition Support Service, University of Rochester, Rochester, NY and Division of Gastroenterology, University of Rochester, Rochester, NY.

We report the largest experience in the medical literature of the management of hyperemesis gravidarum (HG) with nasogastric tube feeding.

**Background:** HG is a common cause for hospitalization during early pregnancy. Patients who fail to maintain hydration and nutrition despite antiemetic treatment are typically managed with intravenous hydration and parenteral nutrition. Risks of parenteral nutrition have been well documented and include catheter related sepsis, thrombosis and various metabolic complications in addition to considerable expense. In contrast, anecdotal reports have suggested that tube feeding can be well tolerated in these patients. Tube feeding may decrease vomiting by reducing the stimulation of taste and smell receptors which initiate the oropharyngeal phase of digestion. Retrospective chart review of our entire cohort of 26 women over 7 years with HG who were referred for persistent vomiting and loss of weight despite antiemetic treatment. Diagnosis was confirmed by standard clinical and laboratory parameters, including liver function tests, urinalysis, thyroid function and abdominal ultrasonography. All patients were administered isotonic tube feeds via a 8 Fr nasogastric tube, starting from 125ml every 12 hours and increasing gradually up to 500ml every 6 hours till 100% of caloric goal was achieved.

Median age of the patients was 25 years. Median presentation was at 8 weeks gestation. Mean duration of symptoms prior to referral was 23 days. Weight loss from onset of symptoms averaged 4.4 kg. Mean time to cessation of emesis after insertion of the feeding tube was 4.5 days. Mean number of days to initiate steady weight gain was 3.6 days. All patients achieved 95–100% of the nutrition goals for pregnancy. Mean duration of hospitalization was 5 days after initiating tube feeds. Average duration of tube feeding was 50 days. 84% of the pregnancies went to term (mean 36weeks) with all the neonates at a weight appropriate for gestational age (mean 3.4kg). There were no significant complications. Self-limiting diarrhea occurred in 15%. Tube dysfunction occurred in 21 patients, with a mean reinsertion of 2.7 tubes per patient.

Severe Hyperemesis Gravidarum with weight loss and dehydration can be safely and effectively managed by nasogastric tube feeding in preference to the risks and expense of parenteral nutrition.

Unusual Presentation of Epstein Barr Virus Hepatitis
Scott H. Mackenzie, M.D., Kathryn Peterson, M.D.*
Gastroenterology, University of Utah, Salt Lake City, UT.

54 year old male with no medical history and no medications originally evaluated at outside emergency department on several occasions with headaches with minimal improvement with narcotics. On third presentation labs including liver function test were done showing an alkaline phosphatase of 870 U/L, Bilirubin 2.3 mg/dL, AST 114 U/L, ALT 157 U/L. Abdominal ultrasound done at that time was normal. Patient continued to complain of headache, photophobia, night sweats, and anorexia with only mild right upper quadrant discomfort. He was then transferred to our institution with continued elevation of LFT's: Alk Phos 883, AST 134, ALT 209, bilirubin 5.8. A CT abdomen showing complicated acalculus cholecystitis. Repeat ultrasound showed thickened gallbladder wall. LFT's continued to rise over the next few days. ERCP was performed, revealing normal biliary anatomy and without stones or sludge. A laparoscopic cholecystectomy was subsequently performed along with intraoperative liver biopsy. The gallbladder was grossly normal and pathology returned with mild inflammation. Liver biopsy showed dense chronic inflammatory cell infiltrate within the portal tract. Periportal cholestasis noted with rare neutrophils within bile ductules. The conclusion was this was non-specific finding and could be consistent with acute or unresolved viral hepatitis, autoimmune, drug induced, or possibly extrahepatic biliary obstruction with superimposed cholangitis. The patient was seen in GI clinic one week after discharge and continued to complain of anorexia, pruritus, and fatigue. Bilirubin had dramatically improved to 3.4, Alk Phos 893, AST 125, ALT 152. CMV and EBV PCR along with EBV to capsid IgM were sent. Serologies returned positive for EBV PCR and capsid IgM. Pathology was re-reviewed showing atypical lymphocytes in sinusoids and in situ hybridization studies for EBV were positive. The patient made a full recovery with normalization of his LFT's one month later.

Epstein-Barr virus (EBV) is known to cause acute hepatitis but is usually seen with elevated transaminases. Cholestasis at presentation is an extremely rare presentation with only a few case reports in the literature. EBV is usually self-limited although cases requiring liver transplantation are reported. Costly diagnostic laboratory tests and invasive procedures may be performed to rule biliary obstruction in patients with EBV. EBV infection should be included in the differential diagnosis of cholestatic jaundice especially in those patients who present with only mild right upper quadrant discomfort.

Dysphagia Due to Anastomotic Stricture and Angulation in a Patient with Intestinal Interposition for Benign Disease, Treated with Removable Esophageal Stent

Scott H. Mackenzie, M.D., Kathyrn Peterson, M.D.*
Gastroenterology, University of Utah, Salt Lake City, UT.
This case expands the possible indications for removable esophageal stent complicated jejunal interposition treated with removable esophageal stent. The patient did well post procedure with improved dysphagia and maintenance of weight. The patient was observed for 24 hours in the hospital with resolution of symptoms and no sequelae on follow up.

The patient is a 77 year old female who presented with a six month history of dysphagia and weight loss. The patient did well until three and a half years after surgery when she developed progressive dysphagia and weight loss. At the time of our initial workup, imaging studies suggested a possible diverticulum at the esophago-enteric anastomosis with proximal dilatation of the native esophagus and angulation of the anastomosis. Diagnostic EGD was performed showing the peri-anastomotic stricture and diverticulum. Endoscopic therapy with a removable plastic Polyflex Esophageal Stent (Boston Scientific) was considered as a means to improve angulation, dilate the stricture and bypass the diverticulum. With the patient intubated for airway control, stent was placed with fluoroscopic assistance according to manufacturer guidelines. Stiff guide wire was necessary to allow passage of the deployment lines. Stent guide wire was necessary to allow passage of the deployment apparatus, overcoming the esophageal angulation and preventing passage into the diverticulum. Satisfactory deployment was assessed by fluoroscopy and endoscopy. The patient did well post procedure with improved dysphagia and maintenance of weight. Plan is for eventual removal of the stent and further observation. To our knowledge, this is the first reported case of complicated jejunal interposition treated with removable esophageal stent. This case expands the possible indications for removable esophageal stent in benign disease.

Rectal Varices Masquerading as a Mass

Sajid Jalil, M.D., Roger Saloway, M.D., Robert Wong, M.D., Manoop S. Bhutani, M.D.* Gastroenterology and Hepatology, University of Texas Medical Branch, Galveston, TX.

Rectal varices are a manifestation of portal hypertension and are seen in approximately 60% of patients of liver cirrhosis with esophageal varices according to one study. Diagnostic yield of rectal varices by endoscopy is 44% as opposed to 75% by rectal endoscopic ultrasound in another study. We present a case of rectal varices which presented as an incidental mass on CT of abdomen, endoscopy suggested a submucosal mass, and the diagnosis was clarified using rectal EUS. A 58-years-old male with long standing history of alcohol abuse presented with abdominal distention and shortness of breath. Further evaluation revealed large right hydrothorax and tense ascites. Patient denied any change of bowel habits or bleeding per rectum. CT scan of the abdomen revealed liver cirrhosis and an incidental mass in the rectum. On colonoscopy, two small sessile right colon polyps and a submucosal mass in the rectum encircling about 270 degrees of the circumference were seen. Rectal endoscopic ultrasound was performed which showed multiple anechoic, tubular and serpiginous structures in the submucosa and peri-rectum. Color doppler study showed blood flow, findings confirming a diagnosis of rectal varices. Rectal varices can masquerade as a mass however the diagnosis can be clarified by performing a rectal EUS which may avert a potentially serious bleeding complication from biopsy. [figure1] [figure2]
Drugs, Bugs or Cancer? A Case of Cholestatic Hepatitis
Sajid Jalil, M.D., Shu-Yuan Xiao, M.D., Steven A. Weinman, M.D.*
Gastroenterology and Hepatology, University of Texas Medical Branch, Galveston, TX.

Clarithromycin is a macrolide antibiotic commonly indicated for use in upper and lower respiratory infections and has a well established safety and efficacy profile. Rare case reports of fatal progressive cholestatic and fulminant hepatitis from clarithromycin have been described. We describe a case of acute cholestatic hepatitis from clarithromycin with complete resolution of symptoms on withdrawal. A 48-year-old female with a history of recurrent breast cancer developed Mycobacterium Abscessus pneumonia which was treated with combination of antibiotics including clarithromycin. At the time antibiotics were begun all liver enzymes were normal. Few days after starting treatment she had an isolated increase in alkaline phosphatase to 200 U/dl. Nonetheless, she continued on these drugs for 21 days until it was noted that she had developed jaundice. Liver enzymes revealed a syndrome of cholestatic hepatitis with total bilirubin of 6.9 mg/dl, alkaline phosphatase of 502 U/L, ALT 128 U/L, AST 147 U/L and GGT of 208 U/L. Hepatitis C virus antibody was positive but HCV RNA was undetectable. There was no evidence of extra-hepatic cholestasis on CT of the abdomen. A percutaneous liver biopsy showed acute lobular hepatitis with eosinophilia and cholestasis. A presumptive diagnosis of clarithromycin induced cholestasis was made. Withdrawal of the inciting drug led to a reduction in alkaline phosphatase and bilirubin within 5 days and complete resolution clinically and biochemically in 12 weeks. Clarithromycin is a safe and efficacious macrolide antibiotic. This report emphasizes the possibility of severe idiopathic cholestatic reactions to clarithromycin that are potentially reversible. Therefore awareness and prompt drug discontinuation is critical.

Intramucosal Esophageal Perforation with Nasogastric Tube
Mark J. Coronel, M.D., Kostas Sideridis, D.O., Simmy Bank, M.D.*
Gastroenterology, Long Island Jewish Medical Center, New Hyde Park, NY.

This Clinical Vignette highlights the need for proper attention to the procedural details of Nasogastric tube placement. An 84 year-old woman with a history significant for diverticular bleeding and AAA repair presented to the hospital with 3 episodes of hematochezia and lightheadness. On presentation, vital signs and examination were unremarkable. Initial laboratory data was remarkable for: Hemoglobin 10.7 g/dL. After management with fluids,she had several episodes of rectal bleeding with hypotension and worsening anemia and received 7 units of packed RBCs. Subsequently,she underwent an angiogram which was negative. Given her previous AAA repair and a nondefinitive angiogram,she underwent an
enteroscopy to exclude an aorto-enteric fistula. Colonoscopy was then performed which showed pandiverticulosis with fresh blood and bile in the terminal ileum. She continued to have hematochezia and received another 5 units (total 12 units). Because the bleeding was most likely diverticular in origin, an emergency subtotal colectomy with end ileostomy was performed. After surgery, the patient was noticed to have bright red blood draining from the NG tube placed after surgery. Upper endoscopy was performed to identify the source of the bleed. Under endoscopic visualization, a 14 Fr NG tube was observed entering a false tract in the esophageal mucosa at the level of the GE junction and exiting into the stomach. After removing the NG tube, a gastrografin study showed no extravasation of contrast into the mediastinum. A CT scan of the chest showed no evidence of any pneumomediastinum or extravasation of contrast. The patient recovered uneventfully with supportive care.

There have been no reported cases of the development of an intramucosal sinus tract in the esophagus secondary to gastrointestinal intubation. [figure1] [figure2]

A Report of a False-Positive CT Colonography
Quentin P. Ray, M.D.,∗ Brooks Cash, M.D. Gastroenterology, National Naval Medical Center, Bethesda, MD.

A patient was referred for a screening CT Colonography. The patient underwent a colon preparation with Fleet’s phosphosoda, bisacodyl, barium and gastrografin the night prior to the exam. The CT Colonography was positive for multiple colon polyps from the rectum to the descending colon. The largest of these was a 1 cm polyp seen in the rectum. There were multiple polyps between 5 and 10 mm in size, and numerous polyps less than 5 mm in size. These polyps were seen on both the prone and supine views of the colon, as well as on both the two-dimensional and three-dimensional images. These polyps had the density of soft tissue.

The patient was then referred for a same-day optical colonoscopy. The patient underwent colonoscopy to the cecum. The cecum could not be completely examined as it could not be fully cleared of material. The remainder of the colon was well-visualized. There were no polyps identified. There was some material adherent to the colon wall which could be washed off of the surface. There were several seeds that were seen adherent to the colon wall. The patient was referred for a CT Colonography with biopsies. We suspect that the “polyps” identified on the CT Colonography were in fact material that remained in the colon from the preparation. The material was adherent to the colon wall and thus did not shift position with supine and prone examinations. The material had the density of soft tissue and thus was not barium or gastrografin from the preparation. It is possible that the seeds that were seen on the optical colonoscopy could have been misinterpreted as polyps. [figure1] [figure2]
Autoimmune Hepatitis (AIH) While on beta Interferon (IFN β) and Natalizumab Therapy for Multiple Sclerosis (MS)
Bashra G. Fazili, M.D., Benedict J. Maliakkal, M.D.* Gastroenterology Unit, University of Rochester Medical Center, Rochester, NY.

AIH is a disease of chronic hepatocellular inflammation of unclear etiology. Immunoreactivity to a cellular protein precipitated by a drug or virus exposure has been postulated. Reports of AIH flares have been noted in patients with coexisting HCV infection while on IFN α therapy. IFN β, used in the treatment of relapsing MS, has an immunomodulatory profile similar to IFN α. Alpha 4 integrin is important for activated T cell trafficking into sites of tissue inflammation. Natalizumab is an integrin receptor antagonist that has been used as an immunosuppressive agent for refractory Crohn’s disease and MS.

Our patient, a 52-year-old female, presented with a 10-day history of rising transaminases and 2 days of jaundice, RUQ abdominal pain and nausea. Previous LFT’s were normal. She had been taking IFN β for the past 5 years, monthly natalizumab for 3 months and a methotrexate taper. The methotrexate was stopped at the onset of the transaminitis. She denied any fever, OTC or herbal drug use or family history of liver disease. Exam was notable for stable vital signs, jaundice and RUQ abdominal tenderness. Labs on presentation revealed AST 1984 U/L, ALT 1548 U/L, alkaline phosphatase 256 U/L, TB 6.6 mg/dL, DB 6.1 mg/dL, amylase 68 IU/L, lipase 60 IU/L and a normal complete blood cell count. ANA was positive at 640 AB, IgG 1860 mg/dL and SMA and LKM antibody were negative. CT and ultrasound of the abdomen showed normal liver echotexture, gallbladder wall edema, but no stones. Hepatitis A, B and C serologies were negative. A liver biopsy showed chronic hepatitis with marked activity (HAI 16/18) and marked diffuse portal inflammation with prominent plasmacytic infiltrates. Viral stains for CMV, HSV and EBV were negative. AIH score was positive.

A diagnosis of acute AIH was made. Interferon β and natalizumab were stopped and she was started on 60mg IV methylprednisolone and 75mg oral azathioprine daily. Her steroids were tapered over the ensuing weeks. 6 weeks later she was asymptomatic. Her AST was 64 U/L, ALT 73 U/L, alkaline phosphatase 142 U/L and TB 0.8 mg/dL on 15mg oral prednisone and 75mg oral azathioprine.

This is the first case of AIH reported in a patient on IFN β in combination with natalizumab. It illustrates two points. First, IFN β can cause acute AIH. Secondly, the concurrent use of natalizumab, an immunosuppressive agent, did not prevent the onset of the disease. Discontinuation of IFN β and initiation of standard therapy resulted in a positive clinical response.
The “Tumbling Phenomenon” in Gallstone Ileus
James L. Izanec, M.D., Susan J. Gordon, M.D.* Department of Gastroenterology, Graduate Hospital, Philadelphia, PA.

A 60 yo female without significant PMH presented with four weeks of no bowel movements and two weeks of diffuse abdominal pain, nausea and vomiting. She denied hematemesis, fevers, or chills. Physical exam was notable for dehydration, a soft but distended abdomen, hypoactive bowel sounds and mild diffuse tenderness without rebound or guarding. She had very hard stool palpable on rectal exam. Obstruction series revealed stool throughout the colon and dilated loops of small bowel consistent with partial small bowel obstruction (PSBO) versus ileus. Admission labs showed multiple electrolyte abnormalities consistent with severe dehydration. She received IV fluids and a tapwater enema for presumed fecal impaction and ileus and had two large bowel movements, after which she felt much better. Repeat obstruction series the next morning was normal. Within a few days, her electrolyte abnormalities resolved and she was tolerating a full liquid diet. After being advanced to a full diet, she became nauseous and hypokalemic. Obstruction series showed PSBO versus ileus. Her potassium was repleted and she felt better by the next morning, tolerating full PO’s, with normalization of her x-ray. Two days later she again developed severe nausea and vomiting. Abdominal film showed total small bowel obstruction and follow-up CT showed high-grade obstruction in the mid-jejunum, pneumobilia and a calcified mass at the point of obstruction (Figure 1), confirming the diagnosis of gallstone ileus (GSI). On laparotomy, she had a cholecystoduodenal fistula. Enterolithotomy was performed and the fistula was allowed to heal on its own. The gallstone measured 6.0 cm x 2.5 cm x 2.7 cm.

This case of GSI showed some unusual aspects of the disease. The majority of stones impact in the ileum, with only 15% becoming lodged in the jejunum. Only half of patients with GSI have a history of gallstone disease. GSI is often difficult to diagnose, as it was in this case, because the gallstone “tumbles” down the small intestine, producing intermittent symptoms. As seen in this case, physical findings and radiographs can normalize as the stone moves. Only 50% of cases are diagnosed correctly prior to laparotomy. [figure1]

Combined Therapy of Prednisone and Cyclosporine as Treatment Option for Refractory Coeliac Disease and Clonal T Cell Receptor (TCR) Gene Rearrangement

Juergen M. Gschossmann, M.D.,* Michael P. Bernimoulin, M.D., Rosemarie Weimann, M.D., Zeno Stanga, M.D., Sabine Klineke, M.D., Max Solenthaler, M.D., Ulrich Scheurer, M.D. Department of Gastroenterology, Inselspital / University of Berne, Bern, Switzerland; Department of Hematology, Inselspital / University of Berne, Bern, Switzerland; Department of Pathology, Inselspital / University of Berne, Bern, Switzerland and Department of General Internal Medicine, Inselspital / University of Berne, Bern, Switzerland.

Effective therapy of refractory coeliac disease is still under debate. The necessity for such treatment is underlined by the potential risk of the development of an enteropathy-associated T-cell lymphoma. We report of a male patient with coeliac disease first diagnosed in 1991. Under subsequent gluten-free diet, clinical symptoms of the disease necessitated only intermittent treatment with prednisone. A recent deterioration was treated with azathioprine which had to be stopped because of side effects. When we first saw the patient in August 2004, he had experienced a weight loss of 16 kg within 14 months and suffered from diarrhea, hypoalbuminemia and impaired nutritional state. The diagnostic work-up (blood/stool/x-ray/CT) did not result in any other diagnoses explaining the clinical symptoms. GI endoscopy showed intraepithelial lymphocytosis, villous atrophy with crypt hyperplasia and ulcerative lesions in the small bowel. All biopsies (duodenum/jejunum/ileum/bone marrow/liver/lymph node) but not blood were characterized by monoclonal T-cell receptor-gamma gene rearrangement. Total parenteral nutrition resulted in a weight gain of 14 kg but administration of prednisone at different doses (20–60mg iv/die) was not associated with improved enteral resorption. Therefore, cyclosporine (initially 5mg/kg iv/die) was added to prednisone (60mg iv/die). Consequently, a stepwise reduction of parenteral nutrition was feasible. Within 4 months, the patient gained another 8 kg. A shift from parenteral to oral drug administration was successful under cyclosporine plasma levels between 65 and 96ng/ml (limitation of daily cyclosporine dosage to 2mg/kg because of developing renal insufficiency). The histological analysis of duodenal/jejunal biopsies did not show any change in the modified Marsh classification (IIb).

Conclusion: The combined administration of prednisone plus cyclosporine represents a clinically effective treatment option in patients with refractory celiac disease who are unresponsive to steroids alone and do not tolerate azathioprine.

Vitamin A Toxicity from over the Counter Health Supplements: Every Medicine in Excess Is a Poison
Ankur Sheth, M.D., M.P.H., Vikas Khurana, M.D., F.A.C.G.* Gastroenterology, Overton Brooks VA Medical Center and LSU Health Sciences Center, Shreveport, LA.

Introduction: The growing popularity and availability of over the counter (OTC) health products is of concern. In United States, about 25% of adults ingest vitamin A containing supplements and 5% take supplements of vitamin A alone. We report a case of cirrhosis associated with habitual daily ingestion of OTC dietary supplement of vitamin A.

Case: A 59-year-old white man was referred from primary care physician for massive ascites of six-months duration. He was abstinent from alcohol since 15 years and had been taking variety of unsupervised OTC multivitamin tablets containing an aggregate of 160,000 IU/d vitamin A for two years (Recommended Daily Amount is 5000 IU/d for adults). Laboratory workup was significant for total bilirubin of 0.5 mg/dL, ALP of 154 IU/L, ALT of 40 IU/L, AST of 45 IU/L, albumin of 2.7 g/dL, INR of 1.1, serum aspartic amino transferase gradient of 1.5, vitamin A level of 21 micrograms/L (normal 0.3–0.7 micrograms/L), serum sodium 135 mEq/L, serum potassium 4.6 mEq/L, serum creatinine 1.5 mg/dL, serum calcium 9.9 mg/dL, serum phosphorus 4.7 mg/dL, serum ferritin 59 ng/mL, alpha 1 antitrypsin and negative hepatitis and autoimmune serology. Echocardiogram showed ejection fraction of 55% with normal right ventricular systolic pressure. Ultrasonogram revealed a mildly shrunk liver. Grade I esophageal varices were present on esophagogastroduodenoscopy. Liver biopsy showed chronic hepatitis grade II stage II with hypertrophied stellate cells and perisinusoidal fibrosis consistent with vitamin A toxicity.
Vitamin supplements were discontinued. At two year follow-up patient had minimal ascites with improved liver functions.

Discussion: Symptoms may occur with too much or too little of vitamin A. Vitamin A hepatotoxicity is rare; ranging from elevated liver enzymes to cirrhosis and may be observed in the absence of extra hepatic signs of vitamin A intoxication or increase in serum vitamin A concentration like in our case. Hyperplasia and hypertrophy of perisinusoidal stellate cells and perisinusoidal fibrosis on liver biopsy is consistent with hepatic storage of excess vitamin A. Concomitant alcohol use further potentiates the intrinsic hepatotoxicity of vitamin A. This case highlights the collateral damage caused by OTC vitamin supplements and indicates the need for regulation of medically unsupervised use of such products. As a consequence of increasing use of OTC vitamin A supplements, physicians need to provide information regarding relative safety of such products and elicit history of vitamin A supplements use in evaluation of liver dysfunction.

Xanthogranulomatous Cholecystitis Presenting with Upper G-I Bleed: Case Report and Review of the Literature
George T. Hage-Nassar, M.D., Vlado Simko, M.D., F.A.C.G.*
Gastroenterology, SUNY Downstate Medical Center, Brooklyn, NY and G-I, VA New York Health Harbor Care System, Brooklyn, NY.

Xanthogranulomatous cholecystitis (XGC) is a focal or diffuse destructive inflammatory process of the gallbladder, caused by mucosal damage (likely initiated by gallstones) with subsequent Rupture of Rokitansky-Aschoff sinuses resulting in the accumulation of lipid laden macrophages, fibrous tissue, and acute and chronic inflammatory cells in the gallbladder wall. It is described in less than 1% of cholecystectomy specimen in the United States and up to 8.9% in India and Japan. Extension of the xanthogranulomatous inflammation beyond the G-B wall has been reported, resulting in obstruction of the biliary tree, fistulas into adjacent structures such as duodenum, stomach, colon, and skin, or in hepatic abscesses formation. While there’s no reported cases of XGC complicated by G-I bleed, we report the first such complication: A 66 y/o man with history of Diabetes, presents with palpitations, lightheadedness, and dark loose stools. No history of ETOH abuse, or NSAIDS intake. In the ER he was found to be orthostatic, with mild abdominal tenderness in the RUQ and epigastric region, but no rebound or guarding and the rest of the exam was normal. His orthostasis responded to one liter of Normal Saline. He had positive FOBT. An NG tube was placed and showed few cc of coffee ground material which cleared after lavage. His finger stick was normal and his labs revealed mild microcytic anemia. An EGD showed normal esophagus and stomach, and a 3 cm subepithelial bulge extending from the postbulbar area to the descending duodenum. Minimal oozing of blood was noted from the erythematous, thickened and friable overlying mucosa. Biopsies revealed: duodenal mucosa with acute and chronic inflammation. An abdominal US showed gallstones and thickened G-B wall. A CAT scan and MRI could not rule out G-B carcinoma. EUS revealed a mass arising from the G-B wall extending into the wall of the 2nd duodenum. The patient underwent subtotal cholecystectomy due to difficulty dissecting the thick G-B wall from the adherent duodenum. Pathology: Xanthogranulomatous Cholecystitis (XGC).

Conclusion: Xanthogranulomatous Cholecystitis with extension of the inflammation into the duodenal wall may need to be considered as a possible cause of upper G-I bleed in patients with gallstones.

Posthepatic Portal Hypertension after a Domino Liver Transplantation Due to Pseudo-Budd Chiari Syndrome
Tommy Y. Yen, M.D., Aja Khanna, M.D., Karim Valji, M.D., Marquis Hart, M.D., Tarek I. Hassanein, M.D.* Gastroenterology, UC San Diego, San Diego, CA; Surgery, UC San Diego, San Diego, CA and Radiology, UC San Diego, San Diego, CA.

Portal hypertensive ascites resolve early after liver transplantation (OLT). We report a case of progressive pleural effusion and ascites after a domino OLT. The patient was diagnosed with hepatic hydrothorax attributed to anastomotic stenosis of the donor hepatic vein and the recipient inferior vena cava. A 51 year old Asian male with cirrhosis and a 6cm hepatoma received a domino liver from a donor with Maple Syrup Urine Disease. Trans-arterial chemoembolization and radiofrequency ablation (RFA) was performed prior to OLT. A patient with Maple Syrup Urine Disease received a cadaveric liver transplant and his liver was transplanted into our patient in a domino fashion. Our patient had an uneventful recovery and was discharged with a small right pleural effusion. Progressive right pleural effusions developed two months after OLT. Thoracentesis and pleural biopsies revealed an exudative pleural effusion with repeatedly negative results for infection or malignancy. Abdominal ultrasound revealed a minimal amount of ascites. Therapeutic thoracentesis gave temporary relief but pleural effusions and ascites reaccumulated rapidly. Abdominal MRI and angiogram (MRA) showed a patent middle and left hepatic veins with a patent portal venous system. Hepatic venous pressure gradient was noted to be 8mm Hg between the donor hepatic vein and the recipient vena cava. Balloon venoplasty was performed which reduced the gradient to 2 mmHg. Ascites resolved 2 months after venoplasty with significant decrease in pleural effusion. A stable right pleural effusion remained that was smaller compared to pre-venoplasty; there was no significant ascites on repeat imaging. Serum amino acid levels remained normal during the first year after OLT despite the inherent metabolic defect in the transplanted organ.

Conclusions: 1. Liver grafts from patients with Maple Syrup Urine Disease can be successfully transplanted. 2. Pseudo Budd Chiari syndrome due to anastomotic stenosis of the hepatic vein and vena cava should be considered in recipients of living donor grafts if pleural effusions and ascites do not resolve. 3. Venoplasty can correct major anastomotic stenosis post liver transplantation.

Neuropathy as a Cause of Chronic RUQ Pain: MRI to the Rescue
Susan E. McCormick, M.D.* Gastroenterology, Virginia Mason Medical Center, Seattle, WA.

Chronic abdominal pain can be a frustrating problem for both patient and clinician. Presented here are two cases of chronic right upper quadrant (RUQ) pain with similar unexpected diagnoses.

Case 1: 33 y/o woman, was treated one day ago from another hospital, arrives with a suitcase and a teddy bear and wants cholecystectomy. She has had 5 years of constant, severe, dull RUQ pain just under the ribs with nausea and vomiting (N/V) on most days. She requires daily narcotics. Previous evaluation has been negative, including laboratory studies, multiple EGD’s, ultrasounds (U/S) and CT scans, HIDA scan with CCK ejection fraction, colonoscopy and SBFT. At our institution, thoracic spine MRI showed a syrinx (syringomyelia) extending from T6 to T10. Her pain improved with gabapentin.

Case 2: 23 y/o woman presents with 3 years of RUQ pain in a discrete area, at first intermittent and now constant, often accompanied by right upper back pain. She has no history of back injury. She has lost weight due to poor appetite and N/V when the pain is severe. She requires daily narcotics. Her evaluation by three centers has been negative, including laboratory studies, EGD and multiple U/S’s and CT scans. Examination of the abdomen and back is normal. At our institution, thoracic spine MRI showed a T7–8 right paramedian disc herniation indenting and displacing the spinal cord. Her pain improved with epidural steroid injection.

Discussion: Neuropathic pain related to the T6–10 dermatomes can cause RUQ pain and should be considered in difficult to diagnose cases of chronic pain. Small thoracic spine disc protrusions are common and usually asymptomatic. However, the abnormality seen in our patient is severe. Syringomyelia is rare. It is a cavitary expansion in the spinal cord which is associated with Chiari malformation in 10% (but not in our patient.) It can be acquired due to trauma, infection or tumor, and is probably caused by...
blockage of cerebral spinal fluid outflow. Typical symptoms of syringomyelia are sensory loss, arm weakness and areflexia. Neuropathic pain is usually linear in distribution, but can be focal. Often there are few other symptoms, though both of these women had N/V and even weight loss, likely related to the severity of the pain or perhaps to narcotic treatment. Neither had overt neurological symptoms, though on evaluation by neurology, the patient with the syrinx had decreased pinprick sensation in the corresponding dermatome.

Association of PAN with Hepatitis C – An Unusual Presentation

Sufiyan H. Chaudhry, M.D., ∗ Bradford Waters, M.D., Brad Canada, M.D. Internal Medicine, University of Tennessee, Memphis, TN; Gastroenterology, University of Tennessee, Memphis, TN and Nephrology, University of Tennessee, Memphis, TN.

A 53 year old male with chronic untreated hepatitis C virus (HCV) infection was submitted to cholecystectomy for presumed cholecystitis. Gallstones were not present, and histological examination demonstrated medium sized arteritis, consistent with polyarteritis nodosa (PAN). A biopsy done during surgery showed steatosis with out any evidence of cirrhosis. He presented 2 months later with accelerated hypertension, marked volume overload, and rapidly progressive glomerulonephritis. Serological studies were positive for rheumatoid factor, cryoglobulins, with low C4 and normal C3 concentrations. Kidney biopsy demonstrated cryoglobulinemic glomerulonephritis along with diabetic nephropathy. Because of the severity of the patient’s vasculitic manifestations and cryoglobulinemia, treatment included pulse methylprednisolone followed by oral prednisone and monthly intravenous cyclophosphamide for 6 months. During treatment, mental status, blood pressure control, and volume status markedly improved and serum creatinine stabilized. He subsequently underwent treatment for HCV with interferon with marked decrease in viral load. To this date, the patient has had no relapse of his vasculitis, his creatinine is stable, and viral load remains very low after completing 36 weeks of treatment with interferon.

Major Complications from PEG Tube Placement: Two Case Reports

Dhanasekaran Ramasamy, M.D., C.N.S.P., Mahfuzul Haque, M.D., F.R.A.C.P. ∗ Internal Medicine / Gastroenterology, Brody School of Medicine at East Carolina University, Greenville, NC.

Percutaneous endoscopic gastrostomy (PEG) represents the most common method for enteral access for long term nutritional support. Although it is safely placed in most patients, serious complications can occur during placement of these tubes.

Case Information: Patient A is a 21 y/o male who was involved in a motor vehicle accident and developed prolonged respiratory failure. Enteral access was obtained in the operating room during tracheostomy by placing a PEG tube. Post procedure the patient was noted to have severe abdominal pain. MRl of the abdomen showed the PEG tube traversing through the liver into the stomach. The tube was subsequently removed with complete resolution of the patient’s abdominal pain. Patient B is a 73 y/o male who sustained a cardiorespiratory arrest and underwent a PEG placement at an outside hospital. He was transferred to our hospital due to a fecal leak around his PEG site. Upon arrival, he was noted to have lower gastrointestinal bleed and underwent urgent colonoscopy that showed PEG tube traversing through-and-through the distal transverse colon. He subsequently underwent exploratory laparotomy to remove the PEG tube.

Discussion: Major complications from PEG tube placement include transepithelial placement, colocolutaneous fistula, buried bumper syndrome, necrotizing fasciitis, esophageal perforation and gastric perforation. Complications as illustrated above, although rare, can cause serious complications necessitating the removal of the PEG tube.
Duct of Luschka Leak with an Intact Gallbladder Following EUS

Uzma Siddiqui, M.D., * Adam Gorelick, M.D. Department of Medicine, Yale University, New Haven, CT.

Background: The bile ducts of Luschka are small ducts which directly enter the gallbladder bed and can continue to leak after removal of the gallbladder. While present in up to 25 percent of patients, clinically significant leakage from the ducts is rare, and most commonly occurs following laparoscopic cholecystectomy. Complications of endoscopic ultrasound (EUS) usually occur related to fine needle aspiration (FNA) and include bleeding, infection, perforation, and pancreatitis.

Case: Pt. is a 26 y.o. female complaining of intermittent epigastric pain for one year. Pain is worse after eating and is relieved with vomiting. She has a history of abdominal pain and intestinal malrotation. Approximately two years prior to this presentation she underwent Ladd band lysis for intestinal obstruction. She presented with normal liver function tests and pancreatic enzymes, but mild CBD dilation on abdominal ultrasound. She was referred to gastroenterology for EUS to evaluate the relationship of the annular pancreas to the duodenum and CBD. EUS revealed normal duodenal mucosa without evidence of duodenal or CBD obstruction, normal gallbladder, normal PD, and confirmed an annular pancreas. No FNA was performed. Six hours after the procedure the patient was hospitalized with severe epigastric pain and vomiting. Her labs were noticeable for a WBC 15 (95% neutrophils), AST 150, ALT 140, ALK PHOS 250, and TBLI 2.5. She underwent a HIDA scan which demonstrated a bile leak. ERCP revealed leakage of contrast from a duct of Luschka. A biliary stent was placed, patient’s symptoms resolved, and her labs normalized. She was discharged on oral antibiotics. A follow-up HIDA one month later did not show any evidence of bile leak. Repeat ERCP demonstrated resolution of leak and the biliary stent was removed.

Conclusion: A duct of Luschka leak occurs with a frequency of approximately 0.4% following laparoscopic cholecystectomy, but this is the first report occurring in a patient with an intact gallbladder. Furthermore, a duct of Luschka leak has never been cited as a potential complication of EUS or EGD. It can be hypothesized that with a history of intestinal malrotation and prior surgery, adhesions may have developed, resulting in traction on the gallbladder from endoscope passage with the subsequent development of Lushka leak. Although these conditions are rare, care should be taken when performing EUS and EGD in patients with annular pancreas or malrotation.

Recurrent Tumor of the Rectum in a Young Male

Omar S. Khokhar, M.D., Meenakshy K. Aiyer, M.D.,* Maureen A. Lillicth, M.D. Department of Medicine, University of Illinois College of Medicine-Peoria, Peoria, IL.

A 37-year-old male presented with rectal pain that began eight hours after a surveillance colonoscopy. Pain was associated with a foul-smelling drainage. Review of systems was unremarkable except for anorexia. Past medical history was significant for familial polyposis syndrome and adenocarcinoma of the colon (Stage C2) diagnosed nine years ago with subsequent radiation therapy, proctocolectomy and ileostomy. Physical examination revealed a tender rectal stump that was 1.5 cm in length. Vital signs were within normal limits. Pelvic CT revealed a 2 × 2 cm fluid collection in the rectal region surrounded by a 5.6 × 4.0 cm area of inflammation. A C-reactive protein was elevated at 1.73. Rectal fluid culture was negative. Biopsy revealed acute and chronic inflammatory cell infiltrates with no malignant cells. Endoscopy was normal with no polyps or malignancy. Past records revealed that the patient had similar complaints two years earlier; biopsy revealed a desmoid tumor of the rectal stump.

Desmoid tumors may appear in up to 29% of patients after surgery as a painless or minimally painful mass with a history of slow growth [1]. Retroperitoneal neoplasms are seen more often in familial polyposis coli after abdominal surgery than in other conditions. In addition, a history of surgical trauma at tumor site is noted in 25% of cases [2]. Primary treatment aims are tumor growth cessation regression which can be achieved by surgery and chemotherapy. Current surgery of choice is ileorectal anastomosis with restorative proctocolectomy, while chemotherapy may consist of doxorubicin, dacarbazine, and carboplatin [3]. Desmoid tumors need to be considered in the differential diagnosis of patient with history of local tumor after surgery. In this patient, the rectal fluid was drained and the desmoid tumor left unexcised, since there is a predisposition for recurrence. He was discharged on oral antibiotics with instructions for repeat CT scan in three months and endoscopy in one year.

REFERENCES


An 86 year old Hispanic man from El Salvador was hospitalized with 2 day history of abdominal pain. Pain was sharp, severe in intensity, constant, epigastric in location without any radiation and with no aggravating or relieving factors. Pain was also associated with nausea and multiple episodes of vomiting. Review of Systems was negative for hematemesis, melena, loss of weight or appetite. The patient denied any significant past medical or surgical history. He is a non smoker and denied alcohol or any recreational drug abuse. The patient was not on any medications or using herbal products. On examination, he was afebrile with stable vital signs. Epigastric tenderness was present without any guarding or rigidity. Laboratory Tests were significant for an elevated amylase (274 U/L), lipase (234 U/L) with increased transaminases- aspartate aminotransferase (AST) of 134 and alanine aminotransferase (ALT) of 142. Total bilirubin and alkaline phosphotase were normal. Computerized Tomography revealed a large contrast and air filled duodenal diverticulum with mass effect on the head of the pancreas with stranding within the atrophic head of the pancreas. Small Bowel Series also showed a large smooth, lobular outpouching with a small neck, consistent with a duodenal diverticulum in the third portion of the duodenum. No additional gross diverticula were observed. Patient was managed conservatively with a duodenal diverticulum in the third portion of the duodenum. No additional or chronic liver disease. A hepatic venogram was done which showed no significant stenosis can be successfully treated by percutaneous balloon angioplasty, with resolution of the Budd-Chiari syndrome.

Discussion: Our case demonstrates a rare case of acute pancreatitis due to mass effect of the large duodenal diverticulum on the head of the pancreas. Juxtapapillary duodenal diverticulum is found in 10-15% of patients undergoing ERCP. It is more often found in elderly with a slightly higher frequency in women. Patients are found to have biliary stones in association and had idiopathic pancreatitis twice as often. In an Italian study, Periampullary extraluminal duodenal diverticulum(PEDD) was found in 13% of patients undergoing ERCP for acute pancreatitis. The authors concluded that the presence of PEDD should be verified, mainly in elderly patients, before defining an acute pancreatitis episode as idiopathic.

Not the Usual Suspect: Budd-Chiari Syndrome in a Post-Operative Patient with Hepatic Vein Stenosis in the Setting of Chronic Polyethylenimine from Danazol Use

Cindy W. Tom, M.D., Meredythe A. McNally, M.D.* Internal Medicine, Mayo Clinic, Rochester, MN.

Case: A 65-year-old female was admitted with increased abdominal discomfort, abdominal distension, periumbilical edema, and fatigue one month after undergoing elective laparoscopic cholecystectomy for biliary colic at an outside institution. She had undergone paracentesis for her new ascites, but had recurrence of her ascites and presented for further evaluation. Her history is significant for hypertension, cutaneous vasculitis, low-grade B-cell lymphoma, and a prior cerebrovascular accident. She has a history of mildly elevated transaminases and polyethylenimine that was attributed to chronic danazol use for vasculitis. Her physical exam was remarkable for decreased bisobular breath sounds, a distended abdomen with shifting dullness and bulging flanks, and bilateral pitting edema. Bloodwork was negative for any chronic liver disease. A repeat paracentesis was done, with fluid analysis that was suggestive of portal hypertension. CT of the abdomen revealed irregular enhancement of the liver parenchyma and MRI of the abdomen showed benign-appearing masses of the liver consistent with benign cavernous hemangiomas and a simple liver cyst. An ultrasound-guided biopsy of the liver parenchyma showed venous outflow obstruction with the absence of any primary or chronic liver disease. A hepatic venogram was done which showed focal high grade stenosis of the junction of the right hepatic vein and IVC with a significant 10 mmHg gradient between the right hepatic vein and right atrium. This lesion was thought to be the culprit for her Budd-Chiari syndrome and was dilated percutaneously with subsequent resolution of the gradient. She was started on diuretics and her ascites subsequently resolved. After consultation with her hematologist, her danazol was discontinued.

Discussion: Budd-Chiari syndrome is a rare cause of ascites from hepatic venous outflow obstruction, which, untreated, can lead to chronic hepatic congestion and cirrhosis. Though typically described in cases of thrombotic occlusion of the hepatic veins, this physiology can also be seen with hepatic venous stenosis causing veno-occlusive disease. This case presents an unusual cause of post-operative ascites secondary to Budd-Chiari syndrome from hepatic vein stenosis in the setting of an underlying malignancy and polyethylenimine from her danazol vasculitis treatment. Isolated hepatic venous stenosis can be successfully treated by percutaneous balloon angioplasty, with resolution of the Budd-Chiari syndrome.

A Large Pedunculated Rectal Carcinoid Tumor Resected by Endoscopic Snare Polypectomy: A Case Report and Review of Literature

Theodore M. Perlman, M.D., Kaleem M. Rizvon, M.D., Steven S. Yang, M.D., Paul J. Mustacchia, M.D.* Gastroenterology, Nassau University Medical Center, East Meadow, NY.

A 53 y/o asymptomatic black female with a history of HTN underwent a routine screening colonoscopy which revealed a 18mm pedunculated rectal
polyp as well as a 10mm pedunculated transverse colon polyp. Both were removed by snare cautery. The rectal polyp was grossly atypical. It was pale, firm and nodular with irregular borders on a wide stalk. Pathology reported a rectal carcinoid tumor and a transverse colon tubular adenoma and. An endoscopic rectal ultrasound was performed three weeks later which revealed no invasion of the submucosa. Multiple jumbo biopsies were obtained from the polypectomy site all were negative for any residual carcinoid tumor tissue. Computed tomography of the chest, abdomen and pelvis were negative for metastasis.

Discussion: Carcinoid tumors are derived from the neuroendocrine system. They have the capability of secreting an array of biologically active agents. The incidence of carcinoid tumors has been estimated to be 8.4 per 100,000. 74% of carcinoid tumors are located in the gastrointestinal tract, the ileum, appendix and the rectum are the most common GI sites. The Bronchopulmonary system is responsible for the majority of the other sites. Grossly they are usually submucosal. They are usually yellow tan or pale gray secondary to a high lipid content, as well as firm and rubbery. Histologically they appear as nests, cords or rosettes of uniform round cells with rare mitotic figures. Immunohistochemically, they may be differentiated from other neuroendocrine tumors with chromogranins A,B,C, synaptophysin and enolase stains. They are best visualized endoscopically using EUS and by Somatostatin scintography, PET scans and CT scans. Tumors less than 1cm are very rare and metastasis is rare. Carcinoid tumors have the capability of secreting an array of biologically active agents. Pancreatic islet cell tumors are responsible for most of these syndromes (VIPomas, Glucagonomas, gastrinomas). Carcinoid tumors, however in our case of a pedunculated carcinoid tumor, more studies are needed to determine the prognosis and the most appropriate treatment.

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Superior Mesenteric Artery Syndrome: A Case Report
Kaleem M. Rizvon, M.D., Theodore M. Perlman, M.D., Paul J. Mustacchia, M.D., Ali S. Karakurum, M.D.*
Gastroenterology, Nassau University Medical Center, East Meadow, NY.

A 26 year old white male, prisoner, polysubstance abuser was brought to the Emergency Room with constant, crampy upper abdominal pain occasionally radiating to the back. Patient also experienced multiple episodes of vomiting for 5 days prior to hospitalization. He was unable to eat due to almost continuous vomiting. The patient also reported a loss of appetite with severe weight loss of 27 lb. over 2 months with a documented 20 lb. weight loss in just 6 days after incarceration. He tested negative recently for the human immunodeficiency virus. The patient had an eight year history of Cocaine, Heroin and Alprazolam abuse daily. On examination the patient was a tall thinly built male, weighing 120 lbs with a Body Mass Index of 15 and weight less than the 5th percentile. His vital signs were stable. Oral mucosa was dry and meningeal signs were negative. Abdomen was scaphoid with a right lower quadrant surgical scar of appendectomy. Bowel sounds were well heard with mild epigastric tenderness. Laboratory examination showed severe dehydration on initial presentation. Serum and Urine Toxicology screen were negative. Small bowel obstruction was suspected on a routine abdominal Xray. This was followed by a Computerized Tomography of the abdomen, which showed a significantly distended stomach and proximal duodenum with a cut off at the third part of the duodenum consistent with a Superior Mesenteric Artery (SMA) syndrome. The patient received parenteral nutrition and quickly regained his weight. After 29 days of hospitalization, patient gained back 22 lbs and was discharged to prison with no symptoms after a high caloric oral diet.

Discussion: SMA syndrome also known as Aorto-mesenteric clamp or Wilkie’s Syndrome varies in presentation from a casual finding on radiography to a symptomatic duodenal obstruction. It is characterized by abdominal pain, vomiting and postprandial discomfort that improves in left lateral decubitus, prone or knee chest position and aggravated in supine position. SMA forms an angle of 45 degrees with the abdominal aorta. SMA syndrome occurs due to the compression of the third portion of the duodenum between SMA and Abdominal Aorta. This angle is maintained due to the presence of fatty tissue around the duodenum and pancreas. Clinical symptoms appear when this angle is significantly decreased to between 15–20 degrees, which happens with sudden severe weight loss. Our patient is a typical case of this rare condition and is unique for a quick resolution in less than 5 weeks.

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Pseudotumor Cerebri as a Complication of Obesity in an Adolescent
Allan J. Rosenberg, M.D., F.A.C.G.*
Pediatrics, Tulane School of Medicine, New Orleans, LA.

Significant medical conditions are associated with childhood obesity. Presented is a 16 year old African American male with pseudotumor cerebri. S.B. was seen in the Tulane emergency room with complaints of severe general evidence headache and extremity pain. He was recently evaluated at another hospital for similar complaints in addition to hypertension and difficulty breathing. He was discharged with diagnoses of hypertension, increased intracranial pressure and possible increased intracranial pressure (ICP) treated with antihypertensive, eye drops and analgesic. MRI of the head was normal. LP was not done. He had previous surgery on both legs for Blounts Disease. Family history positive for hypertension and Type 2 Diabetes. His mother weight 350lbs. On admission he weight 182kg, height 164cm, an BP 110/60, BMI greater 95%, slumped in a chair holding his head and complaining of headache and blurred vision. CPAP titration study demonstrated hyperventilation and sleep apnea. Eye exam, iritis, left VI cranial nerve palsy and 2 optic disc edema. LP 58cm opening pressure, cell count and protein normal, culture negative. He underwent lumboperitoneal shunt. Postop headache resolved. Discharged home on CPAP, Vasotec, and Xalatan eye drops. Pseudotumor cerebri is reported in 2,800 obese adolescents and adults. It is characterized by increased ICP and a normal cerebrospinal fluid. Etiology includes changes in CSF absorption and production. Causes are numerous including: metabolic associated with obesity, drugs, infections, hematologic and obstruction of intracranial drainage due to venous thrombosis. Headache is the most frequent symptom. Diplopia secondary to abducens nerve paralysis occurs. Papilledema with an enlarged blind spot is the most common sign. Pseudotumor is mainly self-limited but optic atrophy and blindness can result. Treatment is directed at the underlying cause. Acetazolamide and corticosteroids can be effective. As in this patient lumboperitoneal shunt or subtemporal decompression may be necessary.

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A Tale of Two Sisters: Hereditary Hemochromatosis
Rajalakshmi Iyer, M.D., Mary Jo Atten, M.D., Bashar M. Attar, M.D., Franjo Vladic, M.D., Amila Orucevic, M.D.
Gastroenterology, John H. Stroger Hospital of Cook County, Chicago, IL.

Hereditary hemochromatosis (HH) continues to challenge even the most astute clinician. We describe two sisters of Indian origin who presented with genotype negative primary hemochromatosis. The younger sister (age 46 yrs) first came to attention during work-up of abnormal liver enzymes by her diabetologist. She had been diabetic for 7 years and had attained menopause at age 29 years. She had a mild normocytic anemia and her ferritin was 2398 with transferrin saturation 90%. The second sister (age 55 yrs) was also anemic on incidental blood work-up during treatment of a UTI and her ferritin was 4981 with a transferrin saturation 80%. There was no history of transfusions, hemolytic crisis, skin rash, parenteral iron therapy, familial history of liver disease or anemia. Autoimmune profiles and viral serologies were negative (see table for work-up).

The sisters were started on weekly phlebotomy with erythropoietin support. The response to phlebotomy was remarkable and well tolerated with a steady
normalization of the ferritin. They are now on maintenance phlebotomy q8 weeks.

Symptomatically both have felt invigorated with decrease in arthralgias previously attributed to DJD. Screening of the first degree relatives was negative. Phenotypic HH is the result of C282Y mutation of both alleles in 90% of the cases, whereas the compound heterozygote C282Y/H63D accounts for 3% to 5% of phenotypic hemochromatosis. What was unusual in our patients was the anemia. Anemia in association with primary hemochromatosis is rare but has been seen with Ferroportin1 deficiency. This disorder is due to pathogenic mutations in the SLC40A1 gene encoding a main iron export protein, ferroportin1/IREG1/MP1. It has distinctive clinical features such as early increase in serum ferritin in spite of low-normal transferrin saturation, progressive iron accumulation in organs, predominantly in reticuloendothelial macrophages leading to marginal anemia with low tolerance to phlebotomy. Ferroportin mutations have been reported in many countries regardless of ethnicity. Ferroportin deficiency may be the most common cause of hereditary iron overload beyond HFE hemochromatosis.

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**Gastric Lymphoma in HIV Positive Patient**
Kelleen M. Rizyon, M.D., Theodore M. Perlman, M.D., Fazal Farooqui, M.D., Paul J. Mustacchia, M.D.* Gastroenterology, Nassau University Medical Center, East Meadow, NY.

A 55 year old black male with Acquired Immunodeficiency Syndrome (AIDS) was hospitalized with abdominal pain, nausea and vomiting of one month duration. His most recent CD4 count was 163. Associated relevant symptoms included loss of appetite and 30 lb weight loss over 3 months prior to hospitalization. The patient is closely followed by the AIDS unit and was on appropriate antiretroviral medications. On examination, the patient was in no acute distress with stable vital signs. There was no tenderness of the abdomen and no masses were palpated. Computerized Tomography of the abdomen was obtained in the Emergency Department which showed thickening of the gastric wall. An upper endoscopy revealed a fungating mass in the body and antrum extending to the duodenal bulb with a strong possibility of a malignant lesion. However, pathology showed active chronic inflammation with necrosis and granulation tissue. Budding yeast was also seen. Due to our strong clinical suspicion, the endoscopy was repeated and multiple additional specimens were obtained. A pathological diagnosis of diffuse large B-cell Lymphoma was then confirmed. Further workup showed the tumor confined to the gastrointestinal tract. The patient was referred to oncology for chemotherapy.

**Discussion:** Non-Hodgkin’s Lymphoma of the Stomach is rare accounting for 2% to 8% of all gastric malignancies. Most common site for gastrointestinal lymphomas is the stomach, most often in the distal portion of the stomach. They can appear polyoid, fungating, ulcerative or infiltrative. The primary lesion is submucosal, originating from the lymphoid tissue in the lamina propria. The tumor usually tends to grow through the serosa and then spreads to local and regional lymph nodes. With the improvement of endoscopic and histologic techniques, endoscopic biopsies have become more accurate. Treatment of Gastric Lymphomas has been controversial. Surgical resection can be potentially curative but has an operative mortality of up to 30%. Patients with early stages of the disease (Stages I and II) may be treated with chemotherapy and radiotherapy rather than surgery. The combination of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) is the standard regimen. Surgical intervention is usually not indicated for stage III or stage IV disease unless complications or limited residual disease occurs following chemotherapy or radiation therapy.

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**Exchange Transfusion for Fulminant Hepatic Failure from Sickle Cell Intrahepatic Cholestasis**
Hin W. Lee, M.D., Bruce Runyon, M.D., Zeid Kayali, M.D. Gastroenterology, Loma Linda University, Loma Linda, CA.

Sickle cell disease causes vascular occlusions affecting different organs including the liver. The incidence of liver disease in patients with sickle cell anemia has not been well established. Sickle cell intrahepatic cholestasis is characterized by widespread sickling within the hepatic sinusoids leading to severe ischemia and acute liver failure. About 16 cases have been described in the literature, and five cases of liver transplantation have been performed but with significant postoperative complications including graft failure. Recent reports have described the use of exchange transfusion leading to recovery of liver function. This report describes a case of fulminant hepatic failure from sickle cell intrahepatic cholestasis successfully treated with exchange transfusion.

A 20 year old African American male with history of sickle cell disease was admitted for sickle cell crisis with chest and shoulder pain. Upon admission, he had normal liver enzymes, except total bilirubin of 3.7 mg/dL. On day 4, he developed signs of fulminant hepatic failure with coagulopathy and stage II hepatic encephalopathy. His total bilirubin was 21.5 mg/dL, AST 1231 IU/L, ALT 1102 IU/L, INR 3.78. His mental status deteriorated and he was intubated for airway protection. His CT head showed signs of early cerebral edema and an intracranial pressure (ICP) monitor was placed on day 5. Urgent liver transplantation evaluation was started. Echocardiogram revealed severe pulmonary hypertension with pulmonary arterial pressure of 80 mmHg and patient was deemed not to be a candidate for liver transplant. On day 7, an exchange transfusion of 10 units packed RBC was performed. His liver tests started to decrease the day after exchange transfusion. On day 9, his mental status improved significantly and ICP monitor was removed. One week after exchange transfusion, his total bilirubin was 12.0 mg/dL, AST 81 IU/L, ALT 120 IU/L, and INR 1.31. His liver function continued to improve and he was discharged uneventfully three weeks later. Fulminant hepatic failure due to sickle cell intrahepatic cholestasis is a rare presentation of sickle cell disease. Liver transplantation has been utilized but with significant postoperative complications including graft failure. Pulmonary hypertension from chronic hypoxemia and pulmonary capillary occlusion is a major concern. Exchange transfusion is an effective treatment which can lead to reversal of the sickling process and recovery of liver function.

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**Malignant Melanoma Metastatic to the Duodenum, Case Report and Review of Literature**
Mateen M. Hotiana, M.D., Steven Lichtestein, M.D., F.A.C.G., Fahd Rahman, M.D., Muhammad N. Athar, M.D., Sarba Kundu, M.D. Department of Internal Medicine, Mercy Catholic Medical Center, Darby, PA.
Introduction: Malignant melanoma is the most dangerous skin cancer with a high metastatic potential. It is the sixth commonest cancer in the US and its incidence is rising faster than any other cancer. Location and depth of the primary tumor, and the presence and extent of metastatic disease determines the prognosis. Virtually any organ of the body can be involved but the commonest sites include lungs, lymph nodes, liver, gastrointestinal tract and brain. Death occurs from disseminated disease, usual cause being brain metastases and bowel obstruction. We present a case of a young patient with malignant melanoma metastasizing to the duodenum.

Case Report: A 24 year old male with a known history of malignant melanoma was referred to our gastroenterology clinic for evaluation of severe anemia, fatigue and abdominal pain. An EGD was performed showing a 4 cm friable hard mass in the second part of duodenum (fig 1). Pathology report of the biopsy specimen showed it to be malignant melanoma.

Discussion: Malignant melanoma has a tendency to metastasize to the gastrointestinal tract and the commonest site of involvement is small intestine. Rarely primary malignant melanoma of the duodenum has been reported in the literature. Malignant melanoma metastasizing to the GI tract is diagnosed ante mortem in only 1.5-4.4% patients. Majority, up to 60%, are diagnosed on postmortem examination. According to Bender et al. abdominal pain was the leading symptom at the time of presentation in 60% of these patients followed by obstruction in 47%, nausea and vomiting in 41%, GI bleeding in 30% and a palpable mass in 10% of the patients. Enteroclysis and CT enteroclysis are preferred radiological techniques to diagnose these tumors. The classic finding on imaging is a target lesion or Bull’s eye lesion but is found infrequently.

Conclusion: Patients known to have melanoma presenting with abdominal pain or anemia should be investigated by endoscopy or radiologically. A high index of suspicion is advised in these patients as early detection and complete resection can significantly improve survival. [figure1]

One dose finding study in patients with advanced malignancy found proctitis in 1/3 of patients treated with PPS. We have observed two cases of suspected PPS induced colitis during treatment of IC.

Case 1: A 59yo female developed bloody diarrhea and crampy abdominal pain one month after starting PPS. Flexible sigmoidoscopy revealed aphthous ulcers, friable colonic mucosa with punctuate hemorrhage and exudate. Treatment with sulfasalazine and topical corticosteroids failed to result in clinical improvement. Coloscopy revealed colitis extending from the rectum to the transverse colon. Mucosal biopsies revealed active colitis with patchy involvement with ulcerations and mild architectural distortion. PPS was discontinued with full resolution of symptoms within 2 weeks. Repeat endoscopy revealed endoscopic and histologic resolution of colitis.

Case 2: A 59yo female with a history of irritable bowel syndrome developed increased diarrhea and LLQ abdominal pain 2 weeks after starting PPS. Colonoscopy revealed diffuse erythema with shallow ulcerations and changes consistent with colitis extending from the proximal rectum to splenic flexure. Biopsies confirmed moderately active colitis with patchy involvement and focal fibrosis and necrosis. The patient was treated with mesalamine based treatment and oral prednisone without benefit. Abdominal pain and diarrhea frequency improved upon discontinuation of PPS. Repeat colonoscopy demonstrated endoscopic and histologic resolution of colitis.

PPS has been shown in animal and human studies to be associated with a drug induced proctitis. The clinical setting, time course, histologic findings, endoscopic pattern, failure to respond to anti-inflammatory therapy, and resolution upon withdrawal of PPS suggest a causal relationship. We have described two novel cases of PPS induced colitis during the treatment of IC. Further study is required to elucidate the biologic basis, epidemiology, and the clinical features of PPS induced colitis.

Intestinal Intussusception: A Rare Presentation of Celiac Disease
Adam L. Palance, M.D., Eric H. Shen, M.D., Kiron M. Das, M.D.*
Division of Gastroenterology, Robert Wood Johnson Medical School, New Brunswick, NJ.

To identify and propose unusual presentations of a common disease entity. A 36 year old Irish male was referred to the Crohn’s and Colitis Center of NJ for evaluation of a jejunal intussusception found on CT scan. We were consulted to rule out Crohn’s disease as the cause of the intussusception. He had a history of seminoma, and was status post orchietomy. His oncologist felt that the lesion was unrelated to the seminoma. The patient denied fevers, chills or night sweats. There was no history of diarrhea, blood per rectum or anemia. There was no family history of inflammatory bowel disease. The patient did note recent visual field defects, arthralgias, and a 15 pound weight loss. There was no travel history. Physical examination revealed temporal wasting. Cardiac, pulmonary, abdominal and skin examination was normal. A small bowel follow through was ordered and was normal. With this constellation of symptoms and negative imaging studies, a diagnosis of Crohn’s disease was felt to be unlikely. The patient continued to have weight loss. A follow up CT scan revealed mesenteric adenopathy. An MRI of the brain revealed bilateral optic nerve hypoplasia. Endoscopy was performed to rule out occult celiac disease. At the time of endoscopy an area of questionable jejunal prominence was noted and biopsied. A celiac disease antibody profile was ordered concurrently. Biopsy results revealed subtotal villous atrophy. Tissue transglutaminase antibodies and antigliadin antibodies were all noted to be highly positive. The patient started a gluten free diet. Six weeks after instituting the gluten free diet the patient has gained weight, his arthralgias have improved, and he feels better. His optic nerve hypoplasia has not progressed and is believed to be unrelated to celiac disease.

Celiac disease is a common disease entity. The most common presentation is occult anemia. Weight loss and diarrhea are other clues to this disease process. Jejunal intussusception seen at CT may be an early clue that a patient has celiac disease. Enterocytic intussusceptions are usually nonneoplastic entities. Celiac disease is an example of a functional disturbance that may
cause intussusception without gross mural abnormality. Gluten sensitivity causes muscular flaccidity which may lead to a transient intussusception.

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Intramusosal Gastric Cancer in a Geriatric Patient: Therapeutic Options
Noel R. Fajardo, M.D., Schuyler O. Sanderson, M.D., David E. Larson, M.D.* Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN and Department of Pathology, Mayo Clinic, Rochester, MN.

A 72/F with 6-weeks history of sharp, midepigastric post-prandial abdominal pain was referred to our care. She has a history of gastritis treated with medication. She has no family history of cancer, and denied alcohol nor tobacco use. Examination of the abdomen revealed mild direct tenderness over the upper quadrants, with no evidence of hepatosplenomegaly, and normal rectal examination.

CT of the abdomen was normal and abdominal ultrasound revealed patent celiac and mesenteric arteries. EGD revealed multiple nodules in a 3-cm circumferential pattern in the antrum, biopsies revealed gastric mucosa with high-grade dysplasia. An endoscopic ultrasound visualized the previously observed 3-cm. mass; confirming no evidence of intramural spread and no lymphadenopathy noted.

Our options were to have the patient undergo gastrectomy (either partial or total) or alternatively proceed in a less invasive route, i.e. endoscopic mucosal resection (EMR). The patient decided to undergo EMR. The EMR completely resected the lesion. However, biopsies revealed extensive high-grade dysplasia or intramusosal adenocarcinoma (early gastric cancer). Again, we were confronted with the dilemma to either have the patient undergo gastrectomy or proceed with aggressive endoscopic surveillance, and repeat EMR if necessary.

The patient eventually decided to undergo repeat endoscopic surveillance in six weeks, and perform photodynamic therapy if extensive high-grade dysplasia was again noted.

On repeat surveillance endoscopy, there was no abnormality noted. Multiple random biopsies obtained revealed focal intestinal metaplasia. Symptomatically, her abdominal pain has resolved. The plan at is to continue aggressive follow-up, and have the patient undergo repeat endoscopic surveillance in three months.

Therapeutic options for gastric high grade dysplasia are controversial, although historically, the main consensus favor surgical resection. Over the recent years, the role of endoscopic mucosal resection (EMR) in the management of these lesions has been accepted and recognized. Therefore, factoring the age and medical co-morbidities and careful consideration of maintaining good quality of life, we recommended EMR as a management option.

Overall, the long term survival advantage of EMR over gastric resection in the management of gastric high-grade dysplasia (intramusosal adenocarcinoma) in a geriatric patient remains to be explored.

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Mental Status Changes as the Presenting Feature of Clostridium difficile-Induced Toxic Megacolon
Grant Chu, B.S., Andrea Tom, M.D., Edward Feller, M.D., F.A.C.G.* Medicine, Brown Medical School, Providence, RI and Medicine, Mayo Clinic, Rochester, MN.

Toxic megacolon (TMC) complicating Clostridium difficile toxin-induced pseudomembranous colitis is rare. Similarly, C. difficile presentation without diarrhea is unusual. We report two elderly patients with fulminant colitis who presented with mental status changes to alert clinicians to the diverse, atypical symptoms and signs, and potential for delayed diagnosis in this potentially life-threatening infection.

Case Reports: Case 1: An 88-year old man presented to the emergency department with a one day history of confusion. He also complained of mild obstipation. Four days previously, he had completed cefoxitin treatment for bronchitis. On exam, he was confused and lethargic, temperature = 38.9°C, abdominal distention without tenderness was noted. WBC = 16,300 with 20% bands; lactic acidosis was present. KUB revealed a distended colon with a 12-cm cecum. He was treated with broad-spectrum antibiotics, including oral metronidazole. A pre-op diagnosis of ischemic colitis was made. A subtotal colectomy was performed for TMC. Pathology revealed fulminating, full-thickness colitis with pseudomembranes. He died shortly after surgery.

Case 2: An 87-year old woman was admitted with confusion and lethargy without abdominal pain. She had recent mild constipation. She had recent mild constipation. On exam, temperature = 38.3°C, abdomen was distended but non-tender, and a small amount of fresh blood was present on rectal exam; WBC = 13,400 with 16% bands. Limited endoscopy of the left colon demonstrated severe colitis with rectosigmoid sparing considered to be consistent with ischemia. Three days later, her white count rose to 41,200; KUB revealed an 11–12 cm dilated colon. She was treated with broad-spectrum antibiotics, including IV metronidazole, but continued to deteriorate with increased abdominal distention and decreased responsiveness. At surgery, pseudomembranous colitis with TMC was diagnosed. The patient subsequently expired.

Discussion: Our experience indicates that TMC can present as non-specific mental status changes in the absence of diarrhea. Atypical presentations of C. difficile, including obstipation or constipation, isolated fever, rectal bleeding, recto-sigmoid sparing or mental status changes may result in delay in diagnosis. Clinicians must consider fulminant C. difficile colitis in selected patients recently treated with antibiotics who present with systemic symptoms or signs, such as unexplained mental status changes or isolated fever.

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A Rare Case of Hepatic Splenosis: Initially Interpreted as Metastasis, in a Patient with a Gastrointestinal Stromal Tumor
Kapil Gupta, M.D., Rohit Malik, M.D., Gerald Fruchter, M.D.* Gastroenterology, VA New York Harbor Health Care System, Brooklyn, NY and SUNY Downstate Medical Center, Brooklyn, NY.

Splenosis refers to auto-transplantation of splenic tissue in heterotropic location usually seen after splenic injury or splenectomy. Very few cases of hepatic splenosis have been reported. Here we report an unusual case initially evaluated for submucosal gastric tumor subsequently diagnosed as gastrointestinal stromal tumor, with hepatic splenosis. A 65-year-old male was evaluated for reflux symptoms. Past medical history was significant for hypertension, diabetes mellitus, non-ischemic cardiomyopathy and peripheral vascular disease. There was no history of any major trauma or abdominal surgery. Physical examination was normal. Laboratory results showed mild anemia. Liver function tests were normal. On upper gastrointestinal series a 6.5 × 4 cms, submucosal mass was seen in fundus and body of stomach. Subsequent EGD revealed an umbilicated, submucosal mass involving fundus and proximal body, which appeared to be a leiomyoma vs. leiomyosarcoma. CT scan of abdomen also showed a 7.2 × 6.2 cm submucosal mass. Liver appeared entirely normal. EUS was performed, which showed a gastric leiomyoma, with heterogenous signals consistent with sarcomatous transformation. On laparotomy, a large palpable gastric mass was seen which was close to gastroesophageal junction. Multiple millet-like lesions were also seen involving the left lobe of liver which were assumed to be metastases. Biopsies obtained from these liver lesions revealed benign splenic tissue. Gastric resection was subsequently performed with removal of tumor; pathology was confirmed as gastro intestinal stromal tumor. Hepatic splenosis is a very rare entity. In cases, reported earlier, various diagnoses considered on presentation included hepatocellular carcinoma, hepatic adenoma and metastases. Previously reported cases had a past history of either abdominal trauma, splenectomy or underlying hepatic cirrhosis. To our knowledge this is one of the first cases with hepatic splenosis with no underlying liver disease nor history of splenic trauma in a patient with concomitant gastrointestinal stromal tumor.
Sarcoidosis: A Cause of Obstructive Jaundice

Roberto M. Gamarra, M.D., Roja Ramisetti, M.D., John Frownfelter, M.D., Edward Yousef, M.D., Luis C. Maas, M.D.* Department of Gastroenterology, Providence Hospital, Southfield, MI and Department of Internal Medicine, Providence Hospital, Southfield, MI.

Lung involvement occurs in over 90 percent of patients with sarcoidosis. Extrathoracic manifestations also occur. We describe an unusual patient with extrapulmonary sarcoidosis who presented with clinical, laboratory and imaging findings consistent with obstructive jaundice.

A 42-year-old female presented with painless jaundice and weight loss. There was no history of liver disease, medications use, or travel. The examination of the heart, lungs and abdomen was normal. There was no lymphenadenopathy. The chest radiograph was unremarkable. The total bilirubin was 12 mg/dL, the alkaline phosphatase was 525 IU/L. Liver transaminases, amylase, lipase, calcium, BUN, and creatinine were normal. Intra and extrahepatic biliary dilation was seen on imaging studies. Tumor markers were within normal limits. The ERCP showed an area of stenosis in the mid common bile duct. A stent was placed with clinical and laboratory improvement of the jaundice. Biopsies and brushings taken were negative for malignancy. A 2 × 2 cm lymph node was noted in the porta hepatis on endoscopic ultrasound. Fine needle aspiration was unrevealing. Lymph node biopsies obtained by mediastinoscopy revealed non-necrotizing granulomatous lymphadenitis consistent with sarcoidosis. Special studies and cultures for infections were negative. The patient was started on prednisone, her condition improved, and she remained clinically asymptomatic after six months of follow-up.

Patients with sarcoidosis may present a challenge to various specialists. It frequently presents with bilateral hilar lymphadenopathy, pulmonary infiltration, and ocular and skin lesions, but may affect other organ systems. Sometimes sarcoid granulomas involves only lymph nodes. Enlargement of periportal lymph nodes can produce extrinsic compression of the bile ducts leading to an obstructive jaundice as seen in our patient. Besides the present report, there is only one published case of sarcoidosis that presented with obstructive jaundice in the absence of pulmonary involvement.

Extra-pulmonary sarcoidosis is a challenging diagnosis for physicians when the patient presents without distinct pulmonary involvement. Although rare, sarcoidosis should be entertained in the differential diagnosis of obstructive jaundice associated with portal lymphadenopathy and warrants further work up to exclude this possibility.

Jejunal Obstruction Caused by an Enterolith

Nolan E. Perez, M.D., Cherie R. Phillips, M.A., John Webber, M.D., Murray N. Ehringreis, M.D., F.A.C.G.* Gastroenterology, Wayne State University School of Medicine, Detroit, MI.

Introduction: Small bowel obstruction caused by stone impaction is rare. Most cases are caused by a gallstone after being passed through a biliary-enteric fistula or by an enterolith formed in a small bowel diverticulum. We report a case of an enterolith jejunal obstruction without associated small bowel diverticulum.

Case: A 98 year-old woman presented with several weeks of nausea, vomiting, abdominal pain and anorexia. This was her third admission in the past month for these complaints. Her history included diverticulosis coli, dementia, arthritis, HTN, CVA and CHF.

On examination the patient was afebrile and tachycardic. The abdomen was nontender with normal bowel sounds. White blood cell count was 13,200 and hemoglobin 11.2. Electrolytes, amylase, lipase and liver tests were normal. CT scan revealed a 3 cm calcified mass in the small bowel with dilated proximal loops. There was no pneumobilia and the gallbladder was normal. The patient was treated with IV fluids, no oral intake and a nasogastric tube. A few days later she developed diffuse abdominal pain and absent bowel sounds. At exploratory laparoscopy, a hard non-mobile mass was palpated in the jejunum with dilated bowel proximally. The entire small bowel was run and no diverticula were seen. The gallbladder was intact. The small bowel was resected approximately 2 cm on either side of the 4.5 × 3 × 3 cm mass and sectioning of the stone revealed many layers. [figure1] Her symptoms resolved and she returned to baseline.

Discussion: Primary enteroliths are formed in the small bowel and secondary enteroliths are formed in the gallbladder. Proximal small bowel enteroliths are likely to be composed of bile acids, while those in the distal small bowel are usually composed of calcium or other mineral salts. Gallstone ileus is well described, but there are few reported cases of primary enteroliths causing small bowel obstruction. Given the normal gallbladder, the absence of small bowel diverticula and the radiodensity of the stone, our case likely represents an isolated mineralized enterolith. Only one other case of proximal small bowel obstruction caused by a calcified enterolith has been reported.

Small Bowel Obstruction from Apricot Ingestion

Catherine Tsai, M.D.,* Brian Mulhall Department of Gastroenterology, National Naval Medical Center, Bethesda, MD and Gastroenterology Service, Walter Reed Army Medical Center, Washington, DC.

66 year-old female with cirrhosis from NAFLD, hypothyroidism, type 2 diabetes mellitus, and previous breast cancer presented with symptoms and findings on CT of bowel obstruction. Endoscopy was performed to evaluate for malignancy but instead revealed multiple, unidentified small disc-shaped objects in the stomach and duodenum. Exploratory laparotomy was performed for worsening obstructive symptoms. Thirty-two unmacerated apricot halves were found impacted in the proximal small bowel. The intestinal tract showed no other abnormalities. Despite these findings, the patient denied apricot ingestion. Further examination showed findings consistent with CREST syndrome. Phytobezoars account for 0.4–4% of small bowel obstructions. Among fruits, oranges and persimmons include poor mastication (our patient was edentulous), gastroparesis or small bowel dysmotility, extreme high fiber intake and psychiatric disorders. Clinical presentation ranges from asymptomatic to obstructive symptoms. Various treatments include enzymatic therapy (ie: cellulose, Coca-Cola), mechanical disruption, lavage, or surgical removal. Our patient had evolving obstructive symptoms mandating surgical intervention. In the patient presenting with gastric outlet/proximal small bowel obstruction, a careful history for dental disease and recent food ingestion should
be obtained. In addition, evaluation for evidence of intestinal dysmotility may be warranted. It is important to recognize that phytobezoars may be the culprit etiology in small bowel obstruction in patients with small bowel dysmotility. [figure1] [figure2]

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**Pediatric Intraductal Papillary Mucinous Neoplasia**


Intraductal papillary mucinous neoplasia (IPMN) of the pancreas are premalignant, intraductal, cystic lesions that usually affect men aged 60 to 70. We describe the first reported pediatric case of IPMN. A 14-year-old male presented with recurrent pancreatitis and an amylase of 247 and lipase of 508. Liver function tests were normal. CT scan and ultrasound showed a dilated pancreatic duct, an enlarged pancreatic head, and an atrophied tail. ERCP revealed copious mucus from wide-open, patulous major and minor ampullae. There was pan-dilatation of the main pancreatic duct. Pancreatic fluid cytology revealed benign columnar and cuboidal epithelial cells with macrophages and lymphocytes. Shortly thereafter his abdominal pain subsided with normalization of his pancreatic enzymes. A year after, he had a lipase of 8.1 and an amylase of 167. Repeat ERCP showed continued dilation of the major and minor ampullae with a fish-eye appearance and mucinous plugs. Pancreatic endoscopic ultrasound and pancreatoscopy showed a dilated pancreatic duct of 4–5 mm but no masses or cysts. CT scan revealed a 13mm hypodensity in the pancreatic head. He thus underwent a pylorus-saving pancreaticoduodenectomy for IPMN. Pathology revealed IPMN of borderline malignancy in the pancreatic head involving the main and secondary pancreatic ducts. The parenchyma had multiple cysts lined with tall mucin-producing cells. Epithelial hyperplasia and papillary infoldings with dysplasia were seen and tumor cells stained positive for mucin and cytokeratin 7 and 20. Acinar atrophy, consistent with chronic pancreatitis, was also noted. The patient has done well for over 2 years with no further bouts of pancreatitis. He did develop some mild abdominal discomfort that resolved with pancreatic enzymes and a proton pump inhibitor. Furthermore, levels for serum tumor markers CA 19–9 and carcinoembryonic antigen remain low. This is the first reported pediatric case of IPMN. Although rare, it should be considered whenever the typical fish eye appearance of the ampullae and mucin are noted on ERCP.

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**Metastatic Melanoma Presenting with Abnormal Liver Enzymes**

Todd N. Witte, M.D., Showkat Bashir, M.D., Marie L. Borum, M.D., Ed.D., M.P.H.* Division of Gastroenterology, Department of Medicine, George Washington University, Washington, DC.

**Introduction:** Melanoma is one of the most common malignancies associated with metastatic disease to the GI tract. Although >60% of patients who die of melanoma have gastrointestinal involvement, antemortem presentations are vague and endoscopic identification is <4%. We report a case that presented in an unusual fashion, and was identified by endoscopy.

**Case:** A 56 year old male was referred for abnormal liver enzymes. The patient complained of post-prandial abdominal bloating, decreased appetite, lightheadedness, progressive fatigue, and unintentional weight loss. Past medical history was pertinent for normal colonoscopy three years ago. Physical examination revealed a fit-appearing male with mild bilateral upper abdominal tenderness. Initial liver enzymes from a week prior to consultation were: ALT 772 U/L, AST 666 U/L, Alk Phos 400 U/L, total bilirubin 1.6 mg/dL. The patient was subsequently admitted to the hospital for dehydration and progressive painless jaundice. CT scan revealed numerous pulmonary nodules, kidney and adrenal hypodensities, nodules throughout the small bowel mesentery with retroperitoneal lymphadenopathy, irregularity of the lesser curvature of the stomach, enlargement of the pancreatic head with dilated common bile duct of 1.5 cm with mild diffuse intrahepatic biliary ductal dilation, and multiple enhancing lesions throughout the brain. EGD revealed a single black pigmented spot at the gastroesophageal junction, and multiple pigmented spots and raised fleshy nodules with central umbilication diffusely throughout the stomach and small bowel. Upon further questioning the patient recalled prior removal of a skin lesion for which there was no further follow-up. Histologic evaluation of the pigmented gastric and small bowel lesions confirmed malignant melanoma.

**Conclusion:** Melanoma is not an uncommon source of widely metastatic disease and commonly involves the GI tract. As sensitivity for radiographic evidence of GI involvement is limited and symptoms are often vague, endoscopic evaluation should be considered when melanoma is in the differential of a metastatic malignancy of unknown primary site. [figure1]
Kawasaki Disease Manifesting as Cholangitis

Amy M. Billings, M.D., C. Julian Billings, M.D., Beth M. Rutland, M.D., Karen D. Crissinger, M.D.* Department of Pediatrics, University of South Alabama, Mobile, AL; Department of Medicine, University of South Alabama, Mobile, AL and Department of Pathology, University of South Alabama, Mobile, AL.

Kawasaki disease is a vasculitic disorder usually seen in young children, typically presenting with fever, rash, redness of the lips and tongue, conjunctivitis, lymphadenopathy, and swelling of the hands and feet. Kawasaki’s manifesting with acute cholangitis is exceedingly rare. We describe a 16 year old African American male who was found to have evidence of both Kawasaki’s and cholangitis on liver biopsy.

The patient presented with 3 days of fever, abdominal pain, nausea, vomiting, and a generalized rash. On admission he had a temperature of 102.4°F, a generalized maculopapular rash, sterile pyuria, and a diffusely tender abdomen. Labs included: alkaline phosphatase 330, AST 265, ALT 313, and GGT 247. During his hospitalization, he continued to spike daily fevers for over a week, despite broad spectrum antibiotics. He developed generalized desquamation of his rash on day 6.

CT and MRCP both suggested pericholangitis. A subsequent liver biopsy confirmed cholangitis, as evidenced by the presence of neutrophils within the epithelium and lumens of the bile ducts. [figure1] The biopsy also demonstrated fibrosis and vasculitis consistent with Kawasaki disease.[figure2] He received intravenous immunoglobulin and defervesced two days later. His abdominal pain and elevated liver tests also resolved.

Measurement of liver enzymes can reveal elevated transaminase levels or mild hyperbilirubinemia caused by intrahepatic congestion, and a minority of children develop obstructive jaundice from hydrops of the gallbladder. However, cholangitis in the setting of Kawasaki disease is very rare and has only been described in a handful of cases.

Extensive Necrotizing Fasciitis of the Thigh Secondary to Perforated Colonic Diverticulosis

Kapil Gupta, M.D., Daniel Kaufman, M.D., Michael Zenilman, M.D.* Gastroenterology, Surgery, SUNY Downstate Medical Center, Brooklyn, NY.

Diverticulosis of the colon is very common, and is either asymptomatic or usually presents clinically as diverticular bleeding or diverticulitis. Here we report an unusual case of a patient who presented with necrotizing fasciitis of the thigh resulting from perforated sigmoid diverticulosis.

A 45-year-old male presented to the emergency room with a painful and swollen left thigh of three weeks duration. He denied past medical history or any history of trauma. He complained of fever, but denied nausea, vomiting, or chills. He was afebrile and had normal vital signs. Physical examination revealed a benign abdomen, and an edematous, erythematous, indurated, crepitant, and exquisitely tender left thigh. Blood analysis showed marked leukocytosis (38 K) with a left shift. X-ray of left thigh showed subcutaneous gas. The patient was taken emergently to the OR for treatment of necrotizing fasciitis. Generous medial and lateral incisions of the thigh...
were made, and revealed extensive necrosis with approximately 2L of frank pus. Further extension showed a retroperitoneal abscess, where an additional 1L of pus was drained. Operative cultures grew E. coli, Strep viridians and Enterococcus fecium, and antibiotic coverage was adequate. CT scan with rectal contrast and fistulogram performed subsequently revealed sigmoid diverticulosis and a fistula from the sigmoid colon to the retroperitoneal abscess cavity. The patient was brought back to the OR on several occasions for further wound debridement, vacuum dressing changes, and finally skin grafting. The patient was discharged home and will return for definitive management of his diverticular disease. [figure1] Few case reports of colonic diverticular disease presenting with infectious extraperitoneal manifestations have been reported to date. Of these, only a handful report necrotizing fasciitis of the thigh. Necrotizing fasciitis is a surgical emergency with high mortality rates. Here we show a unique case of necrotizing fasciitis of the thigh as a complication of perforated sigmoid diverticulosis, with good outcome following prompt diagnosis and surgical intervention.

![Image](image1)

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Intrapancreatic Accessory Spleen Mimicking a Neuroendocrine Tumor
Kostas Sideridis, D.O., Samuel Davidoff, M.D., Angelo Fernandes, M.D., Jeremy Bragdon, M.D.,* Gary Gecelter, M.D., Simmy Bank, M.D.
Department of Medicine, Division of Gastroenterology, Department of Surgery and Pathology, Long Island Jewish Medical Center, New Hyde Park, NY.

We present a case of an intrapancreatic accessory spleen (IPAS), which radiologically mimicked a pancreatic islet cell tumor. With the progressive improvement of imaging technologies for the evaluation of the abdominal cavity, the finding of an IPAS will be more common. A 66 year-old white male presented for the evaluation of a mass in the tail of the pancreas. His past medical history and family history were non-contributory. A CT scan showed a 1.6 cm solid, enhancing lesion in the tail of the pancreas (figure A). CBC, electrolytes and neuroendocrine chemistries were normal. A Indium-111 Pentetreotide showed a discrete focus of increased activity in the tail of the pancreas. The risks and benefits of surgical intervention versus further diagnostic work up such as EUS with biopsy were discussed with the patient and he elected to proceed with surgery. A laparoscopic spleen saving distal pancreatectomy was performed. Gross and microscopic examination showed pancreatic tissue adjacent to splenic tissue (Figure B & C). The patient was discharged after the surgery without any complications. The case presented above illustrates how IPAS can be mistaken for neuroendocrine tumors. Although resection of asymptomatic IPAS is unnecessary they are usually resected if they mimic enlarged lymph node or a tumor of the pancreas. Usually IPAS are removed by performing distal pancreatectomy with splenectomy. The newer approach is laparoscopic distal pancreatectomy with preservation of the spleen and splenic vessels. However with future advancements in the diagnostic modalities IPAS can be promptly identified and unnecessary surgery may be avoided. [figure1] [figure2]

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A Case of a 56 y/o Woman with Metasatic Melenoma Post Induction Therapy with Experimental Cytotoxic T Lymphocyte-Associated Antigen 4 Blockade Presented with Diarrhea
Timothy J. Laurie, D.O.,* Gene Chang, M.D., Mani Mahdavian, M.D.
Gastroenterology, Advocate Lutheran General Hospital, Park Ridge, IL.
This is a case of a 56 y/o woman with h/o stage IV melanoma s/p antibody against human CTLA-4 (MDX-010) induction two months prior to admission. Her abdominal exam was benign and complete examination was un-revealing. Stool studies did not grow enteric pathogens. CT of abdomen and pelvis did not identify any radiological evidence of colitis or ileitis. The patient underwent colonoscopic evaluation with visualization of the ileum. There were diffuse ulcerations with nodularity of the ileum(figure 1). The biopsy identified cellular infiltration, and crypt abscess formation(figure 2). The patient was diagnosed with acute ileitis. Melanoma is the sixth most common cancer in the United States. As new therapies are developed clinicians need to be aware of potential side effects. A new biological agent for melanoma is a human antibody against human CTLA-4 termed MDX-010. MDX-010 is currently in phase III clinical trials for treatment of stage III-IV melanoma. Results of phase I trials have indicated that there is risk of autoimmune induction. In phase one trial by Giao et al., 2 of 14 patients developed diarrhea secondary pan-colitis with crypt abscesses. Likewise a study by Weber et al. identify 3 of 17 patients developed diarrhea. The patient reports having 7–8 episodes of watery, non-bloody diarrhea for one week. On exam the patient’s vital sign were stable. Her abdominal exam was benign and complete examination was un-revealing. CT of abdomen and pelvis did not identify any radiological evidence of colitis or ileitis. The patient underwent colonoscopic evaluation with visualization of the ileum. There were diffuse ulcerations with nodularity of the ileum(figure 1). The biopsy identified cellular infiltration, and crypt abscess formation(figure 2). The patient was diagnosed with acute ileitis. [figure1] [figure2] Melanoma is the sixth most common cancer in the United States. As new therapies are developed clinicians need to be aware of potential side effects. A new biological agent for melanoma is a human antibody against human CTLA-4 termed MDX-010. MDX-010 is currently in phase III clinical trials for treatment of stage III-IV melanoma. Results of phase I trials have indicated that there is risk of autoimmune induction. In phase one trial by Giao et al., 2 of 14 patients developed diarrhea secondary pan-colitis with crypt abscesses. Likewise a study by Weber et al. identify 3 of 17 patients developed diarrhea post MDX -010 therapy secondary ileitis diagnosed by CT. Each case was reversible with a course of steroids.

REFERENCES
Diagnosis is made based upon clinical setting, imaging studies, and surgical resection with the pathological hallmark being the normal appearance of hepatocytes arranged in sheets with their cytoplasm containing glycogen and fat with absent portal tracts. Abnormalities of liver enzymes may also be seen.

Management includes discontinuation of oral contraceptives. Surgical resection is generally indicated for multiple lesions, lesions > 5 centimeters in size, symptomatic lesions, and complications of the disease including hemorrhage and malignant transformation. Rarely liver transplantation may be required. Our patient was found to have ten adenomas and had surgical resection at a transplant center entailing approximately 25% of her liver.

**Introduction:** Metastatic Crohn’s disease is the presence of cutaneous granulomas that are noncontiguous with the gastrointestinal tract. Granulomatous cutaneous lesions, an unusual complication of Crohn’s disease, most frequently appear in the skin folds of the anterior abdominal wall and submammary areas. We report a rare case of a woman with metastatic Crohn’s disease involving the face.

**Case:** A 63 year old woman with a history of Crohn’s disease status-post subtotal colectomy with ileostomy (10 years ago) was referred for a second opinion regarding the management of her inflammatory bowel disease. The patient’s Crohn’s disease had been complicated with enterocutaneous and enterovesicular fistulas, lower extremity pyoderma gangrenosum and oral aphthous ulcerations. The patient had been maintained on mesalamine and infliximab. During the past 6 months, the patient reported development of progressive facial erythema, ulceration, swelling and discomfort with persistent severe oral aphthous ulcerations. She denied fever, chills, abdominal discomfort, change in ileostomy output, joint discomfort and active pyoderma gangrenosum. Facial biopsies revealed noncaseating granulomas consistent with Crohn’s disease. Increased frequency of infliximab infusions did not improve the facial lesions or oral ulcerations. Serologic testing demonstrated no evidence of infliximab antibodies. Following consultation, 6-MP and a limited course of topical steroids were added to the medical regimen with significant improvement of the facial lesions and resolution of oral ulcerations.

**Conclusions:** This is an unusual case of Crohn’s disease with metastatic cutaneous lesions involving the face. There have only been 3 previously reported cases of facial involvement and limited information about treatment. The rarity of this cutaneous complication may result in under-recognition of this manifestation. Increased awareness of granulomatous cutaneous involvement in Crohn’s disease will lead to advances in treatment.

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**Metastatic Crohn’s Disease Involving the Face**

David L. Jager, M.D., Christopher R. Entwisle, M.D., Marie L. Borum, M.D., Ed.D., M.P.H.* Division of Gastroenterology, Department of Medicine, George Washington University, Washington, DC.

**Introduction:** Metastatic Crohn’s disease is the presence of cutaneous granulomas that are noncontiguous with the gastrointestinal tract. Granulomatous cutaneous lesions, an unusual complication of Crohn’s disease, most frequently appear in the skin folds of the anterior abdominal wall and submammary areas. We report a rare case of a woman with metastatic Crohn’s disease involving the face.

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**Conclusions:** This is an unusual case of Crohn’s disease with metastatic cutaneous lesions involving the face. There have only been 3 previously reported cases of facial involvement and limited information about treatment. The rarity of this cutaneous complication may result in under-recognition of this manifestation. Increased awareness of granulomatous cutaneous involvement in Crohn’s disease will lead to advances in treatment.

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**An Infant with Autoimmune Enteropathy and Stomach Involvement: Response to Tacrolimus**

Rita Steffen, M.D.,* Alex Green, B.S., Robert Wylie, M.D., Lisa Feinberg, M.D., Lori Mahajan, M.D., Varvara Kaplan, M.D., Vera Hupertz, M.D. Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH and Medical School, Ohio University College of Osteopathic Medicine, Athens, OH.

A female infant presented in the first month of life with failure to thrive, emesis, and protracted diarrhea. Biopsies revealed marked duodenal villous atrophy with surface epithelial lymphocytosis, consistent with autoimmune enteropathy. She also had a large gastric ulcer, showing stomach involvement for the first time in a pediatric case of autoimmune enteropathy. She was also successfully treated with three months of tacrolimus and methylprednisolone, which will be continued for one year. Her duodenal epithelium has healed along with her stomach.

At 17 days of life this infant girl was referred for failure to thrive. During the neonatal period she was treated for necrotizing enterocolitis, which presented with gross blood in the stool. She was vomiting despite formula changes, and diarrhea began at this time. Laboratory studies demonstrated hypoalbuminemia. Her stools were negative for pathogens, but positive for alpha-1-antitrypsin, thus protein-losing enteropathy. Her intestinal biopsies are detailed above, and the gastric ulcer was quite large, measuring 2.0 × 3.0 cm. Its pathology exhibited focal neutrophilic epithelial injury with an increase in the number of chronic inflammatory cells. After a poor response to steroids, the patient was tapered off and subsequently started on oral tacrolimus (FK506, Fugi-sawa Pharmaceuticals, Tokyo, Japan) with a serum concentration goal of 12–15 ng/mL. She responded to tacrolimus and had repeat endoscopic biopsies demonstrating healing of the gastric ulcer and normal small bowel brush border and lamina propria. She is receiving all of her nutrition through her digestive tract. The patient’s gastric mucosa also healed with the immunosuppressive therapy. To our knowledge, this is the first reported case of autoimmune enteropathy in a child that had stomach involvement.

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**Extended Release: Endoscopic Removal of a Medication Bezoar in a Patient with Recurrent Hypotension**

Christopher D. Wells, M.D., Bhavesh M. Patel, M.D., Jonathan A. Leighton, M.D.,* Mohamed Y. Rady, M.D., Joel S. Larson, M.D. Gastroenterology and Hepatology, Mayo Clinic, Scottsdale, AZ and Critical Care, Mayo Clinic, Scottsdale, AZ.

To describe a challenging clinical entity that should be considered in patients presenting with drug overdose and recurrent symptoms, and to pro-
of extended-release nifedipine preparations (Procardia XL). There have been nine previous reports of medication bezoars composed of extended-release nifedipine tablets. In a recent case, a 61-year-old female was admitted to the emergency department with a drug overdose of extended-release nifedipine and venlafaxine. In the emergency department, she was treated with activated charcoal, calcium chloride, and sodium bicarbonate. She exhibited bradycardia, hypotension, and respiratory failure and was subsequently intubated. Within the initial 24 hours, the patient became hemodynamically stable, was extubated, and was transferred to the floor. Approximately 12 hours later, the patient became hypotensive and unresponsive, requiring transfer back to the intensive care unit. A cystic lesion was seen in the abdomen on a radiograph of the abdomen. Because of concern for a medication bezoar, an upper endoscopy was performed. On endoscopy, a mass containing extended-release nifedipine tablets, venlafaxine granules, and charcoal was seen in the fundus. An overtube was placed, and the bezoar was fragmented using a large snare. The pills were then removed using a Roth retrieval net (US Endoscopy, Mentor, OH). In total, 167 extended-release nifedipine tablets were removed. Unfortunately, the patient expired 72 hours later due to multisystem organ failure related to hypotension.

There have been nine previous reports of medication bezoars composed of extended-release nifedipine preparations (Procardia XL®, Adalat XL®, nifedipine gastrointestinal system). None of the prior cases described ongoing or recurrent symptoms related to the active medication. This is the first known report of the endoscopic removal of a bezoar containing an antihypertensive medication in a symptomatic patient. A medication bezoar should be considered in any patient with recurrent symptoms following a drug overdose. Endoscopic removal is the treatment of choice for symptomatic bezoars.

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Gatifloxacin Induced Liver Failure in Patient with Underlying Fibrin Ring Granuloma Caused by Q Fever
Mohammad Otahbachi, M.D., Elias Ghandour, M.D., Houssam Kharrat, M.D.∗ Department of Internal Medicine, Gastroenterology Section, Texas Tech University Health Sciences Center, Lubbock, TX.

To review differential diagnosis of fibrin ring granuloma in liver biopsy. The patient is 55-year-old male with four days history of malaise, aches, chills, sweats and questionable fever. He had negative Strept throat and influenza screening. He was given gatifloxacin (tequin) by his PCP. The patients’ symptoms improved; however, his urine turned darker. His attempt to stop the medication failed secondary to symptom recurrence. By the time he followed up with his PCP, he had developed abnormal liver function tests and jaundice. He works as a welder. Denies alcohol intake. His exam: Sclera is icteric, mild RUQ abdominal tenderness with no rebound or guarding. WBC 14.3, Total bil. 3.8, AST 73, ALT 83, Alk P 289, INR 1.76. The patient underwent a negative ERCP and CT of his abd/pelvis. He continued to spike a fever. Liver function and ammonia levels continued to rise. The gatifloxacin had been stopped and the picture was more suspicious of a gatifloxacin-induced liver failure. With supportive care, the liver function and synthetic function of the liver normalized. However, the patient continued to spike a fever and remained with an elevated white count. His sepsis workup was negative. A liver biopsy was done which exhibited fibrin ring granuloma. The patient underwent Q fever serology which was positive. And he responded well to doxycycline. We believe that the gatifloxacin causes the patient to have acute decompensation of his liver as evident by abnormal synthetic function of the liver. Although injury caused by gatifloxacin was acute, it was transient. The persistent fever triggered further workup, resulting with final diagnosis of Q fever. Q fever with liver involvement is rare. It is one of the conditions that can cause the patient to have fibrin ring granuloma. Others include CMV, EBV, MAI, hepatitis A, infectious mononucleosis, visceral leishmaniasis, Lyme disease, Boutonneuse fever, toxoplasmosis, Hodgkin disease, non-Hodgkin lymphomas, and drug reactions. [figure1]

Liver Biopsy Demonstrating Fibrin Ring Granuloma.

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Markedly Elevated CA 19–9 Levels in a Patient with Jaundice: Searching for the Mass That Did Not Exist
Srinivas R. Pulagam, M.D., Tarun Madappa, M.D.,∗ Loren Kirchner, M.D. Internal Medicine, Canton Medical Education Foundation (NEOUCOM), Canton, OH.

Carbohydrate antigen 19–9 (CA 19–9) can be elevated in pancreatic adenocarcinoma, other GI malignancies, and a host of benign conditions. Few cases however have been reported with values markedly elevated in a benign condition. We report a case of a patient with a markedly elevated CA 19–9 that led to an exhaustive workup to find a non-existent pancreatic “mass”.

Case: A 43-year-old male was admitted for evaluation of abdominal pain, nausea, and vomiting. He also noted progressive jaundice and a 50 lb weight loss over 6 months. Prior to admission, he was on a 6 month alcholic binge. Exam revealed jaundice, scleral icterus, and hepatomegaly. Initial labs: Total bilirubin 27.2 mg/dl, direct bilirubin of 17.5 mg/dl, AST 136 IU/L, ALT 126 IU/L, and alkaline phosphatase 359 IU/L. CT of the abdomen showed a 7 cm pancreatic pseudocyst with suspicion of mass. Because of the “suspicion of mass”, and profound jaundice, a CA 19–9 was obtained (5275 U/ML). Because the CA 19–9 was elevated, an extensive workup was undertaken to evaluate the “mass”. MRCP showed fatty infiltration of liver, pancreatic pseudocyst, and chronic pancreatitis, but no dilatation of the common bile duct. A viral hepatitis panel, EBV, CMV, and HIV were negative. The patients bilirubin increased to 38 mg/dl by one week after admission. Because of continued concern for malignancy, an ERCP was performed which showed no abnormalities. Dulcet brushings were negative for malignant cells. A Fine needle aspiration of the pseudocyst showed no malignant cells. After one week, the bilirubin started to fall and by 1 month, it was 1.1 mg/dl. A repeat CA 19–9 at 1 month was 8584 U/ml. An endoscopic ultrasound again revealed no mass. CA 19–9 levels decreased to 171 U/ml at 2 month follow up. A repeat CT scan 6 months after presentation showed a decrease in the size of the pseudocyst and no “mass”. At 6 months, the patient has stopped drinking and is asymptomatic.

Conclusions: Markedly elevated serum levels of CA19–9 are associated with pancreatic cancer, however, it can also occur in some non-malignant conditions. Ordering a CA 19–9 test in a situation where there is limited suspicion of pancreatic carcinoma (questionable mass) may lead to an unnecessary, risky, and expensive work-up.
An Unusual Etiology of Upper Gastrointestinal Bleeding

Adeyinka O. Laiyemo, M.D., Momodu Jack, M.D., Fitzroy Dawkins, M.D., Duane T. Smoot, M.D.* Medicine, Howard University Hospital, Washington, DC.

To increase awareness of other causes of gastrointestinal bleeding in young men.

A Case Report: We described a 22-year-old black gentleman who presented with a 2-week history of worsening scrotal and leg swelling. He had been having intermittent melonotic stools for 2 weeks with associated abdominal pain, and epigastric fullness. His medical history was significant for testicular cancer for which he had undergone orchectomy, lymphadenectomy, and multiple courses of chemotherapy until he defaulted from treatment.

Physical examination revealed an irregular mass in epigastrium, hepatomegaly, but with a normal bowel sound. He had swollen edematous scrotum and penile shaft, but rectal examination revealed external hemorrhoids, brown stool which was guaiac positive.

EGD performed which revealed polyloid mass lesions in the 2nd and 3rd portions of the duodenum, biopsy revealed mixed germ cell tumor with immature teratoma the same histology of his testicular cancer. He underwent chemotherapy, and repeat EGD five months later revealed a complete disappearance of the mass lesions.

We reviewed the literature regarding similar cases of duodenal metastasis from testicular cancer. To our knowledge, this is the twenty –third reported case in the English literature.

We advocate a detailed physical examination including testicular examination in young men presenting with upper gastrointestinal bleeding.

A Case of a Small Hyperplastic Polyp with Malignant Transformation

Praveen Rapolu, M.D., Robin Baradarian, M.D., Kadirawel Iswara, M.D., Jian Jun Li, M.D., Scott Tenner, M.D., M.P.H.* Division of Gastroenterology, Maimonides Medical Center, Mount Sinai Medical Center, Brooklyn, NY.

Small (less than 1 cm) hyperplastic polyps are a common finding on colonoscopy. These polyps are typically removed by gastroenterologists because of an inability to endoscopically distinguish hyperplastic polyps from adenomatous polyps. There is also a controversy whether the presence of hyperplastic polyps pose an increased risk of proximal colonic polyps and risk of future adenomatous polyps and/or carcinoma in the colon. Additionally, virtual colonoscopy (computed tomography colography) has a decreased sensitivity for these small polyps. Arguments for the use of virtual colonoscopy has included that small polyps which may not be detected are typically hyperplastic polyps that do not warrant removal. We report a case of a patient who underwent a colonoscopy and was found to have an infiltrating colon adenocarcinoma arising from a small hyperplastic polyp. A 60 yr old female patient presented with rectal bleeding and subsequently underwent colonoscopy. During colonoscopy a smooth 0.8 cm polyp was identified in the cecum. The polyp was removed by cold snare. Pathology revealed an infiltrating adenocarcinoma arising within the hyperplastic polyp with the margins negative for the tumor. Immunohistochemically, p53 and Ki-67 were positive in the carcinoma portion of the hyperplastic polyp. Although dysplastic (adenomatous) changes in hyperplastic polyps has been reported, the presence of carcinoma arising in these polyps is rare. This case report suggests that hyperplastic polyps should be removed. Although the risk of carcinoma increases with the size of the polyp and degree of dysplasia, colorectal cancer screening strategies must recognize that all polyps, even small hyperplastic polyps, pose a risk of carcinoma.

Mycobacterium Avium Intracellulare Presenting as a Small Bowel Obstruction

Kiran Jagarlamudi, M.D., Suresh Jayatilaka, M.D., Theodore Dacosta, Jr., M.D., Joseph DePasquale, M.D., Robert Spira, M.D.* Department of Gastroenterology, Seton Hall University School of Graduate Medical Education, South Orange, NJ.

Introduction: In patients infected with HIV, Mycobacterium avium intracellulare (MAI) infection usually presents as disseminated disease. The risk of MAI increases as the CD4 cell number declines below 50 cells/mm³. The most common symptoms of disseminated MAI are non-specific and include: fever, night sweats, abdominal pain, diarrhea, and weight loss. We report a case of MAI presenting as a small bowel obstruction.

Case report: A 48 year old male with history of AIDS (CD4 count 71), and past history of MAI was admitted with a two day history of generalized abdominal pain related with bilious vomiting. He denied any changes in bowel habits, weight loss or fever. Medications included Kaletra, Viread and Ziagen.

On examination he was afebrile, with abdominal tenderness in the epigastric region as well as the right upper quadrant. Laboratory studies were essentially normal. Abdominal X-ray on admission was negative for any obstruction. CT scan done the same day revealed markedly dilated stomach, duodenal and proximal jejunal loops with nondilated portion of the remainder of the jejunum and the ileum, consistent with a partial small bowel obstruction. Upper endoscopy with small bowel enteroscopy was done, which showed a perianpillary mass, with ulceration and a large friable mass in the proximal jejunum with ulceration, causing obstruction to the bowel lumen. Multiple biopsies were taken, the pathology results showed jejunal mucosa with acid-fast bacilli, which on culture was identified as Mycobacterium avium intracellulare. On exploratory laparotomy, there was a nearly obstructing mass in the proximal jejunum, approximately 5 × 6 cm, with surrounding fibrotic inflammatory tissue and lymphadenopathy. He underwent resection of the proximal jejunal mass and primary anastomosis. Post surgical recovery was uneventful. [Figure1]

Conclusion: Mycobacterium avium intracellulare has been reported to cause ileal obstruction in AIDS patients. We present the first case of Mycobacterium avium intracellulare presenting as a jejunal obstruction.

Diffusely Infiltrating Melanoma Mimicking Acute Alcoholic Hepatitis: A Case Report

Mitchell S. Kaplan, M.D., Sushama Gundlapalli, M.D., Shiriram Jakate, M.D., Stanley M. Cohen, M.D.* Hepatology, Rush University Medical
Diffuse malignant hepatic infiltration by melanoma leading to acute liver failure is exceedingly rare. The few existing case reports all had a prior history of primary cutaneous or uveal melanoma. We report a case of a 65 year old Caucasian male with a history of consuming 3–4 alcoholic beverages daily for 40 years was noted to be jaundiced and was admitted for further evaluation. Laboratory evaluation on admission revealed an AST 92 U/L, ALT 56 U/L, alkaline phosphatase 225 U/L, total bilirubin 9.2 mg/dL, albumin 2.7 g/dL, LDH 1841 U/L, and INR 1.40. Serologic work up for other causes of liver disease was negative. Ultrasound and MRI of the abdomen revealed no hepatic masses. Despite supportive care and steroids for presumptive acute alcoholic hepatitis, the patient had worsening of his liver function tests and prothrombin time. A transjugular liver biopsy showed diffuse sinusoidal infiltration of the liver with poorly differentiated malignant tumor cells within the sinusoids which stained strongly positive for S-100 and HMB-45 and negative for keratin. The morphology and the immunoprofile was that of melanoma. Ophthalmologic and dermatologic exams were done and revealed no primary lesion. The patient developed progressive encephalopathy, ascites, and multi-organ failure resulting in death one week later. The patient’s family refused an autopsy.

Our case represents a unique clinical presentation of melanoma; diffuse hepatic infiltration with resultant fulminant hepatic failure. Despite negative ocular and cutaneous exams (the most common primary sources of metastatic melanoma), the hepatic sinusoidal pattern of infiltration suggested metastatic disease.

Our case is also unusual because of the significant potential for an incorrect diagnosis. Given the classic clinical picture of acute alcoholic hepatitis, biopsy may not have been deemed necessary. Prior studies evaluating the role of liver biopsy in alcoholic liver disease suggest that without histological confirmation the diagnosis may be inaccurate in 10–20% of patients. This case supports the concept of considering a liver biopsy in patients with alcoholic hepatitis.

A Stone Overturned: Persistent Cholestasis after Cholelith Extraction

Patrick E. Young, M.D., Mark H. Johnston, M.D.* Gastroenterology, National Naval Medical Center, Bethesda, MD.

A 41 y.o. male with a history of cholecystectomy five years prior presented with a two month history of post-prandial right upper quadrant pain consistent with biliary colic. He denied fever, chills, dark urine, acholic stools, nausea, or melena. Initial laboratory analysis— to include complete blood count, serum chemistries and liver associated enzymes— was normal. A right upper quadrant ultrasound revealed a surgically absent gallbladder, a common bile duct (CBD) measuring 4.4 mm, and a normal pancreatic head.

His symptoms worsened over the next few days with increased abdominal pain and the onset of jaundice. Repeat bloodwork showed the following: total bilirubin 6.2 mg/dL, alkaline phosphatase 201 U/L, alanine aminotransferase 223 U/L, and aspartate aminotransferase 117 U/L. An MRCP revealed a long cystic duct remnant with low insertion but no evidence of biliary obstruction. An ERCP was attempted, but the CBD cannulation failed. Amoxicillin/sublactam was started. His liver associated enzymes remained abnormal, but stable. Repeat ERCP 48 hours later revealed 2 small CBD stones and no visualization of the cystic duct. Balloon stone extraction and sphincterotomy was performed. Despite this, the patient’s pain and lab abnormalities persisted. A third ERCP performed 2 days later revealed an 8mm stone in the long cystic duct remnant. This was extracted, and the ductal system was cleared with an occlusion cholangiogram. Though the patient’s pain abated immediately, his lab abnormalities persisted and he became progressively more pruritic. We were confident that ductal obstruction was no longer causing his symptoms. While the differential diagnosis for persistent lab abnormalities post stone extraction includes thrombus and stricture, he had no evidence of these by ERCP. He had, however, been given a medicine, ampicillin/sublactam, which may cause cholestasis.

William of Occam once remarked “Pluralitas non est ponenda sine necessitate [Plurality must not be posited without necessity]”. When changes in clinical circumstances dictate, though, one must be ready to shift focus from one foe (a stone) to the next (iatrogenesis). Two hundred and eight cases of cholestasis associated with amoxicillin/clavulanic acid have been reported. This is only the second reported case of cholestasis secondary to ampicillin/sublactam.

Our case illustrates the importance of diligence in the approach to a case that dull’s Occam’s razor.

Massive Pneumoperitoneum after EUS FNA of the Pancreas

John D. Horwhat, M.D.,* Allan H. Andrews, M.D. Department of Medicine, Gastroenterology Svc, Walter Reed Army Medical Center, Washington, DC.

Endoscopic ultrasound (EUS) is becoming more popular for the diagnosis and staging of lesions within the pancreas. Fine needle aspiration (FNA) of the pancreas can be safely performed from the stomach or duodenum to obtain tissue with a low risk of complications. Although abdominal pain following EUS FNA is occasionally reported [Eloubeidi et al, AJG 2003: 98(12)], a thorough search of the literature was unable to determine a reported incidence of pneumoperitoneum following pancreatic EUS FNA. We report the case of a patient undergoing EUS FNA of the pancreatic head who experienced massive pneumoperitoneum.

A 60 yo female with midgastrointestinal pain was found to have a mass in the pancreatic head/uncinate process and underwent EUS FNA. 3 needle passes were made from a duodenal approach into the lesion using a 22ga needle. The patient complained of pain following the procedure which was severe but not out of character for her pre-procedure symptoms. She was subsequently discharged home.

Followup staging CT scan performed 6 days later revealed massive pneumoperitoneum. Figure 1 pre-EUS, Figure 2 post-EUS FNA. At this point, the patient’s degree of discomfort was no different than pre-EUS FNA. Abdominal Xray at a clinic visit 2.5 weeks later showed complete resolution of the pneumoperitoneum.

This case reveals massive pneumoperitoneum that might not have been reported had it not been for the staging CT scan performed 6d later. The
Eosinophilic Gastroenteritis and PSC: A Case for Azathioprine
Patrick E. Young, M.D., David A. Sachar, M.D., Eric M. Osgard, M.D.*
Gastroenterology, National Naval Medical Center, Bethesda, MD; Patrick E. Young, M.D., David A. Sachar, M.D., Eric M. Osgard, M.D.
Eosinophilic Gastroenteritis and PSC: A Case for Azathioprine
FNA. We plan to perform a prospective study to determine the incidence of
post-EUS FNA pneumoperitoneum. [figure1] [figure2]

A 25 y.o. male presents with a several-month history of episodic nausea,
emesis, and fatigue. He initially denied fevers, chills, diarrhea, hematochezia,
melena, weight loss, or night sweats. Laboratory analysis revealed a normal
WBC count, but a mildly elevated eosinophil level of 900. An EGD showed
nodular gastric mucosa with diffuse erythema and focal erosions. Gastric
biopsies revealed increased eosinophils, but the sample was not diagnostic
for eosinophilic gastritis. His symptoms persisted despite promethazine as
needed. Repeat EGD was performed and this time gastric biopsies returned
consistent with eosinophilic gastritis. He was placed on prednisone at 40 mg
daily for 2 months with only a mild decrease in symptoms. He was referred
to our center for further evaluation. A thorough evaluation for infectious
etiologies was entirely negative. Skin tests to 77 allergens were normal.

52 year old male with a history of lymphoma and prior chemotherapy (4
yrs ago) presented with new onset ascites. He also had splenectomy as part
of staging for lymphoma. Physical exam revealed moderate ascites, jugular
venous distension, bilateral lower extremity edema and hemocult positive
stool. Liver Function tests: serum albumin 4.2 gm/dl ALT 34 I U/L, AST
36 I U/L, total bilirubin 1.1 mg/dl. Serum creatinine and electrolytes were
normal. Bone marrow was normal with no recurrence of lymphoma. Ascitic
fluid showed albumin of 2.3 mg/dl, with negative cytology. Ascitic fluid LDH,
amylase and bilirubin were normal. Ascites with a serum albumin ascitic fluid
gradient (SAAG) greater than 1.1, led to the following investigations for the
etiology of portal hypertension (Portal HTN).

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An Unusual Cause of Portal Hypertension
Shamita B. Shah, M.D., Satheesh Nair, M.D.*
Gastroenterology/Hepatology, Ochsner Clinic Foundation, New Orleans,
LA and Hepatology, Ochsner Clinic Foundation, New Orleans, LA.

Can a Cardiac Pacemaker Save a Patient from PEG Tube Placement?
Muhammad M. Heif, M.D., Amar Al-Juburi, M.D.*
Geriatrics/Gastroenterology, CAVHS, Little Rock, AR.

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83 year old male referred for PEG tube placement because of unusual swallow-
ing induced syncope and shaking of 6 months duration. While swallowing
large sips of water and occasionally large bites of food he developed ligh-
theadedness and at times had slurred speech and loss of consciousness. The
episodes lasted about a minute. He learned to drink fluids in small sips but

both endoscopically and histologically. He is currently tolerating a gradual
steroid taper.
Eosinophilic gastroenteritis is an uncommon condition which may involve
any part of the digestive system, including the biliary system. This case
illustrates several rare events. First, to our knowledge it is only the third re-
ported case in the English language of biliary involvement with eosinophilic
colitis or gastritis. Second, it is the only reported case in which the biliary
tract did not show marked eosinophilia. Third, it is the first reported case of
improvement with antimetabolite therapy.
A 31 Year Old Male with Abdominal Pain and Anemia

Yogesh J. Patel, D.O.* Department of Gastroenterology, Lutheran General Hospital, Park Ridge, IL.

Our patient is a 31 year old male who presented with 6 weeks of colicky intermittent epigastric abdominal pain which had been getting progressively worse and more constant over the last week. His review of systems was positive for anorexia, weight loss, constipation, headache, nausea, and emesis. This admission had been his third in the past 6 weeks. Previously he had been found to have elevated LFTs, lipase, as well as anemia. On his first hospitalization, our patient had undergone a CT scan of the abdomen, EGD, colonoscopy all of which were negative. Eventually he was given the diagnosis of pancreatitis and recently underwent ERCP and sphincterotomy. His symptoms however did not improve.

Our patient did not have any past medical or surgical history. His family history was significant only for HTN. He was of Indian origin, but had been living in the U.S. for the past twenty years. He smoked one to two cigarettes per day, did not drink alcohol, and denied IVDU. He worked as a computer programmer. He was recently married on a trip to India four months prior to admission where he stayed for one month. His medications on admission were Ultram, hydrocodone, and Protonix.

During this most recent hospitalization his examination was significant for epigastric area abdominal pain and tenderness with hypoactive bowel sounds. He was again noted to have slightly elevated ALP, bilirubin, and a lipase. He was found to have progressively worsening microcytic anemia. A CT scan of the abdomen had failed to demonstrate evidence of pancreatitis. A repeat ERCP had shown normal CBD and pancreatic duct. On hospital day number 5 a peripheral smear was reviewed and revealed basophilic stippling. A diagnosis of lead poisoning was suspected and confirmed with a serum lead level of 123 mcg/dl. He was treated with succimer and at a 2 month follow up he was asymptomatic. A specific source of his lead poisoning was not found.

This case illustrates the need to include diseases such as lead poisoning and porphyria in the differential of abdominal pain when more common diseases have been ruled out. Also the value of a simple test such as a peripheral smear is demonstrated. In our case this test led to the diagnosis. [figure1]
Gastroenterologists make clinical risk-benefit assessments when offering interferon-α based therapies (IFN) to treat Hepatitis C virus (HCV) infection. The fear of precipitating or worsening psychiatric co-morbidity is a frequent trigger for psychiatric consultation to address the probability of IFN-induced neuropsychiatric adverse effects. Several risk factors are thought to increase the risk of IFN emergent psychiatric co-morbidity and include the following: a previous history of any psychiatric illness; a family history of psychiatric illness; and a history of suicidal ideation. In contrast to the variable influence of these psychiatric risk factors, the decreased likelihood of sustained virologic response (SVR) from HCV in response to IFN is associated with several predictive and additive factors. We propose a comprehensive assessment model that integrates both the psychiatric and medical factors pertaining to HCV treatment. Case 1: IFN is clearly indicated in the case of a 35 YO slender white women with no history of psychiatric illness who is infected with a low HCV viral load of either genotype 2 or 3.

Case 2: In the absence of advancing cirrhosis IFN should be delayed in the case of a 50 YO obese African American man with history of psychosis and substance use disorder who is infected with a high viral load of HCV genotype 1. Ongoing psychiatric follow-up is certainly indicated when a patient has one or more psychiatric risk factors. In cases where a low estimated likelihood of SVR from HCV is combined with an intermediate to low probability of psychiatric adverse effects an evaluation incorporating the patient’s IFN treatment preferences can help sway the decision. This model is intended to assist clinicians in making an individualized and balanced risk-benefit analysis incorporating HCV-disease specific factors as well the potential for psychiatric complications prior to offering IFN treatment. [figure1]

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A Rare Case of Peritoneal Sarcoidosis Associated with Struma Ovarii

Sarabjeet Singh, M.D., Bharat Motwani, M.D., Jasleen Duggal, M.D., Frank Maldonado, M.D. Medicine, Rosalind Franklin University of Medical & Sciences-CMS, North Chicago, IL.

Sarcoidosis rarely involves peritoneum and infrequently associated with ovarian masses. We herein present a case of 36-year-old female who presented with abdominal pain and was found to have sarcoidosis of the peritoneum associated with struma ovarii. Case Report: A 36 year old female was admitted to the hospital with complaint of diffuse abdominal pain. Clinical and laboratory findings revealed diffuse tenderness on abdominal palpation and high values of serum ACE, CA 125, CA 19–9. Pelvis imaging revealed bilateral adnexal masses. Histological examination after laparotomy confirmed non-caseating granuloma from peritoneal biopsy while ovarian biopsy revealed struma ovarii. This is the first case report of sarcoidosis, to our knowledge, which is associated with struma ovarii. Also we found only 17 cases of sarcoidosis in the literature with peritoneal involvement, most of which presented with ascites. However, our patients presented with diffuse abdominal pain rather than signs and symptoms of ascites. Longcope and Freiman stated that “the serious surfaces of the body cavities appear as though almost immune to the disease”. This statement has exceptions, and peritoneal sarcoidosis should be considered in the differential diagnosis of peritoneal nodules in addition to tuberculosis, fungal infections, and carcinomatosis. Once again it proves that despite of all the medical progress diagnosis of sarcoidosis continues to be challenging, presents a clinical dilemma and requires high index of suspicion. [figure1] [figure2]
A 77-year-old female presented with one day of severe right upper quadrant (RUQ) pain, nausea, and vomiting. Two years previously, she had undergone excision of a superficial spreading melanoma on her back. She was a non-smoker and had undergone resection of a stage IV squamous cell lung cancer resulting in a right lobectomy. In addition, she had a prior episode of gastrointestinal bleeding secondary to arteriovenous malformations (A VMs). She currently denied hematemesis, hematochezia or rectal bleeding. Her exam was significant for marked tenderness in the RUQ with no fever, jaundice, or peritoneal signs. Laboratory studies revealed a WBC = 13.1 x 10^9/µL. CT scan demonstrated extensive luminal air in a markedly distended gallbladder with a thickened wall without intramural gas. An open cholecystectomy was performed. The surgical specimen revealed biliary sludge and a nodule in the wall of the gallbladder protruding into the lumen; the tumor was not obstructing the cystic duct. Pathologic exam showed emphysematous, gangrenous cholecystitis and confirmed that the nodule was a metastatic melanoma. No microorganism was isolated. Subsequent CT scans confirmed widespread malignancy.

Discussion: Melanoma accounts for 50–60% of gallbladder metastases at autopsy, but is rarely diagnosed ante-mortem. When symptomatic, the usual clinical presentation is acute cholecystitis. Less frequent initial manifestations include jaundice, chronic non-specific abdominal discomfort, isolated fever, or a sepsis syndrome. The uncommon development of emphysematous cholecystitis should be considered when severe direct or rebound tenderness or sepsis is present or when imaging reveals gas in the gallbladder wall or lumen. CT scan is also useful for visualizing fulminant sequelae of this disorder, including gangrene, perforation, and pericholecystic abscess. The majority of cases are acalculous. In patients with known melanoma, unexplained acute abdominal symptoms or atypical or uncertain gallbladder lesions on imaging studies should prompt consideration of metastatic disease. Acute abdominal complaints may also be the initial clue to undiagnosed cutaneous malignancy. This case underscores the need for clinicians to be alert to the possibility of melanoma metastases masquerading as common abdominal disorders.

Lung cancer infrequently metastasizes to the small bowel (SB). Diagnostic modalities to evaluate SB lesions are not optimal. The advent of wireless capsule endoscopy (WCE) has allowed for more complete investigation of the SB. We present a case of a patient with gastrointestinal bleeding secondary to metastatic squamous cell lung carcinoma that was diagnosed by WCE.

Case: A 65-year-old male presented to the Emergency Department with complaints of dyspnea and weakness for 3 days. He had a remote history of squamous cell lung cancer resulting in a right lobectomy. In addition, he had a prior episode of gastrointestinal bleeding secondary to arteriovenous malformations (A VMs). He currently denied hematemesis, hematochezia or abdominal pain. Medications included valsartan, hydrochlorothiazide and albuterol. He had an 80-pack-year smoking history. Family history was non-contributory. On presentation, blood pressure was 80/50 mm Hg and pulse was 112. Physical exam was significant for a benign abdomen and melena on rectal exam. Laboratory results revealed a hemoglobin of 6.8 g/dL. The remainder of laboratory values including platelets, coagulation profile and comprehensive metabolic panel was normal. Gastric aspirate was devoid of blood. Work-up including endoscopy, colonoscopy, and a bleeding scan were normal. WCE revealed several non-bleeding AVMs throughout the SB and a large polyoid obstructing ulcerated mass with active bleeding. The patient required a total of nine units of blood during his hospitalization. He left against medical advice with a hemoglobin of 8.8 g/dL.

He then presented to the emergency department several days later with continued gastrointestinal bleeding. A small bowel series with follow through revealed a mid SB stricture with pre-stenotic dilation. There was passage of contrast beyond the stricture, indicating a partial SB obstruction; however, the capsule was lodged within the stricture. The patient was subsequently taken for laparotomy and underwent palliative resection. The final pathology confirmed a poorly differentiated squamous cell carcinoma, most likely representing metastatic disease from a lung primary.

Conclusion: Although metastasis to the SB is much more common than primary SB lesions, lung cancer only rarely spreads to the SB. Our case is unique in that it is the first report of a SB tumor from a lung primary diagnosed by WCE. In addition, it also highlights the potential risk of capsule retention requiring surgical intervention.

Metastatic Melanoma of the Gallbladder Presenting as Acute Emphysematous Cholecystitis
Nicole L. Grenier, B.S., Samir A. Shah, M.D., F.A.C.G., Richard Gold, M.D., Edward R. Feller, M.D., F.A.C.G.† Medicine, Brown Medical School, Providence, RI and Diagnostic Imaging, Brown Medical School, Providence, RI.

Symptomatic metastatic melanoma of the gallbladder is rare. Similarly, this tumor is an exceptional cause of acute cholecystitis. We report a patient with acute emphysematous cholecystitis as the presenting feature of metastatic melanoma. This unusual association highlights the need to consider malignancy when evaluating unexplained abdominal complaints in patients with a known history of melanoma.

Case Report: A 77-year-old female with a prior episode of gastrointestinal bleeding secondary to metastatic squamous cell lung carcinoma that was diagnosed by WCE. The gallbladder was a thickened wall without intramural gas. CT scan demonstrated extensive luminal air in a markedly distended gallbladder. An open cholecystectomy was performed. The surgical specimen revealed biliary sludge and a nodule in the wall of the gallbladder protruding into the lumen; the tumor was not obstructing the cystic duct. Pathologic exam showed emphysematous, gangrenous cholecystitis and confirmed that the nodule was a metastatic melanoma. No microorganism was isolated. Subsequent CT scans confirmed widespread malignancy. Clinical presentation is acute cholecystitis. Less frequent initial manifestations include jaundice, chronic non-specific abdominal discomfort, isolated fever, or a sepsis syndrome. The uncommon development of emphysematous cholecystitis should be considered when severe direct or rebound tenderness or sepsis is present or when imaging reveals gas in the gallbladder wall or lumen. CT scan is also useful for visualizing fulminant sequelae of this disorder, including gangrene, perforation, and pericholecystic abscess. The majority of cases are acalculous. In patients with known melanoma, unexplained acute abdominal symptoms or atypical or uncertain gallbladder lesions on imaging studies should prompt consideration of metastatic disease. Acute abdominal complaints may also be the initial clue to undiagnosed cutaneous malignancy. This case underscores the need for clinicians to be alert to the possibility of melanoma metastases masquerading as common abdominal disorders.
A Case of Chron’s Disease Presenting Only as Gastric Outlet Obstruction

Herve C. Boucard, M.D., Weizhong Wang, M.D.* Gastroenterology, UMDNJ-New Jersey Medical School, Newark, NJ.

Crohn’s disease involving the upper GI tract is very rare, representing only 1 to 5% of the cases. The antrum and the duodenal bulb are then the most common affected areas and upper GI Crohn’s disease is usually preceded by lower GI symptoms.

We present the case of a 23-year-old previously healthy male from Ecuador complaining of relentless vomiting and a 45-pound weight loss over the last 3 months. The patient reported emesis of both liquid and solid intakes within 15 to 20 minutes after ingestion, preceded by epigastric discomfort. No abdominal pain, constipation, diarrhea, fever or chills were noted. The patient further denied blood per rectum, history of peptic ulcer disease or family history of IBD. He immigrated into the United States 3 years earlier and denied any travel history since that time. The patient was a non-smoker who reported no sick contacts and no personal history of tuberculosis. Physical examination revealed a cachectic male in no distress. There was no]

Metastatic Adenocarcinoma in a Pregnant 21 Year-Old Survivor of the Kasai Procedure for Congenital Biliary Atresia

William F. Shaheen, M.D., Arthur J. DeCross, M.D.* Digestive and Liver Disease Unit, University of Rochester Medical Center, Rochester, NY.

We describe the complication of metastatic adenocarcinoma, probably cholangiocarcinoma, in a pregnant long-term survivor of a Kasai procedure for congenital biliary atresia. She is the oldest such patient described to date who developed a neoplasm.

Congenital biliary atresia is rare (1:10,000 births), but the prognosis for the untreated condition is poor, with death from liver failure occurring in the first 2 years. Effective treatment has been surgical hepatopancreatoenterostomy, or Kasai procedure, but the usual course after surgery is one of gradual cirrhosis, with the common need for liver transplantation by the second decade. Although rare, tumors including hepatoma and cholangiocarcinoma have been reported in this population. Some patients with the Kasai procedure have survived to reach reproductive age, with successful pregnancy outcomes described.

A 21-year-old female with congenital biliary atresia corrected by Kasai procedure at age 2 months, with known cirrhosis and variceal hemorrhage by age 17 but normal baseline liver function tests, presented at 17 weeks gestation with a 7 week history of nausea, vomiting, jaundice, a bilirubin of 6mg/dl and an AST/ALT of 302/513 U/L. Viral A,B,C, CMV and EBV serologies were negative. She improved on antibiotics for presumed cholangitis and was discharged, but was readmitted 5 days later for intractable emesis. EGD showed trace varices and pyloric stricture in the setting of NSAID use. Stricture balloon dilation was performed, but repeat EGD a week later to assess persistent symptoms revealed a closed, deformed pylorus and a deep, ragged ulcer in a deformed duodenal bulb. Exploratory laparotomy with intended gastrojejunostomy was performed after abdominal CT showed gastric outlet obstruction and an adjacent gas collection concerning for a penetrating ulcer of the outlet. During surgery, multiple omental nodules were seen, revealing metastatic adenocarcinoma with mucinous features, but the origin could not be determined by biopsy. A clinical diagnosis of cholangiocarcinoma was made based on a CA19–9 level of 4746 U/ml, which doubled to 9957 U/ml in 34 days, and the absence of mass or infiltrating disease on the CT scan and endoscopies. We believe the cancer infiltrated from the hepatico-jejunostomy to the gastric outlet. A nonviable fetus was delivered at 24 weeks, but persistent hyperbilirubinemia prevented use of palliative chemotherapy, and she was discharged to outpatient hospice care.
Abstracts

Introduction: Supra-anal neoplasms very close to the dentate line may be technically difficult for endoscopic resection and are frequently referred to surgery. Band ligation may be an option in these cases. We describe band ligation of a large supra-anal rectal polypoid lesion close to the dentate line in a patient who refused surgery.

Case Report: A 60-year-old woman underwent endoscopic mucosal resection of a rectal tubular adenoma with high grade dysplasia, located 1 cm from the dentate line, 7 years ago, and was subsequently lost to follow-up. On a surveillance colonoscopy, local recurrence of a 3 cm rectal polypoid lesion close to the dentate line was noted (Figure 1) – biopsies revealed a hyperplastic polyp. EUS confirmed a mucosal polyp without involvement of the submucosa and muscularis propria. Due to the recurrence of the lesion and a concern of missing underlying dysplasia (although biopsies showed hyperplastic polyp only), surgical resection was suggested, but the patient refused it. After magnification endoscopic confirmation of the benign nature of the lesion based on pit pattern, band ligation was performed on two sessions, 3 bands during the first session and two during the second session 4 weeks later (Figure 2).

Follow-up: Two months later, a small whitish scar was noted; biopsies revealed colonic epithelium. The remaining area appeared normal.

Conclusions: Band ligation may be an option in the management of supra-anal rectal polyps in patients who refuse surgery. Further studies are needed.

575 Eosinophilic Gastroenteritis Presenting as Pyloric Stenosis with EUS Demonstrating Thickened Pyloric Channel
Bhavani Moparty, M.D., Manoop S. Bhutani, M.D., Karen Szauter, M.D.* Internal Medicine, University of Texas Medical Branch, Galveston, TX.

The diagnosis of eosinophilic gastroenteritis is based on clinical history and biopsy findings of more than 20 eosinophils per high power field. We describe a case of eosinophilic gastroenteritis presenting as pyloric stenosis. Endoscopic ultrasound (EUS) was used to aid in assessing the extent of disease and ultimately influenced patient management.

Case: 62 year old woman presented with vomiting solids and liquids immediately after eating. She reported a 40 pound weight loss. Her only medication was sertraline. Physical exam was unremarkable. Laboratory tests including a CBC with differential, electrolytes, liver panel, IgE were normal; stool studies revealed no ova or parasites. Upper endoscopy revealed pyloric stenosis (Figure 1) and dilation to 10mm was done. Biopsies revealed severe chronic antral gastritis with eosinophilia. Helicobacter pylori was not detected. No
eosinophils were noted on small bowel or esophageal biopsies. EUS showed thickening of the pyloric channel wall to 7mm with loss of the five layer echopattern. (Figure 2) The muscularis propria was visible in some areas but persistent improvement in symptoms.

Discussion: Eosinophilic gastroenteritis is generally treated with a short course of steroids. Our patient’s prior episodes of pyloric stenosis had been treated with 4–6 weeks of steroids. The extent of disease was not evaluated due to the patient declining surgical intervention. EUS findings provided us useful information regarding extent of disease, guiding further management.

Introduction: Diarrhea can be one of the initial manifestations of hyperthyroidism however, other important causes of diarrhea such as inflammatory bowel disease should be evaluated in these patients to direct appropriate treatment. We describe a case of diarrhea in a patient with new onset of Graves disease simultaneously with ulcerative colitis and discuss treatment options. We also review and summarize the literature regarding the association of these autoimmune disorders and the proposed shared immunologic mechanisms.

Case: A 32 year-old woman with no prior medical illness presented with complaints of 3 weeks of nausea, vomiting, palpitations, fatigue, and bloody diarrhea. Physical examination revealed a diffuse goiter, exopthalmos, resting tremors, tachycardia, and wide pulse pressure. A diagnosis of hyperthyroidism was made based on above features and elevated free thyroxine (T4 and T3) levels with markedly suppressed thyroid stimulating hormone. Stool studies revealed a neutrophil predominant elevated fecal leukocyte count however cultures were negative. A colonoscopy was performed which revealed erythema and superficial ulcerations extending from rectum to hepatic flexure. Mucosal biopsies from the affected segments, were consistent with inflammatory bowel disease (IBD). Therapy with protonolol and propylthiouracil was initiated for hyperthyroidism and subsequently, prednisone and sulfasalazine were started for inflammatory bowel disease. Patient had a significant improvement in her symptoms prior to discharge.

Discussion: The co-existence of IBD and thyroid disease is uncommon with a prevalence of 0.84–3.7% based on published studies. In most cases, the diagnosis of thyroid disease precedes that of IBD. Although both diseases are classified as autoimmune disorders, the pathogenesis of both while sharing an immunologic basis may not be identical. Several theories have been suggested to explain the concurrent occurrence of both IBD and hyperthyroidism in this small subset of patients including increased Th2 helper T-cell activity secondary to Th1/Th2 imbalance or autoimmunity triggered by cross-reactive microbial antigens. This case serves to emphasize the need to consider inflammatory bowel disease in patients presenting with hyperthyroidism and vice versa, to direct appropriate therapy as both share some common clinical features.

Endoscopic Ultrasound-Guided Transluminal Endovascular Embolization of Visceral Pseudoaneurysms: Case Series

Damien B. Mallat, M.D.,∗ J. D. Meler, M.D., Mathew Lovitt, M.D., Jeffery Lamont, M.D. Gastroenterology, Baylor University Medical Center, Dallas, TX and Surgery, Baylor University Medical Center, Dallas, TX.

Pseudoaneurysms of visceral arteries are serious complications of pancreatic and systemic infections. Rupture of pseudoaneurysms is associated with significant mortality and morbidity. First line therapy includes percutaneous transcatheter embolization. Generally, surgical repair is reserved for patients who failed percutaneous transcatheter embolization. However, surgery has significant morbidity and mortality.

Objective and design: We report a case series of 3 splanchic peripancreatic arterial pseudoaneurysms in 2 patients complicated by retroperitoneal bleeding. Percutaneous transcatheter embolization failed in both patients. Surgical repair was considered to have grave consequences.

Interventions: Endoscopic ultrasound (EUS) guided transluminal endovascular embolization was attempted.

Results: In both patients, pseudoaneurysms were successfully treated with injection of thrombin directly into the pseudoaneurysm lumen. Retroperitoneal bleeding had stopped in all 3 treated pseudoaneurysms. Confirmation of complete and persistent embolization were documented in all 3 cases. No complications were seen several days after therapy. Local recurrence was not seen in any case.

Conclusion: We believe EUS-guided transluminal endovascular embolization is a new frontier in the management of difficult splanchic pseudoaneurym. Larger study is needed to assess this new therapy and its complications.

Acute Liver Failure Due to Natural Killer-Like T-Cell Leukemia/Lymphoma: A Case Report and Review of the Literature

Evan S. Dellow, M.D., Shannon R. Morris, M.D., Wozhan Tang, M.D., Cherie H. Dunphy, M.D., Mark W. Russo, M.D.∗ Medicine, University of North Carolina, Chapel Hill, NC and Pathology, University of North Carolina, Chapel Hill, NC.

We describe an unusual case of a patient who developed acute liver failure (ALF) due to natural killer (NK)-like T-cell leukemia/lymphoma. While case series have found that this malignancy can involve the liver, we believe this is the first report of it presenting as ALF.

A previously healthy 63 year-old man was admitted with 1 month of increasing abdominal girth, 2 weeks of jaundice, and 1 week of confusion. He also noted fatigue, low-grade fevers, and weight loss. He took no medications. Though he had used alcohol heavily in the past, he was sober for more than 10 years. There were no other risk factors for or family history of liver disease. On physical examination he had jaundice, slurred speech, asterixis, moderate ascites, a normal liver size, and splenomegaly.

Routine labs revealed hyponatremia, hypoalbininemia, hyperbilirubinemia, thrombocytopenia, and prolonged INR. The WBC was 5,100 with atypical lymphocytes present. Serologic evaluation for routine causes of liver failure was negative. Abdominal ultrasound showed a normal liver size with heterogeneous echotexture, splenomegaly, ascites, and patent vasculature. Paracentesis revealed a SAAG >1.1, 1,247 RBCs, 1,875 WBCs with 1% neutrophils, 4% monocytes, and 95% lymphocytes with atypical forms. Flow cytometry yielded CD2+, CD3+, CD7+, CD56+, CD4+, CD5+, CD8-, CD57-, CD16- cells. Transjugular liver biopsy revealed diffuse infiltration by a malignant lymphoid population with the same markers present; there was no cirrhosis.

The patient was diagnosed with NK-like T-cell leukemia/lymphoma as the cause of liver failure on hospital day 4. This was a contraindication to liver transplantation. On days 4–6, high-dose methylprednisolone failed to induce remission and his synthetic function and mental status worsened. On days 10–11, a salvage regimen of gemcitabine was unsuccessful. On day 12, neutropenia, fever, and hypotension developed, the patient’s jaundice and encephalopathy progressed, and he expired.
This is the first report of NK-like T-cell leukemia/lymphoma presenting as ALF. This unusual diagnosis was suggested by close attention to abnormal peripheral blood and ascitic fluid differentials. Liver biopsy plays a crucial role when the etiology of liver failure is unknown. Hematologic malignancy is an uncommon cause of ALF, but if present, it is a contraindication to transplant.

First Endoscopic Dilation of a Documented 60 Year Old Stricture: The Legacy of Chevalier Jackson

Chevalier Jackson was a Philadelphia otolaryngologist who pioneered rigid endoscopy and bronchoscopy, and chaired Otolaryngology at Jefferson College in Philadelphia. Deaths among children from foreign body ingestion were common in the early 1900s, and his pioneering endoscopic foreign body removal techniques saved many lives. We present a patient first diagnosed by Chevalier Jackson, who was definitively treated 60 years later. This 69 yo man presented with dysphagia of more than 60 years duration. At age 9, in 1935, while living in Philadelphia, the patient developed aphagia with complete esophageal obstruction, after swallowing a peanut, and underwent rigid esophagascopy by Chevalier Jackson with extraction of a large peanut obstructing the esophagus above a congenital distal esophageal stricture. We have obtained with the help of the American Institute of Otolaryngology, a copy of Chevalier Jackson’s diary confirming the procedure done in December 1935. In 1943 while in the service a barium swallow which also showed a “distal esophageal stricture” (actual report available). 5 years before being seen patient had endoscopy with conscious sedation following a food impaction. He became combative during the procedure and no dilation was done.

Patient first came to us in 1995 with chronic dysphagia. He had not lost weight and his physical examination was normal. Barium swallow showed a tight benign distal esophageal stricture. Endoscopy was undertaken with a 9.8 mm Pentax 2901L endoscope. A 7mm distal stricture was found, and gradually dilated to 12mm diameter with Savary guidewire dilators, without fluoroscopy. Biopsies were benign. His symptoms markedly improved, and he was maintained daily PPI’s. A subsequent endoscopy with Savary dilation to 12 mm was again performed in 2000. He has been asymptomatic since. We present one of the few still living patients of Chevalier Jackson, a pioneering endoscopist with a stricture that he diagnosed, but which was not treated until 60 years later. Copy of Chevalier Jackson’s foreign body diary will be presented on the poster courtesy of: Tracy L. Sullivan –Director, The John Q. Adams Center for the History of Otolaryngology–Head and Neck Surgery American Academy of Otolaryngology.

A Rare Case of Rapunzel’s Syndrome (Trichobezoar)

A 29 year old African American female presented to the ER complaining of progressively worsening epigastric pain and N/V over a three month period. She was previously healthy and her physical examination was normal. A CT scan of the abdomen showed only a large volume of retained gastric contents. She was admitted to the surgery service for suspected gallbladder disease. Further evaluation showed evidence of biliary sludge and a gallbladder EF of 30%. A gastroenterology consultation was obtained to exclude other potential GI related disorders prior to planned laparoscopic cholecystectomy. Upper Endoscopy showed a large trichobezoar extending from the gastrosophageal junction, filling the entire lumen of the stomach, and extending to the second portion of the duodenum. An overtube and foreign body forceps were utilized in an attempt to remove the trichobezoar, but was unsuccessful due to its size. The trichobezoar was subsequently removed surgically and the patient made an uneventful recovery. It measured 25 cm by 15 cm with a 15 cm duodenal tail (Figures 1 and 2).

Trichobezoars are rarely encountered in adult gastroenterology practice. They are formed by swallowed hair (trichophagia). Trichotillomania and trichophagia result from an underlying psychiatric disorder. Most cases are discovered in the pediatric population. Hair material is not digested by the stomach and tends to tangle rapidly forming a bezoar. When the trichobezoar extends beyond the stomach into the small intestine, it is referred to as Rapunzel’s Syndrome.

Options are very limited for endoscopic removal. Small trichobezoars have been removed with the aid of various forceps and Nd:YAG laser. Larger trichobezoars are better approached surgically, and carry a low morbidity.
Duodenal Varices: A Rare Manifestation of Portal Hypertension


Duodenal varices are a rare but potentially serious consequence of portal hypertension in the event of a bleed. We report two patients with duodenal varices secondary to portal hypertension.

The first is a 19-year-old female with significant portal hypertension with cavernous transformation of the portal vein secondary to portal vein thrombosis acquired as a child following umbilical vein cannulation. Multiple esophageal varices, a small fundal varix and a solitary post-bulbar duodenal varix approximately 2 cm in diameter were noted at endoscopy. The esophageal varices were successfully obliterated by band ligation after a total of seven sessions and she is on a beta-blocker. The size of duodenal varix was unchanged at follow up endoscopies. Abdominal CT also demonstrated several large intraabdominal varices (mesenteric and splanchnic) not visible at endoscopy. The second patient was a 56-year-old gentleman with severe coronary artery disease and decompensated liver disease with portal and splenic vein thrombosis. He presented with an episode of severe upper gastrointestinal bleeding and was found at endoscopy to have large duodenal varices. He underwent a mesocaval shunt that successfully controlled the bleeding but he died several days post-operatively due to a cardiac event.

Two-thirds of all reported cases of duodenal varices have portal venous hypertension caused by hepatic cirrhosis. In the remaining one-third, prehepatic portal hypertension as a consequence of either a compromised portal venous circulation (portal vein thrombosis) or a primary hematological disease is the underlying cause. There is currently no consensus with regards to management and very little evidence on which to base clinical decision-making. Isolated case reports have reported treatment of active hemorrhage with endoscopic sclerotherapy (i.e. injection of sclerosant or band ligation) whereas others have reported treatment with decompressive shunting. We note that there is no reported literature on prophylaxis of patients who have yet to have a bleed. A review of the literature and possible management strategies will be discussed.

Ischemic Colitis Following Use of Tegaserod (Zelnorm) in a Patient with Narcotic-Induced Gastroparesis

Nazir A. Rahim, M.D., Erina Foster, M.D., Walter Trudeau, M.D.* Gastroenterology, UC Davis Medical Center, Sacramento, CA.

Background: Rare cases of ischemic colitis have been reported following use of tegaserod (Zelnorm), primarily in females with underlying irritable bowel syndrome (IBS). The occurrence of ischemic colitis in non-IBS subjects has not been previously reported.

Aim: To present a case of tegaserod-induced ischemic colitis in a non-IBS subject treated with tegaserod for narcotic-induced gastroparesis.

Case: A 40 y.o. white female (non-diabetic, non-smoker and non-IBS) with gastroparesis due to narcotics presented with 2-week history of worsening left, lower quadrant abdominal pain, fever and bright red blood per rectum. She had been taking tegaserod 6 mg twice daily for 6 months with good control of her gastroparesis without any significant adverse effects due to tegaserod. Colonoscopy was performed and revealed multiple ulcers extending from the descending colon to the transverse colon, consistent with ischemic colitis. Histopathologic evaluation revealed acute ischemic changes consistent with ischemic colitis. Laboratory evaluation was negative for bacterial or protozoal stool infection, including Clostridium difficile. Tegaserod was discontinued and the patient had resolution of her symptoms. Repeat colonoscopy performed six weeks later revealed normal colon examination.

Conclusion: Ischemic colitis should be suspected and sought for in non-IBS patients taking tegaserod.

Was It a Case of “Crying Wolf Too Many Times”?

Muhannad M. Heif, M.D., Amar Al-Jaburi, M.D.* Geriatrics and Gastroenterology, Central Arkansas Veterans Healthcare System, Little Rock, AR.

67 year old man presented to the urgent outpatient clinic with one month history of diffuse colicky postprandial abdominal pain radiating to the back. The pain was severe and associated with nausea but no vomiting. The patient also reported chills but no fever. He was seen four times in the emergency department and the outpatient clinic over the 1 month period for the same complaint. Laxatives, proton pump inhibitor and antacids were prescribed but didn’t help. His past medical history is significant for hypertension, hyperlipidemia, gastroesophageal reflux disease and severe chronic back pain with only mild degenerative disc disease. Suspicion of drug seeking behavior was mentioned several times in his record. Patient denied using any illicit drugs.

On physical examination, he was afebrile and had normal vital signs. Abdominal exam was significant for epigastric tenderness with no rebound. The rest of the exam was unremarkable. Lab tests including metabolic profile, complete blood count, amylase, lipase and liver enzymes were all within normal limits. The patient was admitted to the hospital for observation and further work up. His condition continued to deteriorate and a CT scan few hours after admission showed extensive mesenteric, portal and splenic veins thrombosis with possible bowel infarction. Exploratory laparotomy confirmed the presence of infracted small bowel and the extensive mesenteric venous thrombosis. Extensive investigations for determining the etiology of his pro-thrombotic event were unrevealing. The patient gradually improved and was discharged after several weeks on Warfarin with diagnosis of idiopathic mesenteric, portal and splenic venous thrombosis.

The most common cause of mesenteric venous thrombosis is inherited thrombophilic, other risk factors include portal hypertension, abdominal infections, blunt abdominal trauma, pancreatitis, and malignancy in the portal region.

The hallmark of mesenteric ischemia is abdominal pain that is not explained by the physical findings. Mesenteric venous thrombosis is a rare cause of intestinal ischemia. These factors makes it difficult to be diagnosed early especially in the patient with history of drug seeking behavior. High index of suspicion and thorough investigation are important in diagnosing mesenteric vein thrombosis.

Esophageal Pseudopolyps a Unique Endoscopic Finding in Patient with Active Crohn’s Disease

Raffat Jabar, M.D., Geoffrey Gardiner, M.D., David S. Condon, M.D.* Medicine, Division of Gastroenterology, Loma Linda University, Loma Linda, CA.

Purpose: Esophageal pseudopolyps: a unique endoscopic finding in a patient with active crohn’s disease.

Background: Crohn’s disease with esophageal involvement is uncommon. Reported esophageal manifestations include erythema and friability, aphthoid and deep ulcerations, strictures, fistulas and nodular masses. We report a case of Crohn’s disease with esophageal pseudopolyps. To our knowledge, there are only two other cases of esophageal polyposis in patients with active Crohn’s disease and neither case reported pseudopolyps.
Case Report: A 53 year old male with known history of Crohn’s disease was referred to us for EGD evaluation of abnormal esophagogram with a concern for distal esophageal masses. The patient was diagnosed with Crohn’s disease in 1973. More recently he underwent a total abdominal colectomy for multiple fistulae and intra-abdominal abscess. At the time of endoscopy he was complaining of dysphagia, odynophagia, nausea and vomiting and diarrhea. He was currently taking mesalamine and 6MP. The EGD showed what appeared to be extensive pseudopolyp formation in the distal esophagus and two areas possible developing fistula tracts without active inflammation or ulceration and Schatzki’s ring were also present. Biopsies revealed benign squamous mucosa with mild basal cell hyperplasia, focal hemorrhage and mixed leukocytes, including eosinophils. No granulomas were found. Patient presented several weeks later with nausea, vomiting and was found to have partial small bowel obstruction on CT scan. Symptoms improved with prednisone.

Conclusion: Esophageal Pseudopolyposis is a rare manifestation of Crohn’s disease. Crohn’s disease should also be considered in the differential diagnosis of esophageal polyposis.

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Ovarian Mature Teratoma Presenting as a Rectal Mass; Report of a Case
Masahiro Iwabuchi, M.D., Nobuo Hiwataishi, M.D.,∗ Mikako Sugimura, M.D., Hiroki Takahashi, M.D., Ken Saijo, M.D., Kenji Kimura, M.D., Yutaka Mano, M.D., Nobukazu Tanabe, M.D., Kenji Noguchi, M.D., Motoki Oyauchi, M.D., Hiromichi Ito, M.D., Osamu Kimura, M.D., Satoshi Awabuchi, M.D., Satoko Sato, M.D., Katsutoshi Shiozuka, M.D., Gen Yumone, M.D., Kazutsugu Iwamoto, M.D., Toshiihoro Saito, M.D., Hiroshi Suzuki, M.D., Nobuyuki Chida, M.D. Gastroenterology, Sendai Medical Center; Sendai, Miyagi, Japan; Surgery, Sendai Medical Center; Sendai, Miyagi, Japan; Pathology, Sendai Medical Center, Sendai, Miyagi, Japan; and Gastroenterology, Iwaki Municipal Hospital, Iwaki, Fukushima, Japan.

We present a rare case of ovarian mature teratoma ruptured into the rectum. The case was a 39 year-old woman who presented with a symptom of rectal bleeding. Colonoscopy revealed a diverticulum-like structure in the rectum. The structure measuring approximately 1.5cm in diameter, was filled with a lot of hairs. Inside of that was covered with skin-like component. Biopsy specimen from the lesion revealed squamous cell with no malignancy. After barium enema and the abdominal computed tomography examination, she was diagnosed as an ovarian teratoma ruptured into the rectum. Laparoscopy-assisted anterior resection of the rectum and right salpingo-oophorectomy were undergone. Macroscopically, a lot of hairs were found in the cystic mass in the right ovary. In the cut surface of the surgical specimen, cystic tumor measuring 3.5 cm in diameter, located adjacent both to the rectal wall and the right ovary. In addition, the tumor tightly adhered to the rectal wall and made the fistula with the rectal mucosal surface. Histopathologically, inside of the tumor was covered with squamous epithelium, contained adipose tissue, cutaneous appendage, and mature omentum. In this case, it was suggested that a mature teratoma arising from the right ovary perforated to the rectum. This type of complication for benign ovarian teratoma is thought to be unusual and the possible mechanisms of rectal perforation by this teratoma will be discussed herein.

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Eosinophilic Proctocolitis in 3-Months Japanese Infant; Report of a Case
Masahiro Iwabuchi, M.D., Nobuo Hiwataishi, M.D.,∗ Kenji Kimura, M.D., Mikako Sugimura, M.D., Hiroki Takehashi, M.D., Kenji Noguchi, M.D., Motoki Oyauchi, M.D., Nobukazu Tanabe, M.D., Yutaka Mano, M.D., Satoshi Awabuchi, M.D., Hiromichi Ito, M.D., Osamu Kimura, M.D., Ken Saijo, M.D., Koji Watanabe, M.D., Yusaku Tazawa, M.D., Hiroshi Suzuki, M.D., Sho Takagi, M.D., Nobuyuki Chida, M.D. Gastroenterology, Sendai Medical Center, Sendai, Miyagi, Japan; Pediatrics, Sendai Medical Center, Sendai, Miyagi, Japan; Pathology, Sendai Medical Center, Sendai, Miyagi, Japan; Gastroenterology, Iwaki Municipal Hospital, Iwaki, Fukushima, Japan and Gastroenterology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan.

The food-induced eosinophilic proctocolitis is one of major causes of bloodtinged stools in early infancy in Western countries, whereas that is still rare in Japan here. We present a case of eosinophilic proctocolitis showing characteristic findings in Japanese 3-month-old male infant. He was a 3-month-old infant who had presented with rectal bleeding since 1-month-old. He was a breast-fed infant. Laboratory test showed hypereosinophilia (eosinophils:20%) and mild anemia (hemoglobin concentration :11.3g/dl). Bacterial, viral, and parasitic infection was excluded. Colonoscopy revealed inflammation with reddishness and severe edema in the rectum and the lower sigmoid colon. Biopsy specimen from the rectum showed diffuse infiltration of eosinophils in the lamina propria. Therefore, he was diagnosed as an eosinophilic proctocolitis. After the elimination of his mother’s milk, he was released from rectal bleeding soon.
This appeared to be a rare case of eosinophilic proctocolitis in Japanese 3-month-old infant caused by mother’s milk.

### Abnormal LFTs in a 25 Year-Old Female with Ovarian Hyperstimulation Syndrome

**Bradford C. Sampson, M.D., Ashok N. Shah, M.D.**
**University of Rochester Medical Center, Rochester, NY.**

Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication associated with in vitro fertilization, typically with the use of exogenous gonadotrophins. Although abnormal LFTs occur in up to 30% of severe cases, it is rarely cited as a cause of LFT abnormalities in the GI literature. A 25 year-old female who 4 weeks into pregnancy with one week of nausea, vomiting, and inability to tolerate solids. She had been treated for infertility with bromocriptine and injectable FSH. Four days prior to admission she noted increased abdominal distention and pain. An outpatient ultrasound had shown moderate ascites and enlarged ovaries with large follicular cysts. There was no personal or family history of liver disease. She denied any alcohol use. Her medications on admission were prenatal vitamins, vaginal progesterone, and prn Zofran. Outpatient labs were significant for AST 65u/l and ALT 64u/l with an albumin of 2.5g/dl and normal bilirubin and alkaline phosphatase. Her AST and ALT climbed to 125u/l and 117u/l respectively, and the GI consult service was called to evaluate her transaminitis. On exam, her abdomen was soft and mildly distended with normal bowel sounds and mild, diffuse tenderness that was somewhat worse in the epigastric area. A viral hepatitis panel was normal and the patient’s symptoms improved with bromocriptine and injectable FSH. Repeat LFTs one month later were completely normal. She remained asymptomatic and was later found to be multi-gravid with 4 embryos.

OHSS has a spectrum of symptoms ranging from asymptomatic lab abnormalities and enlarged ovaries to pronounced capillary leak with ascites, ARDS, hypotension, and hypercoagulability. Prevalence of moderate to severe symptoms ranges from 1–10% at major IVF programs. Pathogenesis is poorly understood but thought to be secondary to capillary leak related to a variety of hormones and cytokines released after overstimulation of the ovaries with the use of infertility medications. Symptoms typically begin as a bloated sensation proceeding to nausea, vomiting, and diarrhea. Management is supportive and resolution of symptoms follows decline in serum hCG levels, typically about 7 days in non-pregnant patients and 10–20 days in pregnant patients.

This is a typical presentation and clinical course of moderate OHSS. Gastroenterologists should be aware of this condition as a cause of abnormal LFTs and be aware of the potential for life threatening complications.

### Neurofibromatosis of the GI Tract: An Unusual Presentation

**Suresh G. Jayatilaka, M.D., Kiran Jagarlamudi, M.D., Ziad Salem, M.D., Bradford C. Sampson, M.D., Ashok N. Shah, M.D.**
**Gastroenterology, University of Rochester Medical Center, Rochester, NY.**

Neurofibromas are benign peripheral nerve tumors composed of proliferating schwann cells and fibroblasts. Approximately 25% of patients with Von Recklinghausen’s disease have neurofibromatous involvement of the upper digestive tract with multiple submucosal neurofibromas or less commonly ganglioneuromas, which may cause dyspepsia, abdominal pain or hemorrhage.

**Case Report:** A 78 year-old female with history of Neurofibromatosis type 1 since childhood and hypertension presented with epigastric and peri-umbilical pain associated with poor appetite and a 15lb weight loss over the last three months. Physical examination was remarkable for multiple skin neurofibromas. Her medications included metoprolol and rabeprazole. Laboratory studies revealed a microcytic anemia with a hemoglobin of 10.9 g/dL. An upper endoscopy showed mild gastritis. A colonoscopy demonstrated diverticulosis and angiodysplasia of the right colon, which could not explain the weight loss. A CT scan of the abdomen was then done which showed thickening of the wall of the distal ileum. The patient subsequently underwent a capsule endoscopy, which revealed multiple polyloid, ulcerated, fungating lesions in the terminal ileum. The patient was then referred for surgical resection. The pathological specimen demonstrated hamartomatous vascular polyps related to neurofibromatosis in the small intestine. The patient had a benign post-intervention course.

### Management of Radiation-Induced Complete Esophageal Obstruction with a Concurrent Antegrade-Retrograde Endoscopic Rendezvous Technique

**John T. Maple, D.O., Bret T. Petersen, M.D., Todd H. Baron, M.D., Jan L. Kasperbauer, M.D., Mark V. Larson, M.D., Louis M. Wong Kee Song, M.D.**
**Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN and Otorhinolaryngology, Mayo Clinic College of Medicine, Rochester, MN.**

**Abstract:** The gastrointestinal involvement in neurofibromatosis is usually incidental and asymptomatic. Our patient demonstrates the first documented case of hamartomatous vascular polyps seen with neurofibromatosis and visualized by capsule endoscopy.

**Conclusion:** The gastrointestinal involvement in neurofibromatosis is usually incidental and asymptomatic. Our patient demonstrates the first documented case of hamartomatous vascular polyps seen with neurofibromatosis and visualized by capsule endoscopy.
Background: Esophageal strictures occur in 3–4% of patients with head and neck cancer who undergo radiation therapy. Some of these patients develop complete obstruction of the upper esophagus. Antegrade dilatation is often unsuccessful and many of these patients require surgery.

Case presentations: We report use of the antegrade-retrograde endoscopic ‘rendezvous’ technique to restore esophageal patency in 7 patients with complete upper esophageal obstruction from radiation injury. The procedural steps include: dilation of an existing gastrostomy tract to facilitate transgastric retrograde endoscopy of the esophagus; concurrent exam of the pharynx and upper esophagus with either laryngoscopy or a 2nd flexible endoscope by a second physician; alignment of instruments on either side of the obstructing stricture using direct vision and fluoroscopy; blunt dissection through the obstructing tissue using a guidewire and cannula; wire-guided stricture dilation using either balloon or bougie dilators; and finally, placement of a nasogastric tube until serial dilations provide persistent patency.

All 7 patients had a laryngeal or pharyngeal carcinoma treated with primary or adjuvant external beam radiation; 6 of the patients were men, and the mean age was 64. The median interval between radiation and the rendezvous procedure was 6 months (range 2–24). In patients in whom the information was available, 5/5 suffered significant acute esophageal radiation toxicity. In our hands, this technique was successful in 6/7 cases and no significant adverse events occurred. Variations in the technical aspects of this procedure are also discussed, as are clinical factors that predict late esophageal toxicity in patients undergoing radiation treatment for nearby malignancies.

Discussion: In summary, an antegrade-retrograde rendezvous technique with subsequent dilation appears to be safe and effective for endoscopic management of complete upper esophageal obstruction induced by radiotherapy, and can obviate the need for esophageal resection. A team approach involving the head and neck surgeon, gastroenterologist, radiation oncologist, speech pathologist, and dietician is recommended in the management of the swallowing and nutritional needs of these complicated patients.

Successful Treatment of Uncontrollable Eructation with Pimozide
Alexander R. Spitzer, M.D., Ann L. Silverman, M.D.* Neurology, Wayne State University, Detroit, MI and Gastroenterology, Henry Ford Health System, Detroit, MI.

Chronic eructation is a common symptom of esophageal reflux caused by the release of swallowed air after gastric distention and the reduction of lower esophageal sphincter pressure. While esophageal reflux is the most common cause of burping, voluntary or involuntary aerophagia will also lead to chronic burping. Pimozide is an antipsychotic approved for treatment of severe Tourette's syndrome that selectively antagonizes dopamine D2 receptors. Tourette's syndrome is a disorder characterized by involuntary motor and vocal movements (tics).

We report the successful treatment of chronic eructation with pimozide. A 57-year old man had a history of chronic regurgitation and bloating with abnormal uncontrolled facial movements and vocalizations. A 54-year old female had back surgery and subsequently noted the development of uncontrollable eructation. Abrupt uncontrollable diaphragmatic movements were noted on examination. Both patients underwent an extensive evaluation for presumed esophageal reflux including EGD and empiric treatment with high dose PPI and prokinetic drugs without improvement. A neurologic consultation was obtained, and pimozide was started in each patient after a clinical diagnosis of tic disorder was made. Abnormal movements dramatically decreased and uncontrollable eructation ceased in both cases after treatment. An underlying movement disorder should be considered as the etiology of uncontrolled aerophagia and eructation unresponsive to treatment of gastroesophageal reflux. These cases suggest that refractory eructation may represent a manifestation of a tic disorder. In such cases, pimozide provides a novel treatment option.

Primary Amyloidosis Presenting as Mental Status Changes, Acute Liver Failure and Hemoperitoneum
Agata A. Bednarz-Volk, M.D., Anna Lok, M.D.* Division of Gastroenterology, Department of Internal Medicine, University of Michigan, Ann Arbor, MI.

Gastrointestinal involvement appears to be rare in primary amyloidosis, with biopsy proven disease and clinically apparent disease occurring in only 8 and 1 percent of patients, respectively, based Mayo Clinic data. Hepatic involvement is much more common, being seen in 70 percent of patients, although it is seldom associated with significant clinical manifestations. We present a case of a primary amyloidosis presenting as mental status changes, acute liver failure and hemoperitoneum. The patient was a 58 year old female who initially presented to an outside hospital with fatigue, weight loss, and easy bruising. The work-up revealed anemia and monoclonal gammapathy of undetermined significance. She underwent a bone marrow biopsy, which excluded multiple myeloma. She was readmitted two months later with worsening mental status and diffuse abdominal pain.

Upon transfer to our institution, she was confused and jaundiced. On physical examination she had multiple spider angiomata and a tender abdomen with ascites and hepatomegaly. She was intubated for airway protection. The ascites were tapped revealing hemorrhagic polymicrobial peritonitis. Her liver function tests were cholestatic with alkaline phosphatase in the range of 700s, total bilirubin in the 20s and AST and ALT in the 200s. She also had coagulopathy, hemolytic anemia, sepsis, and acute renal failure. Based on these findings a bowel perforation was suspected but not confirmed on tomograms. An abdominal CT showed hemorrhagic ascites with a 10 cm hematoma intimately related to the branches of the celiac artery. There were also changes concerning for splenic artery pseudo-aneurysms. Vasculitis work-up including an angiogram prompted by these pseudoaneurysms was negative. Finally, re-evaluation of outside bone marrow biopsy with Congo red stains, showed primary amyloidosis. The patient continued to deteriorate despite maximal support and eventually her family decided to withdraw care. On autopsy, primary amyloidosis involving the liver, spleen, gut, lungs, heart, kidneys, adrenal glands, lymph nodes, and bone marrow was found. In retrospect, had the diagnosis been made in October by evaluating the bone marrow with amyloid stains, the patient could have been offered high dose melphalan therapy and a stem-cell transplant. The learning point for a gastroenterologist is to have a high index of suspicion for amyloidosis in cases of anemia and monoclonal gammapathy as well as liver function abnormalities.

Pulmonary Eosinophilia Associated with Infliximab Treatment of Crohn's Disease
David T. Rubin, M.D., Sunana Sohi, M.D., Rebecca Shilling, M.D., Steven White, M.D. Gastroenterology, University of Chicago, Chicago, IL; Medicine, University of Chicago and Pulmonary and Critical Care Medicine, University of Chicago.

An 18-year-old woman with a history of asthma and Crohn's disease of the terminal ileum and colon with prior perirectal abscess presented with 2 days of sore throat, fever, and dyspnea with non-productive cough. Her Crohn's disease had been treated with three doses of infliximab 5mg/kg (weeks 0, 2, and 6) with concomitant azathioprine, and her symptoms developed approximately 2 weeks after the third dose of infliximab. Pre-treatment PPD was negative. She received empiric treatment with ciprofloxacin, but a subsequent chest radiograph demonstrated bibasilar infiltrates, so therapy was changed to ceftriaxone and azithromycin for presumed community-acquired pneumonia, without relief.

Peripheral blood smear showed a new marked eosinophilia (29%), and a chest CT scan revealed a diffuse patchy nodular infiltrate in all lung fields.
Clinicians should consider pulmonary eosinophilia in the differential diagnosis. It is unclear what role her coexistent asthma may have played. This represents a unique reaction to infliximab therapy, rather than idiopathic improvement after the therapy cleared from her system, is suggestive that pulmonary eosinophilia in relation to the infliximab, as well as the dramatic pleural effusion, and pulmonary edema. In this case, the timing of the pulmonary eosinophilia is consistent with the infliximab, rather than idiopathic chronic eosinophilic pneumonia, which requires longer therapy with corticosteroids. It is unclear what role her coexistent asthma may have played. Clinicians should consider pulmonary eosinophilia in the differential diagnosis of patients receiving infliximab who develop pulmonary infiltrates with dyspnea in this setting.

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Oropharyngeal Dysphagia in a Patient with the LEOPARD Syndrome and the Chiari I Malformation. Is There More Than a Fortuitous Connection?

David M. Manuel, M.D., Jonathan P Pezanoski, M.D., Randall Jacobs, M.D., Luis C. Maas, M.D.* Gastroenterology, Providence Hospital, Southfield, MI.

LEOPARD Syndrome is an unusual medical condition characterized by abnormalities of the skin, the heart, the craniofacial area, and/or the genitalia. We describe a patient with this condition who presented with oropharyngeal dysfunction that was discovered to be secondary to a Chiari I malformation. A 31-year-old male patient complained of dysphagia resulting in weight loss. He was admitted for aspiration pneumonia confirmed by chest radiograph. The patient was diagnosed with the LEOPARD syndrome years earlier. His physical exam was significant for low set ears, normal gag reflex, dysconjugate nystagmus, and multiple lentigines scattered diffusely over his skin. A modified barium swallow demonstrated reduced epiglottic movement, stasis in the vallecula and piriform sinuses, and a moderate amount of aspiration, therefore a gastrostomy tube was placed for nutrition. MRI of the brain and cervical spine revealed herniation of the cerebellar tonsils with mass effect on the posterior proximal cervical spinal cord consistent with Arnold-Chiari I malformation. The patient underwent posterior fossa decompression with duraplasty. A repeat modified barium swallow test was normal four days after decompression.

LEOPARD syndrome is a dysmorphogenic disorder of variable penetrance and expressivity. LEOPARD is an acronym that recalls the distinctive features seen in this disorder: (L)entigines, multiple hyperpigmented skin lesions; (E)lectrocardiographic conduction defects; (P)ulmonary stenosis; (O)varian cysts; (A)rterial hypertension; and (R)etarded growth; and (D)ystrophy. The presence of all findings is not required for a diagnosis. Most patients are asymptomatic, but obstructive cardiomyopathy and cardiac dysrhythmias may cause death in some. Neurological conditions described in this syndrome include mental retardation, sensorineural hearing loss, seizures, nystagmus, and dysphagia. Symptoms, such as headache or dysphagia, in patients with the Chiari I Malformation may develop slowly. MRI is the most reliable means for diagnoses. A similar patient with these two syndromes has been previously reported. LEOPARD syndrome is a rare condition with protein manifestations. Besides careful cardiac evaluation and proper genetic counseling, these patients should have periodic neurological evaluations. Chiari 1 malformations may be seen in patients with LEOPARD syndrome.

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Sclerosing Cholangitis Associated with Autoimmune Pancreatitis: An Unusual Origin of Obstructive Jaundice

Soujanya Chava, M.D.*, John J. O'Brien, M.D., Rhonda Purdy, NP Gastroenterology and Hepatology, Creighton University Medical Center, Omaha, NE.

Background: Autoimmune Pancreatitis (AIP) can be found in association with other autoimmune processes such as Sclerosing Cholangitis (SC). The most characteristic laboratory finding is an elevated serum IgG4 level. A key feature of the illness is a good response to oral corticosteroids.

Case Report: A 52-year-old Caucasian male presented with obstructive jaundice associated with pruritus. A previous outside evaluation including Magnetic Resonance Cholangiopancreatography (MRCP), abdominal CT scan and Endoscopic Retrograde Cholangiopancreatography (ERCP) demonstrated a distal common bile duct stricture and a suspicious lesion in the head of the pancreas. Biopsies of the pancreatic lesion were consistent with inflammation and negative for malignancy. Since malignancies can sometimes be associated with para-inflammatory response, carcinoma of the head of the pancreas could not be ruled out. At surgery, the anatomy was not consistent with carcinoma of the head of the pancreas. Therefore, the operation was modified to a choledochojejunostomy and choledochoduodenostomy. Frozen and permanent section biopsies of the pancreas revealed a diffuse fibrotic process with chronic inflammatory changes, but no evidence of malignancy. Therefore the patient was given the diagnosis of chronic pancreatitis. Postoperatively, the patient developed recurrent episodes of jaundice. The patient subsequently had multiple percutaneous transhepatic cholangiographic (PTC) interventions with drain placement. The PTC procedures demonstrated diffuse sclerosis of both intra- and extra-hepatic biliary ducts. Primary sclerosing cholangitis (PSC) was suspected, however, a liver biopsy did not confirm PSC. A colonoscopy ruled out Inflammatory Bowel Disease. Serological markers including Perinuclear-Antineutrophil Cytoplasmic Antibody, Anti Nuclear Antibody, anti-smooth muscle antibody were negative. However, IgG4 level was significantly elevated which was consistent with AIP. The patient subsequently had a course of corticosteroids and did well. It has been previously known that there is an increased association of pancreatitis (10–25%) with sclerosing cholangitis. This case report supports the conclusion that although AIP with SC and PSC have similar cholangiographic appearance, the former responds well to corticosteroid therapy. A pancreatic biopsy supported by elevated serum IgG 4 levels is necessary for the diagnosis.

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Idiopathic Hyperammonemia in a Cardiac Transplant Patient

Bradford C. Samspon, M.D., Arthur J. DeCross, M.D.* Gastroenterology, University of Rochester Medical Center, Rochester, NY.

This is the first report of idiopathic hyperammonemia (IHA) in a cardiac transplant patient. IHA has been a recognized, yet unexplained, uncommon complication of lung and bone marrow transplant (BMT), and has also been described in 2 heart-lung transplant patients. A 40-year-old woman was found to be hyperammonemic when evaluated for lorazepam-resistant seizures which developed 19 days after a heart transplant for the sequelae of Tetralogy of Fallot. She never received valproate. She had no significant history of alcohol use, clinical risk factors or family history of liver disease. She was on hemodialysis for post-operative renal failure, and remained on a ventilator. On exam, there was no evidence of acute or chronic liver disease. Abdominal ultrasound confirmed a normal liver and
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**Acute Bacterial Endocarditis in a Patient with Purulent Complications of Crohn’s Disease**

Manishkumar Patel, M.D., Nadia Trigg, M.D., Charles Berkelhammer, M.D.* Internal Medicine, University of Illinois, Oak Lawn, IL and Gastroenterology, University of Illinois, Oak Lawn, IL.

**Introduction:** Endocarditis has been rarely associated with Crohn’s disease. We describe a patient with Crohn’s disease who developed acute bacterial endocarditis.

**Case:** A 56-year-old white female with a history of steroid dependent Crohn’s colitis and poor adherence to medical therapy and follow up presented with acute onset of pain in both feet as well as left lower quadrant abdominal discomfort. On physical exam both feet were cold, pale and pulseless. There was tenderness in the left lower quadrant. Doppler ultrasound demonstrated emboli in both iliac arteries. Emergent embolectomy was performed. Gram stain revealed gram-positive cocci within the emboli. Multiple blood cultures were positive for Enterococcus fecalis. A 2-D Echocardiogram showed mitral valve vegetations and mitral regurgitation. CT scan of abdomen revealed a left lower quadrant abscess in continuity with the left colon. She was treated with colectomy and diverting colostomy, a six-week course of intravenous antibiotics and ultimately mitral valve replacement. Her steroids were tapered and discontinued.

**Discussion:** Patients with Crohn’s disease are at risk for purulent complications. They may be immunosuppressed with agents such as steroids, anti-TNF agents and immunomodulators. There have only been a few case reports of endocarditis complicating Crohn’s disease. This case highlights the importance of optimal management and, if possible, prevention of purulent manifestations of Crohn’s disease to prevent additional septic complications, including infective endocarditis.

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**Colonoscopy Bowel Preparation in Patients with Long QT Syndrome**

Manishkumar Patel, M.D., Nadia Trigg, M.D., T. Petropulos, M.D., Charles Berkelhammer, M.D.* Internal Medicine, University of Illinois, Oak Lawn, IL; Cardiology, University of Illinois, Oak Lawn, IL and Gastroenterology, University of Illinois, Oak Lawn, IL.

**Introduction:** Patients with long QT syndrome are at risk for sudden death from arrhythmias. Colonoscopy bowel preparation is known to occasionally cause changes in serum electrolytes, magnesium and calcium. Hypokalemia and hypomagnesemia can prolong QT interval and can lead to life threatening arrhythmias and sudden cardiac death in patients with long QT syndrome.

**Case:** A 44-year-old female with family history of colon cancer requested colonoscopic screening. She had a history of congenital long QT syndrome and had refused implantable cardiac defibrillator. Her baseline serum electrolytes and magnesium levels were normal. Baseline EKG showed a QTc interval of 488 msec. The patient was given sodium phosphate bowel preparation, 45 ml the evening before and 45 ml on the morning of colonoscopy. After colonoscopy preparation her potassium was 3.2 mmol/L and magnesium was 1.6 mg/dl. EKG showed that her QTc interval had increased to 500 msec. She was asymptomatic and cardiac monitoring did not reveal any arrhythmias. She was repleted with intravenous and oral potassium and magnesium. Colonoscopy was performed without any adverse effects.

**Discussion:** Although this patient suffered no adverse consequences this case highlights the importance of avoiding hypokalemia and hypomagnesemia during colonoscopy bowel preparation in patients with long QT syndrome. Options to consider in such patients would be to supplement potassium and magnesium during bowel preparation or to use a magnesium containing bowel preparation.∗


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**Endoscopy-Assisted Placement of a Metallic Stent in a Patient with Crohn’s Disease Presenting with Recurrent Benign Intestinal Strictures**

Roberto M. Gamarra, M.D., Tal Hazan, M.D., Jonathan Pezanoski, M.D., Omar Kadro, M.D., Luis C. Maas, M.D.* Department of Gastroenterology, Providence Hospital, Southfield, MI and Department of Gastroenterology, William Beaumont Hospital, Southfield, MI.

Fibrotic (non-inflammatory) stricture occurrence is common in Crohn’s Disease (CD). Endoscopic placement of metallic stents has been tried as an alternative to surgery. However, the available literature and experience with this technique is limited. This report illustrates a patient with recurrent, post-surgical symptomatic strictures secondary to CD who underwent an endoscopic placement of a metallic stent. The patient is a 51-year-old Caucasian male with history of CD who underwent previous resections for recurrent distal small bowel strictures. Despite medical therapy, strictureplasty was necessary to relieve recurrent obstrusive symptoms that developed as a result of a new stenosis at the site of the ileocolonic anastomosis. Failure of that therapy led to repeated endoscopy-assisted balloon dilations all of which were ineffective. The patient ultimately underwent endoscopy-assisted placement of a metallic stent, which has proved successful in preventing recurrence of his symptoms over the last 36 months.

Although active inflammatory strictures in CD can be treated medically, fibrotic stricture still occurs. Intestinal resection or surgical strictureplasty are often needed. Surgical strictureplasty preserves intestinal length but does not reduce the number of surgical procedures. Endoscopy-assisted balloon dilatation has been tried as a non-surgical alternative, but the outcome, as also observed in our patient, is often transient and requires repeated procedures. Gastrointestinal stenting, already widely used in the treatment of malignant strictures and fistulas, represents a new modality to treat benign fibrotic strictures. Preliminary reports have shown that endoscopy-assisted placement of metallic stents is a safe procedure with minimal complications and lasting effects. After the endoscopic placement of the stent, our patient has experienced complete resolution of his obstructive symptoms.

This report along with others supports the use of metallic stents in selected patients with medically refractory CD associated intestinal strictures with minimal side effects and maximal benefit.
Acute Cytomegalovirus (CMV) Seroconversion after Blood Transfusion, and Fulminant Colitis

Manishkumar Patel, M.D., N. Trigg, M.D., P. Parvathala, M.D., Charles Berkelhammer, M.D.* Internal Medicine, University of Illinois, Oak Lawn, IL and Gastroenterology, University of Illinois, Oak Lawn, IL.

Introduction: Patients with Inflammatory bowel disease (IBD) may require blood transfusions for bleeding and anemia. CMV has been associated with exacerbations of IBD and superimposed CMV enterocolitis, particularly in patients receiving immunosuppressive medications. Patients with IBD may require immunosuppression making them more susceptible to CMV enterocolitis. Acute CMV has also been associated with an alteration of CD4 to CD8 ratio and a flare up in IBD independent of CMV enterocolitis. We describe a CMV negative patient with IBD who developed acute CMV after receiving blood transfusions from a CMV positive donor.

Case: A 43-year-old male with a long-standing history of Crohn’s colitis and bilateral avascular necrosis of hips from steroids was maintained on azathioprine with therapeutic 6-thioguanine levels. He required 2 units of packed red blood cells (PRBC) transfusion because of symptomatic anemia. The transfused PRBCs were CMV positive. Six weeks later he presented with fevers, myalgias and arthralgias. IgM to CMV was positive with low titer IgG to CMV, consistent with acute seroconversion. This was followed by pancytopenia with a drop in leucocytes to 1.7 K/microL; platelets to 55 K/microL. His colitis became fulminant and fulminant colitis. CMV negative IBD patients on immunosuppressants were often colectomy with ileo-rectal anastomosis for ongoing bleeding. There was no change in CT scan findings. After resuscitation, she underwent a colonoscopy, which showed multiple polyps throughout the colon, ranging in size from 3 mm to 5cm. There were no rectal polyps. Some of the larger polyps were friable and oozing blood. There was a moderate amount of fresh blood mixed with clots in the lumen up to the transverse colon. Pathology showed diffuse infiltration of the lamina propria by a monotonous population of atypical lymphocytes that was consistent with mantle cell lymphoma. In addition to the colonic polyps, CT abdomen also showed enlarged mesenteric and retroperitoneal lymph nodes. The liver, spleen and stomach appeared normal. The patient subsequently underwent a subtotal colecotmy with ileo-rectal anastomosis for ongoing bleeding. There were innumerable colonic polyps many of which were hemorrhagic. The small bowel was inspected intra-operatively and found to have no lesions. The uninvolved colonic mucosa was unremarkable. The patient recovered after 6 months of rosiglitazone showed resolution of multifocal nodular fatty liver lesions.

Conclusion: This case illustrates that multifocal nodular fatty liver can mimic metastatic disease to the liver. Rosiglitazone resulted in improvement in insulin resistance and dramatic resolution of nodular fatty lesions on CT scan.
uneventfully and was discharged with follow up in oncology clinic after she agreed to chemotherapy. [figure1]

All That's Yellow Is Not Hepatitis
Fahd Rahman, M.D., Mujeeb Altaf, M.D., M.R.C.P.,* Muhammad N. Athar, M.D., Hotiana Mateen, M.D., Haris Usman, M.D., Nashat Maqsita, M.D.
Int. Medicine, MCMC / DUCOM, Darby, PA.

A 25 year old presented with right sided upper abdominal pain associated with vomiting. She was icteric and had a tender RUQ with hepatomegaly. Murphy's sign was absent but had right costovertebral angle tenderness. Laboratory studies revealed an elevated AST, ALT and alk. Phosphatase.

Urine showed no pyuria. Hepatobiliary pathology was suspected but hepatitis serology was negative. CT abdomen had a right pelviureteric stone, hydronephrosis, biliary duct dilation and a perinephric abscess (fig 1,2). She had antibiotics and a nephrostomy drainage. An immediate clinical improvement and normalization of LFT's was noted. She was discharged home on TMP/SMX to follow up later.

Perinephric abscesses are pus collections surrounding the kidneys. Predisposing conditions are urologic surgeries, UTIs, diabetes and calculi. Common pathogens are the E. coli, if abscess complicates a pyelonephritis, while S. aureus if source is hematogenous. Presentation is with fevers, chills, nausea, vomiting, flank and abdominal pain or masses. Patients can present with obstructive jaundice. Proposed mechanism is extrinsic compression of biliary tree (Fig 1). According to Edelstein H et al, positive urine & blood cultures identify pathogens in 37–58% of patients. Leukocytosis and pyuria are not sensitive or specific. Meng MV and colleagues showed CT scan to be 92% sensitive in diagnosing the site & extent of abscesses. IV pyelograms and ultrasound can be false negative. Treatment entails open or percutaneous drainage. Nephrectomy may be appropriate in staghorn calculi. Initial broad spectrum empiric therapy requires anti staphylococcal penicillin and an aminoglycoside. Further use of antibiotics depend on the pathogen present. Prognosis is good if appropriately treated but in untreated mortality is 40%. [figure1] [figure2]

Squamous Cell Carcinoma: A Rare Primary Malignancy of the Liver
Steve Keilin, M.D., Melchor Demetria, M.D.,* Bashar M. Attar, M.D., F.A.C.G., Amila Orucevic, M.D.
Gastroenterology and Pathology, John H. Stroger Hospital of Cook County and Rush Medical College, Chicago, IL.

Squamous Cell Carcinoma of the liver is an extremely rare primary hepatic malignancy. It comprises less than 1% of all primary liver malignancies and carries a poor prognosis. To date there have been only a few reported cases. A 42 year old Korean female, with no past medical history, presented with a year history of sharp, upper abdominal pain worsening over the last 3 months associated with nausea, low-grade fevers and weight loss of 10 pounds. On exam she had a fever of 100°F, was thin appearing with a firm, tender, palpable mass in the right upper quadrant. Lab values were notable for a normocytic anemia, an alkaline phosphatase of 146 U/L and LDH of 758 U/L. A CT of the abdomen revealed a 6.4 × 5.7 cm gall-bladder fossa mass. The patient underwent a CT guided biopsy and histology revealed squamous cell carcinoma adjacent to normal liver tissue. The patient underwent an exploratory laparotomy that showed a 6.5 × 6.2 cm mass involving the inferior portion of the right lobe of the liver. The patient was considered non-resectable and intraoperative biopsies confirmed the diagnosis of squamous cell carcinoma of the liver. She was treated with a chemotherapeutic regimen of carboplatin and paclitaxel, which was well tolerated, but 4 months into therapy she developed melena with a drop in hemoglobin. EGD showed that the mass had eroded into the 2nd portion of the duodenum. The patient was offered another chemotherapeutic regimen plus radiation, but chose palliative care and died two months later.

Since the first case report in 1975, few cases of primary squamous cell carcinoma of the liver have been reported. In 2001, an extensive case review series found only 18 cases reported in the literature. Of these, 15 were associated with underlying hepatic cysts: 12 solitary non-parasitic hepatic cysts and 3 epidermoid cysts. The majority of cases present at an advanced stage and have a poor prognosis. Surgical intervention is the treatment of choice in those patients considered resectable. Otherwise chemotherapy has been used with little success in several case reports, with a median survival rate of about 8 months. Our case represents a rare primary hepatic malignancy, arising in an otherwise healthy female without any associated underlying hepatic cysts.
Ischemia a New Cause of Colovesical Fistula Resulting from Internal Iliac Artery Aneurysm Coil Embolization
S. Mubashir A. Shah, M.D., Javier L. Parra, M.D., Jamie S. Barkin, M.D., F.A.C.P, M.A.C.G.* Gastroenterology, University of Miami School of Medicine, Miami, FL and Gastroenterology, Mount Sinai Medical Center, Miami Beach, FL.

Diverticular disease is the most common cause of colovesical fistula. Colovesical fistulae are observed in postoperative settings or as a consequence of Crohn’s disease. Iatrogenic fistulae are caused by surgical procedures, radiation, cancer, or infection. Other causes include foreign bodies, like swallowed chicken bones or toothpicks, in the bowel. This is the first report of an endovascular coil causing a colovesical fistula by an ischemic mechanism. A 76-year-old man with a contained rupture of a 12 cm left internal iliac artery aneurysm was treated endovascularly with coil embolization and stent placement. He had a right hemicolectomy for colon cancer; prostate cancer treated with hormonal therapy and had undergone a Billroth II anastomosis with vagotomy for PUD in the past. A colonoscopy two years ago was normal. Eleven days post procedure he had four episodes of hematochezia with a drop in his hemoglobin and hematocrit. Coagulation profile and platelet count were normal. He denied melena, hematemesis, abdominal pain or constipation. Some feces were reported inside his urinary catheter bag but no pneumaturia was reported.

His vital signs were stable. Abdomen was nontender with a central surgical scar. His rectal exam showed heme positive formed stools. Abdominal CT scan revealed no extravasation of IV contrast into the gastrointestinal tract or leak from the vascular stent. On colonoscopy, at 20 cm from the anal verge, a 4 cm fistulous opening was seen with visualization of urinary bladder wall. Cystoscopy confirmed a large fistula between the bladder and rectum at the level of the trigone distal to the ureteral orifices. During surgery a wire from the iliac artery aneurysm coils was seen sitting in the bladder causing a vesiculoaneurysmal fistula as well. The patient made an uneventful recovery post-surgical repair of the fistulas and removal of the vascular coils. Patients with colovesical fistulae may have suprapubic pain, irritative voiding symptoms, urinary tract infections and hematuria. Pneumaturia and fecaluria are seen in 40–60%. CT scanning of the abdomen and pelvis is the most sensitive test for detecting a colovesical fistula. Colonoscopy is helpful in determining the nature of the bowel disease. Treatment of the fistulas depends on the cause. Connections between the colon and urinary bladder can result from ischemia caused by coils placed for embolization.

A Case of Idiopathic Autoimmune Gastrointestinal Dysmotility
Shahana F. Pasha, M.D., Tisha N. Luntford, M.D.*, Fida Lennon, M.D., Ph.D. Dept. of Gastroenterology & Hepatology, Mayo Clinic College of Medicine, Scottsdale, AZ and Dept of Neurology, Mayo Clinic College of Medicine, Rochester, MN.

A 60 year old female presented with post-prandial abdominal pain, nausea, early satiety and weight loss. Gastric scintiscan was abnormal, with less than 10% emptying at 2 hours. Paraneoplastic panel revealed elevated N type calcium channel binding antibodies (CCBA), leading to an extensive and negative workup for malignancy. Ganglionic cholinergic receptor antibody (GCRA) was elevated at 0.08 nmol/L, confirming a diagnosis of Idiopathic Autoimmune Gastrointestinal Dysmotility (AIGD). AIGD is the nonneoplastic form of autoimmune autonomic neuropathy (AAN). AAN is a subacute/chronic disorder of the autonomic nervous system. Onset of autonomic decline often follows resolution of a viral illness. AAN can be associated with myasthenia gravis. GCRAs with specific binding or blocking action target the nicotinic AchRs of autonomic ganglia. AIGD is an immune-mediated inflammatory enteric neuropathy and can involve any part of the GI tract. Pathologic findings include enteric ganglioneuritis, with progressive degeneration and functional impairment of enteric neurons. The diagnosis is supported by the presence of antineuronal antibodies (ANNA) and N type CCBAs, after exclusion of an underlying malignancy.

Clinical presentation of AIGD includes esophageal and LES dysmotility (achalasia), gastroparesis and intractable emesis (most common) and intestinal pseudo-obstruction (Ogilvie syndrome). Our patient had severe gastroparesis, and AIGD was confirmed by the above workup, including an autonomic reflex study which revealed autonomic dysfunction. Treatment with pyridostigmine (30mg/day) led to symptomatic improvement and stabilization of weight.

The diagnosis of AAN should be included in patients with severe gastroparesis. With advances in autoimmune medicine, new diagnostic and management strategies may become available for AIGD, an underrecognized form of AAN. Current management is supportive, with maintenance of nutrition, promotility agents and treatment of complications, including bacterial overgrowth. Definitive treatment includes steroids, immune modulators (azathioprine or cyclophosphamide) or cholinesterase inhibitors (pyridostigmine). AAN should be considered in patients with gastrointestinal dysmotility. A diagnosis of AIGD is established by the presence of GCRAs, after exclusion of a paraneoplastic syndrome. A successful outcome can be achieved with cholinesterase inhibitors, steroids or immunomodulators.
**Acute Abdomen in an Elderly Woman with Mitral Valve Replacement: Is It Intestinal Ischemia or Intestinal Hematoma?**

Jeffery R. Groce, M.D., G. Gomez, M.D., G. S. Raju, M.D.*
Gastroenterology, The University of Texas Medical Branch, Galveston, TX.

**Introduction:** The classic bedside teaching of an approach to acute abdomen in the setting of mitral valve replacement is; “ischemia until proven otherwise.” Although this is true in the majority of cases, one should also seriously consider spontaneous intramural small bowel hematoma (SISBH).

**Case Report:** A 72-year-old woman with mitral valve replacement was hospitalized with 5 days of tarry diarrhea, generalized abdominal pain, nausea & emesis. Examination revealed diffuse abdominal tenderness with rebound, and normal bowel sounds. Her INR was >13, WBC = 14.1, and Hb = 8.6. Nasogastric tube lavage was negative for blood. Initial treatment included intravenous pantoprazole, fluids and antibiotics. Both aspirin and warfarin were held. CT Scan revealed numerous fluid filled, thickened loops of small bowel (Fig 1). Given her past medical history, persistent abdominal pain, and clinical features of peritoneal irritation, intestinal infarction from thromboembolism was a concern. Exploratory laparoscopy revealed an ischemic-appearing section of small bowel (Figure 2). A 20 cm section of necrotic proximal jejunum was resected. Histology revealed marked submucosal hemorrhage, consistent with SISBH. The patient’s hospital course was otherwise uncomplicated. We took this opportunity to review the literature on SISBH.

**Discussion & Conclusion:** SISBH: occurs in 1 per 2500 anticoagulated patients/yr and CT findings are classic. SISBH can be managed conservatively. Surgery is indicated in patients who worsen despite 72 hours of medical management, GI bleeding, or perforation. Our patient underwent surgery because of continued pain. With a high degree of suspicion, early diagnosis, and aggressive medical management one could avoid unnecessary surgery.

![figure1](image1)
![figure2](image2)

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**Tegaserod Use in Opioid Induced Delayed Gastric Emptying**

Muhammad M. Heif, M.D., Amar Al-juburi, M.D.* Geriatrics and Gastroenterology, CAVHS, Little Rock, AR.

A 75 year old man presented with 2 year history of intermittent nausea and vomiting which progressed gradually and became constant in the last 6 months leading to 40 lb. weight loss and significantly impacting his daily function. He also complained of bloating, easy satiety and vague mild abdominal discomfort. He has a history of long standing constipation controlled with laxatives. He has had chronic back pain for the past 35 years secondary to vertebral fractures that required multiple surgeries and resulted in neuropathic pain in the lower extremities. He has been treated with narcotics (Morphine, Oxycodone and Fentanyl patches) to control his pain for the last 10 years. He also has coronary artery disease, hypertension, hyperlipidemia, chronic bronchitis and benign prostate hypertrophy. His physical exam was unremarkable except for abdominal distension. His evaluation included upper gastrointestinal endoscopy which showed mild gastritis and no mechanical obstruction. He tested positive for H. Pylori. Treatment with triple therapy mildly helped his abdominal discomfort but he continued to have nausea and vomiting. Gastric emptying scintigraphy showed severely delayed gastric emptying. Further investigations for causes of gastroparesis were unrevealing. Although opioids were suspected as the culprit for these symptoms he could not be taken off these medications secondary to the disabling back pain. He was treated with Metoclopramide which helped some but was discontinued secondary to extrapyramidal side effects (oculogyric crisis). He was later started on Tegaserod, 12 mg twice a day, with complete resolution of his vomiting and significant improvement in his nausea and other upper gastrointestinal symptoms. During his 4 months post therapy follow-up he has gained 10 lb, and was happy to report that he was able to go out to dinner with his wife for the first time in a long time. Medication-induced gastroparesis is usually acute and presents early. However, in this patient, symptoms were chronic and started after several years of opioid use. Treatment of gastroparesis in the elderly is challenging. They usually have multiple medical problems and are prone to develop side effects to the available medications. Tegaserod is a promising option for treatment of gastroparesis. Effects of Tegaserod on symptoms of gastroparesis have not been reported. Trials to establish the efficacy of Tegaserod on clinical symptoms of gastroparesis of different etiologies would be very helpful.
We report a rare case of malignant peritoneal mesothelioma associated with intestinal obstruction due to peritoneal disseminated metastasis in young man. The patient in early thirties admitted due to exacerbated abdominal pain and rapid body weight loss in Jan 2003. Elevated levels of WBC, CRP and serum CA125 were observed. Barium enema showed marked compression of the transverse colon and the sigmoid colon. Abdominal Computed Tomography examination revealed diffusely thickened peritoneal tumor adjacent to the liver and the spleen. Laparotomy showed a thickened peritoneal tumor and multiple disseminated tumor in large area of the intraperitoneal organs. Construction of catheter cecostomy for intestinal obstruction was underwent. Histopathologically, the tumor was diagnosed as malignant mesothelioma by immunohistological examinations and electron microscopy. The patient received palliative treatment but died 3 months after diagnosis. Autopsy revealed wide spread metastases occupying large part of peritoneal cavity, which involved liver, spleen and gastrointestinal tracts. The unique progressive feature in this rare neoplasm is evaluated and referred to the literature in this report.

A Case of Primary Malignant Melanoma of the Esophagus
Ken Saijo, M.D., Hiroki Takahashi, M.D.* Motoaki Ohyamauchi, M.D., Masahiro Iwabuchi, M.D., Satoko Sato, M.D., Hirokichi Ito, M.D., Osamu Kimura, M.D., Satoshi Iwabuchi, M.D., Mikako Sagimura, M.D., Kenji Noguchi, M.D., Nobukazu Tanabe, M.D., Kenji Kimura, M.D., Yutaka Mano, M.D., Nobuyuki Chida, M.D., Shin Toshima, M.D., Toshihiro Saito, M.D., Hiroyoashi Suzuki, M.D.* Gastroenterology, Sendai Medical Center, Sendai, Miyagi, Japan; Surgery, Sendai Medical Center, Sendai, Miyagi, Japan; Pathology, Sendai Medical Center, Sendai, Miyagi, Japan.

Primary malignant melanoma of the esophagus is extremely rare with only about 200 cases having been reported in Japan. We report a case of malignant melanoma of the esophagus. A 55-year old male visited our hospital complaining of dysphasia. Endoscopic examination revealed a blackish protruded tumor measuring 40mm in diameter in the middle esophagus. In addition, multiple pigmentation of the esophageal mucosa was noted in the middle and lower esophagus. Endoscopic biopsy specimens of the tumor led to a diagnosis of malignant melanoma. The deformity of the esophageal wall was slight in the barium esophaogram, thus the depth of the tumor invasion was estimated as slightly reaching to the submucosa. Chest and abdominal CT showed no evidence of distant metastasis. Thoracic esophagectomy with right thoracotomy was performed. Pathologically, the lesion was T1N1M0, and malignant melanoma in situ in melanosis was recognized. Microscopic findings showed junctional activity which meant tumor cells grew laterally, proliferating in the basal layer of squamous epithelium and destroying the basal lamina. Therefore, this case was diagnosed as a primary malignant melanoma of esophagus with lymph node metastasis. We report here on our patient and refer to the literature concerning this type of tumor in Japan.

A Case of Delayed Healing of Gastric Ulcers Associated with Sirolimus
John Altomare, M.D., Sanoosh Poddar, M.D., Sara Mitchell, M.D.* Gastroenterology, Geisinger Medical Center, Danville, PA.

Sirolimus is an immunosuppressive and anti-proliferative agent used in organ transplantation. Sirolimus is associated with many adverse effects. We present a case of delayed healing of gastric ulcers associated with Sirolimus use.

Case Report: A 65-year-old male with diabetes, ESRD and renal transplant in March 2003 presented with anemia and heme-positive stools. Immunosuppressive therapy consisted of Sirolimus and Prednisone. In May 2004, EGD revealed a gastric ulcer with an underlying inflammatory nodule. He was maintained on PPI therapy. Anemia and heme-positive stools continued and repeat EGD in March 2005 revealed an AVF in the gastric cardia. This was treated endoscopically with good hemostasis. Retained food prevented visualization of past ulcer site. Repeat EGD four weeks later for continued anemia found a large cratered ulcer at the site of the previously AVF as well as several other peptic ulcers including the ulcer site from one year earlier. Sirolimus was felt to be contributing to the ulcers and was stopped. EGD seven weeks later revealed a healing ulcer site with no additional ulcers seen.

Discussion: Sirolimus is associated with a number of side effects including gastrointestinal effects. These include constipation, diarrhea, dyspepsia, nausea and vomiting. To date there have been no report of peptic ulcer disease or delayed ulcer healing in association with Sirolimus. Sirolimus is associated with oral ulcers when used in combination with mycophenolate mofetil.

Our patient however was not using mycophenolate mofetil. The authors felt the ulcers may be a result of Sirolimus’ effect on growth factors and it’s strong anti-proliferative effects rather than infectious from immunosuppression. Similar mechanisms are implicated in Sirolimus’ association with a higher rate of wound healing complications in transplant patients than other immunosuppressive agents. We believe that the gastric ulcers and their delayed healing in this patient could also be associated with Sirolimus’ effect on poor wound healing and anti-proliferative effects. We strongly recommend either dose reduction or alternative medications in patients using Sirolimus who present with peptic ulcer disease.

REFERENCES

Percutaneous Endoscopic Gastrostomy Tube Placement in a Patient with a Biventricular Assist Device
William F. Shaheen, M.D.*, Asad Ullah, M.D. Digestive and Liver Disease Unit, University of Rochester Medical Center, Rochester, NY.

We describe the first successful placement of a percutaneous gastrostomy tube in a patient with a bi-ventricular assist device. Gastrostomy tube placements have been described in the literature in patients with left-ventricular assist devices, but gastrostomy placement in a paracorporeal BIVAD which has twice the number of cannulas has not been described previously. As a bridge to cardiac transplantation, ventricular assist devices, including left ventricular assist devices (LVAD) and biventricular assist devices (BIVAD) are being used with increasing frequency for cardiac failure patients. We describe successful placement of a percutaneous gastrostomy tube in a 21-year-old female who developed post-partum cardiomyopathy and suffered ventricular fibrillation arrest requiring resuscitation. After initial placement of a temporary Abiomed BIVAD, a more permanent BIVAD AB5000 (Biotech) was placed. The patient had a prolonged hospital course, complicated by a lengthy ICU admission and decreased oral intake thought secondary to mental status changes from hypoxic brain injury sustained during her arrest. Albumin was 2.8 g/dl at the time of gastrostomy tube placement. A 20-French gastrostomy tube was placed endoscopically 37 days after BIVAD placement 3cm from her left costal margin in the left upper quadrant, with no immediate complications. Bleeding from the fistula tract did occur while the patient was being anticoagulated with warfarin and a heparin drip for her BIVAD, with negative EGD for internal gastrointestinal hemorrhage and successful hemostasis achieved with silver nitrate application to the tract 9 days after gastrostomy tube placement. The patient tolerated tube feeds afterward with improvement of her albumin to 3.5 g/dl two weeks after the feeding tube was placed but died from cerebral complications not associated with the feeding tube placement 39 days later.

Concern for developing cellulitis that could contaminate the BIVAD cannulae pockets which usually enter the mediastium superior to the gastrostomy pockets.

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site and anticoagulation requirements of the ventricular assist devices which may induce tract and gastrointestinal bleeding remain possible complications to gastrostomy tube placement in this population. Because of their overall debilitated clinical state, adequate nutritional status remains an essential part of their recovery and preparation for possible cardiac transplantation.

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GIST Presenting as an Obscure Gastrointestinal Bleed
Kiran Jagarlamudi, M.D., Suresh Jayatilaka, M.D., Bhuvaneswari Dorai, M.D., Robert Spira, M.D.* Department of Gastroenterology, Seton Hall University School of Graduate Medical Education, South Orange, NJ.

Introduction: Tumors of the small intestine are rare. Gastrointestinal stromal tumor (GIST) is the third most common malignant tumor of the small intestine. Presenting features include abdominal pain, abdominal mass and gastrointestinal bleed. We report a case of GIST presenting as an obscure gastrointestinal bleed.

Case-report: A 57 year old male, was admitted to a community hospital with complaints of dizziness. Hb on admission was 10.9 gm%. While at the hospital, he noticed maroon colored stools. He denied any abdominal pain or weight loss. Repeat Hb was 5.6 gm%. He had an EGD followed by a small-bowel enteroscopy up to the proximal jejunum which showed no obvious source of bleed. Subsequent colonoscopy with intubation of the terminal ileum was normal. Both angiogram and a bleeding scan were normal. During the time period, he received a total of 9 units of PRBC. He was then transferred to our hospital where on the night of admission, he underwent a wireless capsule endoscopy, which revealed active bleeding in the mid-jejunum. No arterio-venous malformations were seen. He had an urgent exploratory laparotomy. There was a 2.6 × 1.7 × 1.1 cm pedunculated mid jejunal tumor. A small bowel resection with enterenterostomy was done. Pathology of the tumor showed a GIST tumor with a mitotic index of 2/10 hpf, with no necrosis and surgical margins free of tumor. Post surgical follow up was uneventful. [figure1] [figure2]

Discussion: GIST is a rare etiology of gastrointestinal bleeding. Wireless capsule endoscopy plays an important role in evaluating patients with obscure gastrointestinal bleed. We report a case of small bowel bleeding secondary to a jejunal stromal tumor whose diagnosis was facilitated by capsule endoscopy.

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Gastrointestinal Involvement of Mantle Cell Lymphoma in a Patient with Previous Negative Colonoscopy: Determining Chronicity of Disease
William F. Shaheen, M.D., Ashok Shah, M.D.* Digestive and Liver Disease Unit, University of Rochester Medical Center, Rochester, NY.

Mantle cell lymphoma (multiple lymphomatous polyposis) a type of Non-Hodgkin’s B-cell lymphoma with known gastrointestinal involvement, can occur independent of marrow or other systemic involvement. Previous cases describe isolated gastrointestinal involvement as well as synchronous gastrointestinal involvement with nodal and marrow disease, but chronological development of gastrointestinal lesions remains to be determined.

We describe a 69 year-old male referred for bi-directional endoscopy with anemia and occult, guaiac positive stools after being diagnosed four weeks previously with mantle cell lymphoma by cervical lymph node biopsy for increasing neck swelling and lymphadenopathy. CD5 and Cyclin D1 were both positive by immunostain and flow cytometry. Though the colon was involved extensively, concentration of lesions was identified in the cecum and terminal ileum. Whole-body CT after endoscopy showed extensive nodal disease and multiple lung nodules but no radiographic evidence of gastrointestinal involvement. Bone marrow biopsy was negative. The patient was begun on chemotherapy with hyper-CVAD (cyclophosphomide, doxorubicin, vincristine, dexamethasone) after Rituxan. After 5 cycles, he remains in clinical remission with no residual gastrointestinal symptoms.

Interestingly, the patient had a negative colonoscopy five months previous to diagnosis of his lymphoma, with a normal mucosa and no identification of mantle cell lymphomatous lesions seen at that time. Gastrointestinal tract involvement has been previously reported in 15% to 30% of patients with mantle cell lymphoma. Recent prospective data, however, shows a much higher prevalence at a microscopic level in the setting of normal macroscopic exams. This patient presented with nodal and gastrointestinal involvement. His initial presentation of cervical lymphadenopathy was rapid, and uniquely, he had a colonoscopy five months prior to diagnosis which showed no macroscopic lesions suspicious for lymphoma. This suggests that macroscopic mantle cell lesion development in the gastrointestinal tract may be rapid as well, and reaffirms that mantle cell lymphoma in the
gastrointestinal tract is neither an indicator of disease severity, progression nor a predictor of response to therapy.

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Mucinous Biliary Obstruction in Intraductal Papillary Mucinous Neoplasm of the Pancreas (IPMN)
Nadia A. Trigg, M.D., A. El-Attar, M.D., Charles Berkelhammer, M.D., F.A.C.G.∗ Gastroenterology, University of Illinois, Christ Hospital, Oak Lawn, IL.

Introduction: IPMN can rarely be associated with biliopancreatic fistula. These fistulae can be benign or malignant. Mucus can appear within the bile duct secondary to biliopancreatic fistulae in IPMN. We describe a case of mucinous biliary obstruction in IPMN.

Case: A 75 year old male presents with jaundice, anorexia, and weight loss. A CT scan showed dilated pancreatic and biliary ducts. There was an associated 4 cm x 5 cm cystic neoplasm in the head of the pancreas. Bilirubin was 16 mg/dl, alkaline phosphatase 550 U/dl, CA 19–9 was 1500 U/dl. ERCP showed a gaping major and minor papilla extruding mucus typical of IPMN. Pancreatogram showed a dilated pancreatic duct with obstructing globules of mucus. Cholangiogram showed a dilated common bile duct without strictures, but with multiple globules of mucus causing biliary obstruction.. At laparotomy, the tumor was inoperable, and a double bypass duct was performed. The patient expired from terminal malignancy 6 weeks later.

Discussion: Our patient had clinical features of IPMN. On CT scan, there was an associated cystic lesion. Loftus et al. [1] have recommended classifying such patients with mucinous cystic lesions seen in conjunction with other features of IPMN as having IPMN. Our patient had an obstructive jaundice caused by large mucous globules in the common bile duct. There was no evidence of any biliary strictures.

Conclusion: Obstructive jaundice in the absence of biliary strictures may be caused by mucinous biliary obstruction in patients with IPMN.

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Is Collagenous Colitis a Manifestation of Burnt-Out Crohn's Disease?
John C. Fucci, M.D., ∗ Oliver A. Cerqueira, D.O., Mei-Chien H. Fucci, M.D. Internal Medicine, The University of Oklahoma College of Medicine, Tulsa, Tulsa, OK.

Two cases are described of patients who initially presented with a segmental colitis with endoscopic and biopsy appearance typical of Crohn’s disease. They were treated and attained remission. Later, they both developed watery diarrhea without bleeding. Colonoscopy showed only mild hyperemia without evidence of Crohn’s disease. However, random right colon biopsies were classic for collagenous colitis.

Case #1: An 83-year-old white female presented with a 6-month history of diarrhea and a 15 pound weight loss. She was noted to be anemic with a hemoglobin of 9.8 and an elevated sedimentation rate of 68. A colonoscopy revealed a severely inflamed right colon with skip areas of ulceration and a cobble-stone appearance. Biopsy showed acute and chronic inflammation. Upper endoscopy, including small bowel biopsy, was negative. She was treated with prednisone and 5-ASA; after several months, she went into remission. She had minimal symptoms over the next 3 years, but then presented with watery diarrhea. Colonoscopy at that time showed mild hyperemia of the right colon and biopsy showed a thickened subepithelial collagen layer with lymphocytic infiltrates in the lamina propria.

Case #2: A 50-year-old white female presented with a 3-week history of bloody diarrhea. Colonoscopy revealed a severe colitis with multiple deep linear ulcers and skip areas typical of Crohn’s colitis. Biopsy showed severe acute and chronic inflammation. She was treated with infliximab and IV steroids. The steroids were tapered over the next 3 months, and she went into remission. She had several flares over the next year requiring treatment with oral steroids and 5-ASA, but then attained a year long remission without medication. She then developed watery diarrhea. Repeat colonoscopy showed only mild hyperemia, but biopsies of the right colon showed lymphocytic infiltration within the lamina propria and a thickened subepithelial collagen layer. These cases illustrate a relationship between Crohn’s disease and collagenous colitis. Previous reports have demonstrated patients with collagenous colitis developing Crohn’s disease, and the presence of focal lymphocytic and collagenous colitis biopsy findings in patients with Crohn’s disease. However, our cases clearly demonstrate, clinically, endoscopically, and histologically, a progression of disease from active Crohn’s disease to collagenous colitis. Collagenous colitis should be suspected in patients who present with watery diarrhea and a history of Crohn’s disease.

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Closure of Gastrostomy Tube Site after Removal of the Feeding Device: A Novel Application for the Use of Fibrin Glue
Rita Steffen, M.D., ∗ Robert Wyllie, M.D., Lori Mahajan, M.D., Lisa Feinberg, M.D., Khudakal Radakrishnan, M.D., Francesza Mohr, M.D., Barbara Kaplan, M.D., Vera Hupertz, M.D. Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH.

Removal of gastrostomy tubes when their course of usefulness is complete is sometimes accompanied by leakage of stomach contents. This leakage of gastric secretions may last for a variable period of time, sometimes resulting in significant epidermal irritation and possibly excoriation. Other times the site must be covered with gauze or other material until the tract has finally sealed in with fibrous tissue.

We report the use of fibrin glue for the purpose of accelerating the closure of leaking gastrostomy tube sites in two children whose tubes were removed and were symptomatic with persistent drainage of stomach contents on to the abdominal wall.

Patient 1: A 14-year-old male with a background history of portal hypertension and esophageal varices. He underwent upper gastrointestinal endoscopy for the purpose of banding esophageal varices. At the time of the procedure fibrin glue was applied on the stoma of the abdominal wall where the gastrostomy tube had been removed. The fibrin glue was seen passing through the gastrostomy tube site, and the endoscope was subsequently removed. Patient 2: a 5-year-old male with a background history of inflammatory bowel disease. His gastrostomy tube had been removed previously and he presented with delayed closure of the tract with nuisance leakage persisting for several weeks. Fibrin glue had to be applied on two occasions to successfully close the gastrostomy tube site. While 94% of gastrostomy sites close within 24 hours, delayed closure can be a significant source of leakage, irritation, and other complications. Some patients have required referral for surgical closure. The application of fibrin glue to gastrostomy tube sites with delayed closure proved to be an effective treatment for these children. Fibrin glue may have a valid role in clinical practice when gastrostomy tubes are removed and the gastrocutaneous fistula persists.

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Idiopathic Eosinophilic Esophagitis and Eosinophilic Gastroenteritis Successfully Treated with Azathioprine or 6-Mercaptopurine
Peter Netzer, M.D., F.A.C.G.∗ Jerzy W. Bielecki, M.D., Juergen M. Gschossmann, M.D. Department of Gastroenterology, Inselspital / University Hospital of Bern, Bern, Switzerland.

Background: Idiopathic eosinophilic esophagitis (EE) is an increasingly recognized inflammatory disorder of the esophagus. The inflammatory
pattern of EE is predominately associated with a T_{H} 2-type allergic response. The disease has often chronic recurrent character and requires long-term treatment with topical or systemic corticosteroids. The aim of our study was to determine whether in severe cases with long-term systemic corticosteroid-dependency an immuno-modulating treatment may have a steroid-sparing effect?

Methods: In three patients with proven severe idiopathic EE (1/3 also suffered from eosinophilic gastroenteritis) and chronically corticosteroid-dependency, we prospectively studied the clinical and histological response under treatment with azathioprine (2mg/kg BW po/die) or 6-mercaptopurine (1mg/kg BW po/die).

Results: All patients experienced both symptomatic and histological resolution once steroid doses were tapered on several occasions. After administration of azathioprine in 2 patients and 6-mercaptopurine in one patient, steroids could be stopped in all 3 patients without clinical relapse. Subsequent histological examinations showed complete disappearance of eosinophilic infiltration over a time span of months up to 8 years. One patient who stopped his treatment with azathioprine relapsed and became again steroid-dependent. In the follow-up, steroids could be stopped again after azathioprine had been reinitiated. In one patient, high blood counts of eosinophilic cells had been originally measured which also disappeared under azathioprine treatment.

Conclusions: In severe steroid-dependent cases of idiopathic eosinophilic esophagitis and eosinophilic gastroenteritis, an immunomodulating treatment with purine analogues may be a helpful alternative to glucocorticoid therapy. At least in our patients, long-term use of immuno-modulating drugs was overall well tolerated and decreased morbidity due to EE. It could be speculated that the beneficial effect of azathioprine/6-mercaptopurine in treating EE is associated with their pro-apoptotic effect on T-lymphocytes.

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Severe Upper Gastrointestinal Bleeding as the Initial Presentation in an Elderly Man with Hereditary Hemorrhagic Telangiectasia
Javier A. Pou, M.D., Maria I. Dueno, M.D., F.A.C.G., Harry Ruiz, M.D., Doris Toro, M.D.* Gastroenterology Section, Veteran Affairs Medical Center, San Juan, PR.

Hereditary hemorrhagic telangiectasia (HHT) is an undiagnosed autosomal dominant disorder characterized by telangiectasias and arteriovenous malformations. The presentation is variable and can be life threatening regardless of age, gender or ethnicity. After epistaxis, gastrointestinal (GI) bleeding is the most common presentation and can pose a diagnostic and therapeutic challenge.

Case report: An 80 year old man with history of essential tremors, mild epistaxis and alcohol use was admitted for massive GI bleeding that required intensive care. He had been in excellent health all his life and hospitalized once for acute alcoholic hepatitis. The epistaxis is never required medical attention. He did not use NSAIDs, anticoagulation or anti-platelet medications.

Six first degree relatives have had epistaxis. He appeared pale but well nourished. Careful examination did not reveal any vascular lesion in the region of the lips, tongue, palate, conjunctiva, chest, back, fingertips, palms, soles or nails. The rest of the physical exam was unremarkable except for black tarry stools. The Hgb was 5g/dl (12.6–17.8), MCV 93.3(80.6–103.7), MCH 26.8(26.1–34.1) and platelets 231(155–371). The AST 27(0–47 U/L), ALT 15(0–45 U/L), AP 112(30–115 U/L), total bilirubin 0.6mg/dl, albumin 2.9(2.6–5.2g/dl), PT14.3sec (11.8–14.3), PTT28.6sec (22.1–38.3) and closure time of 84 sec (81–153).

An EGD showed over 100 flat cherry red vascular ectasias of variable size with central blood vessels and an emanating feathery look. They were friable to light touch, and covered 50–70% of the stomach mucosa. No esophageal or gastric varices were seen. Several courses of Argon plasma coagulation (APC) were directed to the largest and most friable lesions. Colonoscopy did not reveal telangiectasias. A CT scan with IV contrast did not show AV malformation, portal hypertension or cirrhosis. The patient improved with aggressive resuscitation and APC treatments.

Conclusion: We hope to contribute with the ongoing efforts to increase physician awareness by reporting this unusual case. The presentation is atypical due to its very late onset, lack of external visible telangiectasia and lesions almost entirely limited to the stomach. In this case, endoscopic findings became a cornerstone in the definite diagnosis of HHT as defined by The Scientific Advisory Board of the HHT Foundation International.
Olanzapine-Induced Hypersensitivity Hepatitis

Manishkumar Patel, M.D., N. Trigg, M.D., Charles Berkelhammer, M.D.∗
Internal Medicine, University of Illinois, Oak Lawn, IL; Internal Medicine, Univ of Illinois, Oak Lawn, IL and Gastroenterology, Univ of Illinois, Oak Lawn, IL.

Introduction: There have been only a few case reports of olanzapine (Zyprexa) related hypersensitivity hepatitis. Not all of these cases have been confirmed on rechallenge. We describe a case of olanzapine-induced hypersensitivity hepatitis confirmed on rechallenge.

Case: A 41 year old female was hospitalized for schizoaffective disorder. She had been previously stable on stelazine for many years. She had a history of intolerance to olanzapine, manifested by fever, nausea, skin rash and abnormal liver biochemistries shortly after starting it, necessitating its prompt discontinuation. Her baseline liver biochemistries were normal except for a mild chronic increase in alkaline phosphatase (155 U/l, normal <125 U/l) secondary to non-alcoholic fatty liver disease. She was rechallenged with olanzapine. Within three days she developed fevers to 39 Celsius, nausea and an erythematous skin rash. Her liver biochemistries increased to an ALT of 251 U/l (normal <52), AST of 191 U/l (normal <40 U/l), alkaline phosphatase of 349 U/l, and bilirubin of 1.7 mg/dl (normal <1.2 mg/dl). Extensive serological evaluation and imaging studies were negative. Olanzapine was discontinued with complete resolution of her symptoms and return of liver biochemistries to baseline. She was subsequently able to tolerate thiothixene and quetiapine.

Summary: We describe a case of olanzapine-induced hypersensitivity hepatitis confirmed on rechallenge. Patients with this condition can tolerate other atypical antipsychotics without cross-reaction.

Ruptured Hepatic Artery Aneurysm in Acute Pancreatitis

Thomas R. Puetz, M.D.,∗ Vasanth Siddalingaiah, M.D. Gastroenterology, Advanced Healthcare, Mequon, WI.

Bleeding complications occurring during an episode of acute pancreatitis are uncommon. Most episodes are associated with the development of a pseudoaneurysm in patients with chronic pancreatitis. Mortality associated with a bleeding pseudoaneurysm or ruptured splanchnic aneurysm ranges from 10–100% depending on whether prompt diagnosis and treatment is provided. In the case presented, the patient complained of a two day history of right upper quadrant abdominal pain. The admission labs were revealing AST of 40 U/l, ALT of 75 U/l, alkaline phosphatase of 134 IU/ml, and bilirubin of 0.9 mg/dl. Upper endoscopy revealed a clean-based ulcer involving most of the anterior wall of the body and antrum of the stomach. The ulcer was clean-based and had smooth edges. Biopsy specimens of the ulcer showed epithelial atypia similar to that described with hepatic arterial infusion chemotherapy. Preservation of mucosal architecture, atypia associated with marked cellular enlargement, maintenance of a low nuclear to cytoplasmic size ratio, cytoplasmic eosinophilia with vacuolization, few mitosis figures, and recognition of similar atypia in endothelial cells helped to differentiate these SIR-Sphere related changes from gastric dysplasia/carcinoma. Structures consistent with SIR-Spheres were identified in the gastric capillaries. The patient was treated with esomeprazole (40 mg twice daily) with relief of his epigastric pain in one week. Repeat upper endoscopy 6 weeks later revealed near complete healing of the ulcer. Gastroenterologists and pathologists should be aware that gastric ulcers mimicking carcinoma can occur as a late complication of hepatic artery infusion anti-neoplastic therapies.

An Unusual Complication of Midline Abdominal Wall Paracentesis

Muhammad K. Hasan, M.D., Shoaib Saya, M.D., Tauseef Ali, M.D., Thomas L. Whitsett, M.D.∗ Department of Internal Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

A 50 years old Caucasian female with history of Hepatitis C presented to the emergency room with complaints of fever, abdominal pain, abdominal distension and lower extremity swelling. On examination, patient had signs...
of chronic liver disease including chest wall spider angomas, asctes, splenomegaly and lower extremity edema. Laboratory data showed leukocyte count of 12,500 cells per cubic millimeter, hemoglobin 11 grams per deciliter, platelets 47,000 cells per cubic millimeter, PT 37.8 seconds, INR 3.6, albumin 1.6 grams per deciliter, AST 47 units per liter, ALT 102 units per liter and alkaline phosphatase 195 units per liter. Patient underwent midline abdominal wall diagnostic paracentesis, for evaluation of spontaneous bacterial peritonitis (SBP), by emergency room physician. Peritoneal fluid analysis was not consistent with SBP. Patient underwent abdominal CT Scan for further evaluation of abdominal pain. CT-Scan showed ascites, ciritic liver, splenomegaly and an incidental 8.7 × 8.5 × 8.3 cm pelvic mass. For further evaluation of the pelvic mass, patient had transabdominal ultrasound and duplex vascular study done, which showed an 8.1 × 8.2 cm ovarian cyst in open communication with a dilated variceous vein, with venous flow within the cyst. This was thought to be traumatic venous leak, by midline paracentesis, from the distended variceal vein into the ovarian cyst giving rise to pseudoaneurysm of the variceal vein. This ovarian cyst and venous communication was successfully obliterated with ultrasound guided thrombin injection into the cyst. To the best of our knowledge this type of complication from mid line paracentesis and than complete obliteration with thrombin injection has not been reported.

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Post Cholecystectomy Recurrent Acute Pancreatitis Secondary to Sump Syndrome
Viviana T. Caban, M.D., Perry Hookman, M.D., F.A.C.G., Jamie Barkin, M.D., M.A.C.G.* Division of Gastroenterology, Mount Sinai Medical Center, Miami Beach, FL.

The sump syndrome, presents usually with cholangitis and its complications. The aim of this case report is to present a patient with sump syndrome who presented solely with recurrent pancreatitis, normal LFT’s and no cholangiti.

Case Report: A 44-year-old woman with a history of cholecystectomy 15 years ago, followed by a biliary by-pass (choledochoduodenostomy) one year later for choledocholithiasis, presented with recurrent episodes of acute pancreatitis and normal LFT’s without cholangitis. Previously an endoscopic biliary papillotomy for presumed sump syndrome was performed however she continued to experience recurrent pancreatitis. She had experienced 8–10 episodes of acute pancreatitis over the preceding 5 years. There was no history of hypercalcemia, hypertryglyceridemia or abdominal trauma nor was she ingesting any medications. Evaluation included a normal abdominal CT scan; laboratory data showed elevated amylase and lipase. ERCP revealed a normal pancreatic duct with adequate drainage and a choledochoduodenostomy. She had a flat, normal-looking ampulla of Vater with signs of previous sphincterotony that could not be endoscopically extended. Consequently, she underwent surgical closure of the choledochoduodenostomy, pancreatic sphincteropty and cholecchojejunostomy. Subsequently, she progressed to good health and remained well without recurrent episodes of pancreatitis for the following 12 months.

Sump syndrome should be considered as a cause of pancreatitis presumably via an obstructive mechanism.

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Bleeding Secondary to a Meckel’s Diverticulum and a Dieulafoy’s Lesion in an Elderly Male
Fadi T. Mustapha, M.D., Ramon E. Rivera, M.D., Vandanna Singh, M.D., Susan J. Gordon, M.D.* Gastroenterology, Graduate Hospital, Philadelphia, PA.

A 74 yr. old man was admitted with painless hematochezia that occurred one day prior to admission. The bleeding was sudden in onset described as bright red. The pt’s medical history includes HTN, CAD and COPD. He denied any alcohol abuse.

The physical exam revealed mild orthostatic hypotension, increased bowel sounds with no abdominal tenderness. Blood work revealed a Hgb of 7.6. He was transfused with 3U of PRBCs and admitted to the ICU. A colonoscopy revealed normal colonic mucosa with no evidence of active bleed. The following day the patient developed a recurrent episode of hematochezia prompting evaluation with a tagged RBC scan which revealed accumulation of activity in the area of the distal ileum.

Urgent laparotomy revealed a 3 cm ileal diverticulum 15 cm proximal to the ileocecal valve. Palpation of the distal ileum revealed probable intraluminal blood clots. A 20 cm segment of the distal ileum was resected.

Gross and histological examination of the open specimen revealed a Meckel’s Diverticulum with no ectopic mucosa. Additional findings included an adjacent mucosal ulcer and a medium sized submucosal artery (Dieulafoy’s lesion) with an intraluminal blood clot.

Meckel’s diverticulum is the most prevalent congenital anomaly of the GI tract occurring in 2% of the population. The lifetime risk of a complication is 4%. It is a true diverticulum and is regarded as a remnant of the omphalomesenteric duct. It is classically a pediatric disorder presenting with intestinal hemorrhage, perforation, intussusception, volvulus, diverticulitis and abdominal pain.

The majority of complicated cases of Meckel’s diverticulum contain ectopic mucosa, with up to 75% of these being gastric mucosa and up to 15% pancreatic tissue. Acidic and alkaline secreting ectopic tissue can cause ulceration. Diagnosis requires a high index of suspicion. Technetium-pertechnetate scan (Meckel’s Scan) aids in locating the source of painless bleeding. Gastric mucosa readily shows Tc uptake thus revealing any ectopic tissue. In children the scan has a sensitivity of 85%, in adults the sensitivity falls to 62.5%. Angiography and CAT scans occasionally are helpful. Ileal resection has been traditionally the treatment of choice. Dieulafoy’s lesion, also known as caliber-persistent artery occurs in the proximal portion of the stomach but also has been reported throughout the gastrointestinal tract. Its appearance is that of a larger than usual artery found in close proximity to the mucosal surface.

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Four Cases of Patients with Gastrointestinal Granular Cell Tumors

We present four cases of patients with gastrointestinal granular cell tumors (GCT) with a literature review.

Case 1: A 47 yo black female with EGD performed for dysphagia showing a 7 mm nodule in the esophagus at 29 cm. Biopsies revealed GCT with immunohistochemical stain positive for S-100. CT scan of the thorax showed a 21 mm X 21 mm soft tissue mass in the anterior mediastinum. EUS showed a 2.5 cm heterogeneous lesion in the mediastinum. FNA of one of the mediastinal lymph nodes was negative for malignancy. PET scan was negative for malignant disease.

Case 2: A 51 yo black female with EGD for GERD showing a whitish to yellow 7 mm nodule in the distal esophagus. EUS showed that the lesion was submucosal and hypoechogenic. Forceps biopsy confirmed GCT with positive stain for S-100.

Case 3: A 56 yo white female undergoing screening colonoscopy showing a 1 cm submucosal appearing lesion in the transverse colon. Lesion removed with hot biopsy with histology confirming GCT with positive stain for S-100.

Case 4: A 54 yo white male with EGD to evaluate GERD showing a 3 cm X 2 cm smooth nodule in the gastric cardia with biopsies showing a GCT with stain positive for S-100. The patient underwent surgical wedge resection of the GCT with at least 1 cm margins. No recurrence seen on subsequent endoscopies.

GCTs occur in several body areas1,2,3 including the gastrointestinal tract in 1–8% of cases4. The esophagus is the most frequent site followed by the stomach and colon for gastrointestinal tract tumors. It is a benign neural
tumor thought to arise from Schwann cells. The tumors are usually less than 3–4 cm and poorly circumscribed nodules. GCTs occur in multiple sites in 10–15% of patients. Immunohistochemical analysis is positive for S-100 protein.

It is difficult to distinguish GCTs from other submucosal lesions based on endoscopy and EUS alone without pathologic diagnosis. Studies suggest that EUS and endoscopic removal is the treatment of choice for esophageal GCTs if they are small in size (< 2 cm) and do not involve the muscularis propria.

GCTs are malignant less than 2% of the time. Larger GCTs have a higher risk of malignancy. Although most GCTs are benign and can be surveyed endoscopically, the malignant potential warrants evaluation with EUS for possible endoscopic resection.

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Fulminant Hepatic Failure from Budd-Chiari Syndrome Treated with TIPS

Stanley M. Cohen, M.D., * Hector Ferrell, M.D., Sushama Gundlapalli, M.D., Anthony M. Sako, M.D., Forrest Dodson, M.D., Shritam Jakate, M.D.

Hepatology, Rush University Medical Center, Chicago, IL; Radiology, Rush University Medical Center, Chicago, IL; Surgery, Rush University Medical Center, Chicago, IL, and Pathology, Rush University Medical Center, Chicago, IL.

Budd-Chiari syndrome (BCS) is a rare disease caused by hepatic venous outflow obstruction. Presentation can include fulminant hepatic failure. Few treatment options, including emergent surgical decompression and liver transplantation, are available for fulminant BCS. Anticoagulation is generally not effective. Previous case reports and small series have shown TIPS (transjugular intrahepatic portosystemic shunt) to have poor outcomes in fulminant BCS. We present a case of fulminant hepatic failure due to BCS successfully treated with TIPS.

A 27 year old male with no past history presented with abdominal pain, jaundice, and elevated liver function tests (LFT’s). His laboratory data revealed albumin 3.0 mg/dL, bilirubin 58 mg/dL, AST 674 U/L, ALT 434 U/L, and INR 2.62. Ultrasound (US) and CT scans revealed occluded hepatic veins, caudate lobe hypertrophy, and massive ascites. Venogram revealed completely thrombosed hepatic veins, and a stenotic intrahepatic inferior vena cava. Liver biopsy showed dilated sinusoids, peri-central vein (zone 3) necrosis and hemorrhage, and bridging fibrosis. The patient was listed for emergent liver transplantation. Due to worsening mental status with asterixis, worsening LFT’s (bilirubin 8.0, AST 1245, ALT 672) and INR (4.16), an emergent TIPS was placed as a temporizing, decompressive measure. The TIPS was placed from the right hepatic vein stump to the right portal vein using a covered endoprosthesis. The hepatic venous pressure gradient decreased from 52 mmHg to 11 mmHg. Hypercoagulable work-up was negative.

Three months after the TIPS placement (without the need for liver transplantation), the patient has returned to work. His TIPS is patent by US. Except for a bilirubin of 2.1 mg/dL and an INR of 1.75, his LFT’s have normalized. Treatment options are limited for fulminant hepatic failure from BCS. Emergent surgical decompression is limited by the lack of local expertise, and significant morbidity and mortality. Emergent liver transplantation is limited by organ availability. Our case demonstrates that TIPS can be performed successfully and safely in a patient with fulminant hepatic failure from BCS. TIPS can be used as a temporizing bridge to liver transplantation, or possibly as definitive therapy.

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A Case of Duodenal Pigmentation in a Patient with Upper Gastrointestinal Bleeding


Medicine, Loyola University Medical Center, Maywood, IL.

Case Report: This 67-year-old caucasian female with CAD, CHF, DM type 2, GERD, hypothyroidism, COPD, iron deficiency anemia, and multiple serrated adenomas throughout the colon presented to the ED with dizziness and lightheadedness. She had noticed intermittent black stools over the previous two months since being started on oral iron replacement. However, she described melena and maroon stools for two days prior to admission. She denied chest pain, shortness of breath, nausea, or vomiting. Our patient was found to be orthostatic on examination and lab values revealed acute worsening of known iron deficiency anemia. EGD was performed and revealed gastric AVM’s and an antral ulcer (both coagulated using APC).

In addition, upon intubation of the duodenum, punctate black pigmentation was identified diffusely throughout the duodenal bulb and second portion of the duodenum. Duodenal biopsies revealed “focal black pigment deposition into the lamina propria of the villi” and a negative iron stain. Further staining, including Fontana Masson with and without bleach, was performed. The pigment disappeared upon bleaching, which reflects that melanin is the probable origin.

Discussion: These duodenal findings can possibly be attributed to “Pseudomelanosis duodeni” which is a rare endoscopic entity previously reported predominantly in African-American females in the sixth or seventh decade of life. Many reported patients are hypertensive (treated with hydralazine and propranolol in particular), diabetic, have chronic renal disease and have had upper gastrointestinal bleeding. Although exact composition of this pigmentation is unknown, it has been postulated to be melanin, a melanin-like substance, iron, hemosiderin, or lipofuscin. The full clinical significance of this finding has not been elucidated to date.

In a patient with the above findings, we propose that he or she be evaluated for other systemic entities which may be causative. First, the patient should undergo thorough dermatologic examination to assess for malignant melanoma, which has been described to metastasize to intestinal mucosa. Next, the patient should be evaluated for folic acid deficiency previously described to be associated with melanosis of the duodenum. Also, the patient’s full medication history should be obtained (most importantly history of anti-hypertensive therapy).

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Development of Non-Hodgkin’s Lymphoma during Combination Therapy with Viral Breakthrough

Hatem T. Shoukeir, M.D., JoAnn Comas, RN, Larry Riccio, Pharm.D., Ayse Aytaman, M.D. * Gastroenterology, V A New York Harbor HCS, Brooklyn, NY and Gastroenterology, SUNY Health Science Center at Brooklyn, Brooklyn, NY.

Background: Hepatitis C is the most common chronic blood-borne infection in the United States. Liver is the primary site of infection. HCV can also infect and replicate in peripheral blood mononuclear cells leading to monoclonal proliferation of B-cells. Lymphoproliferative disorders have been associated with HCV including essential mixed cryoglobulinemia and non-Hodgkin’s lymphoma. 7–20% of patients with NHL have HCV. Antiviral therapy of the HCV infection has been associated with regression of the NHL. To date there are no reports of lymphoma development during antiviral therapy. We are reporting a case of NHL developing during combination therapy with viral breakthrough.

Case presentation: A 54 year old Vietnam war veteran with history of IDVA in remission and chronic hepatitis C was referred to the GI-Liver clinic. He was found to have genotype 1b, over 5,000,000 copies per ml viral load and stage 3 fibrosis on liver biopsy. He had history of post traumatic stress disorder, depression and hypertention. He underwent therapy with rebetron for 24 weeks with some biochemical but no virologic response and therapy was terminated. With advanced liver disease he was offered retreatment with pegylated interferon alpha 2 b (1.5 mcg/kg) weekly and ribavirin (10.6 mg/kg) daily. He had 2 log decline in HCV RNA to 21,000 copies per ml at 12 weeks with complete normalization of ALT and complete viral eradication at 24 weeks. At week 47 he presented to his primary care physician with 1-week history of a sore throat and an enlarged, tender lymph node in the right posterior cervical chain. He was given azithromycin with no improvement. A CT of the neck revealed a 2 cm lesion involving the right submandibular gland. FNA of the lesion revealed large cell lymphoma, diffuse, B-type. Repeat viral RNA revealed viral breakthrough with 923,167 copies per ml.
The prevalence of breakthrough during interferon therapy ranges between 14% to 21%. The significant viral proliferation during breakthrough in this case has been associated with clonal proliferation of the B-cells and lymphoma development.

The pathophysiologic insights, LN biopsy and patient/virus demographics will be discussed.

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Primary Splenic Lymphoma in an HCV Positive Patient
Steve T. Chen, M.D., Robert J. Martin, CRNP, Shyam Bulepur, M.D.
Gastroenterology, Lancaster Gastroenterology, Inc., Lancaster, PA and Hematology Oncology, Hematology Oncology Physicians of Lancaster, Lancaster, PA.

Case: A 63 year-old woman underwent CT of the abdomen to evaluate complaints of abdominal pain and early satiety. The CT showed multiple splenic masses and marked splenomegaly as well as a normal liver. Her PMH is significant only for HTN. She had remote exposure to blood transfusions incidental to an AIDS. She has had no prior hospitalizations for AIDS. Her past history includes SLE and rheumatoid arthritis. She has had no prior lymphoma development.

The prevalence of breakthrough during interferon therapy ranges between 10–25% of all PI cases. Most frequently, PI in AIDS is incidental and resolves or stabilizes with conservative management. Our patient, however, developed worrisome signs and symptoms requiring laparotomy. Clinicians must be aware that the spectrum of PI-associated lymphoma is diverse. This rare disorder may manifest as an incidental finding, or as unexplained digestive symptoms which may be innocuous or life-threatening. Free intraperitoneal air in this setting may be due to rupture of a subserosal bleb resulting in non-surgical pneumoperitoneum or reflect an intra-abdominal emergency.

Discussion: PI has been reported in AIDS and other immunosuppressed settings, including solid organ transplantation, chemotherapy, and high-dose corticosteroid treatment. Opportunistic infections such as CMV, toxoplasmosis, and cryptosporidium are the most common associations of PI in AIDS which may represent as many as 10–25% of all PI cases. Most frequently, PI in AIDS is incidental and resolves or stabilizes with conservative management. Our patient, however, developed worrisome signs and symptoms requiring laparotomy. Clinicians must be aware that the spectrum of PI-associated lymphoma is diverse. This rare disorder may manifest as an incidental finding, or as unexplained digestive symptoms which may be innocuous or life-threatening. Free intraperitoneal air in this setting may be due to rupture of a subserosal bleb resulting in non-surgical pneumoperitoneum or reflect an intra-abdominal emergency.

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Endoscopic Repair of a Post-Operative Gastro-Cutaneous Fistula
Piyush K. Dhanuka, M.D., Rosario Ligresti, M.D.,† Kaul Ashutosh, M.D., Edward Lebovics, M.D., J. Savino, M.D. Division of Gastroenterology & Hepatology Diseases, New York Medical College, Valhalla, NY and Department of Surgery, New York Medical College, Valhalla, NY.

Post-operative gastrocutaneous or enterocutaneous fistula are frequent surgical complications. They are difficult to treat and have high morbidity and mortality. We present endoscopic repair of one such case with fibrin glue application.

A 33-year-old woman with morbid obesity had undergone open Roux-en-Y gastric bypass surgery two years ago. She then underwent laproscopic redo surgery. Her immediate postop course was complicated by suture line leakage that required repair and jejunostomy tube placement. Three months later she presented with persistent drainage (∼800 mL/day) through two JP drains. Gastrografin study showed a gastro-cutaneous fistula.

Endoscopically both JP drains were visualized intraluminally just distal to the anastomosis site consistent with erosion through the gastric pouch wall. This was confirmed by methylene blue and contrast dye injection. Both JP drains were removed and the tract was infiltrated with 4 ml of fibrin tissue glue using a 7 French catheter. Complete occlusion was documented. Subsequent computerized tomography with oral contrast as well as gastrografin study revealed no extravasation. [figure1] Two repeat endoscopic application of fibrin tissue glue, at one week and four weeks interval, resulted in complete closure of the fistula. Complete closure was documented by gastrointestinal series performed with dilute barium at six weeks.

Fibrin tissue glue is a tissue-compatible glue used in various surgical fields for more than a decade to prevent bleeding. It promotes wound healing by fibroblast proliferation. In our case it successfully treated the post-operative fistula and prevented the need for a complicated surgical repair. Literature review does not reveal any such case from United States. With increasing number of the bariatric surgeries in US, endoscopic repair of such complications is likely to be increasingly valuable, and fibrin tissue glue can be a very useful adjunct to that.

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Pneumatosi s Intestinalis Due to Mycobacterium avium intracellulare in an AIDS Patient
Gregory A. Dadakian, B.A., Edward R. Feller, M.D., F.A.C.G.* Medicine, Brown Medical School, Providence, RI.

Pneumatosi s intestinalis (PI) is characterized by the presence of multiple submucosal and subserosal blood-filled cysts in the small or large intestine. PI associated with AIDS is usually asymptomatic, but uncommonly causes life-threatening disorders potentially producing bowel necrosis or perforation. We report a patient with Mycobacterium avium intracellulare (MAI) and complicated PI to alert clinicians to consider this rare and potentially misleading cause of abdominal complaints when evaluating clinical symptoms in AIDS.

Case report: A 41 y.o. man with AIDS (CD4 = 7) presented to the ER with 2 months of diffuse upper abdominal pain, diarrhea and weight loss. On exam, he was afebrile and had a distended, tender upper abdomen without signs of peritonitis. WBC = 2500 with 85% polys. Abdominal CT scan = widespread lymphadenopathy consistent with disseminated MAI, diagnosed previously. Abdominal pain decreased over several days, but loose, watery diarrhea persisted. On hospital day 10, his pain worsened acutely and new diffuse abdominal tenderness was detected; he remained afebrile with no change in WBC. Repeat CT scan demonstrated extraluminal, submucosal air consistent with pneumatosis of the right colon and sigmoid; a small amount of free intraperitoneal air indicative of intestinal perforation was suggested. He underwent exploratory laparotomy, sub-total colectomy and small bowel resection with ileostomy for severe colitis. Pathology revealed MAI of the ileum, colon and pericolonic mesenteric lymph nodes. No perforation was present.

Discussion: PI has been reported in AIDS and other immunosuppressed settings, including solid organ transplantation, chemotherapy, and high-dose corticosteroid treatment. Opportunistic infections such as CMV, toxoplasmosis, MAI and cryptosporidium are the most common associations of PI in AIDS which may represent as many as 10–25% of all PI cases. Most frequently, PI in AIDS is incidental and resolves or stabilizes with conservative management. Our patient, however, developed worrisome signs and symptoms requiring laparotomy. Clinicians must be aware that the spectrum of MAI-associated PI in AIDS is diverse. This rare disorder may manifest as an incidental finding, or as unexplained digestive symptoms which may be innocuous or life-threatening. Free intraperitoneal air in this setting may be due to rupture of a subserosal bleb resulting in non-surgical pneumoperitoneum or reflect an intra-abdominal emergency.
Discussion:
chemotherapy. The patient died of disseminated, undiagnosed malignancy 6 weeks after a painless mass in his right groin. On exam, he was afebrile; a hard, smooth, mobile, irreducible 4 cm mass was palpated just above the inguinal ring. Abdominal CT scan confirmed an incarcerated right inguinal hernia. At laparotomy, the mass was discovered to be indurated omentum. Pathologic examination of the resected omentum with special stains revealed metastatic adenocarcinoma consistent with a gastrointestinal (GI) primary. Review of the abdominal CT revealed a normal pancreas with some thickening of the gallbladder wall. No evidence of hepatic metastases was found. Ultrasound confirmed minimal thickening of the gallbladder wall with multiple small stones. Complete blood count, liver chemistries, alpha-fetoprotein and CEA were normal, but CA 19–9 was slightly elevated. Colonoscopy confirmed minimal thickening of the gallbladder wall. No evidence of hepatic metastases was found. Metastatic adenocarcinoma consistent with a gastrointestinal (GI) primary. We report a patient with this association to alert clinicians to this exceptional etiology of a groin hernia.

Case Report: A 73-year-old man presented to his physician 3 weeks after the discovery of a painless mass in his right groin. On exam, he was afebrile; a hard, smooth, mobile, irreducible 4 cm mass was palpated just above the inguinal ring. Abdominal CT scan confirmed an incarcerated right inguinal hernia. At laparotomy, the mass was discovered to be indurated omentum. Pathologic examination of the resected omentum with special stains revealed metastatic adenocarcinoma consistent with a gastrointestinal (GI) primary. Review of the abdominal CT revealed a normal pancreas with some thickening of the gallbladder wall. No evidence of hepatic metastases was found. Ultrasound confirmed minimal thickening of the gallbladder wall with multiple small stones. Complete blood count, liver chemistries, alpha-fetoprotein and CEA were normal, but CA 19–9 was slightly elevated. Colonoscopy confirmed minimal thickening of the gallbladder wall. No evidence of hepatic metastases was found. Metastatic adenocarcinoma consistent with a gastrointestinal (GI) primary. We report a patient with this association to alert clinicians to this exceptional etiology of a groin hernia.

Discussion: adenocarcinoma found in inguinal hernia sacs is most commonly gastrointestinal, ovarian, prostatic or due to tumors associated with ascites. Unusual benign lesions, including pancreatic pseudocysts or abdominal abscesses may also present as a groin hernia. Increased intraabdominal or local pressure may contribute to its development. Hernia as the initial manifestation of carcinoma of unknown primary is exceedingly rare. A new, irreducible, or rapidly expanding inguinal hernia may, exceptionally, be due to cancer. As in our case, evaluation uncommonly detects the primary site. Physicians should be aware of malignancy presenting as a groin hernia. Gross abnormalities within a hernia sac should be studied histologically, though routine examination of all hernia sacs is unwarranted.

Pylephlebitis: Still Present in the Modern Era?
Christopher Boatin, M.D., Roger Montenegro, M.D., Shrutii Sawnhey, M.D., Mary Jo Atten, M.D., Harry Richter III, M.D., Bashar M. Attar, M.D. F.A.C.G.* Medicine, John H. Stroger Hospital of Cook County, Chicago, IL and Surgery, John H. Stroger Hospital of Cook County, Chicago, IL.

Pylephlebitis, supplicative thrombophlebitis of the portal vein, is a potentially fatal condition that is usually associated with severe intra-abdominal or pelvic infections. In the antibiotic era this infectious complication should be expected to be extremely rare, but given its high mortality, it is a condition requiring prompt diagnosis and treatment. This previously healthy 62-yr old male presented with a one month history of abdominal pain and fever. He had gone to an outside clinic and was given a one week course of an antibiotic for a UTI. On exam he had a temperature of 100.5 and LLQ tenderness. Labs showed a leukocytosis of 19,000 and albumen of 2.9. Abdominal CT showed wall thickening in the sigmoid colon with two adjacent abscesses and a thrombus in the portal vein with extension into the superior mesenteric vein. Blood cultures were drawn and he was started on broad-spectrum antibiotics and anticoagulation with LMW heparin. The abscesses were not accessible for aspiration/drainage by percutaneous or transrectal routes. The fever, leukocytosis and abdominal pain/tenderness resolved over the next several days and he was discharged on oral antibiotics and LMW heparin with plans for colonoscopy in 4–6 weeks. Over the course of the next 6 weeks he was admitted twice for recurrent abdominal pain; one time he also had diarrhea and C. difficile colitis that was treated. Colonoscopy showed diverticulosis. Repeat CT showed resolving thrombus and recanalization of the portal vein. He underwent left hemicolectomy and did very well post-operatively with no evidence of portal hypertension. Anticoagulation was discontinued after 6 months, and work-up for a hypercoagulable state was negative. Pylephlebitis should be a disease of the past in developed countries with easy access to medical care and the availability of broad-spectrum antibiotics. However, there may be resurgence in this potentially fatal condition, perhaps related to increasing numbers of uninsured patients without easy access to medical care. Wide-spread use of high resolution CT scanning may merely be diagnosing this condition more readily. However, this patient illustrates severe, prolonged intra-abdominal infection (at least one month) leading to pylephlebitis. Whatever the cause of this resurgence, it is a condition requiring rapid diagnosis and treatment in order to keep mortality low.

Cardiac Tamponade Secondary to Infrathoracic Gastric Volvulus
Paula M. Dionisio, M.D.,* Christopher D. Wells, M.D., Patel M. Baves, M.D., Leighton A. Jonathon, M.D., Heigh I. Russell, M.D. Internal Medicine, Mayo Clinic Hospital Scottsdale, Phoenix, AZ., Gastroenterology, Mayo Clinic Hospital Scottsdale, Phoenix, AZ and Critical Care Medicine, Mayo Clinic Hospital Scottsdale, Phoenix, AZ.

A 69-year-old male with a known paraesophageal hernia underwent bilateral partial nephrectomies for bilateral renal cell carcinoma. On his first post-operative day, the patient developed acute shortness of breath with tachycardia and hypotension. Pulmonary embolism was suspected so an emergent computed tomography (CT) of the chest was obtained. The CT revealed a distended, entirely intrathoracic stomach with evidence of an organo-axial volvulus. The distended stomach caused moderate-to-severe compression of the left atrium. The patient returned to the intensive care unit where he was intubated and pressors were initiated for continued clinical deterioration. Due to clinical and radiographic evidence of cardiac tamponade, an emergent upper endoscopy was performed in an attempt to decompress the stomach. Once the endoscope was successfully advanced to the esophago gastric junction a snare was used to drag the nasogastric tube into the twisted stomach, and the stomach was decompressed. A rapid improvement in the patient’s hemodynamic status was noted following the procedure and within several hours he was extubated and requiring no hemodynamic support.

Gastric volvulus is an infrequently encountered clinical entity. Cardiac tamponade secondary to a gastric volvulus is exceptionally rare and there have been only 3 previous case reports. Although few have described this clinical circumstance, all describe fatal or near fatal situations. Timely endoscopic management, via decompression or reduction, can quickly restore hemodynamic stability. This diagnosis should be considered in the appropriate clinical setting in patients with a predisposing condition, such as a paraesophageal hernia.
**Behcet’s Ileocolitis: Dramatic Response to Infliximab Infusion**

Sripathi R. Kethu, M.D. ∗ Division of Gastroenterology, Brown Medical School and Rhode Island Hospital, Providence, RI.

**Introduction:** Behcet’s disease (BD) is a chronic, relapsing, multisystem, immune-mediated, inflammatory disorder of unknown etiology. Gastrointestinal tract involvement is seen in 3%-26% of patients with BD. The diagnosis of BD can be made if the patient has oral ulceration occurring at least three times a year, with 2 of the following: recurrent genital ulcers, skin lesions, eye lesions or a positive pathergy test. There are three published case reports so far describing the efficacy of infliximab in treating Behcet’s ileocolitis. Here we describe a case where patient with Behcet’s ileocolitis responded dramatically to infliximab infusion.

**Case Presentation:** A 35-year-old woman presented with right lower quadrant pain and diarrhea of 6 weeks duration. The stool was watery, non-bloody, approximately 8–10 times per day. She had a 5-pound weight loss in 6 weeks and low-grade fever. She also complained bilateral knee pains on admission, which she had on and off for the past 8 years. She gave history of recurrent orogenital ulcers for the past 3 years for which etiology could not be found. Approximately 2 years ago she had an episode of uveitis that was treated conservatively. Her C-reactive protein (CRP) level was elevated to 24.7 mg/L (range 0–8.0 mg/L) and erythrocyte sedimentation rate (ESR) was 72 mm/hr (range 0–20 mm/hr). Stool studies were negative for any infection. Colonoscopy revealed multiple well-demarcated, penetrating ulcers throughout the colon and ileum. The histology of these ulcers revealed acute inflammation without granulomas. Antisccharomyces cervicase antibody was negative. Based on these symptoms, Behcet’s disease with ileocolitis was diagnosed. Initially she was tried on high-dose intravenous corticosteroids with poor response. Then she was given infliximab 5mg/kg infusion. Less than 24 hours after the infusion, her diarrhea stopped and knee pain resolved. The patient received second infusion at week 2. After the second infusion, colonoscopy was repeated which showed complete healing of all the ulcers. Random biopsies of the colon revealed minimal residual inflammation. CRP and ESR were normal. Then she received the third infusion at week 6. The patient remained in remission without any additional therapy at the end of 4 months after the last infusion.

**Conclusion:** Infliximab is effective in treating ileocolitis associated with Behcet’s disease. Patients who do not respond to intravenous corticosteroids, should be considered candidates for therapy with infliximab.

**A Patient with Schistosomiasis Presenting as Colonic Ulcers, Severe Iron Deficiency Anemia and Esophageal Varices**

Mamoon M. Elbedawi, M.D., Khalid A. Khambal, M.D., Samuel Giday, M.D., Joseph Nidiry, M.D., Duane T. Smoot, M.D. ∗ Internal Medicine, Howard University Hospital, Washington, DC.

Schistosomiasis is endemic mostly in the tropical regions. Its life cycle has human and snail host. Adult worms of S. mansoni reside in mesentery and portal veins. The eggs produced cause intense granulomatous inflammation and fibrosis which result in the formation of portal hypertension, and in the colon ulceration, inflammatory polyps and in severe cases strictures. This is the first case in the literature with complication in the liver and colon. A 21 year old male with no past medical history, recently migrated to the US from Guinea presented with 3 weeks of painful LUQ mass. Also he had weight loss, heartburn and bloody diarrhea. On physical exam he had LUQ abdominal tenderness and splenomegaly with a total span of 20 cm. CBC showed Hb of 5.4, HCT of 19.1, with microcytosis and low serum iron. LFTs were normal. Stool was negative for ova and parasite. HIV, Hepatitis B and C tests were negative. Sickle cell and malarial smears were also negative. CT scan and ultrasound of the abdomen showed splenomegaly. BM biopsy showed normocellular to hypercellular BM with absent iron stores. Patient also underwent EGD that showed grade 2 esophageal varices with no stigmata of recent bleeding. Colonoscopy showed rectosigmoid ulcers. Histopathology of the colonic ulcerations revealed a calcified schistosoma egg.

This is a case of Schistosomiasis that resulted in portal hypertension with esophageal varices, splenomegaly, colonic ulceration and severe iron deficiency anemia. Therefore Schistosomiasis should be entertained in the differential diagnosis in patients with severe iron deficiency anemia and splenomegaly on a background of recent travel to endemic area or recent migration to the US. [figure1] [figure2]

**Incidental Finding of a Chronic Gastric Volvulus: An Underdiagnosed Entity Associated with Increased Mortality**

Julie T. Yang, M.D., Geoffrey Gardiner, M.D., David S. Condon, M.D. ∗ Medicine, Division of Gastroenterology, Loma Linda University Medical Center, Loma Linda, CA.

**Background:** Gastric volvulus is defined as abnormal rotation of the stomach of more than 180 degrees and can result in incarceration and strangulation. It was first described in 1866 and remains a rare clinical entity. It is defined by the classic triad of severe epigastric pain, retching without vomiting, and inability to pass a nasogastric tube. Diaphragmatic defects and gastric ligament defects are the most common causes of secondary gastric volvulus in adults in 43 and 32% of cases, respectively. Patients with gastric...
volvulus often present with nonspecific symptoms and therefore are often misdiagnosed as having cholelithiasis or peptic ulcer disease. We report a case of a patient who presented with one episode of coffee-ground emesis and melena associated with epigastric pain without previous gastrointestinal signs and symptoms, and who was subsequently found to have large hiatal hernia, camelion ulcers and gastric volvulus.

Case Report: A 71-year-old man with previously diagnosed peptic ulcer disease and hiatal hernia presented with one episode of coffee-ground emesis and melena associated with epigastric pain. Patient did not report early satiety, intermittent abdominal pain associated with eating, or previous episodes of retching or vomiting. Upper endoscopy revealed a large hiatal hernia, ulcers within the hiatal hernia and a duodenal diverticulum. The EGD scope was also noted to coil up and undergo a longer and skewed path inside the stomach. An upper GI barium-contrast study showed a large hiatal hernia, two duodenal diverticula and an organoaxial volvulus of the stomach without evidence of obstruction. Patient's signs and symptoms resolved with proton pump inhibitor. He remained asymptomatic and was referred for surgical evaluation.

Conclusion: Gastric volvulus can present with nonspecific or no symptoms and is often misdiagnosed or underdiagnosed. Chronic gastric volvulus has up to 13% mortality rate and acute gastric volvulus with up to 20% mortality rate. Surgery is the definitive treatment, even though endoscopic treatments have been reported. We need to increase our awareness of such an entity and should also consider upper GI barium-contrast study in patients who present with nonspecific abdominal complaints.

Six Month Safety and Efficacy of Polyflex® Stent for Treatment of Benign Esophageal Stricture
Shilin Y. Lakhani, M.D., R. Martin Bashir, M.D., F.A.C.G., F.A.C.P.
Department of Medicine, Washington Hospital Center, Washington, DC.

Options are limited for the management of individuals who have failed proton pump inhibitor therapy and esophageal dilation for treatment of benign, distal esophageal stricture. This is a report of an 80 y/o woman with a 3 year history of a benign esophageal stricture who presented with increasing dysphagia to liquids and solids with secondary 30 lb. weight loss. Her past management had included repeated esophageal dilation with biopsies and twice daily proton pump inhibitor therapy. At upper endoscopy, she had a distal esophageal stricture extending from 37 to 40 cm from the central incisors. The stricture was at the level of the Z line with no evidence for a hiatal hernia. Multiple biopsies were consistent with gastroesophageal reflux disease with no evidence of Barrett's metaplasia, dysplasia, or malignancy. Endoscopic ultrasound demonstrated thickening of the distal esophagus and no mass or adenopathy. A 12 cm x 18 mm Polyflex® stent (Boston Scientific Corp.) was placed under fluoroscopic guidance (Figure 1). At follow-up 8 weeks later, she reported complete resolution of dysphagia and had regained 12 lbs. At that time she refused to have the stent removed, as recommended by the manufacturer. She was then followed bimonthly and had no signs or esophageal symptoms to suggest stent occlusion or migration. Repeat endoscopy at 6 months demonstrated a completely in tact Polyflex® stent in excellent position. Since placement of the stent, she had gained 32 lbs. and was asymptomatic.

Conclusion: In select individuals with benign esophageal strictures, placement of a Polyflex stent provides a safe and effective long-term option for management of dysphagia and weight loss.

Reversal of Liver Cirrhosis in a Nonresponder with Chronic Hepatitis C
Ayodele T. Osowo, M.B.B.S., Vinodh Jeenavatham, M.B.B.S., M.P.H., Taran Kohari, F.A.C.P.* Medicine, Unity Health System (Park Ridge Hospital), Rochester, NY and Gastroenterology, Unity Health System (Park Ridge Hospital), Rochester, NY.

Background: Chronic hepatitis C virus (HCV) infection is a leading cause of liver cirrhosis and hepatocellular carcinoma, thereby increasing the population in need of liver transplantation. The Use of interferon and ribavirin has reduced the morbidity and mortality of this disease.

Case: A 49-year old African American female seen in clinic with elevated ALT 68 and AST 99(alanine and aspartate aminotransferases) on routine checkup. She quit alcohol and intravenous drug use 14 years ago. Vital signs and physical examination were unremarkable. Hepatitis profile was positive for only HCV, genotype was 2A. Complete blood count, electrolytes, Iron studies, thyroid function, amylase, lipase and alpha 1-antitrypsin were normal. Hepatic panel was normal except for elevated ALT and AST. Alpha fetoprotein and screening for autoimmune hepatitis were unremarkable. Pre-treatment liver biopsy showed severe piecemeal and bridging necrosis (grade 3) and cirrhosis (stage 4). She received two 12month courses of Ribavirin and interferon alpha 2b with partial viral response without viral clearance. Five months after her last treatment viral count was 279,000 copies/ml. She received another 12month trial of Pegylated interferon alpha-2b and ribavirin with partial response after 12 months. Lowest viral count during treatment was 224,000 copies/ml but the 6 months post treatment count was 700,000 copies/ml. Repeat liver biopsy showed mild piecemeal necrosis (grade 1) and mild fibrosis (stage 1).

Conclusion: The goal of treatment in Hepatitis C infection is to prevent complications. Infection is considered eradicated when there is sustained Virologic response (SVR), defined as absence of virus in serum by RNA testing 6months after 1 year of treatment. The primary benefit of treatment is histological, that is prevention of cirrhosis and hepatocellular carcinoma. Several studies have shown that there is histological advantage in treatment of nonresponders even in the absence of viral clearance. As seen in this case there was complete reversal of cirrhosis without eradication of the virus. Hopefully as more data becomes available there will be a stronger recommendation for treatment of nonresponders who can tolerate the medications.

Efficacy of Rifaximin in Steroid Dependent Crohn’s Disease
Wojciech Blonski, M.D., Rabi Kandi, M.D., Gary R. Lichtenstein, M.D.* Division of Gastroenterology, Wroclaw Medical University, Wroclaw, Poland and Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA.

Case: 43 yo white female with known colonic Crohn’s disease (CD) for 15 yrs duration with peripheral arthropathy in both knees presented with a CD flare having 4–5 BMs/day, hematochezia, tenesmus, abdominal cramping, low grade temperature 38.3C and arthropathy. She had 3 flares of her CD in her life each treated with a course of corticosteroids. The last flare was 7 yrs ago.

Labs: Hgb 11.2 gm/dl (baseline 13.0 gm/dl), WBC 10.4/mm3, ESR 35 mm/hr and CRP 12 mg/l

Colonoscopy: Active CD was present from the distal sigmoid colon to the midtransverse colon with serpiginous ulcers in mid transverse colon and relative rectal sparing. Colonoscopic biopsies from the area of active ulceration showed histologic evidence of CD.

Course: The pt was treated initially with mesalamine 4g/day and had no response to therapy over a course of 8 wks. She was started on Prednisone 40mg/day for 2 wks which resulted in resolution of symptoms to 1 BM/day. Prednisone was tapered at a rate of 5mg/wk to 15 mg/day and she developed fecal urgency, loose stools (5 BMs/day). Her prednisone dose was increased to 40 mg/day, symptoms resolved but she developed moon face, acne, anxiety and depression. She refused treatment with immunomodulators, infliximab or further steroids due to concerns about potential toxicity.

Given the persistence of symptoms and her disease being colonic in location, Rifaximin (Xifaxan®) 400 mg BID for 2 wks was instituted with resolution of symptoms. Subsequently steroids were tapered off. She has now been off corticosteroids and is symptom free for the past 8 mos.
Discussion: Oral antibiotics have demonstrated therapeutic efficacy for multiple enteric conditions treated by gastroenterologists. CD has been demonstrated to be effectively treated with antibiotics in the past in several trials: (Sutherland et al. Gut 1999;32:1071) Efficacy of metronidazole demonstrated in colonic CD; (Steinhaert et al. Gastroenterol. 2002;123:33 and Prantera et al AJG 1996;91:328) Efficacy of ciprofloxacin + metronidazole (especially in colonic CD- in Steinhart’s study). Preliminary data for Rifaximin has been presented for Crohn’s disease (Pinto et al Eur J Clin Res 1997;9:217 and Kornbluth A et al gastro 2005 DDW Abstract and Bosworth BP et al gastro 2005 DDW abstract) however none have suggested its use for steroid dependent patients. The efficacy of Rifaximin in steroid dependent patients might be appropriate to further investigate.

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Anorectal Plasmablastic Lymphoma in an HIV+ Patient: An Uncommon Site
Gilbert Simoni, M.D., Robert S. Spira, M.D.∗ Division of Gastroenterology; Seton Hall University School of Graduate Medical Education, South Orange, NJ. St. Michael’s Medical Center, Newark, NJ.

Introduction: Plasmablastic lymphoma (PBL) is a newly described and unique subtype of diffuse large B-cell lymphoma predominantly in HIV positive patients involving unusual sites, commonly in oral cavity and the jaw. Its immunophenotypically, PBL is negativity for CD20 and immunoreactive for VS38, CD79a and CD138. This particular type of non-Hodgkin lymphoma has a rapidly progressive course that carries a poor prognosis if not treated properly. We present a case of PBL in the rectum which was diagnosed with difficulty but treated successfully.

Case report: A 48 year-old HIV positive African American male with CD4 count of 80 cells/mm3 presented with rectal bleeding for two months, fatigue and weight loss. Colonoscopy showed a large rectal mass. Biopsy revealed granulation tissue with marked inflammation. MRI of pelvis showed a 4 cm and weight loss. Colonoscopy showed a large rectal mass. Biopsy revealed granulation tissue with marked inflammation. Preliminary data for Rifaximin has been presented for Crohn’s disease (Pinto et al Eur J Clin Res 1997;9:217 and Kornbluth A et al gastro 2005 DDW Abstract and Bosworth BP et al gastro 2005 DDW abstract) however none have suggested its use for steroid dependent patients. The efficacy of Rifaximin in steroid dependent patients might be appropriate to further investigate.

Discussion: In HIV positive patient anorectal masses can occur from a wide spectrum of causes with most common lesions being condyloma and rectal ulcers that are usually idiopathic but some associated with HSV and CMV. Malignancies in the anorectum are less common but when present, they are commonly associated with Kasposi’s sarcoma, Non-Hodgkin’s Lymphoma, squamous-cell carcinoma, and adenocarcinoma. To date and to the best of our knowledge, there have only been three cases of anorectal PBL reported in the literature all of which have focused on its histopathology.

Conclusion: Our case illustrates the difficulties in diagnosis of PBL. The unusual and unique immunohistochemical characteristics of PBL warrants a high index of suspicion. Gastroenterologists should be aware of this rare malignancy, especially in the HIV infected patients who present with rectal mass, because of its fatal outcome if it is improperly treated or left untreated.

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Esophageal “Piercing”
Susana Lopes, M.D., Guilherme Macedo, Ph.D.∗ Fernando Tavarela Veloso, Ph.D. Gastroenterology Department, H.S.Joao, Porto, Portugal.

A 42 years old male was referred to us for a suspected foreign body implanation in upper esophagus. In a routine chest X-ray, an opaque ring, 0.8 cm diameter, was seen apparently in the upper esophagus. He was totally asymptomatic, and denied a previous accidental or volunteer ingestion of any foreign body. A CT scan was performed, confirming the presence of a luminal foreign body and some parietal thickening.

Endoscopy revealed a suspended metallic (golden) ring over a mucosal bridge, at 22 cm from dental arcade. We proceeded to its retrieval, after cutting the mucosal bridge with papillotome knife. The patient kept asymptomatic, with normal endoscopy 2 weeks later. At this appointment, he recalled from his mother that a golden ring was missing when he was 1 year old!

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Acute Cholestatic Hepatitis Associated with Reinitiation of Statin Treatment
Ken Song, M.D., Sherman Chamberlain, M.D., William Salazar, M.D., Subbaramiah Sridhar, M.B.B.S.∗ Medicine, Medical College of Georgia, Augusta, GA.

We report a case of acute cholestatic hepatitis after reinitiation of a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (HMG-CoA RI). A 51 year old patient with a remote history of heavy alcohol abuse was admitted with jaundice, epigastric pain, and weakness. 2 years previously he received atorvastatin. Subsequently, he was found to have elevated aspartate and alanine aminotransferase and alkaline phosphatase with a normal bilirubin level. Liver biopsy at that time was consistent with chronic hepatitis and stage 3 fibrosis. The liver enzymes returned to normal after discontinuing atorvastatin. 6 weeks before his most recent admission, he was started on a medication containing simvastatin and ezetimibe. He developed worsening fatigue and jaundice, and presented to our institution.

A hard, enlarged, minimally tender liver was noted. Serological tests of viral hepatitides, iron studies, auto-antibodies against the liver were either normal or negative. Contrast CT scan showed an enlarged liver with fatty change. Liver biopsy showed stage 4 fibrosis with focal cannuicular cholestasis. Over the next 4 days of hospitalization of all medications, his symptoms resolved, and he was discharged.

Patients taking HMG-CoA RIs’ rarely develop mild serum transaminase elevations, however, acute cholestatic hepatitis is seldom reported. The exact mechanism is unknown. Our patient developed an acute cholestatic hepatitis induced by an HMG-CoA RIs on two separate occasions, explained by the temporal relationship to the initiation of therapy, and development of liver injury, followed by improvement in symptoms and laboratory data after discontinuing the therapy. This case is compatible with the diagnosis of severe acute cholestatic hepatitis due to the reintroduction of an HMG-CoA RI, to which this chronic liver disease patient had been previously sensitized. HMG-CoA RIs occasionally cause acute cholestatic hepatitis. Further liver injury related to re-initiating HMG-CoA RIs has been reported previously. Our case highlights that a patient with underlying chronic liver disease, who develops mild liver toxicity when an HMG-CoA RI is initiated, may develop a more severe liver toxicity if this drug class is reintiated even after a long time lag. This suggests a possible immuno-allergic mechanism of liver toxicity which may develop against the entire class of HMG-CoA RIs. Thus, it is important to avoid the reintroduction of HMG-CoA RIs in those who have underlying chronic liver disease.

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Management of Hepatic Arteriovenous Malformations in Hereditary Hemorrhagic Telangiectasia
Emeline F. Helou, M.D., Patrick Kamath, M.D.∗ Karen Swanson, M.D. Gastroenterology, Mayo Clinic, Rochester, MN.

A 62 year old woman with a twenty-five year history of hereditary hemorrhagic telangiectasia (HHT) presented with right upper quadrant pain and dyspnea on exertion. Physical exam was remarkable for mucocutaneous telangiectasias, jugular venous distension, clear lung fields, a right upper
quadrant bruit, and lower extremity edema. CT of the abdomen demonstrated multiple enhancing lesions throughout the liver with enlarged hepatic arterial branches, consistent with HHT involvement of the liver. Echocardiogram and right heart catheterization revealed high output cardiac failure. Her symptoms progressed despite medical management of the cardiac failure. Hepatic artery embolization and liver transplantation were considered. Liver involvement is reported in up to 30% of cases of HHT. Most commonly blood is shunted from hepatic arteries to hepatic veins, but hepatic artery to portal vein and portal vein to hepatic vein shunting may occur. Of those with hepatic involvement, up to 40% develop high output cardiac failure. Decreasing the amount of arteriovenous shunting improves symptoms and reverses the hemodynamic changes of high output cardiac failure. Hepatic artery embolization and liver transplantation in the management of HHT with hepatic involvement was reviewed. Between 1990 and 2004, twenty-six cases of hepatic artery embolization were reported. Improvement in cardiac output was demonstrated. Repeat embolization was required in many cases because of revascularization and collateral development. Complications were common and included cholangitis and biliary necrosis. Three patients required liver transplantation because of complications. Overall mortality was 35%. Between 1995 and 2004, twenty-four liver transplants for HHT were performed. Right heart catheterizations demonstrated improved hemodynamics. Hepatic artery ligation, banding or embolization was previously performed in six of these patients. Transfusion requirements were greater when compared to liver transplantation for other indications. Overall mortality was 24%. Follow-up was incomplete. In cases of HHT with hepatic arteriovenous shunting, hepatic artery embolization is temporizing and is associated with life threatening complications. Liver transplantation should be considered. It is associated with lower mortality, but longer follow-up is required. Further study is required to determine the optimal timing of transplantation, taking into consideration the reversibility of the cardiac failure as well as the degree of hepatic dysfunction.

AL Amyloidosis Presenting as Hematochezia and a Colonic Mass
Lisbeth A. Selby, M.D., Charlotte Gill, M.D., Mary B. Duke, M.D.*
Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY; General Internal Medicine, University of Kentucky, Lexington, KY and Pathology, University of Kentucky, Lexington, KY.

AL amyloidosis (ALA) is an unusual result of a plasma cell dyscrasia, with an incidence of 8/106, that usually presents with renal, cardiac or hepatic findings. Tissue damage results from deposition of amyloid protein, which is derived from immunoglobulin light chains. ALA only rarely presents with lumenal GI findings.

We report an 81 year old woman with a several month history of left lower quadrant pain, hematochezia, iron deficiency anemia, and constipation. The onset of abdominal pain preceded the other symptoms by 18 months. She had a significant PMH of MI, nephrectomy several years prior for renal cell cancer, and multi-infarct dementia. Colonoscopy revealed marked sigmoid diverticulosis with significant angulation. A near-obstructing, hemorrhagic, necrotic mass was noted in the mid sigmoid. Passage of the endoscope beyond the mass was deferred due to concern for perforation. Multiple biopsies were obtained. The chief endoscopic differential diagnoses were colon carcinoma, inflammatory mass associated with diverticulitis, and mass effect secondary to colonic ischemia. CT scan was unremarkable. Intraoperative findings mirrored the endoscopic appearance.

Pathologic examination of the resection specimen revealed an area of submucosal hemorrhage and ischemic necrosis. No evidence of carcinoma was noted. The walls of submucosal arteries were markedly thickened by deposition of an amorphous substance suspicious for amyloid. Congo red stains confirmed this substance as amyloid. The urine immunofixation electrophoresis (IFE) for the detection of Bence Jones proteins revealed free lambda monoclonal light chains. Immunostain revealed prominent staining of the arterial walls with antibody to lambda light chains. The development of the colonic mass lesion was probably related to ischemic necrosis and hemorrhage, which were a consequence of vascular damage by amyloid deposition. Although her chief manifestations were gastrointestinal, the urine IFE suggested systemic involvement. It is possible that she would have developed more typical manifestations over time, had she survived for longer term follow up. Subclinical ALA features were not explored due to a complicated post-operative course.

In summary, this case illustrates an unusual presentation of ALA which mimicked much more common disorders such as colon carcinoma and diverticulitis.

Argon Plasma Coagulation for Treatment of Watermelon Colon
Rishi Pawa, M.D., Ritesh Patel, M.D., Anil Gopinath, M.D., Jyothi Reddy, M.D., F.A.C.G.* Department of Gastroenterology, V.A. Medical Center, University of Illinois at Urbana Champaign, Danville, IL.

We report a rare case of iron deficiency anemia secondary to sigmoid colon vascular ectasia with endoscopic appearance of watermelon colon. Other than the stomach, watermelon lesions are rare in other parts of gastrointestinal tract. To our knowledge, only seven cases of watermelon colon have been reported, only one of which had sigmoid colon involvement. Associated conditions have included eosinophilia, chronic anemia, protein loosing enteropathy, watermelon stomach, systemic sclerosis and mitral valve disease with supraventricular tachycardia.

Chart review and review of available literature using Medline and relevant bibliographies of published articles.

Patient was found to have iron deficiency anemia after having presented to his primary care physician with complaints of weakness and fatigue. Colonoscopy was performed which revealed circumferentially arranged red-dish stripes in the sigmoid colon, biopsy of which revealed submucosal edema with chronic inflammatory cell infiltration and vascular ectasia. These lesions were treated by Argon Plasma Coagulation (power 45W, flow 1.2 L/min.). Argon Plasma Coagulation was performed again via flexible sigmoidoscopy 4 weeks later. EGD and laboratory screening for autoimmune diseases came back as normal and over the next 4 months, patient’s hematocrit improved and remained stable. [figure1] [figure2] Review of literature has revealed limited data on endoscopic therapy for watermelon colon. However, Argon Plasma Coagulation appears to be appropriate and effective therapy for watermelon colon based on the clinical outcome in our case.
Systemic mastocytosis results in accumulation of mast cells in various tissues. Here we report a case of systemic mastocytosis mimicking drug-induced hepatitis in a 60 year-old African-American woman. She presented with nausea, diarrhea and a 50 lb weight loss as well as hepatosplenomegaly and a cholestatic pattern on liver tests. The patient was not taking medications. Liver biopsy revealed prominent mixed inflammatory infiltrates including eosinophils in the portal tracts with bile duct injury and bile ductular proliferation. Tryptase and CD 117 staining showed prominent mast cells. Bone marrow biopsy confirmed mast cell infiltration with underlying myelodysplasia.

Systemic mastocytosis is due to persistent clonal proliferation of progenitors of mast cells associated with activating c-kit gene mutations. While 85% of adults have skin involvement, a minority of patients present with systemic disease only as was the case with our patient. There are only six published reports on cholestatic patterns of liver involvement by systemic mastocytosis (Table 1). Our case is the first to describe hepatic involvement of systemic mastocytosis presenting like drug-induced hepatitis. Clinicians and pathologists should have a high index of suspicion for systemic mastocytosis in a patient with cholestatic pattern of liver tests and bile duct inflammation and injury in the absence of drug exposure.

### Table 1. Case Reports of Cholestatic Pattern of Liver Involvement in Systemic Mastocytosis

<table>
<thead>
<tr>
<th>Reference</th>
<th>Presentation</th>
<th>Liver biopsy histology</th>
<th>Pattern of cholestatic abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our Case (2005)</td>
<td>60yo female</td>
<td>eosinophil &amp; mast cell infiltrate in portal tract; bile duct injury and proliferation</td>
<td>drug-induced pattern</td>
</tr>
<tr>
<td>Baron et al. (1995)</td>
<td>75 yo female; ERCP with tapered strictures of intrahepatic ducts</td>
<td>mast cell infiltrate in portal tract with concentric periductal fibrosis</td>
<td>sclerosing cholangitis pattern</td>
</tr>
<tr>
<td>Safyan et al. (1997)</td>
<td>35 yo female with AML</td>
<td>edematous portal tracts with mast cells; patchy canicular cholestasis</td>
<td>intrahepatic cholestasis pattern</td>
</tr>
<tr>
<td>Kyriakou et al. (1998)</td>
<td>60 yo male; ASMA +</td>
<td>hepatic mast cell infiltration</td>
<td>autoimmune cholangitis pattern</td>
</tr>
<tr>
<td>ibid</td>
<td>72 yo male; ASMA +</td>
<td>histologic lesions compatible with autoimmune cholangitis</td>
<td>autoimmune cholangitis pattern</td>
</tr>
<tr>
<td>ibid</td>
<td>47 yo female; ASMA +</td>
<td>not done</td>
<td>autoimmune cholangitis pattern</td>
</tr>
<tr>
<td>ibid</td>
<td>75 yo female; ASMA +</td>
<td>mast cell clusters in liver</td>
<td>autoimmune cholangitis pattern</td>
</tr>
</tbody>
</table>

ASMA = anti-smooth muscle antibody.

**Systemic Mastocytosis May Mimic Drug-Induced Hepatitis**

Sonia S. Kapfer, M.D., John Hart, M.D.,* Smruti R. Mohanty, M.D.
Section of Gastroenterology, University of Chicago Hospitals, Chicago, IL.

We report the case of a 44 year old male with chronic hepatitis C (CHC) infection and insulin-requiring diabetes mellitus (DM) who developed a severe insulin resistance syndrome (IRS). At age 41 the patient presented with glucose intolerance, and the diagnoses of CHC and type 2 DM were made. The patient was lean, HIV negative, and did not have a family history of DM. He admitted to occasional alcohol use. The patient did not have a liver biopsy and was not considered a candidate for antiviral therapy. Over the next six months, his diabetes was controlled with intermediate acting insulin in doses up to 100 units daily. Within a year of the diagnoses of CHC and DM, the patient’s insulin requirements rose dramatically, resulting in additional hospitalizations for symptomatic hypoglycemia. Plasmapheresis was initiated on the assumption that the IRS was associated with the underlying CHC infection; it was unsuccessful due to hypotension and discontinued. Anti-insulin-receptor antibody testing was negative. At age 44 the patient died due to complications of DM.

Although liver disease of any etiology may alter glucose metabolism, evidence is accruing to support an association between CHC and DM [1]. The mechanism behind this link is unknown. Mechanisms postulated include tumor necrosis factor’s effect on tyrosine phosphorylation and subsequent downregulation of insulin receptors, and beta cell dysfunction [2,3]. The majority of reported cases of DM in linked to CHC appear to be of the non insulin dependent variety and occur in relation to interferon therapy. The patient represents an unusual and as yet unreported example of a severely insulin resistant, treatment-naïve CHC patient.

**REFERENCES**

An eight-month-old previously healthy infant presented with a recent history of abdominal distension and post-prandial vomiting. She was ultimately taken for exploratory laparotomy, was diagnosed with a hepatoblastoma, and had a left hepatectomy and cholecystectomy at that time. The patient’s post-operative course was complicated by a persistent bile leak which did not respond to treatment with a pigtail catheter. Her total bilirubin rose to 9.1. This led to the decision to perform an ERCP.

An ERCP was performed under general anesthesia using a standard adult Olympus JF 140F side-viewing duodenoscope. The exam lasted approximately 2 hours. After biliary access was obtained, fluoroscopic images revealed a stricture in the RHD as well as another at the junction of the CHD and CBD, with proximal CHD dilation. After reviewing our diagnostic images, the surgeons decided to perform a second exploratory laparotomy. This revealed the cause of the strictures to be suture ligation from the previous surgery. A T-tube was placed and the patient’s bile leak resolved and her LFTs improved.

Images
The safety and efficacy of ERCP in the pediatric population has been established in several reasonably large retrospective case series done at major centers. These series depict ERCP success and complication rates comparable to those of ERCP performed in the adult population. Most authors report that, particularly in the infant population (less than 1 year old), as well as in a majority of cases in children less than 7 to 10 years old, a specially designed pediatric duodenoscope (IPF: Olympus) was used. The concern expressed by some is that using scaled-down instruments may limit technical procedural success. Although the data has not demonstrated this to be true, there are selected cases in which this concern is valid.

Our experience demonstrated that an eight-month-old infant weighing 7.7kgs was able to tolerate, without complication, a successful 2-hour diagnostic ERCP. To our knowledge, this is the first reported case over the past twenty years of a successful ERCP done using adult-scale equipment in an infant of this age and size. This is noteworthy because, in the appropriate clinical circumstance, this technique can be extremely useful in improving efficacy, particularly of therapeutic ERCP, in the pediatric population.

PMH: She had recurrent nose bleeds since childhood and UGIBs secondary to gastric and duodenal AVMs requiring interventions and numerous blood transfusions.

FAMHs: Maternal grandfather had recurrent epistaxis.

Results: INF was started based on telangiectasia resolution in one case report. Our pt had facial telangiectasia regression as well as diminished frequency and severity of nose bleeds which decreased from a daily occurrence to once weekly, approximately twelve weeks after INF was initiated. She had no reported GI bleeds after INF was begun.

Discussion: This is the third case report of pts with HHT noting regression of telangiectasias using INF and the first case describing epistaxis resolution. Subsequent to our implementation of INF, a second case of INF therapy resulting in regression of telangiectasias in a pt with HHT was reported.

Conclusion: INF is a promising new therapy for HHT. Clinical trials are needed in order to determine the efficacy of this drug in pts with HHT.
A 58-year-old male presented with hematemesis and melena. He was recently diagnosed with HCC and had two prior episodes of GVB. Prior investigations had revealed a large right liver mass, PVT, splenomegaly, dilated splenic vein with gastric varices.

On examination, he was hypotensive and had tender hepatomegaly. Investigations: Hb: 7 g/dl, platelets: 88,000/cmm, alkaline phosphatase: 139 U/l, AST: 90 U/l, ALT: 132 U/l and INR: 1.3. An upper endoscopy revealed a large cluster of gastric fundic varices and no esophageal varices. He was not a candidate for TIPS as CT scan redemonstrated PVT. This was suspected to represent invasion of HCC into the intra-hepatic vasculature. He was deemed to be at a high risk for re-bleeding and was not a candidate for splenectomy. He underwent SAE; two 8 mm Nestor coils were deployed within the distal splenic artery and six 10mm coils were deployed in the mid-distal aspect of the splenic artery. He tolerated the procedure well and there was no re-bleeding. A CT scan obtained 2 weeks later showed an approximately 80% splenic infarction with reduction in gastric varices.

Discussion: HCC is the fifth most common cancer and tends to invade the intrahepatic vasculature especially the portal vein. Portal vein tumor thrombosis (PVT) can be detected in 30–62% of reported patients and portends a poor prognosis. The incidence of variceal bleeding as the presenting feature in HCC ranges from 1–15%. GVB is a common complication of portal hypertension and is associated with high morbidity and mortality rates. Endoscopic sclerotherapy is difficult to perform for GVB and has had varying success rates. Although splenectomy is an option, it is has a high risk of severe hemorrhage and high operative mortality. SAE is an alternative treatment for this group of patients. SAE leads to cessation of GVB by decreasing splenic inflow. Metallic coils and Gelfoam are the most commonly employed agents. Close monitoring is suggested in patients with a volume of splenic necrosis > 50%. The post-embolization syndrome (pain, fever, vomiting) is the most frequent side effect and typically resolves rapidly. Other complications reported include transient ascites, splenic abscess, pneumonia, pleural effusion and sepsis.

In conclusion, SAE offers an attractive alternative for treatment of GVB associated with HCC and PVT in patients with high surgical risk.
not commonly thought of as a potential cause of diarrhea in an HIV patient, although HIV and Crohn’s can certainly co-exist. Case reports by James in 1988 and Yoshida in 1996 showed resolution of CD symptoms in patients who contracted HIV. Reports by Bernstein in 1994 and Lautenbach in 1997 showed that patients with HIV can have active CD even in the setting of markedly decreased CD4 counts. This is the first reported case of newly diagnosed CD in a patient with long-standing HIV. Reports by Bernstein in 1994 and Lautenbach in 1997 showed resolution of CD symptoms in patients who contracted HIV. Reports by Bernstein in 1994 and Lautenbach in 1997 showed that patients with HIV can have active CD even in the setting of markedly decreased CD4 counts. This is the first reported case of newly diagnosed CD in a patient with long-standing HIV. With great advances in the treatment for HIV, patients are maintaining normal immunity, and living, for longer periods of time. As a result, IBD may become more commonly seen in patients with HIV.

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Spontaneous Colonic Perforation without Dilatation in a Patient with Ulcerative Colitis (UC) and the Role of Imaging Modalities in the Diagnosis of Colonic Perforation

Laith H. Jamil, M.D., Thomas Alexander, M.D.* Gastroenterology, William Beaumont Hospital, Royal Oak, MI.

Describe an uncommon complication in a patient with UC.

64 year old, non-compliant female, with an 8-year history of UC currently on Asacol presents to the EC with 3 days of flu like symptoms, intermittent lower abdominal pain, nausea, vomiting, and diarrhea. Physical examination was unremarkable except for mild abdominal distention and mild tenderness in the lower quadrants. Labs showed a WBC 22.4, Hg 11.0, BUN 17, and Cr 2.0. Acute abdominal series (AAS) was worrisome for distal mechanical SBO without free air. Clinical condition deteriorated as the patient was being prepped for CT. CT abdomen and pelvis 6 hours following the AAS showed severely dilated bowel loops with inflammatory changes in the small bowel mesentery and evidence of perforation with free fluid without again free air. Patient underwent exploratory surgery, revealing a perforated sigmoid colon. Free colonic perforation without dilatation in patients with UC is uncommon. Free perforation occurred in only 7/702 patients with UC (1%) without toxic dilatation seen at Mount Sinai Hospital (1960–1981). These 7 patients represented 30% (7/23) of all colonic perforations seen in patients with UC. Classic physical signs of peritonitis were absent in 6/7 patients. All had a marked deterioration in general condition after perforation. Mortality was high (57%). Comparatively longer histories of colitis, prolonged current attacks, and slightly greater delays between presumed perforation and operation were characteristics of these patients.

Several studies have evaluated the use of various imaging studies in the diagnoses of visceral perforation. One study showed that combined radiography, US and CT showed signs of perforation in 71% of cases. When free air was present (1/3 of cases), free intraperitoneal fluid was the only radiological finding. Another study showed that CT demonstrated the presence of free intraperitoneal gas in more patients than an AAS (92% vs. 74%). Possibility of free perforation in UC must be considered in fulminating cases, even in the absence of colonic dilatation. Careful clinical monitoring and early surgical intervention may be the keys to reducing mortality. AAS is still the primary tool to evaluate for visceral perforation. Free air when present may be detected in nearly 100% of cases. When there is no free air detected and symptoms persist, CT should be performed after at least 6 hours interval to allow the radiological picture to change.

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Use of Biclip To Close a Gastrocutaneous Fistula

Raymond B. Bedgood, D.O., Ayaz J. Chaudhary, M.D.* Gastroenterology/Hepatology, Medical College of Georgia, Augusta, GA.

The closure of gastrocutaneous fistulas can be challenging to gastroenterologists and patients alike. Surgery is usually needed to close gastrocutaneous fistulas. We present a unique endoscopic closure technique, using Quickclips manufactured by the Olympus Corporation.

29 year old Paralyzed Hispanic Male presented to our Gastroenterology Clinic for removal of a PEG tube by endoscopic retrieval. Four months later after removal, the patient returned to our clinic complaining of continuous discharge from the stoma since removal of the PEG tube, especially after eating. A gastrocutaneous fistula was suspected. The patient was endoscoped and the patency was confirmed by the introduction of a guidewire through the skin via the fistula to the stomach. The fistula as seen in Figure 1 was closed by the application of four Quickclips as seen on Figure 2.

The patient returned to the clinic 6 weeks after the clips were applied and denied any drainage around the fistula site. The patient was satisfied with the outcome. After 4 months of follow up, the patient had no further discharge. This procedure prevented him from undergoing surgery. Endoclips have been FDA approved for hemostasis. Their use can be versatile as demonstrated in this case. If the fistula fails to close on first attempt, a second endoscopic procedure is usually warranted.

Quickclips for the closing of uncomplicated fistulas, and possibly stomas, may be an added therapy for the skilled endoscopist. The Quickclips are allowed to fall off without any additional procedures. This procedure avoids general anesthesia risks, additional surgical procedures to the patient along with medical savings costs. Lastly, this patient had immediate improvement in his quality of life. [figure1] [figure2]
Epstein-Barr Virus-Positive Primary Intestinal Hodgkin’s Lymphoma Complicating Crohn’s Disease
Joseph H. Shelton, M.D., Daniel E. Polter, M.D.* Gastroenterology, Baylor University Medical Center, Dallas, TX.

Inflammatory bowel disease and immunosuppressive therapy are thought to confer an increased risk of lymphoma. However, debate persists on this issue. We present a case of EBV-positive Hodgkin’s lymphoma arising in a Crohn’s patient on azathioprine.

Our patient is an 81-year-old man, an Auschwitz survivor, who was diagnosed with Crohn’s Disease 50 years ago. He received two ileocolonic resections 27 and 8 years ago. His Crohn’s disease has generally been most active at the ileocolonic junction. He has been in clinical remission, and taking daily azathioprine, for 5 years.

He presented to clinic with weight loss and malaise. He had no bleeding, abdominal pain, fever or lymphadenopathy. Colonoscopy revealed a mass (pictured below) at the ileocolonic anastomosis, but was otherwise normal. Biopsies revealed Hodgkin’s Lymphoma, with presence of EBV. Abdominal CT scan and bone marrow biopsy were normal. Chemotherapy was administered (ABVD), and follow-up colonoscopy showed significant shrinkage of the tumor.

Our patient illustrates a rare complication of Crohn’s disease. To the best of our knowledge, this is the fourth reported case of Hodgkin’s lymphoma arising in a Crohn’s patient on azathioprine.

Inflammatory bowel disease (IBD) patients are suspected to be at increased risk for lymphoma, but the evidence is mixed. One cohort study (Gut 2000;47:514) found that IBD patients were at a 31-fold increased risk of non-Hodgkin’s lymphoma, but only if they were on immunosuppression. Population-based studies have found no increased risk of lymphoma in IBD (Am J Gastroenterol. 2000;95:2308).

Primary intestinal lymphoma is a rare complication of Crohn’s disease. A recent review (J Clin Gastroenterol 2003;36:332) identified only 31 published cases. Of these, three were Crohn’s patients who developed Hodgkin’s lymphoma while taking azathioprine. Like our patient, they all responded well to chemotherapy.

With longer treatment courses of azathioprine, clinicians should remain alert to the possibility of lymphoma. [figure1]

Esophageal Polyps in a HIV Infected Patient with Upper GI Bleeding: A Case Report
Dhanasekaran Ramasamy, M.D., C.N.S.P., Mamun Shahrier, M.D., Ph.D., Mauricio Zapiach, M.D., Mahfuzul Haque, M.D., F.R.A.C.P.* Internal Medicine / Gastroenterology, Brody School of Medicine at East Carolina University, Greenville, NC.

To highlight esophageal polyps in the setting of upper GI bleeding in a HIV infected patient.

Case Report: 40 y/o male was referred for follow up EGD two months after an episode of massive upper gastrointestinal bleed. Initial upper endoscopy (EGD) had revealed multiple esophageal polyps with ulcerations and the patient was subsequently placed on proton pump inhibitors. Follow up EGD revealed multiple small and large polyps in the esophagus with severe candidal esophagitis. A single large pedunculated polyp (7 cm in length) was seen in the upper esophagus that extended from 15 cm to 22 cm from the gums. Barium esophagogram also revealed the multiple esophageal polyps and the large pedunculated polyp was clearly seen in the proximal
esophagus, measuring 2 cm in transverse diameter. Biopsies from the polyp showed candida esophagitis with granulation tissue and ulceration. No dysplasia or malignancy were noted. Viral cultures were negative. The patient was treated with a two week course of oral fluconazole. He was noncompliant with subsequent follow up. Two months later, HIV testing was found to be positive and his CD4 count was 6. He developed respiratory failure and died shortly afterwards at an outside institution.

**Discussion:** Esophageal polyps in the setting of HIV infection is seen rarely. Primary esophageal lymphomas and inflammatory fibroid polyps of the esophagus have been reported in HIV infected patients and they usually present with dysphagia. Esophageal polyps as a possible cause of upper GI bleeding, as illustrated in our case, is extremely rare.

**Conclusion:** In patients with HIV infection, esophageal polyps should be considered in the setting of upper GI bleeding.

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**Worm Infestation Seen on Capsule Endoscopy in a Patient with Abdominal Pain: A Case Report**

Dhanasekaran Ramasamy, M.D., C.N.S.P, Stefan Marcuard, M.D., F.A.C.G.* Internal Medicine / Gastroenterology, Brody School of Medicine at East Carolina University, Greenville, NC and Carolina Physicians, Greenville, NC.

To illustrate the unusual finding of parasites on Capsule Endoscopy (CE) in a patient with unexplained abdominal pain.

**Case Report:** A 77 y/o old female was referred by an internist with complaints of abdominal pain and fevers of several months duration. She denied nausea / vomiting, diarrhea, weight loss or travel outside the United States. EGD, Colonoscopy and CT abdomen was negative. She was referred to us for small bowel evaluation. On CE, the first gastric image was seen at 4 minutes of capsule activation. The first duodenal image at 33 minutes. There were several whitish highly motile worm-like structures noted in the duodenum and jejunum, starting at 60 minutes and ending at 150 minutes. These findings were strongly suspicious for parasitic infection. No bleeding, erythema, or mass lesions were visualized in the small intestine during the study. Stool studies for ova and parasites were negative. In view of the CE findings, the patient was treated with Mebendazole for one week. Her abdominal pain resolved following the eradication therapy.

**Discussion:** Thus far CE has been shown to be useful in the evaluation of occult gastrointestinal bleeding, crohns disease and other small bowel mucosal pathology. Our findings of parasites in the small bowel has rarely been reported. Further studies in patients with unexplained abdominal pain will be needed to assess its role in the evaluation as well as detection of parasitic in the small bowel. Whether CE is more sensitive than stool studies for parasites also needs to be determined.

**Conclusion:** CE may be useful in the the detection of parasites, especially in patients with unexplained abdominal pain.

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**Enteropathy Type T-Cell Lymphoma**


**Introduction:** T-cell lymphomas of the GI tract are much less common than those of B-cell origin. The majority of small intestine T-cell lymphomas are termed Enteropathy Associated T-cell Lymphoma (EATL) due to their connection with celiac disease. Occasionally T-cell lymphomas display similar microscopic appearance and immunohistochemical characteristics of EATL, but test negative by antibodies specific for celiac sprue. These are termed enteropathy type T-cell lymphomas. We will present a case of a patient with an enteropathy type T-cell lymphoma.

**Case Report:** A 40-year-old male with no significant past medical history presented with complaints of diarrhea and a twenty pound weight loss over the previous three months. Upper endoscopy with small bowel biopsy revealed heavy lymphocytic infiltration in the lamina propria and submucosa with broadened, attenuated villi, changes consistent with celiac sprue. A gluten free diet did not improve his symptoms and antibody testing for celiac disease returned negative. Empiric treatment for tropical sprue did not alleviate the patient’s symptoms. Colonoscopy with ileoscopy revealed small ulcers in the terminal ileum suspicious for Crohn’s disease. Maximal therapy for Crohn’s was begun, however the patient’s clinical course continued to deteriorate. CT scan of the abdomen was consistent with a small bowel obstruction and the patient underwent a laparoscopic right hemicolectomy with terminal ileal resection. Again symptoms of diarrhea and weight loss recurred. Push enteroscopy was performed and biopsies taken from the small intestine showed atypical lymphocytes. Laparoscopy with full-thickness biopsy revealed small intestinal mucosa with flattening of the
Appendiceal Mucocele: A Diagnostic Dilemma
Dia T. Simmons, M.D., Tony E. Yusuf, M.D., Mark V. Larson, M.D.*
Gastroenterology and Hepatology, Mayo College of Medicine, Rochester, MN.

Case Presentation: A 53-year-old male underwent a colonoscopic exami-
nation after a single episode of small-volume hematochezia. Colonoscopy
revealed sigmoid diverticulosis and a 2 × 2 cm friable mass in the ce-
cum, obscuring the appendiceal orifice. [figure1] Mucosal biopsies from the
mass revealed mild, chronic inflammation, with no evidence of malignancy.
Contrast-enhanced CT scan of the abdomen and pelvis demonstrated a fluid
filled appendix, and a tubular mass with an attenuating rim and a low at-
tenuation center at the base of the appendix; the mass appeared to prolapse
into the cecum. The remainder of the abdomen and pelvis appeared normal.
Despite the surface biopsies, because of the concern that this mass could
still be a malignant lesion, surgical resection was undertaken. 
Laparoscopic resection of the cecum and terminal ileum was performed.
Pathology revealed a chronically inflamed appendix containing a large mucus
plug, consistent with a benign mucocele of the appendix. Six of 6 regional
lymph nodes were benign.

Discussion: An appendiceal mucocele typically describes a dilated, mucin-
filled appendix. Patients may present with RLQ abdominal pain, bleeding, or
a palpable abdominal mass, with or without obstructive symptoms. Alterna-
tively, a mucocele may be an incidental operative finding. More overt clinical
presentations tend to be associated with malignant processes. An association
with synchronous malignancy, particularly colonic, has been established.
The underlying pathology associated with appendiceal mucocele includes
cystadenoma, cystadenocarcinoma, adenocarcinoma, or a benign mucin-
filled cyst. The distinction between benign and malignant mucocele is dif-
ficult to establish preoperatively, thus surgical resection is recommended.
Rupture of a mucinous cystadenoma or cystadenocarcinoma can occur, and
may result in pseudomyxoma peritonei. In expert hands laparoscopic resec-
tion can be successful, although open resection for appendiceal mucocele is
generally recommended, in order to avoid potential spillage and peritoneal
seeding.
A 38-year-old male with a history of untreated latent tuberculosis presented with abdominal pain and melena. He reported ten years of intermittent, dull, right-lower-quadrant pain with no radiation, alleviating or aggravating factors. He denied weight loss, vomiting or hematochezia. He noted three episodes of melena in the 10 days prior to admission. On exam, his abdomen was soft and mildly tender throughout. Bowel sounds were present. There were no masses or organomegaly. Rectal exam was hemoccult positive without perianal disease. CT scan revealed moderate wall thickening of the ascending colon (figure 1). Colonoscopy showed a large, irregular, ulcerated cecal mass arising from an incompetent ileocecal valve (figure 2). Biopsies revealed granulation tissue with mucosal inflammation. Histopathologic exam after a right hemicolectomy revealed submucosal fatty infiltrates consistent with Ileocecal Valve Lipohyperplasia (ICVL).

ICVL is characterized by infiltration of adipose tissue within the submucosa. This causes outpouching of the valve into the cecum, resulting in varied symptoms. The pathogenesis is uncertain, but may be related to hormonal effects, tissue hypoxia or local inflammatory mediators. ICVL presenting with melena has only been reported in one prior case. Endoscopically, it may be indistinguishable from conditions such as neoplasm, infection or inflammatory bowel disease. A patient with vague abdominal symptoms and melena whose endoscopic exam is suggestive of neoplasia, infection or inflammatory bowel disease, ICVL must be considered in the differential diagnosis. Operative excision is the only effective treatment in those who are symptomatic or whose diagnosis is in doubt. [figure2] [figure1]

REFERENCES

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Lipohyperplasia of the Ileocecal Valve: An Unusual Etiology of Melena
Shahrooz Bemanian, M.D., Kenneth Lee, M.D., Michael M. Kline, M.D.*
Dept of Medicine, Division of Gastrointestinal and Liver Disease, Keck
USC School of Medicine LAC-USC Medical Center, Los Angeles, CA.

A 38-year-old male with a history of untreated latent tuberculosis presented with abdominal pain and melena. He reported ten years of intermittent, dull, right-lower-quadrant pain with no radiation, alleviating or aggravating factors. He denied weight loss, vomiting or hematochezia. He noted three episodes of melena in the 10 days prior to admission. On exam, his abdomen was soft and mildly tender throughout. Bowel sounds were present. There were no masses or organomegaly. Rectal exam was hemoccult positive without perianal disease. CT scan revealed moderate wall thickening of the ascending colon (figure 1). Colonoscopy showed a large, irregular, ulcerated cecal mass arising from an incompetent ileocecal valve (figure 2). Biopsies revealed granulation tissue with mucosal inflammation. Histopathologic exam after a right hemicolectomy revealed submucosal fatty infiltrates consistent with Ileocecal Valve Lipohyperplasia (ICVL).

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A CT scan of her head revealed no signs of bleeding, stroke or injury. Lumbar puncture revealed normal CSF findings. Erythrocyte transketolase level was drawn to test for Thiamine deficiency and she was administered 100 mg of thiamine, along with folate and Vitamin B₁₂. She regained normal extracranial motor function within 8 hours of Thiamine administration. Serum B₁₂ and folate levels were normal, however her Thiamine levels were found to be 38 (normal = 68–107). MRI of the brain was contemplated, but could not be performed because the patient had a pacemaker. She was kept on parenteral Thiamine replacement for the next 6 weeks.

With morbid obesity reaching pandemic levels over the past decade, bariatric surgery is becoming an increasingly popular and publicized. Likewise, the incidence of postoperative complications like Wernicke encephalopathy have definitely increased and reached medical practice beyond the realm of bariatric surgery. Wernicke encephalopathy classically presents as a triad of ophthalmoplegia, ataxia and confusion but may also manifest as unexplained hypotension, hypothermia, or even coma progressing over a few days without any components of the classic triad. Described as an acute manifestation of thiamine deficiency, it is thought to develop following 2 to 3 months of vitamin deprivation during starvation. The association with the roux-en-Y procedure is linked primarily to lack of gastric capacity. Diagnosis is mainly clinical and institution of therapy should not await radiographic findings of hyperintensity in the midbrain and mamillary bodies using magnetic resonance imaging. Parenteral replacement remains the mainstay of therapy; however, prompt diagnosis in the correct clinical setting dictates long-term prognosis and morbidity.
assuming a 1% incidence of PEG site metastases in patients with oropharyngeal and esophageal malignancy. To demonstrate a 50% reduction in PEG site metastases using an overtube, a total of 1240 patients would need to be included to achieve statistical significance with a p value of <0.05.

Conclusions: Cancer metastatic to a gastrostomy site is a rarely reported yet serious complication of PEG tube placement in patients with oropharyngeal and esophageal cancer. The use of an overtube during endoscopic PEG tube placement to prevent direct implantation of malignant cells by means of instrumentation warrants further investigation.

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Diffuse Colonic Angiomatosis: A Rare Cause of Severe Lower Gastrointestinal Bleeding

Dustin G. Case, D.O., David L. Limauro, M.D.,* Anthony M. Colatrella, M.D., Mark A. Cedar, D.O. Department of Gastroenterology, Mercy Hospital, Pittsburgh, PA.

Introduction: Vascular lesions are important sources of gastrointestinal tract hemorrhage. The vascular abnormalities commonly encountered by gastrointestinal endoscopists are categorized as vascular ectasias, arteriovenous malformations and capillary telangiectasias, or angiodyplasias which may or may not be associated with systemic syndromes. These lesions tend to have their own defining clinical, endoscopic and/or angiographic characteristics. Angiomatosis is a descriptive term to signify the existence of multiple dilated vascular channels in the intestinal wall. This report describes a patient with diffuse colonic angiomatosis who eventually required subtotal colectomy for the treatment of life threatening colonic hemorrhage.

Case Study: A 59-year-old presented with abdominal cramping, diarrhea, and hematochezia. He noted a remote history of a right hemicolectomy secondary to localized adenocarcinoma of the colon eleven years prior to the current episode. The remainder of his history and physical exam was unremarkable with the exception of bright red blood on digital rectal exam. Colonoscopy performed two years prior to admission revealed granular appearing mucosa and biopsies showed lymphoid aggregates in the lamina propria. Colonoscopic findings during his present illness revealed deeply erythematous colonic mucosa with loss of normal appearing mucosal pattern. There were also multiple punctate and linear ulcers and diffuse wall edema. Random biopsies of the colon wall showed proliferation of tortuous capillaries and in many areas, the surface epithelium was denuded with only endothelial cells separating the capillary lumen from the colonic lumen. Diagonal consensus from the home hospital as well as send out pathology laboratory was termed “mucosal angiomatosis”. Recurrence of the patient’s bleeding required surgical intervention and the patient underwent a subtotal colectomy with end ileostomy. He has had no further episodes of bleeding.

Conclusion: Angiomatosis, a striking endoscopic finding and apparently a very rare cause of GI bleeding, is defined by diffusely dilated vascular channels in the intestinal wall. It is endoscopically and pathologically distinct from other causes of bleeding in the gastrointestinal tract. Although no final conclusion can be made as to the etiology of this patient’s condition, it is probable that this angiomatosis was an acquired condition, as it was not described on gross pathology at his initial right hemicolectomy.

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Symptomatic Acute Hepatitis C Virus: A Case Report

Theodore M. Perlman, M.D., Shafeeq Ahmed, M.D., Kaleem M. Rizvon, M.D., Steven S. Yang, M.D., Paul J. Mustacchia, M.D.* Gastroenterology, Nassau University Medical Center, East Meadow, NY.

19 year old white male with a pmlx. of ADHD, Bipolar disorder, recently incarcerated was admitted to the hospital complaining of abdominal pain, fatigue, elevated liver function tests and dark urine. Six weeks prior patient admitted to using IV heroin with a friend who had known Hepatitis C virus. ROS was negative for fever or chills, recent travel, diarrhea, changes in medications, alcohol ingestion. Socially he was an active IV drug abuser and cigarette smoker. His vital signs were within normal limits. Physical exam was negative for scleral icterus, adrenopathy and positive for RUQ tenderness. Initial labs 4 weeks prior to admission: AST-1403, ALT-3303, ALP-137, TBR-.16, INR-.1, WBC 8.1, HB-14.9, PLT-250, Hepatitis A,B,C serologies were negative. On admission: AST-1717, ALT-3786, ALP-151, TBR-.2, Anti HCV positive, HCV RNA-138 IU/ml. Genotype-1b. Clinically patient improved over one week as his transaminases decreased. 12 weeks after contracting the virus his liver tests improved but never completely resolved: AST-50, ALT-112, ALP-73, TBR-.6. His HCV RNA increased to 368 IU/ml. RUQ US was unremarkable.

Discussion: An estimated 15–20% of newly infected persons with hepatitis C are symptomatic. Therefore acute hepatitis C is a rare diagnosis. The incubation period is 15–75 days with an average of 50 days. The first biochemical marker in the acute phase is HCV RNA which usually is detectable within the first two weeks. The Preicteric phase begins with the rise of serum aminotransferases (4–12 weeks)non specific symptoms occur at this time. The icteric phase follows which lasts 4–6 weeks. Anti HCV is the last of the markers which are detected which is detected after symptoms begin. Diagnosis is made by the combination of serological tests including HCV RNA, new elevations of aminotransferases, newly converted ANTI HCV, ANTI HCV core IgM, ANTI HCV titers and the patient's history. Upto 50% of patients have spontaneous HCV RNA clearance usually within the first 12 weeks. Patients with higher spontaneous clearance rates are those who had symptomatic acute disease, young patients and females. HCV RNA levels have not been shown to predict the natural history of acute infection. Treatment is usually initiated after 3 months if the patient is not able to clear his HCV RNA and his aminotransferases have not normalized. Treatment options include: interferon monotherapy, pegylated interferon alone or in combination with ribavirin for 24 weeks or more.

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Endoscopic Retrograde Removal of Gallbladder Remnant Calculi

Joseph H. Shelton, M.D., Damien B. Mallat, M.D.* Gastroenterology, Baylor University Medical Center, Dallas, TX.

Currently, therapy of symptomatic gallbladder remnant calculus is surgical removal. However, surgery in these patients is more complex, due to their prior cholecystectomy. A recent case series (Surg Endosc 2002;16:981–4) describes 7 patients with symptomatic gallbladder remnant calculus. Most of them received laparotomy as definitive treatment. Patients who are poor operative candidates have limited options for treatment of gallbladder stones: dissolution therapy, extracorporeal lithotripsy and percutaneous cholecystostomy. We report endoscopic removal of a gallbladder remnant stone using ERCP. Our patient is a 40-year-old male, with cholecystectomy 3 years ago, who presented with crampy severe RUQ abdominal pain associated with jaundice. He was afebrile with a tender abdomen. His ALT was 455, and total bilirubin was 5.2. Work-up at an outside hospital included ultrasound as well as CT scan of the abdomen. CT scan suggested a bile duct stone and a gallbladder remnant stone. ERCP was attempted to remove the bile duct stone. ERCP confirmed a 12 mm common bile duct stone and an 8 mm stone in the gallbladder remnant. The cystic duct was patent. The CBD stone was removed after mechanical lithotripsy. Subsequently, a 0.35 jagwire was inserted into the gallbladder remnant. A Boston Scientific mechanical lithotriptor was inserted into the gallbladder over the wire. The gallbladder stone was crushed, then removed through the ampulla. Balloon sweep of the gallbladder and CBD removed sludge. The final cholangiogram showed no filling defects. The patient has been asymptomatic since the procedure.

This report describes a novel method of treating gallbladder remnant calculi. We are not aware of any other reported case of gallbladder stone removal using ERCP. Gallbladder remnant calculus removal by ERCP appears to be a quick and effective treatment. This technique is attractive for patients in whom surgery...
would be high-risk or technically difficult. Further study is needed before it can be routinely recommended. [figure1]
onset of severe crampy lower abdominal pain associated with 10 episodes of hematochezia followed by passage of clots. She denied fever. There was no recent history of sick contacts, antibiotic use or travel. Past medical history was also significant for adrenalectomy for an aldosterone-secreting tumor, right breast lumpectomy and depression. There was no family history of inflammatory bowel disease or colon cancer. Medications included tamofoxifen, hydrochlorothiazide and rizatriptan as needed. Of note, the patient reported recent daily rizatriptan usage within the week prior to admission. Physical examination revealed normal vital signs without orthostasis. Abdominal exam was remarkable for tenderness to deep palpation in left upper and lower quadrants. Rectal exam revealed gross blood. Laboratory data was significant for WBC 8,000/ul, hematocrit 41% and normal coagulation studies. Stool culture and C. difficile toxin assay were negative. Abdominal CT scan revealed bowel wall thickening of the transverse colon. A colonoscopy was notable for swelling, erythema and ulceration in transverse colon and splenic flexure, consistent with ischemic colitis. The patient was managed conservatively and improved; rizatriptan was discontinued.

The ischemic colitis observed in this case is likely attributable to the rizatriptan. Another possible etiology could be related to the 4% increased risk of thromboembolic events associated with tamoxifen, although, this patient had been on tamoxifen for years. This case highlights the potentially serious adverse effects of triptans. Evaluation of patients with ischemic colitis should include review of medicines, including triptan use, as a potential cause of the ischemia.

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**Transient Colocolic Intussusception at Initial Diagnosis in a Patient with Crohn’s and Salmonella typhimurium**

Deborah Flomenhoff, M.D., Cynthia Harris, M.D., Luis Pena, M.D., " Ein Lee, M.D. Gastroenterology, University of Kentucky, Lexington, KY and Pathology, University of Kentucky, Lexington, KY.

Colocolic intussusception is unusual in adults and rarely reported in association with Crohn’s disease or infection. IBD-associated intussusceptions have been largely described with underlying pseudopolyps. A single case report of ileocolic intussusception in association with S. typhimurium was reported in 1994. The combination of IBD and infection has not been reported. We report a case of colocolic intussusception associated with undiagnosed Crohn’s and superimposed Salmonella infection.

A previously healthy 30 year old man presented with a 4 day history of severe right lower quadrant pain, nausea and diarrhea. He reported 10-20 watery stools per day during this course. He denied any history of fever or vomiting and denied sick contacts. However, on review of systems he did report lancinating pelvic pains occurring without warning over the previous eight months and difficulty gaining weight since adolescence. The patient remembered a similar episode at age ten characterized by severe right lower quadrant pain. An UGI at that time revealed “stomach ulcers;” no further treatment or evaluation was pursued. At this admission the diarrhea was guaiac positive without microscopic evidence of WBCs. Electrolytes were consistent with a secretory diarrhea.

A 10 cm colocolic intussusception was seen on CT at the time of admission. On subsequent CT the intussusception was non-obstructing with oral contrast clearly moving through the area of involvement to the distal colon. Surgery was consulted. The incidence of malignancy in colocolic intussusception is reported to be greater than 50%; surgery has been advocated as initial therapy. However, in view of the childhood history and thin body habitus, a colonoscopy was performed. On examination the colon showed patchy edema, erythema and friability involving segments from the sigmoid to the cecum. Aphthae were seen in the terminal ileum to 25 cm. Endoscopy was consistent with Crohn’s and the patient was begun on antibiotics and steroids while awaiting pathology. Two days after endoscopy stool cultures were positive for Salmonella typhimurium. Pathology showed chronic transmural inflammation involving the entire colon and the TI; findings were most consistent with Crohn’s and not with acute Salmonella infection. Intercurrent Salmonella infection and chronic intussusception led to intussusception and unmasked Crohn’s.

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**How Reliable Are Nutritional Indices in Guiding Treatment – “Pre-Albumin Chase Is a Misadventure”**

Shahina Hakim, M.D., Lin Shu, M.S, RD, Diane Parrington, Ph.D., Rakesh Nanda, M.D. Gastroenterology, Carl T Hayden VAMC and Clinical Nutrition Department, Carl T Hayden VAMC, Phoenix, AZ.

Pre-albumin (PAB) is a traditional index for assessing nutritional status. Our observations suggest that independently, it might not be an accurate indicator as: a) it is a negative acute phase reactant; b) it is affected by other factors: medications, disease, etc.

Proteins are produced in the liver. In the presence of severe disease production may be switched off and levels may not reflect nutritional status alone.

A 55 y old man with h/o valley fever, s/p R upper and middle lobectomy 1992; Mycobact. kansasii infection in 1999 had R pneumonectomy in 2003. He had polymicrobial empyema, multiple admissions and surgeries since 10/2004 – muscle flaps, thoracotomy, and rib resection. On admission he was malnourished-Wt. 70% IBW, BMI = 17 with 10 lb wt,loss in last 5 months.

Work up revealed a large esophago-pleural fistula.

He was made NPO, feeding initiated with a GJ tube. As he didn’t show the predicted improvement in PAB and weight, TPN was started. He received huge amounts of supplementation (Enteral and TPN). Despite escalation in the intake it was hard to achieve weight gain.

Despite aggressive feeding based on PAB values,desired results were not obtained for initial 6 weeks (upto 5000 calories/day) until there was a reduction in CRP, with. weight gain (116 lbs to 134 lbs).(fig)

Followed serially, an inverse relationship between CRP and weight/PAB was noted. (fig).

In sick patients PAB alone may not be a true marker of nutritional status and CRP/ weight may be used together to make an assessment. There is no single indicator that can reliably predict a patient’s nutritional status.Further studies are required. [figure1] [figure2]
Autoimmune enteropathy is an increasingly recognized cause of intractable diarrhea, usually affecting infants and children. To our knowledge, there are no prior adult cases of coexisting autoimmune enteropathy, myasthenia gravis and thymoma.

74 year old white male presented with insidious 25 lb weight loss, poor appetite, vague abdominal pain and constipation. Treatment with lactulose resulted in intractable diarrhea for 6 weeks. He also complained of early satiety, nausea and shortness of breath which he attributed to deconditioning. Esophagogastroduodenoscopy and colonoscopy were normal. However small bowel and colon biopsies, revealed chronic enteritis with absent goblet cells, increased crypt lymphocytes and apoptotic bodies. Serum anti-goblet IgG was strongly positive, all consistent with autoimmune enteropathy. CT scan of the chest for dyspnea revealed a stable upper anterior mediastinal mass. [figure1] He promptly responded to prednisone 40 mg taper.

After completing steroid taper, he complained of constipation, proximal muscle weakness, dysphagia and worsening shortness of breath. Swallowing evaluation showed aspiration, deltoid muscle biopsy showed inflammation and atrophy. Serologies showed positive Anticholinesterase Receptor binding / modulating Antibody and GAD 65 antibodies in high titers. Symptoms responded slowly to 80 mg prednisone taper. The anterior mediastinal mass was resected and pathology showed a confined 4.5 × 4.0 × 1.5 cm thymoma. Two weeks after steroid reintiation and thymectomy, dysphagia resolved, weakness and weight improved. Constipation is being treated with Miralax. This patient demonstrated features of autoimmune enteropathy, myasthenia gravis and thymoma. Enteropathy responded to steroids, but myasthenia required thymectomy.

Conclusions:
1. rhGH was associated with a decreased ostomy output without reduction in oral intake in a patient with SBS.
2. rhGH allowed for the reduction of PN fluid and nutrient requirements per week and days of PN infusion per week.

Recombinant Human Growth Hormone Reduces Fluid Requirements in a Parenteral Nutrition Dependant Patient with Short Bowel Syndrome
Neha R. Parekh, M.S., RD, CNSD, Ezra Steiger, M.D., FACS.∗ Douglas L. Seidner, M.D., F.A.C.G. Dept of General Surgery, Cleveland Clinic Foundation, Cleveland, OH and Dept of Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH.

Short bowel syndrome (SBS) follows extensive intestinal resection and results in impaired absorption, malnutrition and dehydration. Spontaneous adaptation of the remaining bowel begins shortly after resection, however many patients will need to rely on parenteral nutrition (PN) indefinitely due to persistent malabsorption. Recombinant human growth hormone (rhGH) was recently approved for use in SBS to promote intestinal adaption and enhance function of the residual bowel. The utility of rhGH was tested in a 49 year old female SBS patient (initials MD) dependent on PN for 5 days/week since November 1984. MD has a history of complicated Crohn’s disease requiring multiple abdominal surgeries and leaving approximately 90 cm jejunum ending in an ostomy. In November 2004, MD began a specialized diet and maximal anti diarrheal therapy with no change in weight, ostomy output or PN requirements by April 2005. MD then received a subcutaneous injection of rhGH (0.1 mg/kg/day) for 4 consecutive weeks. On the last day of rhGH administration, MD’s weight was up 0.7 kg and ostomy output decreased an average of 520 mL/day. PN administration was then reduced to 3 days/week and PN fluid requirements were decreased to 5.5 L/week (55% reduction). PN calorie provisions were thereby reduced to 3660 kcal/week (60% reduction) and PN protein provisions were reduced to 150 g/week (60% reduction). Two weeks after rhGH therapy, MD’s weight, ostomy output and PN provisions were unchanged.

Parameters for PN Reduction During rhGH Therapy

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Start of rhGH</th>
<th>End of rhGH</th>
<th>2 weeks post-rhGH</th>
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<td>Weight (kg)</td>
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<td>Serum albumin (g/dL)</td>
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<td>Ostomy output (average mL/day)</td>
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<td>PN days per week</td>
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<tr>
<td>PN protein per week (g)</td>
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</tbody>
</table>

Conclusions:
1. rhGH was associated with a decreased ostomy output without reduction in oral intake in a patient with SBS.
2. rhGH allowed for the reduction of PN fluid and nutrient requirements per week and days of PN infusion per week.

Pneumoperitoneum Complicating an Endoscopic Retrogradecholangiopancreatography (ERCP)-Rendezvous Procedure
Seth A. Cohen, M.D.,∗ Young Lee, M.D., Franklin E. Kasmin, M.D., Jerome H. Siegel, M.D. Division of Digestive Diseases, Beth Israel Medical Center, New York, NY.

A 92 year-old woman presented with symptomatic choledocholithiasis. ERCP failed because the papilla was not visible within a large peripanillary diverticulum. We sent the patient for a right-sided percutaneous transhepatic cholangiogram (PTC) that demonstrated large CBD stones, a pigtail drain was placed in the duodenum. Two days later the patient underwent a rendezvous ERCP. With the PTC catheter in the place the papilla was endoscopically accessible. An endoscopic sphincterotomy was performed.
and the percutaneous catheter was removed without incidence. The sphincterotomy was inadequate to deliver the large CBD stones, therefore it was extended. At the completion of the sphincterotomy the patient developed pneumobilia and pneumoperitoneum. A biliary stent was placed and the ERCP was terminated. The patient remained clinically stable. Surprisingly, the abdominal computer assisted tomography (CT) revealed no retroperitoneal air, but rather intraperitoneal air and no leak of duodenal contrast. The patient had focal abdominal tenderness and mild leukocytosis but no evidence of peritonitis. The patient was seen in surgical consultation and given her age and comorbidities it was decided to treat her non-operatively. The patient was treated with broad spectrum antibiotics and observed in the ICU. Abdominal exam remained benign and repeat CT scan again showed no evidence of duodenal perforation. The patient was discharged after 4 days. We hypothesize that duodenal air from endoscopic insufflation entered the biliary tree through the enlarged sphincterotomy and leaked out through the puncture site on the liver capsule, from the percutaneous drain, and entered the peritoneal cavity. This correlates with what we observed during fluoroscopy, explains the presence of pneumoperitoneum in the absence of a duodenal perforation, and is consistent with the patient's benign clinical course. Usually when we remove a PTC drain during a rendezvous ERCP, it has a mature track and therefore the air leaks outside the patient to the skin. In this patient, the percutaneous drain was only 2 days old and there was no mature track to the skin and so the air leaked into the peritoneum. Although the rendezvous technique for ERCP is safe and well established, we feel it is prudent to wait 7–10 days after a PTC is placed to allow the track to mature before removing it during ERCP.

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An Unusual and Interesting Presentation: Neuroendocrine Carcinoma of Parotid Gland with Mets to the Pancreas

Nebu V. Koshy, M.D., Khalid Nour, M.D., Mashood Quadri, M.D., M. Raza Anees, M.D.* Department of Medicine, Overton Brooks VAMC, Shreveport, LA and Department of Medicine, Louisiana State University Health Sciences Center, Shreveport, Shreveport, LA.

A 70 year old white male with history of small cell carcinoma of the left parotid gland, status post total parotidectomy presents with 4 week history of worsening upper abdominal pain, mainly in the epigastric region. A CT scan of abdomen showed a large ill-defined inhomogeneous mass involving the head, neck and uncinate process of the pancreas with peri-pancreatic lymphadenopathy. EUS with FNA was performed, which revealed a large 4.5 cm mass in the head of the pancreas with a large 1.5 cm peri-pancreatic lymph node and a 2.5 cm celiac lymph node were seen. Cytology from the pancreatic mass and lymph nodes revealed a neuroendocrine carcinoma with small cell features. Immunohistochemistry showed positive staining for neuron specific enolase, synaptophysin and cytokeratin 20. These immunostains support a diagnosis of neuroendocrine tumor and showed an identical pattern with the parotid tumor.

Small cell neuroendocrine carcinoma is extremely rare and is often difficult to distinguish from malignant lymphoma, adenoid cystic carcinoma, and undifferentiated carcinoma. This is a rare and interesting case of neuroendocrine tumor of parotid gland, now presenting with a metastatic disease involving pancreas. We will present EUS, CT and histological images of small cell neuroendocrine tumor, both from the pancreas and parotid gland.

Myocobacterial tuberculous involvement of the gastrointestinal tract is a frequent site of extra pulmonary tuberculosis but esophageal involvement is rare. Here, we describe a patient with unique presentation of esophageal tuberculosis.

Patient was a 25-year-old Indian woman who had immigrated to U.S. at age of 16. Two weeks prior to her hospitalization, she developed odynophagia and substernal chest discomfort. She was started on a proton pump inhibitor without resolution of her symptoms. An upper GI series revealed large esophageal ulcer with possible perforation. Patient was healthy and without any medical or surgical history. She had no allergies and was taking lansoprazole 30 mg once a day. At the time of immigration, her purified protein derivative test (PPD) was negative. She had not been to India since her immigration. Her vital signs were normal and she appeared comfortable. There was no palpable lymphadenopathy. The lungs were clear on auscultation. Neurologic examination revealed no abnormalities. All laboratory-test results were normal.

Barium swallow revealed linear esophageal ulceration on the right side of mid-esophagus but no perforation. CT scan of chest, abdomen, and pelvis revealed 2.3 × 3.4 × 5.0 cm enhancing subcarinal mass that was inseparable from the esophagus. Esophagogastroduodenoscopy revealed a 4-cm deep, friable ulcer with a sinus/fistula tract in the mid-esophagus. Cytology and biopsies with special stains for AFB, fungus, viruses were negative. Bronchoscopy revealed hyperemia of the airways and bulging in the medial aspect of the right mainstem bronchus. Bronchoalveolar lavage culture and cytology was negative.

On video mediastinoscopy, multiple small lymph nodes surrounding a large, rubbery mass were identified. Multiple biopsies of the mass and the lymph nodes revealed noncaseating granulomas and cultures were positive for Mycobacterium tuberculosis. PPD was positive at more than 15 millimeters. A diagnosis of isolated esophageal tuberculosis was made and patient was started on four-drug regimen of ethambutol, isoniazid, pyrazinamide, and rifampin. Cultures were subsequently positive for Mycobacterium tuberculosis. With treatment, fistula has healed on subsequent endoscopies. In conclusion, tuberculosis should be suspected in patients with odynophagia and large esophageal ulcerations in a patient with appropriate demographic history. Invasive methods may be needed to make the diagnosis.

Cryptococcus Cellulitis and Myositis without Systemic Cryptococcosis

Kuntal M. Thaker, M.D., Kuldip S. Banwait, M.D., Maya Spodik, M.D., Steven K. Herrine, M.D., Victor Navarro, M.D.* Division of Gastroenterology and Hepatology, Thomas Jefferson University Hospital, Philadelphia, PA.

Cutaneous involvement is an uncommon manifestation of cryptococcal disease, but it may be the initial manifestation of systemic cryptococcosis in solid-organ transplant (SOT) recipients and other immunocompromised hosts. Only 36 cases have been described in the literature and majority of them are in renal transplant recipients. No cases of cellulitis with fascitis and myositis without systemic involvement have been described for liver transplant patients. We describe the first case of a liver transplant recipient with cellulitis with fascitis and myositis as the only presentation of cryptococcosis.

50 year old white male presented with erythema and swelling of both lower extremities. His medical history was significant for liver transplant five years ago for alcoholic cirrhosis. Post transplant, he had developed mitral valve insufficiency with heart failure, and pulmonary hypertension. His immunosuppressive regimen consisted of prednisone 10mg and sirolimus 1mg once a day.

On physical exam, patient had temperature of 100.8F. Multiple, irregularly shaped, deep ulcers with surrounding erythema without any evidence of necrosis were seen on both lower extremities. There was significant edema present as well.
Imatinib Mesylate (Gleevec) Induced Hepatitis
Madhavi Rudraraju, M.D., Nadeem Chaudary, M.D., Javid Fazili, M.D.*
Digestive Diseases, University of Oklahoma Health Sciences Center,
Oklahoma City, OK.

Introduction: Imatinib Mesylate (Gleevec) is used for treatment of CML and gastrointestinal stromal tumors. It is generally well tolerated and severe hepatotoxicity is not common. Here we present a case of acute hepatitis associated with imatinib.

Case Report: A 34-year-old Caucasian male with CML was initially treated with Hydroxyurea, but did not have much response and Imatinib was started. His baseline liver function was normal. He presented a year after starting Imatinib with epigastric and upper abdominal pain. There was no history of recent travel, toxin exposure, blood transfusion or intravenous drug use. He denied use of alcohol or over the counter medications. Physical examination was unremarkable. Laboratory data revealed severe transaminitis. Additional laboratory tests, which included viral hepatitis and immune serologies, were negative. Alpha-1 anti-trypsin, ceruloplasmin and iron studies were normal. Ultrasound and CT scan of the abdomen were normal. Transaminases started trending down on day 2 after stopping Imatinib and became normal in 3 weeks. Imatinib is re-challenged twice in our patient as he did not have any other treatment alternatives and had recurrence of biochemical abnormalities. The transaminases normalized after stopping imatinib.

Discussion: Imatinib inhibits the enzyme tyrosine kinase and is currently approved for use in patients with CML. This inhibition blocks proliferation and induces apoptosis in the leukemic cells. Hepatic CYP3A 4 is the main enzyme responsible for its metabolism. Hepatotoxicity has been reported in the initial trial of imatinib. The rate of occurrence of elevated alkaline phosphatase <5%, elevated ALT <1% to 4%, elevated bilirubin <1% to 4%, elevated AST <1% to 3%. Severe hepatotoxicity has been reported in only a few cases. Two cases of deaths due to liver failure, possibly related to imatinib therapy have been reported. Autopsy showed an enlarged liver with fibrin thrombi and acute hepatic necrosis. Two cases of liver injury with biopsy showing acute hepatitis have been reported. Imatinib was “re-challenged” twice in our patient with recurrence of transaminitis. After looking at the temporal relationship between the drug and the liver function test abnormalities we conclude that this hepatitis was secondary to the imatinib. Fortunately his liver enzymes returned to normal after discontinuation of imatinib.

Clinicians should be aware and vigilant of this adverse effects in patients using imatinib as it can be life threatening.

Imatinib with epigastric and upper abdominal pain. There was no history of

HCV Ab Negative HCV Infection in a Kidney Transplant Recipient
Juan A. Guerrero, M.D., Kermit V. Speeg, M.D. Gastroenterology, University of Texas Health Science Center, San Antonio, TX.

Hepatitis C virus (HCV) infection in patients receiving immunosuppression or hemodialysis (HD) has been associated with serum HCV Ab negative infection confirmed by PCR. We present a renal transplant pt who developed HCV Ab negative, HCV PCR confirmed infection which led to cirrhosis and eventual liver transplant.

A 54 yo female presented for evaluation of abnormal liver tests. She complained of fatigue, but denied other symptoms of chronic liver disease. Her past history was significant for prior cholecystectomy, kidney disease from diabetes and a kidney transplant 2 years prior. Active medications included Prograf, prednisone, glipizide, and HCTZ. She had no ETOH exposure and never used IV drugs. She did receive blood products at transplant, but denied other risk factors associated with HCV.

Physical exam was significant for a soft abdomen, healed surgical incisions, and no organomegally or ascites. She had no asterixis or skin manifestations of chronic liver disease. Lab data before transplant showed normal liver tests and a negative HCV Ab. On our evaluation her labs were significant for platelets 71, creatinine 1.1, AST 170, ALT 121, bilirubin 3.9, alk phos 199, GGT 336, albumin 2.9 and INR 1.9. CT and RUQ sono revealed a CBD of ~11mm. Subsequent serologic work up included multiple negative HCV Abs. TheHAV, HBV, CMV, HIV and HSV tests were all normal. Autoimmune markers were negative and her Fe saturation was normal. An HCV PCR was ordered, but cancelled by our lab. ERCP revealed a mild dilatation of her CBD, no filling defects, and rapid drainage of contrast. Her liver tests did not significantly change over a year and a follow up MRI showed a nodular liver with associated ascites and varices. Transjugular liver biopsy revealed a nonspecific chronic hepatitis in the presence of cirrhosis. Liver transplant work up led to another HCV PCR request, which was completed and revealed an HCV viral load of over 1 million. Her liver tests worsened over the ensuing year and she successfully underwent OLT 4 years after her kidney transplant.

HCV Ab negative HCV infection has been reported in immunocompromised and HD pts. One report involving over 310 dialysis pts revealed up to 10% being HCV Ab negative yet having a positive PCR. Our case also illustrates the aggressive course HCV can take in the setting of immunosuppression and suggests that any immunocompromised or HD pt with persistently abnormal liver tests and negative HCV Ab should be evaluated with the more sensitive PCR exam.

Primary Malignant Lymphoma of the Duodenum in a Patient with AIDS
Madhavi Rudraraju, M.D., Nadeem Chaudary, M.D., William Tierney, M.D.* Digestive Diseases, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

Introduction: Biliary tract obstruction in patients with AIDS is most often related to infectious or idiopathic AIDS cholangiopathy. Extensive review of the literature reveals only one report of primary Non Hodgkins Lymphoma (NHL) of duodenum manifesting as obstructive jaundice.

Case Report: A 49-year-old homosexual white male was admitted to the hospital for jaundice and right-sided abdominal pain. He also had pruritus, early satiety and 20 lb weight loss. Physical examination revealed jaundice, but there was no peripheral lymphadenopathy or hepatosplenomegaly. Bilirubin was 6.4 mg/dl, AST 341 U/L, ALT 561 U/L, alkaline phosphatase 913 IU/L, LDH, amylase, lipase, WBC, hemoglobin were normal. CD4 count was 267/µL. Ultrasound of the biliary tree visualized dilation of the common bile duct and pancreatic duct. Abdominal CT scan demonstrated common bile duct dilatation and circumferential thickening of the third part of the duodenum. EGD revealed a mass in the second part of the duodenum, which was biopsied. Pathology demonstrated malignant large cell lymphoma. Bone marrow biopsy revealed marrow involvement with lymphoma. He received chemotherapy with Rituximab, Cyclophosphamide, Doxorubicin and Prednisone and went into remission.

Discussion: The most common biliary cause of jaundice in AIDS is AIDS cholangiopathy which is usually seen in patients with a CD4 count below 100/mm3. NHL is an infrequent cause of jaundice. NHL is primarily encountered in patients with more advanced HIV infection (CD4 below 100/µL).

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The gastrointestinal tract is one of the most frequent extranodal sites of presentation. The major presenting features of these tumors are pain and weight loss; life-threatening complications such as bleeding, perforation and obstruction occur in about 40% of these patients. Patients with gastrointestinal tract lymphoma may be more likely to respond to aggressive therapy and survive longer than those with the predominant bulk of the tumor in other organs. Chemotherapy induced tumor lysis can be associated with perforation in large transmural lesions. Fortunately, our patient did not experience perforation despite the large size of the primary tumor. However our report does highlight the importance of perianpillary lymphoma as an opportunistic cause of biliary obstruction in patients with AIDS and also highlights the importance of prompt diagnosis and aggressive treatment as it improves quality of life and survival given the good response to chemotherapy.

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Pyogenic Liver Abscess Following Colonoscopy in a Patient with Ulcerative Colitis
Christopher D. Wells, M.D., Vijayan Balan, M.D.*, Jerry D. Smilack, M.D., Mauricio Orrego, M.D., Hugo E. Vargas, M.D., Russell I. Heigh, M.D., Elizabeth J. Carey, M.D., Gastroenterology & Hepatology, Mayo Clinic, Scottsdale, AZ and Infectious Diseases, Mayo Clinic, Scottsdale, AZ.

To provide the initial description of a liver abscess developing following a surveillance colonoscopy in a patient with ulcerative colitis.

Medline search using various combinations of the following term(s): “liver abscess,” “endoscopy,” “colonoscopy,” “ulcerative colitis,” “inflammatory bowel disease,” “ fusobacterium nucletum.” Additionally, a review of the references in the citations provided by this search was performed.

A 62 year-old male with a twenty-year history of chronic ulcerative colitis (UC) presented to the emergency department with an approximate two-week history of fevers as high as 40.0°C, shaking chills, as well as malaise. He reported mild febrile urgency and mucus in his stool, but no overt gastrointestinal bleeding or abdominal pain. Additionally, he had undergone a surveillance colonoscopy four weeks earlier which included two polypectomies and a total of 29 biopsies. There were no immediate complications following this procedure. In the emergency department the patient was febrile, had a leukocytosis, mildly elevated transaminases, and an elevated alkaline phosphatase. Contrast-enhanced computed tomography (CT) of the abdomen revealed multiple low-attenuation lesions in the right hepatic lobe, the largest of which measured 9.0cm x 6.0 cm x 8.7cm, consistent with abscesses. This lesion was aspirated under CT guidance and the cultures were positive for Fusobacterium nucletum. His abscess resolved with intravenous antibiotics.

Liver abscess (LA) is a recognized complication of inflammatory bowel disease, although it occurs much more frequently in Crohn’s disease. There have been only six prior cases of LA in the setting of UC. LA has rarely been reported following endoscopic procedures, but there are no previous reports following colonoscopy with polypectomy and/or biopsy.

This is the first description of a pyogenic liver abscess developing after a surveillance colonoscopy in a patient with ulcerative colitis. This diagnosis should be considered in any patient with inflammatory bowel disease presenting with fever.

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Idiopathic Splenic Vein Thrombosis
Savio C. Reddymasu, M.D., Raza Anees, M.D., Larry E. Slav, M.D.* Internal Medicine, LSU Health Sciences Center, Shreveport, LA and Gastroenterology, VA Medical Center, Shreveport, LA.

A 70-year-old man with a history of diabetes, hyperlipidemia, obesity, and peptic ulcer disease presented to the Emergency Department with hematemesis, melena, and epigastric abdominal pain. Physical examination was otherwise unrevealing. Complete blood count, hepatic function tests, and coagulation studies were normal. Computerized tomography (CT) of the abdomen revealed splenic vein thrombosis (SVT) and gastric varices, without evidence of intra-abdominal malignancy or hepatic cirrhosis. Upper endoscopy (EGD) revealed isolated gastric varices and a healed duodenal ulcer. Evaluations for hypercoagulability and paroxysmal nocturnal hemoglobinuria were negative. The clinical diagnosis was portal hypertension secondary to idiopathic SVT, with upper gastrointestinal (UGI) bleeding from gastric varices. Propanolol and warfarin were initiated. Portal vein doppler ultrasound after six months of anticoagulation revealed resolution of SVT.

Discussion: Splenic vein thrombosis with sinus portal hypertension is a rare cause of upper gastrointestinal bleeding which is characterized by the triad of isolated gastric varices, splenomegaly, and normal hepatic function. Most commonly, SVT results from repeated attacks of pancreatitis or mass effect from adenocarcinoma of the pancreas. Other etiologies include retroperitoneal fibrosis, non-pancreatic intra-abdominal neoplasms, and peptic ulcer disease. Rare causes are hypercoagulable states, including polycythemia vera, myelofibrosis, Protein C and S deficiency, antiphospholipid antibody syndrome, and paroxysmal nocturnal hemoglobinuria. Diabetes, hyperlipidemia, obesity, and metabolic syndrome, which predispose venous thromboembolism, may also be risk factors for SVT. The definitive diagnostic study is mesenteric angiography. Ultrasound and CT are diagnostic if they reveal occlusion of the splenic vein. Non-selective beta-adrenergic blockade and anticoagulation with warfarin are the mainstay of treatment of SVT. Splenectomy or splenic artery embolization is recommended for UGI bleeding which is refractory to conservative management. Rarely, streptokinase has been used in acute SVT. Duration of anticoagulation is a matter of debate.

Conclusion: As the prevalence of diabetes, hyperlipidemia, obesity, and metabolic syndrome increases, UGI bleeding secondary to SVT may become more common. Additional studies are needed to establish this relationship conclusively and to determine the optimal duration of anticoagulation.

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Hydrocodone Induced Pancreatitis
Savio C. Reddymasu, M.D., Kenneth Manas, M.D.*, Paul Jordan, M.D. Internal Medicine, LSUHSC, Shreveport, LA and Gastroenterology, LSUHSC, Shreveport, LA.

A 30-year-old white female was referred to our hospital for complaints of abdominal pain, anorexia, and dyspepsia. The patient had recently been hospitalized at another facility with pancreatitis. Her lipase was persistently elevated at approximately 900 U/L and abdominal CT scan had revealed mild inflammation of the tail of the pancreas. Medical records from that hospital indicated that she had become dependent on hydrocodone and carisoprodol (Soma) for analgesia following a motor vehicle accident four months earlier. She had been taking these medications regularly throughout the course of her illness. At the time of admission to our hospital, the patient had not taken either of these medications for approximately two days. Initial laboratory studies revealed lipase 184 U/L, subsequently decreasing to 150 U/L, AST 128 U/L, ALT 195 U/L, and total bilirubin 1 mg/dL. CT scan of the pancreas at our facility was normal. Additional studies revealed no evidence of gallstones, hypertriglyceridemia, hypercalcemia, alcohol intake or other substance abuse. The patient’s presenting symptoms improved spontaneously. She left the hospital against medical advice, unhappy about the fact that she was not receiving hydrocodone or Soma. At home, she apparently resumed these medications. Two days later, she again presented to our institution with the same complaints. Once again, symptoms promptly improved while the patient was not taking the two medications. The possibility of drug-induced pancreatitis secondary to hydrocodone was raised.

We are not aware of any case reports of hydrocodone causing pancreatitis; however, a related drug, codeine, has been suggested as a cause of drug-induced pancreatitis. The likely pathophysiological mechanism involves constriction of the sphincter of Oddi and/or the pancreatic duct. Constriction occurs within 5 minutes of consuming the drug and lasting up to 2 hours. This response is not dose dependent. In one study, pancreatic enzymes increased
approximately 2 hours after subcutaneous administration of codeine and lasted for 1–2 days. Associated pancreatitis is usually mild and development of chronic pancreatitis has not been reported. Diagnosis is made by either resolution of symptoms on discontinuing the drug and/or by rechallenging with reproduction of symptoms, either in a controlled setting or unintentionally, as in our patient. Patients generally have a good recovery once the drug is discontinued. Narcotic analogues can be a potential cause of acute pancreatitis.

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Spontaneous Pneumomediastinum
Savio C. Reddymanus, M.D., Fatihali Borhamanesh, M.D.,∗ Larry E. Stay, M.D. Internal Medicine, LSUHSC, Shreveport, LA and Gastroenterology, LSUHSC, Shreveport, LA.

A 25-year-old black male presented to the Emergency Department with complaints of worsening dysphagia, nausea, and severe vomiting. There was palpable crepitus over the chest wall and neck. Chest X-ray (CXR) revealed pneumomediastinum (PM) and bilateral pleural effusions. Upper endoscopy (EGD) pursued soon after for presumed achalasia, revealed a narrow and tight distal esophagus. The esophagus was found to be cheesy with no obvious esophageal rupture. A gastrografin esophagram after the EGD was consistent with achalasia without leakage of dye into the mediastinum. Non-contrast computerized tomography (CT) of the chest revealed PM, and was consistent with achalasia without leakage of dye into the mediastinum. A gastrografin esophagram after the EGD pursued soon after for presumed achalasia, revealed a narrow and tight distal esophagus. The esophagus was found to be cheesy with no obvious esophageal rupture. A gastrografin esophagram after the EGD was consistent with achalasia without leakage of dye into the mediastinum. Non-contrast computerized tomography (CT) of the chest revealed PM, and a second scan the following day did not reveal any leakage of gastrografin into the mediastinum. Esophageal biopsy showed candidal esophagitis without evidence of malignancy. The C4 lymphocyte count was normal, and human immunodeficiency virus testing and urinalysis were negative. The patient’s symptoms improved with balloon dilatation of the esophagus and fluconazole therapy. Patient was discharged home with a diagnosis of achalasia, candidal esophagitis, and PM. Since there was no obvious etiology for the PM, it was presumed to be spontaneous pneumomediastinum (SPM).

Discussion: SPM is a rare, self-limiting entity usually occurring in young men. Hamman first characterized it in 1939 as free air around mediastinal structures without any apparent etiology such as trauma. The pathophysiology involves a spontaneous rise in intrabronchial and intraalveolar pressure following vomiting (as in this patient), coughing, sneezing, shouting, labor and delivery, or the valsalva maneuver. If a sufficient pressure gradient is generated, alveolar rupture occurs, allowing air to penetrate peribronchial and perivascular spaces into the mediastinum (the so-called Macklin effect). SPM is diagnosed by CXR in the appropriate clinical setting. Additional studies, including CT of the chest and esophagogram, are recommended to exclude other etiologies of PM. SPM resolves spontaneously when the triggering factor is removed. Management is conservative, typically with patient observation for 24 hours. A thoracostomy tube is required if pneumothorax is present. Rare complications include tension pneumomediastinum and “malignant pneumomediastinum”. Endoscopy was performed in this case because of the suspicion of achalasia. SPM is a subtle condition, which requires a high index of suspicion to diagnose. Achalasia with coexistent SPM has not been reported so far.

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Secretory Diarrhea: A Simple Assay That Saved the Patient Another “Million-Dollar” Work-Up
Noah M. Devicente, M.D., Marcelo F. Vela, M.D.,∗ Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, SC.

A 69 year old white female transferred for further work-up of secretory diarrhea.

Case description. 4 months prior, she developed diarrhea after antibiotics for UTI. C. difficile toxin was positive, diarrhea resolved with 14-day metronidazole course. Diarrhea recurred 2 weeks later and after 2 months of progressively worse diarrhea, she was admitted to her primary hospital with 10–12 watery, non-bloody bowel movements per day, with urgency, occasional incontinence, nighttime diarrhea, nausea, rare vomiting, mild abdominal tenderness and 10 lb weight loss. No inciting/relieving factors, fasting had no effect on diarrhea. No fevers, chills, rash, arthralgias, recent travel, sick contacts, well water or recent new medications (except antibiotics mentioned above). Stool culture, leukocytes, hemoccult, ova and parasites, qualitative fat, two C. difficile toxin assays, and cathartic screen all negative. Stool osmolar gap of 6 (Na 61, K 81) indicated secretory diarrhea. CT abdomen and small bowel series unremarkable. Colonoscopy showed petechiae; biopsies were negative (no microscopic colitis). EGD: mild gastritis; small bowel biopsies negative, (no increased lymphocytes, parasites, or amyloid). Plasma VIP, gastrin, calcitonin, ACTH, and TSH, and urinary 5-HIAA all normal. She had minimal improvement on lomotil, and required fluid/electrolyte replacement. At this point, she was transferred to our hospital for further work-up of secretory diarrhea. Exam: afebrile, HR 76, BP 104/70. No rashes, oral mucosa moist, no lymphenadenopathy. Cardiopulmonary exam normal. Abdomen: soft, nontender, nondistended, no masses or organomegaly; bowel sounds normal. Rectal sphincter tone normal. CBC, electrolytes LFTs normal. EGD was normal, small bowel biopsies unremarkable. Colonoscopy revealed patchy superficial colitis throughout entire colon, without ulceration/pseudomembranes. First C. difficile toxin negative, second one positive. Metronidazole resulted in only partial improvement; diarrhea finally resolved after starting oral vancomycin.

While a low stool osmolar gap may prompt an extensive search for rare causes of secretory diarrhea, it is important to focus the work-up on more frequent etiologies and possibly unusual presentation of common diseases. A recent history of C. difficile colitis should raise a high index of suspicion for this infection and should prompt aggressive testing for this organism, keeping in mind that several toxin assays may be needed, and pseudomembranes may be absent.

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Dietary Chaos Syndrome
Savio C. Reddymanus, M.D., Paul Jordan, M.D.,∗ Kenneth Manas, M.D. Internal Medicine, LSUHSC, Shreveport, LA and Gastroenterology, LSUHSC, Shreveport, LA.

Dietary chaos syndrome. A 50-year-old African American male presented to the emergency department with severe epigastric pain, nausea and vomiting. On exam, he was emaciated with a body mass index of 16kg/m². Physical exam was positive for epigastric tenderness and sluggish bowel sounds. At the time of admission, Lipase was 609 U/L, total bilirubin was >0.2 mg/dl, AST 257 U/L, ALT 212 U/L, albumin 2.8 g/dl and serum triglycerides and calcium were normal. There was no prior history of cholelithiasis or alcohol abuse. Computerized tomography (CT) scan of the abdomen revealed pancreatitis and no gallstones were identified. His prior medical history included malnutrition secondary to major depressive disorder. Prior to the episode of abdominal pain, the patient was reported to be anorexic after he stopped taking his psychotropic medications. He had lost about 9 lbs. He had resumed feeding again when this episode occurred. His condition improved with conservative management and lipase decreased to 56 U/L in two days. Patient recovered spontaneously, raising the specter of “dietary chaos” syndrome.

Discussion: Malnutrition has been described to be associated with acinar cell atrophy and injury, epithelial metaplasia, and increased zymogen granule release in the pancreas. This may cause high trypsinogen levels. Weight loss may also cause compression of internal organs. This situation may lead to conversion of trypsinogen to trypsin within the pancreas and subsequent activation of other proteases, triggering inflammatory processes leading to pancreatitis. This has been termed the “dietary chaos” syndrome. Though this condition is described in anorexia nervosa and bulimia, it would be reasonable to consider it in our cachectic patient with a similar syndrome. Recurrent episodes of acute pancreatitis could lead to chronic pancreatitis. This condition resolves with normalization of dietary patterns or resolution of the “dietary chaos.” The “Dietary chaos” syndrome should thus be considered in all malnourished or anorexic patients with idiopathic pancreatitis, particularly during refeeding after prolonged starvation.
High-Grade Small Bowel Obstruction in a Patient with HIV Due to Strongyloides Stercoralis

Kathleen Viveiros, M.D., Hyun S. Kim, M.D., Cynthia A. Behling, M.D. Gastroenterology, University of California, San Diego, San Diego, CA and Pathology, University of California, San Diego, San Diego, CA.

Patients with Strongyloides stercoralis infections have a variety of gastrointestinal complaints including diffuse or epigastric abdominal pain, diarrhea, vomiting, malabsorption and weight loss. Intestinal obstruction due to Strongyloides stercoralis infection is rare yet has been reported in a patient with HIV-1. In patients from endemic areas with HIV, Strongyloides stercoralis should be suspected as a potential cause of small intestine obstruction and excluded before surgical procedures are performed. A 20 year-old HIV infected African woman presents with persistent nausea and vomiting, epigastric pain, anorexia and a ten pound weight loss for a month. One year prior, the patient, as part of the HIV clinic testing for refugees, had Strongyloides stercoralis detected in her stool. She was treated with ivermectin at that time. The patient was admitted for her symptoms of vomiting with weight loss. On exam, the patient was afebrile, mildly anxious with discomfort in the epigastrium and right upper quadrant upon palpation. Her laboratory values included a normal hematocrit and MCV and a CD4 count > 1500 and VL < 50 on no HIV medications. CT of the abdomen and pelvis demonstrated a distended stomach, dilated loops of small bowel and transition zone near the proximal ileum. Multiple enlarged mesenteric lymph nodes were seen on CT as well. Mycobacterium avium-intracelulare (MAI), tuberculosis (TB) and lymphoma were considered as possible causes of obstruction based on CT appearance. Small bowel series showed an irregular narrowing of the third portion of the duodenum associated with mucosal edema. Endoscopy showed an area of marked erythema and edema in the duodenum and random biopsies were taken. The pathology revealed ova and adult forms of parasitic organisms in the duodenal mucosa and submucosa consistent with Strongyloides. She was treated with ivermectin and discharged with symptom improvement. Months later, stool studies are negative and the patient remains asymptomatic. Strongyloides stercoralis is an intestinal nematode endemic in tropical areas of Africa, Asia and Latin America as well as southeastern parts of the United States and eastern Europe. HIV infected patients from these endemic areas presenting with intestinal obstruction should have Strongyloides infection excluded as part of their workup. Prompt diagnosis and treatment obviates the need for surgical exploration in these patients.

EUS and FNA Needle-Assisted Combined Antegrade and Retrograde Dilation of a Complex Esophageal Stricture: A Novel Approach

Gilbert K. Ong, M.D., Ronald Szyszkowski, M.D., Bipin Saud, M.D. Gastroenterology, SUNY-Upstate Medical University, Syracuse, NY.

Background: Combined antegrade and retrograde dilation (CARD) is a safe and effective technique for dilation of complex esophageal strictures. We present such a case aided by the use of an endoscopic ultrasound (EUS) and FNA needle.

We present a 61 y/o male with stage III SCCA of the tongue s/p hemiglossectomy and neck dissection in 2000 followed by radiation. In 2004 he was found to have local recurrence treated with partial pharyngectomy, wide local excision, and reconstruction. A G-tube was placed surgically. He presented in early 2005 with dysphagia to both solids and liquids. Barium swallow showed no passage of contrast into the esophagus. EGD revealed benign appearing thin membrane completely obstructing the lumen just beyond the upper esophageal sphincter. After serial balloon dilation of the G-tube stoma the stomach was intubated. The gastroscope was advanced retrograde towards the stricture. A guidewire could not be advanced across the stricture and complete obstruction was reconfirmed by fluoroscopy with air contrast. A second gastroscope was introduced through the mouth with no opening or fistulous tract seen. An EUS 12mHz probe was placed through the retrograde scope and radial scanning performed. The stricture was thick but avascular. The two scopes were approximated fluoroscopically and transillumination confirmed position. A 22G FNA needle was inserted through the retrograde scope 2 cm into the stricture. The stylet of the needle was then removed and a guidewire threaded from the retrograde scope into the channel of the antegrade scope. The antegrade scope was withdrawn and sequential Savary dilations up to 33F were performed. The retrograde scope was advanced over the wire and into the oropharynx where inspection revealed no tumors. He returned for several more regular EGDs with Savary dilations up to 60F. He was eventually able to tolerate both solids and liquids.

Discussion: The use of EUS enhances the safety of CARD procedures by enabling the operator to identify blood vessels, fistulas, and other strictures. The FNA needle with wire placement is another technique that can be used to traverse strictures.

Successful Identification and Drainage of Giant Hepatic Echinococcal Cyst by Endoscopic Ultrasound

Rohin Baradarian, M.D., Scott Tenner, M.D., M.P.H., Isaac Mosheynat, M.D., Gulam Khan, M.D., Jian Jun Li, M.D.∗ Division of Gastroenterology, Maimonides Medical Center, Mount Sinai School of Medicine, Brooklyn, NY.

Hepatic alveolar echinococcosis is a rare but potentially life-threatening parasitic disease, developing as a result of intrahepatic growth of Echinococcus multilocularis larvae. A high index of suspicion and specific radiologic findings are helpful in the diagnosis of the disease. The only curative treatment of the disease is surgical resection; however, percutaneous ultrasound-guided drainage is an acceptable method of treatment combined with oral albendazole. We report a case of a patient who presented with a symptomatic echinococcal cyst who was successfully treated with endoscopic ultrasound fine needle aspiration. The patient is a 32 year old female from Uzbekistan (Central Asia) who presented with worsening abdominal pain for six months duration. There was no fever, chills, melena, hematochezia, jaundice, or history of liver disease. On physical examination, her vital signs were stable. There was a low grade fever, mild hepatomegally and mild right upper quadrant tenderness. Complete blood count and electrolytes were normal. Liver function tests revealed an albumin decreased to 2.7 mg/dl. The bilirubin and transaminases were normal. After an abdominal ultrasound revealed a mass in the liver, a computed tomograph (CT) was performed. CT revealed a 11 × 9 × 15 cm well circumscribed cyst in the right lobe of the liver. The wall was well defined. Echinococcus was suspected. Echinococcal titters were submitted and albendazole was given. Due to the location of the cyst adjacent to the duodenum, an endoscopic ultrasound with fine needle aspiration was performed. During the EUS, the classic findings described on trans-abdominal ultrasound of an echinococcal cyst were appreciated: triple-layered echogenic wall. A 22 gauge Olympus EUS FNA Needle was placed through the wall of the cyst with no difficulty. The cyst was drained. After the procedure, the patient remained well with stable vital signs. This case suggests that endoscopic ultrasound is safe and effective in the diagnosis and treatment of hepatic echinococcal cysts.

Type I Choleodochal Cyst with Abnormal Union of the Pancreaticobiliary Junction Presenting with Ruptured Gallbladder Carcinoma

Matthew T. Nicholls, M.D., Raj Shah, M.D., Yang Chen, M.D., Mainor Antonill, M.D., Cyrus Piraka, M.D., Krishnavel V. Chatbadi, M.D.∗ Division of Gastroenterology, Denver Health Medical Center, Denver, CO.

A 43-year-old female presented with nausea, vomiting, fever, hypotension, tachycardia and right upper quadrant abdominal pain. Laboratory values revealed leukocytosis and cholesterol.
Transabdominal ultrasound showed a thickened gallbladder wall (2 cm) without surrounding fluid as well as a markedly dilated (2 cm) extrahepatic biliary system. Abdominal CT revealed a dilated extrahepatic biliary duct and additionally, a large poorly defined hypodensity in liver segment V suggestive of gallbladder rupture or focal abscesses. ERCP was performed to further characterize the patient’s anatomy and process prior to surgical intervention. ERCP demonstrated fusiform dilation of the extrahepatic biliary system of up to 2.8 cm suggestive of a type 1A choledochal cyst. Contrast injection of the gallbladder revealed an irregular wall with contained contrast extravasation into the hepatic parenchyma suspicious for gallbladder cancer with associated rupture. Cholangiogram of the distal biliary system revealed a smoothly tapering common bile duct proximal to the junction with the pancreatic duct without any stricture. Aside from mild tortuosity in the head, the pancreaticogastrogram was normal. A borderline abnormal pancreatobiliary junction with a 10 mm long common channel was appreciated distally. A double pigtail biliary stent was placed across the papilla and into the proximal dilated portion of the bile duct. As a result of the cholangiogram, CT scan and intra-operative findings, the patient underwent an extended left hepatic lobectomy with en bloc cholecystectomy, excision of the choledochal cyst and hepaticojejunoscopy reconstruction. Pathology revealed a poorly differentiated adenocarcinoma of the gallbladder and fibrosis and chronic inflammation of the bile duct wall suggestive of a type 1A choledochal cyst.

Primary gallbladder carcinoma is an uncommon but highly malignant tumor with a poor 5-year survival rate. Anomalous union of the pancreatobiliary ductal junction without associated choledochal cyst is a rare congenital anomaly and a known risk factor for development of gallbladder cancer. We present a case of advanced gallbladder carcinoma in the setting of abnormal pancreatobiliary ductal junction with an associated choledochal cyst. Radiographic images (including CT, MRCP and ERCP images) as well as both gross and microscopic pathology images will be displayed.

Fine Needle Aspiration of Peritumoral Lymph Nodes in Esophageal Cancer with Endobronchial Ultrasound

Kyoung W. Noh, M.D., Massimo Raimondo, M.D., Michael B. Wallace, M.D., M.P.H., Herbert C. Wolfson, M.D., Timothy A. Woodward, M.D.* Division of Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL.

Peritumoral lymphadenopathy detected on EUS examination poses a significant challenge in the staging of esophageal cancer. Biopsy of lymph nodes through the primary tumor causes concern for contamination and seeding. We demonstrate a new technique of sampling these lymph nodes using endobronchial ultrasound (EBUS).

A 70-year-old male with a new diagnosis of squamous cell carcinoma of the esophagus was referred for staging EUS. Chromoendoscopy using Lugol’s solution performed prior to EUS revealed abnormally stained mucosa from 34 cm to 22 cm from the incisors. Biopsies demonstrated severe dysplasia or carcinoma-in-situ. EUS examination demonstrated circumferential thickening of the esophageal wall and a 5 mm, diffusely hypoechoic, round periesophageal lymph node with sharp margins. This was located in the area adjacent to the previously documented area of squamous cell carcinoma. EUS guided fine needle aspiration (EUS-FNA) was not performed due to concerns of contamination of the needle as it traversed the cancerous tissue. Thus, the patient underwent EBUS to sample the suspicious lymph node. Under ultrasound guidance, FNA of the periesophageal lymph node was performed. Cytology was negative for malignancy. The patient underwent transthoracic esophagectomy without neoadjuvant therapy. Surgical pathology revealed severe dysplasia/squamous cell carcinoma-in-situ of the esophagus. The periesophageal lymph nodes were free of tumor.

The use of EBUS has been limited to stage lung cancers. We describe a new indication for EBUS. As peritumoral lymph nodes can be accessed through the bronchial wall without traversing the tumor tissue, the presence of malignant cells can be interpreted as a malignant lymph node. In addition, there is no risk of introduction of the malignancy into a benign lymph node.

The presence of malignant peritumoral lymph nodes is important as it helps to determine therapy and predict survival. The detection of these lymph nodes is of increased importance in the cases in which non-operative therapy is planned such as photodynamic therapy and endoscopic mucosal resection. We demonstrate the feasibility and safety of EBUS-FNA of peritumoral lymph nodes in the setting of esophageal carcinoma that would not be otherwise accessible via EUS-FNA. We believe that lymph node staging of esophageal cancer will be an added indication for EBUS.

Constipation and Bloating as an Unusual Presentation of Celiac Disease. A Case Report

Ramu Raju, M.D., Daniel Moore, M.D., Andrew Ukleja, M.D.* Gastroenterology, Cleveland Clinic Florida, Weston, FL.

We present a case of celiac disease (CD) with an atypical presentation. A 34-year old female with a remote history of iron deficiency presented with chronic constipation associated with bloating. She has been suffering from constipation for the last five years that has become more progressive. Despite, trying fiber supplementation, milk of magnesia, and doxecat sodium, she moved her bowels every 3–4 days with little improvement of her symptoms. She denied any heartburn, regurgitation, or any blood or melonetic stools. The patient does not take any NSAIDS. Family history was negative for any GI malignancy or celiac disease. She denied any use of alcohol or tobacco consumption. Physical exam revealed a slender female with no pallor or skin rash. Her exam was unremarkable. Laboratory Tests: WBC 6.9 (K/uL), Hemoglobin 12.2 (g/dL), Platelets 431,000 (K/uL), MCV 80.6 (fL) Complete metabolic panel was normal. Because of the history of anemia and gastrointestinal complaint a celiac panel was obtained. All celiac antibodies were positive: TTG-IgA 136 U/mL, AGA-IgG 126 U/mL AGA-IgA 24 U/mL AEMA-IgA 1:160. Therefore an upper endoscopy was performed and revealed flattened duodenal folds. Biopsies of the duodenum revealed severe villous blunting with focal cryptitis and lymphoplasmacytosis of the lamina propria consistent with CD. Patient was started on a gluten-free diet (GFD) and her symptoms subsided over the next several weeks.

In conclusion, we found CD in the patient with the predominant symptom of constipation which is extremely rare. This case illustrates the importance of considering the work-up of celiac disease in patients with a history of anemia and constipation. Clinical improvement is expected in case of underlying celiac disease with GFD.

Sarcoidosis Presenting with Dysphagia. Diagnosis Confirmed with Endosonography Guided Fine Needle Aspiration (EUS-FNA). Review of the Literature

Laith H. Jamil, M.D., Gehad Ghait, M.D., Gregory Kuleza, M.D.* Gastroenterology, William Beaumont Hospital, Royal Oak, MI.

Describe an unusual presentation for Sarcoidosis and an underutilized method for diagnosis 57-year-old female with history of DM, GERD and Sarcoidosis since 1983 with stable mediastinal lymphadenopathy (ML) presents with new onset intermittent dysphagia and odynophagia. EGD showed mild proximal and mid extra-esophageal compression. CT scan of the chest and abdomen showed ML and abdominal lymphadenopathy suspicious for Lymphoma. An upper EUS-FNA was performed on the para-esophageal and peri-pancreatic lymph nodes with an 18-gauge needle. Histology of the para-esophageal lymph nodes showed non-caseating granulomas consistent with Sarcoidosis. Dysphagia has been described as a symptom in patients with enlarged ML from any cause. It is not usually mentioned as a presentation of Sarcoidosis. Our patient had an EGD 2 years ago with no signs of extra-esophageal
compression. In addition, she had long standing history of GERD and DM, both of which can cause dysphagia and odynophagia.

In regards to EUS-FNA and the diagnosis of Sarcoïdosis, we came across a few series. Annema et al described 51 patients with suspected Sarcoïdosis who underwent EUS-FNA. 36 patients had a previous non-diagnostic bronchoscopy. EUS-FNA demonstrated non-caseating granulomas without necrosis in 41 of 50 patients with the final diagnosis of Sarcoïdosis. Fritscher-Ravens et al studied 19 patients with suspected Sarcoïdosis with EUS-FNA and showed the specificity and sensitivity to be 94% and 100%, respectively. EUS revealed certain suggestive echo patterns for Sarcoïdosis. However, it was not capable of differentiating the lesions from tuberculosis or malignancy.

Other studies have described the diagnosis of Sarcoïdosis via EUS-FNA during the workup for ML. Mishra et al described the diagnosis of Sarcoïdosis in 7/108 consecutive patients during the workup of ML. Wildl et al diagnosed Sarcoïdosis in 28/124 patients who were investigated for ML of unknown origin.

Sarcoïdosis can present with dysphagia at any stage of the disease. Bronchoscopy with transbronchial lung biopsy is non-diagnostic in 30% of patients with suspected Sarcoïdosis and has a risk of pneumothorax and hemoptysis. Diagnosis of Sarcoïdosis in patients with hilar and ML can be achieved with EUS-FNA, which provides a non-surgical alternative with high accuracy and with little or no complications. In addition, mediastinal lymph nodes in Sarcoïdosis appear to have suggestive echo characteristics.

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Obscure GI Bleeding Due to Gastrointestinal Stromal Tumor (GIST) - Diagnosed by Capsule Endoscopy

Hari B. Ancha, M.D., Madhavi Rudravajjula, M.D., Son Nguyen, M.D., Matthew Blankenship, M.D., Verapan Vonghavaravat, M.D.* Section of Digestive Diseases, Department of Internal Medicine, OU Health Sciences Center, OKC, OK.

Gastrointestinal stromal tumor (GIST) is a submucosal tumor which is most commonly found in the stomach and less commonly seen in small bowel. Small bowel GIST is very difficult to diagnose by conventional upper endoscopy. We report a case of massive obscure GI bleeding from small bowel GIST diagnosed by capsule endoscopy.

Case Report: 81-year-old male presented with recurrent gastrointestinal bleed (malena) and anemia. Upper endoscopy and colonoscopy did not show any obvious source of bleeding. He also had small bowel enteroscopy which was normal. Patient continued to have melena, profound weakness, and anemia. Capsule endoscopy was performed to evaluate the bleeding source in the small bowel. A polypoid mass in mid-jejunum was seen by capsule endoscopy. He underwent limited resection of the small bowel. An 8 cm mass was found in the small intestine. The pathology result was compatible with small bowel GIST.

Discussion: GIST can arise in any part of the alimentary tract that contains smooth muscle within its wall. The most common site is the stomach (50 percent), followed by small bowel (25 percent). Colon (10 percent), omentum/mesentery (7 percent) and esophagus (5 percent) are less common primary sites. Small bowel GIST is most commonly found in the jejunum followed by the ileum and the duodenum. Small bowel GIST is often large when it is discovered. By histology, GIST predominantly has spindle-shaped to epithelioid cells. The symptomatic GIST can present as GI bleeding (40 percent), abdominal mass (40 percent) and abdominal pain (20 percent). GIST frequently metastasizes to the liver, and rarely to regional lymph nodes and virtually never metastasizes to the lungs. Thus, small bowel GIST commonly presents with ulceration and bleeding, which can be massive. Surgical resection of the entire tumor is the treatment of choice; resection of lymph nodes is usually unnecessary. The prognosis of malignant GIST involving the small intestine depends upon the adequacy of resection. Five-year overall survival rates are 42 and 8 percent for those undergoing complete and incomplete resections, respectively. Small bowel GIST is a challenge as it cannot be localized by conventional endoscopy; capsule endoscopy is a very valuable diagnostic tool and should be considered.

Capsule endoscopy is a newer non-invasive and highly effective method in the evaluation of obscure gastrointestinal bleeding due to GIST.

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Myasthenia: An Unusual Adverse Effect of Azathioprine Therapy

Arati S. Karhadkar, M.B.B.S., Jeffrey H. Schwartz, M.D., Sudhir K. Dutta, M.D.* Gastroenterology, Sinai Hospital of Baltimore, Baltimore, MD; Gastroenterology, Northwest Hospital, Baltimore, MD and Medicine, University of Maryland School of Medicine, Baltimore, MD.

Azathioprine, an analogue of 6-mercaptopurine has been used as a steroid-sparing agent in the treatment of inflammatory bowel disease for over 30 years. Hypersensitivity reactions to azathioprine including fever, myalgia, arthralgia, rash are well documented in the literature. Here, we report two cases of azathioprine hypersensitivity in patients with IBD manifesting with the unusual symptom of profound muscular weakness resulting in inability to perform simple tasks such as lifting even light objects, sitting upright and walking a few steps. Development of severe myasthenia raised concerns about myositis, rhabdomyolysis, myopathy and sepsis in these patients. Discontinuation of azathioprine resulted in prompt improvement of muscular weakness, and rechallenge led to recurrence of profound myasthenia within hours. Hypersensitivity to azathioprine has been reported to manifest as an aggravation of myasthenia in patients with myasthenia gravis, however, myasthenia has not been reported as an expression of azathioprine hypersensitivity in patients with IBD without a neuromuscular disorder. Azathioprine has been shown to inhibit the enzyme phosphodiesterase and potentiate the neuromuscular block due to succinylcholine, a depolarizing muscle relaxant in the in-vivo experiments utilizing cat soleus muscle preparation. It is well recognized that inhibition of phosphodiesterase can cause increased release of acetylcholine at the neuromuscular junction. We hypothesize that in certain patients, as in the current cases, phosphodiesterase inhibition by azathioprine may be resulting in excessive amount of acetylcholine at the neuromuscular junction, possibly leading to depolarizing neuromuscular blockade.

Development of myasthenia in patients on azathioprine should raise concern about a possible adverse effect of the drug. Failure to clinically recognize this adverse outcome can lead to prolonged periods of muscular weakness in this group of patients.

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Guillain Barre Syndrome Presenting as Nausea and Vomiting

Robert Spitzer, M.D.* Neurology, Wayne State University, Detroit, MI.

I report a case of the autonomic variant of Guillain Barre syndrome presenting with nausea and vomiting.

A 40 year old woman awoke with nausea and vomiting one day after feeling some abdominal discomfort. She became unable to eat with recurrent nausea and vomiting. A workup for ulcer disease was negative. Gastroprasis was diagnosed. She began to develop dizziness and syncope, and orthostatic hypotension was noted. A cardiac workup was negative. She also complained of some tingling of the extremities, fatigue, and unilateral ptosis. Symptoms persisted for eight months and a neurological consultation was obtained, and the autonomic variant of Guillain Barre syndrome was diagnosed. Electrophysiology confirmed sympathetic dysfunction.

Guillain Barre syndrome usually presents with generalized motor weakness. The autonomic nervous system is invariably involved as well. However, a rare variant form involves only the autonomic nervous system, with minimal involvement of the somatic nervous system. Onset is fairly rapid, often in occurs in young individuals, and has a good prognosis for eventual recovery. Recovery typically takes two to three years. Recognition of this variant may be very difficult. Because recognition is usually delayed, the time window for treatment with plasmapheresis or IVIG has usually passed. The clinical presentation usually involves cardiac and gastrointestinal manifestations. Clinicians need to be alert to this possibility when seeing patients with unexplained autonomic dysfunction.
**Case of a Patient with a Jejunal Tubular Adenomatous Polyp Diagnosed by Wireless Capsule Endoscopy**

Kamlesh M. Shah, M.D., George Ahtaridis, M.D.* Division of Gastroenterology, Graduate Hospital, Philadelphia, PA.

The aim of this case report is to illustrate a case of a patient with iron-deficiency anemia who underwent wireless capsule endoscopy revealing a jejunal tubular adenomatous polyp with low-grade dysplasia. Mr. VC is a 78 year old African-American male who presented to us as an outpatient for evaluation of iron-deficiency anemia with heme-occult positive stools. He underwent colonoscopic and upper endoscopic evaluation revealing hyperplastic and tubular adenomatous polyps in his sigmoid colon as well as chronic gastritis. He was referred for wireless capsule endoscopy for continued occult, iron-deficiency anemia. Wireless capsule endoscopy revealed a large polypoid lesion in his mid-jejunum as seen in the following figure. He subsequently was referred for enteroscopy. On enteroscopy, the polypoid lesion visualized by wireless capsule endoscopy was found. The polypoid lesion appeared multi-tubular and sessile as seen in the above figure. Multiple biopsies were taken and pathologic evaluation confirmed the polyp to be a tubular adenoma with low-grade dysplasia. An attempt to completely reset the polyp endoscopically is being considered. This case report of an iron-deficient, anemic patient diagnosed with a jejunal tubular adenomatous polyp with low-grade dysplasia illustrates the utility and importance of wireless capsule endoscopy in our diagnostic armamentarium.

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**Metastatic Sigmoid Adenocarcinoma Presenting as Pseudomyxoma Peritonei**

Naarin Ghesani, M.D., Lilian F. Pliner, M.D., F.A.C.P., Yiyan Liu, M.D.,* Lionel Zackier, M.D., Sita Chokhavatia, M.D. Radiology, New Jersey Medical School, Newark, NJ.

Pseudomyxoma peritonei (PP) is characterized by the production of copious amounts of mucinous fluid that gradually fills the peritoneal cavity resulting in the characteristic “jelly belly”. It is thought to originate either from progressive growth of an appendiceal adenoma/adenocarcinoma that eventually leads to obliteration of the lumen and perforates into and seeds the peritoneal cavity or a primary ovarian tumor. Carcinomatosis peritonei (CP) occurs in metastatic adenocarcinoma arising from varied sites in gastrointestinal tract and may mimic PP clinically and radiographically.

50 year old woman with insignificant medical and family history was evaluated for 6months of increasing abdominal girth, nausea and vomiting. Clinical examination revealed marked abdominal distention and diffuse tenderness. CT scan was consistent with PP and revealed extensive multiloculated ascites with thin septations and omental caking. At the presentation, CA 125 was 269u/ml, CEA was 145.5ng/ml. Colonoscopy revealed a mass with appearance of grape-like cluster at 32 to 45 cm from the anal verge. At exploratory laparotomy, omentum and peritoneal cavity were noted to have massive, diffuse, mucinous deposits of tumor. The debulking surgery included TAH/BSO, total colectomy, splenectomy, distal pancreatectomy and resection of omental tumor mass. The histopathology revealed: well-differentiated metastatic mucinous adenocarcinoma involving ovaries and fallopian tubes; 7 × 4.5 × 2 cm mucin producing well differentiated sigmoid colon adenocarcinoma, involving half of the luminal circumference; metastatic mucious adenocarcinoma to the capsule of the spleen. Both gross and microscopic examination of appendix was unremarkable. She subsequently underwent 6 cycles of FOFOX4 chemotherapy. Multiple repeat CT scans showed persistent PP. Most recent CT scan at two year follow-up shows increasing PP findings. F 18 flurodeoxyglucose (FDG) PET-CT performed after chemotherapy demonstrated low grade radiotracer uptake in the areas of peritoneal disease seen on CT scan, as it would be seen with CP arising from mucinous adenocarcinoma or with PP. Patients presenting with PP may have metastatic intestinal mucinous adenocarcinoma ie CP as demonstrated in this patient. For PP patients debulking surgical intervention is the treatment of choice and chemotherapy is ineffective. Mucin may accumulate several years post surgery but neither CT nor PET scans help differentiation of PP from CP.
The question of whether AHY confers any increased risk for liver disease in the pediatric and adult population remains debated. Several articles have indicated that A1AT heterozygotes (AH) are not represented disproportionately in populations with identified causes of end stage liver disease. However, there are reports that AH are overrepresented among those with cryptogenic cirrhosis. It is possible that AHY may increase susceptibility to a co-existent but as yet unidentified hepatic insult. We report a series of 5 children, ages 6–14, who were referred for elevated transaminases. Evaluation included markers for metabolic, autoimmunne, and infectious etiologies. All were shown to be AH: 4 MZ, 1 SZ. All 5 children had a BMI >95% for age and sex. The four available ultrasounds showed fatty liver. Four had acanthosis nigricans (AN). Four had strong family history of Type 2 DM. A fifth had a family history of cryptogenic cirrhosis and thyroid disease. Three were hypertensive for age. The one child who underwent liver biopsy had 90% fatty infiltrate in the absence of predisposing factors other than obesity and IR. One child whose BMI normalized also had normalization of transaminases. 

All of the children whom we have identified as AH also have clinical markers for IR, including obesity and AN. These children make up a disproportionate number of our patients whom we have classified as NAFLD: of the 10 children with evidence of IR who have had a complete evaluation since 2001, 5 are AH.

In this series we report an association between AHY, IR, elevated transaminases and fatty liver. In our small group of 10 children AHY is overrepresented (50%). Recent studies indicate that mitochondrial dysfunction plays an important role in the hepatic damage seen in both NAFLD and A1AT deficiency. Studies which have shown a disproportionately high number of AHY among those with cryptogenic cirrhosis did not specifically address the issue of NAFLD. We hypothesize that AHY provides a biological milieu that increases the risk of patients with IR to develop liver disease, possibly through a mechanism that increases the susceptibility to fat-related liver injury. This finding suggests that patients with IR and AHY should be treated more aggressively.

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Acute Recurrent Pancreatitis Secondary to an Obstructing Pseudoaneurysm with Antegrade Cannulation of the Main Pancreatic Duct Using Endoscopic Ultrasound  
Robert D. Anderson, M.D.*, Damien Mallat, M.D.  
Gastroenterology, Baylor University Medical Center, Dallas, TX.

Endoscopic retrograde cholangiopancreatography (ERCP) is evolving as a therapeutic procedure of pancreatobiliary diseases. Multiple studies have shown a therapeutic role of pancreatic stenting in the treatment of chronic pancreatitis. However, deep cannulation of the desired duct is not always successful. We present a case of endoscopic ultrasound (EUS) assisted cannulation of the pancreatic duct.

**Method:** A 57-year-old man was referred to our hospital for evaluation of obscure, recurrent gastrointestinal bleeding and acute recurrent pancreatitis. His prior history consisted of multiple episodes of acute pancreatitis. These episodes were followed by melena and a drop in hematocrit 2 to 3 days post pancreatitis. Colonoscopy and upper endoscopy were normal. EUS was performed to assess the etiology of acute recurrent pancreatitis. The examination revealed chronic pancreatitis, a 2 × 3 cm pseudoaneurysm of the gastroduodenal artery with compression of both distal common bile and ventral pancreatic ducts as well as dilation of the pancreatic duct proximal to the compressing pseudoaneurysm. The pseudoaneurysm was successfully emboledizing using coils.

As an outpatient, the patient’s hematocrit was stable without evidence of melena. However, the patient continued to have acute episodes of pancreatitis with cholestatic liver enzymes. Approximately 2 months post emboledization, ERCP was attempted for endoscopic management of acute recurrent pancreatitis and cholestasis. ERCP showed stricture of the ventral pancreatic duct with adequate filling of the pancreatic duct in the body and tail. The pan-creatic duct was dilated proximal to the stricture. Despite multiple attempts, deep cannulation of the pancreatic duct failed. Subsequently, a linear EUS scope was introduced into the stomach and a 19 gauge EUS needle was inserted the pancreatic duct. A 0.035 jagwire was deployed antegrade into the pancreatic duct past the ampulla. The EUS scope and needle were then removed, leaving the wire in place. The wire then was snared in a rendez-vous fashion. A 5 Fr x 7 cm pancreatic stent was deployed retrograde across the ampulla. He was discharge home the next day. There were no further episodes of pancreatitis or bleeding after 3 months of follow-up.

**Conclusion:** This case illustrates the safety and feasibility of new endoscopic intervention of EUS antegrade cannulation of the pancreatic duct.

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Cytomegalovirus-Associated Discrete Gastrointestinal Masses: All That Glitters Is Not Gold  
Houssem E. Mardini, M.D., Talal El Adhami, M.D., Alvero Koch, M.D.*  
Division of Gastroenterology, Hepatology and Nutrition, University of Kentucky, Lexington, KY.

Cytomegalovirus (CMV) infection of the gastrointestinal tract is common in immunocompromised patients. However, CMV as a mass lesion in the GI tract is rare and often mimics malignancy. Since this type of pseudotumor often responds to medical treatment, it is important that the physician be aware of it in treating severely immunocompromised patients.

We report 2 cases of CMV-induced mass / pseudotumor in the 3rd part of duodenum in one pt and in cecum in another pt. The first pt was a 51 yr old black male who is status post kidney transplant 6 weeks prior to presentation. He has been receiving prednisone and tacrolimus. He presented with significant hematochezia and severe anemia. The pt had recent upper and lower endoscopies prior to transplant and were unremarkable. Pt was admitted to the hospital and underwent a repeat endoscopic evaluation. He was found to have a large fungating ulcerated mass in the 3rd portion of the duodenum which was biopsied. The findings including Immunostaining for CMV antigens were consistent with CMV infection with focal inflammation extending to the subserosa. The second pt was a 73 y white male with advanced COPD who has been treated frequently with steroids and antibiotics in the previous few years. He presented with near-syncope and melena. He was found to be severely anemic and was admitted and received blood transfusion. A diagnostic colonoscopy was performed and showed a medium-size ulcerated mass in the cecum. Biopsies of the mass showed ulceration and severe acute and chronic inflammation and numerous inclusion bodies diagnostic of CMV infection. Both patients were successfully treated with Gancyclovir intravenously and did not require surgery.

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A Case of Superior Mesenteric Artery (SMA) Syndrome Responding to Surgical Management  
G. Koshy, M.D., I. Donepudi, M.D., N. Kiyici, M.D., H. Hertan, M.D., F.A.C.G.* Division of Gastroenterology, Our Lady of Mercy Medical Center, Bronx, NY.

**Introduction:** Superior Mesenteric Artery (SMA) syndrome is a rare, under reported but well recognized clinical entity that is characterized by compression of the third portion of the duodenum against the aorta by the SMA resulting in partial or intermittent duodenal obstruction. The incidence is 0.013–0.3%. The SMA forms an angle of 45 degrees with the aorta. Any factor that sharply narrows this angle to about 25 degrees causes SMA syndrome. It usually occurs in the setting of acute weight loss in patients with burns, whole body casts, trauma, cancers due to loss of the mesenteric fat pad between SMA and the Aorta. The patient presents with abdominal pain and persistent vomiting. It is usually managed medically, with patients rarely being considered candidates for surgery. The clinical index of suspicion should remain high in appropriate settings as delay in diagnosis and treatment can lead to dehydration, malnutrition, electrolyte abnormalities and even death.
Objective: To report a case of Superior Mesenteric Artery Syndrome that responded to surgical management.

Methods: A 32 year old female presented to the emergency room with a one-week history of nausea, vomiting and epigastric pain. Her lab chemicals and physical examination were unremarkable and she was admitted for further observation. Radiological imaging studies identified the presence of gallstones and thickened stomach wall with no evidence of obstruction. Upper endoscopy revealed a thickened stomach wall but no pyloric obstruction. Her gastric biopsy showed that she had adenocarcinoma with a signet ring appearance. The tumor was found to be unresectable due to local spread. Her hospital course was complicated by bouts of persistent vomiting and continued weight loss. An upper GI series done subsequently revealed a dilated stomach and an abrupt cut-off in the third part of the duodenum that was suggestive of SMA syndrome. The patient did not respond to conservative management and underwent gastrojejunostomy, with resolution of symptoms.

Conclusion: Although rarely seen, the clinical index of suspicion for SMA syndrome should remain high in patients with acute weight loss and persistent vomiting. Surgical options should be considered earlier rather than later to avoid complications of malnutrition, electrolyte imbalances and death in this subset of patients.

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A Case of Ciguatera Poisoning in a 35-Year Old Male from the Bronx, NY

G. Koshy, M.D., I. Donnepudi, M.D., H. Hertan, M.D., F.A.C.G.* Division of Gastroenterology, Our Lady of Mercy Medical Center, Bronx, NY.

Introduction: Ciguatera poisoning, linked to the consumption of contaminated reef fish such as barracuda, grouper and snapper, is the most commonly reported marine toxin disease in the world. Under-diagnosis and under-reporting (especially in endemic areas such as the Caribbean) make it difficult to know the true worldwide incidence of Marine Toxin Diseases. CDC and others estimate that only 2–10% of Ciguatera cases are actually reported in the United States. The dinoflagellate Gambierdiscus toxicus produces the toxin, ciguatoxin, which is responsible for the cases of ciguatera poisoning that occur in the tropical regions of the world. Patients present with gastrointestinal, cardiac and neurological symptoms.

Objective: To report on a case of ciguatera poisoning in the Bronx, NY.

Methods: A 35 year old man presented with abdominal pain, vomiting, diarrhea and dizziness after consuming cooked barracuda the previous evening. The patient became hypotensive and required ICU monitoring. The patient responded to surgical management.

Conclusion: Ciguatera poisoning occurs with consumption of reef fish. Identification of a contaminated fish is not easy as its appearance, taste and smell are normal. Further, the process of cooking does not destroy the ciguatoxin. It is also possible for the poison to be sexually transmitted. Vertical transmission from the mother to the developing fetus has also been reported. Diagnosis is based on clinical findings. Radioimmunoassays of fish toxin are not completely reliable. It is recommended that all fish, caffeine, alcohol, sweets and nuts be avoided as these agents could result in recurrence of his symptoms.

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Cryoglobulinemia: A Most Unusual Cause of Diarrhea

Richard Prudencio, M.D., Manish Mehta, M.D., Manish Tandon, M.D., Saleem Desai, M.D., Julio C. Ayala, M.D.* Internal Medicine, Department of Gastroenterology, Cambridge Health Alliance, Harvard Medical School, Cambridge, MA.

Cryoglobulins are proteins that precipitate in the cold. Cryoglobulinemia is usually asymptomatic, but in some instances it manifests as a disease affecting one or all organs. The prevalence of cryoglobulinemia is reported as approximately 1:100,000. Intestinal involvement in cryoglobulinemia occurs infrequently and can mimic inflammatory bowel disease. We present an atypical case of cryoglobulinemia with gastrointestinal manifestation. A 54 year old female with history of hepatitis C and schizophrenia presented to the emergency department with diarrhea, fever and rash for 1 week. She had completed a course of antibiotics two weeks prior for an upper respiratory infection. She reported 7–10 watery non bloody bowel movements and denied prior similar episodes. She denied nausea or vomiting, sick contacts, recent travel or unusual food intake. Her medications included risperdal, xanam and valium.

On physical exam: T 102.2, BP of 100/67 mm of Hg, RR 22, and O2 sat 92% on room air. She was ill appearing. Her oropharynx was notable diffusely erythematous mucosa with ulcerations, she had no lymphadenopathy. Her lung exam revealed bibasilar crackles. Heart and Abdominal exams were unremarkable. Rectal exam revealed guaiac positive brown stool. Skin exam was consistent with non blanching malar rash on her face as well as scattered, weeping nodules.Significant labs included, WBC 3.2 th/l, hct 33%, MCV 87. Platelet count 192 th/cumm. AST 186 IU/l, ALT 103 IU/l,
that this patient’s acute diarrhea was due to intestinal vasculitis and there were several rounds of plasmapheresis following which her pericarditis and pleuritis subsided and her diarrhea resolved.

We believe this puzzling case illustrates cryoglobulinemia with multiple organ involvement. Acute diarrhea can be a frequent presentation of many common conditions but after ruling out other potential causes we believe that this patient’s acute diarrhea was due to intestinal vasculitis and that may be a manifestation of cryoglobulinemia.

Disseminated Herpes Zoster in an Immunocompetent Host: A Rare Cause of Acute Upper GI Bleed

Manish Mehta, M.D., Kusum Asudani, M.D., Manish Tandon, M.D., Julio C. Ayala, M.D., Saleem Desai, M.D.∗ Department of Gastroenterology, Cambridge Health Alliance, Harvard Medical School, Cambridge, MA.

Herpes zoster is a common systemic disorder with predominant dermal and neurological manifestations. Varicella appears to be the response to a primary infection in a non-immune person whereas herpes zoster results from recrudescence of a latent infection or rarely due to a new infection. We describe a patient with an unusual presentation of pathologically confirmed herpes zoster.

A 35 year old male from El Salvador presented to the emergency department with multiple episodes of melena and hematemesis for 3 hours. He also reported non-radiating epigastric pain which he had been experiencing for 1 day. He reported fever for 3 days in associated with a wide spread vesicular rash. He reported no history of NSAID use, helicobacter pylori infection or peptic ulcer disease.

On admission the patient was afibrile, tachycardic and orthostatic. His examination was remarkable for an extensive vesicular rash involving his entire body but sparing the palmar and plantar regions. Rectal exam showed melena. Significant lab values were WBC 11 thousand/μl, hct 24%, platelet 136 thousand/μm, albumin 2.4 g/dl.

The patient presented with hematemesis and recent melena in the background of active varicella zoster infection. A nasogastric tube was placed which drained coffee-ground material and fresh blood. Urgent esophagogastroduodenoscopy revealed greater than 50 vesicles, many with active bleeding which were treated with local injection of epinephrine. Volcano ulcers, depressed shallow ulcers covered with white exudates and a reddened mucosa were also noted. No peptic ulcers, varices, Mallory-Weiss tears or Dieulafoy’s lesions were observed. The patient was admitted to the ICU, transfused and stabilized. He was started on Acyclovir upon consultation with infectious diseases. Immunohistochemistry, Tzanck smears and serology returned positive for herpes zoster.

This case report is one of the rare instances when herpes zoster presents as acute upper gastrointestinal bleeding in an immunocompetent patient. Most cases of disseminated herpes zoster with gastrointestinal bleed have been described in immunocompromised individuals. Based on our literature review there was only one other case report of herpes zoster causing gastrointestinal bleed in an immunocompetent patient. We conclude that although disseminated herpes zoster is an entity that could be encountered in immunocompetent patients, its association with acute gastrointestinal bleeding is exceedingly rare.

Bronchobiliary Fistula Secondary to Radiofrequency Ablation of Liver Metastases

Thomas Tran, M.D., Howard Hampel, M.D., Waqar Qureshi, M.D., Yasser Shaib, M.D.∗ Dept of Medicine, Baylor College of Medicine, Houston, TX.

Purpose: Bronchobiliary fistula is an extremely rare condition defined as a passageway between the biliary and the bronchial tracts. The pathognomonic sign is the presence of bile in the sputum (biliotysis). Treatment is traditionally surgical repair. Endoscopic interventions have been increasingly used with variable success.

Methods: The patient is a 65 year-old man who was diagnosed with adenocarcinoma of the right colon in January 2004. He underwent right hemicolectomy that showed malignant invasion of the pericolonic adipose tissue, vessels, and lymph nodes. He was started on a course of chemotherapy. A CT and MRI showed enlarging lesions in the liver suggestive of metastatic disease. The patient underwent laparotomy and intra-operative radiofrequency ablation of the liver lesions in September 2004. He was re-admitted for three weeks of a persistent cough. The cough was productive of up to 1 liter a day of thin green-yellow sputum. Coughing increased with lying down, to the point of choking, and improved with sitting upright. The patient slept sitting in a chair and complained of shortness of breath and pleuritic right-sided chest pain. On physical examination, the patient had normal vital signs. He was standing upright coughing incessantly. Breath sounds were decreased on the right lower lung field. The abdomen was noted for a midline surgical scar. There was no tenderness, distension, or hepatosplenomegaly. The rest of the physical examination was unremarkable. Bilirubin level in the sputum was 10.2. Chest X-ray showed a right pleural effusion. Computed tomography scan showed an 11 cm hypodense lesion in the dome of the liver due to the effect of the recent radiofrequency ablation. A hydroxy iminodiacetic acid (HIDA) scan showed tracer activity in the liver, the biliary tree, the intestine and also in the right lung, the trachea, and the oral cavity. An endoscopic retrograde cholangiopancreatogram (ERCP) showed contrast extravasation into the right lung field. The patient was therefore diagnosed with bronchobiliary fistula as a complication of radiofrequency ablation. The patient underwent endoscopic sphincterotomy and common bile duct stent placement. His symptoms significantly. The amount of biliotysis decreased to about 30-40 milliliters a day. The patient was able to sleep in bed again. He was discharged in stable condition.

Conclusions: ERCP bile drainage produces satisfactory results in management of bronchobiliary fistula.

A Case of Acute Colonic Ischemia Due to Routine Diagnostic Colonoscopy

Mitchell A. Mah‘moud, M.D., F.A.C.G.,∗ Mark W. Anderson, M.D., Camilla Proctor, M.D., Sandra Giles, RN, Pamela Johnson, RN, Amy Camp, RN, Kelly Nichols, LPN, William Pittman, M.D. Department of Internal Medicine, Boice-Willis Clinic, Rocky Mount, NC and Department of Medicine, NashHealth Care Systems, Rocky Mount, NC.

Background: Colonic ischemia (CI) is the commonest form of intestinal ischemia and is composed of spectrum of entities namely: reversible colopathy, transient colitis, chronic colitis, stricture, gangrene and fulminant universal colitis. The colon is unusually prone to ischemic injury due to its low blood supply per gram of tissue compared to the other gastrointestinal organs and is associated with cardiovascular surgery, hemodialysis, medications, physical exertion and potentially obstructing lesions of the colon. Furthermore, it may be precipitated by systemic conditions such as hypotension, infections, coagulopathies and vasculitides. We present a case report of CI due to routine diagnostic colonoscopy.

Case Report: Patient is a 54 year old lady without any significant past medical history who was referred for screening colonoscopy. She denied any history suggestive of IBS, coagulopathy or any of the above predisposing conditions of colonic ischemia. After standard bowel prep with oral fleet phosphosoda, she came to the Endoscopy Unit for the screening colonoscopy. Pre-procedure evaluation revealed an healthy lady with normal and stable vital signs as well as cardiopulmonary examination. The diagnostic colonoscopy was subsequently performed after optimal conscious sedation had been established and completed within fifteen to twenty minutes. Throughout the procedure and at the recovery room her vital signs remained stable and normal. Less than 24 hours after the uneventful colonoscopy patient began...
Oxygen desaturation with associated cyanosis after esophagogastroduodenoscopy (EGD) is commonly thought to be related to events such as oversedation, aspiration, and underlying cardiac or pulmonary disorders. We described impairment of oxygenation with cyanosis due to methemoglobinemia in an healthy female after routine EGD.

**Case Report:** Patient is a young healthy adult female except for recent history of gastric bypass surgery for obesity who was referred for endoscopic evaluation of hematemesis. At the Endoscopy Unit, patient denied any history of significant symptoms suggestive of symptomatic anemia or hemolysis. She also denied any history of known drug allergy, significant cardiac or pulmonary disorders. Initial examination revealed stable vital signs including oxygen saturation of 100% on room air and hemoglobin within the normal range. The EGD was thereafter performed after 2% xylocaine spray of the oropharynx and the administration of intravenous conscious sedation. Even though her vital signs and oxygen saturation remained stable most of the time, shortly before the end of the routine procedure patient became progressively cyanotic with oxygen desaturation as low as 60% even with 100% supplemental oxygen by face mask. Arterial blood gas analysis confirmed impaired oxygenation. Based on her clinical status, which raised the suspicion of methemoglobinemia, a blood methemoglobin level was obtained and this confirmed elevated methemoglobin level of about 11%. Patient was treated immediately with intravenous methylene blue with remarkable improvement in her oxygenation. Subsequent work-up revealed normal methemoglobin reductase enzyme activity and absence of M Hemoglobin. She also denied any history of known drug allergy, significant cardiac or pulmonary disorders. Initial examination revealed stable vital signs including oxygen saturation of 100% on room air and hemoglobin within the normal range. The EGD was thereafter performed after 2% xylocaine spray of the oropharynx and the administration of intravenous conscious sedation. Even though her vital signs and oxygen saturation remained stable most of the time, shortly before the end of the routine procedure patient became progressively cyanotic with oxygen desaturation as low as 60% even with 100% supplemental oxygen by face mask. Arterial blood gas analysis confirmed impaired oxygenation. Based on her clinical status, which raised the suspicion of methemoglobinemia, a blood methemoglobin level was obtained and this confirmed elevated methemoglobin level of about 11%. Patient was treated immediately with intravenous methylene blue with remarkable improvement in her oxygenation. Subsequent work-up revealed normal methemoglobin reductase enzyme activity and absence of M Hemoglobin.

We conclude that in this patient,(1) the cyanosis and the oxygen impairment were due to methemoglobinemia (2) this was a case of acquired methemoglobinemia due to lidocaine.

**Conclusion:** Although considered the best tool for diagnosis of CI, colonoscopy may also precipitate this condition as reported in this patient. There may be few possible explanations for the pathogenesis of CI due to diagnostic colonoscopy in this patient.

**OUTCOMES RESEARCH**

**Assessing Variations in Medication Use Related to Ursodiol Therapy in a Large Hawaii Gastroenterology Clinic**

Naoky Tsai, M.D.,* Stephen George, M.S., Jennifer Lee, ARNP, Kathy Soto Alvarez, Pharm.D., Robert V. Jao, M.D., Medicine, Division of Gastroenterology, Saint Francis Medical Center, Honolulu, HI and Health Outcomes, Conexus Health, Tampa, FL.

**Purpose:** Patients with liver disease face many challenges with their treatment regimens. One challenge is drug therapy compliance. Ursodiol can be prescribed for this patient population. Compliance with this therapy can impact the bioavailability differences between the various dosage forms. Compliance and response to therapy analysis have been conducted in patients with hypertension and diabetes. However, naturalistic studies examining response and compliance in patients with liver disease are lacking.

**Methods:** This retrospective assessment was designed to review patient response and compliance with ursodiol in the treatment of liver disease. We examined patient medical records to assess response to ursodiol and surveyed patients to assess compliance. Using the clinic database, patients were identified based on ICD-9 codes associated with targeted liver diseases. The medical records were reviewed for demographics, ursodiol dose, liver function tests, co-morbid conditions, and resolution of symptoms. Afterwards, the patients were administered a questionnaire by a trained nurse. The questionnaire was designed to assess the patients’ perception, knowledge, and understanding of compliance. Statistical tests compared patient perceptions and knowledge of compliance with ursodiol dose, length of diagnosis, changes in liver function tests, and resolution of symptoms.

**Results:** A total of 77 patients were identified from the claims report. The patient population was comprised of 42 females; the largest ethnicity represented were Asian (41). The two diseases with the highest frequency of occurrence were hepatitis C virus (34) and non-alcoholic fatty liver disease (28). The average daily dose for patients receiving ursodiol tablets and capsules were 833 mg and 1057 mg, respectively. The mean changes in liver function tests from baseline for ursodiol capsules were 28% for both ALT and AST, while the ursodiol tablets were ALT 24% and AST 25%. The difference between the two dosage forms had a statistically significant difference (p<0.05). Patients receiving ursodiol tablets reported less symptoms than did patients receiving ursodiol capsules.

The patient compliance questionnaire is research in progress and the results will be correlated to the medical record review.

**Conclusions:** Overall, the complete study is research in progress and the final results will be presented.

**Milestones in Research in Gastroenterology by Canadians**

Ivan T. Beck, M.D. Ph.D. MACP* Medicine, Gastroenterology, Queen’s University, Kingston, ON, Canada.

**Purpose:** To review historical and recent Canadian contributions to gastrointestinal research.

**Methods:** Investigate history and archives on research in gastroenterology by Canadians

**Results:** For modern contributions the poster provides the names of awardees of the Canadian Association of Gastroenterology (CAG) and the Canadian Association for the Study of the Liver (CASL). These include the “Research Excellence Lecturers,” “Young Investigator Lecturers,” “Visiting Research Professors,” “Ivan T. Beck Lecturers,” and “Education Excellence Lecturers” for the CAG, and the “Gold Medalist Lecturers” and the “Andrew Sass-Kortas Lecturers” for CASL. Historical sections depict with pictures and text the life and work of past investigators. Beginning with the first Canadian research subject, Alexis St. Martin, a courer de bois who was treated by Dr William Beaumont for a gunshot wound, and as a result developed a gastric fistula. They established in the mid 19th century that gastric juice is acid and digests food. The poster portrays Dr. Boris Petrovitch Babkin, who is considered the father of the concept of gut-brain interaction. Hans Selye found that stress causes gastric ulcers. Frederick G. Banting and Charles H. Best extracted insulin from dog pancreas. Dr. John C. Brown described Motilin and Gastric Inhibitory Peptide. Jean A. Morisset provided new aspects on pancreatic islet cell function. Charles Philippe Leblond demonstrated that the crypt cell is the stem cell of the gut. Dr. Leslie S. Valberg worked on iron metabolism and hemochromatosis. Dr. Edwin E. Daniel made contributions to gastrointestinal motility; Dr. Aron M. Rappaport, established the pathologic concept of three zones of the hepatic acinus. Dr. Carl A. Goresky’s understanding of the metabolism of copper and the genetic aspects of Wilson’s disease.
Conclusions: Canadians made major present and historical contributions to the science of digestive organs.

Captions of the History of the Canadian Association of Gastroenterology
Ivan T. Beck, M.D., Ph.D., MACP* Medicine, Gastroenterology, Queen's University, Kingston, ON, Canada.

Purpose: Objective is to review the history of the Canadian Association of Gastroenterology (CAG) from its inception in 1962 until 2005, when it hosted the World Congress in Montreal Quebec.

Methods: Historical investigation of archives.

Results: The poster presents the original signatures and names of the founding members. Dr. Richard D McKenna was the initiator and first President. A lecture series has been established in his name. The list of speakers is provided. Amongst these are the most well respected scientists from Canada, USA, England and France. A section shows the pictures of the Presidents from 1962 to 2004. Other segments portray the growth of membership, the history of the Canadian Journal of Gastroenterology and the sites of the meetings. The section on education describes the well-recognized “Residents in Training” course. The panel on membership education describes the role of the CAG in the “Maintenance of Certification,” required to keep one’s specialty current. A section deals with public education by the Canadian Digestive Health Foundation. Research support is the most important program of the CAG. The Association has been successful in obtaining large amounts of research funds. The poster describes the functions of the Research Committee, which judges applications for research funds and annually recommends to the Board of Directors the investigators who ranked highest to obtain grant support. It also proposes the names for the different research awards, amongst others the “Research Excellence Lecturer” and the “Young Investigator Lecturer.” Looking into the future, the poster describes the strategic plans of 1991, the objectives of which have now been achieved and the new plan for 2004 to 2009.

Conclusions: The Canadian Association of Gastroenterology has achieved its goal to become a major factor in supporting research and education in gastroenterology in Canada and internationally.

Gum Chewing Accelerates Recovery of Bowel Function after Intestinal Resection: Multi-Institutional Prospective Randomized Trial
Robert Garvin, M.D., James T. McCormick, M.D., Thomas E. Read, M.D., Pavlos K. Papasavas, M.D., Philip F. Caushaj, M.D.* Department of Surgery, The Western Pennsylvania Hospital, Clinical Campus Temple University, Pittsburgh, PA.

Purpose: The purpose of this study is to determine whether chewing gum can accelerate recovery of bowel function and shorten hospital stay after intestinal resection.

Methods: All patients undergoing elective bowel resection on the colorectal surgery service at three tertiary care centers were evaluated. Patients were randomized to a control group (no gum) or study group (gum). Data was collected prospectively and included return of bowel function (flatus and defecation), initiation of diet, and length of hospital stay. Statistical analysis was performed using students T-test, and significance determined at p < 0.05.

Results: 62 patients have been enrolled and complete data sets are available for 57 patients; 25 in the control group and 32 in the gum group. Although passage of flatus was similar between the two groups, the first defecation was significantly earlier in the in the gum-chewing group than control group. There was a strong trend towards shorter hospital stay in the gum-chewing group.

Conclusions: From interim analysis we can conclude that gum chewing accelerates the return of defecation bowel function after elective bowel resection and will likely result in shorter length of hospital stay. Gum chewing is an effective, inexpensive, and safe therapy for shortening the duration of postoperative ileus.

Sargramostim Improves Quality of Life as Measured by the Inflammatory Bowel Disease Questionnaire in Patients with Moderate to Severe Crohn’s Disease
Suzanne Laplante, BPharm, Brian Dieckgraefe, M.D., Joshua Korzenik, M.D.* Corporate Outcomes Research, Schering AG, Berlin, Germany; Division of Gastroenterology, Washington University School of Medicine, Saint Louis, MO and Inflammatory Bowel Disease Center, Harvard Medical School, Boston, MA.

Purpose: Patient reported outcomes (PROs) and especially quality of life (QOL) are important tools used to evaluate the benefit of therapeutic interventions in chronic diseases such as Crohn’s disease (CD). The Inflammatory Bowel Disease Questionnaire (IBDQ) is the standard instrument for assessment of health-related QOL in patients with inflammatory bowel diseases. The New Opportunities to Verify Evolving Logic in Crohn’s disease (N.O.V.E.L.) clinical trials program uses QOL to assess sargramostim (GM-CSF) as a potential new therapy for CD.

Methods: A placebo-controlled phase II study (N.O.V.E.L. 1) was conducted to assess the efficacy and safety of sargramostim 6 µg/kg/day for 8 weeks in patients (N = 124) with moderate to severe CD. The IBDQ was completed at baseline; Days 15, 29, 43, and 57 of treatment; and 30 days after treatment. Differences between treatment groups were analyzed by the Wilcoxon Rank Sum Test.

Results: On follow-up Day 30, patients who received sargramostim had a 20% improvement in their total IBDQ score from baseline, as compared to a 7% improvement in the placebo group (P = 0.0145). Patients who received sargramostim had improvements in Bowel and Systemic subscores ranging from 23% to 33% at Day 29 and thereafter, as compared to 4% to 18% in the placebo group (P = 0.0009 to 0.0438). The Social subscore was improved by 14% on follow-up Day 30 for patients who received sargramostim, as compared to 4% in the placebo group (P = 0.0383). No statistically significant difference was observed for the Emotional subscore. There were moderate to large improvements in QOL as indicated by the effect size that ranged between 0.45 and 1.21.

Conclusions: Treatment with sargramostim for 56 days was associated with improved and maintained QOL in patients with CD as measured by the IBDQ. Clinically meaningful improvements of the IBDQ scores were seen as early as Day 29 of treatment including significant improvements in the Social subscore. Sargramostim is a novel agent that is being developed for the treatment of CD and appears to improve the QOL of patients with CD, and important outcome to patients, clinicians, and healthcare providers.

Quality of Life Measured by Short Form 36 Is Improved by a 56-Day Treatment with Sargramostin in Patients with Moderate to Severe Crohn’s Disease
Suzanne Laplante, BPharm, Dieckgraefe Brian, M.D.* Korzenik Joshua, M.D. Corporate Outcomes Research, Schering AG, Berlin, Germany; Division of Gastroenterology, Washington University School of Medicine, Saint-Louis, MO and Inflammatory Bowel Disease Center, Harvard Medical School, Boston, MA.

Purpose: The quality of life (QOL) of patients with Crohn’s disease (CD) is significantly lower than that of a healthy population. New medications developed for CD should demonstrate improvements in patient reported outcomes (PROs) such as QOL.

Methods: As a part of the New Opportunities to Verify Evolving Logic in Crohn’s disease (N.O.V.E.L.) clinical trials program, a placebo-controlled
phase II study evaluated the efficacy and safety of sargramostim (GM-CSF) 6 µg/kg/day for 8 weeks in patients (N = 124) with moderate to severe CD. Short Form 36 (SF-36) was completed at baseline; Days 15, 29, 43, and 57 of treatment; and 30 days after treatment. Differences between treatment groups were analyzed by the Wilcoxon Rank Sum Test.

Results: There was a 30–38% improvement from baseline on Day 15 and thereafter in the General Health subscore of CD patients treated with sargramostim, as compared to a 5–14% improvement in the placebo group (P = 0.0032 to 0.0448). Patients who received sargramostim had a 68–70% improvement in Vitality subscore on Day 57 and on follow-up Day 30, compared to 22–23% in the placebo group (P = 0.0307 and 0.0252, respectively). The Social score was improved by 25% on follow-up Day 30 in patients who received sargramostim compared to 5% in the placebo group (P = 0.0301). Treatment with sargramostim improved Bodily pain by 39–45% on Day 57 and on follow-up Day 30, as compared to 14–25% for the placebo group (P = 0.0481 and 0.0015). The Role Physical subscore was improved by 125% on Day 43 with sargramostim as compared to 39% with the placebo (P = 0.0285). There were no statistically significant differences from baseline in the Physical Function, Role Emotional, and Mental Health subscores in patients receiving sargramostim or placebo. There were moderate to large improvements in QOL as indicated by the effect size that ranged from 0.49 to 1.03.

Conclusions: Significant improvements in the General Health score were observed in patients with CD as early as Day 15 of the sargramostim treatment period. Vitality and Social subscores, as well as other subscores of the SF-36, were improved at different times during and/or after treatment with sargramostim. Sargramostim appears to significantly improve the QOL in patients with CD, which may allow them to live a more active life.

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Preference and Satisfaction with Treatment for Constipation: Development and Validation of New Instruments
K. Fox, V. Barghout, I. Bottoli, M. Chancellorn* Strategic Healthcare Solutions, Monkton, MD; Novartis, E. Hanover, NJ and Univ. of Pittsburgh, PA.

Purpose: Constipation is a highly prevalent disorder affecting up to 28% of North Americans. Satisfaction with therapy has not been fully evaluated. This study was designed to develop and validate new self-administered questionnaires on preference and satisfaction with treatment for constipation.

Methods: Two questionnaires were developed by a literature review and assessment of existing treatment satisfaction instruments across multiple diseases. The first questionnaire is a single binary question on patient preference for constipation treatment. The second questionnaire is 8 items assessing satisfaction with treatment for: 1) amount of warning time before bowel movement 2) lack of liquid stools 3) relief of abdominal bloating 4) medication taste 5) medication administration convenience 6) ease of use 7) willingness to continue using medication and 8) recommend medication to others with constipation. Content validity was assessed through in-depth patient interviews. Construct validity was determined through factor analysis and Spearman’s rank correlation analysis. Constipation patients were recruited from physician practices in Pittsburgh, PA according to ROME II criteria.

Results: Initial patient testing among 13 female patients demonstrated that the questionnaires were easy to very easy to complete and understand (score = 4.6 on 6-point scale). Content validation with 20 patients demonstrated good clarity and comprehensiveness of the questionnaires. 90% of patients indicated that the preference question was easy to understand. 40% found the lack of liquid stools question to be confusing because they were unfamiliar with the term even though “watery or loose stools” was added. Willingness to continue using the medication question was noted to be lengthy because the medication features are listed. However, patients indicated that they would not consider these features unless they were stated in the question. Construct validation was tested among 40 patients and demonstrated good internal consistency (Cronbach alpha = 0.81) and 3 domains for the satisfaction questionnaire (1 = bowel habits 2 = willingness to continue using and recommend to others 3 = medication taste, convenience and ease of use).

Conclusions: The preference and satisfaction questionnaires have strong psychometric validity. Patient preference and satisfaction with constipation treatment now can be captured in clinical practice and research studies through the use of these validated instruments.

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Development and Validation of a Questionnaire To Evaluate Severity of Symptoms in Patients with IBS-C and IBS-A in Canada: The LOGIC Study
P. Pare, M.D.*, S. Lam, M.D., R. Balshaw, Ph.D., I. Morin, Ph.D., S. Khosraveh, M.A., M. Barbeau, M.A., S. Kelly, Ph.D., C. R. McBurney, Pharm.D. Centre Hospitalier Affilie Universitaire de Quebec, QC, Canada; Havos Clinic, Calgary, AB, Canada; Syreon Corporation, Vancouver, BC, Canada; Novartis Pharmaceuticals Inc (Canada), Dorval, QC, Canada and Novartis Pharma AG, Basel, Switzerland.

Purpose: LOGIC (Longitudinal Outcomes study of Gastrointestinal symptoms in Canada) is an ongoing pharmacoepidemiologic study of the Tx pat-
Objective: To develop and validate a self-report questionnaire measuring severity of IBS Sx in pts with IBS-C and IBS-A.

Methods: IBS pts Sx questionnaire has 15-items that measure frequency, intensity, and distress/bother associated with the following IBS Sx: constipation, gas, abdominal pain/discomfort, bloating, and diarrhea. Measured on a 0 to 5-point scale. Principal component analysis (PCA) was performed and correlations between the baseline severity scores and the baseline IBS-QOL overall scores, EQ-5D tariff scores, and EQ-5D VAS were calculated. Mean severity scores were compared between 3 Tx groups: usual care pts (various non-tegaserod Tx), new tegaserod users and previous tegaserod users (used tegaserod in the preceding 6 months).

Results: 1557 subjects completed the IBS severity of Sx questionnaire at baseline. PCA revealed that the 1st, 2nd, and 3rd components provide a good summary of the data, accounting for 37%, 20% and 13% of the total variability, respectively. Other components contribute <10% each. The first component approximates a simple average of Frequency, Intensity, and Distress/Bother scores for all Sx except diarrhea. The resulting Severity Score (0–60 sum) significantly correlates with the IBS-QOL total score (r = 0.549, p < 0.001), the EQ-5D tariff score (r = 0.378, p < 0.001) and the EQ-5D VAS (r = 0.361, p < 0.001). Mean severity score was 37.7 (SD = 10.13) for usual care pts, 42.4 (SD = 10.14) for new tegaserod users, and 41.8 (SD = 9.07) for previous tegaserod users. These findings have been validated by data from ILOS, a similar study conducted in the US.

Conclusions: IBS Severity questionnaire appears to efficiently and comprehensively measure severity of IBS Sx in pts with IBS-C and IBS-A. The severity score appears to be an effective measure of overall IBS Sx severity, although more extensive testing is appropriate.

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Achieving Complete Remission in Patients with Erosive Gastroesophageal Reflux Disease (GERD): Pantoprazole Is Comparable with Esomeprazole

Karna Dev Bardhan, Prof,* Alexander Achim, M.D., Thomas Riddermann, M.D., Peter Sander, Ph.D., Bernd Pfaffenberger, Ph.D. Department of Medicine, District General Hospital, Rotherham, United Kingdom; Private Practice, Iselohm, Germany; Private Practice, Marl, Germany and Department of Gastroenterology, ALTANA Pharma AG, Konstanz, Germany.

Purpose: GERD symptoms can persist despite healing and vice versa. We have therefore redefined complete remission as both endoscopically confirmed healing and symptom relief assessed by the validated ReQuestTM.

Methods: 581 patients with erosive GERD (LA grade A-D) were randomly allocated to once daily treatment with either 40 mg of pantoprazole (PANTO) (n = 288) or esomeprazole (ESO) (n = 293). Treatment was for a maximum of 12 weeks unless complete remission was achieved earlier at 4 or 8 weeks. Esophageal healing was defined as disappearance of all erosive changes. Symptom relief was achieved if the score of the subscale ReQuestTM GI fell below the predefined GERD symptom threshold of 1.725. Complete remission at 12 weeks was the primary variable and at 4 and 8 weeks the secondary ones. The non-inferiority of PANTO vs. ESO was determined by the one-sided 97.5%-Confidence Interval (CI) (Blackwelder method) assuming a non-inferiority margin of -15%. To allow comparison with published reports, endoscopically confirmed healing and symptom relief were also analyzed separately. The efficacy of PANTO and ESO was compared by the two-sided 95% CIs according to the standard normal approximation (non-inferiority margin of -15%).

Results: Complete remission per protocol (PP) at 12 weeks was 92.6% for PANTO and 90.2% for ESO (97.5% CI for the difference above -15%; [-2.9%; +∞]).

Conclusions: Multiple music choices offered through Apple I-Pod technology reduced patient anxiety level scores from baseline prior to undergoing elective endoscopy. The magnitude of the change achieved statistical significance. Patients were generally supportive of the introduction of music in the ambulatory surgery center. I-Pod hard drive storage allowed a wide range of musical selections to match the patients’ pre-existing bias toward acceptable music. Music may improve patients’ acceptance of endoscopy and improve enrollment into screening programs. The clinical utility of music in reducing pre-endoscopy anxiety requirements should be addressed with randomized control trials.

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Major GI Events among Cox-2 Inhibitor, NSAID, and Aspirin Users

C. Daniel Mullins, Ph.D.,* Bac V. Tran, Ph.D., Fadia T. Shaya, Ph.D., M.P.H., John F. Naradezay, Kimberly B. Howard, Pharm.D., M.S.
Pharmaceutical Health Services Research, University of Maryland School of Pharmacy, Baltimore, MD and US Outcomes Research, Pfizer, Inc., New York, NY.

Purpose: This retrospective cohort analysis examined major gastrointestinal (GI) event rates among osteoarthritis (OA) and rheumatoid arthritis (RA) patients prescribed cyclooxygenase-2 inhibitors (COXIBs) or traditional nonsteroidal anti-inflammatory drugs (NSAIDs) alone or with concomitant aspirin (ASA).

Methods: This analysis utilized a retrospective cohort from the GE Logistician database (Centricity EMR), an electronic medical records database of over 3 million patients seen by 5,000 physicians across 27 states. Inclusion criteria: NSAID or COXIB prescribed in 1999–2002, age 65 or older on index date (date of first COXIB or NSAID), diagnosis of OA or RA, at least one year of follow-up without drug switch, or a major GI event before drug switch or end of follow-up. Major GI events were defined as GI hemorrhage including melena: ICD-9 codes 578, 578.0, 578.1, and 578.9. The multivariate logistic analysis examined how the rates of major GI events within a year of the index date differed across the COXIB alone, NSAID alone, COXIB + ASA, and NSAID + ASA groups. We controlled for major GI events in the year prior to the index date, gender, age above 75, and concomitant drug use.

Results: Of the 24,310 patients in our study, 8,574 used COXIB alone (54 major GI events in the year prior and 88 in the year following the index date), 7,207 used NSAID alone (49 and 79), 4,597 used COXIB + ASA (51 and 73), and 3,932 used NSAID + ASA (33 and 63). Compared to patients starting on COXIB alone, those on NSAID + ASA had a statistically significantly higher adjusted rate of major GI events (OR = 1.403, p = 0.05, 95% CI: 1.005–1.906). Those on NSAID alone and those on COXIB + ASA did not have a statistically significantly higher adjusted rate of major GI events (OR = 1.157, p = 0.35, 95% CI: 0.849–1.577; and OR = 1.249, p = 0.18, 95% CI: 0.906–1.722, respectively).

Conclusions: Major GI event rates were numerically highest in NSAID + ASA users, followed by those on COXIB + ASA, NSAID alone, and COXIB alone (lowest). However, only the NSAID + ASA group had a statistically significantly higher rate than the COXIB alone reference group. The addition of ASA did not significantly increase major GI events among Cox-2 inhibitor users. Our results compare to those of Rahme (2004) who found that the lowest rate of GI hospitalizations is associated with COXIB alone, while the highest rate is associated with NSAID + ASA.

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ERRP: A Potential Anti-Angiogenic Agent
Bakesh K. Parikh, M.D., Arun K. Rishi, Ph.D., Anil Weli, Ph.D., Sudha Reddy, M.D., Adhip PN: Majumdar; Ph.D.* Gastroenterology, Wayne State University School of Medicine, Detroit, MI; Veterans Affairs Medical Center, Detroit, MI and Karmanos Cancer Institute, Detroit, MI.

Purpose: Activation of EGFR (epidermal growth factor) and its family member(s) stimulates many processes of carcinogenesis, including angiogenesis. Thus interference with EGFR activation represents a promising strategy for the development of novel and selective anticancer therapies. ERRP (EGFR Related Protein) is a negative regulator of EGFR. The present study was undertaken to determine whether ERRP would affect angiogenesis and the regulation this process.

Methods: Colon cancer and rat endothelial cells were maintained in enriched medium. Cell growth was assessed by MTT assay. ERRP dependent apoptosis was determined using the Cell Death Detection ELISA kit. ERRP-dependent regulation of genes in colon cancer cells was investigated utilizing Atlas human 1.2 array membranes (Clontech). Secretion of basic fibroblast growth factor (bFGF) and vascular endothelial growth factor (VEGF) following treatments with ERRP was investigated by utilizing immunoassay kits for respective growth factors. Tubule formation by aortic endothelial cells, a measure of angiogenesis, was carried out utilizing the In-vitro Angiogenesis Assay Kit. Migration of cells through the matrigel in the absence or presence of ERRP was studied by utilizing the cell invasion assay kit. The invasive cells were stained, photographed and counted in random fields.

Results: ERRP inhibited the growth of rat endothelial cells in a dose-dependent manner resulting in a 65% reduction with the highest dose of ERRP (10 µg/ml) after 48 hrs. In the absence of ERRP (controls), tubule formation was completed by 6 hrs and remained stable for the next 3 hrs. In the presence of ERRP, tubule formation was disrupted at 6 hrs, and after 9 hrs there was a complete disintegration of the tubules. In addition 30–40% of colon cancer cells failed to pass through the matrigel in the presence of ERRP. Treatment also resulted in attenuated levels of proangiogenic factors such as bFGF, VEGF and TGF-α.

ERRP attenuated expression of several genes regulating the processes of proliferation, angiogenesis and invasion, while inducing expression of apoptosis promoting molecules. ERRP inhibited expression of proliferation regulatory genes such as Stat3, FAK and MEK-2.

Conclusions: ERRP inhibits pathways of angiogenesis and proliferation by specifically attenuating multiple mediators of EGFR signaling pathway and by causing diminished secretion of proangiogenic growth factors.
Utilization Patterns of Gastroprotective Agents among NSAID Treated Subjects with Varying Gastrointestinal and Cardiovascular Risk Profiles in a Health Benefits Population


Purpose: The purpose of this study was to gain an understanding of the patterns of Gastroprotective Agent (GPA) utilization among users of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) with varying Gastrointestinal (GI) and Cardiovascular (CV) risk profiles.

Methods: A cross-sectional analysis was completed using the claims of a large health benefits company. A total of 24-months of claims data were analyzed for all eligible subjects. Subjects included those 18 years of age and older, with a prescription claim (i.e. the index claim) for an NSAID between 1 April 2003 and 30 June 2003, who maintained continuous plan enrollment during the study period. Subjects were also required to maintain chronic NSAID utilization, defined as at least 90 days supply of the index medication during the 12-month post-index period. Study subjects were stratified into the following three cohorts based upon their index medication: (1) Cox-II selective inhibitors, (2) non-selective NSAIDs (excluding naproxen), and (3) naproxen. Subjects were further stratified based upon the presence or absence of concomitant GPA utilization during the 12-month post-index period. Finally, subjects were assessed for the presence or absence of risk factors associated with CV and/or GI events during the 12-month pre-index period.

Results: The study population consisted of 27,827 subjects, with a mean age of 61.4 (± 13.5) years. Of the population, 13,408 subjects (48.2%) were treated with non-selective NSAIDs, 5397 (19.4%) with naproxen, and 9022 (32.4%) with Cox-II inhibitors. The proportion of GPA utilization was significantly different (P < 0.0001) among the non-selective NSAID, naproxen, and Cox-II cohorts, with 22.2%, 19.2%, and 29.2%, respectively. Additionally, the proportion of subjects with at least one risk factor for a GI event was significantly different (P < 0.0001) among the cohorts, with 84.6% of non-selective NSAIDs, 84.4% of naproxen, and 48.2% of Cox-IIs. Finally, no significant difference (P = 0.1842) was found in the proportion of subjects with CV risk factors among study cohorts.

Conclusions: The distribution of subjects with at least one GI risk factor was found to be significantly higher in the non-selective NSAID and naproxen cohorts; however, GPA utilization was significantly lower in these cohorts when compared to users of Cox-II inhibitors.

New-Onset Diabetes Confers Increased Risk for Pancreatic Cancer in a Large Cohort of US Veterans

Samir Gupta, M.D., Dan Berenthal, M.P.H., Hui Shen, M.S., Eric Vittinghoff, Ph.D., Kenneth McQuaid, M.D.* GI Division, VA Medical Center, Univ. of California, San Francisco, CA; Health Services Research Enhancement Award Program, VA Medical Center, San Francisco, CA and Epidemiology and Biostatistics, Univ. of California, San Francisco, CA.

Purpose: Many individuals with pancreatic cancer (PCA) have diabetes of recent onset, but the exact incidence of PCA following new-onset diabetes mellitus (DM) and risk factors associated with PCA are unknown.

Objective:
1. To determine the incidence of PCA within 3 years of new-onset DM.
2. To evaluate risk factors associated with PCA in new-onset DM.


Exposure: New-onset diabetic subjects defined by ≥ 2 ICD9 codes for DM within a 12 month period who have at least 2 years diabetes-free enrollment prior to diabetes diagnosis and 6 years follow up.

Primary outcome: New pancreatic cancer by ICD9 coding.

Measurements: Age, sex, race, ICD9 coding for common gastrointestinal complaints.

Results: From a cohort of 1,579,043 Veterans, 36,643 new diabetics were identified with 179,108 person-years of follow up. Among new diabetics, 160 PCAs were recorded, yielding an age-adjusted rate of 89.3/100,000 person years and a RR 2.61 (95% CI, 2.37–2.87) vs. non-diabetics over 6 years follow up. PCA incidence was highest within the first two years after DM diagnosis: RR 5.17 (95% CI, 2.40–6.37) for year 0–1 and RR 2.97 (95% CI, 2.27–3.90) for year 1–2. A significant decreasing trend across years post-DM diagnosis was observed (p < .0001).

Advancing age, and coding for bowel habits change, constipation, diarrhea, dyspepsia, dysphagia, epigastric pain, gas, and malnutrition were identified as risk factors for PCA among new diabetics.

Conclusions: In a large cohort of US Veterans, new diabetes was associated with increased risk of PCA over 6 yrs of follow up. Risk was particularly elevated over the first 2 yrs of follow-up after DM diagnosis, increasing with advanced age. GI complaints in new diabetics were significantly associated with subsequent PCA.

Future research should elucidate risk factors that identify new diabetics at high risk for pancreatic cancer, and consider the benefit of targeted surveillance.

Cancer Risk 0–12mo After New Diabetics vs. Non-Diabetics by Age

<table>
<thead>
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<th>Age</th>
<th>RR</th>
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<tr>
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<td>2.81–13.81</td>
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<td>55–59</td>
<td>10.15</td>
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Incidental Luminal GI Findings on 18FDG PET-CT

Pranav D. Patel, M.D., Jonathan M. Koff, M.D.,* Jaime L. Montilla, M.D., Inku Hong, M.D. Department of Internal Medicine, Walter Reed Army Medical Center; Gastroenterology Service and Department of Radiology, Walter Reed Army Medical Center, Washington, DC.

Purpose: PET-CT combines physiologic imaging based on uptake of 18FDG by metabolically active cells with anatomic localization. There is limited information on the incidence and nature of gastrointestinal (GI) luminal findings on PET-CT done for non-GI indications. We evaluate these findings.

Methods: PET-CT scans performed at a tertiary care center for any indication were reviewed retrospectively. Studies were performed between 26Feb2003 and 11Dec2003. Patients were excluded from analysis if they were <18 years old. An incidental luminal GI finding was defined as abnormal uptake in the GI tract in patients without a primary GI luminal indication (e.g. colorectal cancer, esophageal cancer, gastric cancer, small bowel cancer). GI endoscopy data base was searched for corresponding endoscopy within 6 months of the PET-CT scan. Data analyzed included demographics, indications for PET-CT, GI finding on PET-CT, endoscopic findings, and histopathologic diagnosis.

Results: A total of 587 PET-CT scans on 481 patients were reviewed. Of these, 537 scans (443 patients) were for non-GI indications. There were 18 (4.06%) patients with incidental, abnormal 18FDG uptake in the luminal GI tract. Mean age was 55 and there were 5 (27.8%) females. The indications for the PET-CT scans were: lymphoma (6), lung cancer/pulmonary nodule (5),
leukemia (1), cervical cancer (1), melanoma (1), liver lesions (1), gallbladder cancer (1), and cancer of unknown primary (2). In the 18 patients there were 21 different sites of uptake as follows: colon (12), esophagus (5), small bowel (2), stomach (1) and rectum (1). 11/18 patients underwent endoscopy. 5/11 (45.5%) had endoscopic findings in the distribution of the PET-CT, 4/11 (36.4%) had other findings that were not seen on PET-CT, and 2/11 (18.2%) had normal exams. Endoscopic findings and tissue sampling that correlated with PET-CT included: colon cancer (1), CMV colitis/mass (1), large cell lymphoma (1), esophageal adenocarcinoma (1), pancreatic adenocarcinoma (submucosal esophageal mass) (1).

Conclusions: In this ongoing study, we found that incidental GI luminal findings on PET-CT are uncommon, but when found, occur most commonly in the colon. Due to the relative infrequency of incidental GI luminal findings and the likelihood of endoscopic correlation, we believe that PET-CT findings in the luminal GI tract should be evaluated with endoscopy.

Purpose: Presently, patients referred for colonoscopy at our institution are required to have an initial encounter (closed access). Due to the clinic backlog for appointments, this initial visit may take up to three months. There is an additional wait time from the clinic visit to the colonoscopy. The concern was that the initial physician clinic visit might reveal a finding that would significantly impact the procedure preparation or performance.

The aim of this study was to determine if the wait time, from consultation request to colonoscopy, could be reduced by eliminating the initial clinic visit. It was postulated that instead of a formal clinic visit, a medical provider could review the request for appropriateness, speak with the patient over the phone, and then schedule the colonoscopy.

Methods: The records of all patients having colonoscopy for the calendar year, 2004, were reviewed. Inpatient colonoscopies, repeat colonoscopies, and inflammatory bowel patients were excluded. This left 786 patients who had consultations prior to their colonoscopy.

The goal was to determine if any recommendations, other than a colonoscopy, were made during the initial consultation, and if such changes required physician input. The primary endpoint was the number of GI clinic patients whose treatment plan was simply "colonoscopy". Secondary endpoints were the average wait time for a GI consultation and for a colonoscopy.

Results: 529 of the 786 (67%) consultations did not result in any interventions during the clinic visit other than recommending colonoscopy. 197 (25%) patients had some type of intervention, other studies, labs, or adjustment of medications. The remaining 60 (8%) patients had their GERD addressed, in addition to ordering a colonoscopy during the consultation.

The average wait from the request of the consultation to the clinic visit was 107 days. The time from clinic to colonoscopy was 109 days. Therefore, the total wait time from initial request to the actual colonoscopy was approximately 7 months.

Conclusions: Our closed access system appears to be inefficient since more than 2/3 of the patients did not benefit from the mandatory consultation prior to scheduling the colonoscopy. The average wait time of 7 months for a colonoscopy is worrisome, especially for patients who subsequently had significant pathology diagnosed by their colonoscopies. Patients could be better served by having the consultation request reviewed by a medical provider and referred directly to colonoscopy when appropriate. This would immediately reduce wait time by half.
Conclusions: The roles of the BECs are not clear to gastroenterologists. Although our results ought to be verified by other studies it is proposed that this can provide a framework for developing a gastroenterology specific biomedical ethics curriculum beside the regular activities of our institutions.

An Economic Comparison of Biological Therapies for Crohn’s Disease

Russell D. Cohen, M.D.* Medicine, The University of Chicago, Chicago, IL.

Purpose: Create a cost–comparison 2-year continuous therapy model for current biological therapies available for use in Crohn’s disease

Methods: Comparisons between infliximab iv 5 mg/kg (Ifx) dosed 0.2,6, then q8 weeks; adalimumab sc high-dose 160 mg load, 80 mg qweek (AdLow); adalimumab sc high-dose 160 mg load, 80 mg qweek (AdHigh); natalizumab iv 300 mg q4weeks (Nat); and Gmcsf 300 mg sc qd (8-week cycles separated by 4-week drug-free periods) were made. Labs: CBC3, CPNL q6 months, except Gmcsf (q2 weeks x2 then q month), PPD test for anti-TNF agents. Administration costs at Medicare reimbursement rates for infusions (Ifx, Nat) or for nurse teaching for injections (others; first 3 doses only). Dose escalation: Ifx: increase 2.71% after 1st dose, 1.15% after first year (Cohen et al. Am J Gastroenterol 2004;99(10):S228); AdLow: 37% increase to qweek injections within 6 months (Sandborn et al. Gastroenterology 2005;128(4):A111–2); none for others. Indirect costs – 1 hour for blood tests and PPD (tests and travel). Ifx: 2 hour infusion, 2 hours prep/travel; Nat: 1 hour infusion, 1 hour observation, 2 hours prep/travel; others: 1 hour teaching for first 3 injections. Value of indirect costs calculated from US Department of Labor Bureau – Labor Statistics November 2003 National Occupation Employment and Wage Estimates. Drug costs as reported in AWP-June 2005. Therapy calculated on a continuous 2-year time frame. Treatment regimens as published in peer-reviewed manuscript form; abstract from national meetings used if no available published manuscript.

Results: See table. 1st and 2nd year overall costs lowest for Ifx and AdLow; highest for Gmcsf. Administration costs lower for drugs given as injections than as infusions. 2nd year costs decrease due to no additional need for loading doses, rescreening for TB, or self-injection teaching. Indirect costs lower for injections than infusions, especially after initial teaching period.

Conclusions: 2-year projected costs are lowest for infliximab and low-dose adalimumab therapy for Crohn’s disease. This model needs to be refined with prospective long-term efficacy studies and their associated impact upon healthcare utilization and indirect costs.

Diagnostic Yield of ASGE Appropriateness Criteria of Upper GI Endoscopy. An Italian Multicenter Study at 44 Open-Access Digestive Endoscopy Services

Gianluca Bersani, M.D., Marcello Anti, M.D., Maria Antonietta Bianco, M.D., Luigi Buri, M.D.,* Emilio Di Giulio, M.D., Giovanni Di Matteo, M.D., Leonardo Ficano, M.D., Pietro Loriga, M.D., Sergio Morini, M.D., Vincenzo Pietropaolo, M.D. Digestive Endoscopy, Osp Malatesta N., Cesena, Italy; Osp. Belcolle, Viterbo, Italy; Osp Maresca, Torre Del Greco, Italy; Osp Cattinara, Trieste, Italy; Università La Sapienza, Roma, Italy; Osp De Bellis, Bari, Italy; Università Giaccone, Palermo, Italy; Osp SS Trinità, Cagliari; Osp Nuovo Regina Margherita, Roma and Pol. Umberto I, Roma.

Purpose: The aim of this study, which involved 44 Italian endoscopy services, uniformly distributed at national level, was to assess the occurrence and the possible typology of factors affecting the appropriateness of upper GI endoscopy (EGD)

Methods: 44 open-access endoscopy services participated in this survey which involved 6270 subjects. EGD was classified as appropriate or inappropriate according to American Society of Gastrointestinal Endoscopy (ASGE) criteria. Endoscopy findings were considered relevant if they in some way influenced the patient’s subsequent treatment (i.e. neoplasms, ulcers, varices, erosive esophagitis). For each center, the rate of appropriate EGDs was matched with the different clinical data (patients average age, prevalence of relevant diseases,% of urgent EGDs,% of hospitalized patients,% of patients referred by general practitioner [GP],% of follow-up EGDs) by utilizing either a simple or a stepwise multiple regression model

Results: The appropriateness rate varied from center to center (mean value 77%; range 51.5%-96%). A low correlation was documented between appropriateness and the individual clinical items considered, as shown in the Table 1. A model was selected by means of stepwise multiple regression which demonstrates a significant correlation between appropriateness and% of patients referred by a general practitioner [GP],% of urgent EGDs and prevalence of relevant diseases (F = 7.53, p < 0.05), and explains more than 40% of the variability of the data recorded (R² = 0.41)

Conclusions: The differing appropriateness observed among the centers could be partly explained by the operative characteristics of the endoscopy services. Nevertheless, a sizeable amount of the variability remains to be explained and will require further study

Correlation Between% of Appropriateness and Characteristics of the Centers

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pearson’s r</th>
</tr>
</thead>
<tbody>
<tr>
<td>% patients referred by GPs</td>
<td>−0.41</td>
</tr>
<tr>
<td>% Hospitalized patients</td>
<td>0.40</td>
</tr>
<tr>
<td>% relevant endoscopic findings</td>
<td>0.40</td>
</tr>
<tr>
<td>% urgent EGDs</td>
<td>0.35</td>
</tr>
<tr>
<td>% follow-up EGDs</td>
<td>−0.21</td>
</tr>
<tr>
<td>Mean age</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Upper GI Endoscopy Appropriateness and Operative Features of Endoscopy Services; a Multicenter Audit of 44 Italian Open-Access Endoscopies

Gianluca Bersani, M.D., Marcello Anti, M.D., Maria Antonietta Bianco, M.D., Luigi Buri, M.D.,* Emilio Di Giulio, M.D., Giovanni Di Matteo, M.D., Leonardo Ficano, M.D., Pietro Loriga, M.D., Sergio Morini, M.D., Vincenzo Pietropaolo, M.D. Endoscopy Digestiva, Osp Malatesta N., Cesena, Italy; Osp. Belcolle, Viterbo, Italy; Osp Maresca, Torre Del Greco, Italy; Osp Cattinara, Trieste, Italy; Università La Sapienza, Roma, Italy; Osp De Bellis, Bari, Italy; Università Giaccone, Palermo, Italy; Osp SS Trinità, Cagliari; Osp Nuovo Regina Margherita, Roma and Pol. Umberto I, Roma.

Purpose: The aims of this prospective study were: i) to examine the appropriate use of upper gastrointestinal endoscopy (EGD), in 44 open-access Digestive Endoscopy Units distributed all over Italy, using the American Society of Gastrointestinal Endoscopy (ASGE) guidelines. ii) to verify whether the ASGE guidelines were associated with the endoscopic demonstration of relevant diseases and with consequent changes in patient management

Methods: In a cohort of 6270 consecutive patients (male 49%, median age 59 yrs, range 7–100) referred for EGD to 44 Italian GI Endoscopy centers during 1-month period, the percentage of patients who underwent EGD for
appropriate and inappropriate indications, according to ASGE guidelines (2000) was assessed. The relationship between appropriateness of use and the presence of relevant endoscopic findings (foreign body, polyps, neoplasms, ulcers, esophagitis, erosive gastritis/duodenitis, stenosis, varices) was assessed calculating the likelihood ratios (positive, LR+ and negative, LR-).

**Results:** The rate of EGD generally not indicated (according to the ASGE guidelines) was 22.9%. Comparison between patients with ASGE indications and those without indications was as in Table 1. The likelihood ratios (LR) to find a relevant endoscopic disease according to appropriateness were as in Table 2.

**Table 1.** Appropriateness According ASGE Criteria

<table>
<thead>
<tr>
<th>Normal EGDs</th>
<th>Relevant findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGD Appropriate</td>
<td>11.3%</td>
</tr>
<tr>
<td>EGD not-appropriate</td>
<td>24.6%</td>
</tr>
<tr>
<td>p &lt; 0.05</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>

**Table 2.** Likelihood Ratio to Find a Relevant Endoscopic Disease

<table>
<thead>
<tr>
<th></th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGD Appropriate according ASGE</td>
<td>1.247</td>
<td>.429</td>
</tr>
<tr>
<td>EGD Not-appropriate</td>
<td>.429</td>
<td>1.247</td>
</tr>
</tbody>
</table>

**Conclusions:** The use of appropriate indications can improve patients selection for EGD, and thus can contribute to efforts aimed at enhancing the quality and efficiency of care in an open-access system. However due to values of LR not very different from 1.0, this must be tailored to the specific clinical setting where the guidelines has to be applied, in order to avoid to miss serious diseases.

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**Retrospective Study of Clostridium Difficile Colitis in a Community Hospital**

**Irfan Nawaz, M.D., Taofeek Owonikoko, M.D., Sunil Saroha, M.D.**

**Purpose:** Clostridium difficile colitis causes significant morbidity and mortality in hospitalized patients. We analyzed patient demographics, risk factors, management and outcomes in a community hospital.

**Methods:** Retrospective analysis of all cases of C. diff colitis managed between January to December 2004 in our hospital. Patients presenting with symptoms of diarrhea and pain abdomen with a positive stool toxin were included. Patients with negative stool toxin were excluded. Records were analyzed for demographic information- sex and age, predisposing factors like recent hospitalization, use of antibiotics within 1 month, recent chemotherapy and nursing home residence. Management details including choice of antibiotics, ICU stay and duration of hospitalization, need for colonoscopy or surgery were also studied. Microsoft excel software was used for statistical analysis.

**Results:** 79 of 114 patients met the inclusion criteria for final analysis. 32 were females and 47 males. Mean age was 70.3 yrs, 68.2 for males and 72.4 for females (p = 0.2). Mean duration of hospitalization after diagnosis was 19 days (21.1 for males vs. 17.6 for females, (p = 0.35). 50 patients (63%) were on antibiotics at the time of diagnosis of which 11 (22%) were on 2 or more agents. There was a trend towards longer hospitalization with more antibiotics usage. 20 patients (25%) required oral vancomycin, but this showed no correlation with duration of hospitalization, need for surgery or mortality. There was a positive correlation between ICU stay and mortality (r-value = 0.61). There were 11 mortalities (13.9%) attributable to C. diff colitis: 7 (63%) from sepsis, 3 (27%) from toxic megacolon and 1 (9%) due to post surgical complications.

**Conclusions:** C-diff colitis leads to prolonged hospital stay. No significant difference was noted between the sexes in terms of morbidity and mortality. Requirement for ICU stay, suggestive of severe infection, correlates with increased mortality. However, prolonged duration of symptoms and need for additional vancomycin therapy showed no such correlation. A larger and more controlled study will help to further elucidate these findings.

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**Clinical Features and Outcomes of Permanent Capsule Retention in 245 Consecutive Patients Undergoing Capsule Endoscopy**

**Matthew M. Baichi, M.D., Razi M. Arifuddin, M.D., Parvez S. Mantry, M.D.**

**Purpose:** The most significant complication of capsule endoscopy is permanent retention which occurs at a frequency from 1–6%. There is little literature describing the clinical features and outcomes of such patients. The purpose of our study was to document the frequency, findings, and management of permanent capsule retention at a single referral center.

**Methods:** The medical records of all patients who underwent CE at our institution between June 2002 and February 2005 were reviewed. The study population consisted of all patients with permanent capsule retention which was defined as retention requiring intervention (obstructive symptoms, obstructing lesion seen, retention > 3 weeks). The following data was recorded for each patient: age, gender, procedure indication, relevant medical history, prior small-bowel x-ray, capsule findings, clinical course/outcome, and final diagnosis for capsule retention.

**Results:** 245 consecutive cases were reviewed. The mean age was 63 years. Indications were obscure bleeding n = 220 (90%), Crohn’s n = 15 (6%), polyposis n = 5 (2%), and malignancy n = 5 (2%). Permanent capsule retention occurred in 5 cases (2%). Indications were obscure bleeding (n = 4) and polyposis (n = 1). Two patients had a history of Crohn’s in remission. Three patients had a normal SBFT. One patient had symptomatic small bowel obstruction associated with capsule retention. Two cases had successful endoscopic retrieval; three cases required surgical retrieval. Case 1 had a history of Hereditary Non-Polyposis Colorectal Cancer (HNPCC) and was diagnosed with small bowel adenocarcinoma; he subsequently underwent resection followed by chemo-radiation therapy. Case 2 had idiopathic small bowel stricture and underwent stricture dilation with resolution of symptoms. Case 3 and 5 had stricturing Crohn’s disease. Case 3 (newly diagnosed) started mesalamine; case 5 underwent segmental small bowel resection. Case 5 had post-surgical adhesions and underwent extensive lysis of adhesions.

**Conclusions:** Capsule endoscopy is very safe with a low frequency of permanent capsule retention (2%). The frequency of symptomatic small bowel obstruction from capsule retention is very low (0.4%). Crohn’s disease is a significant risk factor for retention. A normal SBFT cannot exclude retention. The majority of patients with permanent retention had clear benefit resulting from the capsule findings.
Esomeprazole (ESO) Versus Alternative Proton Pump Inhibitors (PPI) in Erosive Esophagitis (EE): A Meta-Analysis of Trials Reporting Healing Rates and Symptom Relief

Ian M. Graubeln, M.D., M.S.H.S.,* Gareth S. Daluai, M.D., M.S.H.S., Brian Fennerty, M.D., Brennan M.R. Spiegel, M.D., M.S.H.S. GI, VA Greater Los Angeles, Los Angeles, CA; GI, David Geffen School of Medicine at UCLA, Los Angeles, CA and GI, Oregon Health Sciences University, Portland, OR.

Purpose: There are limited head-to-head data comparing the effectiveness of available PPIs in EE. Published pH and clinical trial data suggest ESO may be more efficacious than other PPIs, but the determinants and magnitude of benefit are uncertain. We performed a meta-analysis to calculate the pooled effect of ESO on healing rates, symptom relief, and adverse events vs. competing PPIs in EE.

Methods: We performed a structured search of MEDLINE & EMBASE to identify randomized clinical trials from 1995–2005 comparing healing rates, symptom relief, and adverse events with ESO vs. alternative PPIs in EE. Two reviewers (IG & BS) independently selected titles, abstracts, and manuscripts for inclusion in the analysis. The reviewers independently abstracted data and assigned a quality score for each study. We performed meta-analysis with both fixed and random effects models to compare the relative risk (RR) of EE healing, symptom relief, and adverse events between study arms, and calculated the number needed to treat (NNT) with ESO vs. alternative PPI for each outcome. We performed an Egger’s test to assess for publication bias.

Results: We identified 84 titles, of which 11 were selected for final review (κ=0.8 for agreement). Meta-analysis of 8 studies (N=14,779 subjects) comparing rates of healing at 4 & 8 weeks revealed a 10% (RR = 1.10, 95% CI = 1.08,1.12; NNT = 10) and 5% (RR = 1.05; 1.03,1.08; NNT = 20) relative increase in the probability of healing, respectively, with ESO vs. alternative PPIs. ESO conferred an 8% (RR = 1.08; 1.05,1.11; NNT = 20) relative increase in the probability of symptom relief at 4 weeks. The effectiveness of ESO was proportional to severity, as the NNTs for LA Grades A-D were 50, 33, 14, and 8, respectively. There was a significantly higher rate of headache with ESO than other PPIs (RR = 1.22; 95% CI = 1.03,1.44), but no difference in diarrhea, abdominal pain, nausea, or total adverse events. There was no publication bias.

Conclusions: As compared with other PPIs, ESO confers a statistically significant, yet clinically modest overall benefit in 4 and 8-week healing and 4-week symptom relief in all-comers with EE. The benefit of ESO appears negligible in less severe disease (NNT = 50 in LA Grade A), but may be clinically important in more severe erosive disease (NNT = 8 in LA Grade D).

The Evaluation of Nausea and Vomiting in Hospitalized Patients: Are Extensive Investigations Warranted?

Sameer Barkatullah, M.D., Michael D. Brown, M.D.* Gastroenterology & Nutrition, Rush University Medical Center, Chicago, IL.

Purpose: The symptoms of nausea and vomiting (N/V) are frequent reasons for inpatient gastroenterology consults. An aggressive evaluation of N/V in these patients is usually undertaken to ascertain the cause and correct it. It is not clear that this approach leads to a definitive diagnosis, or that it alters the natural history of N/V in hospitalized patients. These investigations could prolong hospital stays and do little to correct the problem.

Methods: We retrospectively reviewed the outcomes of inpatient N/V evaluations by the gastroenterology service at a large urban teaching center. All inpatient consults for N/V received by the GI inpatient service were reviewed for the admitting diagnosis, past medical history, medications, hospital course, relevant diagnostic work-up, and the presumed etiology, treatment, and resolution of N/V 105 consults were seen from January 2003 to December 2004.

Results: A diagnosis was made in only 52% (n = 54) of patients. In those the etiology was unifactorial in 81% (n = 44) and multifactorial in 19% (n = 10). N/V resolved in 76% (n = 80) of patients during the hospital stay. Gastroparesis, medication effects, and ileus/small bowel obstruction accounted for N/V in 57% (n = 31) of patients with a known diagnosis. Diagnostic studies used to evaluate symptoms included abdominal radiographs, EGD, CT, ultrasound, UGI radiography and gastric emptying studies. Of these studies, the gastric emptying study was associated with the highest percentage of positive results; 84.62% of all gastric emptying scans performed revealed abnormalities. 100% of these abnormal examinations revealed the cause for N/V i.e. gastroparesis. This was statistically superior to EGD (p ≤ 0.001) Upper endscopic exams often revealed abnormalities such as gastritis or esophagitis. However, these are more likely the result of emetogenic injury, or are unrelated to N/V altogether. Overall, only 19% (n = 9) of upper endoscopies showed abnormalities clearly accounting for N/V, such as peptic ulcer.

Conclusions: In summary, N/V in the hospitalized patient often defies diagnosis, but typically resolves spontaneously. Among patients with a diagnosis, medications and gastroparesis are the culprits in almost 50% of cases. A more conservative approach to patients without physical evidence of a bowel obstruction may be a review of medications and a gastric emptying study. This may reduce unnecessary testing in a condition destined to resolve spontaneously in most.

Outcomes Research in Clinical Practice—Barriers, Design, Results, Cost and Benefits

John I. Allen, M.D., M.B.A.* Gastroenterology, Minnesota Gastroenterology PA, Minneapolis, MN.

Purpose: In theory, outcomes research identifies clinical variation, facilitates adoption of evidence-based practice and improves procedural results. Barriers to achieving these goals include physician resistance, inability to collect data, size of most GI practices and lack of consensus around important metrics. Minnesota Gastroenterology (46 MD GI practice, 5 AECs, >100,000 patient contacts, 69,738 procedures in 2004) developed a Quality Department to monitor process outcomes, clinical and procedural results, patient satisfaction and cost. Results from this private practice are useful as quality benchmarks.

Methods: A 5-step process was used to initiate outcomes research: (1) agreement among partners to be measured, (2) embedding quality outcomes measures in the EMR, (3) identification of practice variation, (4) measurement and 5) internal and external communication of results. Process outcomes include access metrics and cycle time analysis. Clinical results were measured for Hepatitis C treatment (% patients reaching week 12 of treatment), immunomodulator therapy for IBD (% compliance with lab monitoring) and colonoscopy (cecal intubation and adenoma find rate). 10,210 patient satisfaction surveys were received 2001–2004. Cost data was collected for the total cost of colonoscopy within our ambulatory endoscopy centers versus hospital-based practices.

Results: Access: Average time to first available consultation was 28 days (range 4–45 by clinic site) and time to screening colonoscopy was 22 days (9–44 by AEC). Mean cycle time for 27,310 colonoscopy procedures in 2004 (time from colonoscopy referral to results mailed) was 36 (SD=2.3) days (Referral-scheduling 71 hrs, scheduling to pre-op evaluation 3 days, pre-op to appointment 22 days, in-facility time 121 minutes, procedure time 17.4 minutes, recovery 34 minutes, procedure to biopsy results mailed – 36 hours). Example of clinical results: Colonoscopy – 96.7% cecal intubation rate, 27% adenoma find rate in males, >50 years. Cost dataAverage total cost for colonoscopy (professional and facility reimbursement + pathology charges generated + radiology costs for incomplete exams) averaged $1100 vs $3600 for hospital based practices with pre-procedure consultations.

Conclusions: Meaningful outcomes measurement is difficult in current gastroenterology practices. Minnesota Gastroenterology (because of its size and EMR) has produced business, cost and clinical measures that can serve as a benchmark for private GI practices. Consensus on metrics and further comparison examples are needed.
Purpose: *Helicobacter pylori* (H. pylori) infection causes gastric inflammation and gastritis which increase the risk for peptic ulcer disease (PUD). Several genes of *H. pylori* such as *cagA*, *vacA* and *iceA* genes may play an important role in pathogenesis of this disease. The aim of this study was to examine the prevalence of genes *cagA*, *vacA* and *iceA* of *H. pylori* in patients with PUD compared with patients with non-ulcer dyspepsia (NUD) and to determine the association of these genes with PUD.

Methods: In this study, 40 *H. pylori* isolates were obtained from PUD patients and 40 isolates from NUD patients. Genes *cagA*, *vacA* and *iceA* of *H. pylori* were identified by using polymerase chain reaction (PCR) with specific primers.

Results: The result of this study demonstrated that *cagA* positive, *vacA* s1, m2 and *iceA2* genes were found predominantly in *H. pylori* in Thailand. The presence of either *cagA*, allelic variant *vacA* and *iceA* alone does not have a predictive value as a risk marker for clinical outcome of *H. pylori* infection. In addition, high prevalence of mixed *iceA* isolates (48.75%) was found in Thai patients. All of these isolates contained single *vacA* genotype which suggests the presence of mixed *iceA* genotype in one strain. From analysis, *vacA* s1a, mixed *iceA* genotype was found to be significantly associated with PUD (P = 0.04, OR = 2.51, 95% CI = 1.05–6.04).

Conclusions: Genes *vacA* s1a and mixed *iceA* genotype may play important roles in the pathogenesis of peptic ulcer disease and might be regarded as marker for predicting peptic ulcer disease in Thailand.

Therapeutic Yield of Capsule Endoscopy for Obscure GI Bleeding
Matthew M. Baichi, M.D., Razi M. Arifuddin, M.D., Parvez S. Mantry, M.D.* Small Bowel Imaging Center, University of Rochester, Rochester, NY.

Purpose: Capsule Endoscopy (CE) can determine the type and location of previously unrecognized bleeding lesions. This information factors heavily in determining the utility and modality of further interventions. The primary purpose of this study was to review the utilization and therapeutic yield of follow-up procedures based on positive capsule findings. A secondary goal was to determine if any pre-test factors were predictive of capsule findings.

Methods: The medical records of all patients who underwent CE between June 2002 and February 2005 for obscure bleeding were reviewed. The following data was recorded for each patient: age, gender, mode of presentation (overt vs. occult), lowest hematocrit (Hct) within 4 months prior to exam, CE findings, and post-capsule procedural investigations/interventions based on positive findings.

Results: A total of 213 cases were reviewed. Positive findings were seen in 125 cases. Arteriovenous malformation (AVM) was the most common finding (n = 79). 52/213 patients (24%) had a targeted procedure based on positive capsule findings. In this group, AVM was the most common lesion (31/52) and push enteroscopy was the most common procedure (43/52). 30/79 cases of small bowel AVM prompted subsequent investigation with cautery performed in 16/30 (53%) cases. 5/29 cases of ulcer/erosion prompted subsequent investigation with cautery performed in 1/5 (20%) cases. Blood without definitive lesion (n = 10) and mass (n = 4) prompted 100% subsequent investigation with a high therapeutic yield (blood 67%, mass 75%; table 1 for details). Overall, a therapeutic procedural intervention was performed in 33/52 procedures (therapeutic yield 63%). Age, gender, Hct, and mode of presentation did not predict findings.

Conclusions: This data supports the high clinical utility of capsule endoscopy in obscure GI bleeding. Positive capsule findings prompted further procedural investigation in 52/213 cases (24%) with a procedural therapeutic yield of 63%. Age, gender, hct, and mode of presentation were not predictive of capsule findings.

Randomized Controlled Trial of Long-Term Proton Pump Inhibitor (PPI) in the Prevention of Esophageal Variceal Bleeding in Cirrhotic Patients
Hajime Kawayama, M.D.,* Ryoichi Nishiki Gastroenterology and Hepatology, University Hospital at Koshigaya, Dokkyo University School of Medicine, Koshigaya, Minami-Koshigaya, Saitama Prefecture, Japan.

Purpose: Acute bleeding from esophageal varices is a fatal major complication of cirrhotic patients with portal hypertension. In primary and secondary prophylaxis of variceal bleeding, beta-blockers are the mainstay of pharmacotherapy, but are only partially effective. In most patients, variceal bleeding is observed in the distal esophagus, near the esophago-gastric junction, suggesting the possible involvement of gastric acid. We investigated the effect of gastric acid inhibition with PPI in prevention of esophageal variceal bleeding in cirrhotic patients using a randomized controlled trial design.

Methods: We enrolled 136 patients with confirmed cirrhosis and esophageal varices. 35 of these patients had at least one previous episode of confirmed variceal bleeding, and had been treated with endoscopic ligation. The 136 patients were randomized to receive either PPI (oral rabeprazole 20mg/day, N = 68) or no anti-secretory treatment (N = 68), and followed for up to 4 years. Patient demographics (age, gender, Child-Pugh score, variceal size, red color signs, and previous variceal bleeding) were not significantly different in both groups.

Results: The rate of variceal bleeding was significant lower in the PPI-treated group (8.8%, 6/68) than the untreated group (41.2%, 28/68, P < 0.0001). Four-year rate for occurrence of variceal bleeding, calculated by Kaplan-Mayer analysis, was 10.0% in the PPI-treated group, which was significantly lower than the rate of 49.0% in the untreated group, P = 0.003 by log rank test. Subanalysis of patients with pre-study variceal bleeding (secondary prevention) showed that variceal re-bleeding rate was significant lower in PPI-treated pts (12.5%, 2/16) than untreated patients (47.4%, 9/19, P = 0.002). Four-year rate for recurrence of variceal bleeding, calculated by Kaplan-Mayer analysis, was 14.5% in PPI-treated patients, significantly lower than the 50.5% rate in untreated patients, P = 0.06 by log rank test.

Conclusions: Long-term PPI treatment was effective in prevention of esophageal variceal bleeding and recurrent variceal bleeding in cirrhotic patients.

Cost-Effectiveness of Entecavir vs. Lamivudine with Adefovir Salvage as First-Line Treatment in HBeAg-Positive Chronic Hepatitis B: Analyses Based on Two-Year Results from a Randomized Clinical Trial
David L. Veenstra, Ph.D.,* Uchenna H. Iloeje, M.D., Sean D. Sullivan, Ph.D., Eskinder Tafesse, Ph.D., Anne Cross, Ph.D., Adrian Di Bisceglie,
Purpose: To estimate the incremental cost effectiveness of entecavir versus lamivudine with adefovir salvage for the treatment of HBeAg-positive chronic hepatitis B.

Methods: We developed a Markov disease-simulation model with 14 health states to evaluate the impact of 2 years of treatment with entecavir versus lamivudine with adefovir salvage in a hypothetical cohort of 30-year-old patients with HBeAg-positive chronic hepatitis B. A lifetime analysis was conducted from a U.S. payer perspective. Efficacy data were derived from BMS Study AI424-022 (N = 709), a multi-center randomized trial. Disease progression, direct HBV-related medical costs, and quality of life data were derived from a systematic evaluation of the literature and congress abstracts. Sensitivity analyses were conducted on all parameters in the model.

Results: For entecavir treated patients, the modeled life expectancy was greater than for lamivudine with adefovir salvage (40.38 vs. 39.85 years), and the estimated 10-year cumulative incidence of cirrhosis was lower (22.1% vs. 23.6%). The discounted drug cost for entecavir was $12,354 vs. $7,081 for lamivudine with adefovir salvage, and the non-drug healthcare cost was lower ($21,534 vs. $22,994). The incremental cost/QALY was $10,900 in the base-case analysis, and ranged from $5,000 to $20,000 in the sensitivity analyses. An analysis assuming 4-year drug treatment resulted in an incremental cost/QALY of $8,430.

Conclusions: The results of our analysis indicate that initiating treatment with entecavir in HBeAg-positive CHB patients is a cost-effective strategy, as the estimated incremental cost-effectiveness ratio falls below the often cited threshold of $50,000/QALY. Controlled clinical trials beyond one year, such as utilized in this study, are needed to accurately evaluate treatments for CHB.

Validation of an Objective Assessment for GI Medical Knowledge Competency in Internal Medicine Residents
Robert E. Sedlack, M.D.,* Joseph C. Kolers, M.D., Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

Purpose: Medical Knowledge is one of the six primary competencies trainees are expected to acquire. Developing a means for meaningful assessments of these basic competencies is drawing ever increasing emphasis within the education community. Subspecialty education of Gastroenterology is no exception. It has been shown that staff assessment of a trainee’s fund of knowledge is subjective and largely inaccurate. We developed an end-of-rotation exam for IM residents on a GI sub-specialty rotation and validated its usefulness as a surrogate measure of medical knowledge in GI.

Methods: An end-of-rotation (EOR) exam in gastroenterology (GI) was constructed and introduced as a requirement following internal medicine (IM) residents second year two month experience on this subspecialty rotation. These EOR exams were compared to the GI subsection scores of their third year National In-Training Exam sponsored by the American College of Physicians.

Results: Over a three year period, 138 IM residents completed both exams. The Spearman’s correlation between exam scores was $r = 0.54$ ($p < 0.0001$).

Conclusions: Medical knowledge assessment by this subspecialty EOR exam correlates well with a bench mark measuring tool of medical knowledge and has significant predictive value of future knowledge assessment testing. Because medical knowledge is one of the least objective competency measurements, it is imperative that educators continuously improve and validate the accuracy of our assessment methods as we have shown here.

The Ideal Product Profile for Mild to Moderate Sedation: A Preference Study of Gastroenterologists

Purpose: Gastroenterology procedures frequently require mild to moderate (procedural) sedation. This study evaluated the preference levels of gastroenterologists (GEs) for key attributes of a sedation product.

Methods: In February 2005, GEs were asked to complete an internet-based questionnaire on a blinded procedural sedation product. Eligible participants were required to spend 10% of their professional time in both office and hospital settings to evaluate the impact of 2 years of treatment with entecavir versus lamivudine with adefovir salvage, and the non-drug healthcare cost was lower ($21,534 vs. $22,994). The incremental cost/QALY was $10,900 in the base-case analysis, and ranged from $5,000 to $20,000 in the sensitivity analyses. An analysis assuming 4-year drug treatment resulted in an incremental cost/QALY of $8,430.

Results: A total of 150 GEs were recruited to complete the online questionnaire. Most GEs (61%) reported performing procedures that required procedural sedation in an office setting. The figure indicates the importance (% of influence) that each attribute has in the decision to select a particular product. Surrogates of safety, such as the product requiring anesthesiologist oversight (monitored anesthesia care [MAC] requirement) and levels of respiratory depression (ie, decreased O2 saturation), were the most important attributes affecting treatment choice (22% and 21%, respectively). The ideal product for the office setting, based on preference levels, is one that is given by IV bolus over 30 sec, and has a 5-min offset of action, a full recovery period of 22 min, an amnestic effect lasting until full recovery, a decrease in O2 saturation only to 94%, and no MAC requirement. Similar preferences were observed for the hospital setting.
Determinants and Outcomes of Curative Intent Surgery for Pancreatic Cancer in the United States
Yasser H. Shaib, M.D., M.P.H.,* Jessica A. Davila, Ph.D., Hashem B. El-Serag, M.D. M.P.H., Health Services Research and Gastroenterology, Michael E DeBakey VA Medical Center, Baylor College of Medicine, Houston, TX.

Purpose: Pancreatic cancer is the fourth leading cause of cancer death in the United States. Curative intent surgery (CIS) is presumed to be the only curative option in the treatment of pancreatic cancer. The determinants and the outcomes of CIS are not clear at the population level.

Methods: Using data from 9 registries of the Surveillance Epidemiology and End Results (SEER) program we examined the predictors of receiving CIS between 1987–2001. We identified 32,348 cases of pancreatic cancer. Of those 3,545 (10.9%) received CIS. The proportion of patients receiving CIS decreased significantly with age (p < 0.0001), was similar across all racial groups (10.8% in Whites, 11.4% in Blacks, 11.5% in Asians and 11.2% in Hispanics) and differed significantly with age (p < 0.0001), was slightly higher in males (11.3% vs. 10.5%, p = 0.02), decreased with advanced disease stage (p < 0.0001) and progressively increased over time (7.5% in 1987–89, 9.1% in 1990–92, 10.4% in 1993–95, 12.4% in 1996–98 and 13.4% in 1999–2001, p < 0.0001) and differed significantly across different SEER registries (p < 0.0001) in the multi-variable logistic regression analysis, more recent time periods, younger age, early disease stage and geographic location, but not race or gender were independent predictors of receiving CIS.

Results: We identified 32,348 cases of pancreatic cancer. Of those 3,545 (10.9%) received CIS. The proportion of patients receiving CIS decreased significantly with age (p < 0.0001), was similar across all racial groups (10.8% in Whites, 11.4% in Blacks, 11.5% in Asians and 11.2% in Hispanics), was slightly higher in males (11.3% vs. 10.5%, p = 0.02), decreased with advanced disease stage (p < 0.0001) and progressively increased over time (7.5% in 1987–89, 9.1% in 1990–92, 10.4% in 1993–95, 12.4% in 1996–98 and 13.4% in 1999–2001, p < 0.0001) and differed significantly across different SEER registries (p < 0.0001). In the multi-variable logistic regression analysis, more recent time periods, younger age, early disease stage and geographic location, but not race or gender were independent predictors of receiving CIS (Table). [figure1]In the Cox survival analysis, younger age, early disease stage, more recent time period, geographic location and receipt of CIS were independent predictors of improved survival and Black race was an independent predictor of decreased survival.

Conclusions: Early stage disease, younger age, geographic location and more recent time periods are predictors of receiving CIS. Early disease stage and receipt of CIS are the strongest predictors of improved survival. Black race is an independent predictor of shorter survival.

Management of Acute Gastrointestinal Bleed without Blood Transfusion; a Specialized Unit Experience
Irfan Nawaz, M.D., Rabu Kandu, M.D., George Aitaridis, M.D., Susan Gordon, M.D.* Internal Medicine, Div.of Gastroenterology, Graduate Hospital, Philadelphia, PA.

Purpose: Blood transfusion is a standard practice in management of acute gastrointestinal bleed. Our hospital is a specialized unit to manage patients refusing blood transfusions due to religious or personal reasons.

Methods: A retrospective chart analysis of patients presenting to our hospital with acute gastrointestinal bleed from Jan. 2002 to July 2004. Bloodless care patients were compared with standard care patients that accepted blood transfusion. Inclusion criteria were Hemoglobin drop 2 Gm/dl or more and/or hemodynamic deterioration. We reviewed parameters including demographic and risk factors. Presenting complaints, time to endoscopy, duration of...
ICU and hospital stay, erythropoietin dose, re bleed rate and mortality were also reviewed.

**Results:** 32 patients satisfied the inclusion criteria in study group and 73 patients in control group. There was no significant difference in patient demographics, presentation and risk factors. Mean time to endoscopy in study group was 21.9 hours as compared to control 45.6 hours. Difference between mean was 24 hours (p = 0.009). Mean ICU stay was 2 days in study group and 1 day in control (p = 0.02). There was no significant difference in duration of hospitalization and rebleeding rates between two groups. There was 1 mortality in each group. All patients in study group received Iron, while 78% (25/32) patients received erythropoietin (mean dose 465 U/kg).

There was no significant difference in patient demographics, presentation and risk factors. Mean time to endoscopy in study group was 21.9 hours as compared to control 45.6 hours. Difference between mean was 24 hours (p = 0.009). Mean ICU stay was 2 days in study group and 1 day in control (p = 0.02). There was no significant difference in duration of hospitalization and rebleeding rates between two groups. There was 1 mortality in each group. All patients in study group received Iron, while 78% (25/32) patients received erythropoietin (mean dose 465 U/kg).

**Conclusions:** The outcome of bloodless care patients was comparable to standard care group. We emphasize early endoscopy, close ICU monitoring and support with iron and high dose erythropoietin.

### Table 1.

<table>
<thead>
<tr>
<th>Patient Parameters</th>
<th>Bloodless Care</th>
<th>Standard Care</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age in years</td>
<td>70.7</td>
<td>68.8</td>
<td>0.56 (ns)</td>
</tr>
<tr>
<td>Male:Female</td>
<td>7:25</td>
<td>29:44</td>
<td>0.07 (ns)</td>
</tr>
<tr>
<td><strong>Presentation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper GI bleed</td>
<td>19</td>
<td>43</td>
<td>ns</td>
</tr>
<tr>
<td>Lower GI bleed</td>
<td>13</td>
<td>30</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NSAIDs</td>
<td>13</td>
<td>15</td>
<td>0.06</td>
</tr>
<tr>
<td>Coumadin</td>
<td>7</td>
<td>8</td>
<td>0.24</td>
</tr>
<tr>
<td>Antiplatletes</td>
<td>4</td>
<td>20</td>
<td>0.09</td>
</tr>
<tr>
<td>History of GI bleed</td>
<td>6</td>
<td>28</td>
<td>0.07</td>
</tr>
<tr>
<td>Mean Hb.at</td>
<td>9.62</td>
<td>10.21</td>
<td>0.35 (ns)</td>
</tr>
<tr>
<td>presentation (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to endoscopy</td>
<td>21.9</td>
<td>45.64</td>
<td>0.0009</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>2.03</td>
<td>1.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Total duration of hospitalization (days)</td>
<td>6.8</td>
<td>6.7</td>
<td>0.9 (ns)</td>
</tr>
</tbody>
</table>

**Table 2.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Bloodless Care (No.)</th>
<th>Standard Care</th>
<th>Cost Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presentation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bright red blood PR</td>
<td>14</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Anemia/malena</td>
<td>14</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Coffee ground vomitus</td>
<td>2</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td><strong>Findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastritis/Duodenitis</td>
<td>14</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>5</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Esophagitis</td>
<td>3</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Diverticulosis</td>
<td>13</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>CoLitis</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Polyps</td>
<td>2</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>9</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastritis</td>
<td>11</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Ulcers</td>
<td>4</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>H.pylori</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Adenoma</td>
<td>4</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Although hospitalization for bleeding and perforation resulting from colonoscopy is uncommon, the cost of these complications is high. These data need to be considered when evaluating the overall cost of screening for colorectal cancer.
or to receive basic disease counseling (6 centers, 68 subjects, 32/36 English-/French-speaking) at baseline and at 1 month. Physicians only provided one type of counseling and followed a template to provide the counseling in a standardized manner for both patient groups. The CI group received education about the natural history of the disease, the mechanism of symptoms, lifestyle modifications, available drug therapies and expectations about symptom relief and reasons for consulting. If eligibility criteria were met, all patients received esomeprazole 40 mg once daily for 1 month; management of the patient from months 1 to 7 was at the discretion of the individual physician. The Quality of Life Questionnaire in Reflux and Dyspepsia (QoLRAD) was administered at baseline and 1, 4 and 7 months.

Results: After 1 month of treatment with esomeprazole, all patients had a statistically significant improvement in QoL when compared with baseline (p < 0.001). The change in overall QoLRAD score from baseline to 4 months in the CI group, showed a trend towards improved QoL. As shown in the table, the change in overall QoLRAD score from month 1 to month 4 in the CI group was statistically significant when compared with the basic counseling group.

<table>
<thead>
<tr>
<th>Mean change in overall QoLRAD from month 1 to</th>
<th>CI LS mean</th>
<th>No CI LS mean</th>
<th>Difference (CI – No CI) (95% Conf. Interval)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 4</td>
<td>−0.098</td>
<td>−0.511</td>
<td>0.413 (0.125, 0.701)</td>
<td>0.005</td>
</tr>
<tr>
<td>Month 7</td>
<td>−0.197</td>
<td>−0.439</td>
<td>0.242 (−0.079, 0.563)</td>
<td>0.139</td>
</tr>
</tbody>
</table>

CI = Counselling Intervention.

Conclusions: After 1 month of treatment, disease counseling and education maintains the improved QoL in baseline patients with GERD patients in the short-term.

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Impact of Feedback and Educational Sessions on Physician Reporting of Upper GI Endoscopic Findings
Adil Abdalla, M.D., Kassandra Gruenwald, Bret Petersen, M.D., Beverly Ott, Mary Fredericksen, Cathy Schleck, M.S., Teresa Zais, Alan Zinsmeister, Ph.D., Yvonne Romero, M.D.* Gastroenterology & Hepatology, Mayo Clinic, Rochester, MN and Biostatistics, Mayo Clinic, Rochester, MN.

Purpose: Guidelines to grade reflux esophagitis (RE), Barrett's esophagus (BE) and hiatal hernia (HH) have been developed to improve consistency and communication. At our institution, results are relayed by means of free text dictation. Educational sessions and feedback were provided to endoscopy and GI Assistants. The aims of our study were to assess, among the subset of patients diagnosed with HH, RE and/or BE: 1) the percent time landmarks were dictated in accordance with guidelines; and 2) the impact of education and feedback on reporting behavior.

Methods: Cross-sectional retrospective chart reviews were performed for Time 1 (03/01/04–04/31/04), Time 2 (07/01/04–08/31/04) and Time 3 (03/01/05–04/31/05). Education began two years prior to Time 1. No intervention took place between Times 1 and 2; data was collected at both times to assess for secular change. Between Times 2 and 3, anonymous individual and group feedback, and brief refresher sessions were given. Patients had to provide research authorization. We excluded patients who had esophageal surgery, cancer of the esophagus or stomach, were ≤ age 17, or who had a complex, limited or incomplete EGD.

Results: 6717 EGD's were performed, of which 1304 were excluded [1ack of research authorization (N = 588), complex EGD (N = 348) or young age (N = 290)]. Of the remaining 5413 cases, 2675 had at least one non-exclusive outcome of interest. The table below shows, for each time period: total eligible EGD's; the number of cases with an outcome of interest; and the number & percent of time landmarks were dictated correctly.

<table>
<thead>
<tr>
<th>Findings</th>
<th>Baseline</th>
<th>Time 1</th>
<th>Baseline</th>
<th>Time 2</th>
<th>After Feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eligible EGD's</td>
<td>2069</td>
<td>1759</td>
<td>1585</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HH total</td>
<td>837</td>
<td>697</td>
<td>759</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dictated N (%)</td>
<td>[95% CI]</td>
<td>599 (72%)</td>
<td>458 (66%)</td>
<td>657 (87%)</td>
<td></td>
</tr>
<tr>
<td>[95% CI]</td>
<td>[68, 75]</td>
<td>[62, 69]</td>
<td>[84, 89]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RE total</td>
<td>280</td>
<td>208</td>
<td>166</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dictated N (%)</td>
<td>[95% CI]</td>
<td>259 (93%)</td>
<td>175 (84%)</td>
<td>144 (87%)</td>
<td></td>
</tr>
<tr>
<td>[95% CI]</td>
<td>[89, 95]</td>
<td>[79, 89]</td>
<td>[81, 92]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BE total</td>
<td>229</td>
<td>203</td>
<td>164</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dictated N (%)</td>
<td>[95% CI]</td>
<td>140 (61%)</td>
<td>136 (67%)</td>
<td>133 (81%)</td>
<td></td>
</tr>
<tr>
<td>[95% CI]</td>
<td>[55, 68]</td>
<td>[60, 73]</td>
<td>[74, 87]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CI = Counselling Intervention.

Conclusions: Anonymous individual and group feedback, in combination with brief, structured educational sessions, can statistically significantly improve compliance with established guidelines for the reporting of hiatal hernia and Barrett's esophagus. There is likely a ceiling effect for the grading of esophagitis once the LA Classification System has been incorporated into clinical practice.

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Warfarin May Not Be a Risk Factor for In-Hospital Mortality in Acute Gastrointestinal Hemorrhage
Layla Hajjarfar, M.D., Gregory S. Cooper, M.D., Thomas E. Love, Ph.D., Richard C.K. Wong, M.B.B.S.* Gastroenterology and Hepatology, University Hospitals of Cleveland, Cleveland, OH and Center for Health Care Research, Case Western Reserve University, Cleveland, OH.

Purpose: The impact of warfarin use on mortality in acute gastrointestinal hemorrhage (GIH) has not been clearly defined. The goal of this study is to determine whether the use of warfarin is a risk factor for in-hospital mortality in the setting of acute GIH.

Methods: The dataset used is derived from a consortium of 30 regional hospitals, prospectively collected between 1991 and 1999. All patients in this cohort were documented as having a principal discharge diagnosis of GIH. Using the primary diagnosis code, patients were categorized as having either an upper or lower GIH. Using logistic regression analysis, a propensity score for the likelihood of warfarin treatment was calculated using the variables age, race, sex, history of GIH, diabetes, coronary artery disease, dialysis, and cirrhosis (NSAID and ASA use were not available). Patients on warfarin were matched on a 1:1 ratio to controls by propensity score and source of bleed. A McNemar's Chi-Square test was performed for death and warfarin use on this matched cohort. Other variables evaluated with Wilcoxon signed-rank test were length of stay (LOS), blood transfusion requirements, and use of endoscopy.

Results: Of the 11088 patients in the initial dataset, 7927 had a primary diagnosis code specifying an upper vs. lower GIH. In this cohort, the overall mortality was 3.5%: 1.4% in lower and 4.3% in upper GIH. The 270 patients on warfarin (average presenting INR of 2.8 vs. 1.1 in controls) were matched to controls within a standard error of 60% based on propensity score and source of bleed, producing 269 well-matched pairs. The resulting association between warfarin use and in-hospital mortality was not significant (p = 0.65). The median LOS was 6 days for patients on warfarin vs. 5 days for controls (p = 0.51). 62% of patients were transfused with a median of 3 units in both warfarin users and controls. Of the upper GIH patients, 90% of the warfarin patients and 87% of the matched controls had EGDs performed: 79% of patients with lower GIH in both groups had a colonoscopy (overall p > 0.5).

Conclusions: In contrast to perceived differences, in this community-based sample, the use of warfarin was not a risk factor for in-hospital mortality in patients with acute GIH. Furthermore, patients on warfarin did not differ from their matched controls with respect to blood transfusion requirements, use of endoscopy, or length of stay.
Therapeutic Use of Alum in Radiation Proctitis

Rateesh Khillan, M.D., Kamudi Sonnay, M.D., F.A.C.G.* Raj Wadgaonkar, Ph.D. Medicine, SUNY Downstate Medical Center, Brooklyn, NY.

Purpose: Lower gastrointestinal bleed resulting from radiation colitis is a challenging condition for the gastroenterologist. Radiation colitis is commonly seen after radiation treatment given for pelvic malignancies. There is no effective treatment available for radiation colitis. We propose to use Alum (Aluminum potassium sulfate) in the treatment of radiation induced bleeding from the rectum due to radiation injury. The mechanism of action of Alum is thought to be its astringent effect on the epithelium together with the induction of protein coagulation. There is some evidence about the anti-aggregation effect of Alum on the platelets which if true can be detrimental to our proposed study. Thus we first decided to study the effect of different concentrations of Alum on platelet aggregation in vitro.

Methods: Use of 1% Alum on the platelet rich plasma PRP found to be causing precipitation which was later on tested on tyrodes buffer, serum as well as platelet poor plasma. Then we came up with three concentrations of Alum which did not cause any precipitation (1mM, 10 mM, and 25 mM). These concentrations were used to make stock solution. 50 cc of blood was obtained after consent from the medical residents. None of them was taking any aspirin or NSAIDS in past 10 days. Platelets were extracted after centrifuging whole blood at 1000 rpm for 20 minutes. Platelets were then washed three times with buffer containing inhibitors. We used optical aggregometer from (Chrono-log Corporation) to study the platelet aggregation. 450 ml of prp was taken in glass aliquots with a magnetic pallet. These were placed in the aggregometer at 1000 rpm and 10 ml of fibrinogen was added both in control and test aliquots. Different concentrations of Alum were used to incubate platelets for 3–5 minutes. After this 10 ml, 5ml, of TRAP or 1ml,3ml of thrombin was added and effect was monitored graphically with the attached software (aggregolink).

Results: Alum by itself does not cause any effect on platelet aggregation in any concentration. With 0.5 mM Alum there was 18% inhibition of TRAP induced aggregation, at 1 mM there was 14% inhibition, at 1.5 mM there was no inhibition, at 2.5 mM there was 56% inhibition of TRAP induced aggregation

Conclusions: Alum is safe, cheap compound that should be used cautiously in the treatment of radiation induced bleeding as it can cause inhibition of platelet aggregation. This in vitro study will guide us to use Alum safely in vivo for possible treatment of radiation proctitis.

Predictors of Tolerance to Endoscopic Procedures

Hoassam E. Martini, M.D., Luis R. Pena, M.D.* Nicholas Nickl, M.D. Division of Gastroenterology, Hepatology and Nutrition, University of Kentucky, Lexington, KY.

Purpose: Despite conscious sedation, up to 1/3 of patients may be dissatisfied during endoscopy with sedation, leading to poor procedure tolerance or procedure avoidance. Reliable methods to predict patient aversive experience or to direct patients to appropriate options do not exist. Our group has been developing a questionnaire to reliably identify patients who will experience endoscopy adversely. The aim of this study is to identify factors associated with aversive endoscopic experience in a group of outpatients.

Methods: The study was conducted in 2 phases: the first aimed at identifying factors predictive of poor endoscopic outcomes and the other at validating the questionnaire. 303 unselected patients for routine endoscopy were included. Two questionnaires were given to patients pre- and post-procedure respectively. The first questionnaire elicited demographics, education level, prior endoscopic experience, history of drugs or alcohol use, and levels of anxiety and nervousness before the test. After endoscopy, procedure tolerance and willingness to repeat the examination were determined. The primary outcome of “averse endoscopic experience” was defined as a score of 5 or greater on the post-procedure overall level of satisfaction or unwillingness to repeat the endoscopy. Non-parametric tests and logistic regression models were used to assess the associations, estimate the odd ratio (OR) and 95% confidence intervals (CI) of these association and to control for potential confounders.

Results: Among 298 subjects (112 males and 186 females) who completed the study 32 (11%) had an adverse endoscopic experience. Subjects who reported poor experience had significantly higher levels of nervousness prior to endoscopy (5.0 vs 3.2; p = 0.013). Chronic SSRIs and benzodiazepine use was also associated with poor tolerance (OR 1.9 & 1.7; 95% CI: 1.08–4.1 & 1.1–5.2 respectively). There was a trend of association between alcohol use and poor experience (OR 1.4; 95% CI 0.92–3.1).

Conclusions: We have identified some of the factors associated with poor endoscopic experience and dissatisfaction. These factors include nervousness before procedure and chronic SSRIs use and benzodiazepine use. Subjects with these risk factors should be considered for alternative sedation methods such as performing procedures using propofol. A prospective randomized trial is being conducted to test these predictors in guiding sedation method.

Practice Patterns and Treatment Outcomes in the Management of Chronic Hepatitis C (CHC) Infection in a Large Managed Care Cohort

Manjula Bobbola, M.D., Jasminster Momi, M.D., Joseph K. Lim, M.D., Joanna Ready, M.D., Ramsey C. Cheung, M.D.* Department of Medicine, Kaiser Permanente Santa Clara Medical Center, Santa Clara, CA and Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Stanford, CA.

Purpose: Chronic hepatitis C (CHC) infection remains a leading cause of chronic liver disease, and is of significant concern to insurers and health planners. Although the efficacy of antiviral therapy for CHC is well documented in controlled research populations, its effectiveness in community practice remains less clearly defined. Assessment of practice patterns and treatment outcomes in a large community cohort may inform policy-making among third-party payers.

Methods: We reviewed the administrative, laboratory, and pharmacy databases of selected sites within the Kaiser Permanente Northern California Health System, a large health maintenance organization with 3.1 million members. We identified subjects with CHC infection using ICD-9 diagnoses (070.54) and anti-HCV antibody records. Administrative files were used to obtain demographic information on age, gender, and ethnicity. Laboratory records were used to obtain data on HCV RNA, HCV genotype, AST, ALT, CBC. Pharmacy records were used to obtain data on use of interferon (IFN)/ribavirin (RBV), pegylated interferon (PEG-IFN)/ribavirin (RBV), procrir, neupogen, antidepressants, and trans fusions.

Results: We identified 1470 patients with a documented ICD-9 diagnosis of CHC infection between 1999–2004. Of these patients, 246 underwent treatment with either IFN/RBV (n = 119) or PEG-IFN/RBV (n = 123). The mean age was 47.1 years (95% CI 33.3–60.91), and 158/242 (65.3%) were male. The average duration of therapy was 29.2 weeks. The overall rate of sustained virologic response (SVR) was 48/242 (19.8%), including 14/119 (11.8%) for IFN/RBV and 34/123 (27.6%) for PEG-IFN/RBV.

Conclusions: Many patients with CHC infection in a large community cohort do not undergo antiviral therapy. The rate of SVR following antiviral therapy is significantly lower than what is observed in controlled trial settings. Further research is needed to identify the key barriers to treatment and therapeutic success in these patients.

Comparing 2 Revolutions: Impact of H. pylori Eradication and Introduction of COX-2 Selective Inhibitors on Ulcer Hospitalizations in the United States

Gurkiran Singh, M.D., Alka Mithal, M.D., George Triadafilopoulos, M.D.* Gastroenterology, Stanford University, Stanford, CA and ICORE, Palo Alto, CA.
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Purpose: *H. pylori* eradication has revolutionized the management of peptic ulcer disease. A second major revolution occurred when COX-2 selective inhibitors were introduced in 1999 with a GI safety advantage. We assessed the impact of COX-2 selective inhibitor use by examining trends of hospitalizations due to complicated gastric (GU) and duodenal ulcers (DU) over a period of 11 years and relating them to the total prescriptions of NSAIDs, *H. pylori* eradication, and PPI use.

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of US community hospitals with information on all inpatient care regardless of insurance status. We studied all inpatient hospitalizations in NIS from 1990 to 2001 with a primary diagnosis of complicated GU, DU, or peptic ulcer disease (PUD) with hemorrhage, perforation, and/or obstruction, and analyzed them as a proportion of total NSAID prescriptions (data from IMS) during the same time.

Results: From 1990–2001 there were 423,558,416 hospitalizations in 3.2 billion person-years of observation. Of these, 1,865,687 hospitalizations (0.44% of total) were for a primary diagnosis of a complicated GU, DU, or PUD (58.4 per 100,000 US population). During this time, there were 982.2 million NSAID prescriptions in the US. Annual NSAID prescriptions increased from 67.6 million (1990) to 112.8 million (2001), with the largest increase from 1998 (79.2 million) to 2001 (112.8 million). PPI prescriptions rose from 3.9 million in 1992 to 73.6 million in 2001. Complicated GU, DU, or PUD hospitalizations declined from 163,173 in 1990 to 139,597 in 2001. The rate of GU, DU or PUD hospitalizations per 100,000 NSAID prescriptions declined by almost 50%, from 241.5 in 1990 to 123.8 in 2001 (P < 0.0001). While such hospitalizations declined steadily from 1992 (perhaps reflecting PPI use), there were 2 periods of additional sharp declines: the first (10.8%, 1995) following the NIH consensus conference recommending *H. pylori* eradication, and the second (22.4%, 1999) after the introduction of COX-2 selective inhibitors.

Conclusions: These data strongly suggest that the introduction of *H. pylori* eradication therapy, increasing use of PPIs and the introduction of COX-2 selective inhibitors account for the trend toward fewer hospitalizations for complicated ulcer disease in the US. The impact of COX-2 selective agents on ulcer hospitalizations and mortality is twice as much as that of *H. pylori* eradication.

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Responsiveness of the Work Productivity and Activity Impairment Questionnaire for Irritable Bowel Syndrome with Constipation (WPAI:IBS-C) to Clinically Meaningful Change

M. C. Reilly, MA,* C. R. McBurney, PharmD, A. Bracco, PharmD
Margaret Reilly Associates Inc, New York, NY and Novartis Pharma AG, Basel, Switzerland.

Purpose: The work productivity and activity impairment measures of the Work Productivity and Activity Impairment Questionnaire for Irritable Bowel Syndrome (WP AI:IBS) have been shown to discriminate among patients with different disease severity. The purpose of this investigation was to test the responsiveness of these measures to clinically meaningful changes in symptom severity among IBS patients with constipation.

Methods: Female patients 18–65 years old who met Rome II criteria for IBS, excluding those with frequent diarrhea, were assessed during a randomized, double-blind, placebo-controlled, multicenter study of tegaserod 6 mg bid or placebo for 4 weeks. Absenteeism, presenteeism, overall work productivity loss and activity impairment due to IBS symptoms during the prior 7 days were measured with the WP AI:IBS-C, which excludes diarrhea as an IBS symptom. Patients were classified as responders at Week 4 if they reported satisfactory relief of abdominal discomfort or pain, or relief of overall IBS symptoms in at least 3 of the 4 treatment weeks. The association between WP AI:IBS-C scores and responder status was tested using a Cochran-Mantel-Haenszel stratified test stratified by treatment group.

Results: 2,660 women were randomized and of these 1,675 ( tegaserod [n = 1,363], placebo [n = 312]) were employed and completed WP AI:IBS-C questionnaires. At Week 4, compared to non-responders, responders with relief in abdominal discomfort or pain reported significant reductions in absenteeism (p = 0.02), presenteeism (p < 0.0001), overall work productivity loss (p < 0.0001), and activity impairment (p < 0.0001). When overall IBS symptom relief was considered, compared to non-responders, responders reported significant reductions in all measures (p values < 0.0001), except absenteeism where the reduction was not significant.

Conclusions: The WP AI:IBS-C work productivity and activity impairment measures are responsive to clinically meaningful change in IBS symptom severity and are useful tools for measuring outcomes in IBS-C.

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Assessment of Serum Thiamine Levels Following Gastric Bypass Surgery

Michael E. Herman, DO,* Chris Hym, M.D., Tao W. Jack, M.D., D Phil Consultative Medicine, Naval Hospital, Jacksonville, FL.

Purpose: Prospective pilot study of serum thiamine levels and development of polyneuropathies before and after gastric bypass surgery.

Methods: The cohort consisted of 17 females and 5 males, two were excluded secondary to improper follow-up. All patients had normal thiamine levels prior to surgery with no neuropathies.

Results: Results demonstrated a decrease in serum thiamine levels (3 months, −9%; 6 months −7%) and BMI (3 months, −3%; 6 months, −7%). Although polyneuropathies were reported, deficits on examination at 3 months (4%) and 6 months (1%) were rare. The change in BMI correlated with the change in serum thiamine levels (p < 0.05).

Conclusions: While there was a transient increase in polyneuropathies at three months, there were no long-term neurological deficits noted. We have developed a database to continue following gastric bypass patients and further evaluate potential complications of thiamine deficiency after gastric bypass surgery.

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Compliance with Dyspepsia Guidelines among Primary Care Physicians

Michael E. Herman, DO,* Chris Hym, M.D. Consultative Medicine, Naval Hospital Jacksonville, Jacksonville, FL.

Purpose: All patients over the age of 50, with either new onset or chronic GERD greater than six months should have at least one upper endoscopy to evaluate Barrett’s esophagus. We did a retrospective pilot study comparing compliance with endoscopic guidelines between two fields of primary care medicine.

Methods: Data was obtained from chart reviews of patients enrolled to either the Internal Medicine (IM) or Family Practice (FP) Clinic at our facility over the last two years. Inclusion criteria were male patients, over the age of fifty, taking proton pump inhibitors for at least six months for GERD symptoms.

Results: With a cohort of 418 patients, 178 (81%) of FP patients and 176 (89%) of IM patients met the standards of care with respect to upper endoscopic evaluation. Of those falling out of standard of care, 43% (FP) and 27% (IM) patients met the standards of care with respect to upper endoscopic evaluation. Of those falling out of standard of care, 43% (FP) and 27% (IM) were for a primary diagnosis of a complicated GU, DU, or PUD (58.4 per 100,000 US population). During this time, there were 312.2 million NSAID prescriptions in the US. Annual NSAID prescriptions increased from 67.6 million (1990) to 112.8 million (2001), with the largest increase from 1998 (79.2 million) to 2001 (112.8 million). PPI prescriptions rose from 3.9 million in 1992 to 73.6 million in 2001. Complicated GU, DU, or PUD hospitalizations declined from 163,173 in 1990 to 139,597 in 2001. The rate of GU, DU or PUD hospitalizations per 100,000 NSAID prescriptions declined by almost 50%, from 241.5 in 1990 to 123.8 in 2001 (P < 0.0001). While such hospitalizations declined steadily from 1992 (perhaps reflecting PPI use), there were 2 periods of additional sharp declines: the first (10.8%, 1995) following the NIH consensus conference recommending *H. pylori* eradication, and the second (22.4%, 1999) after the introduction of COX-2 selective inhibitors.

Conclusions: These data strongly suggest that the introduction of *H. pylori* eradication therapy, increasing use of PPIs and the introduction of COX-2 selective inhibitors account for the trend toward fewer hospitalizations for complicated ulcer disease in the US. The impact of COX-2 selective agents on ulcer hospitalizations and mortality is twice as much as that of *H. pylori* eradication.

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Patient Characteristics Irritable Bowel Syndrome with Constipation (IBS-C): Baseline Results from Logic (Longitudinal Outcomes Study of GI Symptoms in Canada)

P. Pare, M.D.,* S. Lam, M.D., R. Balshaw, Ph.D., P. Keown, Ph.D., S. Khosreesh, MA, M. Barbeau, BA, M.Sc., S. Kelly, Ph.D., C. R. McBurney, PharmD Centre Hospitalier Affilie Universitaire de Quebec, Quebec, QC.
Purpose: Abdominal pain/discomfort, bloating and constipation are gastrointestinal dysmotility and sensory symptoms of IBS-C and are associated with impaired quality of life (QoL) and increased health care utilization. LOGIC is an ongoing, prospective, observational study to evaluate the Tx patterns and health outcomes of patients with IBS symptoms in Canada.

Methods: 1,553 patients with IBS-type symptoms were enrolled from 147 community/specialist physician sites across Canada. Clinical data and patient-reported outcomes (PROs) were collected at baseline; PROs were completed at months 1, 3, 6, 9 and 12. QoL and patients’ health state were assessed using IBS-QOL and EQ-5D, and work productivity using the WPAI:IBS. Resource utilization included number and type of physician visits, procedures and Tx.

Results: Baseline data were obtained from 1,553 patients (1,321 [85%] women), mean age = 46 years, mean disorder duration = 11 years (1 month–69 years). Self-reported bowel patterns were predominantly constipation (39%) and alternating constipation/diarrhea (57%). The mean overall IBS-QOL (0–100 scale) was 66; food avoidance (52) and health worry (59) were the most serious concerns, followed by body image (61), dysphoria (67) and interference with activity (67). The WPAI:IBS indicated a 6% loss of work time, 34% impairment in overall work and 37% impairment in daily activities. In the preceding month, patients had on average, 0.76 consultations with a family doctor and 0.07 specialist visits, and fiber (30%), laxatives (28%) and analgesics (39%) were the most commonly reported non-prescription (Rx) medications used. At baseline, the most common Rx medications reported included tegaserod (26%) and pinaverium bromide (9%).

Conclusions: These baseline data are consistent with previous findings showing significant use of medications and healthcare resources with concomitant low QoL in patients with IBS symptoms. This study will follow patients for 1 year, providing insights into the assessment, Tx and outcomes of IBS symptoms in Canada.

Z.A.Q (Zelnorm Advancing Quality of Life) Study Outcomes. Treatment with Tegaserod in a Naturalistic Setting Is Associated with Reductions in Presenteeism and Absenteeism

N. Flook, M.D., G. Choueri, M.D., S. Kelly, Ph.D.,* M. Barbeau, M.Sc. Novartis Pharmaceuticals Inc (Canada), Dorval, QC, Canada and University of Alberta, AB, Canada.

Purpose: Abdominal pain/discomfort, bloating and constipation are symptoms of the lower gastrointestinal (GI) dysmotility disorder, IBS-C. They are associated with impaired quality of life (QoL) and IBS is the second most common cause of work-related absenteeism. ZAQ was a prospective naturalistic study designed to evaluate the impact of Zelnorm treatment on presenteeism and absenteeism in women with IBS-C.

Methods: 2381 patients with lower GI symptoms were enrolled at 481 community physician sites across Canada. Patients completed questionnaires on medication use, absenteeism and presenteeism at baseline and 4 and 12 weeks after starting Zelnorm treatment.

Results: Baseline data were obtained from 1542 patients. Week 4 and/or Week 12 questionnaires were returned by 483 patients (31.3%) who were included in the ITT analysis. The mean age was 49.5 years. Mean disease duration was ≥2 years for 77.5% and ≥6 years for 46.2% of the population. The most common prescription (Rx) medications reported at baseline were PPIs (33.2%), pinaverium bromide (15%) and H2RA (13.3%). Fiber (23%), laxatives (20%) and stool softeners (18%) were the most commonly reported non-Rx medications. With Zelnorm treatment, there was a significant reduction in presenteeism and absenteeism as shown in the table.

<table>
<thead>
<tr>
<th>Days/month missed at</th>
<th>% patients</th>
<th>% patients</th>
<th>% patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>work/school</td>
<td>improved</td>
<td>remained the same</td>
<td>worsened</td>
</tr>
<tr>
<td>Days/month left</td>
<td>27.2*</td>
<td>65.6</td>
<td>7.2</td>
</tr>
<tr>
<td>work/school early</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days/month arrived</td>
<td>17.2*</td>
<td>75.5</td>
<td>7.3</td>
</tr>
<tr>
<td>work/school late</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days/month accomplished less at work/school</td>
<td>49.8*</td>
<td>34.6</td>
<td>15.7</td>
</tr>
<tr>
<td>Days/month accomplished less at home</td>
<td>50.0*</td>
<td>40.3</td>
<td>9.7</td>
</tr>
<tr>
<td>Days/month cancelled/rescheduled activities</td>
<td>39.5*</td>
<td>50.8</td>
<td>9.8</td>
</tr>
</tbody>
</table>

*p < 0.001.

Conclusions: These data, collected over 12 weeks in a naturalistic treatment setting indicate that treatment with Zelnorm is associated with a significant decrease in self-reported presenteeism and absenteeism in patients with symptoms of abdominal pain/discomfort, bloating and constipation.

Predictors of High Levels of Nervousness Prior to Endoscopic Procedures

Housam E. Mardini, M.D., Luis R. Pena, M.D.,* Nicholas Nickl, M.D. Division of Gastroenterology, Hepatology and Nutrition, University of Kentucky, Lexington, KY.

Purpose: Despite conscious sedation, up to a quarter of patients may be dissatisfied during endoscopy with sedation, leading to poor procedure tolerance or procedure avoidance. Previously, we have reported that levels of nervousness before a procedure may predict poor tolerance and dissatisfaction. The aim of the current study is to identify factors associated with higher levels of nervousness before routine endoscopic procedures.

Methods: 303 unselected patients presenting for routine endoscopy were included. Two questionnaires were given to patients pre- and post-procedure respectively. The first questionnaire elicited demographics, education level, prior endoscopic experience, history of drugs or alcohol use, and levels of anxiety and nervousness before the test. After endoscopy, procedure tolerance and willingness to repeat the examination were determined. Nervousness was measured using a visual analogue scale (higher levels indicate higher levels of nervousness). Non-parametric tests were used to assess the associations and correlations.

Results: 298 subjects (112 males and 186 females) completed the study. 46 subjects (16%) were younger than 40 year old, 196 (66%) were 41–60 year old and 54 (18%) were older than 60 year old. Females had higher levels of nervousness (4.1 vs 3.2; p = 0.007). Nervousness levels were higher among patients younger than 60 years old and among patients with educational level of high school or less (3.9 vs 2.7; p = 0.012 & 4.5 vs 3.4; p = 0.015). Furthermore, chronic narcotic use was associated with higher level of nervousness before procedure (3.3 vs 2.6; p = .023). Fear of pain during procedure as reflected by higher levels of expected pain strongly correlated with nervousness before procedure (r = 0.59, p = .0001).

Conclusions: Nervousness before procedure may predict poor endoscopic tolerance. Female gender, age younger than 60 years, educational level of high school or less and fear of pain during endoscopy predict high levels of nervousness prior to endoscopy.

DPEJ Tube Placement Prevents Aspiration in High-Risk Patients

Panagiotis H. Panagiotakis, M.D., Kristen Hilden, M.S., Maydeen Ogar, James A. DiSario, M.D., John C. Fang, M.D.* Gastroenterology, University of Utah, Salt Lake City, UT.
**Purpose:** Many patients with aspiration require feeding tubes. However, PEG feeding has not been shown to decrease aspiration. Feeding more distal in the GI tract may decrease aspiration risk. PEG-J is the most common procedure for providing more distal enteral feeding, however it also has not been shown to decrease the risk of aspiration and/or aspiration pneumonia and tube malfunction is common. Direct Percutaneous Endoscopic Jejunostomy (DPEJ) was developed to address the disadvantages of PEG-J feeding. There is no data on the incidence of aspiration and/or aspiration pneumonia before and after DPEJ placement in patients at risk for aspiration.

**Hypothesis:** DPEJ decreases aspiration and aspiration pneumonia in patients at risk for aspiration.

**Methods:** Retrospective review of all patients receiving DPEJ for aspiration from 1999 to the present. Demographics, incidence of aspiration/pneumonia and outcomes of were collected and compared before and after the DPEJ placement.

**Results:** 11 patients (4 women, 7 men) were identified with median age 37 (17–94). The indications were: neurologic disease (9), esophageal surgery (1) and severe debilitation (1). Median follow-up was 7 months (range 0–45). Weight increased from 44.5 kg (19–55.5) to 49.5 kg (30.5–62.7) after placement (p < 0.03). The total number of documented aspiration episodes decreased from 33 (median 3.0, range 1–6) before DPEJ placement to 3 (median 0, range 0–2) after the DPEJ placement, (p < 0.0001).

**Conclusions:** DPEJ placement may decrease recurrent aspiration and pneumonia in patients with a history of aspiration and/or pneumonia. [figure1]

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**The Impact of Rising Gasoline Price on Gastroenterology Clinic Show-Up Rate: A Longitudinal Study**

Houssam E. Mardini, M.D., Talal El Adhami, M.D., Alvero Koch, M.D., Willem J.S. de Villiers, M.D.* Gastroenterology, University of Kentucky, Lexington, KY.

**Purpose:** Transport is important as a means of gaining access to good quality healthcare services. However, the lack of public transport and limited income particularly of residents in many rural areas requires reliance on private transport. More than 90% of people living in rural areas use automobiles for travel to hospital; this compares with 70% of adults in urban areas. Gasoline prices have increased dramatically (50–60%) in the past 2 years particularly in 2004. The aim of the current study is to determine if the surge in gasoline prices influence the show up rate in a tertiary care center associated gastroenterology clinic that provides specialized care for a large population of residents in many rural areas.

**Methods:** A review of the clinic census between January 2003 and March 2005 was performed and the rates of new and follow-up patients show up were recorded. State specific regular gasoline prices over the same period of time were determined from the Energy Informations Administration web site, a sub division of the Department of Energy. Non-parametric tests were used to compare variables and correlations between monthly gas prices and the corresponding show up rate were assessed.

**Results:** 38% of our clinic patients have Medicare/Medicaid insurance and 54% have private/HMO insurance while the rest are self-paid. The median driving distance in our population (determined from a random sample of 100 patients selected from our data base) was 42 miles. The average gas price per gallon (before tax) was 1.094 in 2003, 1.38 in 2004 and 1.51 in the 1st quarter of 2005 (p = 0.0001). The average monthly number of patients scheduled during the period evaluated was 164 for new patients and 352 for follow up patients. The show up rate for new patients was 79.4 in 2003, 75.8 for 2004 and 74.9 for 2005 (p = 0.38). The show up rate for follow up patients was 74.3 in 2003, 71.6 in 2004 and 68.3 in 2005 (p = 0.06). Monthly gas prices significantly and inversely correlated with the show up rate for both new and follow up patients (r = −0.46 and −0.52; p = 0.028 and 0.016 respectively).

**Conclusions:** The significant rise in gasoline prices may have limited the access of certain population groups to health services. Further research is needed to determine the practical significance of our findings.

**Trends in Lack of Sigmoidoscopy or Colonoscopy in Screening for Colorectal Cancer in the United States**

Houssam E. Mardini, M.D., Talal El Adhami, M.D., Willem J.S. de Villiers, M.D.* Gastroenterology, University of Kentucky, Lexington, KY.

**Purpose:** Screening sigmoidoscopy or colonoscopy is recommended every 5–10 years for people aged 50 years or older. Despite its proven effectiveness, colorectal cancer screening is used far less than screening for other cancers. The aim of the current study is to assess recent trends in the prevalence of lack of screening sigmoidoscopy or colonoscopy in US population age 50 or older.

**Methods:** Data were collected from the reports on Risk Factors and Use of Preventive Services published by the National Center for Chronic Disease Prevention and Health Promotion (part of the Center for Disease Control). Chi-square test was used to compare proportions in a sample of a 1000 persons.

**Results:** Two reports assessing trends in 1999 and 2002 were reviewed. The prevalence of not having had a sigmoidoscopy or colonoscopy during the previous 5 years among Americans aged 50 years or older was 66% in 1999 and 60% in 2002 (p = 0.006) and ranged from 54% in Delaware to 77% in Nebraska in 1999 and 45% in Minnesota to 70% in Oklahoma and Wyoming in 2002. Women had significant improvement in their rate (69.2% in 1999 & 62.5% in 2002; p = 0.003) compared to men (62.7% & 58.3%; p = 0.33). White Americans reported the lowest rate both in 1999 (62.8% in 1999 and 58.3 in 2002) followed by Blacks (67.5% in 1999 vs 59.7% in 2002) and lastly Hispanics (70.5% in 1999 and 68.3% in 2002). Applying these proportions to a population of 1000 people, these trends would be significant in all groups except Hispanics.

**Conclusions:** The prevalence of lack of sigmoidoscopy or colonoscopy in screening for colorectal cancer in the United States has improved but remains very disappointing particularly in Hispanics. Education campaigns and strategies to improve access to preventive health services should be implemented.

**Health Resource Use and Medical Costs in Patients with Fecal Incontinence**

Elise M. Pelletier, M.S., Ann Karpierz, M.P.H., James Fleshman, M.D.* Health Economics and Outcomes Research, Boston Scientific Corporation, Natick, MA and Washington University, St. Louis, MO.

**Purpose:** While the majority of economic research on fecal incontinence (FI) has focused on patients with both urinary incontinence (UI) and FI, data on costs associated with treating patients with FI alone is limited. This study evaluated health outcomes, health resource use, and medical costs in non-UI patients with a diagnosis of FI.

**Methods:** All patients receiving a diagnosis of FI (ICD-9 787.6) in 2002 with no UI diagnosis (ICD-9 788.3, 625.6) were identified from a nationally representative private payer database. A matched cohort of non-FI patients
Risk of Death among Percutaneous Endoscopic Gastrostomy (PEG) Consult Patients

G. Koshy, M.D., I. Donnepudi, M.D., N. Kiyici, M.D., E. P. Norkas, Ph.D., H. Hertan, M.D., F.A.C.G.* Division of Gastroenterology and Dept. of Medical Research, Our Lady of Mercy Medical Center, Bronx, NY.

Purpose: There is limited data on which subset of patients will benefit most from feeding via PEG. The procedure was originally designed for use in patients with neurological disorders. With rising health care costs, the present trend is to use PEG to shorten length of stay (LOS) and to expedite discharge to the nursing home (NH).

Objective: To identify those variables that are likely to predict an increased risk of mortality in patients undergoing PEG.

Methods: sample of 191 consecutive patients [mean age of 81 yrs (range 49–105 yrs), 58% female and 81% from NH] referred for PEG placement between March 2003 and March 2005 were examined at our University teaching hospital. Twenty-one percent of patients were being seen for new PEG insertion vs.79% for replacement PEG. Data on patient age, gender, BMI, race, community vs. NH, new PEG vs. replacement, reason for PEG, MICU vs. floor, LOS, clinical lab values, comorbidity, nutritional status classification score and outcome (discharge vs. death) was collected.

Results: Logistic regression analysis determined that mortality was predicted by [figure1]but was not predicted by patient age, gender, community vs. NH, race, new vs. replacement PEG, asthma, cancer, CHF, dementia, diabetes, hypothyroidism or deep vein thrombosis.

Conclusions: This study identified 10 significant predictors of mortality among PEG consult patients. These findings could be useful in the evaluation of patients prior to PEG placement.

Quality Assessment of Colonoscopy—Colonoscopic Miss Rates for Colon Cancer in the Private Practice Setting

John F. Johanson, M.D.,* Sean Burke, M.D. Rockford Gastroenterology Associates, Rockford, IL.

Purpose: Data from the national polyp study indicates that surveillance colonoscopy with removal of adenomatous polyps reduces the incidence of colorectal cancer. Recent data from Canada indicates that 4% of patients with cancers located in the right colon had colonoscopy within 36 months of their diagnosis suggesting that these lesions may have been missed by colonoscopy. The aim of this study was to identify the rate of missed colon cancers in a large private practice to provide benchmark data for use in colonoscopy quality assessment programs.

Methods: Medical records were reviewed from a 13 man single specialty private practice group located in Rockford, IL. All partners are board certified and have all performed a minimum of 2,000 colonoscopies. Cecal intubation rates exceed 98% for all participating colonoscopists. Patients who developed colon cancer between 2003 and 2004 were identified. Colonoscopy records were reviewed and patients who had a previous colonoscopy between 6 and 36 months were considered to have missed lesions. Colonoscopies performed within 6 months of the diagnosis were considered to be the index procedure. Additional data collected included patient demographics, location of cancer, number of previous colonoscopies, and family history of colon cancer.

Results: During the period from 2003 to 2004, 16147 colonoscopies were performed. Colon cancer was identified in 206 patients for a rate of 1.3%. Of these 206, 10 (4.9%) had a colonoscopy between 6 and 36 months prior to their diagnosis suggesting that these lesions were missed. The mean age of these patients was 66.3 years with a range of 49 – 82 years; 8 were female and 2 males. 80% of the missed lesions were in the right colon and the other 20% in the rectosigmoid. Four of the six had a family history of colon cancer but none had a first degree relative.

Conclusions: The rate of missed colon cancers in a large private practice group is similar to that observed in other studies suggesting that this rate is likely to be accurate. This data can be utilized to provide a starting point for determining benchmark rates to be used in future quality assessment of colonoscopy.

INFLAMMATORY BOWEL DISEASE

Allopurinol Optimizes 6-Thioguanine Production in Inflammatory Bowel Disease Patients Not Responding to Azathioprine or 6-Mercaptopurine

Miles P. Sparrow, M.D., Scott A. Hande, M.D., Sonia Friedman, M.D., Sarah Reddy, M.D., Wee Chian Lim, M.D., Stephen B. Hanauer, M.D.* Department of Gastroenterology and Nutrition, University of Chicago Medical Center, Chicago, IL and Division of Gastroenterology, Brigham and Women’s Hospital, Boston, MA.

Purpose: At least 50% of IBD patients do not respond to 6-mercaptopurine (6-MP) and azathioprine (AZA). Many of these patients have (high) normal thiopurine methyltransferase (TPMT) activity and preferentially metabolize 6-MP to 6-methylmercaptopurine (6-MMP) instead of the active metabolite 6-thioguanine (6-TGN). The aim of this report is to describe the use of allopurinol, which competitively inhibits xanthine oxidase (XO), as a therapeutic adjunct in 6-MP/AZA non–responders to deliberately shunt metabolism of 6-MP towards the active metabolite 6-TGN.
Patients were defined as having chronic pouchitis (CP) if analysis showed that patients with post-operative complications (53%) were more likely to develop CP (p = 0.126). Multivariate analysis showed that patients with post-operative complications (53%) were more likely to develop CP (p = 0.06). Multivariate analysis showed that patients with post-operative complications (53%) were more likely to develop CP (p = 0.06). Multivariate analysis showed that patients with post-operative complications (53%) were more likely to develop CP (p = 0.06).

Conclusions: Chronic pouchitis (CP) is a frequent complication following IPAA. In this study patients with PSC or other EIMs of UC were not more likely to develop CP. Patients with post-operative complications following IPAA were more likely to develop CP and may benefit from early strategies to prevent pouchitis.

Methods: Fifteen outpatients from two tertiary referral IBD clinics who were clinical non-responders to 6-MP/AZA, and whose metabolite studies demonstrated preferential metabolism towards 6-MMP instead of 6-TGN were included. Eligible subjects were commenced on allopurinol 100 mg daily and the dose of 6-MP/AZA was, initially or subsequently, reduced to 25–50% of the original dose. Patients were then followed clinically and with serial metabolite measurements for 6-TGN and 6-MMP. The metabolite levels and white blood cell counts before and after commencing allopurinol were compared with the non-parametric Wilcoxon Signed Rank Test for matched pairs.

Results: After allopurinol was started, 6-TGN levels increased significantly from a mean of 185.73 (± standard error) ±17.7 to 385.4 ± 41.5 pmol/8 × 10^6 RBCs (p < 0.001) while 6-MMP decreased significantly from a mean of 10,380 ± 1,245 to 1,732 ± 502 pmol/8 × 10^6 RBCs (p < 0.001). The addition of allopurinol led to a significant decrease in WBC from a mean of 8.28 ± 0.95 to 6.1 ± 0.82 × 10^9/L (p = 0.01). Five patients developed leukopenia that resolved with thiourea dose reduction. All fifteen patients appeared to improve clinically, although formal disease activity assessments were not performed.

Conclusions: The addition of allopurinol to thiopurine non-responders demonstrating preferential shunting to 6-MMP metabolites appears to be an effective and safe means of shifting metabolism towards the active moiety 6-TGN. The exact mechanism of action is not known, but inhibition of TPMT by allopurinol is a hypothetical means of explaining these results. Follow up is necessary to determine clinical efficacy and safety of increasing 6-TGN levels.

**Predictors of Pouchitis Following Ileal Pouch Anal Anastamosis: A Retrospective Review**

Judit F. Collins, M.D., Katherine M. Hoda, M.D., Kandice L. Knigge, M.D., Karen E. Deveney, M.D.* Division of General Surgery and the Division of Gastroenterology/Hepatology, Oregon Health & Science University, Portland, OR.

**Purpose:** Primary endpoint is to determine risk factors that predict chronic pouchitis in those patients having ileal pouch anal anastomosis (IPAA.)

**Methods:** 237 patients with ulcerative colitis (UC) and undergoing IPAA by one surgeon at Oregon Health & Science University from 1993–2003 were evaluated. Data were gathered via retrospective chart reviews and by a questionnaire administered by telephone in 2004. Patients were excluded if there was less than one year follow-up documented in the chart or they could not be contacted by telephone (n = 63), post-operative diagnosis of Crohn’s disease (n = 3), failed ileoanal procedure (n = 1), and 1-stage IPAA (n = 3). Patients were defined as having chronic pouchitis (CP) or having no pouchitis (≤3 episodes of pouchitis) or having no pouchitis (≤3 episodes of pouchitis). Potential risk factors included number of operations used to perform IPAA, fulminant UC with 2-stage operation, duration of diverting ileostomy following pouch formation, primary sclerosing cholangitis (PSC), other extra-intestinal manifestations (EIMs) of UC, pre-operative liver function tests, duration of UC, and the occurrence of post-operative complications. Initial univariate analysis was performed on all risk factors. Multivariate analysis was performed on all univariate risk factors with p values < 0.2.

**Results:** The prevalence of CP in our population was 46%. The following variables were identified during univariate analysis and entered into a multivariate model: pre-operative serum albumin (p = 0.07), PSC (p = 0.126), duration of diverting ileostomy (p = 0.111), fulminant UC with 2-stage operation, (p = 0.05), and occurrence of post-operative complications (p = 0.007). Patients who did not undergo diverting ileostomy at the time of their IPAA trended towards a lower likelihood of developing CP (p = 0.06.) Multivariate analysis showed that patients with post-operative complications (53%) were more likely to develop CP (p = 0.009.) 8% of patients had PSC and 11% of patients had at least one EIM of UC. Patients with PSC and EIMs were not more likely to develop CP (p = 0.273, p = 0.126.)

**Conclusions:** Chronic pouchitis (CP) is a frequent complication following IPAA. In this study patients with PSC or other EIMs of UC were not more likely to develop CP. Patients with post-operative complications following IPAA were more likely to develop CP and may benefit from early strategies to prevent pouchitis.

**Hormonal Replacement Therapy after Menopause Is Protective of Disease Activity in Women with Inflammatory Bowel Disease**

Susananda V. Kane, M.D.,* Deepa Reddy, M.D. Department of Medicine, University of Chicago, Chicago, IL.

**Purpose:** The effect of menopause and hormone replacement therapy (HRT) has not been previously studied in patients with inflammatory bowel disease (IBD). Experimental data suggest that estrogen is a potent anti-inflammatory agent. The aim of our study was to assess disease course in women as it related to hormonal replacement therapy following menopause.

**Methods:** We performed a retrospective review of female IBD patients followed at a tertiary care center. Women who had documented loss of menses for at least one year with elevated FSH or who had undergone total abdominal hysterectomy with bilateral oophorectomy were eligible. Medical records were reviewed as well as patient interviews conducted when records were incomplete. Disease activity was measured using either the modified Truelove and Witts score for patients with ulcerative colitis (UC) or the CDAI for patients with Crohn’s disease (CD) at each visit. A flare was defined as an increase in score of at least 2 points in the Truelove and Witts score or a CDAI > 150. Information regarding age of onset of menopause, use of HRT, smoking, and medications used for the treatment of IBD were recorded.

**Results:** A total of sixty-five women were studied, twenty-five with UC and forty with CD. The average age of menopause was 48.2 years (range 38–53). Twenty-five patients had disease indices consistent with a flare within two years of menopause, 14/40 (35%) with CD and 11/25 (44%) patients with UC respectively. Twenty women (31%) in the cohort had a history of HRT use following menopause. The Odds Ratios for disease activity are presented below in Table 1. The Odds Ratio did not change when adjusted for use of immunomodulators or steroids, or type of preparation of hormonal therapy.

**Conclusions:** Women who were taking HRT were less likely to experience a flare of their disease in the first two years following the onset of menopause. This apparent protective effect is strengthened by the dose-response seen with extended vs. limited use. Studies with larger numbers of women observed for longer periods of time need to be done to verify this association. This research was sponsored by a research grant from Procter and Gamble Pharmaceuticals.

**Table 1.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio with 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ HRT use</td>
<td>0.18 (0.04–0.72)</td>
<td>0.001</td>
</tr>
<tr>
<td>+ HRT use and CD</td>
<td>0.22 (0.08–1.3)</td>
<td>0.07</td>
</tr>
<tr>
<td>+ HRT use and UC</td>
<td>0.16 (0.2–1.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>&lt; 1 year use</td>
<td>0.45 (0.12–1.7)</td>
<td>0.10</td>
</tr>
<tr>
<td>&gt; 1 year use</td>
<td>0.20 (0.07–0.65)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

**Thrombocytopenic Purpura Following Hemorrhagic Colitis Associated with Immunosuppressive Agents**

Giorgio Corinaldesi, M.D., Ph.D.,* Christian Corinaldesi, M.D. Medicina Generale, ASL 7, Ancona, Italy and Universita’ Politecnica delle Marche, Ancona, Italy.

**Purpose:** Treatment in refractory, relapsed aggressive hemorrhagic colitis is frequently unsatisfactory leading to prolonged hospitalisation and always severe complications occurring in patients undergoing intensive immunosuppressive agents particularly thrombocytopenia, anemia, and neutropenia.
Methods: Treatment of patients with extensive colitis in an advanced stage or not responder or short relapsed or refractory only to oral aminosalicylate drugs, is based upon immunosuppressive drugs such as high dose azathioprine 2.5mg/kg/day, or high dose mercaptopurine 15mg/kg/day, with mesalazine 500mg/twice daily and cortisone which can be used in foamy, enterocolitis, or intravenously (methylprednisolone 60mg/day), and/or cyclosporine 4mg/kg/day, TNF-alpha antagonist (pentoxifilline, infliximab, enterercept, onecept, and thalidomide), or else Fk 506 with micofenolate, or tacrolimus or sirolimus, and monoclonal antibodies such as dactilumab, basiliximab, natalizumab, or timoglobulins have demonstrated its effectiveness and the benefit in maintaining long term remission and an increased quality of life. However, the most frequent, serious, and toxic effect is myelo-suppression resulting in leukenopia, thrombocytopenia, and anemia that often occur in this patients; for the management will be necessary a tailored therapy on the basis of risk profile requiring a therapeutic approach with TPO, IL-1, IL6, SCF.

Results: We identified 4 patients with ulcerative colitis who has intractable intestinal bleeding; the initial treatment consisted of azathioprine (2.5mg/kg/day) and cyclosporine, all received mesalazine 500mg/twice daily, all patients notwithstanding the disappearance of hemorrhagic expressions showed a syndrome characterized by thrombocytopenia, microangiopathic hemolysis and transitory renal dysfunction, in particular it was the thrombocytopenia ( < 40.000 platelets with diffused purpura and several confluent mucol-papular plaques mainly acrodised), and microangiopathic hemolytic anemia.

Conclusions: Allogenic platelet concentrates for transfusion into bleeding thrombocytopenic patients and RBC transfusion if the patients is also anemic is a gold standard therapy, into the other approaches to treating thrombocytopenias we have preferred the recombinant activated factor VII (80mg/kg for the first dose following 120mg/kg every 3 hours for up to additional dose), and HLA-reduced platelet, novel strategies with platelet substitutes or platelet derived microparticles are under examination.

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Severity of Inflammation Predicts Progression to Colorectal Neoplasia in Ulcerative Colitis
Roopali Bansal, BA, Steven Itzkowitz, M.D., Noam Harpaz, M.D., Sabera Hossain, M.Sc., Sierra Matula, M.D., Carol Bodian, Ph.D., Thomas Ullman, M.D.∗ Medicine, The Mount Sinai School of Medicine, New York, NY and Pathology, The Mount Sinai School of Medicine, New York, NY.

Purpose: Although it has long been assumed that greater severity of inflammation (INF) predisposes to colorectal neoplasia in UC, to our knowledge demonstration of this concept has been limited to one case-control study.

Aim: To determine whether INF is an independent risk factor for neoplastic progression among patients (pts) with UC.

Methods: We studied a cohort of UC pts with a colonoscopic surveillance exam in 1996–7, who at that time had a disease duration ≥7 years, had no dysplasia detected on initial exam, and had ≥1 exam with histologic follow-up. We reviewed all available prior and subsequent pathology reports. Each biopsy site was scored for histologic degree of INF using a validated scoring system: 0 - no INF or quiescent/inactive colitis; 1 - mildly active; 2 - moderately active; 3 - severely active. Proportional hazards analysis was used to assess INF severity as a time-changing covariate to evaluate its effect on the endpoints advanced neoplasia (high-grade dysplasia, HGD or colorectal cancer, CRC) or any neoplasia (low-grade dysplasia, LGD, HGD, or CRC). For each colonoscopy, INF scores at each colonic site were summed and averaged.

Results: 418 pts met inclusion criteria. 92% had extensive UC; median [range] duration of UC at the time of inclusion was 16 [8.08] yrs, number of surveillance colonoscopies was 5 [2,17], time to advanced neoplasia was 5.8 [5,14.9] yrs, and the length of follow-up for the non-progressors was 6.7 [3,15] yrs. 18 progressed to advanced neoplasia; 74 progressed to any neoplasia. Using average cumulative INF over time as a time-changing covariate, univariate analysis demonstrated a significant relationship between severity of INF and development of advanced neoplasia (HR, 2.1; P < 0.05). A similar, albeit not significant trend was observed for progression to any neoplasia (HR, 1.3; P = 0.3). Excluding polypoid neoplasia as an endpoint (because these lesions are often managed conservatively with polypectomy), INF was significantly associated with progression to both advanced neoplasia (HR, 2.4; P = 0.03) and any neoplasia (HR, 2.0; P = 0.01). Other variables did not meaningfully alter the relationship of INF to progression in multivariable modeling.

Conclusions: This is the first cohort study demonstrating that severity of histologic inflammation over the course of surveillance in UC patients is a risk factor for developing colorectal neoplasia.
Methods: 18 pts with active Crohn’s disease were treated with 5mg/kg Infliximab infusion. CRP and CPT were assessed the day before treatment and at 4 and 8 week. All pts were in clinical remission at 8 weeks follow-up. Median CRP before treatment was 16 (N < 10 mg/L) and for CPT 2137 (N < 50 mg/kg). At week 4 and 8, the CRP and CPT levels were 3 and 3 mg/L vs. 235 and 48 mg/kg respect.

Results: Both CRP and CPT were elevated before treatment with Infliximab, but CRP was only elevated about 50% above the normal cutoff limit of 10 mg/L were as CPT was more than 40 fold increased. At follow-up, CRP normalized in 16/18 pts at week 4, and three showed elevated values at week 8. In contrast, the CPT levels dropped of more slowly than CRP which may reflected mucosal inflammation still present at week 4. At week 8, 9/18 pts showed normalization of CPT (< 50 mg/kg) indicating mucosal healing and 8 pts (two missing) had moderate elevated CPT levels indicating a persistent smoldering inflammation. All pts were in clinical remission.

Conclusions: Calprotectin appears to be more sensitive than CRP in determining the effect of Infliximab treatments and should be considered during stratification of pts in future drug trials.

Purpose: To study the characteristics of microscopic colitis as seen in a metropolitan community setting.

Methods: A retrospective study of patients seen between 1/95 – 1/2005 was undertaken via chart review from our private community practice.

Results: 32 patients were diagnosed with microscopic colitis, 22 (72%) female, 10 (22%) male. Mean age was 61 years, with a range of 10–83 years. 13 patients had collagenous colitis (CC), with a 5:1 female (F)/male(M) ratio. 15 patients had lymphocytic colitis (LC) with a 1:1 F/M ratio. 4 patients had both CC and LC on pathology with a 3:1 F/M ratio. 3 patients had concomitant celiac sprue, 2 with CC and one with LC; all were female. Diarrhea was of sudden onset in 47% and insidious in 53%. 22% patients had associated abdominal pain and 22% weight loss. Most cases were diagnosed within 6–8 weeks of onset of symptoms (75%), with 63% of patients having resolved diarrhea within 8 weeks. 66% patients had only a single episode of colitis, whereas 34% had either recurrent bouts (22%) or chronic continuous symptoms (12%). Prednisone was the most successful treatment followed by Entocort and azulfidine. Lomotil was only 50% effective.

Conclusions: Microscopic colitis is still uncommon, but in recent years the diagnosis is being made earlier because of better awareness of these disorders. It is primarily a disease of middle aged women, presents as a single episode in 66% of cases, and is almost uniformly responsive to low dose prednisone therapy. 10% of our patients had concomitant celiac sprue.

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Surveillance for Dysplasia in Patients with Ileal Pouch-Anal Anastomosis for Ulcerative Colitis: An Interim Analysis

Jorge D. Melendez, M.D., Carlos Jimenez, M.D., Esther A. Torres, M.D.∗
Carmen Gonzalez-Keelan, M.D., Juan J Lojo, M.D. Medicine, University of Puerto Rico School of Medicine, San Juan, PR; Pathology, University of Puerto Rico School of Medicine, San Juan, PR and Surgery, University of Puerto Rico School of Medicine, San Juan, PR.

Purpose: The risk of developing cancer in the ileal pouch-anal anastomosis (IPAA) of patients who had ulcerative colitis has not been defined. Some have found dysplasia within the pouch mucosa to be quite rare. Although some investigators suggest that pouch surveillance should be based on the results of previous histological assessments, there are no current guidelines for endoscopic surveillance of patients who have undergone IPAA for ulcerative colitis. The aim of our study was to investigate that risk and identify crucial time intervals to guide ileoanal pouch surveillance.

Methods: Endoscopy of the ileal pouch was performed in all consenting patients at 3, 6 and/or 12 months after their IPAA became functional. Pouch biopsies were taken to assess evidence of dysplasia. Biopsies were evaluated by a single pathologist using Riddell’s criteria to ensure standardized interpretation. Interim data analysis using descriptive statistics is reported here.

Results: Twenty nine patients have entered the study. The average patient age at 3, 6 and 12 months of surveillance were 40.7 (SD, 12.2; range, 21–67 years), 39.4 (SD, 13.0; range 21–68 years) and 40.1 years (SD, 12.8; range, 22–77 years) respectively. Average disease length was 8.0 years (SD, 6.8; range, 0.7–27.8 years). Nine of 29 cases (31%) had colonic dysplasia prior to IPAA surgery. Dysplasia within the pouch was reported in only one patient, 6 months after IPAA became functional. This patient demonstrated no evidence of dysplasia on further surveillance at 12 months or statistically divergence by age, duration of disease or history of colonic dysplasia prior to IPAA. No significant subgroup of patients with pouch dysplasia was identified to calculate cumulative risk or to perform comparative statistical analysis.

Conclusions: At this moment, evaluation of the results of long-term follow up of IPAA should precede any attempt to support routine surveillance. However, the finding of dysplasia early after surgery underscores the importance of early pouch surveillance in our population, at least until definite predisposing variables are identified.

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Lymphocytic and Collagenous Colitis in a Community Setting, a 10 Year Review

Douglas J. Sprung, M.D., F.A.C.G.∗ Gregory M. Sprung Medicine, Gastroenterology Group, Maitland, FL.

Methods: A total of 687 patients with mild to moderate UC were randomized into the study, of which 423 analyzable patients had moderate UC. Of these, 223 received 2.4 g/day (400 mg tablet) mesalamine, and 200 received 4.8 g/day (800 mg Tablet) Versus 2.4 g/day (400 mg Tablet): Analysis of Data from Two Randomized, Double-Blind Clinical Trials in Patients with Moderately Active Ulcerative Colitis

James F. Marion, M.D.∗ Michael Saffi, M.D., David A. Schwartz, M.D., Gino Regoli, M.D., Rachelle A. Eusebio, M.S., Linda Law, M.D. Dept of Medicine, Mt Sinai School of Medicine, New York, NY; Greater Cincinnati Gastroenterology Associates, Cincinnati, OH; Vanderbilt University, Nashville, TN and Procter & Gamble Pharmaceuticals, Cincinnati, OH.

Purpose: To evaluate the time to resolution of the cardinal symptoms associated with ulcerative colitis (UC) (stool frequency, rectal bleeding, and both stool frequency and rectal bleeding) in patients with moderately active UC taking mesalamine dosed at 4.8 g/day with an investigational 800 mg tablet, and 2.4 g/day dosed as a currently-marketed 400 mg tablet.

Methods: Data from 2 randomized, double-blind, 6-week, parallel-group studies (ASCEND I & II) conducted in patients experiencing a flare of active UC were pooled and analyzed. Time to resolution of UC symptoms was based on first day of resolution according to daily diaries kept by the patients through an integrated voice response system. In this pre-specified analysis, resolution of stool frequency (SF) was defined as a patient’s return to his/her normal number of stools per day, and resolution of rectal bleeding (RB) was defined as the absence of visible blood in stools. Results: A total of 687 patients with mild to moderate UC were randomized into the study, of which 423 analyzable patients had moderate UC. Of these, 223 received 2.4 g/day (400 mg tablet) mesalamine, and 200 received 4.8 g/day (800 mg Tablet) Versus 2.4 g/day (400 mg Tablet): Analysis of Data from Two Randomized, Double-Blind Clinical Trials in Patients with Moderately Active Ulcerative Colitis
g/day (800 mg tablet) mesalamine. The 2 treatment groups were balanced with regard to baseline and demographic characteristics, disease history, and baseline disease state characteristics. The 4.8 g/day dose was well tolerated and there was no increased risk of adverse events. Results of the median time to resolution analysis are shown in the figure. [figure 1]

**Conclusions:** Mesalamine at a dose of 4.8 g/day (800 mg tablet) significantly decreases the median time to resolution of RB and the composite of both SF and RB compared to mesalamine at a dose of 2.4 g/day (400 mg tablet) in patients with moderately active UC.

**The Frequency of C3435T MDR1 Gene Polymorphism in Iranian Patients with Ulcerative Colitis**

**Alma Farnood, M.D., Nosratollah Naderi, M.D., Babak Noorimayer, M.D., Seyed Javad Mirhasani Moghadam, M.D., Farzad Firoozi, M.D., Rahman Aghazadeh, M.D., Nasser Ebrahim Daryani, M.D., Mohammad Reza Zali, M.D., F.A.C.G.* IBD Department, Research Center for Gastroenterology and Liver Diseases, Shaheed Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran and Gastroenterology Department, Tehran University of Medical Sciences, Tehran, Islamic Republic of Iran.**

**Purpose:** To determine the frequency of C3435T polymorphism of MDR1 gene in Iranian patients with ulcerative colitis.

**Methods:** In a case-control designed study, 150 ulcerative colitis patients and 150 sex, age and ethnicity-matched controls were enrolled from a teaching hospital during a one year period (2002–2003). The C3435T polymorphism was assessed on DNA of peripheral blood leukocyte cells, by PCR (Polymerase Chain Reaction) and RFLP (Restriction Fragment Length Polymorphism) methods.

**Results:** The frequency of 3435T allele was significantly higher in ulcerative colitis patients compared with controls (p < 0.008, OR, 1.579, 95% CI, 1.126–2.217). The frequency of heterozygote genotype (C/T) was also significantly higher in patients with ulcerative colitis (p < 0.028, OR, 1.669, 95% CI, 1.056–2.638).

**Conclusions:** This study suggests that the higher frequency of 3435T allele has an association with ulcerative colitis in Iranian population as previously reported in western countries.

**The Frequency of Three Common Mutations of CARD15/NOD2 Gene in Iranian Patients with Inflammatory Bowel Disease**

Nosratollah Naderi, M.D., Alma Farnood, M.D., Farzad Firoozi, M.D., Mohammad Reza Rezavani, Ph.D., Arash Javeri, M.D., Ali Babari, M.D., Rahim Aghazadeh, M.D., Mohammad Reza Zali, M.D., F.A.C.G.* IBD Department, Research Center for Gastroenterology and Liver Diseases, Shaheed Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran.

**Purpose:** To evaluate the frequency of three main mutations of CARD15 gene (Arg 702 Trp, Gly 908 Arg and Leu 1007 fsinsC) in Iranian patients with Inflammatory bowel disease.

**Methods:** In a case control designed study, 100 ulcerative colitis patients, 40 Crohn’s disease patients and 100 sex, age and ethnicity-matched controls were enrolled from a teaching hospital during a one year period (2003–2004). Three mutations of CARD15 gene (Arg 702 Trp, Gly 908 Arg and Leu 1007 fsinsC) were assessed on DNA of peripheral blood leukocyte cells, by PCR (Polymerase Chain Reaction) and RFLP (Restriction Fragment Length Polymorphism) methods.

**Results:** Among the CARD15 gene mutations evaluated, only the Arg 702 Trp was associated with Crohn’s disease (p < 0.001, OR, 47.667; 95% CI, 5.967 – 380.779) in Iranian patients and none of these mutations had an association with ulcerative colitis.

**Conclusions:** This study shows that Arg 702 Trp mutation of CARD 15 gene has association with Crohn’s disease in Iranian population.

**Comparison of the Efficacy and Safety of SPD476, a Novel, Once-Daily, High-Dose Formulation of Mesalamine, and Asacol with Placebo for the Induction of Remission of Mild-Moderate Ulcerative Colitis: A Phase III Study**

Michael A. Kamm, M.D.,* William J. Sandborn, M.D., Miguel Gassull, M.D., Stefan Schreiber, M.D., Lechoslaw Jackowski, M.D. Department of Gastroenterology, St. Mark’s Hospital, London, United Kingdom; IBD Clinic, Mayo Clinic, Rochester, MN; Dept of Gastroenterology and Hepatology, Hospital Universitari Germans Trias i Pujol, Badalona, Spain; 1st Dept of Medicine, Christian-Albrechts-Universität, Kiel, Germany and NZOZ GCP; Dobra Praktyka Lekarska, Grudziadz, Poland.

**Purpose:** This double-blind, multi-centre study (MATRx2) compared the efficacy and tolerability of Asacol and SPD476, a novel formulation of mesalamine (5ASA) that uses multimeric (MMx) technology to deliver 5ASA (1.2 g/tablet) to the entire colon, with placebo.

**Methods:** 343 patients (pts) with mild-moderate ulcerative colitis (UC) were randomised to receive placebo, Asacol 2.4 g/d three times daily (0.8 g TID), SPD476 2.4g once-daily (QD) or 4.8g QD for 8 weeks.

**Results:** At week 8, a statistically significant greater proportion of pts receiving SPD476 2.4g QD or 4.8g QD achieved remission (defined as a UC disease activity index [UC-DAI] of ≤ 1 with a rectal bleeding and stool frequency score of 0 and ≥ 1-point reduction in sigmoidoscopy score from baseline [BL]) and clinical remission (complete resolution of symptoms) compared with placebo. Asacol was not statistically superior to placebo for either endpoint. A higher proportion of pts receiving active treatment achieved significant clinical improvement (reduction in UC-DAI score of ≥ 3 points from BL) vs placebo. Four pts (2 from placebo group) withdrew from the study due to disease-related adverse events.

**Comparison of the Efficacy and Safety of SPD476, a Novel, Once-Daily, High-Dose Formulation of Mesalamine, and Asacol with Placebo for the Induction of Remission of Mild-Moderate Ulcerative Colitis: A Phase III Study**

Gary R. Lichtenstein, M.D.,* Michael J. Kamm, M.D., William J. Sandborn, M.D., Prabhakar Boddu, MD, Natalia Gabergits, Ph.D. Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA; Dept of Gastroenterology, St. Marks Hospital, London, United Kingdom; Inflammatory Bowel Disease Clinic, Mayo Clinic, Rochester, MN; Dept of Gastroenterology, Osmania General Hospital, Afsalgunj, Hyderabad, India and Dept of Internal Diseases, Donetsk State Medical University, Donetsk, Ukraine.
Purpose: Current mesalamine (5ASA) preparations demand inconvenient multiple daily dosing. MATRx1 is a multicenter phase III, prospective, double-blind study to assess the efficacy and tolerability of SPD476, a novel formulation of 5ASA that uses multimatrix (MMx) technology to deliver 5ASA (1.2 g/tablet) to the entire colon.

Methods: 280 patients (pts) with acute, mild-moderate ulcerative colitis (UC) were randomised to receive placebo, SPD476 2.4 g/d twice-daily (1.2 g BID) or 4.8 g/d once-daily (QD) for 8 weeks. Intention to treat analysis (ITT) was performed for remission (primary endpoint: UC disease activity index [UC-DAI] of ≤ 1, with a rectal bleeding and stool frequency score of 0 and ≥ 1-point reduction in sigmoidoscopy score from baseline [BL]) at week 8 (W8) and clinical response (reduction in UC-DAI score of ≥ 3 points from BL).

Results: The percentage of pts achieving remission, clinical improvement, clinical remission and improved sigmoidoscopy score was statistically significantly higher for SPD476 2.4 g/d BID and 4.8 g/d QD compared to placebo. 79 pts withdrew from the study (41, 17, and 21, from the placebo, 2.4 g/d BID and 4.8 g/d QD groups). 7 serious AE were reported; 3 placebo, 4 SPD476 (aggravated UC [1], pancreatitis [2], viral gastroenteritis [1]). Only pancolitis was considered possibly or probably related to study medication.

Conclusions: SPD476 2.4 g/d BID or 4.8 g/d QD, using novel MMx technology, is effective and well tolerated for the induction of remission of mild-moderate UC. In comparison with the 2.4 g/d BID group, pts receiving 4.8 g/d QD tended towards better clinical response and sigmoidoscopic improvement. It is perceived that the efficacy and convenience of once daily SPD476 is likely to improve pt adherence and enhance treatment success.

Clinical Evaluation of Leukocytapheresis and Granulocyte/Monocyte Apheresis for Active Ulcerative Colitis
Masami Ogawa, M.D., Eisai Cho, M.D., F.A.C.G.* Kenjiro Yasuda, M.D., Masatsugu Nakajima, M.D. Gastroenterology, Kyoto Second Red Cross Hospital, Kyoto, Japan.

Purpose: The purpose of this study is to compare the efficacy of Leukocytapheresis (LCAP) and granulocyte/monocyte apheresis (GCAP) for active ulcerative colitis (UC).

Methods: We treated 26 patients with moderate to severe active UC with extracorporeal circulation therapy. From January 2003 to December 2003, GCAP was performed in 13 patients (7 men, 6 women). Ages ranged from 16 to 70 (mean 35.8) years. Extent of disease consisted of 9 of pan-colitis, 4 of left-sided colitis. Clinical types were 5 of first attack, 4 of relapse-remitting, and 4 of chronic-continuous. In LCAP apparatus, Cellsorba removes leukocytes and monocytes selectively. In LCAP apparatus, Cellsorba removes leukocytes non-selectively. Both extracorporeal circulation therapies were performed once a week for 5–10 weeks. In several severe patients, steroids were combined. We assessed the efficacy of both therapies as follows, (1) excellent; neither diarrhea nor bloody stool and remission by endoscopy, (2) effective; decrease number of bowel movement and bloody stool and improvement by endoscopy, (3) no change; unchanged clinical symptoms and endoscopic findings, (4) exacerbated; worsening of clinical symptoms or endoscopic findings. We assessed endoscopic findings according to Matts’ grading (Grade 1 to 4) before and after treatment.

Results: 7 of 13 patients had good response to GCAP (53.8%). There were 1 with excellent, 6 with effective, 3 with no change and 3 with exacerbated. Matts’ grading changed from 3.30 (mean) to 2.46 (mean). 9 of 13 patients responded well to LCAP (69.2%). There were 6 with excellent, 3 with effective, 3 with no change, and 1 with exacerbated. Matts’ grading became from 4.23 (mean) to 2.54 (mean) after treatment. Combination therapy with steroids was done for 7 in all improved patients with GCAP and for 3 in improved 9 patients with LCAP. Mean response time was 1.71 weeks with GCAP and 2.55 weeks with LCAP. The adverse effects were mild headache (3 with GCAP, 5 with LCAP), dizziness (2 with LCAP) and nausea (2 with LCAP).

Conclusions: GCAP and LCAP are safe and useful therapies for active UC. Extracorporeal circulation therapy, especially LCAP, could be the first choice of treatment alternative to steroid therapy in any stage of UC.

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Infliximab Results in Reduction of Inflammation and Inflammatory Markers in the Mucosa of Ulcerative Colitis Patients: The ACT 1 Trial
K. Geboes, M.D., P. Rutgeerts, M.D., A. Olson, M.D., C. W. Marano, Ph.D.* Dept of Pathology, Katholieke University Leuven, Leuven, Belgium; Dept of Internal Medicine, University Hospital Gasthuisberg, Leuven, Belgium; Clinical Research & Development, Centocor, Inc., Malvern, PA and Clinical Pharmacology & Experimental Medicine, Centocor, Inc., Malvern, PA.

Purpose: In ACT 1, effects of infliximab (IFX) on histological inflammatory activity and inflammatory markers in colonic mucosa of ulcerative colitis (UC) pts was assessed.

Methods: 364 pts with moderately-to-severely active UC (endoscopy score ≥ 2, Mayo score 6–12) despite corticosteroids or AZA /6-MP were randomized to placebo (PBO), IFX 5 mg/kg, or IFX 10 mg/kg at wks 0, 2, 6, 14, and 22. The primary endpoint was clinical response at wk 8 (decrease in Mayo score ≥ 30% and ≥ 3 points, with a decrease in rectal bleeding score of ≥ 1 or rectal bleeding score of 0 or 1, at wk 8). Colonic biopsies were collected at wks 0, 8, and 30 and formalin-fixed from ~35 pts per group. Hemotoxylin & eosin-stained sections were scored for inflammation severity by a blinded pathologist. HLA-DR, tenascin, CD3, myeloperoxidase (MPO), and gelatinase B (MMP-9) expression was evaluated by immuno-histochemistry.

Results: Baseline biopsies had histological features of inflammation characterized by neutrophils in the epithelium, crypt destruction, and the presence of ulcers and erosions (grade 3–5) (63.6% [PBO]; 76.4% [combined IFX])

Table 1. Inflammatory Marker Expression

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Biopsy collection time</th>
<th>PBO</th>
<th>Combined IFX</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wk 0</td>
<td>Wk 8</td>
<td>Wk 30</td>
</tr>
<tr>
<td>Pts HLA-DR positive</td>
<td>72.7</td>
<td>51.9</td>
<td>38.5</td>
</tr>
<tr>
<td>Increased tenasin patients (epithelium)</td>
<td>63.6</td>
<td>48.1</td>
<td>34.6</td>
</tr>
<tr>
<td>Increased tenasin patients (lamina propria)</td>
<td>60.6</td>
<td>55.6</td>
<td>42.3</td>
</tr>
<tr>
<td>CD3 positive*</td>
<td>14.0</td>
<td>15.6</td>
<td>16.4</td>
</tr>
<tr>
<td>MPO positive*</td>
<td>6.8</td>
<td>6.0</td>
<td>0.2</td>
</tr>
<tr>
<td>MMP-9 positive*</td>
<td>3.4</td>
<td>2.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*p Median proportion of cells staining positive
with ~ 11.9% with structural change only. At wks 8 and 30, 35% of IFX and 24% of PBO pts showed structural change unaccompanied by inflammatory changes (grade 0) which equals healing. These histological changes were accompanied by decreased expression of proinflammatory mediators that were more pronounced in the combined IFX group vs PBO (Table 1).

Conclusions: IFX promotes histological healing and down regulation of inflammatory changes. IFX induced down regulation of HLA-DR, tenascin, and CD3-, MPO- and MMP-9-positive cells at wk 8; only tenasin (indicating normal mucosa) and CD3 expression differed from PBO at wk 30.

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Infliximab Therapy for Pediatric Crohn’s Disease, a Long-Term Evaluation
Gary Fanjiang, M.D., M.B.A., Aubrey J. Katz, M.D.* Pediatric Gastroenterology & Nutrition, Tufts-New England Medical Center, Boston, MA.

Purpose: To assess response, complications, and effectiveness of long-term use of infliximab in pediatric patients with Crohn’s disease.

Methods: The charts of 93 pediatric patients with Crohn’s disease who were treated with infliximab for up to 6 years were reviewed. The Pediatric Crohn’s Disease Activity Index (PCDAI) was calculated at 0, 1 and 2 months after infliximab and at yearly intervals for the duration of their follow-up. Patients were successfully treated if they tolerated infliximab, were weaned off steroids, and avoided surgery.

Results: Seventy percent of patients were successfully treated. Of successfully treated patients, 22% required an increased infliximab dose of 10 mg/kg and 24% were weaned off infliximab. Seventeen percent of patients failed therapy because they required surgery; 6% could not be weaned off steroids; and 5% could not tolerate infliximab therapy (after mean of 8.8 infusions). Patients had a mean of 13 (range 2–41) infliximab infusions with a mean follow-up of 7 (range 1–44) months after their last infusion. Successfully treated patients had a mean follow-up of 5 (range 1–44) months after receiving a mean of 15 (range 3–41) infusions. Patients who failed infliximab had a mean follow-up of 13 (range 1–36) months after receiving a mean of 9 (range 2–20) infusions. By 1 month, the mean PCDAI improved from 31.9 to 8.6 (p = 0.0001). By 2 months, the mean PCDAI improved to 4.5 (p = 0.0001) with persistently improved scores thereafter. The mean PCDAI of successfully treated patients improved from 30.1 to 7.1 at 1 month and 3.7 at 2 months (p = 0.0001). Patients who failed infliximab had mean PCDAI improve from 36.5 to 12.4 at 1 month and 6.7 at 2 months (p = 0.0001). The net PCDAI change in successfully treated patients after 2 months was not significantly different than those who failed (p = 0.20). The mean daily prednisone dose in all patients decreased from 16.6 to 5.7 mg by 2 months (p = 0.0001). Patients who were successfully treated were able to significantly wean their prednisone more during the first 2 months compared to those who failed (p = 0.04).

Conclusions: (1) Infliximab is an effective therapy for pediatric patients with Crohn’s disease. (2) Increasing the infliximab dose in patients who did not initially respond may improve its effectiveness. (3) The ability to wean steroids during the first 2 months may predict the long-term success of infliximab. (4) Some patients can be successfully weaned off infliximab. Long-term maintenance therapy with infliximab may thus be unnecessary although further studies are needed.

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Response and Remission Are Associated with Improved Quality of Life in Patients with Ulcerative Colitis
Robarts Research Institute, University of Western Ontario, London, Canada; Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN; Roberts Research Institute, University of Western Ontario, London, Canada; Division of Gastroenterology and Hepatology, University Hospital Vienna, Vienna, Austria; Outcomes Research, Centocor, Inc., Malvern, PA and Division of Gastroenterology, Hospital Leuven, Leuven, Belgium.

Purpose: To examine the impact of infliximab (IFX) on health related quality of life (HRQL) in ulcerative colitis (UC) patients.

Methods: 728 pts were enrolled in two trials: ACT 1 and 2. Pts were randomized (1:1:1) to placebo (PBO), IFX 5 mg/kg, or IFX 10 mg/kg. Treatment was administered at baseline, wks 2, 6, and then q8 wks. HRQL was assessed using the inflammatory bowel disease questionnaire (IBDQ) and the Short Form 36 questionnaire (SF-36). Analysis of variance on van der Waerden scores was used to compare the groups, on the pooled data from the trials.

Table 1. Wk 30 Mean Total IBDQ, PCS, and MCS Scores and Change from Baseline

<table>
<thead>
<tr>
<th></th>
<th>Nonresponder (NR) (n = 137)</th>
<th>Respondersa (n = 150)</th>
<th>Remission (n = 206)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Mean change</td>
<td>Mean</td>
</tr>
<tr>
<td>IBDQ</td>
<td>143.0</td>
<td>11.7</td>
<td>137.3</td>
</tr>
<tr>
<td>PCS</td>
<td>39.8</td>
<td>1.7</td>
<td>45.1</td>
</tr>
<tr>
<td>MCS</td>
<td>44.1</td>
<td>3.8</td>
<td>48.8</td>
</tr>
</tbody>
</table>

aResponders not in remission; *p < 0.001 vs NR.

Conclusions: Pts who achieved remission/response had significantly greater improvements in HRQL than non-responders. Pts in remission had HRQL scores similar to the general U.S. population.

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Infliximab Therapy Improves Health Related Quality of Life in Ulcerative Colitis Patients
Robarts Research Institute, University of Western Ontario, London, Canada; Division of Gastroenterology, Hospital Leuven, Leuven, Belgium; Department of Gastroenterology and Nutrition, University of Chicago, Chicago, IL; Outcomes Research, Centocor, Inc., Malvern, PA; Biostatistics, Centocor, Inc., Malvern, PA; Clinical Research and Development, Centocor, Inc., Malvern, PA and Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

Purpose: To examine the impact of infliximab (IFX) on health related quality of life (HRQL) in ulcerative colitis (UC) patients.

Methods: 728 pts were enrolled in two trials: ACT 1 and 2. Pts were randomized (1:1:1) to placebo (PBO), IFX 5 mg/kg, or IFX 10 mg/kg. Treatment was administered at baseline, wks 2, 6, and then q8 wks. HRQL was assessed using the inflammatory bowel disease questionnaire (IBDQ) and the Short Form 36 questionnaire (SF-36). Analysis of variance on van der Waerden scores was used to compare the groups, on the pooled data from the trials.
Results: Baseline IBDQ and SF-36 scores were similar among groups. The baseline mean total IBDQ score was 126. The baseline mean physical and mental component summary scores (PCS = 39 and MCS = 41) of the SF-36 were ~1 standard deviation below the general U.S. population means (50), indicating impaired HRQL. At wk 8 and wk 30, the combined IFX group had greater improvements (p < 0.001, Table 1) from baseline in total IBDQ, PCS, and MCS scores vs PBO. All 4 IBDQ dimensions had improvements in the combined IFX group vs PBO (p < 0.001), at both time points. All 8 scales of the SF-36 showed improvement in the combined IFX group vs PBO at both timepoints, with significance (p < 0.05) in all but one scale at wk 30 (role-emotional, p = 0.081). There were no notable differences between the trials or the IFX groups.

Table 1. Mean (Median) Improvements from Baseline in Total IBDQ, PCS, and MCS Scores

<table>
<thead>
<tr>
<th>Pts randomized</th>
<th>PBO 5 mg/kg</th>
<th>IFX 5 mg/kg</th>
<th>IFX 10 mg/kg</th>
<th>IFX combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>WK 8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBDQ</td>
<td>21 (15)</td>
<td>40 (39)</td>
<td>36 (33)</td>
<td>38 (35)</td>
</tr>
<tr>
<td>PCS</td>
<td>3.7 (0.3)</td>
<td>6.8 (5.7)</td>
<td>5.9 (4.5)</td>
<td>6.4 (5.1)</td>
</tr>
<tr>
<td>MCS</td>
<td>3.0 (0.0)</td>
<td>5.9 (3.1)</td>
<td>6.4 (3.8)</td>
<td>6.1 (3.5)</td>
</tr>
<tr>
<td>WK 30</td>
<td>18 (0)</td>
<td>33 (24)</td>
<td>35 (32)</td>
<td>34 (28)</td>
</tr>
<tr>
<td>IBDQ</td>
<td>3.0 (0.0)</td>
<td>5.6 (4.0)</td>
<td>5.4 (2.8)</td>
<td>5.5 (3.3)</td>
</tr>
<tr>
<td>MCS</td>
<td>3.8 (0.0)</td>
<td>5.3 (1.6)</td>
<td>7.2 (4.1)</td>
<td>6.2 (2.7)</td>
</tr>
</tbody>
</table>

Compared to Placebo: a−p < 0.001; b−p < 0.01; c−p < 0.05; d−p = 0.066.

Conclusions: IFX 5mg/kg or 10mg/kg results in substantially improved HRQL vs PBO, as measured by both disease specific and generic instruments.

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5-Aminosalicylates Are Associated with Higher 6-Thioguanine Levels in Stable IBD Patients on Azathioprine or 6-Mercaptopurine

Scott Hande, M.D., Noah Wilson-Rich, B.S., Rie Maurer, Athos Bousvaros, M.D., Sonia Friedman, M.D.* Gastroenterology, Brigham and Women's Hospital, Boston, MA and Gastroenterology, Children's Hospital, Boston, MA.

Purpose: Small uncontrolled trials have suggested that 5-aminosalicylate (5-ASA) medications increase 6-thioguanine (6-TG) nucleotide levels in adults with Inflammatory bowel disease (IBD). We sought to characterize the relationship between AVN, IBD, and corticosteroid therapy.

Methods: This retrospective cohort study, we identified all children and adults treated with AZA or 6-MP for IBD at two institutions. Patients were included if TPMT genotype was known and 6-TG and 6-MP levels had been measured after at least 3 months of clinical remission in the absence of steroids, infliximab, or other immunomodulators. 6-MP dosage (mg/kg) was determined for each patient, using standard conversion factor for AZA (2.07). 6-TG and 6-MP levels were compared between patients taking a 5-ASA medication and those who were not. Linear regression was used to evaluate and adjust for potentially confounding variables.

Results: 120 patients were included, with median age 21 (range 6–79). 65 (54%) patients were male. 94 (78%) had a diagnosis of CD, 26 (22%) had UC. 84 (70%) were taking a 5-ASA medication (median dose 51mg/kg, range 25–87 mg/kg). 111 (92%) were TPMT genotype +/− and 9 (8%) were TPMT −. Patients on a 5-ASA agent had a significantly higher mean 6-TG level compared with those who were not (248.2 vs 195.7 pmol/8 × 10^8 RBCs, p = 0.0248) despite comparable mean 6-MP dosage (1.12 vs 1.16 mg/kg, p = 0.6358). This difference remained significant when adjusted for IBD type and TPMT genotype (p = 0.0122). Age, gender, institution, and choice of AZA/6-MP had no effect on mean 6-TG levels (all p-values > 0.1).

Conclusions: 5-ASA therapy is associated with higher mean 6-TG levels in children and adults with UC or CD in remission on AZA or 6-MP. These data suggest that 5-ASA medications can be used with AZA or 6-MP to increase 6-TG levels. 5-ASA agents may be helpful in patients who are 6-MP refractory due to preferential metabolism towards the 6-MMP pathway.

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Crohn’s Perianal Fistulas and the Incidence of Fecal Incontinence

Arnab Ray, M.D., Chase Herdman, M.D., Tatsuki Koyama, Ph.D., Alan J. Hertline, M.D., Paul E. Wise, M.D., Roberta Muldoon, M.D., David A. Schwartz, M.D.* Gastroenterology, Vanderbilt University Medical Center, Nashville, TN; Surgery, Vanderbilt University Medical Center; Nashville, TN and Biostatistics, Vanderbilt University, Nashville, TN.

Purpose: Crohn’s disease (CD) perianal fistulas can cause significant morbidity including fecal incontinence. The rate of fecal incontinence in these patients varies in the literature. The purpose of this study was to assess the rate of fecal incontinence in pts with CD perianal fistulas and to determine if there is a difference in outcomes between those pts who have undergone primarily medical or surgical treatment for their perianal disease.

Methods: The medical records of pts who presented to the GI Clinic at a single academic medical center between 1/01 and 1/04 with perianal CD were reviewed. Demographic data and information regarding treatment was recorded. Mailed questionnaires and telephone interviews were conducted to determine the Fecal Incontinence Severity Index (FISI) score and patient satisfaction.

Results: Of 77 pts identified with CD perianal fistulas, a total of 40 (52%) completed the questionnaire. 25 (63%) pts had surgical treatment while 15 had medical treatment only. The baseline demographic data was similar in both groups. The overall rate of fecal incontinence was high with 64% of all pts having ≥ 1 episode a week of solid stool incontinence. There was no difference between the medical and surgical cohorts (67% vs. 60%; p = 0.75). The median FISI for the medical group was 37, (range 0–59) while the median FISI for the surgical cohort was 33 (range 4–56; p = 0.54). The type of surgical treatment did not affect outcome. Surgical pts who had less invasive operations (incision and drainage or seton placement) had a median FISI of 31, and pts who underwent more aggressive surgical treatment (fistulotomy, fistulectomy, or advancement flap) had a median FISI 42 (p = 0.52). Surgical pts were asked to rate their degree of satisfaction (1 = poor and 5 = excellent). Pearson’s product moment analysis revealed there was not a strong relationship between level of satisfaction and FISI score (correlation = 0.6, p = 0.78). The rate of fecal incontinence in pts with perianal CD is high. There is not a significant difference in the degree of fecal incontinence between pts treated medically or surgically for perianal CD, nor is there a significant difference in fecal incontinence with the different surgical procedures. Surgical pts with higher FISI scores are not necessarily less satisfied with their surgical results.

Conclusions: The rate of fecal incontinence in pts with perianal CD is high. There is not a significant difference in the degree of fecal incontinence between pts treated medically or surgically for perianal CD, nor is there a significant difference in fecal incontinence with the different surgical procedures. Surgical pts with higher FISI scores are not necessarily less satisfied with their surgical results.
Methods: A centralized diagnostic index identified all patients (pts) with IBD and AVN evaluated at Mayo Clinic Rochester between 1976 and 2003. Medical records were abstracted for pt demographics, subtype and duration of IBD, treatment received including corticosteroids, other potential AVN risk factors, AVN stage and joints involved, and AVN treatment and outcomes. Results: We identified 52 ulcerative colitis patients (71% male) and 42 Crohn’s disease patients (52% male). Median age at AVN diagnosis (dx) was 45.9 years (ys) (range, 16.5–82.2), and median duration from IBD to AVN dx was 9.2 ys (0.5–41.2). Of all 94 pts, only 6 pts (6%) had no history of systemic corticosteroid exposure. Steroid-naïve IBD-AVN pts were older at both IBD dx (51.8 ys) and AVN dx (67.3 ys) than steroid users. All 88 steroid users had received oral corticosteroids, and 26 had also received IV steroids (24%). Among pts with available data, median cumulative duration of steroid therapy prior to AVN dx was 12.2 months (range, 2–70.2), median daily prednisone dose was 20.4 mg (12.1–50), and median cumulative prednisone dose was 9,205 mg (2,770–42,660). Overall, 41% had a prior arthropathy and 40% had a history of smoking, with similar rates for those with and without corticosteroid use. The mean number of joints involved was 2.3 among those who had received steroids (55% femoral head, 23% upper extremities) versus 1.2 among those who had not (57% femoral head, 0% upper extremities). The prevalence of stage III-IV AVN was 77% in steroid users versus 67% in the steroid-naïve. Median follow-up time after AVN dx was 4.4 ys (0–27.3). Treatment included arthroplasty in 36%, conservative therapy in 20%, core decompression in 10%, and bone grafting in 7%. Despite treatment, 16% of pts developed worsening symptoms, and 17% had AVN involvement of new joints—none of this progression was seen in the 6 steroid-naïve pts. Conclusions: Osteonecrosis is a rare but serious complication seen in IBD. In a minority of pts, AVN may occur in the absence of corticosteroid therapy. These pts are older at IBD and AVN dx, have fewer joints involved, and have less progression of the joint disease. The etiology of AVN may be multifactorial with contributions from IBD itself, systemic corticosteroid therapy, and other AVN risk factors.

Long Term Remission of Crohn’s Disease Using Infliximab without Human Anti-Chimeric Antibody (HACA) in Absence of Anti-Metabolites

Kevin T. Kao, M.D., Amy McClune, M.D., Chris N. Contreas, M.D.* Division of Gastroenterology, Department of Medicine, Southern California Kaiser Permanente Medical Group, Los Angeles, CA.

Purpose: Optimal medical management of Crohn’s disease has long been a challenging process. Currently, it is common practice to “stack” medica- tions to induce remission by starting with the less toxic 5-aminosalicylic acid, then adding Azathioprine or 6-mercaptopurine and finally Infliximab. Concomitant immunosuppressive therapy is employed to reduce the magni- tude of the immunogenic antibody response to Infliximab so as to enhance its medical efficacy (Baert F. et al NEJM 348:601–8). However the use of multiple agents, especially the immunomodulators, is not without its downsides such as cost, compliance, drug interactions and intrinsic toxicity of the medica- tions. Given these concerns, it can be hypothesized whether Infliximab either alone or in combination with a less toxic first line agent could suffi- ciently control disease without the use of immunomodulators. Additionally, if a serial rather than random infusion method of Infliximab administration is employed, is there a lower rate of both infusion reactions and formation of HACA in the absence of immunomodulators?

Methods: We reviewed our Crohn’s patients taking Infliximab who for med- ical reasons could not use an anti-metabolite. Between the years 2000 to 2005, we were able to identify 3 patients from the hospital and clinics of the Kaiser Permanente Medical Center at Los Angeles who have clinically moderate/severe Crohn’s disease and were placed on Infliximab (1 patient) or a combination of Infliximab and Mesalamine (2 patients). All were place on the standard regimen of 5 mg/kg infusions at 0, 2, and 6 weeks with maintenance dosing every 8 weeks for 3, 4 and 2 years respectively.

Results: All 3 patients are in remission clinically without the usage of im- munomodulators. No significant side effect from Infliximab, measurable level of HACA or infusion reaction was reported in any of the 3 patients.

Conclusions: In conclusion, serial infusion of Infliximab in treatment of moderate to severe Crohn’s disease seems to be well tolerated within our small sample population of patients who are not taking immunomodulators. Despite the limited data, clinical remission in all of our patients suggests that Infliximab, by itself or in combination with other less toxic classes of medications can achieve and maintain clinical remission in moderate to severe Crohn’s disease using continual therapy rather than infusions as needed to treat flares.

P53 Mutations Are Associated with Dysplasia and Progression of Dysplasia in Patients with Crohn’s Disease

Jeffrey W. Nathanson, M.D., Jeanne Farnan, M.D., Nicole Yadron, BA, Sydney Glynear, John Hart, M.D., David T. Rubin, M.D.* Department of Medicine, Section of Gastroenterology, University of Chicago Hospitals, Chicago, IL.

Purpose: Patients who have long-standing inflammatory bowel disease (IBD) are at risk of developing colorectal cancer (CRC). In ulcerative colitis, studies have suggested that mutations in the tumor suppressor gene p53 are associated with pre-cancerous dysplasia and CRC, but little is under- stood of the genetic mutations in Crohn’s disease (CD) that contribute to this transformation. The purpose of this study was to evaluate the utility of p53 immunohisto- chemical (IHC) staining as a marker of dysplasia in CD patients.

Methods: Using existing tertiary center pathology and IBD databases, we performed a retrospective review of all CD patients who underwent p53 IHC staining of endoscopic biopsies or surgical resections between 1995 and 2003. Clinical variables including duration of disease, length of follow- up, and degree of dysplasia were reviewed. Fisher’s exact test was used to determine differences between p53 positive and p53 negative patients.

Results: 14 CD patients had p53 IHC staining of colon (13) or ileum (1). p53 mutations were found in 8 patients (p53-+) and were absent in 6 patients (p53-). 7 out of 8 p53+ patients had histologic evidence of dysplasia (6 with low-grade dysplasia (LGD), 1 with high-grade dysplasia (HGD)) while only 1 out of 6 p53- patients had dysplasia (LGD) (p = 0.03). There was no significant difference between the two groups in gender (female: 6/8 vs. 4/6; p = NS), mean age of onset of CD (27.1 y vs. 27.7 y; p = NS) or in the mean duration of disease at the time of p53 staining (17.0 y vs. 17.0; p = NS). In each group, four patients had subsequent surveillance exams or surgical resections. In the p53+ group, 2 out of 4 patients progressed from LGD to HGD after 0.5 y and 2.25 y, respectively, and were referred for partial colectomy. In the p53- group, 3 patients without dysplasia on initial biopsy did not progress to dysplasia after 1 y, 1 y, and 7 y, respectively. The one p53- patient with LGD on initial biopsy underwent colectomy and had no evidence of dysplasia in the surgically resected specimen.

Conclusions: p53 mutations in CD patients are associated with dysplasia in this population and may predict progression to a higher grade of dysplasia over time. Testing for p53 mutations may aid in stratification of CD patients at risk for CRC.

This research was funded in part by Proctor & Gamble.

An Evaluation of Vaginal Symptoms in Women with Crohn’s Disease

Marie L. Borum, M.D., EBD, M.P.H.,* Deborah B. Graham, M.D., Todd N. Witte, M.D. Division of Gastroenterology, Department of Medicine, George Washington University, Washington, DC.

Gynecologic involvement has been reported as a manifestation of Crohn’s disease. However, there is limited available data addressing the frequency of vaginal complaints in women with Crohn’s disease. This study assessed the
frequency of vaginal involvement and types of vaginal symptoms in women with Crohn’s disease managed at a university inflammatory bowel disease program.

Consecutive women with Crohn’s disease seen during a 3 month period at a university inflammatory bowel disease program were evaluated for the presence of vaginal involvement. The intestinal distribution of Crohn’s disease [colonic, small bowel (SB), colonic/SB] was determined. The presence of vaginal symptoms and types of complaints were assessed. All women with a history of Crohn’s disease were included in the study. There were no exclusion criteria. Statistical evaluation was performed using chi-square analysis.

Fifty women with Crohn’s disease were seen at a university inflammatory bowel clinic during a 3 month period. Twenty-three women had colonic involvement, 7 had SB involvement, 20 had colonic/SB involvement. Eleven of the fifty women (22%) described vaginal symptoms (8 with colonic disease, 1 with SB disease, 2 with colonic/SB disease). Vaginal complaints included labial swelling concurrent with intestinal symptoms (7 with colonic disease, 2 with colonic/SB disease), labial swelling and pain without intestinal symptoms (1 with SB disease and labial granulomas on biopsy) and stool passage through the vagina (1 with colonic disease and fistulas). All women with labial swelling concurrent with intestinal symptoms also had perineal manifestations. There was a significant difference (p < 0.001) between the women with and without vaginal complaints. Women without vaginal complaints had no perineal disease or fistulating complications.

This study suggests that vaginal involvement in Crohn’s disease may be a more frequent phenomenon than previously reported. Most of the women with vaginal symptoms had perineal involvement. However, granulomatous infiltration and fistulization can also result in vaginal complaints. Further study is needed to assess the prevalence of vaginal symptoms in women with Crohn’s disease. Increased awareness of vaginal involvement can enhance knowledge regarding disease manifestations and can potentially improve the management of women with Crohn’s disease.

**Conclusions:**

The sub-analysis confirms previous trial experience that inclusion of patients with mild baseline UC may significantly impact the placebo response rate and therefore has the potential to impact the outcome of the study. Careful consideration should be given in future studies to exclude patients with mild baseline disease activity. [figure1]
Long-Term Safety of Fully Human Anti-TNF Adalimumab in Worldwide Rheumatoid Arthritis Clinical Trials

M. H. Schiff, M.D.*, G. R. Burmester, Prof Dr. Med., A. L. Pangan, M.D., H. Kupper, M.D., G. Spencer-Green, M.D., J. D. Kent, M.D. Research, Denver Arthritis Clinic PC, Denver, CO; Rheumatology, Charité University Medicine, Berlin, Germany; Immunology, Abbott, Abbott Park, IL; Rheumatology, Abbott GmbH & Co. KG, Ludwigshafen, Germany and Immunology, Abbott, Parsippany, NJ.

Purpose: To assess the safety of adalimumab in the long-term treatment of patients with rheumatoid arthritis (RA) in randomized controlled trials (RCT), open-label extensions (OL), and in the Phase IIIb Act (US) and ReAct (EU) trials.

Methods: All patients with RA in adalimumab RCT were eligible to enroll in OL. Safety data were collected at each visit from all patients in RCT/OL/Act/ReAct and reported via routine methodology. Rates of serious adverse events (SAE) were tabulated in events per 100-patient-years (E/100PY) of exposure.

Results: As of Aug. 31, 2004, 10,050 patients (12,066 PY) with long-standing RA had enrolled in adalimumab RCTs worldwide; of these, 271 had ≥5 years of adalimumab exposure. Baseline characteristics were indicative of moderate to severe RA. Rates of selected SAE observed in RCT/OL/Act/ReAct trials were comparable to rates reported as of Aug. 31, 2002 (table) and to published rates of adalimumab safety in global RA clinical trials(1). Overall, the rate of serious infections observed was comparable to rates in published reports of RA patients treated with DMARDs, including TNF antagonists(2,3). Cancer rates were similar to expected rates reported in the National Cancer Institute's Surveillance, Epidemiology, and End Results database. The standardized mortality ratio for adalimumab-treated patients was 0.6 when compared to age-matched controls.

Conclusions: The adalimumab safety profile in RA clinical trials was stable over time. Rates of AE were comparable to rates in adalimumab-naïve RA populations—no new safety signals were identified. There was no apparent drug-associated mortality.


Infliximab vs. Hydrocortisone for Crohn’s Disease Patients Requiring Hospitalization

Jyoti K. Bhattach, M.D., Burton I. Korelitz, M.D., M.A.C.G.,* Georgia Panagopoulos, Ph.D., Efrat Lobel, M.D., Felice Mirsky, M.D., Keith Sultan, M.D., William DiSanti, M.D., Alexander Chun, M.D., Greg Keenan, M.D., Khalid Mamun, B.S. Division of Gastroenterology, Department of Medicine, Lenox Hill Hospital and New York University School of Medicine, New York, NY and Centocor Inc., Malvern, PA.

Purpose: Clinical response measured for a group of patients hospitalized for severity of their Crohn’s disease (CD) who received infliximab (IFX) as first-line therapy is compared to data from a previously published study wherein hydrocortisone was used under the same circumstances.

Methods: In the IFX study, patients aged >17 with a CD of ≥3 months, a Crohn’s and Colitis Foundation of America-International Organization of Inflammatory Bowel Disease (CCFA-IOIBD) score >5, and who had not received IFX for >8 weeks prior to study entry but were receiving stable dose of steroids or other immunomodulators for at least 2 weeks were eligible for the study. A single therapeutic goal was selected for each patient including: elimination of bowel symptoms (12 patients), closure of fistula (2), reduction of abdominal mass (1), and treatment of pyoderma gangrenosum (1). IFX 5mg/kg was administered on admission after negative PPD. Sixteen patients that received IFX were matched to 16 who received hydrocortisone based on a similar goal of therapy. Response was measured by the CCFA-IOIBD score on days 0, 3, 5 and at discharge for patients in the two groups. Admission IOIBD score for the IFX and hydrocortisone group were 13.5(4.4) and 17.8(7.1) respectively. Clinical response guided by that score coincided with a 50% reduction in the score. Patients were discharged at the physician’s discretion when the established goal was achieved.

Results: It was observed that there was no difference in regard to response to treatment during hospitalization between the two groups. On average, the IFX group showed clinical response by 4 ± 2.6 days. This coincided with a mean score of 7 ± 3 or a 48% reduction in the CCFA-IOIBD score, while the hydrocortisone group showed clinical response by 8.4 ± 2.6 days with a mean score of 6 ± 3.2 or a 66% reduction by discharge. Median duration of hospitalization was 4 days for the IFX group & 8 days for the hydrocortisone group. This difference was statistically significant: p < 0.001.

Conclusions: IFX may be as effective as hydrocortisone when used in sick patients with Crohn’s disease requiring hospitalization. Patients receiving IFX may anticipate a shorter hospitalization and an early opportunity to consider an alternate form of therapy when it fails.

The Treatment of Pediatric Ulcerative Colitis with Infliximab, a Long-Term Evaluation


Purpose: We evaluate the indications for infliximab to treat pediatric ulcerative colitis (UC) and report long-term follow-up.

Methods: The charts of 27 pediatric patients with UC who were treated with infliximab were reviewed. All patients would have otherwise been candidates for colectomy. The acute group included patients with new onset UC refractory to IV steroids for 5–7 days and patients with non-steroid dependent UC with a fulminant exacerbation; the chronic group included patients with chronic steroid dependent UC. Lichtiger colitis activity index (LCAI) was measured for all patients at 0, 1, and 2 months after infliximab. Patients were considered as successfully treated if they remained off steroids and avoided colectomy.

Results: The acute and chronic groups included 16 and 11 patients respectively. The acute group had a mean LCAI score of 11.4 at induction and a mean net change of 11.1 after 2 months. The chronic group had a mean LCAI score of 11.2 and a mean change of 5.7. The acute group had a significantly greater net LCAI change than the chronic, p = 0.001. The net LCAI change in the patients treated successfully was not significantly different than those who failed, p = 0.43. The mean follow-up time from last infliximab was 13 months. Infliximab was successful in 75% of patients in the acute group and 27% in the chronic. Infliximab is no longer required in 80% of patients (83% of acute; 67% of chronic) who were successfully treated. These patients had a mean of 10 infusions and a mean follow-up of 10 months from last infliximab.

Conclusions: (1) Infliximab appears to be effective for patients with acute UC refractory to IV steroids and non-steroid dependent UC with fulminant
Crohn’s Disease Presenting as a Life Threatening Retropharyngeal Abscess

Sobia Ali, M.D.*, Saima Ansari, M.D., Shakeel Ahmed, M.D., Michael Disalvo, M.D. Internal Medicine, Unity Health System, Rochester, NY.

Purpose: Metastatic abscess formation is a rare complication of Crohn’s disease. Retropharyngeal abscess as a complication of Crohn’s disease has not been reported in the literature.

Case report: A 34 Year old female with a medical history of mild intermittent asthma presented with severe respiratory distress due to stridor. Her prodomes consisted of one month’s duration of malaise, dysphagia, progressive dyspnea, nausea, vomiting, 30lb weight loss and four days of hematoczezia. Patient looked toxic, was hypotensive, tachycardiac and febrile with 9, 400 WBC’s and 22% bands. She had cervical opisthotonus, an audibl stridor and coughing which precipitated intermittent airway obstruction, thus necessitating urgent endotracheal intubation, by an anesthesiologist. A CT scan of head and neck revealed a large retropharyngeal abscess that necessitating urgent endotracheal intubation, by an anesthesiologist.

Discussion: When compared to enteral crohn’s disease, pulmonary involve-

Purpose: The risk for colorectal cancer (CRC) increases considerably in pa-
tients with chronic ulcerative colitis (UC). Although molecular mechanisms underlying UC-associated carcinogenesis remains incomplete, mutation of p53 gene is frequently detected early in the progression of UC-associated CRC and considered to play an important role. For early detection of UC-associated CRC, surveillance program using colonoscopy is recommended in patients at high risk. However, certain proportion of patients are not enrol-
ed in surveillance program because of poor acceptability for surveillance colonoscopy and its low cost-effectiveness. Therefore, surrogate marker for selecting patients at high risk of developing neoplasms is needed. In this study, we attempted to evaluate the usefulness for measurement of anti-p53 Abs (p53 Abs) by ELISA using sera samples from UC patients with or without UC-associated neoplasms.

Methods: Blood samples were obtained from 206 patients with UC, 85 pa-
tients with sporadic CRC and 63 healthy controls (HC). Serum p53 Abs were detected in duplicate with ELISA method. Immunohistochemical detection of p53 protein overexpression was performed in UC patients who developed dysplasia or adenocarcinoma.

Results: Only one subject (1.6%) was positive for serum p53 Abs in HCs, 45 patients (52.9%) were positive in sporadic CRCs, and 32 patients (15.5%) were positive in UC patients. Among 206 UC patients, 17 patients had UC-associated neoplasms (11 carcinomas and 6 dysplasias) and 12 patients (70.6%) were positive for serum p53 Abs (81.8% in carcinomas and 50.0% in dysplasias), which was significantly high compared with that in non-
neoplastic UC patients (10.6%). The positivity for p53 staining was fairly consistent with those of serum p53 Abs by ELISA.

Conclusions: The present study revealed that serum p53 antibodies are associated with the progression of CRC in patients with ulcerative colitis, suggesting that serological detection of p53 Abs by ELISA is a surrogate method of surveillance colonoscopy by selecting patients at high risk for the development of CRCs.

Effect of the Anti-TNF Agents, Adalimumab, Etanercept, Infliximab, and Certolizumab PEGOL (CDP870) on the Induction of Apoptosis in Activated Peripheral Blood Lymphocytes and Monocytes

Gianluca Fossati, Ph.D., Andrew M. Nesbitt, Ph.D.* Biology Department, Antibody Centre of Excellence, UCB, Slough, Berkshire, United Kingdom.

Purpose: There are contradictory data in the literature regarding the effect of anti-TNF agents on the apoptosis of leukocytes. This is the first study to compare the effect of the anti-TNF agents etanercept, infliximab, adal-
imab, and certolizumab pegol on the induction of apoptosis directly in vitro in normal activated lymphocytes and monocytes.

Methods: Lymphocytes were stained in whole blood with the directly fluores-
cineated anti-TNF reagents or relevant controls and analyzed by flow cytometry after isotypic lysis of red cells. Peripheral blood mononuclear cells were prepared using density gradient centrifugation. Lymphocytes were then iso-
lated from this population by negative selection and monocytes by positive selection using MACS beads. Lymphocytes were cultured with anti-CD3 and anti-CD28 for 24 hours and the monocytes with IL-4 and GMCSF. The effect of the anti-TNF agents on apoptosis of these cells over this period was determined by Annexin V binding using flow cytometry.

Results: All four anti-TNF agents bound to peripheral blood neutrophils, monocytes, and a subset of lymphocytes in comparison with negative control reagents. Infliximab, adalimumab, and etanercept were equally potent at causing apoptosis of the activated monocytes and lymphocytes in this system. Certolizumab pegol did not mediate apoptosis of any cells above the level of the negative control.

Conclusions: This study confirms the data in the literature regarding the induction of apoptosis of activated monocytes and lymphocytes in vitro by infliximab and adalimumab. However in our system, etanercept was found to mediate mononuclear cell apoptosis in a similar manner to infliximab and adalimumab, which contradicts other published reports. Therefore, our study indicates that the exact conditions used for in vitro experiments may...
In Vitro Complement-Dependent Cytotoxicity and Antibody-Dependent Cellular Cytotoxicity by the Anti-TNF Agents Adalimumab, Etanercept, Infliximab, and Certolizumab Pegol (CDP870)

Gianluca Fossati, Ph.D., Andrew M. Nesbitt, Ph.D.* Biology Department, Antibody Centre of Excellence, UCB, Slough, Berkshire, United Kingdom.

Purpose: To determine the ability of the anti-TNF agents adalimumab, etanercept, infliximab, and certolizumab pegol to kill cells expressing membrane TNF by complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC).

Methods: NS0 cells transfected with human TNF (TNF 6.5 cell line) were used for this study. These cells express high levels of membrane TNF on their cell surface. Directly fluoresceinated reagents were used to determine the level of binding of the anti-TNF agents compared with negative control reagents on the TNF 6.5 cell line by flow cytometry. CDC of the TNF 6.5 cell line by the different reagents was determined by measuring lactate dehydrogenase release from the cells and by measuring propidium iodide (PI) staining using flow cytometry. ADCC was performed on the TNF 6.5 cells using monocyte-depleted peripheral blood mononuclear cells as the effector cells. Cell killing was also quantified using PI staining measured by flow cytometry.

Results: All four anti-TNF agents bound to the membrane TNF on the TNF 6.5 cells, although etanercept bound to a lesser degree than the other reagents. However, CDC and ADCC of TNF 6.5 cells were mediated only by adalimumab, etanercept, and infliximab, which all have an active human IgG1 Fc. Certolizumab pegol did not kill cells by either method because it is a PEGylated Fab’ fragment that does not have an Fc region.

Conclusions: It has been reported that etanercept does not mediate CDC or ADCC. However, in this model system, etanercept was clearly capable of killing TNF 6.5 cells by both methods, similar to infliximab and adalimumab. Owing to its unique structure, certolizumab pegol is the only anti-TNF agent that did not mediate killing by CDC or ADCC of cells expressing TNF on their membrane.

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Co-Occurrences of Rheumatoid Arthritis, Ankylosing Spondylitis and Systemic Lupus Erythematosus in Inflammatory Bowel Disease Patients


Purpose: To compare the occurrence rates of RA, AS and SLE in inflammatory bowel disease (IBD) patients to those without IBD.

Methods: Adults (age ≥ 17) continuously enrolled in a group of US managed care organizations from 1/1/2001–12/31/2002 from the PharMetrics Patient-centric Database (PharMetrics Inc., Watertown, MA) with medical and drug benefits were selected. All diagnostic fields and levels of care with an appropriate ICD-9 were used to identify disease populations and study events. Crohn’s disease (CD), ulcerative colitis (UC) and IBD (either UC or CD) patients were matched (1:4) to controls (those without IBD) based on gender, age, region, and previous-time-in-plan. The Charlson Comorbidity Index (CCI) and the Chronic Disease Score (CDS) were used to compute overall chronic disease burden. Relative risk (RR) was estimated to compare risks of RA, AS and SLE in CD, UC and IBD patients, relative to controls.

Results: Most CD, UC and IBD patients were female (57%, 54% and 56%, respectively). The average age was 46, 47 and 47 for CD, UC and IBD patients, respectively. The co-occurrence rates for RA, AS and SLE were similar across controls (Table 1). Compared with controls, CD, UC and IBD patients had significantly higher risk for RA [RR (CI) = 2.91(2.51–3.38), 2.71(2.35–3.13) and 2.68(2.38–2.98)], AS [RR (CI) = 8.97(5.95–13.53), 7.15(4.67–10.96) and 7.75(5.58–10.78)] and SLE (RR = 1.93(1.39–2.67), 1.89(1.42–2.52) and 1.91(1.51–2.41)]. CD, UC and IBD patients had higher CCI and CDS scores than patients in the control groups (Table 1).

Conclusions: IBD patients had increased co-occurrence rates of RA, AS and SLE. Overall chronic disease burden was similar between CD and UC patients.

Table 1. Disease Burden and Co-occurrences of RA, AS and SLE in IBD Patients

<table>
<thead>
<tr>
<th>Disease</th>
<th>RA</th>
<th>AS</th>
<th>SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age and gender adjusted co-occurrence rate (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diseases</td>
<td>N</td>
<td>CCI Mean (95% CI)</td>
<td>CDS Mean (95% CI)</td>
</tr>
<tr>
<td>CD controls</td>
<td>37068</td>
<td>1.02 (1.01–1.03)</td>
<td>1587.42 (1567.48–1607.36)</td>
</tr>
<tr>
<td>UC controls</td>
<td>44880</td>
<td>1.05 (1.04–1.06)</td>
<td>1645.93 (1626.46–1665.40)</td>
</tr>
<tr>
<td>UC</td>
<td>11220</td>
<td>1.60 (1.57–1.63)</td>
<td>2968.80 (2908.19–3029.41)</td>
</tr>
<tr>
<td>IBD controls</td>
<td>66969</td>
<td>1.04 (1.03–1.05)</td>
<td>1620.09 (1648.72–1635.46)</td>
</tr>
<tr>
<td>IBD</td>
<td>18603</td>
<td>1.64 (1.61–1.68)</td>
<td>3050.27 (3082.67–3097.87)</td>
</tr>
</tbody>
</table>

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The Role of Endoscopy in the Treatment of Active Ulcerative Colitis

Michael F. Picco, M.D., Ph.D.*, Jeremy C. Davis, M.D., John R. Cangemi, M.D., Donna Shelton, A.R.N.P. Gastroenterology, Mayo Clinic, Jacksonville, FL.

Purpose: Endoscopy is frequently performed to assess activity and extent in active ulcerative colitis (UC). However, endoscopy correlates poorly with activity and may not influence treatment in UC. We tested the hypothesis that therapy for active UC can be based on clinical grounds without the need for endoscopy.

Methods: Retrospective analysis of 100 consecutive outpatients with clinically active UC who underwent endoscopy. Investigator blinded to endoscopy result predicted therapy based on clinical disease activity (partial Mayo score), gross extent at previous colonoscopy and current medications. Partial Mayo score (stool frequency, rectal bleeding and physician global assessment) classified activity as mild, moderate or severe. Predicted therapy was either maximizing mesalamine or corticosteroids/surgery. Maximizing mesalamine was increasing oral mesalamine (Asacol ≥ 3.6g, Colazal≥6.75g, Pentasa≥3g, sulfasalazine≥4g) and/or adding topical mesalamine. Activity (endoscopy component of Mayo Score) and extent based on current colonoscopy, actual treatment and response by 6 months were recorded.

Results: Clinical criteria were more accurate for predicting maximizing mesalamine therapy compared to corticosteroids/surgery (p < 0.001). Of the 78 patients we predicted maximizing mesalamine therapy, 74 (95%) received this therapy after endoscopy. Of the 4 given steroid therapy, 3 had flared after a recent steroid taper. Of the 22 patients we predicted maximizing corticosteroids/surgery, 15 (68%) received this therapy. Of the 7 who did not, colonoscopy showed less extensive disease compared to previous colonoscopy in 2, quiescent disease in 1, less activity compared to partial Mayo score in 1 and in 3, steroids were withheld because of patient/physician preference. Adjusted accuracy for corticosteroids/surgery was 82% (18/22). Endoscopy demonstrated a poor correlation (coefficient = 0.54, p < 0.001) with clinical activity. Response rates for mesalamine and corticosteroids were 87 and 59% respectively.

Conclusions: Clinical criteria are accurate to begin treatment among patients on suboptimal mesalamine therapy. However, in 20% patients where corticosteroids/surgery was predicted, endoscopy resulted in avoidance of this therapy.
An Association Between Crohn’s Disease and Carcinoid Tumors?
Natalie E. West, M.D., Alan J. Herline, M.D., Paul E. West, M.D., Roberta Muldoon, M.D., David A. Schwartz, M.D.*
Gastroenterology, Vanderbilt University Medical Center, Nashville, TN and Surgery, Vanderbilt University Medical Center, Nashville, TN.

**Purpose:** The increased risk of colon cancer in inflammatory colitis has been well defined. The coexistence of other intestinal neoplasms, including carcinoid tumors (CN), in patients (pts) with Crohn’s disease (CD) has also been reported, but the evidence showing an increased risk of CN with CD has been mixed. We present a series of pts with CD with associated CN.

**Methods:** Cases: We present 4 patients with CD and a 1-cm appendiceal CN found. None of the four had carcinoid syndrome and there were no surgical morbidities. The individual patient details are listed below:

**Case One:** 37-yo female, 10 year history of CD with chronic diarrhea and right lower quadrant pain, initially responded well to steroid therapy but became refractory to treatment. She underwent an ileocolic resection for refractory symptoms. Pathology demonstrated transmural inflammation, and an incidental 1mm CN in the cecum.

**Case Two:** 25-yo female with CD and perianal fistulas, presented with persistent diarrhea and fistulouos drainage. A 3.5cm ileal mass was found on CT. She underwent an ileal resection and app. A 3mm CN was found in her appendix along with chronic ileitis and granulomas.

**Case Three:** 52-yo male with CD and perianal fistulas, presented with perianal pain. He had previously had a diverting colostomy for perianal disease that was subsequently reversed. He underwent a proctocolectomy with ileostomy. A 7mm CN was found in the transverse colon.

**Case Four:** 36-yo male, 5 year history of colitis, presented with rectal bleeding and diarrhea. Colonoscopy showed skip lesions consistent with CD. He underwent a colectomy for refractory disease. Pathology was consistent with CD and a 1-cm appendiceal CN was found.

**Conclusions:** There was an increased incidence of CN in our CD pts over historical controls. Pts with CD may be at increased risk for developing carcinoid tumors. Two of the 4 pts had fistulizing CD suggesting a possible association to this phenotype.

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PET/CT: A Novel Non-Invasive Assessment of Disease Activity in Inflammatory Bowel Disease (IBD)
Randall S. Meissner, M.D., Sigurdar Einarsson, M.D., Scott B. Perlman, M.D., Jesus A. Bianco, M.D., Andrew J. Taylor, M.D., Christine J. Jaskowiak, B.S., Kathleen M. Massoth, M.S., Mark Reichelderfer, M.D.*

PET/CT scans were read by an evaluator blinded to the clinical information. Results were scored according to five regions: small intestine and ascending, transverse, descending and rectosigmoid colon. A score of 0–3 was assigned to each region. Activity less than or equal to liver was considered grades 0 and 1, activity of 3 times the liver or greater being grade 3 and grade 2 being intermediate. A score of 0–1 was interpreted as inactive disease while 2–3 was considered active. Clinical disease activity (by findings from colonoscopy, small bowel imaging, current or previous CT scan) was assessed using the same regional analysis.

**Results:** PET/CT scan showed activity in 45 of 50 possible regions with CT being very helpful in identifying anatomy. In 36 regions, PET activity correlated well with clinical activity (16 inactive, 20 active). In 7 of 10 patients, there were 4 or more regions of correlation of disease activity with the average number of correlating regions in all 10 patients being 3.6. PET appeared to be more sensitive for identifying inflammation with 11 regions showing PET activity and clinical inactivity, and 3 regions showing clinical activity and PET inactivity.

**Conclusions:** PET/CT scan is a novel and non-invasive method to quantify disease activity in patients with IBD. Future studies to assess its clinical role in diagnosis and management of patients with IBD are needed.

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NSAID Use and Flare of Inflammatory Bowel Disease
Faten N. Aberra, M.D., M.S.C.E, Gary R. Lichtenstein, M.D., Colleen Brensinger, M.S., James D. Lewis, M.D., M.S.C.E* Department of Medicine, University of Pennsylvania, Philadelphia, PA.

**Purpose:** Controversy exists regarding whether use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with flare of Crohn’s disease (CD) and ulcerative colitis (UC). The aim of this study was to examine the association between prescription NSAID use and exacerbation of CD and UC.

**Methods:** We used data from the General Practice Research Database (GPRD) from 1988 to 1997 to conduct a case-crossover study. We used our previously validated algorithm to identify periods of remission and identification of new flares of disease (Gastroenterology 2004;126:665). Start of remission periods were identified if there was no prescription for corticosteroids (CS) or 5-aminosalicylic acid (5-ASA) for > 122 days. Newly diagnosed flares were identified by a new prescription for CS or 5-ASA following a remission period. We randomly selected one date during each remission period and the first date of each new flare. Use of NSAIDs was defined as receipt of a prescription within the preceding 60 days. Secondary analyses explored shorter time windows and more than one prescription. Conditional logistic regression was used to assess the association between NSAID use and flare of disease. Adjusted models included use of aspirin, antibiotics, azaithioprine/6MP, season of the year, and calendar year as potential confounders.

**Results:** 1112 CD (62%female, mean age 41 years) experienced 2622 flares and 2029 UC subjects (50%female, mean age 47 years) experienced 5227 flares. NSAIDs were prescribed during the 60 days preceding 134 CD flares (5.1%) and 206 UC flares (3.9%). For CD and UC, the adjusted odds ratio
Purpose: Patients with inflammatory bowel disease (IBD) are at increased risk of developing osteopenia and osteoporosis. The aim of the present study was to investigate the prevalence of decreased bone density and related risk factors in Iranian patients with IBD.

Methods: Totally, 126 patients with ulcerative colitis (UC) and 39 with Crohn’s disease (CD) were enrolled. Dual-energy x-ray absorptiometry technique was used to measure bone density at lumbar (L1-L4 and L2-L4), femoral neck and radius 33% sites. Demographic data were gathered by a questionnaire, and blood samples were obtained to measure biochemical markers. Student’s t-test, ANOVA, and chi-square were used for data analysis. To find predictive variables for BMD, stepwise regression analysis was carried out.

Results: 53(32.1%) IBD patients had diminished bone mineral density at either lumbar spine (L1-L4) or femoral neck. Of these, 9(5.4%) had osteoporosis (5.1% in CD and 5.5% in UC patients, NS), however, 44(26.7%) were osteopenic (23.1% in UC vs. 38.5% in CD patients, NS). Femoral neck bone density was significantly decreased among CD patients (p < 0.04). There was no significant difference in BMD between males and females. 94 (57%) were corticosteroid ever-user. We have found significant differences in BMD T-scores at lumbar L1-L4, L2-L4, and femoral neck in corticosteroid ever-users (p < 0.002, p < 0.001, p < 0.003, respectively). There was no significant difference in biochemical markers between UC and CD patients, except for the calcium, where more CD patients were hypocalcemic (p < 0.001). Stepwise regression analysis have revealed lumbar spine T-score was predicted by age (p < 0.0001), corticosteroid use (p < 0.002), and BMI (p < 0.005), however, femoral neck was predicted by age (p < 0.0001), BMI (p < 0.0001), smoking (p < 0.009) and corticosteroid use (p < 0.028).

Conclusions: Low bone density in both Iranian UC and CD patients is in accordance with western societies. Treatment with corticosteroid has increased this possibility. Corticosteroid use, age, smoking and BMI are predictive factors for low bone density.
patients reported flare of IBD following a flu shot, 1 had flare after MMR, and 1 patient associated IBD onset with HBV vaccine.

**Conclusions:** Patients with IBD are at increased risk for VPD, yet few are adequately vaccinated. Given the unpredictable likelihood of immunosuppression and transfusion, patients should be screened at the time of diagnosis for vaccine history and risk factors. In particular, varicella exposure should be assessed. When possible, patients should be immunized prior to initiation of immunosuppressive medications. Efforts to increase compliance with guidelines should be undertaken in the GI community in order to minimize preventable morbidity in this susceptible population.

### Analysis of DNA Mutations in Stool Is a Novel Method To Detect Neoplasia in Patients with Inflammatory Bowel Disease

**Francis A. Farraray, M.D., M.Sc., Charles Andrews, M.D., Samir A. Shah, M.D., James M. Becker, M.D., Ronald Bleday, M.D., Stanley Ashley, M.D., Richard Hodin, M.D., Marcia Eisenberg, Ph.D., Barry Berger, M.D., Robert D. Odze, M.D.** Gastroenterology, Boston Medical Center, Boston, MA; Brown University, Providence, RI; Brigham and Women’s Hospital, Boston, MA; Massachusetts General Hospital, Boston, MA; Laboratory Corporation of America, Research Triangle Park, NC and Exact Sciences, Marlborough, MA.

**Purpose:** Patients with ulcerative colitis (UC) or Crohn’s colitis (CC) have an increased risk of developing colorectal cancer (CRC). There are limitations to surveillance colonoscopy including compliance issues and sampling error. Therefore, we performed this pilot study to examine the utility of stool DNA-based assays in detecting neoplastic lesions in patients with UC or CC.

**Methods:** DNA from stool samples collected from 13 UC patients and 3 CC patients, M/F ratio: 10/6, mean age: 50.1 years (range: 26–81), mean duration of illness: 19.6 years (range: 1–45 years) was extracted, amplified with PCR and analyzed for 21 mutations within the K-ras, APC and p53 genes, deletions in BAT 26 and for DNA integrity (DIA). DIA identifies long DNA strands (1300–2400 bps, non-apoptotic DNA), which are distinct from shorter strands (200 bps) that develop as a result of normal programmed cell death. DNA results were correlated with the pathologic findings in either the patients' biopsy (n = 5) or resection (n = 11) specimens.

**Results:** Of the 16 patients, 5 had CRC, 5 had flat low-grade dysplasia (LGD), 1 had polyoid LGD and 5 patients had no evidence of dysplasia or carcinoma (Ca) on surveillance colonoscopy (3) or colectomy (2). Overall, 11/11 study patients with dysplasia or Ca had a molecular abnormality compared to only 2/5 (40%) controls (P = 0.018). The DIA assay was positive in 7/11 (64%) patients with either previous or current dysplasia or Ca compared to 2/5 (40%) controls without dysplasia/Ca. K-ras mutations were detected in the four DIA negative patients with either flat (K13p2, K13p2) or polyoid LGD (K13p2) or cancer (K13p2, K13p1) in their colectomy specimens but in none of the 5 control patients. None of the patients had mutations in APC or p53 or deletions in BAT 26.

**Conclusions:** Evaluation of DNA mutations and alterations in stool is a promising new technique that may serve as a useful adjunct to colonoscopic surveillance for the detection of dysplasia or Ca in patients with IBD. Larger studies are needed to determine the sensitivity and specificity of this surveillance approach.

### Magnetic Resonance Imaging in Crohn’s Disease: Evaluation of Activity – Correlation with Crohn’s Activity Index

**Khalid M.Z. Darwish, M.D.,* Kamal M. Okasha, M.D., Abidemonem M. Mourad, M.D., Department of Internal Medicine, Faculty of Medicine – Tanta University, Tanta, Egypt and Department of Radiology, Faculty of Medicine – Assiut University, Assiut, Egypt.**

**Purpose:** We investigated magnetic resonance imaging (MRI) as a tool to evaluate CD activity in newly diagnosed and follow up patients in correlation with clinical and laboratory markers represented by crohn’s Disease Activity Index (CDAI).

**Methods:** This study included 27 patients with proven CD. Twelve patients were included in their 1st month from initial diagnosis. Fifteen patients were regular follow up CD patients. Patient evaluation included: careful clinical evaluation, laboratory tests, colon ileoscopy, and if needed barium studies. MRI evaluation was performed at the level of the pathological bowel loops for the following parameters: bowel-wall thickness (WT); wall enhancement (WE); and wall signal on T2-W [SPIR] images.

**Results:** Clinically active disease with CDAI score above 150 was noted in fifteen patients. All 27 patients had ileal CD. Ten patients had ileocolonic CD. One patient had gastric in addition to her ileocolonic disease. Magnetic resonance imaging (MRI) findings: WT was normal in all patients with inactive disease, while in patients with active disease WT was mild in 2 patients, moderate in 4 patients, and severe in 9 patients. WE was normal in 10 patients, and mild in 2 patients of the inactive disease patients while severe in 7 patients, and mild in 8 patients of the active disease patients. In inactive disease patients T2W signal was mild in 1 patient, and absent in 11 patients, while it was high in 7 patients, and mild in 8 patients of the active disease patients. Statistically significant correlation was noted between WT and CDAI, WE and CDAI, and T2W and CDAI. Also, significant correlation was noted between WT and WE, and T2W and WE.

**Conclusions:** MRI can play a larger role in the clinical assessment of CD activity. MRI has shown good accuracy in detecting the inflammatory changes of CD and in differentiating non-active form active disease.

### Wireless Capsule Endoscopy in the Assessment of Iron Deficiency Anemia in Patients with Ileal Pouch-Anal Anastomosis

**B. Shen, M.D.,* F. Remzi, M.D., A. Brzezinski, M.D., B. Lashner, M.D., J.-P. Ackhar, M.D., J. Santisi, R.N., K. Sherman, R.N., V. Fazio Gastroenterology, Cleveland Clinic, Cleveland, OH and Colorectal Surgery, Cleveland Clinic, Cleveland, OH.**

**Purpose:** Ileal pouch-anal anastomosis (IPAA) has become the surgical treatment of choice in patients ulcerative colitis (UC) & familial adenomatous polyposis who require surgery. Persistent iron deficiency anemia without overt GI bleeding can occur after IPAA. The identification of etiologic factors can be challenging. Wireless capsule endoscopy (WCE) may provide a useful tool to assess small bowel mucosal diseases but its role in patients with IPAA has not been studied. Our aim was to compare diagnostic role of EGD/pouch endoscopy with small bowel histology and WCE in IPAA patients with persistent iron deficiency anemia.

**Methods:** Seven patients with IPAA who had iron deficiency anemia (Hb < 10) > 12 months after IPAA that persisted >12 months were enrolled in the study. The patients who had obvious contributing causes of iron deficiency anemia such as persistent hematochezia or heavy menstrual periods were excluded. EGD with small bowel biopsy and pouch endoscopy with neo-terminal ileum, pouch, and cuff biopsy, and serology for celiac disease were performed. WCE was administered after partial small bowel obstruction was excluded based on clinical, endoscopic, and radiographic evaluation. Final diagnosis of the etiology of anemia was based on a combined assessment of clinical, laboratory, endoscopic, and histologic data.

**Results:** A total of 7 patients included 4 females (57%) with mean age 39.3 ± 17.6 years, mean time since IPAA 4.8 ± 5.0 years. 6 patients had underlying UC and 1 had juvenile polyposis. Five patients had active pouchitis and 2 had normal pouches on pouch endoscopy. None of the patients regularly used NSAIDs. WCE was administered in all 7 patients with successful passage. Mucosa of small intestine was adequately visualized. The cause of iron-deficiency anemia was identified in 4 patients (57%) – 3 patients (43%) by WCE and 2 patients (29%) by EGD, pouch endoscopy, and small bowel histology (P > 0.05).
Conclusions: WCE is safe and well-tolerated in patients with IPAA. A combined assessment of EGD, pouch endoscopy, WCE, and small bowel histology is helpful for the identification of patients with iron deficiency anemia in patients with IPAA.

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The Natural History of Surgery for Ulcerative Colitis in a Population-Based Cohort from Olmsted County, Minnesota


Purpose: To describe the “natural history” and long term outcomes of surgical therapy in a population-based cohort of ulcerative colitis.

Methods: All Olmsted County, MN residents diagnosed with UC between 1940 and 2001 have been identified. Community medical records were reviewed to ascertain all surgeries, including abdominal surgery, lysis of adhesions, perianal surgery, abscess drainage, stomal revision, and stomal hernia repair. Ileostomy takedown after first stage of ileal pouch-anal anastomosis (IPAA) was not counted as a subsequent surgery. The cumulative incidences of proctocolectomy from time of diagnosis and subsequent surgeries from time of colectomy were estimated using the Kaplan-Meier method.

Results: The 378 incidence cases of UC (56.1% male) were followed for a total of 6,360 person-years (median follow-up per patient, 15.1 years; range, 0.1 – 58 years). Eighty-one (21%) underwent a surgical procedure for UC, of whom fifty-six (69%) underwent more than one procedure. Table 1 shows the cumulative incidence of colectomy and subsequent surgeries from time of diagnosis and cumulative incidence of colectomy from time of diagnosis.

<table>
<thead>
<tr>
<th>Causes of Anemia</th>
<th>Detected by EGD/ WCE</th>
<th>Detected by EGD/ Pouch Endoscopy/ Small Bowel Histology</th>
</tr>
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<tbody>
<tr>
<td>Celiac disease, N = 1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Arterio-venous malformations, N = 2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Small bowel polyps, N = 1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>No identifiable causes, N = 3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

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High-Grade Dysplasia in Adenoma-Like Mass Lesions Is Not an Indication for Colectomy in Patients with Ulcerative Colitis

Rabi Kandu, M.D., Wojciech Błonski, M.D., Chin-yu Su, M.D., James D. Lewis, M.D., Faten N. Aberra, M.D., Leonard Baidoo, M.D., Julius J. Deren, M.D., Gary R. Lichtenstein, M.D.* Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA and Division of Gastroenterology, Wroclaw Medical University, Wroclaw, Poland.

Purpose: The management of polypoid dysplasia in ulcerative colitis (UC) is evolving. There are at least 3 reports of polypectomy as a safe alternative to colectomy in pts with adenoma-like mass lesions (ALMs) (Rubin, et al Gastro 1999;117:1295 [n = 30]; Odez, et al Clinical Gastro Hep 2004;2:534 [n = 24]; Kundu et al. Gastro 2005;5128(4):A579 [n = 30]). The management of high grade dysplasia (HGD) in ALMs is not well characterized. Aim of this study was to ascertain the course of pts with HGD in ALMs in the absence of any synchronous flat dysplasia. We hypothesize that colectomy is not mandated in pts after complete excision of ALMs with HGD.

Methods: Pathology/clinical databases were systematically searched for dysplastic lesions in inflammatory bowel disease from 1997–2004. Pts were identified with UC who had ALM lesions, and a subset with high-grade dysplastic polyps were defined as our study cohort. Pt demographics, disease characteristics, surveillance protocol, histopathology of biopsies and colectomy specimens were evaluated.

Results: 113 pts were identified with dysplastic lesions.102 (90%) of these had UC, 5(4%) had Crohn’s disease and 6(6%) had indeterminate colitis. 30 of the 102 (29%) pts with UC had HGD in ALMs in the absence of synchronous flat dysplasia; of which 9(30%) had HGD in these polyps. The mean age of cohort was 61 yrs (28–75 yrs); 9(66%) were male. The mean duration of disease was 16.3 yrs (6–26 yrs). 7/9 (77%) pts had pancolitis.9 pts had 10 ALMs with HGD. 9/10 (90%) of these polyps were within the area of colitis. The polyps were found in: 1(10%) in cecum, 3(30%) in ascending colon, 1(10%) in descending colon, 3(30%) in sigmoid colon, and 2(20%) in rectum. Most polyps (8/10) were adenomatous and 2/10 were villous. The mean polyp size was 5.4 mm (2–12mm). 32 surveillance colonoscopies were performed (mean 3.6 colonoscopies/pt). The pts were followed for a mean of 64.5 mos (40–87 mos). 3/9 pts (33%) had colectomy. No pts in this cohort were detected to have carcinoma in surveillance biopsies and/or in their resection specimens.

Conclusions: Our data suggests that the presence of high grade dysplasia in ALMs does not mandate colectomy. Continued close observation is suggested in this pt cohort after complete excision of polyps. Further prospective evaluation of this pt population is merited.

821

Risk Factors for Osteopenia and Osteoporosis in Patients with Ulcerative Colitis Following Ileal Pouch-Anal Anastomosis

B. Shen,* V. Fazio, F. Remzi, M. Skugor, A. Brzezinski, J.-P. Achkar, R. Lopez, A. Bennett, K. Sherman, B. Lashner IBD Center, Cleveland Clinic, Cleveland, OH.

Purpose: Bone mineral density (BMD) can be adversely affected by ulcerative colitis (UC) and steroid therapy. Ileal pouch-anal anastomosis (IPAA) is the surgical treatment of choice for patients with UC who require proctocolectomy. Data on bone loss in IPAA patients are limited. Our aim was to assess the risk factors for bone loss in patients with UC and IPAA in a tertiary referral center.

Methods: 140 consecutive patients with UC and IPAA were enrolled from the Pouch Clinic, DEXA was performed as part of routine clinical care. Patients were classified as having the normal BMD, osteopenia, or osteoporosis based on T scores of World Health Organization criteria. 25 variables were evaluated. Logistic regression analysis with a stepwise selection was performed.

Results: Of 140 patients (61 M; 79 F), 35%, 37%, 28% had normal BMD, osteopenia, & osteoporosis, respectively. Gender, race, extent and duration...
of UC, stage, configuration, duration and indication of IPAA, primary scle-
roting cholangitis, arthralgias, steroid use before and after IPAA, estrogen
deficiency, history of renal stones or hyperthyroidism, weight loss, calcium &
vitamin D supplement, smoking, alcohol use, history of long-term TPN or
bedridden status, and family history of osteoporosis, were not associated
with an increased risk for bone loss. Of the 25 variables, 4 remained in the
final models: advanced age, low body mass index (BMI), history of fractures,
and modified Pouchitis Disease Activity Index (mPDAI) scores measuring
pouch inflammation. The risks for bone loss increased by 25% for every
5-year increase in age (both males & females); decreased by 41% for every
3 kg/m² increase in the BMI; were 5 times higher for subjects who have
a history of fractures compared to those who have not; and increased by 17%
for every 1 point increase in the mPDAI score.

Conclusions: Bone loss is common in UC patients with proctocolectomy
& IPAA with a prevalence of 65%. Advanced age, lower BMI, history of
non-trauma-related fractures, and pouch inflammation were associated with
an increased risk for osteopenia or osteoporosis. Early identification and
intervention of the risk factors may help to prevent or appropriately manage
osteopenia or osteoporosis.

822
Postoperative Ileus after Laparoscopic Cholecystectomy: Treatment
Using Itopride Hydrochloride
Jean-Rene Basque, R. Gürlich, R. Frasco, P. Maruna, I. Chachkhiani
Scientific Affairs, Clinical Research, Axcan Pharma, Inc., Mont Saint
Hilaire, QC, Canada.

Purpose: Postoperative ileus is a distressing and frequent adverse event
following laparoscopic cholecystectomy (LCE).
Aims: The goal of this investigation was to evaluate the effects of the proki-
netic drug itopride hydrochloride (ITOPRIDE) on gastric motility in the
early postoperative period following LCE.
Methods: Transcutaneous electrogastrography (EGG), a noninvasive diag-
nostic method allowing a monitoring of gastric myoelectric activity, was
used to evaluate variations in gastric motility. 50 patients undergoing LCE
were observed for 3 days beginning at the day of surgery. In a randomized,
double blind manner, patients were administered ITOPRIDE (50 mg/day) or
placebo (sacharose). EGG records were performed at 6, 24, and 48 hours
post surgery in a fasting state and after stimulation with a liquid bolus. EGG
data were recorded by a Microdigitrapper device and analyzed using spectral
analysis and Fourier transformation.

Results: When comparing both groups (ITOPRIDE and placebo), nausea
was found significantly more frequently in the placebo group at the day of
surgery as well as on postoperative days 1 and 2. The incidence of vomiting
did not differ between groups. Differences in the EGG records were ob-
served; on the day of surgery, 56% and 40% of the patients in the ITOPRIDE
and the placebo group showed a physiological EGG curve, respectively. On
the 1st postoperative day it was 68% and 56% and on the 2nd postoperative
day 88% and 80%. However, these differences failed to reach a significance
level of p < 0.05, most likely because of the relative small group sizes.

Conclusions: The perioperative use of ITOPRIDE accelerates the normal-
ization of the EGG curve after LCE. ITOPRIDE was well tolerated, and
no serious adverse events were observed during therapy. Thus, these re-
results suggest that ITOPRIDE can be a useful enhancer of postoperative ileus
restoration following LCE.

823
Extent of Disease in Mild To Moderate Ulcerative Proctitis:
Comparison of 2 Mesalamine (5-ASA) Suppositories in a Randomized
Trial
Danielle de Montigny, T. Peak, M. Lamet, C. Dallaire, U. Shah, J. Spendar
Scientific Affairs, Clinical Research, Axcan Pharma, Inc., Mont Saint
Hilaire, QC, Canada.

Purpose: In ulcerative proctitis (UP), the extent of the disease, not taken
into account by the disease activity index (DAI), along with its severity is a
significant characteristic of the disease. This study looked at the effect of 2
modes of treatment by mesalamine suppositories on disease extent.

Methods: In a randomised clinical trial, patients with mild or moderate UP
limited to 15 cm of the anal margin, evidenced by a Disease Activity Index
(DAI) between 4 and 11, were randomized to mesalamine 500 mg sup BID
(n = 44) (Canasa®, Axcan Pharma) or 1 g HS (n = 39) for 6 weeks. The
extent of UP from the anal margin was measured by endoscopy at baseline,
and after three weeks, and six weeks of treatment. The effect of treatments on
disease extent was compared after 6 weeks of treatment within each group
by Student t-test for paired data and between groups by ANCOVA.

Results: There was a significant decrease (p < .001) in mean (sd) length
of disease extent between baseline and after six weeks in both groups: from
12.4(5.4) cm to 3.5(7.8) cm for 500 mg BID and from 10.5 (4.2) cm to 1.5
(3.2) cm for 1 g HS. There was no significant difference between the groups
at six weeks for disease extent when adjusting for baseline values. A significant
reduction (p < .001) also occurred in scores of mucosal appearance from
baseline to six weeks (greater than 70%) within both groups, with the greater
decline occurring within three weeks.

Conclusions: Both mesalamine suppository treatments were effective in
significantly reducing the length of disease extent after six weeks. This effect,
along with the reduction of disease activity, is important for the overall patient
well-being.

824
The Role of M2 Patency Capsule in Small Bowel Strictures:
Only a Test before M2A Capsule Endoscopy or Diagnostic Tool?
Pietro Occhipinti, M.D., Silvia Saettone, M.D., Laura Broghia, M.D.,
Paolo Gorini, M.D., Ferruccio Rossi, M.D., Gastroenterology and
Digestive Endoscopy Unit, Ospedali Riuniti ASL 13, Novara, Italy.

Purpose: The small bowel is the most commonly affected site of Crohn’s
disease. Localized disease with transmural inflammation can lead to stric-
tures. Small bowel strictures are a diagnostic issue. Radiology offers some
options but false negative examination can occur. M2A Capsule Endoscopy
(Pillcam) seems to be a promising noninvasive diagnostic tool for the study
of entire small bowel. Due to the risk of retention, the capsule is controindi-
cated in patients with suspected bowel strictures. The M2 Patency Capsule
(M2PC) consists of an ingestible, time-controlled, dissolvable capsule that
is the same size as Pillcam. M2PC is composed of a dissolving lactulose
body surrounding a Radio Frequency Identification tag, that can be relayed by
a Radio Frequency scanner. Purpose of the study is to assess the ability
and the safety of M2PC in detecting bowel strictures in patients (pts) with
small bowel Crohn’s disease and clinically suspected strictures.

Methods: Ten pts, 5 male and 5 female, mean age 45 yr (± 17.6), with
clinical pattern of recurrent cramping abdominal pain and/or abdominal
mass, received small bowel follow-through (BFT) and subsequently ingested
M2PC. Patients were scanner tested 36–48 hours after ingestion.

If M2PC was detected after this time, the presence of a stricture was suggested
Results: BFT showed reduction of small bowel lumen only in 4/10 pts.
Instead after M2PC ingestion in 8/10 pts could be suspected an ileal stenosis:
4/10 patients experienced abdominal pain and nausea or vomiting probably
due to the blockage of the patency capsule in the strenosis (the capsules
dissolved after within a mean of 56 hours and the patients then clinically
improved) and 4/10 pts were asintomatic, but the patency capsule was de-
tected in abdomen after 48 hours. Only in 2/10 pts (one with reduction of

822
Postoperative Ileus after Laparoscopic Cholecystectomy: Treatment
Using Itopride Hydrochloride
Jean-Rene Basque, R. Gürlich, R. Frasco, P. Maruna, I. Chachkhiani
Scientific Affairs, Clinical Research, Axcan Pharma, Inc., Mont Saint
Hilaire, QC, Canada.

Purpose: Postoperative ileus is a distressing and frequent adverse event
following laparoscopic cholecystectomy (LCE).

Aims: The goal of this investigation was to evaluate the effects of the proki-
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Methods: Transcutaneous electrogastrography (EGG), a noninvasive diag-
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were observed for 3 days beginning at the day of surgery. In a randomized,
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Conclusions: The perioperative use of ITOPRIDE accelerates the normal-
ization of the EGG curve after LCE. ITOPRIDE was well tolerated, and

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Conclusions: Bone loss is common in UC patients with proctocolectomy
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non-trauma-related fractures, and pouch inflammation were associated with
an increased risk for osteopenia or osteoporosis. Early identification and
intervention of the risk factors may help to prevent or appropriately manage
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small bowel lumen at BFT) M2PC was retrieved intact from the stool and Pillcam was uneventfully performed.

Conclusions: Our preliminary results indicate M2PC is a simple and safe procedure. If a small bowel stricture is clinically suspected, M2PC has to be used before Pillcam in spite of normal BFT. M2PC seems to have better sensibility then BFT in diagnosis of small bowel stricture.

825
The Natural History of Surgery for Crohn’s Disease in a Population-Based Cohort from Olmsted County, Minnesota
Shamina Dhillon, M.D., Edward V. Loftus, Jr., M.D.,∗ William J. Tremaine, M.D., Debra A. Jewell, R.N., W Scott Harmsen, M.S., Alan R. Zinsmeister, Ph.D., L Joseph Melton III, M.D., John H. Pemberton, M.D., Bruce G. Wolff, M.D., Eric J. Dozois, M.D., Robert R. Cima, M.D., David W. Larson, M.D., William J. Sandborn, M.D. Gastroenterology, Mayo Clinic College of Medicine, Rochester, MN; Colon and Rectal Surgery, Mayo Clinic College of Medicine, Rochester, MN; Biostatistics, Mayo Clinic College of Medicine, Rochester, MN; Epidemiology, Mayo Clinic College of Medicine, Rochester, MN. M.D., Bruce G. Wolff, M.D., Eric J. Dozois, M.D., Robert R. Cima, M.D., David W. Larson, M.D., William J. Sandborn, M.D. Gastroenterology, Mayo Clinic College of Medicine, Rochester, MN; Colon and Rectal Surgery, Mayo Clinic College of Medicine, Rochester, MN; Biostatistics, Mayo Clinic College of Medicine, Rochester, MN; Epidemiology, Mayo Clinic College of Medicine, Rochester, MN.

Purpose: To describe the “natural history” and long-term outcomes of surgical therapy in Crohn’s disease (CD) in a population-based cohort.

Methods: All Olmsted County, MN residents diagnosed with CD between 1940 and 2001 have been identified. Community medical records were reviewed to ascertain all surgeries, including intestinal resection, stricturoplasty, gastrojejunostomy, exam under anesthesia, lysis of adhesions, wound debridement, diversion procedures, stomal hernia repair, abdominal exploration, and perianal surgeries (seton placement, fistulotomy, exam under anesthesia, and perianal abscess drainage). The cumulative risks of first, second, and third intestinal resection, lysis of adhesions, and perianal surgery alone were evaluated using the Kaplan-Meier method.

Results: The 314 incidence cases of CD (49.4% male) were followed for 4,946 person-years (median follow-up per patient, 13.2 years; range, 0.01–54 years.) Altogether, 181 (58%) underwent a surgical procedure, of whom 91 (50%) had at least two surgeries. One hundred nine (60%) had ileocolonic resection as their first surgery after diagnosis of CD. The cumulative risk of first intestinal resection was 24% at year 1 after diagnosis, 49% at year 10, 59% at year 20, and 64% at year 30. The cumulative risk of a second intestinal resection was 5% at one year after first resection, 31% at year 10, and 48% at year 20. The cumulative risk of a third intestinal resection was 4% at one year after second resection, 28% at year 10, and 54% at year 20. The cumulative risk of requiring lysis of adhesions for obstruction after the initial surgery was 6.2% at year 10. The cumulative risk of requiring a perianal surgery was 12% at year 10 after CD diagnosis.

Conclusions: In this population-based cohort of CD patients, nearly one-quarter had undergone bowel resection within the first year of diagnosis, and approximately half had required resection by year 10. Second and third resections were not uncommon. These results highlight the need for early medical intervention in Crohn’s disease.

826
Inflammatory Bowel Disease: An Analysis of Disease Characteristics in an Urban Minority Population at a Community Teaching Hospital
Rajalakshmi V. Iyer, M.D., Melchor V. Demetria, M.D.,∗ Bashar M. Attar, M.D. Gastroenterology, John H. Stroger Hospital of Cook County and Rush University, Chicago, IL.

Purpose: To analyse and review the disease characteristics of inflammatory bowel disease (IBD) in an urban minority population.

Methods: We reviewed demographic and clinical data of 177 consecutive minority patients with IBD, 100 with Ulcerative Colitis (UC) and 77 with Crohn’s disease (CD) seen at our community teaching hospital over the past 2 years.

Results: The racial distribution and disease characteristics of the study population are shown in Tables 1 and 2. Disease distribution in UC was proctitis 13%, left sided colitis 27% and pancolitis 56%. With CD, one patient had perianal involvement, 31% colonic disease and 67.5% ileocolonic disease. Strictures were seen in 36.6% of CD patients. Of the UC patients 86% needed 5ASA compounds for maintenance of disease remission, 33% required corticosteroids and 16% were on aziathioprine. Only one patient required cyclosporine. In the CD group 88.3% were on 5ASA, 27.1% were on long term antibiotics, 44.1% required steroids, 42% were on maintenance azathioprine and 10.4% (all African American) required maintenance infliximab. Two patients were on adalimumab for ankylagous spondylitis and had not required any other medication for maintenance of remission in CD. One patient developed a colon cancer after 24 yrs of UC and 2 patients had dysplasia on surveillance biopsies after 8 and 14 yrs of UC respectively.

Racial Distribution

<table>
<thead>
<tr>
<th></th>
<th>UC n = 100(%)</th>
<th>CD n = 77(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>47 (47%)</td>
<td>59 (76.6%)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>35 (35%)</td>
<td>15 (19.4%)</td>
</tr>
<tr>
<td>Asian</td>
<td>14 (14%)</td>
<td>2 (2.6%)</td>
</tr>
<tr>
<td>Middle eastern</td>
<td>2 (2%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>African</td>
<td>1 (1%)</td>
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</tbody>
</table>

IBD Characteristics

<table>
<thead>
<tr>
<th></th>
<th>UC (n = 100)</th>
<th>CD (n = 77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg Age (yrs)</td>
<td>36 ± 12</td>
<td>32 ± 14</td>
</tr>
<tr>
<td>M:F</td>
<td>1.2:1</td>
<td>1.05:1</td>
</tr>
<tr>
<td>Smokers (%)</td>
<td>18.3</td>
<td>36.4%</td>
</tr>
<tr>
<td>Abdominal pain and bloody diarrhea at presentation (%)</td>
<td>89</td>
<td>68</td>
</tr>
<tr>
<td>Weight loss at presentation (%)</td>
<td>12</td>
<td>71.4</td>
</tr>
<tr>
<td>C. difficile colitis at presentation (%)</td>
<td>3</td>
<td>1.2</td>
</tr>
<tr>
<td>Fistulizing disease (%)</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>Disease related surgery (%)</td>
<td>28.6</td>
<td>5</td>
</tr>
<tr>
<td>Extraintestinal manifestations</td>
<td>26</td>
<td>41.5</td>
</tr>
</tbody>
</table>

Conclusions: This is probably one of the largest studies of IBD in a minority population. The disease characteristics in minorities are starting to parallel those in the general population. With a trend towards increasing incidence of Crohn’s disease in African Americans the slightly older age at diagnosis, even a conceivable delay in diagnosis, may be a function of access to health care. This underlines further the importance of reviewing disease characteristics in minorities.

827
Safety of a Rapid One-Hour Infusion of Infliximab in Crohn’s Disease Patients
Micha Rojany, M.D., Walter Trudeau, M.D., Thomas Prindiville, M.D.* Division of Gastroenterology, UC Davis, Sacramento, CA.

Purpose: Infliximab is indicated for use in moderate to severe Crohn’s disease (CD). However, infusions are not without risk. Approximately 4% of infusions will be associated with an infusion reaction. Infusions are typically given over 4 hours and then shortened to 2 to 3 hours in tolerant patients.

Aim: To determine if patients with CD would be able to tolerate a rapid 1 hour infusion safely with an acceptable rate of infusion reactions

Methods: We retrospectively reviewed the charts of all adult patients with CD who received Infliximab infusions between January 2003 and September of 2004 at our institution. All patients started with a standard infusion of 5mg/kg and received an induction dose at 0, 2, and 6 weeks followed by maintenance therapy every 8 weeks. Patients without history of any moderate or severe infusion reaction to Infliximab, severe systemic disease, prior MI,
CVA, or renal failure, were eligible to receive a 1-hour infusion of Infliximab. All patients were monitored for infusion reactions that were categorized as acute or delayed. All infusion reactions were further classified as mild, moderate, or severe. Patients with any prior history of transfusion reaction were pretreated with 1g of acetaminophen and 180mg of fexofenadine. Statistical analysis was performed using the Mann-Whitney test. **Results:** 95 patients received a standard infusion (39 M 56 F). 92% (87/95) of patients were on immunomodulators. There were a total of 478 standard infusions with a mean of 5 infusions per person (range 1–19). The standard infusion group had a total of 27 infusion reactions (14 mild, 1 moderate, 2 severe). 49 patients received rapid infusions (22 M 27 F). There were a total of 253 rapid infusions with a mean number of infusions per person of 5 (range 1–13). 96% (47/49) patients were on immunomodulators. The rapid infusion group had a total of 13 infusion reactions (7 mild, 6 moderate). 9/49 (18%) patients in the rapid infusion group had to return to standard infusions due to infusion reactions. The rate of infusion reactions for standard infusions compared to rapid infusions is comparable: 5.6% vs. 5.1% (p = NS). However, when taking into account those who had received both standard and rapid infusions, the rapid infusions had a slightly higher rate of infusion reactions, but this was not significant (0.05 vs. 0.11, p = NS). **Conclusions:** A rapid 1-hour infusion of Infliximab is well tolerated by a select group of patients and is not associated with an increased rate of transfusion reactions.

**Characterization of Large Polyps in Ileal Pouch-Anal Anastomosis in Patients with Underlying Ulcerative Colitis**

Benjamin Schaus, D.O., Bo Shen, M.D.* Department of Gastroenterology, Cleveland Clinic, Cleveland, OH.

**Purpose:** Restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA) are the procedures of choice for patients with ulcerative colitis (UC) who require surgery. Polyps may occur in a patient’s pouch or rectal cuff. The etiology, malignant potential, and management of these polyps are not known. The aim was to characterize clinical features of large polyps in IPAA in patients with UC.

**Methods:** We searched our 3000-case Pouch Database for UC/IPAA patients with large polyps of the pouch (size ≥ 1 cm). Patients with other underlying diseases of the colon requiring total proctocolectomy and IPAA were excluded. Clinical, endoscopic, and histologic data were analyzed.

**Results:** Twenty patients (10 males and 10 females; mean age of 45.4 ± 14.6 yrs) with polyps in the IPAA were identified with a prevalence of 0.8%. The mean time interval from IPAA performed to pouch polyp diagnosed was 7.1 ± 3.8 years. Indications for proctocolectomy and IPAA were refractory UC (N = 16; 80%) or UC with dysplasia (N = 4; 20%). Of the 20 patients, 66% had polyps at the pouch and 34% had polyps at the rectal cuff; 85% had a single polyp and 15% had 2 or more polyps; 80% had pedunculated polyps; 95% had inflammatory polyps; 1 patient (5%) who had a dysplastic/neoplastic polyp (adenocarcinoma) in the rectal cuff who had initially undergone proctocolectomy and IPAA for UC with dysplasia. The average size of these polyps was 1.93 ± 1.77 cm. 19 patients (95%) with polyps were symptomatic and the all polyps arose from the background of mucosal inflammation with chronic pouchitis, cuffitis, or Crohn’s disease of the pouch. In addition to medical therapy (antibiotics, 5-ASA, steroids, or immunomodulators), endoscopic polypectomy was performed in 16 patients. The pre- and post- polypectomy Pouchitis Disease Activity Index symptom scores were 3.13 ± 1.77 and 1.13 ± 1.24 (P = 0.043), respectively; 2 patients underwent pouch resections for dysplasia/neoplasia of the cuff and chronic refractory pouchitis, respectively.

**Conclusions:** While the majority of large pouch polyps in UC and IPAA patients were benign and inflammatory types, this study found one neoplastic polyp in a rectal cuff. In patients, particularly, with pre-operative dysplasia, polyps at the rectal cuff can be dysplastic or neoplastic. The fact that all large pouch polyps arose from the background of chronic pouchitis, cuffitis, or Crohn's disease, would suggest possible etiology of inflammation.

Polyectomy combined with medical therapy may lead to improvement in symptoms.

**Comparison of Safety and Mortality of Infliximab Therapy to Immunomodulator Therapy in Crohn’s Disease: A Cohort Study**

Jhony Dounit, Aaron Brzezinski,* Bret Lashner, Jean-Paul Achkar, Rocio Lopez, Bo Shen Center for Inflammatory Bowel Disease, Cleveland Clinic, Cleveland, OH.

**Purpose:** While infliximab is indicated for the treatment of Crohn’s disease, blockade of TNF may result in severe immune suppression. Several case series suggested an increase in severe infections, malignancies, and possibly mortality in patients receiving infliximab. Our aim was to assess serious complications in Crohn’s disease patients receiving infliximab compared to Crohn’s disease patients receiving immunomodulator therapy.

**Methods:** We searched all the patients seen at the Cleveland Clinic between 1999 and 2003 with a diagnosis of Crohn’s disease. We included all 322 eligible patients who received at least one dose of infliximab with or without concurrent immunomodulators (the infliximab group) and compared with 217 patients who received 6-mercaptopurine (6MP), azathioprine (AZA), methotrexate (MTX) or corticosteroids for at least 3 consecutive months (the immunomodulator group). We compared the frequency of severe infection, neoplasm, and mortality between the 2 groups. The exclusion criteria were 1) age < 20 at the time of entry; 2) enrollment in the ACCENT trials; and 3) infliximab infusion for diseases other than Crohn’s disease. Severe infection was defined as an infection which occurred within 2 months of the last infliximab infusion requiring hospitalization and IV antibiotics, infection by opportunistic organisms or causing a near death experience. All neoplasms were included except basal cell carcinoma.

**Results:** The 2 groups were comparable in age, gender, disease location, and mean number of IBD- related surgeries (2.1 ± 3.2 vs 1.7 ± 1.9). In the infliximab group, 322 patients received a total of 2168 infusions with a mean follow-up of 2 years after the start of infliximab therapy and a mean of 13.7 years since diagnosis. 26.7% of patients received infliximab prior to any other immunomodulators and 11.8% of patients received no concurrent immunomodulators. Of 217 patients in the immunomodulator group with a mean follow-up of 15.6 yrs since diagnosis, 48.4% had 6MP/AZA, 5% had steroids, 4.1% had MTX, 42.5% received more than one immunomodulators.

<table>
<thead>
<tr>
<th>Infliximab N = 322</th>
<th>Immunomodulators N = 217</th>
</tr>
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<tbody>
<tr>
<td>Severe Infections 17 (5.2%)</td>
<td>10 (4.6%)</td>
</tr>
<tr>
<td>Neoplasm 7 (2.2%)</td>
<td>5 (2.3%)</td>
</tr>
<tr>
<td>Mortality 8 (2.5%)</td>
<td>4 (1.8%)</td>
</tr>
</tbody>
</table>

**Conclusions:** There were no statistical differences in the frequency of severe infection, neoplasm, and mortality in Crohn’s disease patients between the infliximab and immunomodulator groups. Mortality of the 2 groups was 2.5% and 1.8% respectively.

**Do Probiotics Reduce PPAR-γ in Ulcerative Colitis? An Open Labeled Pilot Study**

Noel B. Martins, M.D., David S. Fefferman, M.D., Charlotte Anderson, Ph.D., Munir Zaman, Ph.D., Richard J. Farrell, M.D., Steven D. Freedman, M.D., Sunil G. Sheth, M.D.* Gastroenterology, Beth Israel Deaconess Medical Center, Boston, MA.

**Purpose:** Evidence is mounting that bacteria play a role in the pathogenesis of IBD. Probiotics have shown efficacy in the treatment of ulcerative colitis (UC) although the mechanism of action is unknown. PPAR-γ is expressed...
in colonic epithelial cells and inhibits cytokine activation. In UC, PPAR-γ levels are low. The aim of this study was to determine whether probiotics (VSL#3) up-regulate PPAR-γ as their mechanism of action. 

Methods: Patients with active and inactive UC were screened for eligibility, consented and the disease activity index (DAI) calculated from a questionnaire and a sigmoidoscopy with biopsy. In this open labeled study, patients were treated with VSL#3 orally for 4 weeks. Concurrent use of mesalamine was permitted, but steroids, antibiotics or immunomodulators were prohibited. At the end of 4 weeks, a sigmoidoscopy with biopsy was repeated and the DAI calculated. Real time PCR was performed to assess the level of PPAR-γ from the biopsy samples pre and post VSL#3. 

Results: 15 patients were enrolled; 8 with active and 7 inactive disease. Baseline DAI was 5.6 ± 2.6 for patients with active disease and 0.7 ± 0.8 in the inactive group (p = 0.001). Following VSL#3 treatment, 75% of patients with active disease achieved remission (DAI ≤2) with the DAI decreasing by 66% from 5.6 ± 2.6 to 1.5 ± 1.8 (p = 0.01). This was due to statistically significant reductions in stool frequency, sigmoidoscopy scores and global assessment. DAI also decreased in those with inactive disease (p = ns). However, only the endoscopic subscore was significantly decreased at 4 weeks (p = 0.04). At baseline, PPAR-γ levels were similar between patients with active and inactive disease (p = 0.8). Following VSL#3, PPAR-γ RNA levels were reduced by 45% (p = 0.001) in active disease and by 45.6% (p = 0.1) in those with inactive disease. At 4 weeks, PPAR-γ levels were similar between patients with active disease that achieved remission and patients with inactive disease (p = 0.6).

Conclusions: 75% of patients with active disease achieved remission with VSL#3. This was associated with a significant reduction in PPAR-γ levels from baseline in patients with active disease. Overall there was no significant correlation (p = 0.25) between reduction in the DAI and reduction in PPAR-γ. This data indicates that the mechanism of action of probiotics is not through an upregulation in PPAR-γ but is perhaps the result of immune tolerance. Supported by NIH grant M01-RR0132.

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Can Disrupted Sleep Predispose Flare-Up in Inflammatory Bowel Disease (IBD)?

Ziba Ranjaran, M.D., Laurie A. Keefer, Ph.D., Shahriar Sedghi, M.D., Edward Stepanski, Ph.D., A.B.S.M., Ali Keshavarzian, M.D., F.A.C.G.*
Section of Gastroenterology and Nutrition, Rush University Medical Center, Chicago, IL and Gastroenterology, Mercer University School of Medicine, Macon, GA.

Purpose: The etiology of flare-up in IBD is unknown but is believed to be partially related to environmental factors. Sleep disruptions have been implicated in worsening of disease course in many inflammatory conditions such as rheumatoid arthritis, lupus erythematosus and asthma. Links between sleep and inflammation are also supported by studies. We questioned whether sleep disturbance could also be a trigger for inflammation in patients with IBD. The aims of our study were to determine (1) the prevalence of sleep disturbance in patients with inactive IBD and (2) whether there are perceived links between disease activity and sleep disturbance.

Methods: Eighty inactive IBD subjects (33 Ulcerative Colitis and 47 Crohn’s Disease) were compared to 15 healthy controls and 24 Irritable Bowel Syndrome (IBS) subjects. In IBS, sleep abnormalities have been frequently documented and therefore this group served as a positive control group. Quality of sleep was assessed using the validated Pittsburgh Sleep Quality Index (PSQI). These PSQI questions were modified to include questions about the perceived relation between sleep and gastrointestinal symptoms. Non-parametric data is represented with medians; Mann-Whitney-U tests were used to compare groups.

Results: IBD subjects in remission reported significant sleep disturbance: 1) Sleep onset latency in minutes was more prolonged in IBD (20) and IBS (32.5) than controls (10, p = 0.004); 2) The number of awakenings during the night in IBD was similar to IBS and was higher than controls (p < 0.001); 3) Overall quality of sleep in IBD patients was similar to IBS and was worse than controls (p < 0.0001); 4) 65% of IBD subjects reported a correlation between onset of poor sleep and disease flare up.

Conclusions: While data is limited by self-report, our preliminary findings support the presence of sleep disturbances in IBD patients. First, sleep disruptions in IBD appear to be as common as in IBS patients. Further, the majority of IBD patients linked poor sleep as a potential trigger for disease flare. It remains to be seen if these sleep disruptions are due to IBD itself (i.e. newly described extraintestinal manifestation) or an independent problem. Future studies should objectively characterize the type of sleep disruption in these patients, elucidate potential mechanisms and determine whether treatment of sleep disturbances can decrease the rate of flare-ups.

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Rifaximin as a Steroid-Sparing Medication in the Management of Patients with Inflammatory Bowel Disease

Daniel Feldman, M.D., Robin Baradarian, M.D., Kadiravel Iswara, M.D., Jian Jun Li, M.D., Scott Tenner, M.D., M.P.H.* Division of Gastroenterology, Maimonides Medical Center, Mount Sinai School of Medicine, Brooklyn, NY.

Purpose: Broad-spectrum antibiotics are often used in patients with Inflammatory Bowel Disease (IBD) despite the lack of well-designed, placebo-controlled trials. Rifaximin is a new synthetic antibiotic that has a broad spectrum of activity and few side effects due to minimal absorption from the gastrointestinal tract. Unlike ciprofloxacin and metronidazole, rifaximin has similar coverage with no systemic side effects. In order to determine the role of rifaximin in the management of patients with IBD, the following study was undertaken.

Methods: 27 patients with IBD, 11 with Crohn’s disease and 16 with Ulcerative colitis were included in the study. There were 16 female, 11 male patients, mean age 33 ± 8. All patients presented with mild to moderate disease manifested as diarrhea and/or abdominal pain. All patients were currently being treated with mesalamine at high dosage (mean 4.4 ± 0.8 grams). Patients were excluded if they had taken other medications, such as infliximab, 6-mercaptopurine or azathioprine. Due to persistent (n = 9) or recurrent disease (n = 18), the patients were given either (Group 1) prednisone 40–60 mg orally daily or (Group 2) rifaximin 400 mg orally twice daily. If the patients improved, the prednisone was continued for 2 weeks and then tapered, the rifaximin was continued for 2 months and then tapered. Response was defined as induction of remission without the addition of other medications. At the judgement of the clinician caring for the individual patient, additional therapy was provided.

Results: Of the 27 patients included in the study, 14 patients were given prednisone, 13 patients were given rifaximin. All but one patient in the prednisone group responded to therapy. The one patient who did not respond had Crohn’s disease and was subsequently given infliximab resulting in a complete response. Thirteen patients were given rifaximin. Of these patients, all but two responded; both required the addition of corticosteroids, one was hospitalized.

Conclusions: This study demonstrates that the broad spectrum antibiotic rifaximin may be effective in patients with IBD who require further treatment with corticosteroids. However, the steroid sparing efficacy must be considered in a well-defined subset of patients. The use of rifaximin in ulcerative colitis and Crohn’s disease requires further evaluation in larger studies.
Purpose: Medical care for patients with inflammatory bowel disease (IBD) presents an ongoing challenge to gastroenterologists, posing a greater need for rapid diagnostics. The clinical assessment for confirmation of disease becomes even more difficult with the need to differentiate disease activity from episodes of irritable bowel syndrome (IBS) and enteric infections. Recent studies have shown Clostridium difficile (CDiff), a nosocomial pathogen that causes antibiotic-associated diarrhea and pseudomembranous colitis, to be the most frequently identified pathogen in cases of relapsing IBD (10 to 20%). Our aim was to evaluate clinically confirmed Crohn’s disease (CD) subjects for the presence of fecal anti-Saccharomyces cerevisiae antibodies (ASCA), lactoferrin (Lf) and CDiff.

Methods: A total of 23 adult outpatients with Crohn’s disease with a female:male ratio of 1:1.3 were recruited for the evaluation. Fecal specimens were collected and stored frozen prior to analysis. Fecal ASCA and lactoferrin (Lf) levels were measured using polyclonal-based enzyme-linked assays (EIA). CDiff was confirmed by fecal-based EIA for toxins A and/or B, glutamate dehydrogenase (GDH; a common antigen for nontoxicigenic and toxigenic CDiff), and tissue culture assay with confirmation by specific antibody neutralization. Direct PCR on fecal DNA was used to detect the genes for both CDiff toxins (tcdA and tcdB).

Results: Of the 23 CD subjects, 48% (11) had detectable fecal ASCA and 78% (18) had elevated Lf (≥7.25µg/mL) with a mean ± SE of 248.9 ± 82.9 µg/mL, indicating intestinal inflammation. A total of 5 were positive for GDH, 2 of which were strongly positive by EIA for toxin A and/or toxin B. Both EIA-positive stool specimens were cytotoxic by tissue culture assay with complete neutralization, and were positive for tcdA and tcdB. The 2 toxin-positive subjects had elevated lactoferrin (34.5 and 69.1 µg/mL) and a history of colonic inflammatory and ileocolonic perforating disease.

Conclusions: Fecal ASCA and Lf represent a useful panel for assessing subjects for Crohn’s disease and for ruling out IBS. Toxigenic CDiff was confirmed in 9% of all patients and 11% of the 18 patients with active disease, further confirming the need to screen for toxigenic CDiff during the assessment of active IBD.

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Amelioration of Mucosal Injury with Mesalamine Plus Antioxidant Therapy in Dextran Sulphate Sodium Induced Colitis in a Rodent Model
Nadeem A. Chaudhary, M.D., Hanumantha R. Ancha, M.D., Dustin Telesco, Stanley Lightfoot, Ph.D., Richard F. Hurley, M.D.* Department of Medicine, Oklahoma University Health Sciences Center, Oklahoma City, OK.

Purpose: The pathogenesis of mucosal injury in IBD involves enhanced production of reactive oxygen species. The aims of this study were to examine the effects the antioxidant N-acetylcysteine (NAC) alone and in combination with mesalamine (5-ASA) on mucosal healing and repair in dextran sulfate sodium (DSS) induce colitis.

Methods: Colitis was induced by oral administration of 4% DSS in the drinking water for 4 days. SD rats (250-275g) were randomized to five groups. Group 1 control, Group 2–5 received DSS in drinking water and Group 3–5 were further randomized to also receive daily intracolonic treatment with: 5-ASA (100 mg/kg) plus NAC (40mM), (Group3); 5-ASA (Group 4); and NAC (Group 5) for four days. Microscopic indices of colonic injury were scored and tabulated. Histological features examined included epithelial damage and mucosal ulceration. Additional measures included serum CRP and cytokine gene expression in colonic tissues by ribonuclease protection assay (RPA).

Results: DSS treatment produced mild to moderate colitis. The aggregate microscopic injury score for DSS treated animals was 5.5 ± 2.0; maximal score 15. Monotherapy with 5-ASA and NAC caused reduction in aggregate scores (4.1 ± 0.9 and 4.0 ± 1.1, respectively) that were not significantly different from DSS alone, P > 0.1. In contrast, combination therapy with 5-ASA plus NAC reduced global injury by 67% to 1.82 ± 0.8. Furthermore, 5-ASA plus NAC caused significant improvement in epithelial damage when compared to DSS alone: 0.3 ± 0.2 vs 1.5 ± 0.3, P < 0.02. DSS colitis was associated with elevated CRP values; 7.0 ± 0.6 µg/ml. CRP levels were reduced substantially by concurrent treatment with 5-ASA plus NAC (1.0 ± 0.3 µg/ml). Similar reductions in CRP levels were observed with either 5-ASA or NAC. DSS treatment caused marked increases in cytokines IL 1a and IL 1b in colonic tissues and resulted in 6.8 and 12.1 fold increases, respectively, in gene expression above of control values. NAC and 5-ASA, alone or in combination, substantially reduced DSS-induced IL 1a and IL 1b gene expression by 55-90% to levels that approximated control values.

Conclusions: Intraluminal therapy with NAC plus 5-ASA caused significant amelioration of mucosal injury induced by DSS. Combination treatment with the antioxidant NAC plus mesalamine was also associated with substantial reduction in serum CRP levels and proinflammatory cytokine gene expression.
Purpose: Inflammatory bowel disease (IBD) is a chronic inflammatory disease of the gastrointestinal tract with a poorly understood pathogenesis. Pituitary Adenylylate Cyclase Activating Polypeptide (PACAP) potentially regulates the immune system through the activation of PAC1 (Trends Mol Med, 2003, p. 211–7), however, the role of PACAP and its receptor, PAC1, in inflammatory colitis is unclear. The purpose of this study is to elucidate the role of PACAP and its receptor, PAC1, in an experimental mouse model of colitis.

Methods: Colitis was induced in 8 adult PAC1 +/- and 7 PAC1 --/-- mice with 2.5% DSS given orally for 6 days. Measurements of water and food intake, body weight, observations of mice activity and stool appearance were made at baseline and daily thereafter for six consecutive days. On the 7th day the intact colon from both groups of mice were dissected and examined macroscopically and microscopically to determine the degree of ulceration that was scored in a blinded fashion.

Results: PAC1 --/-- and PAC1 +/- mice, both showed significant body weight loss following treatment with DSS. PAC1 +/- mice showed a slightly lower, but statistically insignificant, intake of food (7.7 ± 5.47 g/day vs 9.5 ± 7.31 g/day) and water (11.89 ± 13.4 g/day vs 16.0 ± 14.70 g/day), compared to the PAC1 +/- group. Using a macroscopic score scale with a maximum of 8 and a minimum of 0, the PAC1 +/- mice had a higher macroscopic score (3 ± 0 vs 0 ± 0, p < 0.05, n = 15), compared to the wild type. A score of 0 indicates a normal colon, whereas a 3 indicates a colon with inflammation, ulcer ( < 2cm), and colonic wall thickening. The colonic length to weight ratio was lower (29.07 ± 10.02 vs 14.86 ± 2.60, p = 0.013) in the PAC1 --/-- mice, indicating a higher level of inflammation compared to the wild type group. The H and E stained slides of the distal and proximal confirmed that in the PAC1 +/- group, a dense mucosal infiltrate, containing neutrophils, lymphocytes and macrophages, was significantly more abundant than in the PAC1 +/- group.

Conclusions: PAC1 receptor deficient mice exhibited significantly higher levels of colonic inflammation. These data suggests that the PAC1 receptor plays a protective role against colonic inflammation in mice, and may have the potential to help design future studies for treatment, and or, prevention of IBD.

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High 6-MMP/6-TGN Ratios Predict Non-Response and Hapoteotopy to Thiopurine Therapy in Crohn’s Disease
Ernest G. Seidman, M.D.,* Devendra Amre, M.D. Medicine and Pediatrics, McGill University Health Centre, Montreal, QC, Canada and Pediatrics, Ste Justine Hospital, University of Montreal, Montreal, QC, Canada.

Purpose: Efficient conversion of the thiopurine drugs 6-mercaptopurine (6-MP) or its pro-drug azathioprine (AZA) to the active 6-thioguanine nucleotide (6TGN) metabolite is decisive to clinical efficacy. The principal catabolic metabolite, 6-methylmercaptopurine (6MMP), is formed via the competing thiopurine methyltransferase (TPMT) pathway. We first established the clinical utility of measurement of these intracellular metabolites in IBD in order to optimize outcomes. The aim of this study was to assess the clinical utility of 6-MMP to 6-TGN ratios in predicting efficacy & toxicity to thiopurine therapy.

Methods: 6-MP metabolite levels were measured prospectively at 3–6 monthly intervals, or at the time of a clinical relapse or adverse events, in pediatric patients with Crohn’s disease on 6-MP or AZA (>3 months). Therapeutic response was determined by Harvey Bradshaw index and physical exam at each visit. The clinical utility of 6-MMP to 6-TGN ratios in predicting efficacy & toxicity to thiopurine therapy was assessed.

Results: Results were analyzed as continuous variables for 1787 clinical evaluation points in 267 patients and data were classified into quartiles. One or more relapses were observed in 53.7% of cases. Non-compliance was observed in 6.25% of patients. 6-MMP values greater than 5119 and less than 851 were associated with increased likelihood of relapse (Odds Ratio [OR] 1.41, 95% CI 1.1–1.9, and OR 1.38, 95% CI 1.1 – 1.8 respectively, p = 0.02). A significantly higher risk for relapse was associated with high (>24.3) ratios of 6MMP/6TGN (OR 1.33, 95% CI 1.1–1.8 p = 0.04). Ratios < 4.2 correlated with TPMT deficiency. Clinical remission did not correlate with dose of 6-MP/AZA. Hepato toxicity (25.8% of subjects) was associated with increased 6-MMP levels (OR 6.2, 95% CI 3.2–12.3, p < 0.05) and high 6-MMP/6-TGN ratios (OR 7.2, 95% CI 3.8–13.8, p < 0.05).

Conclusions: Excessive TPMT metabolism, reflected metabolically by high 6-MMP/6-TGN ratios, is associated with lower probability of clinical response and increased likelihood of hepatotoxicity. The determination of 6MMP/6TGN ratios provide the clinician with useful tools for optimizing therapeutic response to thiopurine drugs in IBD
Gastrointestinal Crohn’s Disease (GDC) is an unusual condition manifesting with nausea, emesis, and abdominal pain. GDC can be complicated by duodenal strictures, gastric outlet obstruction, and rarely pancreatitis. We report a rare case of GDC with ampullary reflux of barium contrast into the biliary system.

The patient presented with nausea, vomiting, non-bloody diarrhea, and abdominal pain and two days of left knee pain and tender lumps on bilateral lower extremities. Medications included 6-MP 25mg/d, famotidine, and metaclopromide. Exam revealed mild tenderness at McBurney’s point and EN below the knees. Patient had a white cell count of 15.1, albumin 2.0 and normal Hematocrit, amylase, and liver enzymes.

The patient was diagnosed with a Crohn’s flare and treated with intravenous steroids. Small Bowel radiographs and endoscopy revealed innumerable gastric pseudopolyps, anatomical pyloroduodenal distortion, free-flowing bile from a deformed ampulla, ready reflux of contrast into the common bile duct and pancreatic duct (PD), and a tight mid-duodenal stricture; single-contrast barium enema revealed newly seen terminal ileal string sign. Ampullary and gastroduodenal biopsies revealed chronic inflammation. The patient was discharged on TPN, oral prednisone, 6-MP 50mg/d, acid suppression and promotility agents. Extra-Intestinal manifestations included Erythema nodosum (EN), bilateral knee effusions, and arthritis.

We describe a case of initial GDC causing ampullary destruction with biliary reflux. This patient subsequently developed ileocolitis. Isolated GDC without ileal involvement is extremely rare. There are few case reports describing pancreatitis secondary to Crohn’s disease; ampullary incompetence is postulated to be the etiology. Ampullary reflux into the PD with Crohns has only previously been documented once in literature. Although our patient did not have pancreatitis, it is important to recognize that GDC can have ampullary complications.

Purpose: Gastrointestinal Crohn’s Disease (GDC) is an unusual condition manifesting with nausea, emesis, and abdominal pain. GDC can be complicated by duodenal strictures, gastric outlet obstruction, and rarely pancreatitis. We report a rare case of GDC with ampullary reflux of barium contrast into the biliary system.

Infliximab Induces and Maintains Mucosal Healing in Ulcerative Colitis Patients: The ACT Trails
W.L. Sandborn, M.D., J.F. Colombel, M.D., W. Reinsich, M.D., B.G. Feagan, M.D., D. Raczakiewicz, M.D., A. Olson, M.D., J. Johanns, Ph.D., S. Travess, M.D., D. Present, M.D., B.E. Sands, M.D., S.B. Hanauer, M.D., G.R. Lichenstein, M.D., W.J.S. de Villiers, M.D., P. Rutgeerts, M.D.* Gastroenterology, Hospital Leuven, Leuven, Belgium; CHU de Lelle, Hospital Claude Huriez, Lille, France; Gastroenterology & Hepatology, University Hospital Vienna, Vienna, Austria; Robarts Research Institute, University of Western Ontario, London, Canada; Department of Medicine, Shaare Zedek Medical Center, Jerusalem, Israel; Clinical Research & Development, Centocor, Inc, Malvern, PA; BioStatistics, Centocor, Inc., Malvern, PA; Department of Medicine, Mount Sinai Medical Center, New York, NY; Gastroenterology, Massachusetts General Hospital, Boston, MA; Gastroenterology & Nutrition, University of Chicago, Chicago, IL; Gastroenterology, Hospital of the University of Pennsylvania, Philadelphia, PA; Department of Medicine, University of Kentucky, Lexington, KY and Gastroenterology & Hepatology, Mayo Clinic, Rochester, MN.

Purpose: ACT 1 & 2 evaluated the safety and efficacy of IFX for UC. Data were pooled to determine the effect of IFX on mucosal healing.

Methods: 728 pts with active UC despite corticosteroids/aza6/MP and/or aminosalicylates (ACT 2 only) with endoscopic evidence of moderate/severe UC (endoscopy score ≥2) and a total Mayo score of 6–12 inclusive, were randomized to PBO, IFX 5 or 10 mg/kg at wks 0, 2, 6 and q8 wks. Mucosal healing was defined as endoscopy subscore of 0 or 1.

Results: More IFX 5- (61.2%) and 10 mg/kg (60.3%) pts had mucosal healing at wk 8 vs PBO (32.4%, both p < 0.001). At wk 30, 48.3% and 52.9% of IFX 5- and 10 mg/kg pts, respectively, had mucosal healing vs 27.5% of PBO (both p < 0.001). At endoscopy at wk 8, more pts receiving IFX 5- (25.2%) and 10 mg/kg (24.4%) had no evidence of active colitis (endoscopic score of 0) vs PBO (8.2%, p < 0.001). At wk 30, 27.7% and 30.6% of IFX 5- and 10 mg/kg treated pts, respectively, were free of evidence of active colitis vs. 9.4% of PBO (both p < 0.001). Proportion of pts in clinical remission was similar for the IFX at wks 8 and 30 (range, 29.8% to 36.4% vs 10.2% to 13.1%; PBO; p < 0.001 all comparisons). Proportion of IFX-treated pts in clinical remission at wk 30 was 4 fold greater for pts with mucosal healing at wk 8 (48.3%) vs pts without mucosal healing at wk 8 (9.5%).

Conclusions: IFX is effective in inducing mucosal healing and remission in UC pts. Clinical remission at wk 30 occurred 4 times as often for pts with mucosal healing at wk 8.

Natalizumab Improves the Health Related Quality of Life (HRQOL) in Crohn’s Disease Patients

Purpose: Crohn’s disease is associated with impaired HRQOL. This analysis investigated HRQOL outcomes during maintenance therapy with natalizumab (a humanized monoclonal IgG4 antibody to α4 integrin) in the ENACT-2 trial where higher rates of sustained response and remission were observed compared with placebo.

Methods: Patients who responded to natalizumab induction therapy (n = 339) were randomized to natalizumab 300 mg (n = 168) or placebo infusions (n = 171) given monthly for up to 12 months. HRQOL was measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) and the Short Form-36 (SF-36) at months 0, 3, 6, 9, and 12. Higher scores indicate better HRQOL. A minimally important difference (MID) is defined as 16 pts for Total IBDQ and 5 pts for SF-36 summary scores.

Results: The change for all IBDQ scales from ENACT-1 baseline was significantly greater (p < 0.05) in natalizumab-treated patients at all timepoints. Changes in 7 of 10 SF-36 scales were significant by month 3 and all were significant in months 9 and 12. A significantly greater proportion of natalizumab patients achieved MID on the Total IBDQ at months 6–12 and the SF-36 PCS at months 3–12. Mean scores for physical function, social function, role-emotional, and mental health approximated US norms at month 12.

Change From Baseline [Mean (SD)]

<table>
<thead>
<tr>
<th>Nataizumab</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBDQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBDO Total</td>
<td>53.9 (33.6)</td>
<td>35.5 (40.3)</td>
</tr>
<tr>
<td>Bowel Symptoms</td>
<td>17.7 (11.7)</td>
<td>10.2 (13.6)</td>
</tr>
<tr>
<td>Systemic Symptoms</td>
<td>9.0 (7.1)</td>
<td>6.1 (7.2)</td>
</tr>
<tr>
<td>Emotional Function</td>
<td>17.4 (13.4)</td>
<td>12.8 (15.1)</td>
</tr>
<tr>
<td>Social Function</td>
<td>9.5 (7.2)</td>
<td>6.9 (8.4)</td>
</tr>
<tr>
<td>SF-36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical Component Summary</td>
<td>12.6 (9.4)</td>
<td>6.8 (9.5)</td>
</tr>
<tr>
<td>Mental Component Summary</td>
<td>9.7 (10.6)</td>
<td>6.8 (12.4)</td>
</tr>
<tr>
<td>Physical Function</td>
<td>18.1 (18.2)</td>
<td>15.2 (21.7)</td>
</tr>
<tr>
<td>Role-Physical</td>
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<td>22.4 (48.2)</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>32.1 (22.5)</td>
<td>17.9 (25.1)</td>
</tr>
<tr>
<td>General Health</td>
<td>22.6 (22.2)</td>
<td>11.9 (18.7)</td>
</tr>
<tr>
<td>Vitality</td>
<td>27.3 (25.3)</td>
<td>18.9 (27.2)</td>
</tr>
<tr>
<td>Social Function</td>
<td>30.3 (24.3)</td>
<td>20.5 (28.1)</td>
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<tr>
<td>Role-Emotional</td>
<td>27.8 (42.4)</td>
<td>20.1 (48.7)</td>
</tr>
<tr>
<td>Mental Health</td>
<td>17.2 (19.0)</td>
<td>10.3 (19.2)</td>
</tr>
</tbody>
</table>
Conclusions: Maintenance therapy with natalizumab resulted in significantly improved HRQOL, as evidenced by both disease specific (IBDQ) and general (SF-36) measures.

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Maintenance of Remission over 1 Year in Patients with Active Crohn’s Disease Treated with Adalimumab: Results of a Blinded, Placebo-Controlled Study


Gastroenterology. Mayo Clinic. Rochester, MN; Ctr Advanced Medicine, Univ Chicago, Chicago, IL; Gastroenterology, Charles Univ, Prague, Czech Republic; Gastroenterology; Atlanta Gastroenterology Associates, Atlanta, GA; Ctr IBD Research, UNC Medical School, Chapel Hill, NC; IBD Clinic, Dalhousie Univ, Halifax, NS, Canada; Medicine, Univ Calgary, Calgary, AB, Canada; Gastroenterology, UZ Gasthuisberg, Leuven, Belgium and Immunology, Abbott, Parsippany, NJ.

Purpose: To assess the long-term efficacy and safety of adalimumab (ADA)—a fully human anti-TNF monoclonal antibody approved for the treatment of rheumatoid arthritis (RA)—in maintaining remission in patients (pts) with Crohn’s disease (CD).

Methods: Patients with moderate to severely active CD who completed CLASSIC, a 4-week, placebo-controlled, multi-center study of ADA, were eligible to enter a long-term study of ADA (CLASSIC II). All pts in CLASSIC II received ADA 40 mg sc at Week 0 (Week 4 of CLASSIC) and Week 2. Patients in remission (CDAI < 150) at both Week 0 and Week 4 were randomized to receive ADA 40 mg eow, ADA 40 mg/wk, or placebo for up to 1 year. Patients with CDAI≥150 entered an open-label ADA cohort (results reported elsewhere). CDAI and adverse events (AE) were assessed at each study visit.

Results: Of 275 pts entering CLASSIC II, 55 had CDAI < 150 at both Week 0 and Week 4 and were randomized. Remission was maintained over time in ADA-treated pts but not in pts receiving placebo (table). AE were generally mild to moderate in severity and similar to those previously reported in studies of ADA in pts with RA. Serious AE occurred in 2 pts in the placebo group (intestinal obstruction, back pain) and in 1 pt in the 40-mg-eow group (non-critical coronary artery disease.)

Maintenance of Remission, N (%)

<table>
<thead>
<tr>
<th>Week</th>
<th>Placebo (n = 18)</th>
<th>ADA 40mg eow (n = 19)</th>
<th>ADA 40mg/wk (n = 18)</th>
</tr>
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<tbody>
<tr>
<td>4</td>
<td>16 (89)</td>
<td>18 (95)</td>
<td>18 (100)</td>
</tr>
<tr>
<td>8</td>
<td>10 (56)</td>
<td>14 (74)</td>
<td>16 (89)</td>
</tr>
<tr>
<td>12</td>
<td>9 (50)</td>
<td>16 (84)*</td>
<td>16 (89)*</td>
</tr>
<tr>
<td>16</td>
<td>10 (56)</td>
<td>15 (79)</td>
<td>14 (78)</td>
</tr>
<tr>
<td>24</td>
<td>8 (44)</td>
<td>15 (79)*</td>
<td>17 (94)*</td>
</tr>
<tr>
<td>32</td>
<td>6 (33)</td>
<td>15 (79)*</td>
<td>17 (94)*</td>
</tr>
<tr>
<td>48</td>
<td>8 (44)</td>
<td>15 (79)*</td>
<td>17 (94)*</td>
</tr>
<tr>
<td>56</td>
<td>7 (39)</td>
<td>13 (68)</td>
<td>15 (83)*</td>
</tr>
</tbody>
</table>

LOCF, *p < 0.05 ADA vs. placebo.

Conclusions: In this small exploratory cohort, remission was maintained in pts with CD treated with ADA 40 mg/wk or 40 mg eow for 1 year. ADA was safe and well-tolerated in this study. A larger study, powered to definitively assess the long-term efficacy of ADA, is ongoing.

844

Tacrolimus Therapy for Severe Recurrent Crohn's Disease after Stem Cell Transplant

Erina N. Foster, M.D., Walter L. Trudeau, M.D.* GI/Hepatology, UC Davis Medical Center, Sacramento, CA.

Purpose: We describe the use of tacrolimus as rescue therapy for recurrent Crohn’s disease (CD) post stem cell transplant refractory to all traditional therapies in the face of a fungal infection.

Methods: Case report.

Results: Tacrolimus (FK506) is an oral macrolide antibiotic with immunomodulatory effects which has been used in refractory inflammatory bowel disease. Pilot studies have shown tacrolimus to be safe and effective for fistulizing CD.

We describe a 40 year old Caucasian male with a 7 year history of fistulizing CD who had initially responded to infliximab infusion. Unable to achieve therapeutic levels of 6TG on 6MP, the patient was switched and maintained on 6TG. The progression of his disease resulted in severe inflammation of the rectosigmoid area, spiking fevers, and frequent hospitalizations. The patient then underwent autologous stem cell transplant at an outside facility. The patient’s disease remained quiescent for 2 years and then flared with fever, abdominal pain, distention and diarrhea. After treatment with infliximab and IV steroids, the patient continued to have fever and severe diarrhea with hematochezia. After high dose IV steroids were started at an outside center, subcutaneous methotrexate was tried but discontinued due to neutropenia. Total parenteral nutrition was started for significant weight loss and progressive hypoalbuminemia. He was admitted to our hospital with new onset productive cough, fevers, worsening abdominal pain and diarrhea. Sigmoidoscopy revealed severe friable, ulcerated and intensely inflamed mucosa. Abdominal films showed persistent ileus of the small bowel and colon. Aspergillus infection was also diagnosed by CT guided biopsy of new pulmonary nodules. The patient refused surgery despite medical and surgical advice. Tacrolimus therapy was initiated with IV dosing at 0.03mg/kg/day as continuous infusion and titrated to oral dosing with a goal level of 10–15 ng/ml. Within 2 weeks of starting tacrolimus, the patient responded with firmer nonbloody stools, weight gain, and an increase in serum albumin. One month after therapy began, the inflammation and ulceration had improved on sigmoidoscopy. His pulmonary symptoms cleared with concurrent treatment with voriconazole.

Conclusions: Based on our short term anecdotal experience, tacrolimus is a therapeutic option in this patient with severe recurrent CD refractory to steroids, infliximab, and stem cell transplant who was intolerant to methotrexate.

845

Provision of Preventive Health Services to IBD Patients

Lisbeth Selby, M.D., Housea Mardini, M.D., M.P.H., Willem J.S. de Villiers, M.D., Ph.D.* Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY.

Purpose: Patients (pts) with chronic diseases often do not receive preventive health services at the same rate as the general population. The issue has not been fully explored; hypotheses include such issues as consumption of physician time by the complexity of a chronic condition and the idea that primary physicians, who usually provide such services, are intimidated by the complexity of the chronic disease, remaining only superficially involved in the care, if at all.

We performed a cross-sectional survey of our IBD clinic pts to assess the rates at which they receive 10 US Preventive Services Task Force (USPSTF) recommended services (ones rated either A or B).

Methods: One of several IBD specialists surveyed 49 consecutive adult IBD pts at a single routine clinic visit. We combined chart data and patient report to determine receipt of services. We also gathered data on demographics, insurance coverage, disease duration, and IBD type. Data was recorded on standardized forms. USPSTF recommendations can be found at http://www.ahrq.gov/clinic/ uspstf.htm.

Results: Ulcerative colitis was present in 1/3, while Crohn’s disease was present in the rest. Males comprised 43% of the group. Mean age of the group was 41.8 years. 35%were women aged 40 or older. Only 3/49 pts was 65 or older. Median number of physician visits/yr was 5. Median duration of diagnosed IBD was 8 yrs (range 1–30).

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Rates of receipt of preventive services in 8/10 categories ranged from 90–98%. One pt did not get blood pressure screening, the only service required at age 25, due to lack of health insurance. Another pt continually refused several appropriate services. Mammogram screening rates would have been 98% if women in their 40s were excluded from analysis.

Disturbing trends in under-utilization were noted in screening at risk pts (defined by USPSTF as hypertensives or hyperlipidemics) for diabetes; only 84% had been tested. Even more concerning was the observation that only 69% of pts had ever received dietary advice to lower cardiovascular disease risk.

Small numbers of pts > 65 years old limit analysis in this group.

**Conclusions:** In general, deficiencies in the receipt of these services is likely multi-factorial but merits further attention since mortality in IBD is largely due to the same diseases as in the general population. Study of elderly IBD pts in particular is needed. IBD specialists are uniquely poised to monitor the receipt of these services and facilitate implementation, perhaps by frequent, targeted communication to primary physicians.

**846**

The Effectiveness of Continuing the Induction Dose of Asacol into the Maintenance Phase: Results from the Community Setting

**Purpose:** The FDA indicated dosages of Asacol® (mesalamine) delayed-release tablets are 2.4 g/day for the treatment of mild-moderately active ulcerative colitis (UC) and 1.6 g/day for maintenance of remission. There is anecdotal evidence that maintaining the induction dose may be better than dose-reduction to prevent relapse. This study used a naturalistic, retrospective design to compare the outcomes of UC patients maintained on the dose used to induce remission with those whose maintenance dose was reduced.

**Methods:** The medical records from 411 UC patients from 39 geographically dispersed, community gastroenterology practices who had a disease flare between 1999 and 2003 successfully treated with Asacol without requiring steroids were reviewed. The review included the single flare of interest and the subsequent maintenance period. Outcome measures examined were maintenance of remission at 6 and 12 months post-induction, and% rated “normal” on the physician global assessment of symptom severity (PGA) at final data capture. The primary explanatory variable was the relation between maintenance (M) and induction (I) dose, coded as M = 1 vs. M < 1. Other covariates examined were:

- Final induction dose: grouped on g/day, ≤2.4, 3.2–4.0, >4.8
- Extent of disease: proctitis+rectosigmoiditis vs. left-sided vs. extensive
- Severity of disease: mild vs. moderate vs. severe
- Prior history: 1st flare vs. subsequent flare without immediately prior maintenance medication vs. subsequent flare while on maintenance medication.

**Results:** In logistic regression analyses, no variables were significantly (p < .05) predictive of maintenance of remission at 6 or 12 months. When the initial PGA was forced into the logistic regression model first, to control for severity of attacks and to assess the impact of the other variables, the only significant predictor of final PGA was M = 1 vs. M < 1 (p < .01, OR = 2.21, 95% CI = 1.36–3.58). Results are shown in the table below.

<table>
<thead>
<tr>
<th>Starting PGA</th>
<th>M vs. I</th>
<th>N</th>
<th>% Normal at Final Data Capture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>M = 1</td>
<td>135</td>
<td>65.9</td>
</tr>
<tr>
<td></td>
<td>M &lt; 1</td>
<td>43</td>
<td>51.2</td>
</tr>
<tr>
<td>Moderate or Severe</td>
<td>M = 1</td>
<td>173</td>
<td>78.6</td>
</tr>
<tr>
<td></td>
<td>M &lt; 1</td>
<td>60</td>
<td>53.3</td>
</tr>
</tbody>
</table>

**Conclusions:** Maintaining the same dose of Asacol used to induce remission significantly increased the likelihood of UC patients receiving a physician’s global assessment of “normal” at one year post-induction. This finding was consistent across dosage levels and extent of disease.
Purpose: Patients with inflammatory bowel disease (IBD) are at risk for glucocorticoid induced osteoporosis. However, there is very limited data on the magnitude of this risk, and the duration and dose of steroids required to produce bone loss. The objective of this study is to prospectively determine the rate and degree of bone loss in IBD patients treated with corticosteroids.

Methods: IBD patients who are being started on oral prednisone undergo baseline DEXA to determine bone mineral density (BMD) scanning and lateral vertebral assessment for fracture, baseline labs, and 1,25 (OH) Vitamin D levels. NTX levels are drawn after 1 month of prednisone therapy, and follow-up DEXA scans are repeated at 3, 6 and 12 months after the initiation of prednisone. IBD patients, matched for disease activity, but not being started on prednisone will be studied as controls. Patients on prednisone undergo a standard steroid taper based upon clinical response. All patients are treated empirically with calcium 1500 mg/d and vitamin D 600 u/d. 38 patients will be entered in the steroid and control groups each. Baseline disease activity is scored using the Mayo Score for UC, and the Harvey Bradshaw Index for CD.

Results: To date, 16 patients starting on steroids have entered the study; 12 UC, 4 CD; mean age = 32.1, 10 male and 6 female, mean BMI = 22.2. All women were premenopausal. No patient had a history of fracture. Mean baseline t score of bilateral hips = −0.7. Mean baseline t score of L2–L4 = −0.6. 20% of patients were found to have baseline osteopenia in the hips, and 7% of patients had baseline osteoporosis in the hips. 14% of patients had baseline osteopenia at L2–L4, and 14% had baseline osteoporosis at L2–L4. 50% of patients had low baseline levels of 1, 25 (OH) vitamin D and were supplemented with ergocalciferol 50,000 units TIW. Mean NTX at 1 month = 14.7; no patient had an elevated NTX. At 3 months there was a mean decrease of 1.7% (range 0% – 6%) at the hips, and a mean decrease of 2.7% (range 1% – 6%) at L2–L4. No fractures developed as assessed by lumbar vertebral assessment.

Conclusions: In this interim analysis, significant bone loss as defined by a greater than 5% decline in BMD can be seen as early as 3 months in these patients with active IBD being treated with a tapering course of prednisone, despite concurrent supplemental calcium and vitamin D. Continued prospective follow up at 6 and 12 months is underway.

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A Randomized Placebo-Controlled Trial of Infliximab Therapy for Active Ulcerative Colitis: ACT I Trial Results through Week 54
W. J. Sandborn, M.D., B. G. Feagan, M.D., A. Olson, M.D., J. Johanss, Ph.D., S. Travers, M.D., D. Present, M.D., B. E. Sands, M.D., P. Rutgeerts, M.D., M. * D. Gastroenterology & Hepatology, Mayo Clinic, Rochester, MN; Robarts Research Institute, University of Western Ontario, London, Canada; Clinical Research & Development, Centocor, Inc., Malvern, PA; Biostatistics, Centocor, Inc., Malvern, PA; Dept of Medicine, Mt. Sinai Medical Ctr, New York, NY; Gastrointestinal Unit, Massachusetts General Hospital, Boston, MA and Gastroenterology, Hospital Leuven, Leuven, Belgium.

Purpose: The ACT I trial evaluated the safety and efficacy of infliximab (IFX) in UC.

Methods: 364 pts with active UC despite corticosteroids/AZA/6-MP, with endoscopic evidence of moderate/severe UC (endoscopy score ≥2) and total Mayo score of 6–12 inclusive, were randomized to placebo (PBO), infliximab (IFX) 5- or 10 mg/kg at wks 0, 2, 6 and q8 wks through wk 46. Primary endpoint was induction of clinical response, defined as decrease in Mayo Clinic score of ≥50% and ≥3 points, with decrease in rectal bleeding score of ≥1 or rectal bleeding score of 0 or 1 at wk 8. Secondary endpoints were clinical remission, defined as Mayo score ≤2 with no individual subscores >1, and mucosal healing defined as endoscopy subscore of 0 or 1.

Results: More pts treated with IFX 5- (69.4%) and 10 mg/kg (61.5%) were in clinical response at wk 8 vs PBO (37.2%, p < 0.001 for both). At wk 54, 45.5% and 44.3% of IFX 5- and 10 mg/kg pts, respectively, achieved clinical response vs 19.8% of PBO (p < 0.001, for both). At wk 8, 38.8% and 32.0% of IFX 5- and 10 mg/kg pts, respectively, were in clinical remission vs 14.9% of PBO (p < 0.001 and p = 0.002); this persisted at wk 54 (34.7%, 5 mg/kg; 34.4%, 10 mg/kg vs 16.5%, PBO; p = 0.001 for both). Mucosal healing at wk 8 occurred in 62.0% and 59.0% of IFX 5- and 10 mg/kg pts, respectively vs 33.9% of PBO (p < 0.001, for both); this was maintained at wk 54 (45.5%, 5 mg/kg; 46.7%, 10 mg/kg vs 18.2%, PBO; p < 0.001 for both). Proportion of pts with ≥1 AE in the IFX group was 89.3%, vs 85.1% in PBO. SAE’s occurred in 22.6% vs. 25.6% in the combined IFX and PBO group, respectively. 10.7% of PBO and 11.1% in the combined IFX group experienced ≥1 infusion reaction. In the 5mg/kg IFX group, 1 pt each reported prostatic adenocarcinoma, intestinal dysplasia, and optic neuritis. Serious infections were reported in 4.5% vs. 4.1% in the IFX and PBO groups, respectively. One TB case was reported in the 10 mg/kg IFX group.

Conclusions: In active UC, IFX reduces signs and symptoms, induces and maintains remission, and attains mucosal healing.

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Rapid Response to Human Anti-TNF Monoclonal Antibody Adalimumab in Patients with Moderate to Severely Active Crohn’s Disease in the CLASSIC Study
S. B. Hanauer, M.D.,∗ W. J. Sandborn, M.D., P. Rutgeerts, M.D., R. N. Fedorak, M.D., R. Panaccione, M.D., L. E. Melliti, Dr.P.H., P. F. Pollack, M.D. Ctr Advanced Medicine, U Chicago, Chicago, IL; Gastroenterology, Mayo Clinic, Rochester, MN; Gastroenterology, UZ Gasthuisberg, Leuven, Belgium; Gastroenterology, U Alberta, Edmonton, AB, Canada; Medicine, U Calgary, Calgary, AB, Canada; HEOR, Abbott, Chicago, IL and Immunology, Abbott, Parsippany, NJ.

Purpose: To assess the rapidity of response to adalimumab (ADA), a fully human monoclonal antibody targeting tumor necrosis factor (TNF) approved for the treatment of rheumatoid arthritis, in patients with moderate to severely active Crohn’s disease (CD).

Methods: In the CLASSIC study, patients with moderate to severely active CD (220–450 CDAI) and naïve to anti-TNF therapy were randomized to receive subcutaneous injections at Weeks 0 and 2 with adalimumab 40 mg/20 mg (40/20), 80 mg/40 mg (80/40), or 160 mg/80 mg (160/80), or placebo (PB). Remission (CDAI < 150), response (CDAI decrease ≥70 points), self-administered IBDOQ, and CDAI were assessed at Weeks 1, 2, and 4.

Results: In all, 299 patients were randomized to 40/20 (n = 74), 80/40 (n = 75), 160/40 (n = 76), or PB (n = 74). CDAI and IBDOQ scores did not
differ among groups at baseline (BL). Statistically significant improvements in ADA-treated patients versus PB were observed in clinical response and CDAI and IBDQ scores as early as Week 1 and continued to improve through Week 4 (Table). Remission rates increased at all time points in the 80/40 and 160/80 groups and were significant at Week 4 in the 160/80 group versus PB.

Conclusions: Adalimumab rapidly induced remission, clinical response, and improvements in CDAI and total IBDQ in patients with moderate to severely active CD. Significant improvements in clinical response, CDAI, and total IBDQ were observed as early as Week 1 and continued through Week 4 in patients treated with ADA 80/40 and ADA 160/80 compared to PB. While improvements in CDAI and IBDQ scores were similar in the 80/40 and 160/80 groups, the optimal induction regimen for remission at Week 4 was 160/80.

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Screening for Dysplasia in Primary Sclerosing Cholangitis – A Population-Based Assessment of Physician Practices
Gilad G. Kaplan, M.D., Steven J. Heitman, M.D., Robert J. Hilsden, M.D., Ph.D., Stefan Urbanski, M.D., Samuel S. Lee, M.D., Kelly W Burak, M.D., Robert J. Myers, M.D., Mark Swain, M.D., Remo Panaccione, M.D.*. Medicine (Division of Gastroenterology), University of Calgary, Calgary, AB, Canada and Pathology, University of Calgary, Calgary, AB, Canada.

Purpose: Patients with primary sclerosing cholangitis (PSC) and either ulcerative colitis (UC) or Crohn’s disease (CD) have a high risk of developing colorectal cancer (CRC). Recent recommendations have suggested annual four quadrant multi-segmental biopsies to detect CRC or dysplasia. Physician adherence to this protocol has not been adequately assessed. Aims: 1) to determine the rate of dysplasia in PSC patients with UC or CD and 2) to assess screening practices by gastroenterologists for PSC.

Methods: A population-based study of the Calgary Health Region (CHR) was conducted between April 1, 2000 and March 31, 2005 to identify all patients with a diagnosis of PSC. PSC patients were identified using regional databases (ERCP, health records, diagnostic imaging, transplant and histopathology) and were confirmed by chart review. Histopathology from colonoscopy records was reviewed in CHR patients with PSC and UC or CD for: 1) the number of biopsies taken during screening colonoscopy; 2) frequency of colonoscopies conducted between 2000 and 2005, and 3) the presence of CRC, dysplasia or a dysplasia associated lesion or mass (DALM).

Results: During the study period there were 105 patients with PSC identified, 44 resided in the CHR and had UC or CD. Of the 44 patients who were eligible for screening, 5 (11.4%) were diagnosed with dysplasia (n = 2), DALM (n = 2) or CRC (n = 1) in the 5 year screening period. Two of these patients were diagnosed by screening colonoscopies, while the other three were not being screened regularly and were identified because of the development of symptoms. Of an expected 130 screening colonoscopies for dysplasia, only 56 (43%) were actually conducted and only 32% of patients had more than three quarters of their recommended colonoscopies attempted. Those patients undergoing screening colonoscopies had a median of 27 [19–33] biopsies taken.

Conclusions: Patients with PSC and UC or CD have a high rate of pre-malignant or malignant colorectal lesions. A population-based assessment of the practice of screening colonoscopies for dysplasia demonstrated that the frequency of screening was low and that sampling was inadequate. Suboptimal screening may explain why two thirds of PSC patients with dysplastic or malignant pathology were identified through symptomatic presentation.

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Mesalamine Prevents Dysplasia in Patients with Inflammatory Bowel Disease
Ilan Aharoni, M.D., Sara Safdar, M.D., Asher Kornbluth, M.D., Jian Jun Li, M.D., Robert Kodsi, M.D., Scott Tenner, M.D., M.P.H.* Division of Gastroenterology, Maimonides Medical Center, Brooklyn, NY and Division of Gastroenterology, Mount Sinai School of Medicine, New York, NY.

Purpose: The lifetime prevalence of colorectal cancer in a patient with inflammatory bowel disease (IBD), ulcerative colitis or Crohn’s colitis, is 3 to 6%. Endoscopic surveillance for dysplasia in patients with long-standing colitis is an accepted method of preventing death from colorectal cancer. Recent studies have suggested that the incidence of colorectal cancer in patients with long-standing colitis is decreasing. It is not clear whether the decrease in colorectal cancer is associated with a decrease in the incidence of dysplasia, to changes in the natural history of the disease or increased use of maintenance therapy with mesalamine and/or immunosuppressive agents.

Methods: In order to determine the role of mesalamine in the prevention of colon cancer, we evaluated mesalamine use in patients with long-standing ulcerative colitis and Crohn’s colitis who had a duration of disease greater than 8 years. Demographic information, duration of disease, number of hospitalizations, extent of disease, and other medications taken were recorded. The mean dosage of mesalamine was calculated using the total dose per time period studied divided by the number of days from the time of diagnosis to May 1, 2005.

Results: One hundred-two patients were included in the study. There were 53 female, 49 male patients, mean age 64 ± 18 years. The mean duration of disease was 16.5 ± 8.8 years. All patients had received mesalamine for a mean period of 14.4 ± 7.1 years. The mean dosage of mesalamine in all patients was 2.6 ± 1.2 grams. None of the patients studied developed colon cancer. Four patients developed dysplasia (3.9%). The mean dosage of mesalamine in patients who had not developed dysplasia 2.6 ± 1.2 grams was significantly higher than patients who had developed dysplasia 0.8 ± 0.35 grams (p = 0.003). There were no significant differences between the groups regarding age, gender, duration of disease, extent of disease, or other medications, including 6-mercaptopurine/azathioprine.

Conclusions: We conclude that the incidence of dysplasia and colon cancer in patients with IBD is decreasing. In patients with long-standing IBD, increased total mesalamine exposure appears to decrease the incidence of dysplasia. These results suggest that the decreased incidence of colon cancer in patients with IBD may be related to increased use of mesalamine for maintenance therapy.

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Does Colonoscopy Preparation Cause a Flare of Ulcerative Colitis? Stacy Menees, M.D., Peter Higgins, M.D., Sheryl Korsnes, Grace Elta, M.D.* Gastroenterology, Univ. of Michigan, Ann Arbor, MI.

Purpose: Anecdotally, colonoscopy preparation seems to increase ulcerative colitis (UC) symptoms in some patients. The goal of this study is to determine if there is an association between colonoscopy preparation and disease relapse and to identify demographic factors, disease characteristics, or medications that are associated with increased symptoms after colonoscopy preparation.

Methods: Initial assumption of a 20% flare rate led to a planned study size of 30. Thirty-five outpatients with a history of UC, intact colon and quiescent disease as determined by the patient were enrolled in a prospective ABA crossover study in which the patients served as their own controls (A = no prep B = colonoscopy prep). Patients were clinically evaluated with the Simple Clinical Colitis Activity Index (SCCAI) for the week prior to colonoscopy (A), week 1(B) and week 4(A) after colonoscopy. Data analysis used a mixed model to accommodate non-independence of repeated measurements.

Results: 31 patients completed the study. Mean age was 48 yrs, with 97% Caucasian and 55% men. Patients had UC for an average of 14.1 yrs (1.5–54 yrs), with an average of 0.64 hospitalizations/yr, 3.7 flares/yr, and 1.7 episodes requiring steroids/yr. 68% used 5-ASA, 36% used thiopurines, and 23% used chronic prednisone. 77% used fleets phospho-soda prep. Pre-colonoscopy, 2(6%) patients felt that preps lead to UC flares, while 3(10%) were unsure, and the majority (84%) thought there was no effect. Six (19%) pts required an escalation of their 5-ASA meds post-colonoscopy, 2 of these
Low Grade Dysplasia Preceding Neoplasia in Inflammatory Bowel Disease

Robin Forman, D.O., David Labowitz, D.O., Emily Glazer, M.D., Georgia Panagopoulos, Ph.D., Burton I. Korelitz, M.D.* Digestive Diseases, Beth Israel Medical Center; New York, NY and Gastroenterology, Lenox Hill Hospital, New York, NY.

Purpose: Studies have shown that low grade dysplasia (LGD) progresses to advanced neoplasia (high grade dysplasia or colorectal cancer) in 30% of patients with Ulcerative colitis (UC). The present study investigated whether LGD preceded different types of neoplasia in patients with UC and Crohn’s colitis (CC).

Methods: A retrospective chart review was conducted on 23 UC and CC patients with high grade dysplasia (HGD) and colorectal cancer (CRC) to seek those with LGD on surveillance colonoscopy. Only patients with flat dysplasia were included. Patients were grouped into HGD, Adenocarcinoma (ACA) without mucinous features, and ACA with mucinous/signet ring cell features. Clinical and disease characteristics of patients in the groups were compared. The Chi-square test was used for dichotomous variables and Analysis of Variance was used to compare groups on continuous variables.

Results: There were no differences in demographics and disease characteristics (Table 1). Overall, 48% of neoplasia was preceded by LGD. HGD was preceded by LGD in 83% of patients (5/6). ACA w/o mucinous features was preceded by LGD 50% of the time (6/12). Cases of ACA w/mucinous features were not found to have antecedent LGD (0/5) (Table 2). Theses results were statistically significant (p = .022). All cases with ACA with mucinous features had CC.

Conclusions: These preliminary results suggest that HGD is usually preceded by LGD. However, there may not be a definitive progression of LGD to more aggressive forms of CRC. Patients with CC may have a propensity to develop CRC with mucinous features which is not preceded by LGD. A large scale controlled cohort study is needed to further elucidate the relationship between LGD and advanced neoplasia in IBD.

Table 1. Patient & Disease Characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>HGD</th>
<th>ACA w/o mucinous features</th>
<th>ACA w/ mucinous features</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, N(%)</td>
<td>5 (83)</td>
<td>6 (50)</td>
<td>3 (60)</td>
<td>0.39</td>
</tr>
<tr>
<td>Mean age Sx onset (yr)</td>
<td>37 (18)</td>
<td>31 (14)</td>
<td>42 (20)</td>
<td>0.43</td>
</tr>
<tr>
<td>Mean age Dx (yr) Disease, N(%)</td>
<td>37 (17)</td>
<td>38 (15)</td>
<td>45 (22)</td>
<td>0.71</td>
</tr>
<tr>
<td>CD</td>
<td>2 (22)</td>
<td>2 (22)</td>
<td>5 (55)</td>
<td></td>
</tr>
<tr>
<td>UC</td>
<td>4 (29)</td>
<td>10 (71)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Mean Sx onset to neoplasia Dx (mos)</td>
<td>179 (115)</td>
<td>305 (173)</td>
<td>312 (170)</td>
<td>0.62</td>
</tr>
<tr>
<td>Mean Sx onset to LGD (mos)</td>
<td>106 (97)</td>
<td>148 (103)</td>
<td>NA</td>
<td>0.51</td>
</tr>
<tr>
<td>Mean LGD to neoplasia (mos)</td>
<td>42 (35)</td>
<td>51 (62)</td>
<td>NA</td>
<td>0.78</td>
</tr>
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</table>

Table 2. Relationship Between Neoplasia & LGD

<table>
<thead>
<tr>
<th></th>
<th>HGD, N(%)</th>
<th>ACA w/o mucinous features, N(%)</th>
<th>ACA w/ mucinous features, N(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LGD</td>
<td>5 (83)</td>
<td>6 (50)</td>
<td>0 (0)</td>
<td>0.02</td>
</tr>
<tr>
<td>No LGD</td>
<td>1 (17)</td>
<td>6 (50)</td>
<td>5 (100)</td>
<td></td>
</tr>
</tbody>
</table>

GM-CSF Protective Effects in Experimental Colitis

Satheesh K. Sainathan, Ph.D., Kumar S. Bishnapuri, Ph.D., John Parkinson, Ph.D., Marco Colonna, M.D., Shrikant Anant, Ph.D.,* Brian K. Dieckgreber, M.D., Ph.D. Gastroenterology, Washington University in St. Louis, School of Medicine, Saint Louis, MO; Berlex Laboratories and Pathology and Immunology, Washington University in St. Louis, School of Medicine, Saint Louis, MO.

Purpose: Crohn’s disease is associated with a loss of tolerance to commensal gut flora. In preliminary set of studies on germ-free mice, we observed a 3–4-fold induction in granulocyte-macrophage colony stimulating factor (GM-CSF) expression. These results suggested a potential role of GM-CSF in the mucosal response to commensal flora. To establish a mechanistic understanding of GM-CSF action in the treatment of Crohn’s disease, we examined its effects in experimental model of DSS-colitis.

Methods: Recombinant murine GM-CSF was pegylated (PEG-rmGM-CSF) to increase the half-life and to prevent rapid clearance from circulation. To determine the protective role of GM-CSF, mice were induced colitis by administering 5% DSS in the drinking water for 7 days and subsequently treated with or without PEG-rmGM-CSF. A group of mice was also treated with 440c to probe the involvement of the pDC in the response to GM-CSF. Results were interpreted on the basis of histopathological evaluation, disease activity score as well as cytokine expression by real time RT-PCR and protein arrays.

Results: Treatment of PEG-rmGM-CSF significantly reduced DSS-colitis associated weight loss, reduction in colonic size, bleeding score. However, the administration of mAb 440c along with PEG-rmGM-CSF led to a complete reversal of protective effect. Histopathological observation further demonstrated a profound reduction in inflammatory cell infiltrates. Real time RT-PCR analyses exhibited a significant increase in pro-inflammatory cytokine expression associated with DSS-colitis, however PEG-rmGM-CSF treatment led to a significant decrease in TNF alpha, IL-1 beta expression and its complete reversal was observed following mAb 440 c treatment. The data were further confirmed by protein-array analysis. Administration of CpG DNA (a TLR 9 ligand) in colitis model exhibited protective effect through production of Type I Interferon. We also demonstrated that administration of PEG-rmGM-CSF further amplified CpG DNA induced Type I Interferons, IL-10 and IDO production

Conclusions: These data suggest that GM-CSF protection in DSS-induced colitis may occur through interferon producing plasmacytoid DCs. These results also suggest that GM-CSF may be critical in regulating the mucosal immune response and contributing to a tolerogenic environment.
Clinical Features and Outcomes of Cytomegalovirus Colitis or Pouchitis in Patients with Inflammatory Bowel Disease

Nadim Salfiti, M.D., Edward V. Loftus, Jr., M.D.,∗ William J. Tremaine, M.D., Darrell S. Parh, M.D., William A. Faubion, M.D., William J. Sandborn, M.D. Gastroenterology, Mayo Clinic College of Medicine, Rochester, MN.

Purpose: To evaluate the clinical features and outcomes of cytomegalovirus (CMV) colitis or pouchitis complicating the course of inflammatory bowel disease (IBD).

Methods: A centralized diagnostic index was utilized to identify all patients with confirmed IBD and CMV colitis or pouchitis who were evaluated at Mayo Clinic Rochester between 1992 and 2001. Medical records were abstracted for demographics, clinical features and outcomes.

Results: Fourteen patients with IBD and CMV colitis or pouchitis were identified, ten with ulcerative colitis (UC) (71%), three with Crohn’s disease (CD) (21%), and one with indeterminate colitis (7%). Thirteen patients had a previously established diagnosis of IBD, while one was diagnosed with CMV and IBD concurrently. Present medications included steroids in 86% and immunosuppressives in 35% (only 14% were on neither). In 12 patients, CMV was identified after failure of conventional medical therapy. In two cases, CMV was not suspected preoperatively and was diagnosed by review of the surgical specimen. CMV diagnosis was based on characteristic histologic findings in 13 cases, and on colitic symptoms plus serologies and viral culture of blood in one case. CMV serologies were performed in 7 cases; IgG was positive in 5 (71%) and IgM was positive in 3 (43%). In 2 cases, both IgG and IgM were negative despite positive biopsy findings. In 11, CMV treatment consisted of intravenous ganciclovir and withdrawal of immunosuppressives; in 9 patients (82%), remission of disease was achieved and colectomy avoided. In the 2 other patients with a pre-operative diagnosis of CMV, surgery was the primary treatment due to severity of disease. Two patients presented with CMV pouchitis; one improved with therapy (ganciclovir and withdrawal of immunosuppressives), while the other did not.

Conclusions: CMV colitis or pouchitis may complicate the course of IBD. CMV superinfection should be considered in all patients presenting with a severe IBD exacerbation, especially those who are refractory to steroids and immunosuppressives. Treatment involves anti-viral therapy, mainly ganciclovir, and withdrawal of immunosuppressive agents. This leads to improvement of underlying IBD in most patients, and can often avoid, or at least delay, the need for surgical intervention.

Remission and Clinical Response Induced and Maintained in Patients with Active Crohn’s Disease Treated for 1-Year Open-Label with Adalimumab

William J. Sandborn, M.D.,∗ S. B. Hanauer, M.D., M. Lukas, M.D., D. C. Wolf, M.D., K. L. Isaacs, M.D., D. G. MacIntosh, M.D., R. Panaccione, M.D., P. Rutgeerts, M.D., P. P. Pollack, M.D. Gastroenterology, Mayo Clinic, Rochester, MN; Ctr Advanced Medicine, Univ Chicago, Chicago, IL; Gastroenterology, Charles Univ, Prague, Czech Republic; Gastroenterology, Atlanta Gastroenterology Associates, Atlanta, GA; Ctr IBD Research, UNC Medical School, Chapel Hill, NC; IBD Clinic, Dalfhousie Univ; Halifax, NS; Canada; Medicine, Univ Calgary, Calgary, AB, Canada; Gastroenterology, UZ Gasthuisberg, Leuven, Belgium and Immunology, Abbott, Parsippany, NJ.

Purpose: To assess the long-term efficacy and safety of open-label (OL) therapy with fully human anti-TNF monoclonal antibody adalimumab (ADA), approved for the treatment of rheumatoid arthritis (RA), in patients (pts) with active Crohn’s disease (CD).

Methods: Patients with moderate to severely active CD who completed CLASSIC, a 4-week, placebo-controlled, multi-center study of ADA, were eligible to enter a long-term ADA study (CLASSIC II). All pts in CLASSIC II received ADA 40 mg sc at Week 0 and Week 2. Patients in remission (CDAI < 150) at both Week 0 (Week 4 of CLASSIC) and Week 4 were randomized to a blinded, placebo-controlled cohort (results reported elsewhere). Patients with CDAI ≥150 received OL ADA 40 mg eow for up to 1 year. CDAI and adverse events (AE) were assessed at each study visit. Rates of remission and clinical response, reductions from baseline CDAI of ≥70 (Δ70) or ≥100 (Δ100) points, were calculated. Dose escalation to 40 mg/wk was allowed for flare or persistent non-response.

Results: Of 275 pts entering CLASSIC II, 220 were treated in the OL cohort. At Week 56, 44% of pts were in remission and 68%/59% achieved a70/Δ100 clinical response, respectively (Table). After 1 year, 134 pts (61%) remained on ADA therapy with 54% receiving ADA 40 mg eow and 46% receiving ADA 40 mg/wk. AE were mild to moderate in severity and similar to those previously reported in studies of ADA in pts with RA. Serious AE included infection (11) and CD exacerbation (10).

Long-Term Remission and Clinical Response (% of pts)

<table>
<thead>
<tr>
<th>Week</th>
<th>CDAI &lt; 150</th>
<th>Δ70</th>
<th>Δ100</th>
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<tr>
<td>0</td>
<td>5</td>
<td>40</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>59</td>
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</tr>
<tr>
<td>8</td>
<td>29</td>
<td>62</td>
<td>50</td>
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<td>16</td>
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<td>48</td>
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</tr>
<tr>
<td>56</td>
<td>44</td>
<td>69</td>
<td>62</td>
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LOCF.
Conclusions: Remission was induced in 44% of pts treated with OL ADA, and 69% achieved clinical response within 1 year. Improvements were long-lasting. Adalimumab was safe and well-tolerated.

**NOD2/CARD15 Mutations Are Not Associated with Chronic Pouchitis or Crohn’s Disease of the Pouch**

Jean-Paul Achkar, M.D., Aaron Brzezinski, M.D., Bo Shen, M.D., Feza H. Remzi, M.D., Victor W. Fazio, M.D., Deborah Vogel, Bret A. Lashner, M.D.* Center for Inflammatory Bowel Disease, Cleveland Clinic Foundation, Cleveland, OH.

Purpose: Ileal-pouch anastomosis (IPAA) is the surgical treatment of choice for patients with ulcerative colitis who require surgery. Chronic pouchitis or a subsequent diagnosis of Crohn’s disease (CD) involving the IPAA are uncommon but increasingly recognized complications of this surgery. Because these conditions involve inflammation of the ileum and because NOD2/CARD15 mutations have been associated with ileal inflammation in CD, our aim was to determine the prevalence of NOD2/CARD15 mutations in patients with chronic pouchitis and CD of IPAA.

Methods: Patients and controls were identified from outpatient clinics and blood was drawn for DNA extraction. Chronic pouchitis was defined as 4 or more episodes of pouchitis per year or the need for chronic antibiotic or immunosuppressive therapy to control symptoms, in addition to endoscopic evidence of pouch inflammation. CD of IPAA was diagnosed on the basis of the absence of NSAID use, 3. development of perianal disease. Patients with “typical CD” (who had not undergone IPAA surgery) and non-IBD controls were also recruited and analyzed. The 3 common NOD2/CARD15 mutations (SNP 8,12 and 13) were analyzed using TaqMan (SNP 8 and 13) and Amplifluor (SNP 12) assays.

Results: NOD2/CARD15 mutations were uncommon in patients with chronic pouchitis or CD of IPAA with prevalence rates similar to those seen in healthy controls and less than in patients with “typical CD” (Table). All groups were statistically significantly different from “typical CD” (P = 0.001).

Conclusions: 1. The occurrence of chronic pouchitis or CD of IPAA is not associated with NOD2/CARD15 mutations. 2. Further studies are required to determine whether other genetic mutations may play a role in the pathogenesis of these diseases.

<table>
<thead>
<tr>
<th># NOD2/CARD15 Pouchitis</th>
<th>Chronic CD of IPAA (N = 13)</th>
<th>Typical CD of IPAA (N = 22)</th>
<th>Non-IBD Controls (N = 96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 mutations</td>
<td>10 (83%)</td>
<td>17 (94%)</td>
<td>39 (50%)</td>
</tr>
<tr>
<td>1 mutation</td>
<td>2 (17%)</td>
<td>1 (6%)</td>
<td>35 (45%)</td>
</tr>
<tr>
<td>2 mutations</td>
<td>0</td>
<td>0</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Undetermined</td>
<td>1</td>
<td>4</td>
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**Lack of Response to Infliximab (Remicade®) Therapy in Patients with Crohn’s Disease May Relate to Disease Phenotype**

Tarun Sharma, M.D., Subhashini Poolla, M.D., M.P.H., Asit Panja, M.D., Kiron Das, M.D., Ph.D.* Dept of Medicine-Division of Gastroenterology, UMDNJ Robert Wood Johnson University Hospital, New Brunswick, NJ.

Purpose: Although infliximab has been widely used to treat refractory Crohn’s Disease (CD) with good therapeutic effectiveness, there is a subgroup of patient population that fails to respond to this treatment. Our goal was to determine if there is any relationship between lack of therapeutic response to infliximab treatment and the disease phenotype in CD.

Methods: We performed a retrospective chart review of 83 adult patients who received infliximab from October 1998 to February 2004 at our center. Clinical response was classified as complete response, partial response, and non-response based on patient records at 4 weeks post each infusion. Indications for treatment were: refractory inflammatory disease without fistula (50 patients), termed as CD-Type 1 phenotype and disease with fistula (33 patients) termed as CD-Type 2 phenotype.

Results: Overall response rate in CD-Type 1 and CD-Type 2 individually was 70% and 27.3% respectively. The overall partial response rate in CD-Type 1 was 10%, and 39.4% in CD-Type 2. The overall non-response rates in these groups were 20%, and 33.3% respectively.

Complete response was seen in 73% (n = 11) of CD Type 1 (n = 15) and 50% (n = 1) of CD Type 2 (n = 2) patients with 1st infusion, 63% (n = 17) of CD Type 1 (n = 27) and 33% (n = 7) of CD Type 2 (n = 21) with 3–6 infusions, 83% (n = 5) of CD Type 1 (n = 6) and 25% (n = 2) of CD Type 2 (n = 8) for 7–10 infusions, and 50% (n = 2) of CD Type 1 (n = 2) patients with >10 infusions. No response was seen in 27% (n = 4) of CD Type 1 patients with 1st infusion, 22% (n = 6) of CD Type 1 and 33% (n = 7) of CD Type 2 patients with 3–6 infusions, 25% (n = 2) of CD Type 2 patients with 7–10 infusions, and 50% (n = 2) of CD Type 2 patients with >10 infusions.

Partial response was seen in 50% (n = 1) of CD Type 2 patients with 1st infusion, 15% (n = 4) of CD Type 1 and 33% (n = 7) of CD Type 2 patients with 3–6 infusions, 17% (n = 6) of CD Type 1 and 50% (n = 4) of CD Type 2 patients with 7–10 infusions.

Conclusions: Our results indicate that therapeutic effect of long-term use (up to 10 infusions) of infliximab in refractory Crohn’s Disease is greater (80%) in CD-Type 1 when compared to its effect on CD-Type 2 (67%); p = 0.013. Continuous follow up is needed to ascertain this relationship which may aid in identification of critical feature/s linked to non-responsiveness to infliximab treatment with respect to disease phenotype in patients with CD.

**Safety of Budesonide Capsules for the Treatment of Crohn’s Disease: Post-Marketing Surveillance Data**

Gary R. Lichtenstein, M.D.,* Bengt Bengtsson, M.D., Mervyn Danilewitz, M.D. Department of Medicine, Division of Gastroenterology, Hospital of the University of Pennsylvania, University of Pennsylvania School of Medicine, Philadelphia, PA and AstraZeneca, Lund, Sweden.

Purpose: Budesonide capsules (Entocort® EC) were developed as a medication with similar efficacy as conventional corticosteroids for the treatment of mild-to-moderate Crohn’s disease (CD), but with fewer side effects, due to a high topical glucocorticosteroid (GCS) activity and high first-pass metabolism in the liver. Budesonide capsules have been marketed since 1995 and, as of March 16, 2004, approval has been granted in 45 countries.

Aim: To review the safety profile of budesonide capsules from post-marketing surveillance reports of adverse events (AEs).

Methods: From the time that budesonide capsules were first marketed, all reports of AEs associated with budesonide capsule use have been entered and classified according to the Medical Dictionary for Regulatory Affairs (MedDRA) in a safety database. The data from this safety database were reviewed, with a particular focus on clinically important AEs that could reflect known GCS side effects.

Results: As of March 16, 2004, the clinical experience with budesonide capsules included more than 60 million treatment days, with 520 case reports from post-marketing surveillance; 445 were non-serious and 75 were serious. The most common AEs in the post-marketing safety database were headache, nausea, and rash. The most common serious AEs were hypokalemia (n = 6), peripheral edema (n = 5), and weight increase (n = 5). There were 5 deaths in the post-marketing safety database and these were reported as not causally related to the budesonide capsules. There were 4 reports of adrenal insufficiency; 5 of cataracts (4 non-serious); 4 of increased blood glucose in patients already diagnosed with diabetes (3 non-serious); 2 of osteoporosis; 1
of diabetes mellitus; 1 each of thrombophlebitis, disseminated intravascular coagulation, and deep vein thrombosis; and 1 of osteonecrosis in a patient previously treated with conventional systemic corticosteroids.

**Conclusions:** Based on more than 60 million treatment days, the frequency of reported non-serious and serious AEs following budesonide capsule treatment was low. These results support the findings from both short- and long-term clinical studies demonstrating that budesonide capsules are generally safe and well tolerated for the treatment of mild-to-moderate CD.

### 862

**Is Dysplasia Visible during Surveillance Colonoscopy in Ulcerative Colitis?**
Rabi Kundu, M.D., Wojciech Błonski, M.D., Chinyu Su, M.D., James D. Levis, M.D., Fatem Ahera, M.D., Leonard Baidoo, M.D., Julius J. Deren, M.D., Gary R. Lichtenstein, M.D.* Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA and Division of Gastroenterology, Wroclaw Medical University, Wroclaw, Poland.

**Purpose:** Dysplasia and colorectal cancer (CRC) in Ulcerative Colitis (UC) may develop in flat mucosa indistinct from surrounding tissue. In pts who have a prolonged history of UC and have no demonstrable dysplasia on mucosal biopsy it is recommended to proceed with a strict colonoscopic surveillance program with suggestions that at least 18 jumbo biopsies are necessary to detect either cancer or dysplasia if present with 95% confidence (Rubin CE. Gastro 1992;103:1611). Recently, this has been challenged by at least 2 small retrospective studies claiming adequate sensitivity to detect dysplasia during surveillance colonoscopy. (Rutter GI Endoscopy2004;60:334 and Rubin Gastro 2005 S128(4):A122). Our aim in this study is to determine if dysplasia is visible during surveillance colonoscopy.

**Methods:** Medical records, endoscopy and pathology databases were systematically reviewed between 1997–2004. Only patients with dysplasia were evaluated.

**Results:** 113 pts with dysplasia were evaluated of which 102 (90%) had UC and 5 (4%) had CD and 6 (6%) had indeterminate colitis. 53/102 (52%) of UC pts had inadequately documented colonoscopy or incomplete data and were thus excluded from our analysis. The remaining 49/102 (48%) served as our study cohort, Demographics: mean age-58.2 yrs (median 62 yrs, IQR 46–73 yrs); 32/49 (65%)- males; Disease Extent- pancolitis (29/49–59%), left sided (8/49–16%), proctitis (12/49–25%), 45/49 (92%) of pts who had visually detectable lesions at colonoscopy had dysplasia in these lesions. The total number of lesions detected in these 49 colonoscopies were 62; of which 47 (76%) were polyps (5 were described as pseudopolyps), 11 (18%) were flat lesions (17-LGD, 76%; 8 HGD, 24%).

**Conclusions:** Dysplasia in UC is endoscopically visible in the majority of pts in undergoing surveillance colonoscopy. Our findings do not preclude the need to perform random surveillance biopsies but suggest that attention should be directed to macroscopically visible lesions when performing surveillance colonoscopy. Further prospective trials are merited to validate our observations.

### 863

**A Study To Define the Geographical Overlap in the Incidence of Severe Inflammatory Bowel Disease and Overall Cancer: A Cross-Sectional Study**
Stacie A. Vela, M.D., Brenda J. Hoffman, M.D.,* Merriman Dowdle, Ph.D., Rickey Carter, Ph.D., Division of Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, SC and Department of Biostatistics, Bioinformatics and Epidemiology, Medical University of South Carolina, Charleston, SC.

**Purpose:** Environmental factors may play a role in the development and severity of disease in patients with inflammatory bowel disease (IBD). The Division of Gastroenterology at MUSC has particular expertise in the management of IBD. It is our anecdotal observation that there are specific geographic areas in the state of South Carolina in which we see the most challenging cases of inflammatory bowel disease. Recently the statewide incidences of malignancy were reviewed by geographic location. Demonstrating an overlap of these regions would prompt further investigation of environmental exposures in high-risk areas and perhaps lead to a greater understanding of the etiology of IBD.

We aim to show geographic trends in IBD within the state of SC to demonstrate that the areas with the highest incidence of malignancy overlap with the most severe cases of IBD.

**Methods:** The number of hospital discharges with primary diagnosis for Crohn’s disease or Ulcerative Colitis was obtained from the state of SC using ICD-9 codes. Data were reported as a number per 100,000 people per county. Incidence of overall cancer was obtained and reported in a similar manner. The association of the incidence rates was measured using Spearman’s rho (r). The rates were classified into four categories, and the association of these categories was measured by the Mantel-Haenszel Chi-Square, an ordinal measure of association.

**Results:** The correlation of the overall cancer rate and IBD rate was r = 0.25 (p = 0.1) and the ordinal association measured by the Mantel-Haenszel Chi-Square was ($X^2 = 2.73, df = 1, p = 0.1$). Both measures indicate a trend of association. Counties with higher rates of cancer also observe higher rates of IBD. With data limited only to SC, only 37% power to reject the null hypothesis of no association (i.e., uncorrelated rates, $H_0: r = 0.0$) was obtained. The cross-sectional study design does not imply causality.

**Conclusions:** In SC there are geographical regions that are associated with more severe cases of IBD. These areas also tend to have the highest incidence of cancer. Further prospective studies involving additional states should be conducted to investigate possible environmental exposures accounting for this distribution and to ensure a nominal power of at least 80% is obtained.

### 864

**Inhibition of Neutrophil Elastase Prevents the Development of Murine Dextran Sulfate Sodium-Induced Colitis**
Yuichi Morohoshi, M.D., Katsuyoshi Matsuoka, M.D., Tadakazu Hisamatsu, M.D., Susumu Okamoto, M.D., Toshifumi Hiro, M.D.* Department of Internal Medicine, School of Medicine, Keio University, Japan, Tokyo, Japan.

**Purpose:** Neutrophil elastase (NE) is a major secretory product from activated neutrophils and a major contributor to tissue destruction. However, little is known about the pathogenic contribution of NE to ulcerative colitis (UC). This study was designed to investigate the contribution of NE by measuring NE activity in plasma and colonic mucosal tissue from UC patients and a murine acute colitis model, and to elucidate the therapeutic effect of the NE-specific inhibitor ONO-5046.

**Methods:** The NE enzyme activities in plasma and colonic mucosal tissue from UC patients were directly measured using an enzyme-substrate reaction. Acute colitis was induced in mice by administration of 1.5% DSS for 5 d. DSS-induced colitis mice were then treated with ONO-5046 (50 mg/kg body weight) intraperitoneally twice a day.

**Results:** In UC patients, the NE enzyme activity was significantly elevated in both the plasma and colonic mucosal tissue compared with healthy controls. In DSS-induced colitis mice, the NE enzyme activity increased in parallel with the disease development. ONO-5046 showed therapeutic effects in DSS-treated mice by significantly reducing the weight loss and histological score. ONO-5046 suppressed the NE enzyme activities in both plasma and supernatant of colonic mucosa from DSS-induced colitis mice.

**Conclusions:** A specific NE inhibitor prevented the development of DSS-induced colitis in mice. NE therefore represents a promising target for the treatment of UC patients.
A Case-Control Study of Fragility Fracture Risk among Inflammatory Bowel Disease Patients

William A. Blumentals, Ph.D.,* Richard L. Sheer, B.S., Natalie Borisov, Ph.D., Michael Steinbich, Ph.D. Department of Epidemiology & Pharmacoeconomics, Procter & Gamble Pharmaceuticals, Mason, OH.

Purpose: To determine whether inflammatory bowel disease (IBD) patients have an increased risk of vertebral and non-vertebral fragility fractures compared to a non-IBD population.

Methods: Fracture cases were defined as patients ≥ 18 years of age with a newly diagnosed vertebral or non-vertebral fragility fracture between 1/1/01 and 6/30/03 (index date) in the Ingenix Lab/Rx DatabaseTM and between 1/1/01 and 12/31/02 (index date) in the Medstat MarketScan Database®. We identified fragility fractures by only including patients with closed fractures, and excluding patients with a record of malignant neoplasm and/or trauma ‘E codes’ at any point. A vertebral fracture diagnosis was validated with a record of a radiologic examination ±15 days from the diagnosis date. For each case, 1 control patient with no record of a vertebral or non-vertebral fracture was randomly selected, and matched by age (±2 years), gender, and calendar year. IBD patients were identified based on having a diagnosis of ulcerative colitis or Crohn’s disease or ≥2 5-ASA prescriptions in the year prior to the index date. Odds ratios were computed using conditional logistic regression models and adjusting for age, gender, and glucocorticosteroid use in the 12 months prior to the index date.

Results: After combining both databases, a total of 141,266 fragility fracture cases and 141,266 matched controls were identified. Of these, 1,126 fracture cases and 969 controls were diagnosed with IBD. Overall, IBD patients appeared to have a 62% higher risk for fracture (OR = 1.62, 95% CI = 1.47–1.78). After adjusting for age, gender, and glucocorticosteroid use, the risk remained elevated (adjusted OR = 1.46, 95% CI = 1.33–1.61). Based on crude odds ratios, ulcerative colitis patients were 55% more likely to develop a fracture compared to non-IBD patients (OR = 1.55, 95% CI = 1.33–1.79), and Crohn’s disease patients were more than 70% more likely to have a fracture versus non-IBD patients (OR = 1.71, 95% CI = 1.46–2.00).

Conclusions: The results of this case-control study suggest an increased risk of fragility fractures among IBD patients, even after adjusting for glucocorticosteroid use. It will be important to assess the effect of fracture-prevention treatment in an IBD population.

TNF-α Promoter Gene Polymorphism May Modify Disease Behaviour in Crohn’s Disease Patients with NOD2/CARD15 Polymorphism

Hoessam E. Mardini, M.D., Lisbeth Selby, M.D., Rezaan Arsenescu, M.D., Trevor A. Winter, M.D., Willem J.S de Villiers, M.D.* Division of Gastroenterology, Hepatology and Nutrition, University of Kentucky, Lexington, KY.

Purpose: NOD2/CARD15 gene polymorphism is associated with increased risk of developing CD in Caucasian populations. It has been shown to be associated with certain disease characteristics including younger age at diagnosis, ileal location and possibly complicated behavior (fistulizing and stricturing disease). Little is known about the potential gene-gene interaction between TNF-α promoter gene polymorphism and NOD2 polymorphism. Our aim is to assess the influence of TNF-α promoter gene polymorphism on disease behavior among CD pts with NOD2 polymorphism.

Methods: Using our IBD database we identified CD patients who had genetic testing for both genes polymorphisms (G908R, L1007P and R702W for NOD2 and 308 and 857 for TNF-α). All tests were performed in our institution using PCR techniques. Pts’ characteristics (age at diagnosis, disease location and behavior and the need for surgery during the course of disease) were compared between patients with at least one NOD 2 mutation and wild type TNF-α (group 1) and pts with at least one NOD2 mutation and at least one TNF-α (group 2). Non-parametric tests and logistic regression models were used to assess the associations, estimate the odd ratio (OR) and 95% confidence intervals (CI) of these association and to control for disease duration and smoking status.

Results: Among 226 CD patients 71 had at least one NOD2 mutation. Among those, 33 had at least 1 TNF-α mutation. Compared to group 1, group 2 patients were more likely to have fistulizing phenotype (42% vs 31% (OR 1.3; 95% CI: 1.05–1.9), less likely to have strictureting phenotype (6% vs 18% (OR 0.44, 95% CI: 0.91–0.23), to have more frequent colonic disease (25% vs 15%, OR 1.6; 95% CI: 2.1–1.1). Group 2 pts tended to be older at time of diagnosis (median 24 vs 21 years, p = 0.067). There was no significant difference between the 2 groups with regard to the frequency of resective surgery, extraintestinal manifestations and smoking status.

Conclusions: The concomitant presence of TNF-α promoter gene variation with the NOD2/CARD15 variation may influence disease behavior. Colonic disease, fistulizing phenotype and possible older age at time of diagnosis are associated with having variation in both genes.

Clinical Epidemiology of Inflammatory Bowel Disease in Lebanon: Prevalence, Practice Patterns, and Impact on Quality of Life

Heitham Abdul-Baki, M.D., Lara Zuhabi, M.D., Abd ElHajj, M.D., Cecilio Azar, M.D., Bassem Ayyach, M.D., Fadi H. Mourad, M.D., Kassem A. Baruda, M.D., Elie Aoun, M.D., Aha I. Sharara, M.D.* Internal Medicine, American University of Beirut Medical Center, Beirut, Lebanon.

Purpose: Limited data exists about Inflammatory Bowel Disease (IBD) in Lebanon and the Middle East. The aims of the present study were to estimate overall and specific prevalence of IBD (Crohn’s disease and ulcerative colitis) and to describe practice prevalence trends and patients’ characteristics as well as impact on quality of life in a tertiary care medical center in Lebanon.

Methods: To estimate the prevalence of IBD, computerized records of a University-based health program carrying the diagnosis of Crohn’s disease (CD) or ulcerative colitis (UC) were searched. Prevalence was estimated by age group, sex, and socioeconomic class. In addition, data gathered for a 5-year period from specialty Gastroenterology clinics at the American University of Beirut Medical Center (AUBMC) were analyzed to describe demographic and selected clinical information from patients with IBD. Moreover, Inflammatory Bowel Disease Questionnaire (IBDQ) was analyzed on 50 randomly selected patients from the AUBMC IBD Registry.

Results: Of 15,662 individuals studied, 7 had a diagnosis of CD and 13 of UC. The estimated prevalence per 100,000 was 44.7 for CD, 83.0 for UC, and 127.7 per 100,000 for IBD. Mean age for CD and UC was 43 and 47 years respectively with a slight female predominance. Of 10,381 patients presenting to GI specialty clinics at AUBMC from 2000–2004, 258 or 2.4% had proven IBD (142 UC, 98 CD, and 8 undefined IBD) with a mean age of 38.7 years. Prevalence trends of IBD in clinics did not change significantly over 5 years (range 1.9 to 2.9%). The median IBDQ score calculated in 50 randomly selected patients from the IBD registry was 121.7 ± 30.4 indicating a moderately-severe impact of disease on quality of life.

Conclusions: The estimated prevalence of IBD in this Lebanese population group places it among the middle-range reported for Caucasian populations in Europe and North America. Additional studies must be conducted in Lebanon in order to examine the impact of socioeconomic factors and to confirm the observed findings for health care planning. The psychosocial disease burden of IBD in Lebanese patients is significant.

Rifaximin for Mild to Moderately Active Crohn’s Disease

Leanne Baidoo, M.D.,* Wojciech Blonski, M.D., Rabi Kanda, M.D., Gary R. Lichtenstein, M.D. Division of Gastroenterology, University of Pennsylvania, Philadelphia, PA.

Purpose: Antibiotics, classically metronidazole and ciprofloxacin, are used to treat mild to moderately active Crohn’s disease(CD). Their use is often limited by side effects; metronidazole is commonly associated with development...
of nausea, anorexia, a metallic taste and peripheral neuropathy. Ciprofloxacin has been associated with nausea, drug interactions, tendinitis and spontaneous tendon rupture. Rifaximin, a new orally administered, poorly absorbed (< 0.4%) antibiotic, with virtually no bacterial resistance is approved in the US for traveler's diarrhea. Its utility in CD has not been adequately evaluated. To date 24 pts have been reported with CD in the literature who were fixed with Rifaximin (AJG 2003; 98(9): S250) (Eur J Clin Res 1997;9: 217). We report our open label experience with Rifaximin for Rx of 16 pts with mild to moderately active CD.

Methods: Rifaximin(Xifaxan®) was evaluated in an open label study to assess its efficacy, tolerability, and side effect profile for mild to moderately active CD. 16 pts were evaluated who presented with classic symptoms of mild to moderately active CD and treated at a dose of 400 mg po BID. Pts were subsequently evaluated in the office or via telephone contact and assessed for response (None, < 50%, > 50%, Complete Remission), time to efficacy onset, AEs, and response to prior medications. Standard demographic data was assessed. IRB approval was obtained

Results: Mean age 38 years (range:21–58 years), 44% female, 8(50%) had ileocecal, 4(25%) had ileal, and 4(25%) had colonic CD. 75%(12 of 16) of patients responded to treatment with Rifaximin. 67%(8 of 12) had complete remission and 33%(4 of 12) reported a > 50% response. Mean time to onset of response was 10 days (range: 7–16 days) and to complete remission was 21 days (range: 14–30 days). The 4 pts who did not respond had ileal (n = 1) and ileocolic (n = 3) CD. All pts who responded reported a decrease in frequency of bowel movements (n = 12) and decreased abdominal pain (n = 11) or bloating (n = 1). No significant AEs were noted.

Conclusions: This study suggests that Rifaximin is as effective as but safer than many contemporary treatments for mild to moderate CD. Prospective randomized placebo controlled studies are merited to further evaluate our preliminary findings.

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Septicemia for a Patient with Ulcerative Colitis Treated by Conventional Drug Therapies and Leukocytapheresis

Masatoshi Nitta, M.D., Ichiro Hirata, M.D.,* Tsukasa Iwashita, M.D.
Department of Gastroenterology, Hokuesu General Hospital, 16–23 Kitayamagawachow Takatsuki City, Osaka, Japan and 2nd Department of Internal Medicine, Osaka Medical College, 2–7 Daigaku-machi Takatsuki City, Osaka, Japan.

Purpose: We encountered a patient with ulcerative colitis (UC) occurred septicemia during treated by conventional drug therapies such as prednisolone and leukocytapheresis (LCAP). These therapies are strongly suppress the immune and considerable for the cause of heavy infection. This might be important suggestion for the therapists. So we present the

Methods: A 35-year-old female was admitted to our hospital on October 23, 2002 to receive UC therapies. Her UC type was moderately severe total colitis. Prior to admission to our hospital, her condition had not improved for about 2 months, despite drug therapy such as 5-aminosalicylic acid and oral administration of prednisolone. Thus she was admitted to our hospital. On the admission day, she had bloody stool about 15 times/day, slight fever, and hypoproteinemia. She was treated by intravenous high dose prednisolone and LCAP.

Results: After 3 LCAP sessions, her condition had improved. However, after 4th LCAP, she had high fever with depression of blood pressure. In the blood culture, Serratia marcescens causes opportunistic infection was observed. Therefore, she had discontinued LCAP and reduced prednisolone. She was recovered from septicemia by intravenous antibiotics and endotoxin absorption. After 60 days from admission, remission was observed and the patient discharged.

Conclusions: Combination therapy such as prednisolone and LCAP are effective for active UC. However, they are sometimes excess immunosuppression, and cause of opportunistic infection. This suggests that therapists have to care for the infection during these immunoregulatory therapies.

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Colonie Microflora in Crohn's Is Different Than Normals

Ece Mutha, M.D., Patrick Gillevet, Ph.D., Masi Shiahnoodi, Nancy Liccard, Ali Keshavarzian, M.D.* Section of Gastroenterology and Nutrition, Rush University Medical, Chicago, IL and Department of Environmental Sciences and Policy, George Mason University, Manassas, VA.

Purpose: Clinical observations and animal studies point toward a dysbiosis in IBD, however the changes that make up this dysbiosis in Crohn's disease (CD) are largely unknown. Amplicon length heterogeneity is a sophisticated technology that examines 16s ribosomal DNA of bacteria and can be used to define such changes in CD. We therefore hypothesized that ALH is a tool to study the changes in the mucosal microflora in Crohn's disease and can differentiate Crohn's disease from normals.

Methods: We collected mucosal biopsy samples from the ileum, right colon, and left colon of patients with Crohn's disease (n = 22 for active disease, n = 10 for inactive disease) and healthy controls (n = 10) at the time of colonoscopy. The samples were fingerprinted for bacterial patterns using ALH. The fingerprints were analyzed using principal component analysis with the aid of custom PERL scripts and a multivariate statistical package. ANOSIM was used for statistical analysis.

Results: ALH patterns were unique in each subject. There was a visual separation between normals and Crohn's disease in PCO analysis. ANOSIM statistics revealed a statistically significant difference between active CD, inactive CD and healthy controls. (R = 0.2129, p = 0.001 for comparison of active vs inactive CD/ R = 0.1545, p < 0.001 for comparison of active CD vs controls/ R = 0.3487, p < 0.001 for comparison of inactive CD vs controls). There was no statistically significant difference between endoscopically involved and noninvolved portions of the colon.

Conclusions: Our results show that a dysbiosis exists in the mucosal microflora in CD. ALH is a useful tool in evaluation of dysbiosis in IBD. Further studies are now underway to determine a pattern or set of patterns associated with the presence of CD.

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Repeated Cycles of Sargramostim for Active Crohn's Disease (CD): Update from an Open Label Trial (N.O.V.E.L. 5)

John Valentine, M.D.*, Diana Hausman, M.D. University of Florida and Gainesville, Gainesville, FL.

Purpose: Sargramostim, a hematopoietic growth factor that stimulates the innate immune system has been shown to induce response and remission in patients with moderately-to-severely active CD. We report here experience in patients who have multiple cycles of sargramostim treatment in an ongoing open-label study.

Methods: Patients who participated in any previous trial with sargramostim for treatment of CD are eligible. Treatment consists of repeated cycles of 8 weeks of sargramostim 6 ug/kg/day. Concurrent antibiotics, 5-ASA compounds, and steroids are permitted.

Results: From February 2003 through March 2005, 94 patients initiated treatment, with median age of 41 yrs and median baseline CDAI score of 312. 62 patients had completed at least one cycle of treatment, 32 patients at least two cycles, 18 patients at least three cycles, 8 patients at least four cycles, 5 patients at least five cycles, and 4 patients at least 6 cycles. The majority of patients were compliant with daily dosing of drug throughout treatment, with median age of 41 yrs and median baseline CDAI score of 312. 62 patients had completed at least one cycle of treatment, 32 patients at least two cycles, 18 patients at least three cycles, 8 patients at least four cycles, 5 patients at least five cycles, and 4 patients at least 6 cycles. The majority of patients were compliant with daily dosing of drug throughout each cycle. Median decrease in CDAI score relative to study entry was 79 points after cycle one; 91 points after cycle two; 83 points after cycle 3; 102 points after cycle 4; and 101 points after cycle 5; and 191 points after cycle 6. The most commonly reported adverse events (AEs) included injection site reactions (ISRs), bone pain, nausea, headache, fatigue and back pain. The incidence of ISRs decreased with repeated treatment, from 71% during cycle 1 to 25% during cycle 4. The incidence of bone pain also decreased from 26% during cycle 1 to 8% during cycle 4. White cell counts peaked
between weeks two and four of each treatment cycle, and returned to normal values between cycles.

**Conclusions:** Treatment with up to 6 cycles of sargramostim for active CD was generally safe and well tolerated. Patients were compliant with daily dosing throughout multiple cycles of treatment. ISRs and bone pain decreased with repeated dosing. While this study was designed to evaluate safety, median responses with retreatment are similar to previously reported data.

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A Multicenter, Randomized, Controlled Trial between Weekly and Semiweekly Treatment with Granulocyte and Monocyte Adsorption Apheresis for Active Ulcerative Colitis

A. Sakuraba, N. Inoue, Y. Kohgo, A. Terano, T. Matsui, Y. Suzuki, T. Hibi Division of Gastroenterology, Department of Internal Medicine, School of Medicine, Keio University, Tokyo; Third Department of Internal Medicine, Asahikawa Medical College, Asahikawa; Department of Gastroenterology, Dokkyo University School of Medicine, Tochigi; Department of Gastroenterology, Fukuoka University Chikushi Hospital, Fukuoka and Department of Internal Medicine, Sakura Hospital, Faculty of Medicine, Toho University, Tokyo.

**Purpose:** In contrast to the advances in understanding the pathogenesis of ulcerative colitis (UC), there have been few pivotal improvements in its medical treatment. We have previously reported that granulocyte and monocyte adsorption apheresis (GCAP) is an efficacious and safe treatment for active UC. It is an extracorporeal treatment that selectively removes granulocytes and monocytes (FcγR expressing leukocytes) from the blood of the patient.

The previous weekly GCAP therapy is reported to be effective for two-thirds of active UC patients and required an average of 4 weeks to achieve remission. In this study we compared the efficacy and safety between weekly (x1/week) and semiweekly (x2/week) GCAP therapy for active UC.

**Methods:** The aim of the study was to compare the efficacy and safety between weekly and semiweekly GCAP therapy for moderately active UC. Hundred and twenty active UC patients, with moderate disease, were randomly categorized to receive the previous weekly GCAP therapy (group 1) or the semiweekly GCAP therapy (group 2). Each group received a total of 10 treatments. The rate of inducing remission and the time to achieve remission was compared between the 2 groups. Remission was defined as a Lichtiger's score of equal to or below 4. Incidences of Adverse effects were also compared between the 2 groups. Medical treatment was not altered two weeks prior to and during the treatment. However, the dosage of corticosteroids was allowed to be tapered in line with the improvement of symptoms.

**Results:** The rate of inducing remission was 46.7% (21/45) in group 1 and 73.1% (38/52) in group 2 (P = 0.01). The mean time to achieve remission was 28.1 days in group 1 and 15.9 days in group 2 (P = 0.0002). The incidence of adverse effects was 10.5% and 11.0%, respectively (P = NS).

**Conclusions:** Semiweekly treatment with GCAP is an efficacious and safe treatment for moderately active UC. The rate of inducing and the time to achieve remission was markedly improved by the semiweekly GCAP therapy compared to the weekly GCAP therapy.

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Dysregulated Immune Response in Mesenteric Lymph Nodes of Crohn’s Disease

Toshiro Sato, Atsushi Sakuraba, Nagamu Inoue, Toshifumi Hibi Division of Gastroenterology, Department of Internal Medicine, School of Medicine, Keio University.

**Purpose:** The pathogenesis of Crohn’ Disease has not been determined yet. However, recent studies have revealed that Th1 immune regulation from mesenteric lymph node (MLN) as the initiator of the mucosal Th1 regulation.

**Methods:** Mesenteric lymph nodes were obtained from patients with Crohn’s disease, Ulcerative colitis, colonic cancer and colonic diverticulum. Dendritic cells and T cells were isolated from MLN by density gravity centrifugation, magnetic beads sorting and flow cytometric sorting. Surface marker analysis was examined by flow cytometry and the expression of Th1 transcription factor, T-bet, was analyzed by Real-time RT PCR. To determine the Th1 inducing ability of MLN dendritic cells, we performed allo-MLR assay between isolated MLN dendritic cells and allo-naive T cells from donor peripheral blood, and cytokine production was examined using cytokine beads array.

**Results:** As compared with other disease, significantly higher Th1 cytokine production and the expression of T-bet was observed in T cells from MLN of Crohn’s disease. The isolated dendritic cells from MLN were confirmed morphologically and functionally. Furthermore, MLN dendritic cells from Crohn’s disease had significantly higher Th1-inducing ability in the MLR assay.

**Conclusions:** In Crohn’s disease, Th1 immune regulation is observed in MLN aside from intestinal mucosa. These results suggest that the Th1 immune response observed in the MLN may lead to the mucosal injury in Crohn’s disease. This result may link to the new therapy targeted to the MLN dendritic cells.

**FUNCTIONAL BOWEL DISORDERS**

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The Prevalence of Constipation in Korean Population

Oh Yung Lee, M.D.,∗Dae Won Jun, M.D., Ho Yong Park, M.D., Sung Hee Han, M.D., Sun Yang Yang, M.D., Hang Lek Lee, M.D., Byung Chul Yoon, M.D., Ho Soon Choi, M.D., Joon Soo Hahn, M.D., Dong Hoo Lee, M.D., Min Ho Lee, M.D., Chun Sukh Kee, M.D. Internal Medicine, Hanyang University Hospital, Seoul, Korea.

**Purpose:** Most of studies about bowel habits have been conducted in western countries. This study was conducted to estimate bowel patterns and epidemiology of constipation in the Korean.

**Methods:** A telephone interview was conducted with a total of 1,029 individuals in the Korea 15yr of age or older about their bowel habits. The sampling frame was constructed to be demographically similar to the Korean population based on geographic region, gender, and age. Subjects were given a validated questionnaire using Rome II criteria, which were asked about bowel symptoms, sociodemographic associations, laxative use, and physician visits.

**Results:** Of the whole subjects 95.6% had defecation frequency between three per week and three per day. The most common symptom of constipation was feeling of incomplete emptying. The prevalence was 16.5% for self-reported constipation, 9.2% for functional constipation, 3.9% for constipation type IBS. Of subjects’ self-reported constipation, proportion of functional constipation and constipation predominant IBS were 21.8% and 23.5%, respectively. Of subjects excluding self-reported constipation, proportion of functional constipation was 6.8%. Prevalence of self-reported constipation and constipation predominant IBS were higher in females than in males(p = 0.001). Prevalence of self-reported constipation decreased with increasing age(p = 0.003). Prevalence of functional constipation increased with increasing family incom(ep = 0.044). 30% of those with constipation predominant IBS, 14.1% of self-reported constipation, and 6.3% of functional constipation had visited a physician for it. Of subjects’ self-reporting constipation, 8.2% used laxatives.

**Conclusions:** Constipation was common in the Korean population and discrepancy of prevalence between self-reported constipation and functional constipation was higher in females than in males. Differences in epidemiological profile by age, sex ratio, and relation to other sociodemographical factors were found.
Cyclic Vomiting Syndrome in Adults: A Report of 41 Patients

David R. Fleisher, M.D.,* Blake Gornowicz, M.D., Kathleen Adams, B.S.N., Richard Burch, M.D., Edward J. Feldman, M.D. Department of Child Health, University of Missouri School of Medicine, Columbia, MO; Department of Medicine, University of Missouri Hospital & Clinics, Columbia, MO; Cyclic Vomiting Syndrome Association, Milwaukee, WI; and Department of Medicine, Geffen School of Medicine at UCLA, Los Angeles, CA.

Purpose: Description of the clinical features of CVS, the patients, and the problems of management.

Methods: This is a retrospective study of 41 adults (24 men, 17 women) who presented at 20 to 64 years of age (average, 34 years; median, 34 years) with CVS seen between 1992 and 2003. Follow-up data were obtained by mailed questionnaires.

Results: Age of onset ranged from 2 to 49 years (mean, 21 years; median, 20 years). The duration of CVS at the time of consultation ranged from less than 1 year to 49 years (mean, 12 years; median, 7 years). CVS episodes were stereotypic insofar as their hours of onset (midnight to noon), symptomatology and length. Ninety three percent of patients had recognizable prodromes. Half of the patients experienced a constellation of symptoms consisting of CVS episodes, migraine diathesis, inter-episodic dyspeptic nausea, and a history of panic attacks. Deterioration in the course of CVS is indicated by coalescence of episodes in time. The prognosis of CVS is influenced by the responsiveness by co-morbid triggering factors to treatment.

Conclusions: CVS is a disabling disorder affecting adults as well as children. Although assiduous management of its physical and psychological aspects seems to benefit patients, the relationship between its course and treatment modalities remains to be clarified by future prospective studies. The value of such studies will depend upon an appreciation of the phenomenology of CVS as revealed by naturalistic observation as well as physiologic and prospective clinical investigation.

Visual Feedback Alters Perception of Rectal Distension in Patients with Irritable Bowel Syndrome (IBS)

N. Firooz, M.D., B. Nalibof, Ph.D., B. Dickhaus, M.D., J. Stains, R.N., R. Bolas,* E. A. Mayer, M.D. Center for Neurovisceral Sciences & Women’s Health, UCLA Division of Digestive Diseases, Los Angeles, CA.

Purpose: To determine if visual feedback of stimulus intensity alters perceptual stimulus ratings in IBS patients.

Methods: 21 healthy control subjects (Ctrl) (12F; mean age 39) and 23 Rome II-positive, diarrhea-predominant IBS patients (IBS) (14F; mean age 36) underwent three consecutive periods of intermittent phasic rectal distension. Following a familiarization block, subjects were randomized to either high-feedback (HFB) or low-feedback (LFB) block. Synchronized with each rectal inflation, subjects watched a cartoon simulation of a distending rectum and a gauge showing increasing pressure within the rectal balloon. During the familiarization block, the animated display consistently corresponded to the actual level of distension, while it suggested a higher stimulus intensity during distensions of the HFB block, and a lower intensity during the distensions of the LFB block. Ratings of intensity and unpleasantness of the stimuli, subjective emotional responses, heart rate, and neuroendocrine measures were obtained during the study. Visceral distension was performed using a rectal balloon catheter connected to an electronic device.

Results: Ctrl showed higher intensity ratings during HFB compared to LFB and familiarization. In contrast, IBS showed higher intensity ratings during both HFB and LFB compared to familiarization (p = 0.025). Ctrl showed significantly lower intensity ratings during stimuli with false low feedback than during stimuli with false high feedback. In contrast, IBS rated both false feedbacks similarly (p = 0.0302). During correct feedback, intensity ratings by Ctrl remained constant across all three blocks of inflations. In contrast, IBS had higher ratings during correct feedbacks of the two study blocks compared to those in familiarization (p = 0.0558). IBS generally scored higher than Ctrlts on emotional scales. In IBS, but not Ctrlts, there was a significant rise in plasma levels of both cortisol (0.017) and prolactin (0.006) during the HFB and LFB blocks compared to levels obtained during pre- and post-balloon insertion.

Conclusions: IBS patients showed an increase in intensity and emotional ratings and in hormone levels in blocks of inflations that contained incorrect visual feedback. In IBS, perceived mismatch between actual visceral stimulus intensity and presumed intensity may be associated with higher stimulus ratings in terms of intensity, unpleasantness and affect.

Acupuncture Treatment Effects in IBS Are Predominantly Placebo Effects

Antonius Schneider, M.D., Konrad Streitberger, M.D., Stefan Witte, M.D., Hans-Christoph Friederich, M.D., Stephan Zipfel, M.D., Paul Enck, Ph.D.* General Medicine, University Hospitals, Heidelberg, Germany and Psychosomatic Medicine, University Hospitals, Tuebingen, Germany.

Purpose: Despite occasional positive reports on the efficacy of acupuncture on functions of the gastrointestinal tract, published data not provide conclusive evidence that acupuncture (AC) is effective in the treatment of the irritable bowel syndrome (IBS).

Methods: Forty-three patients with the diagnosis of IBS according to Rome II criteria were randomly assigned to receive either acupuncture (n = 22) or sham acupuncture (n = 21) (SAC) using the so-called “Streitberger needle”, and a standardized acupuncture treatment according to Traditional Chinese Medicine (TCM). Treatment duration was 10 sessions with an average 2 acupuncture sessions per week, and primary endpoint was improvement of quality of life (QOL) using the FDDQOL and the SF36, compared to baseline assessment at the end of treatment. QoL measurement was repeated three months after treatment.

Results: Both the AC as well as the SAC group improved significantly in global QOL by the FDDQOL at the end of treatment (p < .022), with no differences between both groups; the SF36 was insensitive to these changes. This effect was reversely reversed three months later. Based on the small differences found between AC and SAC, a study including 570 patients would be necessary to prove efficacy of AC over SAC. Post-hoc comparison of responders and non-responders in both groups combined revealed a significant prediction of the placebo response by two subscales of the FDDQOL (sleep, coping) (F = 6.746, p < .003) in a stepwise regression model.

Conclusions: Acupuncture efficacy in IBS is primarily a placebo response that may in part be predicted by high coping capacity and low sleep quality in individual patients. (Supported by the German Medical Acupuncture Association, DÄGfA)

Determinants of the Placebo Response in the Irritable Bowel Syndrome (IBS) – A “Meta-Meta-Analysis”

Sibylle Klosterhalfen, Ph.D., Paul Enck, Ph.D.* Psychosomatic Medicine, University Hospitals, Tuebingen, Germany and Institute of Medical Psychology, University Hospitals, Duesseldorf, Germany.

Purpose: The placebo response not only in IBS is incompletely understood. Two recent meta-analyses (Patel et al. 2005, Pitz et al. 2005) have produced conflicting results, e.g. regarding the number of study visits in predicting the placebo response. We evaluated the trial data that were entered into either one or both meta-analyses.

Methods: The total amount of published trials that were found was well above 100 (Pitz et al. 140, Patel et al.: not reported). Patel et al. found 45 of 96 trials that met their entry criteria (at least 2 weeks trial, at least 20 patients per study arm), while Pitz et al. found 53 out of 84 trials, that met criteria (> 1 week, > 10 patients per arm) and that reported global improvement rates of the placebo arm of the study to be analysed further. The studies that
were entered into either one or into both data analyses were subject to our analysis.

**Results:** 1) Only 26 studies were entered into both data set, the remaining studies were selected only by one group (Patel: another 19 studies, Pitz: another 27). It remained open according to which entry criteria these selections occurred (Patel: MEDLINE and other databases between 1960 and 2003; Pitz: PUBMED, time not specified). 2) Of those 26 studies that were common in both samples, complete agreement was found in only 6 studies; in the remaining 20 studies, both groups disagreed at least in one of the following four criteria: Number of study visits (18 studies with disagreement), % drug response (10 studies), % placebo response (8 studies), study design (1 study). When checked for systematic differences between both groups, none was found, since deviations were in both directions. In two cases the discordance on the number of study visits was maximal: While Patel et al. noted 3 visits, Pitz et al. counted 12 for the study of Lucey et al. (1987), and for the study by Rajagopa et al. (1998), Patel counted 12 visits, while Pitz et al. found only one. Disagreement exceeded 20% in regards to drug and/or placebo response rate in 5 studies. 3) When all 72 studies were entered into a statistical analysis, none of the predictors found in either meta-analysis could be confirmed.

**Conclusions:** Meta-analyses not only on published IBS drug trials can only be as good as the studies published; this ‘meta-meta-analysis’ provides evidence that this is not the case in many studies, and that a meta-analysis based on such studies mixes apples and oranges (Moayyedi 2005) (Supported by a grant from DFG).
Irritable Bowel Syndrome: What Do Patients Really Know?
Brian E. Lacy, Ph.D., M.D.*, Kirsten T. Weiser, M.D., Laura Noddin, M.D., Douglas Robertson, M.D., Maria Grau, M.D., Christina Parratt-Engstrom, B.A, Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH; Medicine, White River Junction VA Hospital, White River Junction, VT and Biostatistics, Dartmouth Medical School, Hanover, NH.

Purpose: Despite the high prevalence of IBS, little is known about patients’ understanding of this disorder. This study assessed the knowledge base of IBS patients (Pts) regarding the prevalence, etiology, diagnosis and treatment of IBS.

Methods: 736 Pts diagnosed with IBS (Rome II criteria) at an academic medical center over a 3 year period were eligible for inclusion. Each Pt was mailed a questionnaire, the first part of which requested demographic information. The second part assessed the level of knowledge of each Pt regarding IBS.

Results: Of 682 deliverable questionnaires, 261 Pts responded (38.3%); 84% were women. The mean age of all respondents was 53.7 years; the mean duration of symptoms was 14.2 years. Most respondents did not understand the etiology of IBS. They cited dietary factors (80.7%), anxiety (87.9%), and depression (68.2%) as the most frequent causes of IBS. Regarding the pathophysiology of IBS, 48% of respondents noted that IBS Pts have altered visceral hypersensitivity, while 45.7% stated that IBS Pts have a motility disorder. With regards to prevalence, only 26.9% recognized that IBS is more prevalent than hypertension, while 61.6% knew that IBS occurs more frequently than colon cancer. Most Pts did not recognize that abdominal pain is the cardinal symptom of IBS (30.9%), and nearly half (44.5%) stated that IBS could be diagnosed with colonoscopy. 21.5% of respondents believed that IBS increases the risk of colon cancer, while 30.5% stated IBS increases the risk of developing IBD. Only 5.7% of patients believed that surgery could improve symptoms of IBS.

Conclusions: This is the first study to assess IBS Pts knowledge regarding their disorder. An overwhelming majority reported that anxiety, dietary factors, and depression cause IBS. Pts mistakenly believed that IBS increases the risk of developing both colorectal cancer and IBD. Few Pts understood the relative prevalence of the disease or the primary symptom of IBS. These findings are discordant with physician views, current knowledge, and current practice standards. Our results highlight the need for effective educational programs for IBS patients.

Rifaximin, a Non-Absorbable Antibiotic, Improves the Symptoms of Irritable Bowel Syndrome: A Double-Blind Randomized Controlled Study
Mark Pimentel, M.D.*, Sandy Park, B.A., Yuthana Kong, M.P.H., Robert Wade, Sunanda V Kane, M.D. GI Motility Program, Cedars-Sinai Medical Center, Los Angeles, CA and Gastroenterology, University of Chicago, Chicago, IL.

Purpose: Rifaximin, a newly approved non-absorbable antibiotic is reported to have better efficacy than neomycin in effecting a reduction in gut bacteria. In this study, we aim to demonstrate the effectiveness of rifaximin in improving IBS symptoms.

Methods: Primary care IBS subjects meeting Rome I criteria (all subgroups) were recruited at two centers in the U.S. Subjects with recent antibiotic use, diabetes, history of bowel obstruction, known gastrointestinal disease, abdominal surgery, proton pump inhibitor use or antidepressant use were excluded from study. After consent, a 7-day stool diary was undertaken followed by a questionnaire and a lactulose breath test, the results of which were blinded to subjects and investigators. They were then randomized in double blind fashion to receive either placebo or rifaximin 400 mg p.o. t.i.d. for 10 days. During the 7 days following antibiotic therapy, subjects were asked to repeat the stool diary followed by a symptom questionnaire and lactulose breath test. The primary outcome was global improvement in IBS.

Results: After exclusion criteria were applied, 91 subjects were consented and 87 of these (44 placebo, 43 rifaximin) were randomized. In the intention-to-treat analysis, rifaximin resulted in a 37.7 ± 5.8% overall improvement in IBS compared to 23.4 ± 4.3% with placebo (p < 0.05). With rifaximin, 37% of subjects were deemed clinical responders (defined as > 50% improvement overall) compared to 16% for placebo (p < 0.05). Among subjects with diarrhea, clinical response was seen in 49% with rifaximin compared to 23% with placebo (p < 0.05). Bloating was also improved (p = 0.06). No difference was seen with constipation. As in previous study, methane on lactulose breath test was almost exclusively associated with constipation. Also, the degree of methane production correlated significantly with constipation severity (r = 0.49, p < 0.05), stool frequency (r = −0.622, p = 0.01) and Bristol stool score (r = −0.53, p < 0.05).

Conclusions: Rifaximin is effective in improving the symptoms of IBS. Methane on breath test correlates with constipation in IBS patients.

Significant Overlap between IBS and GERD: A Systematic Review of Literature
Igor Nastaskin, M.D., Edgar Mehdkhani, M.D., Jeffrey Connklin, M.D., Sandy Park, B.A., Mark Pimentel, M.D.* GI Motility Program, Cedars-Sinai Medical Center, Los Angeles, CA.

Purpose: Evidence points to a significant overlap between IBS and GERD. In this study, we evaluate this overlap by conducting a systematic review of the literature.

Methods: Six electronic databases from 1966 through Jan 2005 were screened with multiple search terms to identify all epidemiological evidence linking IBS and GERD. In addition, AGA meeting abstracts for 2003 and 2004 were also screened. All studies were validated by the authors and data extracted according to predefined criteria. As a separate independent search, studies evaluating the prevalence of IBS and GERD in the general population were sought. These articles were obtained to compare the prevalence of IBS and GERD in the community to the degree of overlap.

Results: The search identified 997 original titles with 14 publications that fulfilled our eligibility criteria. Among the 14 studies, 7 determined GERD prevalence in patients already diagnosed with IBS and the maximum mean prevalence of IBS in patients with GERD was 38.6%. The other 7 studies examined the prevalence of IBS in patients already diagnosed with GERD. The maximum mean prevalence of IBS in subjects known GERD was 49.5%. Based on the prevalence of IBS (14.3%) and GERD (25.4%) in the community, the rate of IBS in the non-GERD community was calculated to be only 2.5%.

Conclusions: There is a strong overlap between GERD and IBS that exceeds the individual presence of each condition. In the absence of GERD, IBS is relatively uncommon.

Initial and Sustained Effects of Lubiprostone, a Chloride Channel-2 (CIC-2) Activator for the Treatment of Constipation: Data from a 4-Week Phase III Study

Purpose: To examine data on onset and persistence of effect from a 4-week Phase III study comparing lubiprostone with placebo in subjects with chronic idiopathic constipation.

Methods: In a Phase III multicenter, parallel-group, DB trial comparing lubiprostone with placebo, subjects with a history of chronic idiopathic constipation were randomized to receive oral lubiprostone (24 µg bid) or placebo with food and water for 28 days after a 15-day drug-free period. Chronic constipation was defined as < 3 spontaneous bowel movements (SBMs) per
week, with a minimum 6-month history of hard stools, sensation of incomplete evacuation, or straining during at least 25% of bowel movements (BM). An SBM was any BM that did not occur within 24 h of rescue medication use. Patients with mechanical obstruction, organic disorders of the large or small bowel were excluded, as were patients with conditions or treatments that could affect safety or data validity. Patients were evaluated at baseline, at weekly intervals during treatment, and at follow up. Patient diaries were used to record data on SBM frequency, global assessments, and symptom assessments.

Results: Statistically significant differences in the timing of the first SBM following initiation of treatment were observed; 73 of the 119 subjects (61.3%) receiving lubiprostone vs 37 of the 118 subjects (31.4%) in the placebo group experienced an SBM within 24 h of first dose (p ≤0.0001). Within 48 h, 79.3% of subjects receiving lubiprostone, versus 65.5% of subjects receiving placebo had experienced an SBM (p < 0.05). For the overall analysis of time to first SBM, there was a statistically significant (p < 0.001) treatment effect in favor of lubiprostone. The greater SBM frequency/week for patients receiving lubiprostone compared with those on placebo was statistically significant (p < 0.05) and sustained throughout the treatment period. [Figure 1]

Conclusions: Lubiprostone, 24 µg bid, provides rapid relief of chronic idiopathic constipation that is sustained over the 4-week treatment period.

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Efficacy of Itopride Hydrochloride on Gastric Emptying in Patients with Diabetic Gastroparesis
Jean-Rene Basque, Ph.D., Y. Kikuchi, T. Ohtsubo, G. Sarashina, H. Nakamura Clinical Research, Scientific Affairs, Ascan Pharma Inc., Mont Saint-Hilaire, QC, Canada and Baraki, Japan.

Purpose: Gastroparesis is a chronic disorder defined by delayed gastric emptying. Clinical symptoms include nausea, vomiting, bloating, and post-prandial abdominal fullness.

AIMS: To evaluate the effects of itopride hydrochloride (ITOPRIDE) on electrical gastrography measurements using a Digitrapper electro-gastrogram and gastric emptying tests performed following ingestion of a meal together with a capsule of SITZMARKSTM radiopaque markers.

Methods: 12 NIDDM patients were selected on the basis of having a reduction in vibration sensation in the lower leg and low nerve impulse transmission velocity. Itopride (150 mg/day) was administered orally for two weeks. Electrical gastrography measurements were performed before and immediately after treatment. Gastric emptying tests were performed following ingestion of a meal together with a capsule of SITZMARKSTM radiopaque markers.

Results: At baseline, pre-prandial electrical gastrography measurements revealed a dominant frequency of 58.1%. Following ITOPRIDE administration for 2 weeks, the dominant frequency showed a significant increase to 72.9%. Post-prandial electrical gastrography measurements prior to ITOPRIDE administration showed a dominant frequency of only 41.7%. Thereafter, ITOPRIDE administration revealed a significant increase to 71.4%. Gastric emptying of SITZMARKS prior to ITOPRIDE administration revealed that the bolus of radiopaque markers emptied from the stomach after 2 hours of ingestion was only of 5%. Following a 2-week ITOPRIDE administration, gastric emptying of radiopaque markers was significantly increased to 24%. Finally, acetaminophen blood concentrations measured 1 hour post-prandial showed a significant increase from 9.7µg/mL to 14.0ug/mL following ITOPRIDE administration.

Conclusions: For both pre- and post-prandial periods, administration of ITOPRIDE resulted in a significant increase in the dominant frequency measurements thereby indicating a clear improvement in gastric emptying. Thus, ITOPRIDE appears to be effective in NIDDM patients. Based on these results, additional controlled trials using ITOPRIDE will be needed to fully assess its implication for the treatment of diabetic gastroparesis.
Purpose: Benefits in IBS with a novel probiotic strain, *B. infantis* 35624, have previously been reported. The aim of this analysis was to identify baseline characteristics that have a significant effect on the treatment response.

Methods: Subjects from a randomized, double-blind, placebo-controlled clinical study, were considered treatment responders if they had at least 2 weeks with adequate relief of IBS symptoms during a 4-week treatment phase. Predictors included in the analysis were: 12 symptom variables; 6 variables used in the Rome II classification of IBS sub-types; 6 demographic variables; and treatment effect (n = 87 on active, n = 86 on placebo). The best baseline predictors were obtained by fitting a logistic regression model using a backward elimination technique.

Results: The baseline characteristics most closely associated with responders were the symptom urgency (mean = 1.96, SD = 0.93); the Rome II variables hard stool and straining; and the demographic variable alcohol consumption (mean = 4.67, SD = 5.46). A total of 115 subjects (66.5%) had hard stools and 127 (73.4%) had straining in the last 3 months (Rome II). At the end of the treatment phase there were 55 (63.2%) responders in the active group and 40 (46.5%) in the placebo group (unadjusted OR = 2.08). The table gives the main results of the best logistic regression model. A one-unit score increase for urgency increased the chances of being a responder by a factor of 1.45. Hard stool increased the OR whereas straining decreased it. A one-unit increase in alcohol consumption decreased the chance of response by a factor of 0.88. After adjusting for these baseline predictors, the odds of response in the *B. infantis* 35624 group were 2.15 times that in the placebo group.

Conclusions: The baseline variables urgency, hard stool, straining and alcohol consumption have a significant impact on the chances of being a treatment responder to this probiotic. In the presence of the best baseline predictors, treatment efficacy increased, as measured by the OR, from 2.08 to 2.15.

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**Probiotic Use Results in Normalization of Bowel Movement Frequency in IBS. Results from a Clinical Trial with the Novel Probiotic Bifidobacteria infantis 35624**

E. M. Quigley, M.D., F.A.C.G.* P. J. Whorwell, M.D., L. Altringer, B.S., J. Mord, Ph.D., L. O'Mahony, Ph.D., F. Shanahan, M.D. Alimentary Pharmabiotic Center, University Cork College, Ireland; Department of Medicine, University of Manchester, Manchester, United Kingdom and Procter & Gamble, Mason, OH.

Purpose: Benefits associated with a novel probiotic strain, *B. infantis* 35624 in IBS have previously been reported. The aim of this analysis was to determine the impact of probiotic therapy on bowel movement (BM) frequency.

Methods: Data from a randomized, double-blind, placebo-controlled clinical study in female IBS subjects were evaluated. BM frequency at baseline was calculated using data from the last 7 days of the run-in phase. BM frequency was then evaluated in a similar manner during each week of a 4-week treatment phase. To determine effect of probiotic on BM frequency, *B. infantis* 35624 1 × 10^8 CFU per capsule (n = 85) and placebo (n = 80) were compared for subjects with differing baseline bowel movement frequencies (i.e. ranging from constipation, at one end, to diarrhea, at the other) using analysis of covariance.

Results: At baseline, the median BM frequency was 1.43 BM/day, with an inter-quartile range of 1 BM/day to 2.29 BM/day. The distribution of BM frequencies over the entire range of percentiles is illustrated in the Table. While there were no statistical differences between placebo and *bifidobacterium* at the mid-point of the distribution frequency (inter-quartile range), significant differences (p < 0.05) were noted at both ends (i.e. below the 15th percentile: constipation and above the 81st percentile: diarrhea) of the frequency distribution with the *bifidobacterium* treated group experiencing a normalization of bowel habit in each instance.

Change from baseline comparisons at different baseline values

<table>
<thead>
<tr>
<th>Baseline percentile</th>
<th>Average BM/day</th>
<th>Week 4 B. infantis 35624</th>
<th>Placebo</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>10&lt;sup&gt;th&lt;/sup&gt;</td>
<td>.71</td>
<td>+.57</td>
<td>+.31</td>
<td>+.25</td>
<td>.037</td>
</tr>
<tr>
<td>15&lt;sup&gt;th&lt;/sup&gt;</td>
<td>.80</td>
<td>+.51</td>
<td>+.27</td>
<td>+.23</td>
<td>.049</td>
</tr>
<tr>
<td>25th</td>
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<td>+.36</td>
<td>+.18</td>
<td>+.18</td>
<td>.098</td>
</tr>
<tr>
<td>50&lt;sup&gt;th&lt;/sup&gt;</td>
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<td>-.03</td>
<td>+.07</td>
<td>.457</td>
</tr>
<tr>
<td>75&lt;sup&gt;th&lt;/sup&gt;</td>
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<td>-.58</td>
<td>-.44</td>
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<tr>
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<td>-1.21</td>
<td>-.85</td>
<td>-.36</td>
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</tbody>
</table>

Conclusions: The probiotic *B. infantis* 35624 normalised bowel habit among IBS patients with diarrhea or constipation at baseline by increasing BM frequency in constipated subjects and reducing BM frequency in those with diarrhea at baseline. These results suggest that supplementation with the novel probiotic *B. infantis* 35624 results in normalization of BM frequency for IBS sufferers at both ends of the spectrum.

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**Azithromycin as Novel Treatment for Gastroparesis?**

Baharak Mosheire, M.D., Nicholas G. Verne, M.D., Philip P. Toskes, M.D.* Gastroenterology, Hepatology and Nutrition, University of Florida, Gainesville, FL.

Purpose: Current medical therapy of gastroparesis with prokinetic agents has been disappointing due to the limited options currently available. Erythromycin is a potent prokinetic agent that stimulates gastric emptying. Recently, Erythromycin (EES) has been associated with sudden cardiac death due to prolongation of QT intervals and subsequent torsade de pointes related through its interaction with inhibitors of cytochrome P-450 3A4 (NEJM. 2004 Sep 9; 351 [11]: 1089–96). Azithromycin (AZI) is a synthetic macrolide similar in structure to Erythromycin, however it does not interact with the cytochrome P-450 isoenzymes. The aim of this study was to determine if azithromycin stimulates antral activity in patients with gastroparesis.

Methods: Small bowel manometric data on 30 patients undergoing clinical evaluation for gastroparesis was reviewed. Antral activity was measured after infusion of EES 250mg IV and AZI (500mg IV or 250mg IV) were given at different intervals during the small bowel manometry. The parameters measured included the total duration of effect, mean amplitude of antral contractions, duration of highest antral contraction, number of cycles per minute, and the motility index. The data was analyzed using the repeated measures ANOVA for comparison of each medication.

Results: Comparison of EES and AZI at a dose of 250 mg shows no difference in antral activity measured in terms of mean amplitude (p < 0.327), duration of antral contractions (p < 0.821), or number of cycles per minute (p < 0.258). Comparison of EES with AZI at a dose of 500 mg however shows that the mean amplitude and duration of antral activity were increased with AZI (p < 0.027 and p < 0.17, respectively). The difference in motility index was 3657 ± 1290 mmHg.min with AZI versus 1656 ± 488 mmHg.min with EES (p < 0.025). No significant difference was seen with respect to the total duration of contractions or the number of cycles per minute.

Conclusions: Azithromycin stimulates antral activity similar to Erythromycin and moreover has a longer duration of effect. Azithromycin unlike Erythromycin however, does not have significant drug-drug interactions and may be a potential new medication for treatment of gastroparesis.
Comparison of Visceral and Somatic Pain Sensitivity in Irritable Bowel Syndrome Patients with and without Fibromyalgia
Baharak Moshiree, M.D., Donald D. Price, Ph.D., Michael E. Robinson, Ph.D., Nicholas G. Verne, M.D.* Department of Medicine, University of Florida, Gainesville, FL and Department of Medicine, North Florida/South Georgia Veteran Health System, Gainesville, FL.

Purpose: Recent studies have shown that patients with irritable bowel syndrome (IBS) exhibit both visceral and somatic hyperalgesia. This is similar in effect to the central hypersensitivity mechanism seen in patients with Fibromyalgia (FM). The aim of the present study was to compare the magnitude of visceral and thermal hypersensitivity in IBS patients and Fibromyalgia patients with IBS (FM + IBS) compared to age/sex matched healthy controls.

Methods: Fifteen patients (12 F, 3 M) with IBS, ten patients (10 F) with FMS, and seventeen control subjects (13 F, 4 M), rated pain intensity and unpleasantness to hot water immersion (45° and 47° C) of the hand/foot and phasic distension of the rectum (35.5 mmHg) on a 0–10 M-VAS scale. The data was analyzed with 3 separate one-way ANOVA’s with Post-hoc Tukey tests.

Results: When comparing both thermal and visceral stimuli, the control group had lower pain ratings than either the IBS or FMS + IBS groups (p < 0.001). IBS patients rated rectal distension as more painful than the FMS + IBS group (p = 0.004). During hot water immersion of the foot, the FMS + IBS group had higher pain ratings than the IBS group (P = 0.027). During hand immersion, FMS + IBS and IBS patients did not significantly differ in their pain intensity ratings (P = 0.15). Both patient groups had higher scores than controls to somatic focus, state anxiety, and depression. No significant differences were found between the IBS and FMS + IBS groups on any psychological measures.

Conclusions: FMS + IBS patients show greater thermal hypersensitivity compared to IBS patients. However, IBS patients exhibit higher pain ratings to rectal distension compared to FMS + IBS patients. These data suggest that regions of primary and secondary hyperalgesia are to some extent dependent on the primary pain complaint.

Screening for Celiac Disease in an IBS Population

Purpose: Celiac disease (CD) is a genetically predisposed immune-mediated disorder affecting primarily the GI tract and activated by ingestion of gluten contained in wheat, rye and barley. It may begin in childhood or adult life, and serologic studies indicate the prevalence is relatively common with estimates of 1% to 3% in the general population in Europe and the US. Symptoms are highly variable and may include abdominal pain, bloating, diarrhea, and constipation (1,2). Because these non-specific GI symptoms are also compatible IBS-A, IBS-CM and IBS-DM subtypes were based on prospective assessment of stool habit. Subjects received clinical questionnaires at 3-mo. intervals for 1 yr. (N = 190 evaluable). A Classification and Regression Tree (CART) analysis (SAS V.8) identified, using cross-sectional data from 2-week diary cards, which clinical items discriminated between IBS-A, IBS-CM and IBS-DM, that would otherwise require prospective assessment of bowel habit over at least 1 year.

Results: Screening period for active IBS symptoms, patients had a serum sample ing with the majority of patients coming from US, Canada, Germany, and Australia (1138/1362, 84%). IgA TTG antibody results were obtained for 1355 patients with 7 patients testing positive for CD: 6 females (4 white, 2 Hispanic) and 1 male (white). By history, 2 females were diarrhea-IBS and 1 female had constipation-IBS. Three females and 1 male had mixed diarrhea-constipation IBS.

Conclusions: In this IBS population, IgA TTG antibody testing for CD suggests that the prevalence of CD in IBS (7/1355; 0.5%) is similar to the prevalence observed in general population studies. Cost of screening for CD in a clinical trial may not be justified given the small number of patients with possible CD. Further studies are warranted to confirm these findings.

REFERENCES

An Algorithm Using CART Analysis To Identify IBS-C and IBS-A from IBS-D
Douglas A. Drossman, M.D.,* Carolyn B. Morris, Ph.D., Yuming Hu, Ph.D., Jane Leserman, Ph.D., Brenda B. Toner, Ph.D., Nicholas Diamant, M.D., Shrikant I. Bangdiwala, Ph.D. UNC Center for Functional GI and Motility Disorders, U of North Carolina, Chapel Hill, NC and Centre for Addiction and Mental Health, U of Toronto, Toronto, ON, Canada.

Purpose: In Drossman, Gastro, 2005, we defined by prospective 1-yr evaluation, Rome II compatible IBS alternators (IBS-A) who alternate between IBS-C and IBS-D. IBS-A had similar bowel habit to IBS constipation-mixed (IBS-CM: alternates between IBS-C and IBS-M, but not IBS-D), while IBS diarrhea-mixed (IBS-DM: alternates between IBS-D and IBS-M, but not IBS-C) appears as a separate group. This suggest that treatments for constipation could apply to IBS-CM and IBS-A, but not IBS-DM, and treatments for diarrhea be restricted to IBS-DM. The aim of this study was to develop an algorithm to identify IBS-A, IBS-CM and IBS-DM patients for clinical trials, either as 3 distinct groups or with IBS-CM and IBS-A combined.

Methods: Among 317 women entering an NIH treatment trial, Rome II compatible IBS-A, IBS-CM and IBS-DM subtypes were based on prospective assessment of stool habit. Subjects received clinical questionnaires at 3-mo. intervals for 1 yr. (N = 190 evaluable). A Classification and Regression Tree (CART) analysis (SAS V8) identified, using cross-sectional data from 2-week diary cards, which clinical items discriminated between IBS-A, IBS-CM and IBS-DM, that would otherwise require prospective assessment of bowel habit over at least 1 year.

Results: Several analyses were run to create a model that was parsimonious in the number of predictor items (N = 2–4) and also robust in identifying the defined groups (misclassification range 12.6% to 34.2%). Efforts to classify subjects into 3 groups (IBS-A, IBS-CM, IBS-DM) were unsuccessful because IBS-A could not be separated from IBS-CM, thus confirming our initial findings. The best model contained only 2 items (average stool consistency using Bristol Stool Scale, and stool frequency) with a 14.7% misclassification rate. The final clinical decision rule was: 1) Is stool frequency < 2/day? 2a) If Yes, is the stool consistency < 5 [Yes = IBS-A + IBS-CM; No = IBS-DM] 2b) If No, is the stool consistency < 4 [Yes = IBS-A + IBS-CM; No = IBS-DM]?

Conclusions: Using CART analysis, we developed a simple algorithm using a 2-week assessment of average stool frequency+consistency that identifies with 85% accuracy subjects who will have IBS-A & IBS-CM vs. IBS-DM over the subsequent year. The algorithm may be of value in clinical trials and in planning treatments. Supported by NIH: R01DK49334, and R24 DK067674 and Novartis Pharmaceuticals.
Do All Patients with Small Intestinal Bacterial Overgrowth (SIBO), Based on a Double Peaked Lactulose Breath Test (DPLBT), Need Antibiotics or Is Tegaserod an Option?  
Daniel S. Mishkin, M.D.C.M., David Blank, M.D.C.M., Morty Yalovsky, Ph.D., Seymour Mishkin, M.D.C.M.*  
Gastroenterology / Clinical Biochemistry / Management, McGill University Health Center, Montreal, QC, Canada and Gastroenterology, Boston Medical Center, Boston, MA.

**Purpose:** The goal of our clinical evaluation was to see the effects of tegaserod on patients who presented with constipation and bloating and were found to have a DPLBT. The lactulose breath test (LBT) uses a non absorbed disaccharide broken down by bacterial colonies normally encountered in the cecum. The LBT can be used to identify patients with SIBO based on the presence of a DPLBT, signifying an abnormal proximal location of bacteria. A 72 year old female diabetic patient had resolution of her significant constipation and bloating as well as normalization of her DPLBT while taking tegaserod. She had been previously given a 14 day course of ciprofloxacin and metronidazole and had a transient resolution of her DPLBT; however, her symptoms recurred within 6 months. She refused a second course of antibiotics, and we opted to start tegaserod 6 mg po bid. She sustained resolution of her DPLBT and her clinical symptoms within 2 weeks.

**Methods:** Patients with the clinical syndrome of constipation predominant IBS (IBS-C) based on Rome II criteria were evaluated with LBT. Five female patients (ages 53 – 65) manifested a DPLBT and underwent a trial of tegaserod. None of these patients had any clinical history to suggest dysmotility i.e. diabetes, calcium channel blockers, or evidence of mechanical obstruction based on UGI/SBFT and colonoscopy. After 2 weeks, a repeat LBT and clinical evaluation was performed.

**Results:** Four responded to a 2 week trial of tegaserod 6mg bid with resolution of the DPLBT accompanied by significant symptomatic relief. The fifth patient discontinued tegaserod on the third day due to cramps and diarrhea and did not repeat the LBT. All 4 patients with IBS-C and DPLBT who completed the 2 week trial of tegaserod had clinical improvement and normalization of the LBT. The double peak disappeared and the oral cecal transit time (OCTT) was reduced from a mean of 143 minutes (range 120 – 150) to 79 (range 60 – 90).

**Conclusions:** Patients with an abnormal LBT consistent with SIBO may be relieved with antibiotics. The LBT is an indirect evaluation, yet a clinical response and a normalization of an abnormal test cannot be ignored. Tegaserod, a prokinetic, may alter the findings on LBT, as it is known to decrease the OCTT, and may provide a more physiologic therapy for a selective subgroup of IBS-C.

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Effects of Single Dose Administration of MD-1100 on Safety, Tolerability, Exposure, and Stool Consistency in Healthy Subjects  
Mark G. Currie, Ph.D.,* Caroline Kartz, Ph.D., Shalina Mahajan-Miklos, Ph.D., Robert W Bushby, Ph.D., Angelika Fretzen, Ph.D., Steve Geis, M.D. R&D, Microbia, Inc., Cambridge, MA.

**Purpose:** MD-1100, a Guanylate Cyclase-C agonist that acts in the intestine with minimal oral absorption, is a novel agent that was designed to act in the intestine with minimal oral absorption. The goal of our clinical evaluation was to see the effects of tegaserod on patients who presented with constipation and bloating and were found to have a DPLBT. The lactulose breath test (LBT) uses a non absorbed disaccharide broken down by bacterial colonies normally encountered in the cecum. The LBT can be used to identify patients with SIBO based on the presence of a DPLBT, signifying an abnormal proximal location of bacteria. A 72 year old female diabetic patient had resolution of her significant constipation and bloating as well as normalization of her DPLBT while taking tegaserod. She had been previously given a 14 day course of ciprofloxacin and metronidazole and had a transient resolution of her DPLBT; however, her symptoms recurred within 6 months. She refused a second course of antibiotics, and we opted to start tegaserod 6 mg po bid. She sustained resolution of her DPLBT and her clinical symptoms within 2 weeks.

**Methods:** Patients with the clinical syndrome of constipation predominant IBS (IBS-C) based on Rome II criteria were evaluated with LBT. Five female patients (ages 53 – 65) manifested a DPLBT and underwent a trial of tegaserod. None of these patients had any clinical history to suggest dysmotility i.e. diabetes, calcium channel blockers, or evidence of mechanical obstruction based on UGI/SBFT and colonoscopy. After 2 weeks, a repeat LBT and clinical evaluation was performed.

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**Conclusions:** Patients with an abnormal LBT consistent with SIBO may be relieved with antibiotics. The LBT is an indirect evaluation, yet a clinical response and a normalization of an abnormal test cannot be ignored. Tegaserod, a prokinetic, may alter the findings on LBT, as it is known to decrease the OCTT, and may provide a more physiologic therapy for a selective subgroup of IBS-C.

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**Results:** We observed no SAEs during this study, and the pattern of AEs between placebo and MD-1100 treated subjects was similar with the exception of the intended pharmacodynamic actions from an agent that promotes secretion and transit. MD-1100 was well tolerated at all dose levels and, as anticipated for this luminaly acting compound, we were unable to detect any systemic exposure of MD-1100. MD-1100 elicited an increase in the BSFS post-dose, reflecting a decrease in stool consistency. We also observed other indications of G.I. activity post-dosing of MD-1100, including an apparent increase in stool weight.

**Conclusions:** In this single-dose Phase 1 study, MD-1100 was well tolerated across the dose range studied (30 – 3000 micrograms). As expected for an agent that was designed to act in the intestine with minimal oral absorption, MD-1100 appears to possess G.I. pharmacodynamic activity in healthy subjects with no detectable levels of systemic exposure. To date, the preclinical and clinical data strongly support the potential of MD-1100 for the treatment of G.I. conditions, including IBS-C. In addition to the single dose study described here, a multiple ascending dose study of MD-1100 in 48 healthy subjects has recently completed enrollment. We anticipate advancing MD-1100 further into clinical development with the objective of evaluating whether MD-1100 will act to treat the pain, bloating, and constipation associated with IBS-C.
Methods: A Phase III multicenter, parallel-group, DB, randomized, placebo-controlled trial was conducted in subjects with a history of constipation. Chronic constipation was defined as < 3 spontaneous bowel movements (SBMs)/week, with a minimum 6-mo history of hard stools, sensation of incomplete evacuation, or straining during at least 25% of bowel movements (BM). An SBM was any BM that did not occur within 24 h of rescue laxative use. After a 15-day drug-free period, subjects were randomized to oral L (24 µg bid) or P with food and water for 28 days. Evaluations were performed at baseline and at weekly intervals during treatment and follow-up and included patient global assessments, patient symptom assessments, and physical and lab testing. The primary efficacy variable was SBM frequency; secondary variables included time to first SBM, % of patients with an SBM within 24 h of first dose, and response classification.

Results: 237 subjects were enrolled: 119 to L and 118 to P. L and P populations were similar; both were predominantly female and Caucasian. The mean pretreatment weekly SBM frequency was 1.28 for L vs 1.52 for P; at Week 1, SBM frequency increased to 5.89 in the L group vs 3.99 in the P group (p < 0.0001). Significant differences in SBM frequency persisted throughout the study: Week 2 (p = 0.0487), Week 3 (p = 0.0004), and Week 4 (p = 0.0068). The mean difference in SBM frequency between baseline and Week 1 was 4.61 for L vs 2.47 for P (p < 0.0001). At Week 1, 72.1% of L patients were classified as full responders (> 4 SBM/week without rescue drugs), vs 48.7% of P patients (p < 0.0001). During the 24 h after first intake of study drug 61.3% of L and 31.4% of P subjects had an SBM. In subjects receiving L, significant improvements, which persisted throughout the study, were also observed with respect to stool consistency (p values < 0.0001), straining (p values < 0.002), and constipation severity (p values < 0.03). Although treatment-related adverse events were reported, none were classified as serious. Nausea, the most common AE, occurred in 21% of L and 4.2% of P patients; it was generally mild to moderate.

Conclusions: Lubiprostone, 24 µg bid, is well tolerated and significantly better than placebo in providing rapid, sustained relief of the symptoms of chronic constipation.

Older patients were more likely to have undergone sigmoidoscopy or colonoscopy (47.1% vs 16.9%; p < 0.05). Otherwise, health care utilization between the two IBS groups was similar as evident by number of physician visits per year, use of prescription drugs (23.5 vs 16.9%; p = NS) and alternative medications (10.4 vs 11.8%; p = NS) and being disabled due to IBS (zero vs 3.9%; p = NS).

Conclusions: There is no difference in general health and health care resource use by older IBS patients as compared to the younger counterparts. The greater use of sigmoidoscopy or colonoscopy by older patients is likely to be a reflection of increased popularity of colon cancer screening.
Purpose: To compare patient evaluations of the effects of lubiprostone vs placebo in the treatment of chronic idiopathic constipation.

Methods: In this Phase III multicenter, parallel-group, double-blind trial, following a 15-day drug-free period, 244 subjects with chronic idiopathic constipation were randomized to receive either oral lubiprostone (24 µg bid) or placebo with food and water for 28 days. Chronic constipation was defined as < 3 spontaneous bowel movements (SBMs) per week, with a minimum 6-month history of very hard stools, sense of incomplete evacuation, or straining during at least 25% of bowel movements (BM). An SBM was defined as any BM that did not occur within 24 hours of rescue medication use. Patients with conditions or treatments that could affect safety or data validity were excluded. SBM frequency, BM assessment (constancy and straining), abdominal assessment (bloating and discomfort), and global assessment (constipation severity and treatment effectiveness) were evaluated by patients and recorded in diaries at baseline, on a weekly basis during treatment (4 weeks), and at follow up.

Results: Patients receiving lubiprostone reported statistically significant improvements over baseline for stool consistency (p < 0.0001 at all weeks) and degree of straining (p < 0.03 at all weeks). Compared with placebo, statistically significant differences that persisted throughout the study were seen for SBM frequency (p < 0.0001 at Week 1 and < 0.05 at weeks 2–4), stool consistency (p < 0.0001 at all weeks), straining (p < 0.002 at all weeks), and severity of constipation (p = 0.006 at Week 1 and < 0.03 at weeks 2–4). Patient global assessments of treatment effectiveness reported significantly more effective relief from lubiprostone than from placebo throughout the study period; at Week 1, mean treatment effectiveness was 1.88 for lubiprostone vs 1.22 for placebo (p < 0.0001) on a scale of 0 (not at all effective) to 4 (very effective). Lubiprostone retained a significantly (p < 0.0001) greater effectiveness rating (range 1.86–1.97) relative to placebo (range 1.17–1.22) throughout the treatment period.

Conclusions: Patient assessments indicate that lubiprostone positively affects symptoms of chronic constipation and that the effect persists over at least 4-weeks’ treatment.

Effects of Lubiprostone, a Novel GI Chloride Channel Activator, on Isolated Smooth Muscle

G. P. Perentesis, PharmD,* D. F. Crawford, Ph.D., K. J. Engelke, Ph.D., H. Osama, M.S., R. Ueno, M.D. R&D, Sucampo Pharmaceuticals, Bethesda, MD; Toxicology, Takeda Global R&D, Lincolnshire, IL; R&D, Sucampo Pharmaceuticals, Bethesda, MD and ADME, R-Tech Ueno, Ltd., Osaka, Japan.

Purpose: Lubiprostone (L), a novel bicyclic fatty acid derivative under development for the treatment of chronic idiopathic constipation and irritable bowel syndrome, increases intestinal fluid secretion via selective activation of GI CIC-2 chloride channels without altering blood levels of sodium or potassium. Clinical studies have shown that L relieves constipation and improves associated symptoms, such as bloating and straining. This study aims to characterize the pharmacokinetic profile of L in the mouse, rat, rabbit, dog, and monkey.

Methods: After oral doses of [3H]-L were administered to fasting animals (mouse, rat, dog, rabbit, and cynomolgus monkey), plasma clearance, urine and fecal excretion, and tissue distribution were determined using standard methods. Radiolabeled L was added to plasma from fasted animals (rat and dog), and the protein-bound fraction determined as a measure of in vitro plasma protein binding: in vivo protein binding was determined after oral dosing of fasted rats with 50 µg/kg [3H]-L.

Results: Total plasma radioactivity peaked within 4 h in most species tested. The plasma half-life was < 2.5 h in rats and ~9 h in rabbit and monkey. At 48 h, excretion of radioactivity in rats was nearly equivalent in urine and feces. In contrast, excreted radioactivity was primarily in the urine in dogs, rabbit, and monkey. By 48 h postadministration, 73–95% of administered radioactivity was excreted in all animals. The majority of radioactivity was localized to the GI tract in the rat. Outside the GI tract, 6.8% of radioactivity was found in the liver 1 h postdosing, with very little radiolabel (0.71%) detected by 6 h. In vitro plasma protein binding was reversible, and binding was >90% in mouse, rat, and dog. There were no binding differences with respect to sex or concentration. In vivo protein binding studies indicated reversible binding ranging from 46.1% to 61.1% (of the administered dose) at 1–6 hours after administration.

Conclusions: The majority of radiolabel is found locally in the GI tract and is almost completely eliminated within 48 hours. For all species except the rat, the predominant route of elimination was urinary. In vitro protein binding was reversible and similar across all species, with no sex differences; in vivo protein binding was reversible, and increased as a function of time.

Gastrointestinal Symptoms after Gastric Bypass Surgery

G. Anton Decker, M.B.B.Ch., Ann Schetter, R.N., Carolyn S. Williams, R.N., Lori R. Roast, M.D., James M. Swain, M.D., Michael D. Crowell, Ph.D. Division of Gastroenterology and Hepatology, Mayo College of Medicine, Scottsdale, AZ; Division of Endocrinology, Mayo College of Medicine, Scottsdale, AZ and Department of Surgery, Mayo College of Medicine, Scottsdale, AZ.
Purpose: Gastrointestinal (GI) symptoms are more frequent in obese individuals. Gastric bypass surgery, specifically Roux-en-Y gastric bypass surgery (RYGB), has become an effective and now common treatment for extreme obesity. Little is known about the impact of RYGB on GI symptoms. We evaluated the frequency and severity of GI symptoms in patients before or after RYGB.

Methods: Obese patients (n = 56) attending a support group completed a GI Symptom Checklist. Three groups of patients were identified, pre-GPS (n = 25; 52 ± 11 yrs), early (0–8 months) post RYGB (n = 14; 50 ± 8 yrs) and late (12 months) post RYGB (n = 17; 56 ± 8 yrs). ANOVA was used to detect differences between groups. If a significant difference was detected, post-hoc, pairwise comparisons were made using Tukey’s-b at a significance level of p < 0.05. Results are reported as mean ± SE.

Results: The groups were similar in age and gender. The BMI differed significantly between groups (pre-GPS = 41.7 ± 1.5 kg/m², early post RYGB = 35.3 ± 2.1, late post RYGB = 27.1 ± 1.0). Compared to the non-surgical group, vomiting was more frequent in the early and late post RYGB groups. The severity of vomiting improved in the late post RYGB group. Early satiety and persistent fullness after eating were more frequent and severe early post RYGB, but not late post RYGB. Diarrhea, flatulence and fecal urgency were more frequent and severe in the late post RYGB group compared to the pre-RYGB group. In the post RYGB groups, weight loss correlated with the severity of diarrhea.

Conclusions: Upper and lower GI symptoms are more frequent after RYGB for extreme obesity. These symptoms should be addressed by clinicians as they may influence patient satisfaction and compliance after RYGB.

904

In Vivo Metabolism of Lubiprostone, a Novel GI Chloride Channel Activator, in Mouse, Rat, Dog, and Monkey

G. P. Perentesis, PharmD,* D. F. Crawford, Ph.D., K. J. Engelle, Ph.D., R. Ueno, M.D., Y. Kawai R&D, Sucampo Pharmaceuticals, Bethesda, MD; Toxicology, Takeda Global R&D, Lincolnshire, IL and ADME, R-Tech Ueno, Ltd., Senda, Japan.

Purpose: Lubiprostone (L), in development for chronic idiopathic constipation and constipation-predominant IBS, is a selective GI chloride channel-2 (CIC-2) activator that increases intestinal fluid secretion. These studies compare the in vivo metabolic profiles of L in different species.

Methods: Mouse, rat, dog, and monkey were orally administered [3H]-L: 50 µg/kg for mouse and rat, and 5 µg/kg for dog and monkey. Blood samples were collected periodically from 5 min to 48 h postdosing, and urine and feces collected from 0–144 h postdosing.

Results: The maximum percentage of administered dose of unmetabolized L in plasma of mouse, rat, or dog was 2.18% at 60 minutes, 2.11% at 10 minutes, and 0.8% at 30 minutes, respectively. L plasma levels in the dog declined rapidly to undetectable within 120 minutes and L was not detected in the monkey at any point. L was not detected in urine or feces of any species at any time. Several metabolites (peaks A-M) were detected by HPLC in plasma of nearly all species. Peaks C and D were the major early peaks; peak J was the major late metabolite. C decreased rapidly with time as follows: 0.67% in mouse at 60 minutes, 1.80% in rat at 120 minutes, 0.30% in dog at 180 minutes, and nondetectable (ND) at 90 minutes in monkey. In rats peak D decreased to a minimum by 30 minutes (4.0%) and remained relatively constant (4.9–9.1%); in the mouse, declined rapidly to 4.31% by 60 minutes, and in the dog was 0.53% at 180 minutes. Peak D was detectable (2.13%) at 90 minutes and undetectable at 240 min in monkey. Peak J was at a maximum in plasma after 30 minutes in the rat (37.8%), 10 minutes in mouse (38.97%), and 180 minutes in the dog (25.88%), respectively and undetectable within 90 minutes in the monkey. Peaks C, D, and J were detected in urine/feces as follows: Peak C: rat (0.21/0.95%), dog (ND/3.47%), and monkey (ND/ND); Peak D: rat (0.21%/0.72%), dog (7.87%/2.27%), and monkey (0.73%/0.14%); and Peak J: rat (8.63%/2.63%), dog (2.40%/ND), and monkey (16.45%/2.00%).

Conclusions: Lubiprostone is rapidly and extensively metabolized from the plasma. L was detected only transiently and at very low levels in plasma of mouse, rat, and dog, with no parent compound detected in monkey plasma. Total metabolites were qualitatively similar in all species tested, with notable quantitative differences in the major metabolites that appear early or late in the metabolic pathway.

905

Effects of Lubiprostone, a Novel GI Chloride Channel Activator, on Reproductive and Developmental Toxicity Endpoints in Rats

D. F. Crawford, Ph.D.,* G. P. Perentesis, PharmD, K. J. Engelle, Ph.D., R. Ueno, M.D. Toxicology, Takeda Global R&D, Lincolnshire, IL and R&D Sucampo Pharmaceuticals, Bethesda, MD.

Purpose: Lubiprostone, under development for chronic idiopathic constipation, is a selective GI CIC-2 chloride channel activator. Preclinical assessment of lubiprostone (L) demonstrates minimal toxicity. The following studies evaluate reproductive and developmental effects in rats.

Methods: For reproduction, 0.04, 0.2, or 1.0 mg/kg/day of L was administered by oral gavage. In male rats dosing was for 4 weeks prior to mating and 35 days from mating to end of third mating; female dosing was 14 days prior to mating, 15 days during mating, and 7 days during pregnancy. Male rats were sacrificed on the day following final dosing and females on day 13 of pregnancy. In the developmental study oral doses of L at 0.02, 0.2, and 1.0 mg/kg/day were given from gestation day (GD) 6 to lactation day (LD) 20. Pregnant F0 dams delivered F1 offspring, which were subsequently mated.

Results: Food consumption was intermittently increased or decreased during dosing. No body weight changes were observed in females. In the 1.0 mg/kg/day males, decreased body weight gain, alimentary tract distension,
and large adrenal glands were observed – the absolute weight of epididymis was significantly decreased with no changes in relative weight. No changes were observed in sperm parameters, including motility ratio, viability and sperm number. No treatment-related histopathologic findings were observed in either sex. No significant differences in reproductive endpoints, including corpora lutea number, implantation index, and preimplantation losses, were noted in females, with the exception of decreased numbers of implantation and live embryos in the 1.0 mg/kg/day group. The NOEL was 0.2 mg/kg/day for parental effects and 1.0 mg/kg/day for reproductive effects. In the developmental study, significant decreased food consumption and body weight gain was observed in the F0 dams at 1.0 mg/kg/day, leading to total litter death in half of the pregnant dams following parturition. Lactating dams at the highest dose produced pups with decreased weights and open-field activity. The NOEL for parental and F1 fetal effects was 0.2 mg/kg/day.

Conclusions: No effects on reproductive, fertility, or developmental parameters were observed in the absence of maternal toxicity. The results of these animal studies indicate that lubiprostone exhibits a low likelihood for reproductive or developmental toxicity at clinically relevant doses.

906

Tegaserod Benefits Patients with Constipation Predominant IBS (IBS-C) and Delayed Orocecal Transit Time (OCTT) as Determined Using the H2 Lactulose Breath Test (LB T)
Daniel S. Mishkin, M.D.C.M., David Blank, M.D.C.M., Morty Yalowky, Ph.D., Seymour Mishkin, M.D.C.M.* Gastroenterology, McGill University Health Center, Montreal, QC, Canada; Gastroenterology, Boston Medical Center, Boston, MA; Clinical Biochemistry, McGill University Health Center, Montreal, QC, Canada and Management, McGill University, Montreal, QC, Canada.

Purpose: Symptomatic IBS-C can be very difficult to treat effectively. We proposed that the subgroup with delayed OCTT would respond favorably to tegaserod, a prokinetic, compared to other currently available therapies. LBT testing uses a non absorbed disaccharide that is broken down by bacterial colonies that are normally encountered in the cecum. The OCTT is determined as the time (minutes) from ingestion until there is a rise in H2 > 20 ppm above baseline, coinciding with it’s metabolism by normal colonic bacteria.

Methods: In a retrospective study we identified 12 females aged 22 – 70, with IBS-C as defined by Rome-II criteria whose OCTT was significantly prolonged (≥105 min, range 105 – 180) and without evidence of SIBO. A repeat LBT and a clinical evaluation with respect to stool frequency, pain and bloating were performed after a 2 week course of tegaserod 6 mg bid.

Results: Nine of 12 (75%) patients noted a significant clinical response. In 7/9 (78%) of the clinical responders there was a reduction in OCTT from a mean of 141(range 105 – 180) to a mean of 81(range 45 – 120). In 4/9 (44%), the OCTT was ≤75 minutes. No improvement in the LBT was observed in all three non responders. In view of the severity of IBS-C related symptoms in one initial non- responder, we elected to increase the dose of tegaserod to 6 mg tid. In addition to an increase in stool frequency to > 3.5 complete spontaneous bowel movements/week and a significant reduction in pain and bloating, her OCTT fell from the pre-treatment value of 180 to 45 minutes. These results are consistent with a dose response relationship between tegaserod and the OCTT.

Conclusions: These results suggest that IBS-C patients with significant prolongation of the OCTT may be identifying a selective subgroup of patients who are likely to benefit from a trial of tegaserod. We can only speculate whether titrating the dose of tegaserod to address a prolonged OCTT will lead to a better clinical response for initial non responders.

907

Probiotics in Irritable Bowel Syndrome: A Systematic Review
Mohamed O. Othman, M.D., Praveen K. Roy, M.D.* Department of Medicine, University of New Mexico, Albuquerque, NM.

Purpose: Probiotics are viable microorganisms with beneficial physiologic or therapeutic activities. Probiotics have been reported to be useful in the prevention or treatment of various intestinal diseases. Recent studies have suggested a role for probiotics in Irritable bowel syndrome (IBS). We conducted a systematic review of the efficacy and safety of probiotics in IBS.

Methods: MEDLINE (from 1966–2005) and abstracts of gastroenterology scientific meetings in the last 5 years were searched (search date June 2005). Only randomized clinical trials conducted in adult subjects were included. Studies were assigned a quality score. Standard forms were used to extract data regarding study design, duration of study, outcome measures, and adverse effects by two independent reviewers.

Results: 8 studies satisfied the inclusion criteria with a total of 343 patients. Significant heterogeneity was present among the studies. Most of the studies had a small sample size (range 10–77 patients) and were not adequately powered. Duration of therapy with probiotics ranged from 4 to 8 weeks. Different strains of probiotics were evaluated in these studies: Lactobacillus plantarum, Lactobacillus GG, Lactobacillus salivarius, Bifidobacterium breve, Bifidobacterium infantis, Streptococcus faecium, and VSL #3 (contains 8 different organisms). Six studies reported improvement in IBS symptoms with probiotics compared to placebo. L. plantarum improved IBS symptoms in 3 studies while one study found no effect. VSL #3 was evaluated in one study and showed improvement in abdominal bloating only, with no effect on other IBS symptoms. Two probiotics, Lactobacillus salivarius and Bifidobacterium infantis were evaluated in a single study. Both probiotics decreased abdominal pain, however Bifidobacterium was found to be more superior. Another study evaluated Streptococcus faecium and found clinical improvement with probiotic therapy. Lactobacillus GG did not improve any of the symptoms compared to placebo in another clinical trial involving 25 patients. No significant adverse effects were noted in any of the studies. Limitations of the studies were short duration of therapy, small sample size and lack of uniformity in reporting primary outcome measures.

Conclusions: Various probiotic regimen may be useful in the treatment of IBS. However, larger well designed clinical trials are needed to verify findings from these smaller studies.

908

Gastroparesis: The Impact on Work and Daily Activities
Brian E. Lacy, Ph.D., M.D.,* Victoria Barghout, M.S.P.H., David Bauer, BA Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH and Global Health Economics, Novartis Pharmaceuticals, East Hanover, NJ.

Purpose: Patients (Pts) with gastroparesis (GP) suffer from recurrent symptoms of nausea, vomiting, early satiety, and abdominal pain. The impact of GP on work and daily activities has not been previously reported.

Methods: 491 patients with documented GP over the age of 18 were followed over a 3 year period (1/02 to 1/05). Gastroparesis was documented by the presence of symptoms for more than 6 months (nausea, vomiting, and early satiety) with delayed gastric emptying verified by solid phase gastric emptying scan. Mechanical obstruction was ruled out in all patients. In January 2005, patients were sent a questionnaire which collected demographics, employment status, work and daily activities, and medication use. Utilization of health care resources, including physician visits, diagnostic testing, ER visits, and hospital admissions was also assessed. A reminder postcard was sent to all patients 2 weeks after the initial mailing. Non-responders were sent an identical survey 2 weeks after the postcard was mailed. All responses were anonymous and no incentives were provided. This protocol was approved by the IRB of Dartmouth Medical School. Descriptive statistics were computed using Microsoft Excel XP (2003).

Results: Of the 491 eligible patients, 100 questionnaires were unable to be completed (because of incorrect/outdated address (n = 72); returned but not answered (n = 10); patients were deceased (n = 18)). Of the remaining 391 questionnaires, 228 were completed for a response rate of 58.3%. The mean age was 49.6 (range 19–86), 77.2% were female, and 88.2% were Caucasian. 68.9% of respondents had entered or completed college. In the past 12 months, 67.5% of respondents reported that GP led to a reduction in...
their daily activities, while 21.9% reported that GP caused them to change their school or work schedule. 28.5% of respondents noted that GP had resulted in a reduction in their annual income. 11.0% of patients reported that they were medically disabled due to their GP and 5.7% stated they were unemployed/not working specifically due to their GP.

**Conclusions:** This is the first study to measure the consequences of GP on work and daily activities. This disorder substantially impacts daily activities and leads to a reduction in income due to disability and missed work. Treatment regimens should include strategies to restore productivity and enhance well-being.

**Gastroparesis Impacts Health Care Resource Utilization**

David Bauer, BA, Victoria Barghout, M.S.P.H., Brian E. Lacy, Ph.D., M.D.* Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH and Global Health Economics, Novartis Pharmaceuticals, East Hanover, NJ.

**Purpose:** Gastroparesis (GP) is a chronic disorder of delayed gastric emptying characterized by recurrent symptoms of nausea, vomiting, early satiety, and abdominal pain. Data on health care utilization by gastroparetic patients is lacking.

**Methods:** 491 patients (Pts) with documented GP (≥ 18 years) were followed over a 3 year period. Gastroparesis was documented by chronic symptoms (≥ 6 months of nausea, vomiting, and early satiety) with a delayed solid phase gastric emptying scan. Pts were sent a questionnaire which collected demographics, employment status, work and daily activities, and medication use. Utilization of health care resources, including physician visits, diagnostic testing, ER visits, and hospital admissions was also assessed. A reminder postcard was sent to all Pts at 2 weeks, and non-responders were sent an identical survey 2 weeks later. All responses were anonymous; no incentives were provided. Descriptive statistics were computed using Microsoft Excel XP (2003).

**Results:** Of 491 eligible Pts, 100 questionnaires were unable to be completed (incorrect/outdated address (n = 72); returned but not answered (n = 10); Pts were deceased (n = 18)). Of the remaining 391 questionnaires, 228 were completed (58.3%). The mean age was 49.6 (range 19–86), 77.2% were female, and 88.2% were Caucasian. 68.9% of respondents had entered or completed (58.3%). The mean age was 49.6 (range 19–86), 77.2% were female, and 88.2% were Caucasian. 68.9% of respondents had entered or completed college.

58.7% of Pts had seen their family practitioner/internist in the previous 12 months while 21.5% required 5 or more visits to their internist during the same time period. 62.3% of Pts had seen a gastroenterologist in the previous 12 months, while 15.8% required 5 or more visits to a gastroenterologist. 53.9% of patients reported that they required a visit to the emergency room for treatment of their GP, while 49.6% had been hospitalized due to GP. 20.2% of patients required total parental nutrition for their condition at some point, while 15.8% had been on peripheral parenteral nutrition, and 18.4% had required a feeding tube.

**Conclusions:** This is the first study to measure health care utilization in patients with GP. Patients with GP experience frequent office visits, emergency room treatments and hospitalizations; in addition, one-fifth report using supplemental nutritional support of some kind. This data highlights the substantial consumption of health care resources by patients who suffer from this chronic disorder. Future treatments will need to focus on ways to reduce health care resource utilization in gastroparetic patients.

**Phloroglucinol (Spasfon) in Irritable Bowel Syndrome**

Wasim Jafri, FRCP,* Javed Yakoob, Ph.D., Sajjad Hussain, M.B.B.S., Nadim Jafri, M.B.B.S., Muhammad Islam, M.S.C Medicine, Aga Khan University Hospital, Karachi, Sind, Pakistan.

**Purpose:** To determine the efficacy and tolerability of phloroglucinol (Spasfon), an antispasmodic agent in the treatment of Irritable Bowel Syndrome (IBS).

**Methods:** An open label (quasi interventional) study. One hundred patients coming to the gastroenterology clinics of Aga Khan University Hospital with IBS as defined by the Rome II criteria were enrolled between February 2004 and September 2004 to participate in the trial and were treated as outpatients. Spasfon 50 mg orally three times daily was given for two months. Symptoms were assessed before and during treatment using a questionnaire.

**Results:** One hundred patients were enrolled in the study. Of them 61% (61/100) were males and 39% (39/100) were females. Their mean age was 41 ± 14 years. Sixty-eight patients completed the study and 32 dropped out. On Spasfon treatment there was an overall statistically significant improvement in abdominal pain p < 0.001, frequency of stool per day p < 0.001, urgency p < 0.001, passage of mucus per rectum p < 0.001, sense of incomplete defecation p = 0.001 and bloating p = 0.001. However, no response was seen in the feature of straining in both genders p = 0.676. The difference in response to treatment according to gender separately showed statistically significant improvement in the sense of incomplete defecation in females alone with p = 0.003.

**Conclusions:** Spasfon in a dose of 50 mg three times daily is effective and well tolerated by the IBS patients. It relieves most of the symptoms of IBS.

**Bloating: Prevalence and Risk Factors in a Community Sample**

Ashok K. Tuteja, M.D., Nicholas J. Talley, M.D., Sandra K. Joos, Ph.D., David H. Hickam, M.D.* Gastroenterology, VA Medical Center & University of Utah, Salt Lake City, UT; Gastroenterology, Mayo Clinic, Rochester, MN and Internal Medicine, V.A. Medical Center and Oregon Health & Science University, Portland, OR.

**Purpose:** Abdominal bloating is frequently experienced by patients with irritable bowel syndrome (IBS). However, bloating is not a part of generally accepted case definitions (such as the Rome Criteria), and there is a paucity of data examining the prevalence of bloating in other functional bowel disorders. We performed a cross-sectional study in a community sample of adults to determine the prevalence of bloating in subjects with IBS, diarrhea, constipation and dyspepsia. We also evaluated the association between personal and environmental features and bloating and the impact of bloating on quality of life (QOL).

**Methods:** 1069 employees (age range 24 to 77 years) of a single integrated health care system were mailed a validated questionnaire inquiring about their upper and lower gastrointestinal symptoms, including whether they often feel bloated and actually observe abdominal swelling (Bowel Disease Questionnaire). QOL was evaluated using the SF 36 questionnaire. Rome I criteria were used to define IBS, constipation, diarrhea and dyspepsia.

**Results:** 723 subjects (response rate 72%) returned the survey. Bloating was reported by 149 (21%) of subjects. More females than males reported bloating (OR 1.52, CI 1.04 – 2.23, p = 0.03); after controlling for age this difference was not significant. With increasing age fewer subjects reported bloating (OR = 0.98; 0.96 – 1.00; p = 0.03), and this difference persisted after controlling for gender. Nine percent of subjects met criteria for IBS, 19.4% for constipation, and 10.9% for diarrhea. Symptoms of dyspepsia were reported by 14.7% (6.2% ulcer-like, and 6.1% dysmotility-like dyspepsia). Sixty-four percent of subjects with IBS, 42% with constipation, 35% with diarrhea, 42% with ulcer-like and 71% with dysmotility-like dyspepsia reported symptoms of bloating (all p ≤ 0.01, compared to subjects without one of these disorders). Bloating was not associated with marital status, education, smoking, alcohol, acetaminophen or aspirin use (all p ≥ 0.07). Subjects with bloating had lower scores on all QOL subscales of the SF 36 (P ≤ 0.05).

**Conclusions:** Bloating is a common symptom in working-age persons and is associated with decreased QOL. While bloating is more common among subjects with IBS and dysmotility-like dyspepsia, it does not discriminate well between these and other functional bowel disorders.
### 912

**Translation and Validation of a Japanese Version of the Irritable Bowel Syndrome-Quality of Life Measure (IBS-QOL-J)**

Motoryori Kanazawa, M.D., Ph.D., Douglas A. Drossman, M.D., Masase Shinozaki, M.S., Yasushi Sagami, M.D., Ph.D., Yuka Endo, M.D., Olafar S. Palsson, PsyD, Michio Hongo, M.D., Ph.D., William E. Whitehead, Ph.D., Shin Fukudo, M.D., Ph.D. – Department of Behavioral Medicine, Tohoku University School of Graduate Medicine, Sendai, Japan; Center for Functional GI & Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill, NC; Department of Psychosomatic Medicine, Tohoku University Hospital, Sendai, Japan and Department of Comprehensive Medicine, Tohoku University Hospital, Sendai, Japan.

**Purpose:** To compare quality of life (QOL) for patients with irritable bowel syndrome (IBS) between the U.S. and Japan, it is indispensable to develop common instruments. The IBS-QOL (Dig Dis Sci 1998; 43: 400–11), which is widely used in Western countries, was translated into Japanese as there has been a lack of Japanese disease-specific QOL measures for IBS.

**Methods:** The original 34 items of the IBS-QOL were translated from English into Japanese through two independent forward translations, resolution, back translation, and resolution of differences. Forty nine patients who had GI symptoms but did not have any organic diseases (including 30 IBS patients diagnosed by Rome II criteria) were recruited from Tohoku University Hospital in Sendai, Japan and completed the IBS-QOL-J concomitant with the IBS severity index (IBSSI; Aliment Pharmacol Ther 1997; 11: 395–402) twice within 14 days.

**Results:** The IBS-QOL-J demonstrated high internal consistency (Cronbach’s alpha; 0.96) and high reproducibility (intraclass correlation coefficient; 0.92, p < 0.001). Convergent analyses confirmed that the score of IBS-QOL-J was significantly correlated with overall severity of IBS symptoms on the IBSSI (p < 0.05) and with the individual items on the IBSSI that assess interference with life in general (r = 0.47, p < 0.01) and dissatisfaction with bowel habits (r = 0.32, p < 0.05). Twelve patients who had consulted physicians for their GI symptoms more than 6 times in the past 6 months had significantly lower scores in the IBS-QOL-J than 37 patients who had consulted 6 times or less (59.6 ± 18.9 vs 73.8 ± 19.2, p < 0.05), whereas there was not a significant difference in the severity score of IBS symptoms between both groups (258 ± 117 vs 207 ± 92, p > 0.10). Age, sex, education or marital status did not affect the measure.

**Conclusions:** The IBS-QOL-J is a reliable instrument to assess the disease-specific QOL for IBS. Considering cross-cultural comparison, this measure is likely to be a valuable tool to investigate the QOL in Japanese patients with IBS.

### 913

**Comparison of Non-Ulcer Dyspepsia with H. pylori and H. pylori Infection in an Urban Cohort in Pakistan**

Javed Yakoob, Ph.D.,* Wasim Jafri, F.A.C.G., Shahab Abid, F.C.P.S., Zaigham Abbas, F.A.C.G., Muhammad Islam, M.Sc., Saeed Hamid, F.A.C.G., Hasmain Ali Shah, F.A.C.G., Zubair Ahmed, FCPS Section of Gastroenterology, Department of Medicine, Aga Khan University Hospital, Karachi, Pakistan and Department of Pathology, Aga Khan University Hospital, Karachi, Pakistan.

**Purpose:** To determine the proportion of our patients with dyspepsia associated with and without H. pylori.

**Methods:** One hundred twenty-four consecutive patients presenting with dyspepsia at first visit to gastroenterology outpatient of Aga Khan Hospital from January 2005- April 2005 were enrolled. Clinical symptoms at presentation were noted. All patients were endoscoped and antral biopsy specimens collected for the rapid urease test and histopathology. Dyspepsia was defined as intermittent or persistent discomfort in the upper abdomen or other symptoms related to the upper gastrointestinal tract. A diagnosis of H. pylori infection was made when either rapid urease test or histology was positive. A diagnosis of nonulcer dyspepsia associated with H. pylori was made when intermittent or persistent symptoms related to the upper gastrointestinal tract were associated with normal endoscopy and positive rapid urease or histopathology.

**Results:** These are the preliminary results of an ongoing study. A total of 124 patients, 82 males were studied. Sixty-nine (56%) was H. pylori positive. 49/82 (60%) males and 20/42 (48%) females were H. pylori positive. The major presenting symptoms of nonulcer dyspepsia associated with H. pylori and without were abdominal pain (discomfort 45/69 (65%) and bloating 17/69 (25%) compared to 38/55 (69%) and 9/55 (16%) with odds ratio (OR) 0.8 95% CI (0.4 – 1.8) and OR 1.7 95% CI (0.7 – 4.1) respectively. Endoscopy revealed minimal changes in nonulcer dyspepsia associated with H. pylori positive 21/33 (64%) compared to 12/33 (36%) with H. pylori infection. In 2/30 (7%) moderate antral gastritis was revealed in nonulcer dyspepsia with H. pylori compared to 28/30 (93%) with H. pylori infection alone. On histopathology, mildly active H. pylori associated antral gastritis was noted in 20/23 (87%) in nonulcer dyspepsia with H. pylori and 3/23 (13%) with H. pylori infection while moderately active H. pylori associated antral gastritis in 4/46 (9%) with nonulcer dyspepsia with H. pylori compared to 42/46 (91%) with H. pylori infection.

**Conclusions:** The presenting symptoms of nonulcer dyspepsia with and without H. pylori infection are similar. There are minimal endoscopic and histopathology changes in nonulcer dyspepsia associated with H. pylori compared to H. pylori related diseases.

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**Abstracts**
stools (11.2%). In order to reduce confounding with possible irritable bowel syndrome, we excluded subjects whose main complaint was abdominal pain (12.2%). Response to Tx was defined by an increase of at least 1 complete spontaneous bowel movement (CSBM)/week during the 12-week Tx period.

**Results:** Response to T 6 mg bid was superior to P for patients who complained of any one of the following main constipation Sx during the preceding 6 months: abdominal bloating, straining, feeling of incomplete evacuation, infrequent defecation or hard stool. Tx differences ranged from 13.6% to 22%. Statistical significance was reached for each of the main complaints (table). In addition, regardless of main Sx complaint, 45.5% of pts reported improvement with T, while only 28.0% reported improvement with P (difference of 17.5%, p < 0.0001)

**Conclusions:** T 6 mg bid was superior to P in pts with Sx of CC regardless of their main complaint and demonstrated improvement in each group of pts with a primary complaint of hard stool, bloating, straining, feeling of incomplete evacuation and infrequent defecation.

### Effect of Tegaserod on Colonic Motility

**Subodh Varshney, M.S.,* Gaurav Jain, M.S., Vinod Narkhede, M.B.B.S., Rashmi Jaiswal, M.B.B.S., Swarna Tiwari, B.Sc., Raman Sharma, M.B.B.S., Abhishek Sharma, M.S., Sandesh Sharma, M.S. GI Surgery, Bhopal Memorial Hospital and Research Centre., Bhopal, MP, India.**

**Purpose:** A recent meta-analysis has shown that Tegaserod (selective 5HT4 receptor partial agonist), is a safe and effective treatment for IBS patients with constipation. We studied the objective effect of Tegaserod on colonic motility by colonic manometry.

**Methods:** Eight patients (4 men) with mean age 45 years (range 36 to 58 years) diagnosed to have constipation predominant IBS were studied following informed consent. All patients had normal USG abdomen and pelvis, haemogram, blood biochemistry, thyroid functions and colonoscopy. Following patients were excluded:

1. Age < 18 years or > 60 years.
2. Previous laparotomy or therapeutic laparoscopy.
3. Patient with diabetes mellitus, hypothyroidism, connective tissue disorder or drugs affecting bowel motility.

Symptoms of all patients were recorded. All had colonic manometry as baseline (without medication) and repeat colonic manometry [after Tegaserod 6 mg twice a day for 6 weeks (Bisnorm, Solaris Pharma, Mumbai, India)] using water perfusion static colonic manometry with 8 port perfusion catheter and Redtech GiPC windows software (Redtech, California, USA).

**Results:** The number of colonic contraction > 10 mm of Hg of right and left colon, with (Tegaserod) or without (baseline) drug are shown in Table 1. The symptom score before and after Tegaserod is shown in Table 2.

**Table 1.** Suggests Number of Segmental Colonic Contractions, > 10 mm Hg of Right and Left Colon Before and After Tegaserod

<table>
<thead>
<tr>
<th>Case</th>
<th>Baseline (No. of contractions in 2 hrs)</th>
<th>Study Group (No. of contractions in 2 hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R colon</td>
<td>L colon</td>
</tr>
<tr>
<td>1</td>
<td>120</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>64</td>
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<td>7</td>
<td>56</td>
<td>72</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
<td>62</td>
</tr>
<tr>
<td>Mean(SB)</td>
<td>57(36)</td>
<td>58(26)</td>
</tr>
</tbody>
</table>

*p < 0.0036*  
*p < 0.044*  

**Conclusions:** This investigation provides definitive support for the efficacy of biofeedback for PFD constipation.

### Increased Prevalence of Functional Bowel Disorders in First Degree Relatives of IBD Patients

Lisbeth Selby, M.D., Houssam Mardini, M.D., M.P.H., Sasha Bjork, B.A., Willem de Villiers, M.D., Ph.D.* Digestive Diseases and Nutrition, University of Kentucky, Lexington, KY.
Purpose: There is recent evidence that inflammatory bowel disease (IBD) and functional bowel disorders, such as irritable bowel syndrome (IBS), may have a similar etiopathogenesis. Each is known to show family clustering. But, clustering of both diseases in families has not been studied. Anecdotally, we evaluate many relatives of IBD patients for troubling GI symptoms but rarely diagnose them with IBD. The main aim of our study was to define the prevalence of IBS and the related disorder, functional diarrhea (FD), in first degree relatives of IBD (FDR-IBD) patients versus that in general medical controls (GMC).

Methods: We designed a Rome II-based, self-administered survey for adult FDR-IBD and GMC. We also queried: demographics, current smoking status, relationship to IBD patient, age at time of relatives’ diagnoses, and questions on the duration and nature of contact with the relative since IBD diagnosis. To obscure the study aim, many other symptoms were queried. Subjects were categorized, based on Rome II criteria, as either IBS/FD+ or IBS/FD-.

Non-parametric tests (chi-square and Mann-Whitney U) and logistic regression models were used to assess the associations, estimate the odd ratio (OR) and 95% confidence intervals (CI) of these associations and control for potential confounders.

Results: 92 surveys were evaluated, 42 from FDR-IBD and 50 from GMC. The median age of FDR-IBD was 28. The median age of GMC was 47. The FDR-IBD were 43% male; GMC were 32% male (ns). The prevalence of either IBS or FD in the FDR-IBD was significantly higher than that in the GMC (17/42 v. 10/50; p = 0.032). Alternatively stated, the OR of a FDR-IBD having IBS or FD was 2.7 (CI = 1.08–6.75). Surprisingly, only 30% of such subjects are under the care of a physician.

Of all IBS/FD+ subjects, the FDR-IBD were more likely to have increased stool frequency (>3/day) than GMC (10/17 v 1/10; p = 0.012) and more likely to have mushy loose stools (13/17 v 4/10; OR 3.2).

Also, in IBS/FD+ group, FDR-IBD were more likely to have urinary tract symptoms (13/17 v 4/10; p = 0.04; OR 1.9; CI = 1.17–4.0). Lastly, FDR-IBD who were IBS/FD+ were younger at the time of their relative’s diagnosis with IBD compared to FDR-IBD who were IBS/FD-, regardless of the current age of the respondent (24 yr v 42; p = 0.01).

Conclusions: Our findings are intriguing but do not establish a genetic link between IBD and IBS/FD. Further work will address the possibility that functional bowel disorders in FDR-IBD are learned responses.

A Prospective, Multicenter US Trial To Determine the Yield of Routine Diagnostic Testing in Suspected Diarrhea-Predominant and Alternating IBS Patients

Dong H. Lee, M.D., Allan H. Andrews, M.D., Richard Dohan, M.D., Cecilia H. Kim, M.P.H., Brooks D. Cash, M.D., William D. Chey, M.D.*, Gastroenterology, National Naval Medical Center, Bethesda, MD; Gastroenterology, Walter Reed Army Medical Center, Northwest, DC; Gastroenterology, Naval Medical Center Portsmouth, Portsmouth, VA and Gastroenterology, University of Michigan, Ann Arbor, MI.

Purpose: We sought to evaluate the yield of routine diagnostic testing for organic diseases which might provide an explanation for GI symptoms in patients with suspected IBS.

Methods: Previously unevaluated patients fulfilling the Rome II criteria for IBS were enrolled into this prospective trial from 3 US sites. Patients with constipation-predominant IBS were not included in this trial. Over the course of 6–8 weeks, patients underwent testing with CBC, comprehensive metabolic profile, thyroid function testing, serological testing for celiac sprue, stool studies if appropriate, and colonoscopy with biopsies. Patients with serological evidence of celiac sprue underwent confirmatory testing with EGD and small bowel biopsy.

Results: To date, 100 suspected IBS pts [58 females, mean age 39 (18–80)] have enrolled in this ongoing study. Overall, 19 pts had abnormal test results. 10 pts were mildly anemic. In no pt was the anemia attributed to GI source and in 8 reproductive age females, the anemia was felt secondary to menstruation. Of the remaining 9 pts with abnormal testing, 5 had abnormal TSH levels which were not felt to explain the pts IBS symptoms (3 low, mean TSH = 0.35 and 2 high, mean TSH = 6.9), 2 had biopsy proven celiac disease, 1 had ulcerative proctitis, and 1 developed new onset ascites several months after initial evaluation and was diagnosed with an omental mucinous tumor.

Conclusions: Routine diagnostic testing uncovered abnormalities in 19% of pts with suspected IBS. However, abnormalities felt to possibly explain IBS symptoms were found in only 4% of pts. We report the first prospective, multicenter US experience addressing the yield of routine testing for celiac sprue in IBS pts. According to a recent modeling study (Spiegel, Gastro 2004 Jun:126(7):1721–32), the 2% prevalence of celiac sprue we report may justify more widespread serological screening in pts with suspected IBS.

National Survey on Patient Education in Irritable Bowel Syndrome (IBS)

Albena Halpert, M.D., Christine Dalton, P.A.-C., Yuming Hu, Ph.D., Carolyn Morris, Ph.D., Olafur Palsson, Psy.D., Nancy Norton, Douglas Drossman, M.D.*, Center for Digestive Disorders, Boston Medical Center, MA; UNC Center for Functional GI & Motility Disorders, NC and International Foundation for Functional Gastrointestinal Disorders, WI.

Purpose: To identify patients’: (1) Perceptions about IBS; (2) Preferences on the type of information needed; (3) Preferences about educational media; (4) Expectations from health care providers.

Methods: The study consisted of: (1) Questionnaire item generation using patient focus groups to develop the IBS-Patient Education Questionnaire (IBS-PEQ). (2) Cognitive item reduction of items considered important and relevant by IBS patients and (3) Data acquisition. The IBS-PEQ was administered to a national sample of IBS patients. Analysis: Frequencies of the endorsement of items and their ranking (1–3) were obtained. A weight index = frequency of item endorsements, X mean rating per item was calculated to account for the importance of both endorsement and ranking. A higher index indicated greater importance (range 0–3).

Results: 200 outpatients completed the survey, mean age was 45.6 ± 19.8 yrs., with an educational attainment of 14.8 ± 2.8 yrs., and 89.5% were female. Illness duration was 8.9 ± 4.7 years. The most prevalent misconceptions about IBS included (% of subjects agreeing with the statement and% unsure): 1) IBS will develop into colitis (18%, 28%), 2) malnutrition (17%, 24%), and 3) cancer (14%, 29%). IBS patients were interested in learning about (% of subjects choosing an item,% ranking the item in the top 3 preferences, and weight index): 1) foods to avoid (60%, 16.5%, 1.0), 2) causes of IBS (55%, 16%, 1.05), 3) medications (58%, 15.5%, 0.95), 4) coping strategies (56%, 13%, 0.83), and 5) psychological factors related to IBS (55.5%, 15.5%, 0.81). Choice of presentation methods included: 1) M.D. (67.5%), 2) brochures (42%), and 3) newspapers and magazines (40.5%). 80% of patients expected the M.D. to be available via phone or e-mail following a visit, and to provide information about sources of additional information and research studies. The most desired qualities of the physician were the ability to: 1) listen (80%), 2) provide hope (73%), and support (63%).

Conclusions: Despite increasing education about IBS, many patients hold misperceptions about IBS developing into cancer, colitis, or causing malnutrition, and they most often seek information about dietary changes. They expect physicians to be the primary provider of information, to have good communication skills, and to provide hope and support.

Is Small Intestinal Bacterial Overgrowth (SIBO) Really Prevalent in Irritable Bowel Syndrome (IBS)?

Lucinda A. Harris, M.S., M.D., Michael D. Crowell, Ph.D., John K. DiBaise, M.D., Kevin Olden, M.D.*, Division of Gastroenterology & Hepatology, Mayo Clinic – Scottsdale, Scottsdale, AZ and Division of Gastroenterology & Hepatology, University of Southern Alabama, Mobile, AL.
Purpose: IBS, a multifactorial disorder characterized by abdominal pain and altered bowel habits, affects 10–15% of the population. Recently SIBO has been found by some investigators to occur in 78–84% of IBS patients. Controversy exists as to the results of these studies and the actual prevalence of SIBO in patients with IBS. We suspect that the lactulose breath testing overpredicts the true prevalence of SIBO in IBS patients.

Methods: The charts of 182 consecutive patients referred for glucose hydrogen breath tests (100gm glucose, 2hr observation) for SIBO from March 2004 to April 2005 were reviewed. Charts were reviewed for breath tests results as well as for gastrointestinal symptoms and characteristic symptoms of IBS. Of these, 113 patients (88F, Mean age 58) were identified that met Rome II criteria for IBS. Patients were classified by predominant bowel habit type (A-alternators, C-constipation, D-Diarrhea).

Results: Results of the breath test by IBS bowel type, % of male and female patients and range and median are presented below.

<table>
<thead>
<tr>
<th></th>
<th>% of Male</th>
<th>% of Female</th>
<th>% of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of Total</td>
<td>12 (10.6%)</td>
<td>101 (84.9%)</td>
<td>113</td>
</tr>
<tr>
<td>% of A</td>
<td>1 (7.1%)</td>
<td>13 (92.9%)</td>
<td>14</td>
</tr>
<tr>
<td>% of C</td>
<td>6 (16.7%)</td>
<td>30 (83.3%)</td>
<td>36</td>
</tr>
<tr>
<td>% of D</td>
<td>5 (8.1%)</td>
<td>58 (91.0%)</td>
<td>63</td>
</tr>
<tr>
<td>% of Males</td>
<td>2 (8.0%)</td>
<td>23 (92.0%)</td>
<td>25</td>
</tr>
<tr>
<td>% of Females</td>
<td>10 (11.4%)</td>
<td>78 (88.6%)</td>
<td>88</td>
</tr>
</tbody>
</table>

Median range 37–73, Median 65.5.

Conclusions: Only 11% of our patients had positive glucose hydrogen breath tests. Although differences in the two breath test techniques (lactulose and glucose) exist, it seems highly unlikely that if SIBO were truly involved in IBS as a primary etiologic factor that the two techniques would yield such discrepant results.

Sensitivity of glucose hydrogen breath testing for SIBO has been calculated at 75%, whereas as sensitivity of lactulose for SIBO with scintigraphy to document the accuracy of the “double peak” phenomenon was estimated at 39% (17% without scintigraphy). Our results confirm that other etiologic factors are involved in the pathophysiology of IBS.

REFERENCES

921

Probiotics in Irritable Bowel Syndrome (IBS): Meta-Analysis
Filippo Cremonini, M.D., M.Sc., Noel R. Fajardo, M.D., Nicholas Talley, M.D., Ph.D.* Clinical Enteric Neuroscience, Translational and Epidemiological Research (C.E.N.T.E.R.) Group, Mayo Clinic and Foundation, Rochester, MN.

Purpose: Probiotic supplementation on IBS symptoms has been proposed and tested in several single-center, relatively small trials. However, efficacy of probiotics in IBS is still unclear and some suggest a potential benefit on the individual symptom of bloating.

Methods: Search of the electronic databases MedLine and EMBASE (1966–2005), a hand-search from retrieved papers’ cross-references. Therapeutic responses were defined as 1. binomial improvement according to study definition, 2. improvement of bloating scores, calculated for the individual studies as delta (Probiotic-Placebo) of the percent reduction from baseline bloating scores at the end of treatment periods. A random-effects model was used to pool the binomial results and the number needed to treat (NNT) for study-defined improvement was calculated.

Results: Seven randomized controlled studies were eligible. Three studies used combinations of probiotics, and 4 studies used single strain preparations. There was significant heterogeneity across studies (p < 0.005), although inclusion criteria and probiotic doses were comparable. The pooled odds ratio for study-defined improvement (5 studies eligible) was 2.99 (95% CI 0.83–10.74, upper plot). The NNT was 4 (95% CI 3–7). Effect of probiotics on bloating scores varied widely across studies (5 studies eligible, range 13% worse to 48% better, lower plot).

Conclusions: The benefit from probiotics on IBS improvement and on the individual symptom of bloating is modest. Further larger trials may be needed to show a definite effect.

922

Why Do Irritable Bowel Syndrome Patients Take Multiple Drugs and What Are the Associated Costs?

Purpose: Most IBS patients use multiple medications and supplements. Previous studies have not assessed the reasons, or its relationship to symptom severity or symptom relief. Aims were to assess (1) whether polypharmacy is explained by symptom severity or poor treatment response, (2) the incremental cost of polypharmacy, and (3) health care costs attributable to prescription and OTC drugs, herbs, and dietary supplements.

Methods: In 2001–2002, patients in a large health maintenance organization diagnosed with IBS, constipation, diarrhea, or abdominal pain at a clinic.
visit were invited within two weeks to complete questionnaires and 1,665 (59%) did so (mean age 53 years, 73% females). Completers were sent follow-up questionnaires 6 months later. Physician and hospital costs were calculated from automated medical records for this 6-month period, and out of pocket costs estimated from patient questionnaires. IBS severity at enrollment was assessed by a validated questionnaire (APT 1997:11:395–402), and satisfactory relief was assessed at follow-up. Analysis was limited to 706 patients who met Rome II IBS criteria and had no known organic symptom cause.

**Results:** (1) Number of drugs taken was positively related to IBS symptom severity (regression analysis: beta = .201, p < .001) and negatively related to treatment satisfaction (beta = −.140, p = .001), together accounting for 7% of the variance. (2) 64.1% of IBS patients used 2 or more OTCs, herbs, or dietary supplements. Mean 6-month costs of drugs increased linearly, from $128 if taking 1 medication to $720 if taking 8+, and number of drugs was positively correlated with total cost of care for IBS (rho = 0.476, p < .001). (3) Total 6-month health care costs including out of pocket expenses averaged $3,816. Mean expenses for IBS were $620, including $308 for hospital and physician charges, $104 for prescriptions, $71 for OTCs, $9 for herbal remedies, $57 for dietary supplements, and $69 for complementary/alternative treatments.

**Conclusions:** (1) The number of drugs taken by IBS patients is only in small part explained by IBS severity or unsatisfactory treatment response. (2) Number of drugs taken correlates with total health care costs for IBS. (3) Drugs and diet supplements account for 38.9% of health care costs for IBS, and OTCs, herbs, and dietary supplements make up 56.8% of these costs.

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**Patient Characteristics Determining Clinical Diagnosis of Constipation-Predominant IBS (IBS-C) vs. Chronic Constipation (CC)**

Olafur S. Palsson, PsyD, Rona L. Levy, Ph.D., Andrew D. Feld, M.D., Michael Von Korff, Sc.D., Marsha J. Turner, M.S., William E. Whitehead, Ph.D.* Dept. of Medicine, University of North Carolina, Chapel Hill, NC; University of Washington, Seattle, WA and Group Health Cooperative, Seattle, WA.

**Purpose:** Our prior work (Gastroenterol 2004;126(4) Suppl 2-A:606) showed poor agreement between the Rome criteria and clinical diagnosis of IBS-C and CC. Physicians likely take other patient characteristics than diagnostic criteria into account in assigning diagnoses. This study aimed to identify the patient characteristics that might influence diagnostic decisions and differ between ROME II IBS-C patients diagnosed IBS vs. CC.

**Methods:** 1,658 patients (73% female, mean age 53 years) given clinical diagnoses of IBS, abdominal pain, functional constipation or diarrhea at a visit to health maintenance organization doctors completed mailed questionnaires following their visit (59% response rate). Questionnaires included the Rome Diagnostic Questionnaire, the IBS Severity Scale (IBSS), additionnaires following their visit (59% response rate). Questionnaires included the Rome Diagnostic Questionnaire, the IBS Severity Scale (IBSS), additional constipation severity questions, the Brief Symptom Inventory-18, the Recent Physical Symptoms Inventory (RPSQ) and demographic questions. Healthcare utilization for 1 year prior to the index visit was obtained from the HMO’s electronic record.

**Results:** 255 patients met Rome II IBS-C criteria, of which 109 were clinically diagnosed IBS and 83 diagnosed with CC. Clinically diagnosed IBS patients had higher IBS pain severity (4.89 ± 3.1 vs. 3.65 ± 3.4, p = .008) compared to CC patients, but the groups did not differ in pain frequency, distention severity, dissatisfaction with bowel habits or life interference from bowel problems. Clinical IBS patients, compared to CC, were also less likely to report constant severe constipation in the past 6 months (40% vs. 67%, p < .0001), had more non-GI physical symptoms on the RPSQ (12.2 ± 0.5 vs. 9.0 ± 0.6, p = .003), and were more likely to be female (66% vs. 70%, p = .003) and younger (48.8 ± 1.4 vs. 54.1 ± 1.8, p = .02). Race, education levels, healthcare utilization in the past year and general psychological distress were not different between the groups. All variables distinguishing the groups except age had additive power in predicting diagnostic assignment (binary logistic regression analysis) and collectively explained 25% of the variance (Nagelkerke $R^2 = .25$).

**Conclusions:** Severity of abdominal pain and constipation, as well as gender, age and the amount of non-gastrointestinal symptoms, influence whether patients presenting with constipation receive a clinical diagnosis of IBS or chronic constipation.

924

**Do Comorbid Dyspepsia and Reflux Symptoms Affect Morbidity, Utilization, and Outcome in Irritable Bowel Syndrome (IBS)?**


**Purpose:** The impact of co-morbid gastroesophageal reflux disease (GERD) or functional dyspepsia (FD) on IBS health care costs and utilization, clinical response or symptom status is largely unknown, and was evaluated as a sub-study in a large survey assessing usual medical care for IBS (Aliment Pharmacol Ther 2004;20:1305–15).

**Methods:** Patients given a clinical diagnosis of IBS, abdominal pain, constipation, or diarrhea during a health maintenance organization (HMO) visit completed mail questionnaires within 2 weeks, including the ROME II questionnaires, IBS-QOL, IBS Severity Index and ratings of satisfaction with medical care, and a satisfactory relief of bowel symptoms question (yes/no) at 6-month follow-up. All health care visits were obtained from the HMO’s electronic records for 1 year after the index visit, and charts reviewed by trained abstractors.

**Results:** 1658 patients (ages 18–72, 73% female) completed baseline questionnaires, 73% also completed follow-up, and 87% of the patient records were manually reviewed. Data analyses included all 527 patients who met Rome II IBS criteria, had complete data, and had no organic symptom cause in charts. Patients were classified either IBS-only (n = 201), IBS+GERD (n = 73) if they had current GERD diagnosis in their record, or IBS+FD (n = 255) if they reported upper GI pain often on the ROME II questionnaire and had no GERD diagnosis. Group comparisons are presented in the table (ANOVA and Fischer’s exact tests).

<table>
<thead>
<tr>
<th></th>
<th>IBS-Only</th>
<th>IBS+FD</th>
<th>IBS+GERD</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS Severity Score</td>
<td>208.4 (7.5)</td>
<td>272.8 (6.9)**</td>
<td>250.1 (12.2)**</td>
</tr>
<tr>
<td>IBS-QOL Score</td>
<td>79.2 (1.4)</td>
<td>68.9 (1.6)**</td>
<td>73.8 (2.9)</td>
</tr>
<tr>
<td>6 mo Satisfactory Relief (%) patients</td>
<td>63</td>
<td>57</td>
<td>48*</td>
</tr>
<tr>
<td>Satisfaction with care (0–100%)</td>
<td>69.0 (1.7)</td>
<td>64.7 (1.8)</td>
<td>62.0 (3.2)*</td>
</tr>
<tr>
<td>Total annual outpatient visits</td>
<td>9.8 (0.5)</td>
<td>11.5 (0.8)</td>
<td>10.1 (1.0)</td>
</tr>
<tr>
<td>Annual GI outpatient visits</td>
<td>1.6 (0.1)</td>
<td>2.0 (0.1)</td>
<td>1.4 (0.1)</td>
</tr>
</tbody>
</table>

significance of difference from IBS-only group *p < .05, **p < .01, ***p < .0001; S.E.M. in parentheses.

**Conclusions:** Compared to IBS-only, IBS+FD and IBS+GERD patients have more severe IBS symptoms, IBS+FD have poorer health-related quality of life, and IBS+GERD are less likely to be satisfied with care or to have satisfactory relief after 6 months. Healthcare utilization is not significantly affected by the co-presence of upper GI symptoms in IBS.

925

**Which Medications and Food Supplements Are Associated with Bloating in Patients with Functional Bowel Disorders?**

Olafur S. Palsson, PsyD, Rona L. Levy, Ph.D., Andrew D. Feld, M.D., Michael Von Korff, Sc.D., Marsha J. Turner, M.S., William E. Whitehead, Ph.D.* Medicine, University of North Carolina, Chapel Hill, NC; University of Washington, Seattle, WA and Group Health Cooperative, Seattle, WA.

**Purpose:** To identify the patient characteristics that might influence diagnostic decisions and differ between ROME II IBS-C and CC. Physicians likely take other patient characteristics than diagnostic criteria into account in assigning diagnoses. This study aimed to identify the patient characteristics that might influence diagnostic decisions and differ between ROME II IBS-C patients diagnosed IBS vs. CC.

**Methods:** 1,658 patients (73% female, mean age 53 years) given clinical diagnoses of IBS, abdominal pain, functional constipation or diarrhea at a visit to health maintenance organization doctors completed mailed questionnaires following their visit (59% response rate). Questionnaires included the Rome Diagnostic Questionnaire, the IBS Severity Score (IBSS), additionnaires following their visit (59% response rate). Questionnaires included the Rome Diagnostic Questionnaire, the IBS Severity Score (IBSS), additional constipation severity questions, the Brief Symptom Inventory-18, the Recent Physical Symptoms Inventory (RPSQ) and demographic questions. Healthcare utilization for 1 year prior to the index visit was obtained from the HMO’s electronic record.

**Results:** 255 patients met Rome II IBS-C criteria, of which 109 were clinically diagnosed IBS and 83 diagnosed with CC. Clinically diagnosed IBS patients had higher IBS pain severity (4.89 ± 3.1 vs. 3.65 ± 3.4, p = .008) compared to CC patients, but the groups did not differ in pain frequency, distention severity, dissatisfaction with bowel habits or life interference from bowel problems. Clinical IBS patients, compared to CC, were also less likely to report constant severe constipation in the past 6 months (40% vs. 67%, p < .0001), had more non-GI physical symptoms on the RPSQ (12.2 ± 0.5 vs. 9.0 ± 0.6, p = .003), and were more likely to be female (66% vs. 70%, p = .003) and younger (48.8 ± 1.4 vs. 54.1 ± 1.8, p = .02). Race, education levels, healthcare utilization in the past year and general psychological distress were not different between the groups. All variables distinguishing the groups except age had additive power in predicting diagnostic assignment (binary logistic regression analysis) and collectively explained 25% of the variance (Nagelkerke $R^2 = .25$).

**Conclusions:** Severity of abdominal pain and constipation, as well as gender, age and the amount of non-gastrointestinal symptoms, influence whether patients presenting with constipation receive a clinical diagnosis of IBS or chronic constipation.
**Purpose:** Abdominal distention accompanied by a subjective sensation of fullness or bloating adversely affects quality of life, and is often found to be the most distressing symptom of irritable bowel syndrome (IBS) (Am J Gastroenterol 1999;94:1320–6).

**Aims:** Identify which of 22 types of drugs and food supplements are associated with bloating.

**Methods:** In a large health maintenance organization (HMO), patients with clinical diagnoses of IBS, constipation, diarrhea, or abdominal pain at a clinic visit were invited within 2 weeks to complete questionnaires, and 1,665 (59%) did so (average age 53 years, 73% females). Patients who completed the questionnaires were requested to complete follow-up questionnaires 6 months later. Chart reviews were used to identify patients with organic disease explanations for functional bowel symptoms. This was an observational study of usual medical care, and treatments varied between patients. Patient questionnaires were used to identify which prescription and non-prescription medications and food supplements patients were taking. Patients rated the severity of abdominal distention over the last 10 days on a numeric rating scale (0–100). Nonparametric correlations were used to identify which of 22 drugs and food supplements were significantly (p < .01) correlated with distention, and these were entered into a linear regression analysis. Analyses were limited to 1,041 patients who had a functional bowel disorder, did not have malabsorption, inflammatory bowel disease, or gastrointestinal malignancy, and were not pregnant.

**Results:** (1) 9 types of drugs or supplements were significantly correlated with abdominal distention: fiber, bran, laxatives, glycerin suppositories, antispasmodics, antidepressants, gas-relief meds, and over the counter analgesics. Gas-relief medications, antispasmodics and pain-relievers were likely taken for the treatment of symptoms associated with distention and were consequently not entered into the regression model. (2) Regression analysis showed that 3 categories accounted for an adjusted R^2 of 4.2%: glycerin suppositories, bran and fiber.

**Conclusions:** This study shows that fiber, bran and glycerin suppositories are associated with increased abdominal distention. Laxative use was not an independent predictor (p = .08) because it was correlated with use of bran, fiber and suppositories.

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**926**

**IBS-C Patients Have Greater Treatment Satisfaction with Initial and Repeated Use of Tegaserod (T)**

M. C. Reilly, M.A.,* A. Bracco, Pharm.D., C. R. McBurney, Pharm.D.

Margaret Reilly Associates Inc, New York, NY and Novartis Pharma AG, Basel, Switzerland.

**Purpose:** To assess the impact of T in patients with irritable bowel syndrome with constipation (IBS-C) on treatment satisfaction indices.

**Methods:** Women (≥65 years) with IBS-C (Rome II) were randomized to T 6 mg bid or placebo in a double-blind, placebo-controlled multicenter study. Women underwent a 2-week baseline, and two 4-week double-blind Tx periods (P1, then re-randomized to P2), separated by a Tx-free interval. A nine-item questionnaire assessed patients’ Tx expectations, satisfaction with relief of abdominal pain/discomfort, constipation, and other Sx, greater level of expectations being met or exceeded, greater relief of Sx with study medication vs previous medication use, greater future utilization of study medication, and more recommendations of T to others with IBS.

**Conclusions:** This study demonstrated that patients are more satisfied with T as a treatment for IBS-C compared with placebo.

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**927**

**Patients with Chronic Constipation Who Respond to Tegaserod after 4 Weeks Maintain Symptom Improvement for over 13 Months**

M. Sheteline, M.D.,* M. Dolker, Ph.D., I. Bottoli, M.D., M. Cohard-Radice

Novartis Pharmaceuticals Corp, East Hanover, NJ and Novartis Pharma AG, Basel, Switzerland.

**Purpose:** Tegaserod is approved for the treatment of chronic idiopathic constipation (CC) in both men and women less than 65 years of age. Efficacy in patients with CC has been shown for 12 weeks in large randomized placebo-controlled trials. This study examines efficacy data collected from a long-term (13 month) safety extension study of tegaserod in CC.

**Methods:** In this 13-month, blinded, extension study, symptoms of constipation were assessed monthly for abdominal distension/bloating, bothersomeness of constipation and satisfaction with bowel habits (using a 5-point Likert scale); as well as a composite score for global constipation relief. A responder in the Core trial (12 weeks prior to the 13 month extension) was defined as an average improvement of ≥ one complete spontaneous bowel movement per week during the first 4 weeks of therapy. Patients continued on the same dose of tegaserod at the completion of the core trial into the

---
13 month extension. Data were analyzed using last assessment carried forward to avoid confounding by dropouts with paired t-test of each timepoint against the within-group baseline.

**Results:** After 4 weeks of tegaserod 6 mg bid, 40% of CC patients were responders for the primary efficacy variable. 61% of the 4-week responders completed the extension trial and 88% of this group were responders at the end of the 12-week core efficacy period. After 12 weeks and 13 months, this population continued to manifest improvement in the multiple symptoms of constipation, as well as global measures of bowel habit satisfaction and global constipation relief (Table). This assessment was consistent for patients receiving 2 mg of tegaserod bid. All improvements were statistically significant (p < 0.0001 for all measures) and clinically meaningful (average improvement of 1 point on a 5-point scale).

**Conclusion:** Improvement of 1 point on a 5-point scale).

<table>
<thead>
<tr>
<th>Symptom</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal distension/bloating</td>
<td>111</td>
<td>1.08</td>
<td>0.85</td>
<td>1.09</td>
<td>0.94</td>
<td>1.18</td>
<td>0.94</td>
</tr>
<tr>
<td>Satisfaction with bowel habits</td>
<td>111</td>
<td>1.25</td>
<td>1.19</td>
<td>1.17</td>
<td>1.09</td>
<td>1.28</td>
<td>1.28</td>
</tr>
<tr>
<td>Global relief of constipation</td>
<td>111</td>
<td>1.02</td>
<td>0.89</td>
<td>1.04</td>
<td>1.02</td>
<td>1.06</td>
<td>1.06</td>
</tr>
</tbody>
</table>

*13 months after the 12-week core trial.

**Conclusions:** These results demonstrate the long-term improvement in the symptoms of chronic constipation in patients who respond to tegaserod after 4 weeks.

**928**

Pathologic Findings Are Common during Colonoscopy for Constipation

M. Shethzine, M.D., * D. Lieberman, M.D., N. Mattek, M.P.H., J. Holub, M.P.H., G. Eisen, M.D. Novartis Pharmaceuticals Corp, East Hanover, NJ and Oregon Health and Science University, Portland, OR.

**Purpose:** Constipation is a common medical disorder and affected pts often undergo an increased number of procedures, e.g. colonoscopy. Since pts with constipation have other symptoms in addition to infrequent defecation, including abdominal pain, change in stool form (hard stools), bloating and straining, physicians may be concerned about the possibility of underlying pathology.

**Methods:** To evaluate the risk of pathologic finding in pts with constipation, we evaluated 374,323 colonoscopies performed between 2000–2003 as part of the CORI Program. Of these procedures, 5.8% (21,549) listed constipation as an indication and 2.0% (7,524) classified constipation as the primary/only indication. Data were compared to 46,400 colonoscopies performed in a matched control group of average/routine risk pts and statistical significance approximated (Fishier’s Exact test).

**Results:** Most procedures demonstrated abnormal findings; procedures for constipation revealed hemorrhoids 41.4% (n = 8,919) compared to 30.4% (control population), 29.1% (n = 6,272) and 27.7% (n = 2,086) of procedures for constipation as an indication, or as the primary indication, found a polyp. Multiple polyps were found in 5.8% (n = 1,255) and 4.9% (n = 368) of procedures performed for any constipation and constipation as the primary indication respectively. Polyps (single or multiple) were also present in the control cohort. Other findings significantly increased in colonoscopy performed for any constipation included; solitary ulcer (0.3% vs 0.1% control); fissure/fistula (0.2% vs < 0.1% control); stricture/stenosis (0.3% vs 0.1% control) and tumor (1.2% vs 0.4% control).

**Conclusions:** Procedures performed primarily for constipation or for constipation as an additional reason frequently reveal pathology. Physicians should evaluate pts presenting with infrequent defecation, change in stool form, bloating and straining carefully and consider the possibility of pathology in pts suffering from constipation.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Routine risk only</th>
<th>Any constipation</th>
<th>Constipation primary/only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Findings</td>
<td>49,460</td>
<td>21,549</td>
<td>7,524</td>
</tr>
<tr>
<td>Fissure/fistula</td>
<td>N (%)</td>
<td>N (%)</td>
<td>N (%)</td>
</tr>
<tr>
<td>Hemorrhoids</td>
<td>22 ( &lt; 0.1)</td>
<td>45 (0.2)**</td>
<td>12 (0.2)*</td>
</tr>
<tr>
<td>Solitary ulcer</td>
<td>15,056 (30.4)</td>
<td>8,919 (41.4)**</td>
<td>2,610 (34.7)**</td>
</tr>
<tr>
<td>Stricture/Stenosis</td>
<td>40 (0.1)</td>
<td>69 (0.3)**</td>
<td>19 (0.3)*</td>
</tr>
<tr>
<td>Tumor</td>
<td>32 (0.1)</td>
<td>71 (0.3)**</td>
<td>27 (0.4)**</td>
</tr>
</tbody>
</table>

* < 0.001, ** < 0.0001 (statistically more common in constipation than Routine Risk; approximated with Fishier’s Exact Test).

**929**

Tegaserod Is Superior to Placebo in Normalizing Stool Consistency and in Increasing Frequency of Complete Spontaneous Bowel Movements (CSBMs) in Chronic Constipation (CC) Patients Who Present with Hard Stools

W. D. Chey, M.D., I. Bottoli, M.D., V. Walter, M. Shethzine, M.D., M. Cohard-Radice, M.D. University of Michigan Medical Center, Ann Arbor, MI and Novartis Pharmaceuticals Corp, East Hanover, NJ.

**Purpose:** We investigated how Tegaserod (T), a promotility agent, normalized stool consistency and increased frequency of CSBMs vs placebo (P) in pts with CC with predominant hard stools (HS).

**Methods:** Data from 2 T double-blind, randomized, placebo-controlled pivotal studies were pooled for analysis. Pts with ≥1 spontaneous bowel movement (SBM) and stool consistency (SC) recorded according to the Bristol Stool Form Scale (BSFS: 1 = hard; 7 = watery) at baseline (BL) and on treatment were included in this analysis. SC categories were defined as >50% of recorded SC of SBMs: 1–2 HS, 3–5 normal and 6–7 loose or watery stool (LWS). CSBM response was defined as an average increase of ≥one CSBM/w over wks 1–4 and 1–12. The proportion of patients with normalized SC was compared between treatment groups using logistic regression with treatment, center, study, gender, baseline SC category as factor, treatment subgroup interaction, and complete SBMs at BL as covariate for each week ≥1.

**Results:** 378/775 (48.8%) of pts in the T 6 mg bid group and 377/774 (48.7%) in the P group were classified as having HS at BL. For pts with HS at BL, improvements in SC were greater with T than P. At wk 1, SC had normalized in 41% of those treated with T vs 36% with P (p = 0.23). The proportion of pts achieving normal SC and their differences T vs P increased over time, range 8–15% to reach statistical significance at wk 4 (T 47%, P 36%, p = 0.006). The treatment differences vs P remained significant throughout wk 12 (all p < 0.008) except for wk 11 (p = 0.0502) with 48–56% of T pts normalizing their SC during wks 5–12. In wk 1, 8% of T patients with HS at baseline had LWS vs 2% P. The proportions of patients with LWS tended to become smaller over time (2–3% during w 9–12 in the HS form at BL group across treatments), with the differences between T and P also decreasing. 48% of T group vs 30% P (OR 2.2) were CSBM responders at wks 1–4 (50% vs 34% at w 1–12, OR 2.0, both p < 0.0001). The proportion of responders tended to be higher for those with HS form at BL than for those with other SC at BL.

**Conclusions:** A significantly higher percentage of pts with HS at BL in the T 6 mg bid group normalized their SC as compared with P. As the BSFS correlates with gut transit, this finding supports the prokinetic effect of T. T was superior to P in increasing the number of CSBMs.
Pilot Genetic Association Study of 5-HTT LPR and GNb3 C825T Polymorphisms with Irritable Bowel Syndrome (IBS)

Yuri Saito, M.D., G. Richard Locke, M.D., Janice Zimmerman, Joshua Slusser, Mariza de Andrade, Ph.D., Gloria Petersen, Ph.D., Nicholas Talley, M.D.* Division of Gastroenterology, Mayo Clinic College of Medicine, Rochester, MN; Division of Biostatistics and Division of Epidemiology.

Methods: The study design was a case-control study of 50 outpatients IBS and 53 age-, gender-, and race-matched controls from the Divisions of Gastroenterology and Internal Medicine at a major medical center. Participants completed a symptom questionnaire and donated blood. DNA was extracted from blood leukocytes and genotyped using PCR. t-tests, chi-square or Fisher’s exact tests, and Armitage trend tests were used to compare demographic, symptom, and genotype/allele frequency data between cases and controls.

Results: Demographics of the cases and controls were similar. 82% of cases met Rome II criteria for IBS: 12% constipation-, 46% diarrhea-, 42% mixed-IBS. Genotype and allele frequencies for the 5-HTT LPR and GNb3 C825T polymorphisms are shown in the Table. Genotype and allele frequencies did not differ between overall cases and controls, but allele frequencies differed among subgroups of IBS with controls in this small sample. A sample size of 2362 and 758 will be needed to detect a genetic association for the 5HTT-LPR and GNb3 C825T polymorphisms in a future study.

Conclusions: This pilot study suggests that the polymorphisms may be associated with IBS subtypes but not IBS overall. Large samples sizes will be required in a future case-control study to detect an association between these polymorphisms and IBS.

Which Symptoms Predict Satisfaction with Treatment and Improved Quality of Life in Irritable Bowel Syndrome (IBS)?

Olafur S. Palsson, PsyD, Roma L. Levy, Ph.D., Andrew D. Feld, M.D., Michael Von Korff, Sc.D., Douglas A. Drossman, M.D., William E. Whitehead, Ph.D.* Dept. of Medicine, University of North Carolina, Chapel Hill, NC; University of Washington, Seattle, WA and Group Health Cooperative, Seattle, WA.

Purpose: Satisfactory relief (yes or no) of IBS symptoms in general is commonly used to evaluate the effectiveness of investigational treatments, but limited data are available on how satisfactory relief relates to changes in specific symptoms. The aims of this study were to determine (1) which of 5 specific symptoms on the IBS Severity Scale at baseline predict satisfactory relief at 6 months follow-up, (2) and whether changes in specific symptoms from baseline to follow-up are predictive of satisfactory relief and improvement in quality of life.

Methods: 1,665 health maintenance organization patients with clinical diagnoses of IBS, constipation, diarrhea, or abdominal pain at a clinic visit completed mailed questionnaires within two weeks of their visit and 6 months later. Regression analyses were limited to 529 patients who met Rome II criteria for IBS, did not have a known organic symptom cause, and completed follow-up questionnaires. Patients rated abdominal pain intensity and frequency, severity of abdominal distention, dissatisfaction with bowel habits, and impact of IBS symptoms on everyday activities – and also IBS-QOL – at enrollment and follow-up on validated questionnaires. Satisfactory relief, constipation and diarrhea were measured at follow-up only.

Results: (1) IBS symptoms at enrollment predicted a modest but significant 14.2% of the variance in who reported satisfactory relief at 6 mo. Symptoms
predicting satisfactory relief were lower ratings of pain frequency, dissatisfaction with bowel habits, and impairment of daily activities. (2) Changes in specific symptoms from baseline to 6 mo follow-up accounted for 24.8\% of the variance in satisfaction relief. Reductions in pain intensity and in dissatisfaction with bowel habits were the only significant predictors of satisfaction. Improvements in constipation and diarrhea were independently associated with an increased probability of satisfaction relief. (3) 37.9\% of the variance in IBS-QOL improvement was explained by reductions in abdominal distention (bloating), dissatisfaction with bowel habits, and life interference from symptoms.

**Conclusions:** Satisfactory relief of IBS symptoms depends on improvements in both pain and altered bowel habits, but improved quality of life is more closely tied to improvements in bloating and bowel habits than it is to pain.

**933**

Balsalazide Prevents Acute Radiation-Induced Proctosigmoiditis: Final Results of a Trial in Prostate Cancer Patients

Christopher D. Jahraus, M.D.∗, Doug Bettenhausen, Pharm.D., William H. St Clair, M.D. Ph.D. Dept. of Radiation Oncology, Univ of Alabama at Birmingham, Birmingham, AL; Salix Pharm, Morrisville, NC and Dept of Radiation Med, Univ of Kentucky, Lexington, KY.

**Purpose:** One third of cancer diagnoses in US men are prostate cancer. Many receive pelvic radiotherapy (RT); of these up to 75% will experience acute radiation-induced proctosigmoiditis (RIPS), making it the most significant toxicity associated with pelvic RT. This pilot study examined the effectiveness of balsalazide in preventing RIPS and other toxicities associated with pelvic RT. Pilot preliminary data, though encouraging, did not achieve statistical significance.

**Methods:** In this double-blind, randomized trial, patients undergoing RT for non-metastatic prostate cancer received balsalazide (n = 19) or placebo (n = 17). The primary endpoint was development of clinical proctitis; secondary endpoints were diarrhea, dysuria, fatigue, and weight change. Patients were evaluated for each toxicity and scored according to National Cancer Institute Common Toxicity Criteria v. 2.0. The numeric grade of each toxicity was multiplied by the number of days the patient experienced that grade and summed for the course of treatment to produce the toxicity index. Data were also analyzed by the total number of days patients experienced each toxicity at a numeric grade ≥2.

**Results:** Patients receiving balsalazide had relative reductions in each of the toxicity indices compared with placebo and fewer days with toxicities ≥grade 2, as shown in the table below. [figure1] Weight change and prevalence of diarrhea did not differ significantly between groups.

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Average Index Score</th>
<th>Days of Toxicity ≥Grade 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proctitis</td>
<td>25.7 vs placebo</td>
<td>2.5 vs 18.5</td>
</tr>
<tr>
<td>Dysuria</td>
<td>27.7 vs 41.5</td>
<td>4.4 vs 7.8</td>
</tr>
<tr>
<td>Fatigue</td>
<td>27.8 vs 28.2</td>
<td>1.3 vs 3.9</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>31.5 vs 31.8</td>
<td>6.7 vs 7.8</td>
</tr>
</tbody>
</table>

Conclusions: These results suggest balsalazide is efficacious in preventing multiple toxicities associated with pelvic RT, including RIPS. Patients receiving balsalazide had a significant reduction in the severity of proctosigmoiditis and a marked reduction in the number of days they experienced a toxicity ≥grade 2. Reduction in radiation-associated toxicity may improve quality of life for patients receiving pelvic RT and limit toxicity-associated treatment interruptions, with potential to improve the efficacy of treatment delivered with curative intent.

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Comparison of Rome II Criteria with Patient Reported Bowel Pattern: Results from the IBS Longitudinal Outcomes (ILOS) Study

Jayde Kurland, M.D.,∗, Deborah Caniscoli, M.D., Kristijan H. Kahler, S.M., Homa B. Dastani, Ph.D., Robert Balshaw, Ph.D., Nadia Leskinova, M.S. Gastroenterology, Naval Medical Center, San Diego, CA; Shore Health Group, NJ; Novartis Pharmaceuticals, East Hanover, NJ and Syreon Corporation, Vancouver, BC, Canada.

**Purpose:** Patients with IBS are often sub-classified based on their predominant bowel habit. Rome II uses symptom-based diagnostic criteria to identify and sub-classify patients with IBS. In this study we compared patient’s self-reported bowel pattern with the Rome II criteria. We also compared the symptom burden between those who met the Rome II criteria and those who did not.

**Methods:** ILOS is a 6-month, prospective, observational study of patients with a physician diagnosis of non-diarrhea predominant IBS, conducted in 46 sites in the US. A questionnaire including Rome II criteria items was administered to patients at baseline. In addition, patient’s reported bowel pattern (i.e. normal, constipated, diarrhea and alternating) was determined at baseline and compared with the classification of the symptoms as per the Rome II criteria. The frequency, intensity and bothersomeness of IBS symptoms were evaluated at baseline and compared between those patients who met the Rome II criteria and those who did not.

**Results:** Of the 380 patients enrolled, most patients (78.2\%) met the Rome II criteria for the diagnosis of IBS. Based on the Rome II criteria and the patient’s reported bowel pattern, 34.5\% and 43.9\% of the patients were classified as having constipation predominant IBS, respectively. Based on the symptom assessment, 32.9\% of the patients were classified as alternating. The Rome II criteria could not classify 32.4\% of the patients, suggesting they may be alternating. Based on the Rome II criteria and the patient’s reported bowel pattern, 33.1\% and 23.1\% of the patients were classified as normal, having diarrhea-predominant IBS or were missing responses, respectively. There were no differences in the frequency, intensity or bothersomeness of IBS symptoms such as gas, constipation, abdominal pain or discomfort and bloating, between those patients who did and did not meet the Rome II criteria.

**Conclusions:** In the present study most of the patients met the Rome II criteria for diagnosis of IBS, however, there were no significant differences in the assessment of IBS sub-types between the Rome II criteria and patient’s reported bowel pattern. There were also no differences in the symptom burden between those who met the criteria versus those who did not.

**935**

Tegaserod Reduces Multiple Symptoms across Overlapping GI Disorders: Results from a Self-Reported Patient Questionnaire

Brian E. Lacy, M.D., Ph.D.,∗, Anastasia S. Malicka, Todd D. Phillips, Pharm.D., Jeffrey Kralstein, M.D. Division of Gastroenterology, Dartmouth-Hitchcock Medical Center, Lebanon, NH and Novartis Pharmaceuticals Corporation, East Hanover, NJ.

**Purpose:** To prospectively evaluate the extent of comorbid conditions associated with GI disorders and the degree of symptom relief provided by tegaserod.

**Methods:** Women (ages, 18–74 years; mean, 46 years) who received a first-time tegaserod prescription were randomly recruited (November 2003–February 2004) through flyers in physicians’ offices. Eligible patients received a self-report 8-week diary, follow-up questionnaires, and telephone interview. Results are presented for tegaserod users before their first tegaserod prescription and after their first course of therapy (2–4 months).

**Results:** Two hundred patients were recruited; 174 respondents participated in the study. Pre-tegaserod users had symptoms for an average of 7.3 years, and the majority (64\%) had more than one disorder. The predominant disorders reported were IBS (90\%), constipation (46\%), and GERD (37\%). The majority (58\%) of participants experienced moderate symptoms. Bloating
Cyclic Vomiting Syndrome and Chronic Cannabis Use
Noel R. Fajardo, M.D., Filippo Cremonini, M.D., M.S.C., Nicholas J. Talley, M.D., Ph.D.* Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN.

Purpose: Cyclic vomiting syndrome (CVS) is a rare disorder of unknown etiology, characterized by stereotypical and severe episodes of vomiting separated by symptom-free intervals, occurring almost at regular intervals. Therapeutic options are limited as etiology is unknown. Chronic cannabis use has recently been suggested as a potential cause of CVS. Our aim was to determine the association between cannabis use and occurrence of CVS symptoms through a case-control study.

Methods: All CVS patients referred from local community and referral practice of a tertiary GI center, diagnosed to have cyclic-functional vomiting between 1998 and 2003 (n = 89) constituted the case population. Patients with significant comorbidities (e.g. previous abdominal surgery, diabetes, on medication that may affect gastric motility, etc.) were subsequently excluded from the analysis. Age- and gender-matched controls were selected from patients diagnosed to have irritable bowel syndrome (IBS) with no nausea and vomiting seen at our institution at the same time period. Ascertainment of cannabis use was performed by abstraction of medical records which includes clinical history and self-reported health demographic data.

Results: 48 CVS cases met criteria and were matched to 48 controls. 22% (11/48, 95% CI 13–35%) of cases and 12% (6/48, 95% CI 6–31%) of controls were active or previous cannabis users, giving an odds ratio of 2.1 (95% CI 0.7 to 6.1) for cannabis use. Cannabis use, when found, preceded symptom onset in CVS patients. In both cases and controls, cannabis use was more common in men.

Conclusions: The odds for cannabis use were two-fold higher in CVS patients than in the IBS control group. However, the association was not statistically significant. Chronic cannabis use as an etiology of CVS should further be investigated using larger cross-sectional and prospective studies.

Cancer Use in CVS (cases) and IBS (controls)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CVS</th>
<th>IBS</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>11</td>
<td>6</td>
<td>ns</td>
</tr>
<tr>
<td>Gender</td>
<td>10M:1F</td>
<td>4M:2F</td>
<td>ns</td>
</tr>
<tr>
<td>Age (yrs)*</td>
<td>34±3</td>
<td>36±5</td>
<td>ns</td>
</tr>
<tr>
<td>Age Start Cannabis use (yrs*)</td>
<td>20±2</td>
<td>21±2</td>
<td>ns</td>
</tr>
<tr>
<td>Age Start CVS (yrs)*</td>
<td>29±3</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24±1</td>
<td>25±2</td>
<td>ns</td>
</tr>
<tr>
<td>Education (yrs*)</td>
<td>12±1</td>
<td>15±1</td>
<td>0.04</td>
</tr>
<tr>
<td>Cannabis Use (yrs*)</td>
<td>12±3</td>
<td>16±4</td>
<td>ns</td>
</tr>
<tr>
<td>Recent Active Users</td>
<td>8/11</td>
<td>3/6</td>
<td>ns</td>
</tr>
<tr>
<td>Frequency of Use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Light (&lt; 1 day/week)</td>
<td>4/11</td>
<td>2/6</td>
<td></td>
</tr>
<tr>
<td>Moderate (1–2 days/week)</td>
<td>3/11</td>
<td>0/6</td>
<td></td>
</tr>
<tr>
<td>Heavy (daily)</td>
<td>3/11</td>
<td>4/6</td>
<td></td>
</tr>
</tbody>
</table>

*(±SEM).

936

Gastrointestinal (GI) Symptoms in Underweight Individuals: A Population-Based Study

Purpose: Upper GI symptoms may result from gastric dysfunction. Dyspeptic symptoms in tertiary care have been associated with weight loss (Tack et al. Gastroenterology 1998;115:1346–52). Whether other upper or lower GI symptoms are associated with being underweight remains unknown in the general population. Our aim was to determine whether upper and lower GI symptoms can predict being below normal body mass (BMI < 20 kg/m²) in the general population.

Methods: A short-form questionnaire containing validated items covering common GI symptoms, lifestyle and BMI was mailed to a random sample of Olmsted County population. The associations were tested accounting for age, gender, and behavioral factors by logistic regression, using the normal BMI subjects as the reference group.

Results: Fifty-eight out of 930 responders (6.2%, 95% CI 4.6–7.7, 53 females) reported having BMI < 20 Kg/m². Associations between upper GI symptoms and lower than normal body mass are shown in the figure. Reporting early fullness (OR 2.1, 95% CI 1.1–4.5) and nausea (OR 2.4, 95% CI 1.1–5.6) independently predicted having a BMI < 20 Kg/m², while individuals reporting acid regurgitation were less likely to be underweight (OR...
0.4, 95% CI 0.16–1). Other gastrointestinal symptoms, including diarrhea, constipation and epigastric pain did not predict having a lower than normal BMI.

Conclusions: Early postprandial fullness and nausea are associated with being lower than normal body mass in the general population. These findings confirm observations in functional dyspepsia in tertiary referral centers. GI symptoms may contribute to have lower weight, or, alternatively, a common mechanism might predispose to both GI symptoms and underweight status [figure1]

**940 Drug Utilization Characteristics among Patients with Non-D IBS: Results from the IBS Longitudinal Outcomes (ILOS) Study**

**Deborah Camiscoli, M.D.,† Jayde Kurland, M.D., Robert Balshaw, Ph.D., Nadia Leskinova, M.S., Kristijan H. Kahler, S.M., Homa B. Dastani, Ph.D. Gastroenterology, Shore Health Group, NJ; Gastroenterology, Naval Medical Center, San Diego, CA; Syrecon Corp., Vancouver, Canada and HE&OR, Novartis Pharmaceuticals, East Hanover, NJ.**

**Purpose:** In this study we described the patterns of drug use and characteristics of patients with non-diarrhea predominant irritable bowel syndrome (non-D IBS) based on the drug categories at baseline.

**Methods:** ILOS is a 6-month, prospective, observational study of patients with a physician diagnosis of non-D IBS, conducted in 46 sites in the US. Physician and patient reported over-the-counter and prescription drug use for GI-related disorders were assessed at baseline. Patients were categorized as receiving no drug, monotherapy (mono) or polytherapy (poly). Patient reported quality of life (QOL) assessed by SF-36 and the validated IBSQOL, health care resource utilization, and work productivity using the Work Productivity and Activity Impairment Questionnaire: Digestive Health were collected at baseline. Severity of IBS symptoms were assessed by the frequency, intensity and distress/botherlessness of the symptoms, using a 5-point Likert scale. Differences in patient characteristics between the drug categories were assessed using Kruskal-Wallis or Chi-Square or Fisher’s Exact test as appropriate.

**Results:** Of the 380 patients identified with non-D IBS, 67.1% were on poly, 20.7% were on mono and 12.1% did not report any GI-related medication use. Of those on mono, the top 5 drug categories were tegaserod (29.1%), pain medications (20.3%), acid reducers (12.7%), anti-depressants (11.4%) and fiber (10.1%). A significant trend towards more QOL impairment with increasing drug use was observed in each of the following SF-36 domains (p < 0.01): physical functioning, role physical, role emotional, and vitality. Based on IBSQOL scores, patients on polytherapy had poorer QOL compared to those receiving monotherapy or no drugs (p = 0.003). Patients on polytherapy had higher severity scores on the cardinal IBS symptoms of abdominal pain, bloating and constipation, sought more medical care and had greater daily activity impairment than those receiving monotherapy or no drugs, though these results were statistically non-significant.

**Conclusions:** Most patients with non-D IBS use multiple GI-related drugs to relieve their symptoms. Based on the drug categories at baseline, patients on poly appear to have more severe IBS and had poorer QOL than those receiving mono or no drugs.

**941 Dextofisopam Improves Bowel Function in Men and Women with IBS**

**Steven Leventer, Ph.D.,* Karen Raudibaugh, Allen Mangel, M.D., Ph.D., Kimm Galbraith, Robert Kucharik, Naidong Ye, Ph.D., James Phillips, Dr.P.H., John Keogh, Kevin Keim, Ph.D., M.Sc. Research and Development, Vela Pharmaceuticals Inc., Ewing, NJ; Triangle Research Institute, Research Triangle Park, NC and Sage Statistical Solutions, Inc., Efland, NC.**

**Purpose:** Dextofisopam is a non-sedating antispasmodic agent that modulated autonomic function via a novel hypothalamic receptor, resulting in decreased stimulated autonomic activity. We explored the effects of dextofisopam on bowel function in patients with IBS.

**Methods:** Men and women with diarrhea-predominant or alternating IBS (d-IBS or a-IBS) were randomized to receive 12 weeks of dextofisopam 200 mg BID or placebo in a double-blind study conducted in the US. Stool frequency and stool consistency were the principal measures of bowel function.

**Results:** Of 140 patients, 66 received dextofisopam and 74 placebo, 73% were women, and 78% had d-IBS. Dextofisopam decreased stool frequency and improved stool consistency relative to placebo. These effects were apparent in d-IBS patients, but not in alternators. At Week 12, dextofisopam-treated d-IBS patients had a 70% greater reduction in stool frequency and approximately twice the improvement in stool consistency vs. placebo. In d-IBS patients, decreased stool frequency and improved stool consistency were apparent within 2 days. Interestingly, patients entering the study with higher stool frequency (≥3 stools/day) exhibited a marked reduction in stool frequency, while those who entered the study with lower stool frequency (<3 stools/day) did not. Similar rates of adverse events were seen in the dextofisopam and placebo groups. Worsening abdominal pain occurred more frequently with dextofisopam (12% vs. 4%), and headache occurred more frequently with placebo (5% vs. 12%). Importantly, dextofisopam produced minimal constipation (3.0%, vs. 1.4% for placebo).

Taken together, these data suggest that dextofisopam may be an agent that “normalizes” stool parameters rather than one that retards or stimulates gastrointestinal transit.

**Conclusion:** Rapid reduction in stool frequency and improvement in stool consistency were seen in d-IBS patients treated with dextofisopam. Though a substantial effect was seen on stool frequency, a very low rate of constipation was seen with dextofisopam. Dextofisopam may be “normalizing” gastrointestinal motility rather than inhibiting motility. Dextofisopam shows promise of providing an important new therapeutic alternative for IBS, one that may normalize bowel function without producing significant constipation.

**942 Patients Less Than 65 Years of Age Suffering from Irritable Bowel Syndrome or Constipation Have a High Risk of Being Diagnosed with Ischemic Colitis**

**Dong-Churl Suh, Ph.D.,* Kristijan H. Kahler, S.M., In-Sun Choi, Ph.D., Hyun-chul Shin, Ph.D., Jeffrey Krulstein, M.D. Pharmacy, Rutgers University, Piscataway, NJ and HE&OR, Novartis Pharmaceuticals, East Hanover, NJ.**

**Purpose:** Recent reports have suggested an increased risk of ischemic colitis (IC) among patients with irritable bowel syndrome (IBS) and constipation (C); however, the incidence of IC and its relationship to IBS and C in younger individuals is less understood. In this study, we evaluate the possibility that IBS and C predisposes to IC among those <65 years of age.

**Methods:** Data for this study was obtained from the PharMetrics patient-centric database which includes longitudinal medical and pharmacy claims
data for over 46 million lives. We identified patients $\geq$ 18 years of age, newly diagnosed with IBS or C from 1/1/00 to 12/31/01. The IBS and C cohorts were closely matched 1:1 to control cohorts using the propensity score method. All cohorts were followed from first diagnosis through 12/31/03 for the occurrence of IC. Incidence rates (IR) were assessed using a Kaplan-Meier estimator and a log-rank test.

Results: We identified 12,559 patients newly diagnosed with IBS (94% between 18 and 64 years of age) and 13,538 patients newly diagnosed with C (91% between 18 and 64 years of age). The IR for the development of IC in all IBS patients and those $<65$ was 65.36 (16 cases) and 55.83 (13 cases) per 100,000 p-y, respectively, as compared to 28.74 (7 cases) and 17.29 (4 cases) per 100,000 p-y in the control cohort, respectively. The IR ratio for all IBS patients and those $<65$ was 2.3 ($p = 0.060$) and 3.2 ($p = 0.029$), respectively. The IR for the development of IC in all C patients and those $<65$ was 45.63 (12 cases) and 28.98 (7 cases) per 100,000 p-y, respectively, as compared to 15.27 (4 cases) and 12.25 (3 cases) per 100,000 p-y in the control cohort, respectively. The IR ratio for all C patients and those $<65$ was 3.0 ($p = 0.046$) and 2.4 ($p = 0.196$), respectively.

Conclusions: Consistent with earlier findings, IBS and C appear to be associated with an increased risk of IC by about 2-3 fold. We found that even among younger patients, where IC is less common, this relationship still persists.

### 943

**Appropriate Prescribing of Tegaserod—A Look at a Managed Care Population**

Jay Margolis, RPh,* Jason Tan, M.S., Debra Wertz, Pharm.D., Homa B. Dastani, Ph.D., Kristijan H. Kahler, S.M. Analysis and Medical Writing, HealthCore, Wilmington, DE and HE&OR, Novartis Pharmaceuticals, East Hanover, NJ.

**Purpose:** Tegaserod is a selective 5-HT4 receptor agonist indicated for the treatment of IBS with constipation (IBS-C) and chronic idiopathic constipation. This study assessed the demographic, diagnostic and treatment characteristics of patients receiving tegaserod in a managed care population.

**Methods:** A retrospective analysis of pharmacy and medical claims data of tegaserod users from geographically diverse managed care health plans was conducted. Benefit-eligible members who were continuously enrolled and initiated on tegaserod therapy between 8/1/02 and 12/31/03 were included in the study. The first prescription fill date for tegaserod during this period was considered the index prescription date. Patients' diagnostic and demographic characteristics were evaluated at the index diagnosis visit and during a two-year period (one-year prior and one-year post) around the index prescription date. Patients were categorized as having at least one medical claim for IBS, abdominal pain, bloating, constipation, or other GI-related disorders based on the International Classification of Diseases, Clinical Modification (ICD-9-CM) codes.

**Results:** A total of 2,952 tegaserod users were identified of which 314 did not have any GI-related diagnosis and were excluded from the analysis. Of the 2,638 tegaserod users with an index diagnosis visit for a GI-related disorder, 93.5% were female, and the mean age was 48.6 (SD = 13.7) years. Most of tegaserod users (84.5%) had an index diagnosis for IBS (47.8%), or at least one of the cardinal symptoms of IBS-C: constipation (23.2%), abdominal pain (13.0%), or bloating (0.5%). Throughout the 2-year observation period, 93.5% of the patients had a medical claim consistent with the symptoms of IBS. In the one-year follow-up period, the average days of tegaserod therapy was 105 days (median 60 days). Moreover, 40.8% of the patients received 0–30 days supply of tegaserod, 26.4% received 31–90 days, 14.1% received 91–180 days, and 18.7% of received more than 180 days supply of tegaserod.

**Conclusions:** Most patients receiving tegaserod had a diagnostic claim for IBS or one of the cardinal symptoms of IBS-C (i.e., abdominal pain, constipation or bloating), indicating that tegaserod is being used in the appropriate population.
assess the impact of this education on the appropriateness of EUS referral patterns. [figure1] [figure2]

945

Outpatient Placement of Feeding Gastrostomy (PEG) Prior to Chemo-Radiation for Head & Neck Cancer
Elaine Posluns, RD, Ian Poon, M.D., Lawrence B. Cohen, M.D.∗ Clinical Nutrition, Toronto Sunnybrook Regional Cancer Centre, Toronto, ON, Canada; Radiation Oncology, Toronto Sunnybrook Regional Cancer Centre, Toronto, ON, Canada and Gastroenterology, Sunnybrook & Women’s College Health Science Centre, Toronto, ON, Canada.

Purpose: Patients with Head & Neck cancer (HNCa) undergoing chemoradiotherapy and/or surgery are at high risk for severe weight loss, dehydration, malnutrition, treatment interruptions and hospitalization. The use of PEG in this population offers a safe, effective method of delivering enteral nutrition to compensate for the decline in oral intake. In the past, patients were admitted to hospital for PEG insertion and education when effects of the cancer treatment caused significant dysphagia, mucositis and reduced oral intake. We are reporting initial results of an innovative program for HNCa patients during which out patient PEG is established prior to the start of chemo-radiation. Follow up and education regarding the care and use of the tube are provided on an outpatient basis.

Methods: HNCa patients were selected to have a PEG established prior to chemo-radiation based on individual MD practice. All patients received nutrition counselling and education by a registered dietitian prior to treatment. Weight loss, treatment interruptions and hospitalizations were compared in patients who had vs didn’t have a pre-treatment PEG.

Results: 31 patients received PEG and enteral feeding as an outpatient procedure and were compared to a group of 20 similar patients who did not receive a PEG. In the PEG group, average weight loss following treatment was 6.8% compared to 11.0% in the non PEG group. 100% of the PEG group completed treatment without interruption or hospitalization for malnutrition/dehydration, compared to 29% of the non-PEG patients who required iv-hydration or hospital admission for nutrition support. PEG complications were abdominal pain requiring hospitalization (2), infection (5).

Conclusions: Patients with PEG received more of their prescribed nutrition and fluids, lost less weight, and had fewer treatment interruptions and hospital admissions than non-PEG patients. An average 3–5 day hospital admission for in-patient PEG placement is eliminated saving health care costs. PEG insertion in ambulatory HNCa patients prior to chemo-radiation is safe, well tolerated, cost effective and improves clinical outcome. Our experience supports PEG tube insertion in ambulatory HNCa patients prior to treatment.

946

PEG Placement: Relation between Sepsis and Early Survival
Shahzad Iqbal, M.D.∗, Viren Shah, M.D., Gerald Posner, M.D., Eric Jaffe, M.D., Deepak Mahajan, M.D., Mohammad Forood Hassan, M.D., Mohamad Mansour, M.D., Franklyn Marsh, M.D., Pranjal M. Agrawal, M.D.
Internal Medicine, Interfaith Medical Center, Brooklyn, NY.

Purpose: Gastrostomy tubes are justified for patients who need tube feeding for more than 30 days. The impact of PEG (percutaneous endoscopic gastrostomy) tube placement on patient’s survival depends on the patient’s underlying conditions. In this study, we analyzed whether h/o diabetes mellitus or decubiti were associated with early survival after PEG placement. The results were adjusted for age and gender.

Methods: In this retrospective study, all patients who had PEG placed from 08/2001 to 10/2003 and survived at 8 weeks post-PEG, were included. Patient’s demographics, presence of sepsis (within 2 weeks before PEG), h/o DM or decubiti (stage 2 or greater); and any rise in serum albumin levels at 8 weeks post-PEG were noted. None of the patients were septic at the time of PEG placement. PEG was defined by considering together clinical (fever), biochemical (white cell count, urinalysis, culture results) and radiological criteria (chest or abdominal x-rays, CT scan). The data was analyzed using logistic regression model. The results were adjusted for age and gender.

Results: The study included 89 patients (74% females and 26% males). The average age was 80.3 years (range 45 to 100 years). 45 out of 89 patients had no rise in serum albumin level at 8 weeks. Of those 45 patients, 28 were diabetic and 23 had decubiti. Using logistic regression analysis, diabetes and decubiti were found to have a statistically significant negative association with a rise in serum albumin levels (p-values of 0.036 & 0.057, and odd ratios of 2.76 & 2.79 respectively). H/o recent sepsis didn’t have statistically significant negative association with a rise in serum albumin level (p-value 0.64 and odd ratio 0.77).

In another analysis, we had found that h/o recent sepsis was negatively associated with early survival after PEG placement. But those who survive, sepsis didn’t have a negative effect on the rise in serum albumin levels.

Conclusions: A history of diabetes and decubiti are negatively associated with rise in serum albumin levels post-PEG. These findings are consistent with the known debilitating effects of these conditions, and conversely with their roles as markers of general inanition.

948

Prospective Investigation of Patient-Initiated Procedure Cancellation/“No-Show”

Purpose: Patient-initiated procedure cancellation on “short-notice” and failure to present for scheduled GI endoscopic procedures is costly from per-
Table 1. Stepwise Multiple Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adjusted Odds Ratio</th>
<th>P-value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 55 or more</td>
<td>2.45</td>
<td>0.012</td>
<td>1.22–4.91</td>
</tr>
<tr>
<td>Sense of Incomplete evacuation</td>
<td>0.08</td>
<td>0.011</td>
<td>0.01–0.57</td>
</tr>
<tr>
<td>All/almost all of the time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of Laxative</td>
<td>4.48</td>
<td>0.009</td>
<td>1.46–13.76</td>
</tr>
<tr>
<td>Neurological Disorder</td>
<td>6.61</td>
<td>0.059</td>
<td>0.93–47.13</td>
</tr>
<tr>
<td>More than Zero cc amount left in</td>
<td>2.62</td>
<td>0.057</td>
<td>0.97–7.05</td>
</tr>
<tr>
<td>the Bottle</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of Calcium Supplement</td>
<td>0.49</td>
<td>0.050</td>
<td>0.24–1.00</td>
</tr>
</tbody>
</table>

950
Laparoscopic Cholecystectomy in Japanese Octogenarians
A.-Hon Kwon, M.D.,* Yoichi Matsui, M.D. * Department of Surgery, Kansai Medical University, Moriguchi, Osaka, Japan.

Purpose: The most rapidly growing sector of Japanese society is composed of individuals older than 65 years of age and by 2050 this age group will represent 35.7% of the population. For the elderly, who are generally considered to have diminished cardiopulmonary reserves and who are therefore often less able to withstand the trauma and stress of open abdominal surgery, the advantages of a laparoscopic approach are obvious. However, elderly patients may have an increased risk of conversion to open cholecystectomy and individuals aged 80 years and over are at the greatest risk of experiencing adverse surgical outcomes. The purpose of this study was to evaluate the results of laparoscopic cholecystectomy (LC) in patients aged 80 years and over.

Methods: Between April 1992 and December 2003, 471 patients aged 65 to 79 years (Group 1) and 45 patients aged 80 years and over (Group 2), who underwent LC were included in the study. Laparoscopic exploration of the common bile duct could be performed both to obtain a diagnosis or for the treatment.

Results: The mean age of Group 1 patients (202 men and 269 women) was 71 years; the mean age of Group 2 patients (18 men and 27 women) was 83 years. Choledocholithiasis and gallbladder cancer were both significantly more common in Group 2 patients. Hypertension, diabetes mellitus, and cardiovascular disease were the most common underlying diseases in both groups. There were no deaths in either group. The overall incidence of major complications (bile duct injury, bile leakage and bowel injury) was low and similar in the two groups. The success rate of the intraoperative cholangiography was similar between groups, however the rate of laparoscopic stone clearance was significantly higher in Group 2 patients. Cholesterol stones were the most frequently reported type of stone in both groups. Seventy-five of the 221 patients (34%) in Group 1, and 14 of the 20 patients (70%) in Group 2, had positive bile cultures (p = 0.003). The incidence of GNRs in Group 2 patients was significantly higher than in Group 1 patients.

Conclusions: Octogenarians tolerate LC well, especially in the elective setting. Therefore, primary care physicians should feel comfortable when referring patients for the surgical management of biliary tract disease before complications might develop that would necessitate an urgent operation.

951
A New Method for Food Disimpaction Using a Push Dilator under Fluoroscopy Guidance
Yaser Al-Solaiman, M.D., Samah Bassas, M.D., Mohammad M. Alsolaiman, M.D.* Internal Medicine, Albany Medical College, Albany, NY and Gastroenterology, Central Utah Clinic, Provo, UT.
Evaluation of the Potential Role of Endoscopic Intraluminal Therapy in Postoperative Bariatric Patients

Thomas W. Abernathy, Jr., M.D., Kathleen M. Kennedy-Wilkins, R.N., John R. Kirkpatrick, M.D., Timothy R. Koch, M.D.* Section of Gastroenterology, Washington Hospital Center, Washington, DC and Department of Surgery, Washington Hospital Center, Washington, DC.

Purpose: It has been suggested that endoscopic intraluminal therapy may be useful for management of postoperative bariatric patients. To examine the potential frequency of and role of endoscopic intraluminal therapy, we reviewed the clinical, radiological and endoscopic characteristics and findings of patients referred to a single bariatric surgical specialist for correction of post-operative problems.

Methods: In a retrospective review of the evaluation of their symptoms, 23 patients were included who were seen between 2001 and 2004. Among 14 different GI clinicians in the Orlando community, the average colonoscopic withdrawal time from the cecum was 6.15 minutes, with a range of 2 to 25 minutes. When biopsies or polyps were removed the mean withdrawal time was 8.75 minutes.

Conclusions: Among 14 different GI clinicians in the Orlando community, the average colonoscopic withdrawal time from the cecum was 6.15 minutes, with a range of 2 to 25 minutes. When biopsies or polyps were removed the mean withdrawal time was 8.75 minutes. This data is very similar to publicized recommendations. The data suggests a high level of quality regarding colonoscopic evaluations in this community. Similar studies may be done in communities throughout the United States, providing a report card on the quality of colonoscopic examinations in various regions of our country.
**Purpose:** Visicol is effective and well tolerated as a colonoscopy purgative. The MCC tablet binder may leave a visible residue during procedures. An MCC-free formulation INKP-102, has been developed. The purpose of this randomized, investigator-blinded, multicenter trial was to determine the appropriate dosing regimen for INKP-102.

**Methods:** Eligible, adult colonoscopy pts received one of 6 dosing regimens of INKP-102 or Visicol (see table). Colon-cleansing efficacy was based on response to treatment. A pt was considered to be a responder if Overall Colon Cleansing (OCC) was rated “excellent” or “good” on a 4-point scale based on the amount of retained “colonic contents.” Safety measures were monitored.

**Results:** Most adverse events (nausea, abdominal pain, distention, vomiting) were mild or moderate in intensity and occurred with the same frequency or less in the INKP-102 arms compared with Visicol.

**Conclusions:** INKP-102 is a safe and efficacious purgative. “Next day” dosing is preferred but “evening only” dosing with a 32-tablet dose of INKP-102 is also effective.

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**Comparison between Endoscopic Pappilary Balloon Dilatation and Endoscopic Sphincterotomy for the Treatment of Common Bile Duct Stones**

Hidetaka Watanabe, M.D., Masashi Yoneda, M.D., Kazunari Kanke, M.D., Akira Terano, M.D., Hideyuki Hiraishi, M.D.* Department of Gastroenterology, Dokkyo University, School of Medicine, Mibu, Tochigi, Japan.

**Purpose:** Endoscopic sphincterotomy (EST) has been established as an endoscopic treatment of common bile duct stones, whereas the technique of endoscopic papillary balloon dilatation (EPBD) has recently become widespread. EPBD is simple and preserves the papillary sphincter function. It has been reported that EPBD is associated with a lower risk of bleeding as a complication, but a higher risk of postoperative pancreatitis compared with EST. However, there have been few reports on detailed studies of post-EST and EPBD pancreatitis. Therefore, we conducted a study on the outcomes and early postoperative complications, especially pancreatitis, of EPBD and EST for the treatment of common bile duct stones at our department.

**Methods:** 180 patients with common bile duct stones were randomized to EPBD or EST. For EPBD, an 8-mm dilatation balloon was used. For assessment of postoperative pancreatitis, the Cotton’s criteria were modified to include relatively milder pancreatitis.

**Results:** Complete removal rate of stones was significantly higher in EST group (95.6%) than that in EPBD group (86.6%); however, regarding small stones (< 10 mm), complete removal rate of EPBD (93.8%) was similar to that of EST (98.1%). By modified criteria when milder cases were included, postoperative pancreatitis occurred significantly more often in EPBD (16.7%) than in EST (6.7%). Bleeding was encountered in one patient (1.1%) of the EST, while no patients in EPBD. No fatal complication occurred in either the EPBD or EST group.

**Conclusions:** In regard to small common bile duct stones, EPBD achieves appropriate same outcome as EST, while mild postoperative pancreatitis occurs more often in EPBD.

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**Treatment of Gastric Varices with 2-octyl-cyanoacrylate Glue Injection: A Long-Term (2-Year) Efficacy and Safety Study**


**Purpose:** To prospectively evaluate the efficacy and safety of 2-octyl-cyanoacrylate glue injection for the treatment of gastric varices (GV).

**Methods:** Forty-four consecutive patients with GV were enrolled. Inclusion criteria were: 1) history of GV bleeding or 2) presence of high-risk GV (≥ 2cm in size or presence of red wale marks). Exclusion criteria were presence of hepatorenal syndrome or multi-organ failure.

Glue injection was performed with a standard endoscope (GIF-1T160, Olympus Inc.) and 23-gauge sclerotherapy needles. 2-octyl cyanoacrylate was injected into the varix in 1-mL aliquots. During follow-up endoscopy at 1, 3, 6, and 12 months, repeat glue injection was performed if catheter palpatation did not reveal hard, obliterated varices. After 1 year, patients were followed clinically and endoscopy was performed as-needed. Primary endpoints were acute and long-term hemostasis and related complications.

**Results:** Endoscopic findings of active GV bleed and hemostasis achieved after glue injection are shown (Figures 1–2). Control of active bleeding in 6 patients was 100% (Table 1). At 2-year follow-up, only 5/44 rebled from GV. Two of these patients underwent transjugular intrahepatic portosystemic shunts, 1 had a self-limited bleed, 1 underwent splenectomy, and 1 patient who missed follow-up died at an outside hospital. Side-effects were mild and managed conservatively (Table 2).

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**A**

**B**

**Conclusions:** 2-octyl cyanoacrylate is safe and efficacious in the treatment and long-term prevention of GV bleeding.
Table 1. Efficacy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrest of active bleed</td>
<td>6/6 (100%)</td>
</tr>
<tr>
<td>Acute rebleed (&lt;72 hrs)</td>
<td>2/44 (5%)</td>
</tr>
<tr>
<td>Subacute rebleed (3–90 d)</td>
<td>0</td>
</tr>
<tr>
<td>Late rebleed (&gt;90 d)</td>
<td>3/44 (7%)</td>
</tr>
</tbody>
</table>

Table 2. Complications

<table>
<thead>
<tr>
<th>Event</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>5 (9%)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

957

Analysis of Incomplete Examinations in Capsule Endoscopy

Kevin S. Sieja, M.D., Stephen R. Freeman, M.D.* Medicine, Division of Gastroenterology, University of Colorado Health Sciences Center, Denver, CO.

Purpose: To evaluate procedure and patient related factors that may influence the likelihood of complete small bowel visualization in capsule endoscopy.

Methods: All capsule endoscopy examinations performed at our institution between 3/03–8/04 were analyzed through review of endoscopy reports, medical records and telephone follow-up. One examination was excluded in which there was an immediate technical malfunction upon capsule ingestion. A total of 55 examinations were analyzed. Incomplete examinations were defined as studies in which the capsule did not reach the colon before the battery expired. The Student t test and the Fisher exact test were used for the statistical comparison of means and proportions between the complete and incomplete examinations. Variables not distributed normally were compared using the Wilcoxon rank sum test.

Results: The completion rate or success of visualizing the entire small intestine was 64%. Gastric transit time was significantly longer in incomplete examinations vs. complete examinations (median 37.5 min vs. 16 min, p = 0.04). The indications and findings of the examinations were not significantly different between the two groups. There were no statistically significant differences in patient characteristics between the two groups with respect to age, sex, history of diabetes, abdominal surgery, chronic constipation/diarrhea, or the use of narcotic, anticholinergic or laxative medications.

Conclusions: Prolonged gastric transit time was the only significant factor influencing the completion rate in capsule endoscopy examinations. Further controlled trials are warranted to determine if shortening gastric transit time through the use of prokinetic agents will increase the completion rate and yield of capsule endoscopy.

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String Capsule Endoscopy Versus ESO Pill Cam for the Diagnosis of Barrett’s Esophagus. A Head-to-Head Comparison Study

Richard Shaughnessy, D.O., Rodney Atkins, L.P.N., Mansud S. Shaukat, M.D., Francisco C. Ramirez, M.D.* Gastroenterology, Carl T Hayden VA Medical Center, Phoenix, AZ.

Purpose: The Eso Pill Cam (EPC) is marketed for evaluation of esophageal diseases. The EPC is a two sided capsule which takes twice as many images, and uses a standard protocol of patient positioning to control esophageal transit time. It is unclear if the free-floating EPC can consistently diagnose Barrett’s Esophagus (BE).

AIM: To assess the esophageal transit time of the EPC, and to compare the diagnostic yield and adequacy of the EPC, to String Capsule Endoscopy (SCE) in patients with known BE.

Methods: Patients underwent sequential EPC, SCE, and EGD. For EPC the patient swallowed the capsule while supine and this was followed by elevation of the head of bed as per manufacturer protocol. SCE was then carried out by using SBPC modified with a sleeve and string. The device was swallowed in the sitting position, and the entire esophagus was scanned up and down at least three times for no longer than 10 minutes. The device was then removed from the patient. Finally, EGD was performed, the BE length measured and EPC retrieved by Roth’s net. Esophageal transit time of EPC was measured as the time when both images displayed stomach minus the time of first esophageal image. An independent experienced endoscopist blinded to the diagnosis reviewed the images and rendered a diagnosis.

Results: Ten patients, 4 with LSBE (mean 7.5 cm), and 6 with SSBE (mean 1.4 cm) were studied. SCE resulted in the correct diagnosis in all patients. The mean recording time for SCE was 379 seconds. The mean transit time for the EPC was 119.8 seconds (range 54–405 seconds). The diagnosis of BE could not be definitively established via EPC in 1 patient, was probable in 2 and possible in 1.

Patient Length BE (cm) EPC transit time (sec) EPC Diagnosed BE

| 1 | 6 | 405 | Possible |
| 2 | 14 | 6 | No |
| 3 | 2 | 29 | Yes |
| 4 | 6 | 191 | Yes |
| 5 | 1 | 9 | Probable |
| 6 | 0.5 | 334 | Probable |
| 7 | 4 | 164 | Yes |
| 8 | 2 | 39 | Yes |
| 9 | 2 | 5 | Yes |
| 10 | 1 | 16 | Yes |

EPC was found and retrieved in 40% of patients. There were no complications.

Conclusions: Esophageal transit time is a physiologically dependent variable that cannot be controlled by increasing the number of images per second taken or modification of the patient’s position. EPC transit time through the esophagus was highly variable, despite strict adherence to manufacturer protocol. This precluded the firm visual diagnosis of BE in 40% of patients. SCE eliminates the variability of esophageal transit time, and permits examination of the esophagus on multiple passes. This allowed for the correct diagnosis of BE in all studied patients.

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Endoscopic Pancreatic Exocrine Function Testing Made Easy

Picha Moolsintong, M.D., Frank R. Burton, M.D.* Internal Medicine, Division of Gastroenterology and Hepatology, Saint Louis University School of Medicine, St. Louis, MO.

Purpose: The purpose of this study is to evaluate whether a new drainage tube technique will simplify the endoscopic secretin stimulated pancreatic exocrine test (ESPE) and be valuable in evaluating patients for chronic pancreatitis.

Methods: We conducted a retrospective study of twenty-one patients with chronic abdominal pain and normal pancreatic imaging. These patients had ESPE testing with the following modified endoscopic collection system. ESPE testing was performed with conscious sedation using a Pentax 3430. Porcine synthetic (0.2 mcg/kg, ChirRhoClin, Inc.) or human secretin was given IV 15 minutes before endoscopic duodenal aspiration. Prior to entering the duodenum all gastric contents were evacuated. The first 10 min collection was performed in the 3rd portion of the duodenum. A wire-guided Ligory drainage tube (8.5Fr) with a distal pigtail multiport aspiration tip was placed in the 3rd portion of the duodenum under direct endoscopic visualization. The endoscope was withdrawn as the tube was brought out through the oropharynx and was connected to continuous aspiration. Two additional 10
min-period collections were obtained via the drainage tube at 30 and 45 min after IV secretin. Patients were maintained in the left-lateral decubitus position during the procedure to prevent any gastric fluid contamination. All fluid collections were analyzed for bicarbonate (HCO₃⁻) concentration.

Results: Of the 21 patients studied, 13 were females and 8 were males with a mean age of 48.9 years. Peak HCO₃⁻ concentrations (PHC) at 15 minutes occurred in 11 of the 21 patients (52%). PHC at 30 minutes occurred in 7 of 21 patients (33%). PHC at 45 minutes occurred in 3 of 21 patients (14%). Normal concentrations of HCO₃⁻ were seen in 57%, abnormal concentration in 5%, and equivocal concentrations (60–80 mmol/L) in 38% even after 55 minutes of duodenal collections.

Conclusions: This new drainage tube technique appears to be valuable in detecting HCO₃⁻ peak secretion after 15 minutes without the need for direct endoscopic aspiration. This technique allows the use of a drainage tube without the need for fluoroscopy, prolonged sedation, and continuous direct endoscopic aspiration. Additional studies are necessary to determine whether this drainage tube method can be used adequately for all collections after secretin administration.

960

Oral 48 g INKP-102 Has Improved Safety Profile over 60 g Sodium Phosphate Tablets as a Bowel Purgative Prior to Colonoscopy


Purpose: The safety and efficacy of Visicol (23% microcrystalline cellulose; MCC) is well established. Side effects of nausea, vomiting and bloating are less w/ Visicol (36%, 9%, 47%) vs 4L PEG (54%, 18%, 62%), p ≤ 0.0001; Castenberg 2001. Safety data from 2 trials were collected from 931 adults scheduled for colonoscopy who took either Visicol® Tablets (NaPT;13% MCC) or INKP-102, a new NaP tablet formulation w/o the MCC binder, shown to have excellent bowel cleansing. These multicenter, investigator-blinded studies assessed the safety of 3 oral regimens of INKP-102 compared to NaPT for even greater improvement.

Methods: Patients were randomly assigned to either 60 g NaPT (40 tabs) or doses of INKP-102: 60 g (40 tabs), 48 g (32 tabs) or 42 g (28 tabs).

Results: The incidence of all adverse events (AEs) was less among patients receiving the lower dosing arms. Of all the regimens studied, the overall incidence of AEs, the incidence of GI disorders and abdominal distention (bloating) and vomiting were significantly less among patients who took the 48g INKP-102 dose.

Conclusions: The incidence of superficial mucosal aphthous ulceration detected upon visual exam of the colon for all INKP-102 patients was 4% overall, compared to 5% for NaPT.

<table>
<thead>
<tr>
<th>Number (%) of patients</th>
<th>NaPT 60 g (N = 268)</th>
<th>INKP-102 48 g (N = 272)</th>
<th>P-Value1</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with at least 1 AE</td>
<td>176 (66)</td>
<td>153 (56)</td>
<td>0.0275</td>
</tr>
<tr>
<td>All GI disorders</td>
<td>172 (64)</td>
<td>147 (54)</td>
<td>0.0182</td>
</tr>
<tr>
<td>Abdominal bloating</td>
<td>110 (41)</td>
<td>83 (31)</td>
<td>0.0119</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>68 (25)</td>
<td>62 (23)</td>
<td>NS</td>
</tr>
<tr>
<td>Nausea</td>
<td>81 (30)</td>
<td>72 (26)</td>
<td>NS</td>
</tr>
<tr>
<td>Vomiting</td>
<td>23 (9)</td>
<td>11 (4)</td>
<td>0.0037</td>
</tr>
</tbody>
</table>

*Adverse events experienced by more than 2% of patients. 1Percentages between NaPT and INKP-102 (48g) dose treatment arms were compared using Fisher’s Exact test. Significance at p = 0.05.

Conclusions: INKP-102 has an improved GI safety profile, and 48 g (32 tabs) is significantly better than marketed 60 g NaPT. The smaller dose and fewer side effects may enhance patient compliance while providing excellent cleansing.

961

Capsule Endoscopy Findings Change Patient Management

Cody B. Barnett, M.D., Jack A. DiPalma, M.D., F.A.C.G., Kevin W. Olden, M.D., F.A.C.G.* Division of Gastroenterology, University of South Alabama, Mobile, AL.

Purpose: For capsule endoscopy (CE) to play a significant role in the diagnosis of gastrointestinal disease, changes in patient management and positive patient outcomes must be seen. The purpose of this study was to determine whether CE findings would lead to a change in patient management.

Methods: The study was a retrospective chart review of CE done at our institution. A total of 210 cases were reviewed. Demographic data was collected as well as indications and findings. Charts were reviewed for actual changes in management based on CE findings. When that information was not available, CE findings were used to determine whether a change in management would occur. These findings included active bleeding, especially within reach of a therapeutic endoscope, masses or polyps potentially missed by prior endoscopies, and ulcers or lesions that would necessitate a change in medical management. This would include discontinuation of medications such as NSAIDS or a change in inflammatory bowel disease treatment regimen based on evidence of active disease from CE.

Results: Overall, CE findings would lead to a change in patient management in 38.6% of the study population. For patients with obscure-occult bleeding, 36.6% would have had a change in management. In obscure-ovet bleeding patients, 41.9% would have a change in management. In those patients who had CE for known or suspected inflammatory bowel disease, 36% would have had a change in management based on capsule findings.

Conclusions: This study demonstrates that, in addition to yielding “interesting findings”, CE leads to an actual change in management in a reasonable number of patients with suspected small bowel disorders, inflammatory bowel disease, and overt or obscure bleeding. CE also provides information that reassures patients and eliminates the indication for further testing. Larger prospective studies are indicated to validate these results.

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How Important Is Abdominal Compression and Position Change in Successful Colonoscopy to the Cecum?

Athan P. Kartsonis, M.D.,* Kim Howse, R.N. Melbourne Ambulatory Surgery Center, Melbourne, FL.

Purpose: To determine the utility of abdominal compression and position change in successful colonoscopy to the cecum.

Methods: 268 consecutive patients undergoing elective colonoscopy at an ambulatory endoscopy center were enrolled in the study. Patients having undergone previous colon resections were excluded. Olympus video colonoscopes were used for all procedures. All patients were sedated with diprovane. A stopwatch was used to determine the time from introduction of the colonoscope to cecal intubation. All exams were performed by one endoscopist (apk).

Regions of abdominal compression were divided into Right Upper Quadrant (RUQ), Left Upper Quadrant (LUQ), Right Lower Quadrant (RLQ), and Left Lower Quadrant (LLQ). Position changed referred to transferring the patient from left lateral decubitus to any other position.

Results: The 268 patients enrolled in the study included 130 males (48.5%) and 138 females (51.5%). Mean study participant age was 62 yrs. 266 out of 268 (99%) exams were successful. Identification of the ileocecal valve confirmed all successful exams. The mean time to cecal intubation in successful exams was 3 min 13 sec (range 1min 3sec to 18 min 37sec). The 2 unsuccessful exams involved 1 unsuccessful sigmoid traversal and 1 unsuccessful hepatic flexure passage. Mean withdrawal time for all successful exams was 12 min 3 sec (range 2 mins 36 sec to 39 mins).
Abdominal compression was necessary in 55 out of 268 patients (20.52%). In those patients requiring abdominal compression the RUQ was the most frequent area compressed (25pts. 45%). The frequency for compression of other regions was as follows.

- LLQ 10pts (18%)
- RUQ & LLQ 8pts (15%)
- LUQ 6pts (11%)
- ALL 4 quadrants 3pts (5%)
- RUQ & LUQ 1pt (2%)
- RUQ, LLQ, RLQ 1pt (2%)
- LLQ & LUQ 1pt (2%)

No patient warranted position change from the LLQ position to achieve cecal intubation.

**Conclusions:**
1. Abdominal compression to achieve cecal intubation is necessary in the minority of patients undergoing outpatient colonoscopy.
2. Assisting the colonoscope around the hepatic flexure with gentle RUQ compression appears to be the most useful compressive measure in achieving cecal intubation.
3. Performing routine sigmoid compression at the initiation of all colonscopic exams is not warranted.
4. Position change was not necessary in this study to achieve cecal intubation.
5. Colonoscopy to the cecum can be successful in a high percentage of patients in the private practice setting.

### Comparing the Outcomes of Endoscopic Treatment for Removal of Bile Duct Stones: Endoscopic Papillary Balloon Dilatation or Endoscopic Sphincterotomy?

**Authors:** Akira Hashimoto, M.D., Atsuya Shimizu, M.D., Mutami Koyama, M.D., Katsuya Shinozaki, M.D., F.A.C.G.* Internal Medicine, Saiseikai Matsusaka Hospital, Matsusaka, Japan; Internal Medicine, Mutsuakya Cyuo Hospital, Matsuoka, Japan and 1st Department of Internal Medicine, Mie University, Tsu, Japan.

**Purpose:** Recent reports suggest that endoscopic sphincterotomy (EST) is superior to endoscopic papillary balloon dilatation (EPBD) in terms of stone removal and early complications. In this study we have evaluated the efficacy and safety of EPBD compared with EST in multicenter study.

**Methods:** Two hundred fifty-seven patients with bile duct stones were enrolled and assigned to EPBD (n = 140) or EST (n = 117) in multicenter hospitals. EPBD was carried out using a balloon-tipped biliary catheter with a maximum diameter of 8 mm. Before inflation we inject glyceryl Trinitrate into the common bile duct to decrease biliary pressure.

No inflate the balloon gradually and deflate immediately when the balloon diameter becomes 8 mm. EST was performed according to the conventional method.

**Results:** Complete duct clearance was achieved in 93.2% in the EPBD and 94.2% in the EST (not significant). Mechanical lithotripsy was needed in 51 patients (39.2%) in the EPBD and 36 patients (32.4%) in the EST (not significant). EPBD required a greater mean number of treatment sessions than EST (1.67 vs 1.40, P = 0.03). Complications occurred in 6.9% of patients in the EPBD and 8.1% of those in the EST (not significant). There was no mortality. The frequency of acute pancreatitis was higher in the EPBD than in the EST (6.9% vs. 2.7%; P = 0.10). Hemorrhage occurred only in the EST (0% vs. 5.4%; p < 0.05). Acute cholecystitis and cholangitis were obtained in one EPBD patient and eight EST patients with gall bladder stones in situ (P = 0.02).

**Conclusions:** EPBD and EST were approximately equal in terms of successful clearance of bile duct stones. The frequency of acute pancreatitis was higher in the EPBD than in the EST, whereas hemorrhage occurred only in the EST. EPBD is clinically more effective in decreasing the risk of acute cholecystitis in patients with gall bladder in situ. Therefore EPBD appear to be appropriate treatments for bile duct stones.

### Factors Associated with Nonattendance for Outpatient Colonoscopy

**Authors:** Christopher S. Huang, M.D., Brian C. Jacobson, M.D., Oren Fix, M.D., David R. Lichtenstein, M.D., F.A.C.G., Francis A. Farraye, M.D., F.A.C.G.* Section of Gastroenterology, Boston University Medical Center, Boston, MA.

**Purpose:** To identify specific factors associated with nonattendance for outpatient colonoscopy.

**Methods:** Self-administered questionnaires were given to 271 consecutive patients who attended their colonoscopy appointment over a 5-week period beginning Mar 1, 2004. Similar questionnaires were mailed to 346 consecutive patients who did not attend their colonoscopy appointment, assessing reasons for nonattendance, perceptions and concerns regarding colonoscopy, and logistical considerations affecting attendance. Responses from attendees and nonattendees were compared, and ORs with 95% CI were calculated to determine the association between specific factors and attendance.

**Results:** Overall nonattendance rate 32%. 198 of 271 attendees (73%) responded, compared to 32 of 346 non-attendees (9%). Results shown in table reflect data from 502 subjects, including all 230 questionnaire responders.

**Conclusion:** Factors associated with nonattendance included non-white race, non-English language, open access booking, longer interval between referral and appointment, patient being unaware of indication, absence of GI symptoms, poor self-perceived health, difficulty with bowel preparation, and logistical failures. Interventions that address modifiable factors can potentially improve attendance rates for colonoscopy.

### Wireless Capsule Endoscopy (WCE) in Inpatients with Obscure Gastrointestinal (GI) Bleeding

**Authors:** Brian C. Brauer, M.D., Hari H. Diwakaran, M.D., Gary R. Zuckermand, D.O., Chandra Prakash, M.D.* Division of Gastroenterology, Washington University School of Medicine, St. Louis, MO and St. Charles, MO.

**Conclusion:** Factors associated with nonattendance included non-white race, non-English language, open access booking, longer interval between referral and appointment, patient being unaware of indication, absence of GI symptoms, poor self-perceived health, difficulty with bowel preparation, and logistical failures. Interventions that address modifiable factors can potentially improve attendance rates for colonoscopy.
Purpose: Wireless capsule endoscopy (Given Imaging, Yoqneam, Israel) is a novel imaging technique for evaluating the small bowel, with a high diagnostic yield in obscure GI bleeding. We addressed the impact of WCE in managing patients hospitalized with obscure GI bleeding.

Methods: Inpatients undergoing WCE for obscure GI bleeding over a 3 year period were identified from retrospective chart and endoscopy database review. All patients had undergone conventional endoscopy prior to WCE. Clinical characteristics and hospital course were analyzed to determine if WCE led to changes in management and outcome.

Results: During the study period, 56 successful WCE studies were performed on 55 inpatients (age 67.82 ± 2 yrs, 25F/30M) with obscure GI bleeding, accounting for 30% of WCE studies in the same period. Two-thirds of the studies were performed for obscure-over overt bleeding. Abnormalities were seen in 36 patients (65%). The frequency of finding abnormalities trended higher in obscure-overt compared to obscure-occult bleeding (70% vs. 56%, p = ns). Findings consisted of vascular abnormalities including angiodysplasia (21 patients, 38%), fresh blood (7 patients, 13%), mucosal ulceration (4), and other potential bleeding lesions (4). Findings were in the small bowel in 29 (52%), while 7 (13%) had bleeding lesions in the stomach/oesophagus (4) or colon (3). Intervention was recommended after definitive localization of the bleeding source in 15 (27%) patients, of which two-thirds had obscure-over overt bleeding. Recommendations included push-enteroscopy (4 patients), surgery (5 patients), and other endoscopy (upper endoscopy 2, colonoscopy 3, endoscopic ultrasound 1 patient). Interventions were performed in the small bowel in 8 patients, stomach in 2 patients, colon in 2 patients, and one patient underwent angiography; 2 other patients recommended intraoperative enteroscopy declined. Potentially curative interventions (ablation, surgery) were performed in 5 patients (9%). WCE was misleading in two cases: a) angiodysplasia were seen, but the patient subsequently was found to have bled from an aortoenteric fistula, and b) a patient rebled after small bowel resection directed by WCE.

Conclusions: WCE appears to be of benefit in the inpatient setting, where definitive localization may direct intervention in about a quarter of inpatients presenting with obscure GI bleeding. Inpatient WCE may be more useful in obscure-overt bleeding. WCE findings can be misleading.

Validation of Endoscopic Gastric Analysis (EGA) as a Method To Determine Gastric Acid Output Performed during a Standard Esophagegastroduodenoscopy (EGD)

Hank S. Wang, M.D., David S. Oh, M.D., Gordon V. Ohning, M.D., Ph.D., Joseph R. Piscagna, M.D.* Dept. of Gastro., VA Greater LA Healthcare System, Los Angeles, CA and Dept. of Medicine, David Geffen School of Medicine at UCLA, LA, CA.

Purpose: Conventional gastric analysis (GA) has been used both to diagnose hypersecretory conditions, including Zollinger-Ellison Syndrome (ZES), and to monitor hypersecretory conditions under proton pump inhibitor therapy. Conventional GA using a nasogastric tube requires one hour to perform and results in a high incidence of adverse events. In this study, we have validated endoscopic gastric analysis (EGA) as a replacement technique for accurately measuring gastric acid output.

Methods: In a prospective, cross-over study, 14 patients with ZES underwent gastric analysis, first by the conventional GA and then by an endoscopic approach for 15 minutes with standard conscious sedation performed on the same day. Acid concentration was determined by titration, basal volume was recorded, and acid output was calculated. To assess reproducibility, half the study population underwent repeat testing with both procedures on a later date.

Results: Basal volume, acid concentration and acid output did not differ statistically between the two procedures. The endoscopic method had statistically greater reproducibility in measuring acid output (p = 0.04). Basal volume and acid concentration also had higher reproducibility by EGA compared to GA. One complication, an esophageal submucosal hematoma, was reported in the GA group, which was verified during subsequent EGA. No complications resulted from EGA.

Conclusions: For the first time in the U.S., we introduce a new, rapid, simple endoscopic technique to measure gastric acid secretion without stimulation and report similar values of basal volume, acid concentration and acid output compared to the conventional procedure. This endoscopic approach offers multiple advantages over the traditional exam including increased patient acceptance and improved cost-effectiveness since it can be performed during a standard upper endoscopy. These results indicate that EGA has a similar level of accuracy as the traditional GA but has greater advantages and greater reproducibility.

EUS-FNA as the Initial Diagnostic Modality in Centrally Located Primary Lung Cancers: A New Concept

Alfredo J. Hernandez, M.D., Michel Kahaleh, M.D., Grace E. White, R.N., Juan Olazagasti, M.D., Vanessa M. Shami, M.D.* Digestive Health Center of Excellence, University of Virginia, Charlottesville, VA.

Purpose: The need to safely and accurately diagnose lung neoplasms is crucial as the only prospect for a cure is surgical resection. CT-guided FNA of centrally located lesions is difficult and carries a 10 to 15% risk of pneumothorax in a population of patients with generally poor baseline lung function. A small amount of data exists on the use of EUS-FNA as the initial modality to diagnose primary lung cancer. We evaluated the diagnostic yield and complications associated with EUS-FNA of primary lung neoplasms that were adjacent to the esophagus or invaded the mediastinum at our institution.

Methods: A retrospective review of an established prospective database was performed of all patients undergoing EUS-FNA of a primary lung neoplasm during January 2001 to May 2005. The indications for the procedure, diagnostic accuracy, and complications were reviewed. The electronic medical record was examined for at least 30 days post procedure for any delayed complications or further interventions.

Results: A total of 12 cases of EUS-FNA of primary lung neoplasms were identified. All the lesions were centrally located lung neoplasm that invaded the mediastinum or were adjacent to the esophagus. The mean age was 65 (SD 9). There were 7 lesions in the right lung and 5 lesions in the left lung. The average size of the lung lesions was 52.6 (SD 23.6) × 40.8 (SD 15.5) mm. The median and mean number of FNA passes was three (range 2–4). Nine patients had no associated mediastinal lymphadenopathy. Of the 3 patients with associated mediastinal lymphadenopathy, two had positive FNA cytology for metastatic carcinoma. All the procedures provided an accurate diagnosis of the primary lung lesion without the need for further intervention (9 cases of non-small cell carcinoma, 3 cases of small cell carcinoma, and 1 case of neuroendocrine carcinoma). One patient had a small amount of hemoptysis post procedure requiring hospital admission for observation. No immediate or delayed complications occurred in the other 11 patients.

Conclusions: EUS-FNA allows for a safe and accurate initial diagnostic modality for the diagnosis of lung lesions adjacent to the esophagus or invading the mediastinum. Although further randomized prospective trials are warranted, this modality should be considered as a first step in the diagnostic armamentarium in centrally located lung lesions due to its safety and accuracy.
Purpose: To evaluate changes in renal function over time following bowel preparation with oral sodium phosphate.

Methods: Outpatients undergoing elective colonoscopy were enrolled into two study groups based on concurrent use of selected medications known to affect renal perfusion: Group I – no medications, Group II – angiotensin converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB), or diuretics. Fleet® Phospho-soda® 45 mL was taken the evening before and the morning of the exam (90 mL total, ≥ 10 hour dosing interval). Vital signs, weight, creatinine, serum electrolytes, urinalysis, and serum/urine osmolality were measured at screening, at exam, and serially between 2 days (E+2) and 3 months (E+90) after the exam. Glomerular filtration rate (GFR mL/min/1.73 m²) was estimated using the MDRD equation (Ann Intern Med 1999;130:461–70).

Results: 191 subjects have been enrolled; 121 have completed the 3-month protocol to date (Group I: n = 76, mean age 60.8 yrs; Group II: n = 45, mean age 64.6 yrs). Bowel cleansing was rated excellent or good in 89% (p < 0.001) and serum (p < 0.001) osmolality decreased from screening to exam in both groups. Mean GFR increased from screening to exam in Groups I (p = 0.02) and II (p = 0.02). Between screening and E+90, mean GFR decreased in Group I (p = 0.01), though the change was small (2.9 mL/min). Mean GFR did not change significantly between screening and E+90 in Group II. In the 15 subjects with low baseline GFR (< 60 mL/min), 7 demonstrated an increased GFR from screening to E+90, 7 were unchanged, and 1 decreased by 3 mL/min. [figure1]

Conclusions: Sodium phosphate bowel preparation is not associated with clinically significant changes in renal function in patients with or without concurrent use of ACE-Is, ARBs, or diuretics. Study enrollment is ongoing.

Evaluation of Wireless Capsule Endoscopy Interobserver Agreement Among Four Different Levels of Expertise

Kanwar R.S. Gill, M.D., Andrew K. Roorda, M.D., Margaret Allen, L.V.N., Jungwhan Lee, M.D., Taketo Yamaguchi, M.D., Kenneth F. Binmoeller, M.D.* Interventional Endoscopy Service, California Pacific Medical Center, San Francisco, CA and Department of Medical Education, St. Mary’s Medical Center, San Francisco, CA.

Purpose: To prospectively evaluate multiobserver diagnostic findings and render agreement for lesion and normal anatomical landmarks compared with gastroenterologist capsule expert (E) findings as the gold standard.

Methods: 21 subjects underwent wireless capsule endoscopy (CE). CE video was initially read by E, who has read approximately 600 prior CE cases. 2 board-certified gastroenterologist capsule trainees [1 with no experience reading CE (T#1) and 1 with minimal experience reading CE (T#2)] independently read the same 21 CE videos. A nurse (N) with no prior endoscopy experience, but with experience processing 600 prior CE cases and who received certification from an ASGE-sponsored CE training program also read the same 21 CE videos. Thumbnail findings of E, T#1, T#2, and N were reviewed and were categorized as clinically significant, clinically insignificant, or normal anatomical landmarks. Thumbnail findings of E were considered to be the gold standard and were compared against the findings of T#1, T#2, and E. Kappa and other statistical analysis were performed.

Results: 18 significant lesions were identified by E: A VM (9), bleeding (4), erosion (2), radiation colitis (1), scalpelled mucosa (1), and tumor (1). The number correctly identified by T#1 was 10 (56%), by T#2 was 16 (89%), and by N was 14 (78%). 10 insignificant lesions were identified by E: xanthoma (4) and red spot (6). The number correctly identified by T#1 was 5 (50%), T#2 was 8 (80%), and N was 9 (90%). 55 normal anatomical landmarks were identified: 1st gastric image (20), 1st duodenal image (19), and 1st cecal image (16). The number correctly identified by T#1 was 53 (96%), T#2 was 54 (98%), and N was 49 (89%). For significant lesions, 18 overcalls occurred: T#1 (10), T#2 (4), and N (4). There were 34 overcalls for insignificant lesions: T#1 (9), T#2 (10), and N (15). Kappa was 0.48 (moderate agreement) for significant lesions, 0.43 (moderate agreement) for insignificant lesions, and 0.88 (almost perfect agreement) for normal anatomical landmarks. Overall, kappa was 0.79 (substantial agreement).

Conclusions: Prior endoscopy training alone by gastroenterologists does not assure adequate recognition of pathology on CE. A nurse with no experience reading CE performed remarkably well when compared to three gastroenterologists. The role of a nurse in reading CE warrants further consideration.

Comparison of Two Dosing Regimens of Liquid Sodium Phosphate Against a Low Dose PEG Regimen

David H. Balaban, M.D., Pramod Malik, M.D., William O. Thompson, Ph.D.*, CGA, Charlottesville Gastroenterology Associates, Charlottesville, VA; Gastroenterology Associates of Tidewater, Chesapeake, VA and Biostatistics, Medical College of Georgia, Augusta, GA.

Purpose: To compare the quality of preparation (prep), tolerability and acceptability of two dosing regimens of oral sodium phosphate (NaP) with a low dose regimen of PEG solution + Bisacodyl tablets for patients undergoing elective colonoscopy.

Methods: Commercially available oral NaP, Unflavored Fleet® Phospho-soda® (C. B. Fleet Co., Inc.) and 2 L PEG 3350 solution with 4, 5 mg tablets Bisacodyl [HalfLyte® kit] (Braintree Laboratories) (PEG-L), were evaluated. NaP was administered as two doses, one the evening prior and second in the morning of the procedure. Two dosing regimens of NaP were used: a) 45 mL NaP in the evening, 45 mL in the morning of the exam (NaP-S); or b) 45 mL NaP evening, 30 mL morning (NaP-L). All doses of NaP were diluted with 12 fl. oz. of a non-sugar lemonade flavored beverage; subjects were allowed a low-residue lunch diet regimen the day before the colonoscopy. The PEG-L subjects all followed manufacturer’s prep instructions (4 Bisacodyl tablets at noon, 2 L PEG following the first bowel movement; clear liquids entire day before until after the exam). Subjects were balanced by gender and randomized to the treatment groups. Physicians, blinded to the medication, rated the quality of the prep on a Likert scale (Poor, Fair, Good and Excellent). A residual stool score (RSS, range 0 – 12) was based on the sum of 3 prep quality components: stool amount, consistency and% wall visualized, scored on a 0–4 scale (0 = best to 4 = worst). Subjects rated 12 common side effects on a 4-level scale, and rated acceptability items on a 5-level scale.

Results: Mean age of 55 years was similar in all 3 groups. Bowel cleansing rated by physicians was superior for NaP compared to PEG-L (p < 0.001), 970

<table>
<thead>
<tr>
<th>Prep Quality Group</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair/Poor</th>
<th>RSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaP-L (n = 40)</td>
<td>24</td>
<td>11</td>
<td>5</td>
<td>2.98</td>
</tr>
<tr>
<td>NaP-S (n = 40)</td>
<td>22</td>
<td>17</td>
<td>1</td>
<td>2.34</td>
</tr>
<tr>
<td>PEG-L (n = 41)</td>
<td>5</td>
<td>26</td>
<td>10</td>
<td>3.72</td>
</tr>
</tbody>
</table>
but not different between NaP doses (p = 0.644). RSS scores showed the same findings (p = 0.002). Side effect reports were similar among groups. There were no differences in ease of drinking or taste. Willingness to retake the regimen was significantly different (p = 0.019), with percent positive responses 95, 88, 73 for NaP-L, NaP-S, PEG-L.

Conclusions: Better prep was achieved with both NaP regimens over PEG-L. Subjects reported a higher willingness to repeat NaP prep. All prep had similar profiles of tolerability and acceptability.

Conclusions: Serial EUS surveillance of GIST/Ls appears to be safe for malignant transformation occurs invariably and that surgical intervention is mandatory. Periodic surveillance is another option for lesions of apparent low malignant potential. Endoscopic ultrasound (EUS) allows accurate monitoring of size and internal tissue characteristics. No data exists regarding EUS surveillance for this subset.

Methods: A prospective endoscopic database was interrogated and all cases regarding EUS surveillance for this subset.

Purpose: The natural history of gastrointestinal stromal tumours is not clearly defined. Controversy has emerged with recent guidelines suggesting that malignant transformation occurs invariably and that surgical intervention is mandatory. Periodic surveillance is another option for lesions of apparent low malignant potential. Endoscopic ultrasound (EUS) allows accurate monitoring of size and internal tissue characteristics. No data exists regarding EUS surveillance for this subset.

Results: Between 1995 and 2005, 119 patients were diagnosed with GIST/L at EUS. Median age was 64 (range 30–92), males = 57, median follow-up = 3.75 years. Location was gastric = 82, oesophageal = 34 and duodenal = 1. Median lesion size = 18 mm (range 2.5–65). Surgical resection was performed after index EUS in 26 patients. The diagnosis of GIST/L was confirmed on surgical pathology in 22, with alternative diagnoses of duplication cyst = 1, infiltrating pancreatic cancer = 1, inflammatory mass = 2. Pathology revealed borderline malignant potential in 4 cases and low malignant potential in 18 cases. 93 patients did not undergo surgery after index EUS. Serial EUS has been performed in 22 patients with apparent benign disease with median follow-up of 6.8 years. At index EUS median lesion size was 15 mm (range 5–44). Median number of surveillance EUS examinations was 2 (range 2–6) with median inter-procedure interval of 12 months. Mean lesion growth velocity was 0.82 mm/year, with unchanged size in 13. Surgery was eventually performed in 5 and pathology revealed benign tumour in all cases.

Conclusions: Serial EUS surveillance of GIST/Ls appears to be safe for lesions with benign appearance at index examination. This suggests that the natural history of this subset is characterised by slow growth and that sudden malignant transformation occurs rarely. The need for immediate surgical intervention is obviated by this management approach.

Conclusions: These results suggested that MPD stricture was related with the treatment and recurrence of pancreatic stones and could be eliminated by stenting. However, pancreatic stones can be formed even in cases without MPD stricture, it is necessary to elucidate the natural history of chronic pancreatitis.

Conclusions: There are no clinical and very few laboratory randomized studies comparing different hemoclips and other treatments for ulcer hemostasis. Our purposes were: 1) to compare deployment results of 3 clips/ulcer with InScope (INS) (Ethicon Endo-Surgery) vs. Olympus (OLY) QuickClip2’s, to evaluate long-term hemoclips retention rates, 3) to compare ulcer healing times after treatments and the influence of hemoclips retention on ulcer healing, and 4) to study safety of treatments.

Methods: 6 adult mongrel dogs with prehepatic portal hypertension were heparinized. Gastric ulcers (GU)’s were made with jumbo biopsy forceps (8 mm diameter, open) and randomized in pairs to 1 of 5 endoscopic treatments (INS, OLY, EPI, MPEC, EPI-I-MPEC) or control. Initial hemostasis was the 1 endpoint and closure of ulcers was a 2 endpoint for hemoclips. 3 hemoclips/ ulcer were placed. Animals were treated with oral PPI until ulcers healed. Failure of clip deployment on ulcers and time to initial hemostasis were recorded. At weekly FU endoscopies, ulcer stigmata, size and healing complications; and hemoclips retention were quantitated.

Results: Initial failure of hemoclips deployment was 0% for INS and 7% for OLY. See Table 1 for initial results. The time required for 50% of ulcers to heal was significantly longer for MPEC (3 weeks) or EPI-I-MPEC (3.5 weeks) than EPI (2 weeks) or OLY, INS or control (1.5 weeks). There were no major complications.

Conclusions: 1) Olympus and InScope hemoclips were similar in deployment times, success rates, and influence on ulcer healing. 2) More ulcer
sites had InScope hemoclips retained after 1 month than OLY. 3) MPEC hemostasis was faster than either hemoclip. 4) Retained hemoclips across acute ulcers accelerated healing compared to MPEC, EPI, or combination. 5) No major complications resulted.

### Results to 4 wks

<table>
<thead>
<tr>
<th>Hemostasis times (sec)</th>
<th>NaP</th>
<th>EPI</th>
<th>EPI+MPEC</th>
<th>OLY</th>
<th>INS</th>
</tr>
</thead>
<tbody>
<tr>
<td>% ulcers healed @ 2 wk</td>
<td>83%</td>
<td>8%</td>
<td>42%</td>
<td>0%</td>
<td>75%</td>
</tr>
<tr>
<td>% ulcers healed at 4 wk</td>
<td>100%</td>
<td>83%</td>
<td>100%</td>
<td>83%</td>
<td>100%</td>
</tr>
</tbody>
</table>

*p < 0.05 vs other treatments; + All these healed by 5 weeks.

### Table 2. Ulcer Sites with ≥1 Hemoclips Retained in Long-Term F/U

<table>
<thead>
<tr>
<th>Wks of F/U</th>
<th>QuickClip2</th>
<th>InScope</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 wk</td>
<td>100%</td>
<td>91.7%</td>
</tr>
<tr>
<td>4 wks</td>
<td>50%</td>
<td>58.3%</td>
</tr>
<tr>
<td>8 wks</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>12 wks</td>
<td>0%</td>
<td>33%</td>
</tr>
<tr>
<td>16 wks</td>
<td>0%</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

### 974 Small, Microcrystalline Cellulose (MCC)-Free NaP 32 (INKP-102)

#### Methods

Eligible scheduled colonoscopy pts were randomized to INKP-102 in a Phase 3 investigator-blinded multicenter trial. A Patient Questionnaire showed excellent overall colon and superior ascending colon cleansing to V (p = 0.039). Pts were randomized to either 60 g V (40 tabs), 48 g INKP-102, or 42 g (28 tabs). Blood samples were collected from 931 adults scheduled for colonoscopy who took either Visicol® or INKP-102. The data demonstrate a strong statistical pt preference for the 32 tab INKP-102 dosing regimen over V, as shown by pt responses. INKP-102 32 tabs are smaller and require ingestion of less fluid than V. This is the preferred dosing regimen for bowel preparation. Use of INKP-102 may have a significant and positive impact in pts’ overall decision to schedule a colonoscopy.

### Conclusions

- A total of 816 pts were randomized; 704 pts were included in the All Assessed population. While the study regimen for the INKP-102 arms (60 or 48g) was more easily tolerated by pts compared to the V regimen (p = 0.039), pt preference was most consistent for 48g (32 tab) This abstract addresses only V and INKP-102 32 tab pt preference data, for those questions where ≥90% of the population responded. (Table). There was no difference in h/o of prior colonoscopy among arms.

### Purpose

The transient nature of electrolyte changes following ingestion of NaP bowel prep is well documented (Hookey, 2002). Safety data from 2 trials were collected from 931 adults scheduled for colonoscopy who took either Visicol® or INKP-102, a next generation cellulose-free NaP tablet. These multicenter, investigator-blinded studies evaluated the changes in clinical lab findings of 3 doses of INKP-102 compared to 60 g V.

### Methods

Pts were randomly assigned to either 60 g V (40 tabs) or INKP-102 doses: 60 g (40 tabs), 48g (32 tabs) or 42g (28 tabs). Blood samples were collected in 14 days prior to colonoscopy (screening) and immediately before the procedure.

### Results

Significant elevations from mean screening values were observed for serum levels of P and Na (p < 0.0001). Generally, mean P increases were smaller for INKP-102 (3.64 mg/dL, all doses) than for 60 g V (4.06 mg/dL); p = 0.0002. P changes from screening tended to increase with increasing doses of INKP-102; change from screening P was significantly reduced in pts who took 48 g INKP-102 vs 60 g V (p = 0.0001). Increases in Na from screening levels tended to be smaller with lower doses of INKP-102. Smaller proportions of pts shifted their Na from normal to elevated (7% V vs 12% INKP-102); however for pts with increased Na at screening, the value was WNL at colonoscopy, 83% V vs 75% INKP-102. Significant reductions from mean screening levels were observed in serum Ca, K, Mg and BUN (p < 0.0001). Mean changes in serum K levels were smaller in pts taking 60 g INKP-102 than 60 g V (−0.61 vs. −0.69, p = 0.0120); 21% of 60 g V pts shifted to low K vs 19% INKP-102. Shifts from normal to lower Ca were not observed in 60g V pts; 15 pts shifted to low Ca in the INKP-102 grp. Only 2 pts shifted from WNL for Mg at screening to low; 1 in each treatment grp. Decreases from mean screening values in BUN were smaller in the INKP-102 grp. vs 60g V group (p = 0.0006). Overall, mean serum Cr was similar among the treatments. Pts (n = 28) with elevated screening Cr tended to decrease to WNL at colonoscopy, 3 of 9 V pts and 12 of 19 INKP-102.

### Conclusions

INKP-102 48 g had significantly lower P change from baseline than higher doses. Overall, expected electrolyte changes for INKP-102 and Visicol were mild, self-limiting and followed a dose response trend with smaller changes at lower doses.

### Knowledge of Appropriate Indications for EUS by Physicians In-Training and Practice across Specialties

Parantap Gupta, M.D., Robert F. Wong, M.D., Manoop S. Bhutani, M.D., F.A.C.G.* Internal Medicine, University of Texas Medical Branch, Galveston, TX.
Purpose: EUS has evolved as a useful imaging and interventional modality for work-up and treatment of a variety of lesions. Appropriate referral for EUS requires knowledge, which may be variable, about EUS by non-gastroenterologists. We assessed the knowledge of indications and the utility of EUS among participants at a regional internal medicine (IM) update conference after a lecture about EUS and among physicians working at a large multispecialty academic institution with an active program in EUS.

Methods: A survey was done using a modification of previously published questionnaire. This questionnaire was distributed to all the participating members at a regional IM conference who attended a lecture about EUS and to faculty and residents in IM, gastroenterology (GI) and surgery at University of Texas Medical Branch (Galveston, TX). The correct answers were then compared among various groups of responders and with respect to organ systems.

Results: Table 1 compares the results of the participants in training and practice across specialties about indications of EUS for different organ systems. Gastroenterologists were more likely to be correct than non-GI physicians (p < 0.001). There were no significant differences between the mean scores of faculty vs. residents, surgeons vs. non-surgeons, referring vs. non-referring physicians and participants vs. non-participants. Respondents were more likely to identify an appropriate upper GI indication and less likely to identify an appropriate colo-rectal indication (p < 0.001).

Conclusions: Although EUS has a number of diagnostic and therapeutic clinical applications, non-GI physicians appear to have a reasonable knowledge about its indications. A single lecture on EUS indications can serve as an effective tool in educating practicing non-GI physicians who may be out-of-training for many years and may not have been exposed to this technology in training. Knowledge about lower GI indications for EUS is less when compared to upper GI indications.

Table 1.  

<table>
<thead>
<tr>
<th></th>
<th>Esophageal (%)</th>
<th>Gastrointestinal (%)</th>
<th>Hepatopancreaticobiliary (%)</th>
<th>Colorectal (%)</th>
<th>Mean (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (100%)</td>
<td>68.2</td>
<td>82.4</td>
<td>75.1</td>
<td>63.9</td>
<td>73.6</td>
</tr>
<tr>
<td>Participant (38.8%)</td>
<td>65</td>
<td>76.3</td>
<td>80.5</td>
<td>54.4</td>
<td>69</td>
</tr>
<tr>
<td>Non-participant (61.2%)</td>
<td>70.2</td>
<td>86.2</td>
<td>71.8</td>
<td>84.9</td>
<td>78.3</td>
</tr>
<tr>
<td>Faculty (59.2%)</td>
<td>69.8</td>
<td>81.6</td>
<td>79.3</td>
<td>61.1</td>
<td>72.6</td>
</tr>
<tr>
<td>Resident (37.9%)</td>
<td>66.7</td>
<td>85.9</td>
<td>69</td>
<td>68.6</td>
<td>72.5</td>
</tr>
<tr>
<td>GI (13.6%)</td>
<td>82.9</td>
<td>97.6</td>
<td>91.4</td>
<td>73.2</td>
<td>86.3</td>
</tr>
<tr>
<td>Non-GI (86.4%)</td>
<td>65.8</td>
<td>80</td>
<td>72.6</td>
<td>62.4</td>
<td>70.1</td>
</tr>
<tr>
<td>Referral (51%)</td>
<td>71.5</td>
<td>73</td>
<td>75.6</td>
<td>64.1</td>
<td>71.1</td>
</tr>
<tr>
<td>Non-referral (46.6%)</td>
<td>64.2</td>
<td>81.6</td>
<td>73.8</td>
<td>61.5</td>
<td>70.3</td>
</tr>
<tr>
<td>Surgeon (8.7%)</td>
<td>75.6</td>
<td>77.8</td>
<td>64.4</td>
<td>77.8</td>
<td>73.9</td>
</tr>
<tr>
<td>Non-surgeon (91.3%)</td>
<td>67.3</td>
<td>82.7</td>
<td>76</td>
<td>62.1</td>
<td>72</td>
</tr>
</tbody>
</table>

Conclusions: Patients given consent information via videotape had superior test scores to those who received consent information directly from their physicians. Administration of a multiple-choice test led to increased retention of information provided during the consent process.

Impact of Bowel Habits on Successful Bowel Preparation
Jeremiah Karz, M.D.,* Vinod Kurupath, M.D., Archana Nair, M.D., Deepak Mahajan, M.D., Radhakrishna Kalakontla, M.D., Masi Khaja, M.D., Alex Gershennorn, M.D., Kiran Bhat, M.D., Joseph Quagliata, M.D. Division of Gastroenterology, The Brooklyn Hospital Center, Brooklyn, NY.

Purpose: Incomplete bowel cleansing has ramifications in terms of timely diagnosis and treatment as well as utilization management and overall healthcare efficiency. There may be physiologic factors impacting on bowel cleansing that need to be considered. The goal of this study is to determine whether patients’ perceptions of their bowel habits were in any way predictive of adequate bowel prep using a standard regimen. We also investigated other factors.
which may affect bowel preparation such as presence of diverticulosis and history of abdominal surgery.

**Methods:** Patients referred for elective colonoscopy were included in the study and given standard PEG-3550 bowel preparation. On the day of colonoscopy, the patients were asked about their general bowel habits and bowel frequency. An endoscopist, blinded to the nature of the preparation, judged the result of the bowel cleansing. For purposes of analysis, the colon was separated into left, right, and transverse and the presence of solid, liquid, and semisolid stool in each of these segments was reported separately. A positive finding for each category of stool in each segment was assigned a value of one and the total sum was calculated for a composite stool grade (0 = no stool in entire colon, 9 = all types of stool were seen in all segments).

Standard t-test and ANOVA analysis was used for evaluating composite stool grade data.

**Results:** Data have been collected from 202 patients. The mean age was 60.5. There were 136 females and 66 males. The mean composite stool grades for the groups never, rarely, sometimes and always experiencing constipation were 2.5476, 2.4655, 2.5781, and 2.5667 respectively. (ANOVA P-value = 0.989259.) There was a statistically insignificant trend toward better cleansing in patients without diverticulosis compared to those with diverticulosis (2.35 vs. 2.71, t-test, P value = 0.2750). Presence or absence of prior abdominal surgery did not appear to be a statistically significant factor in bowel cleansing (2.56 vs 2.48, t-test, P value = 0.7435).

**Conclusions:** These preliminary data indicate that patients’ perceptions of their bowel habits are not predictive of successful bowel cleansing. Multivariate analysis may yield patterns of demographics and bowel habits which may be useful in predicting successful bowel cleansing. Bowel preparation could then be adjusted individually for better outcome, thereby saving time and money while optimizing our ability to detect colonic lesions.

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**The Experience of a Newly-Developed Capsule Endoscope**

Haruhiko Ogata, M.D., Koichiro Kamai, M.D., Hirokiyuki Imaeda, M.D., Koichi Ato, M.D., Tadakazu Hisamatsu, M.D., Sasumu Okamoto, M.D., Yasushi Iwao, M.D., Yoshiro Sagino, M.D., Masaki Kitajima, M.D., Toshihumi Hibi, M.D.* Center for Diagnostic and Therapeutic Endoscopy, Keio University Hospital, Tokyo, Japan; Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan; Department of Diagnostic Radiology, Keio University School of Medicine, Tokyo, Japan; Department of Surgery, Keio University School of Medicine, Tokyo, Japan.

**Purpose:** Current limitations of the commercially available capsule endoscopy device include sub-optimal image resolution and sharpness. In collaboration with Olympus Medical Systems Co, Japan, we have developed a new capsule endoscope. The following is the up to date clinical experience with this new device.

**Methods:** Features of a new capsule endoscope are; 1. upgrade resolution, depth of the field, and brightness of the image, by improving the optical system. 2. contains the new function to adjust the level of lighting automatically coordinate with the brightness around, 3. original real time handy display viewer. In a prospective fashion, patients referred for evaluation of the small bowel were included in this study. As part of the inclusion criteria, patients agreed to undergo either small bowel Barium X-ray and/or subsequent push enteroscopy. Capsule images were reviewed by four physicians. Results of capsule exams were compared to Barium X-ray findings and/or push enteroscopy.

**Results:** Up to date this ongoing study has accrued the number of patients, namely, 40 patients have been enrolled, and the total estimated number of patients will be 53. The representative cases include obscure small intestinal bleeding with chronic renal failure, A-V malformation, multiple tiny erosions with SLE, multiple edematous villi with AIDS, and suspicious of malignant lymphoma. This new capsule provided excellent visualization of the precise construction of small intestinal villi, in some cases even a small-sized-erosion was found which was hardly detected by Barium X-ray. Additionally, this new technology allowed for clear real time image interpretation on an LCD display. This handy viewer could be helpful for detecting the retention of capsules in stomach or small intestine, and for the confirmation of capsules passing through ileo-cecal valve.

**Conclusions:** Our preliminary experience suggests that this new capsule endoscopy provides higher resolution images as well as real time small bowel visualization, both of these are significant improvements over currently available technology. This study has been funded by Olympus Medical Systems Co, Japan.

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**Retrograde Double Balloon Endoscopy (rDBE) for Completion Colonoscopy in Patients with Incomplete Examination Using a Conventional Colonoscope**

Shabana F. Pasha, M.D., M. Edwyn Harrison, M.D.,* Ananya Das, M.D., Nancy Malty, R.N., Kristine Arnell, Jonathon A. Leighton, M.D. Dept. of Gastroenterology & Hepatology, Mayo Clinic College of Medicine, Scottsdale, AZ.

**Purpose:** To evaluate the success rate of rDBE for completion colonoscopy in patients who had incomplete examination using a conventional colonoscope.

**Background:** The success rate of colonoscopy with a conventional colonoscope is 80–95%. An estimated 14.2 million screening colonoscopies in the US would lead to at least 710,000 incomplete examinations. There is no standard technique to offer patients with incomplete colonoscopy. Double balloon endoscopy is a new technique to effectively examine the entire small intestine by antegrade and retrograde approach. rDBE similarly may facilitate difficult colon examinations.

**Methods:** A retrospective chart review was conducted of patients who had rDBE after incomplete colonoscopy using a conventional colonoscope.

**Technique:** rDBE was performed by the push and pull method. The double balloon endoscope has a balloon at the tip of the scope and sliding overtube. The endoscope was sequentially pushed and withdrawn with inflation and deflation of the balloons to prevent looping of the colon. The technique allows diagnostic and therapeutic interventions, including biopsies, polypectomy and control of bleeding.

**Results:** Seven patients underwent rDBE after incomplete colonoscopy from April to June 2005.

1. rDBE had a completion rate of 88% (6 of 7 patients). Cecal intubation was achieved in 6 patients and the ascending colon was reached in one patient.
2. Therapeutic success rate was 100%. Seven polyps were resected in 6 patients, inclusive of the patient in whom rDBE was incomplete.
3. rDBE was performed under conscious sedation using fentanyl (165 mcg, range 150–175 mcg) and midazolam (7 mg, range 5–10 mg).
4. Total procedure time for rDBE, including sedation and polypectomy was 60.8 min (range 36–101 min).

**Results of Double Balloon Colonoscopy**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Gender</th>
<th>Completion rate (no of pts)</th>
<th>Therapeutic success (polypectomy)</th>
<th>Procedure Time (minutes)</th>
<th>Conscious sedation (Fentanyl &amp; Midazolam)</th>
</tr>
</thead>
<tbody>
<tr>
<td>78 (67–81)</td>
<td>6F, 1M</td>
<td>6/7 (88%)</td>
<td>7/7 polyps (100%)</td>
<td>60.8 range (36–101)</td>
<td>Fentanyl 165 mcg (range 150–175 mcg) Midazolam 7 mg (5–10 mg)</td>
</tr>
</tbody>
</table>

Mayo Clinic, Scottsdale.

**Conclusions:** rDBE was effective in completing colon evaluation in 88% of patients with incomplete examination using conventional colonoscopy. This technique had a therapeutic success rate of 100%. Like conventional colonoscopy, rDBE could be performed under conscious sedation and in a reasonable time period.
The Early Bird Gets the . . . Cecum? Higher Colonoscopy Completion Rates in the Morning Versus Afternoon
Christopher D. Wells, M.D., Russell I. Heigh, M.D.,* Jose Hernandez, Virender K. Sharma, M.D. Gastroenterology & Hepatology, Mayo Clinic, Scottsdale, AZ and Biostatistics, Mayo Clinic, Scottsdale, AZ.

Purpose: To investigate any differences in colonoscopy completion rates in the morning versus the afternoon, and to identify any factors that may lead to a discrepancy.

Methods: The Clinical Outcomes Research Initiative (CORI) database was searched for colonoscopy completion rates in the morning versus afternoon in outpatient undergoing exams intended to reach the cecum. Additional information regarding quality of bowel preparation was obtained for each procedure. All bowel preparations were initiated on the evening prior to the exam. The CORI database requires assignment of prep quality among various categories: “excellent,” “good,” “fair, adequate exam,” “fair, exam compromised” and “poor,” and these were recorded for each group. The Chi Square statistic was used to compare rates of completion as well as prep quality.

Results: 6078 exams were included over a 12 months period from January 2004–January 2005. Of these exams, 3730 were performed in the morning and 2348 were performed in the afternoon. 3549 (95.2%) of the morning procedures were completed to the cecum while 2201 (93.7%) of the afternoon exams were completed (p = 0.02) A significant difference in bowel preparation quality was observed between the morning and afternoon groups. The afternoon group bowel preparations were of lower quality and were more likely to be rated as “fair, adequate exam” (p < 0.001) “fair, exam compromised” (p < 0.001) or “poor” (p = 0.002) while the morning group bowel preparations were of higher quality and were more frequently recorded as “excellent” (p < 0.001) or “good” (p < 0.001).

Conclusions: Colonoscopy completion rates were lower in the afternoon compared to the morning in outpatient undergoing colonoscopies. Lower quality in colon prep appears to be one of the factors contributing to this lower rate. The impact of several other variables is also being investigated, the results of which are pending at this time.

Use of Tegaserod along with Polyethylene Glycol Electrolyte Solution for Colonoscopy Bowel Preparation: A Prospective, Randomized, Double-Blind, Placebo-Controlled Study
M. R. Sanaka, M.D.,* D. Super, M.D., K. Mullen, M.D., R. Joseph, M.D., A. Kyprianou, M.D., S. Thiruppathi, M.D., R. Ghanta, M.D., R. Ferguson, M.D., A. McCullough, M.D. Gastroenterology, MetroHealth Medical Center, Cleveland, OH.

Purpose: Polyethylene glycol electrolyte solution (PEG-EL) is widely used for colonoscopy preparation. The need to drink a large volume and associated nausea and bloating are impediments to patient tolerance and compliance. A significant number of patients have inadequate bowel preparation despite taking PEG-EL. Aims of our study were to determine the effect of Tegaserod, a prokinetic agent, when given in addition to PEG-EL on patient tolerance, nausea, bloating and the quality of colonic preparation.

Methods: In this prospective, randomized, placebo-controlled, double-blind study, a total of 130 patients scheduled for colonoscopy were enrolled. They were instructed to take three pills of either Tegaserod 6 mg each or placebo (one pill twice on the day prior to and third pill in the morning on the day of colonoscopy). Patients were instructed to drink 4L of PEG-EL in the evening prior to the day of colonoscopy. Patients rated their tolerance of preparation on a 5 point Likert scale (1 = no distress, 5 = unable to finish). A score of 3 or less was considered acceptable, a score of 4 and 5 unacceptable. Nausea and bloating were rated on a 4 point scale (1 = none, 4 = severe). The endoscopist rated the quality of preparation on both left and right sides of colon on a 5 point scale (1 = no retained liquid, 5 = retained solid stool). Willingness of patients to repeat the same preparation in the future was recorded. Mann Whitney U and Chi-Square tests used, p < 0.05 for significance. Assuming that 65% in placebo group and 90% in Tegaserod group will have acceptable tolerance, a sample size of 56 per group is required for detecting the difference with a power of 90% and a Type I error of 0.05.

Results: 55 patients in placebo group and 58 patients in Tegaserod group completed the study.

Conclusions: Addition of Tegaserod to PEG-EL with this dosing strategy during colonoscopy preparation does not improve nausea, bloating, patient tolerance or the quality of colonic preparation.

A Two Year Experience of Propofol/Meperidine in a Community Based Surgery Center
James A. Sinnott, M.D.,* Edward J. Fricker, M.D., Shawn Rogers, R.N., Tana Maccara, R.N. Gastroenterology, South Georgia Medical Center, Valdosta, GA.

Purpose: To evaluate the safety of propofol/meperidine administered by a physician and registered nurse in a community based surgical center.

Procedures Propofol/Meperidine

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopy</td>
<td>2254</td>
<td>64%</td>
</tr>
<tr>
<td>EGD</td>
<td>1248</td>
<td>36%</td>
</tr>
<tr>
<td>Total</td>
<td>3502</td>
<td>100%</td>
</tr>
</tbody>
</table>

Methods: For the last two years we have used a combination of Propofol/Meperidine in a community based surgical center. Prior to the use of Propofol all staff members underwent additional training including ACLS and airway management techniques.

Results: All complications observed were transient and none required hospitalization excluding post polypectomy bleeds.

Complications with propofol/meperidine

<table>
<thead>
<tr>
<th>Type of Complication</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total complications</td>
<td>135</td>
</tr>
<tr>
<td>O2 decrease</td>
<td>41</td>
</tr>
<tr>
<td>Hypotension</td>
<td>67</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>1</td>
</tr>
<tr>
<td>Vasovagal</td>
<td>3</td>
</tr>
<tr>
<td>Narcan admin</td>
<td>1</td>
</tr>
<tr>
<td>I.V. fluids</td>
<td>4</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>7</td>
</tr>
<tr>
<td>Local reaction to propofol/meperidine</td>
<td>2</td>
</tr>
<tr>
<td>Solu-Cortef admin.</td>
<td>2</td>
</tr>
<tr>
<td>Nasal airway placement</td>
<td>4</td>
</tr>
<tr>
<td>Post polypectomy bleed</td>
<td>3</td>
</tr>
</tbody>
</table>

May 2003- May 2005
Conclusions: This study has demonstrated the continued safety of propofol/meperidine after two years of use in a community-based ambulatory surgical center. These complications are similar to our previously published midazolam/meperidine data.

Improvement in Discharge Time with the Use of Propofol/Meperidine vs. Midazolam/Meperidine in a Community Hospital

James A. Sinnott, M.D., Edward J. Fricker, M.D., Tana Macera, R.N.
Gastroenterology, South Georgia Medical Center, Valdosta, GA.

Purpose: This study was initiated to identify improvement in the procedural time with the use of propofol/meperidine compared to midazolam/meperidine in our community hospital.

Methods: A sampling of charts was drawn comparing the procedure start time to discharge from the hospital GI-Lab recovery room for propofol/meperidine and versed/meperidine. Patients were discharged based on standardized alertness criteria.

Results:

EGD Time from Procedure Start Till Discharge

<table>
<thead>
<tr>
<th>Drug given</th>
<th>propofol/meperidine</th>
<th>midazolam/meperidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of procedures</td>
<td>118</td>
<td>115</td>
</tr>
<tr>
<td>average patient age</td>
<td>51.3 years</td>
<td>63.0 years</td>
</tr>
<tr>
<td>Time</td>
<td>50.31</td>
<td>70.57</td>
</tr>
</tbody>
</table>

Difference in time to discharge 20.26 min.

Colonoscopy Time Till Discharge

<table>
<thead>
<tr>
<th>Medication used</th>
<th>propofol/ meperidine</th>
<th>midazolam/ meperidine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>108</td>
<td>106</td>
</tr>
<tr>
<td>Average patient age</td>
<td>56.5 years</td>
<td>60.2 years</td>
</tr>
<tr>
<td>Time from procedur start till discharge</td>
<td>64.45 min</td>
<td>78.33 min</td>
</tr>
</tbody>
</table>

Difference in time to discharge 13.88 min.

Conclusions: This study demonstrates the improvement in recovery time observed with the use of propofol/meperidine. It combines several improvements that propofol offers, including rapid onset of sedation and improvements in recovery time.

A Prospective Outcomes Study and Cost Analysis of Post-Procedural Radiologist’s Interpretation of ERCP X-Ray Films

Steve Kucera, M.D., Gerard Isenberg, M.D., Amitabh Chak, M.D., Richard Wong, M.B.B.S., Ashley Fauls, M.D., Michael Sivak, M.D.
Gastroenterology, Case Western Reserve University/University Hospitals of Cleveland, Cleveland, OH.

Purpose: The aims of this study are to prospectively determine if post-ERCP x-ray film reading by radiologists alters clinical decision-making and to determine whether the current standard of care is a cost-efficient practice.

Methods: A preliminary, prospective analysis of 145 patients undergoing ERCP over the course of 4 months was performed. A separate endoscopist (E), not involved in the patient’s care, reviewed the radiologist’s (R) report of the ERCP x-ray films to determine if there was either concordance or discordance with the procedural findings. The patients’ clinical courses were prospectively followed to determine if clinical decision-making was affected by the R’s interpretation of the x-ray films. Secondarily, a cost analysis was performed.

Results: Of the 145 patients, there was an overall discordance between the E and R in 80 of the cases (55%). One patient underwent a laparoscopic common bile duct exploration based on R’s interpretation that was discordant to the E’s, however, the abnormality reported by the R was not confirmed surgically. In two further cases, additionally imaging studies (liver MRI and abdominal CT scan) were ordered based upon R’s readings which were discordant from the E’s; again, the E’s findings were validated by the further imaging. In the other 77 cases, no additional procedures, imaging, or laboratory tests were ordered. In total, 130 cholangiograms with 61 discordances (47%), and 72 pancreatograms with 27 discordances (38%) were evaluated. Radiologists were reimbursed $5,395 for interpretation of ERCP x-ray films, and over the course of a year, their reimbursement would be greater than $17,000. Extra testing based on discordant reports resulted in an additional $2,510 of reimbursement for 3 patients.

Conclusions: The R’s interpretation of ERCP films was inadequate, with a 47% discordance rate among cholangiograms and a 38% discordance rate among pancreatograms. The routine practice of post-procedure ERCP x-ray film interpretation by R altered clinical practice in only 3 of the 80 discordant cases; subsequent care did not confirm R’s findings and imparted increased risk to the patients. This practice proved to be a misallocation of resources and should not be continued. Additional patient enrollment, multicenter involvement, and continued cost analysis are needed to verify these preliminary findings.

Colonoscopy Withdrawal Times and the Presence or Absence of Colonic Adenomas at Screening Colonoscopy

Athan P. Kartsonis, M.D., Kim Howe, R.N. Department of Gastroenterology, Melbourne ASC, Melbourne, FL.

Purpose: To determine the relationship between colonoscopy withdrawal time, adenoma detection, and adenoma size during screening colonoscopy in an ambulatory private practice setting.

Methods: 97 consecutive patients undergoing screening colonoscopy included 46 males (47%) and 51 females (53%). No patient had undergone previous colonoscopy or colon resection surgery. Patients with first degree family members suffering from colon cancer were excluded from the study. The examination was performed with Olympus colonoscopes after either phosphosoda or PEG lavage purge. Diprovan was used for sedation and all exams were performed by one endoscopist (apk). Upon entering the cecum and identifying the ileocecal valve withdrawal timing was initiated with a stop watch.

Results: The mean age of the study patients was 60.7 years. All exams were successful to the cecum. The average age of patients with no adenomas was 59.1 yrs, with adenomas 64.3 years.

Adenoma Incidence:

- Patients with adenomas: 26 (27%)
- Patients with adenomas >1 cm: 13 (13%)
- Patients with adenomas >2 cm: 3 (3%)

Colonoscopy Withdrawal Times:

Mean withdrawal time all patients: 12 min 37 sec
Mean withdrawal time in patients with no adenomas: 10 min 59 sec
Mean withdrawal time in patients with adenomas: 14 min 9 sec
Mean withdrawal time in patients with adenomas >1 cm: 21 min 37 sec
Mean withdrawal time in patients with adenomas >2 cm: 30 min 50 sec

Conclusions: 1. The adenoma incidence rate at screening colonoscopy in this study was 27%.
2. Withdrawal time for patients with no adenomas detected (10:59) was longer than the recently recommended 6 minute minimum time for withdrawal in negative exams.
3. Withdrawal times for more complex adenomas (>1 cm) were substantially longer than withdrawal times for the total adenoma subset. (p < .01)
4. 3% of patients harbored adenomas >2 cm in diameter.
5. Screening colonoscopy in private practice should be successful to the cecum in a very high percentage of patients.

Oral INKP-102 Provides Effective Colon Cleansing for Afternoon Colonoscopies

David M. Kastenberg, M.D., David Stanton, M.D., Nav Grandhi, M.D., Martin Rose, M.D., Rohn Karlstadt, M.D., Sandra Lottes, Pharm.D., Nancy Ettinger. GI, Thomas Jefferson Univ, Philadelphia, PA; GI,
Purpose: Afternoon colonoscopy is predictive of an incomplete procedure. In patients (pts) using a PEG purgative, this is largely due to poor bowel cleansing (Shah et al., GIE 2005; 61:AB155). The aim of this study is to assess the effectiveness of a new microcrystalline cellulose-free sodium phosphate (NaP) tablet purgative (INKP-102) in pts undergoing afternoon colonoscopy.

Methods: A prospective, multicenter, randomized investigator-blinded study to assess the safety and efficacy of 2 oral regimens of INKP-102 compared to Visicol® Tablets (NaP). For all study arms, medication dosing was split between the evening before (eve) and the next morning (morn) 3–5 hours before the colonoscopy. 704 adults were randomized to either Visicol 60 g (20 tabs eve, 20 tabs morn), taken 3 tabs q 15 min, or to INKP-102: 60 g (20 tabs eve, 20 tabs morn), taken 4 tabs q15 min, or INKP-102: 48g (20 tabs eve, 12 tabs morn), taken 4 tabs q15 min. Colon cleansing was scored as poor, fair, good, or excellent using a 4-point scale on a Physician Questionnaire. Effective colon cleansing was defined as achieving a “good” or “excellent” score. Combining “good” and “excellent” scores, a post-hoc analysis of morning (before 12 pm) vs. afternoon (after 12 pm) colon cleansing was performed to assess efficacy.

Results:

Comparison of Pts Achieving Good/Excellent Cleansing Scores

<table>
<thead>
<tr>
<th>Visicol</th>
<th>INKP-102</th>
<th>INKP-102</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 g (40 tab)</td>
<td>60 g (40 tab)</td>
<td>48 g (32 tab)</td>
</tr>
<tr>
<td>N = 235 (%)</td>
<td>N = 233 (%)</td>
<td>N = 236 (%)</td>
</tr>
</tbody>
</table>

AM Colonoscopy

Overall Colon Cleansing

138/146 (94) 144/149 (97) 144/151 (95)

Ascending Colon Cleansing

131/146 (90) 141/149 (95) 142/151 (94)

PM Colonoscopy

Overall Colon Cleansing

84/89 (94) 82/84 (98) 81/85 (95)

Ascending Colon Cleansing

77/79 (86) 79/84 (94) 78/85 (92)

P value¹ NS NS NS

¹Comparison of proportion of pts with good or excellent colon cleansing between AM and PM within each treatment group; NS defined as ≥ 0.05 level

Conclusions: Visicol and INKP-102, both 60 g and 48 g, are highly effective purgatives for afternoon colonoscopy. Flexibility of either AM or PM scheduling is maintained without the risk of an incomplete procedure due to inadequate bowel prep.

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Polyflex® Stent Placement for Palliation of Dysphagia Due to Locally Advanced Gastroesophageal Junction and Esophageal Malignancy during Neoadjuvant Therapy

Michael Saunders, M.D., Scott Lee, M.D., Bruce Tang, M.D., Roanne Selinger, M.D., Brant Oelschlager, M.D., Michael Kimney, M.D.*

Gastroenterology, University of Washington, Seattle, WA.

Purpose: Combined modality therapy with preoperative chemoradiotherapy followed by surgery is commonly used for patients with stages IIb and III disease. Such patients may experience dysphagia with weight loss due to the malignant stricture. This has been traditionally managed with surgical feeding jejunostomy. We report our experience with the use of Polyflex® (Boston Scientific), an expandable, removable silicon stent, as an alternative to feeding jejunostomy in this setting.

Methods: Nine consecutive patients with locally advanced (Stage IIb, III) esophageal or gastro-esophageal junction carcinomas underwent Polyflex® stent placement by standard upper endoscopy with fluoroscopic guidance. All patients had significant dysphagia and progressive weight loss requiring consideration for feeding jejunostomy. All patients were to undergo planned neoadjuvant chemoradiotherapy prior to surgical resection.

Results: see Table

<table>
<thead>
<tr>
<th>Patient</th>
<th>Stage</th>
<th>Stent length, body diameter</th>
<th>Palliation of dysphagia and malnutrition?</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T3N0M0</td>
<td>12 cm, 16 mm</td>
<td>Yes</td>
<td>Stent removed at restaging after 6 weeks</td>
</tr>
<tr>
<td>2</td>
<td>T3N1M0</td>
<td>9 cm, 16 mm</td>
<td>Yes</td>
<td>Received primary chemo/XRT; stent remains patent at 6 months</td>
</tr>
<tr>
<td>3</td>
<td>T3N0M0</td>
<td>9 cm, 16 mm</td>
<td>Yes</td>
<td>Stent migrated after neoadjuvant therapy; removed at esophagectomy</td>
</tr>
<tr>
<td>4</td>
<td>T3N1M0</td>
<td>9 cm, 16 mm</td>
<td>Yes</td>
<td>Stent migrated after neoadjuvant therapy; removed at esophagectomy</td>
</tr>
<tr>
<td>5</td>
<td>T3N1M0</td>
<td>9 cm, 18 mm</td>
<td>Yes</td>
<td>Stent migrated after neoadjuvant therapy; removed at esophagectomy</td>
</tr>
<tr>
<td>6</td>
<td>T3N1M0</td>
<td>9 cm, 21 mm</td>
<td>No</td>
<td>Esophageal perforation; local invasive, metastatic disease at surgical exploration</td>
</tr>
<tr>
<td>7</td>
<td>T3N0M0</td>
<td>9 cm, 18 mm</td>
<td>Yes</td>
<td>Received primary chemo/XRT; stent remains patent at 6 months</td>
</tr>
<tr>
<td>8</td>
<td>T3N1M0</td>
<td>12 cm, 18 mm</td>
<td>Yes</td>
<td>Received primary chemo/XRT; stent remains patent at 4 months</td>
</tr>
<tr>
<td>9</td>
<td>T3N1M0</td>
<td>9 cm, 18 mm</td>
<td>No</td>
<td>Stent migrated proximally, replaced; feeding jejunostomy placed due to persistent nausea/vomiting</td>
</tr>
</tbody>
</table>

Conclusions: Polyflex® stent placement was successful in all patients, was effective in palliation of dysphagia and malnutrition in the majority (7 of 9), and associated with infrequent complications (1 tumor perforation associated with stent placement; stent migration following neoadjuvant therapy occurred in 3 patients but did not cause symptoms and the stents were easily removed at the time of esophagectomy). Polyflex® stent placement should be considered as a management option for patients with dysphagia and weight loss due to locally advanced esophageal or GE junction carcinomas.

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Large Balloon Dilatation with Sphincterotomy for Management of Common Bile Duct Stones Difficult To Extract with Standard Methods in Poor Surgical Candidates

Khalid M.Z. Darwish, M.D.* Internal Medicine Department, Faculty of Medicine – Tanta University, Tanta, Egypt.

Purpose: Bile duct stones are still present in 10–14% of patients after the application of conventional endoscopic extraction techniques and require additional procedures for duct clearance. Elderly with chronic illnesses and patients with other co-morbidities represent challenge for surgical intervention. This work is a prospective evaluation of large balloon dilatation with sphincterotomy for extraction of difficult CBD stones in poor surgical candidate patients.

Methods: Twenty two patients in whom stone extraction have failed with standard endoscopic sphincterotomy and standard balloon and/or basket extraction were then used to remove the stones. Stone extraction with this method was successful in 17 patients (77.3%), in 5 patients (22.7%) either 2nd session with re-dilatation with a larger balloon alone or together with mechanical lithotripsy were required to clear the CBD. No major complications occurred.

Conclusions: Large diameter balloons dilatation with sphincterotomy is a viable alternative for removal of difficult CBD stones when standard methods fail in poor surgical candidates.
A Prospective Assessment of the Diagnostic Utility and Complications of Endoscopic Ultrasound-Guided Fine Needle Aspiration: A Large Single Endosonographer’s Experience from a Newly Developed Program

Mohamad A. Eloubeidi, M.D., M.H.S.,∗ Ashutosh Tamhane, M.D., M.S.P.H. Division of Gastroenterology and Hepatology, University of Alabama at Birmingham, Birmingham, AL.

Purpose: It is currently unknown, whether with adequate third tier EUS training, a newly developed EUS program can produce results similar to those of experienced EUS centers. We, therefore, prospectively evaluated the diagnostic accuracy and major complications of EUS-FNA performed by a single endosonographer in a newly developed program and compared our results to those of expert centers.

Methods: We prospectively evaluated EUS-FNA in consecutive patients over a 28 month period (July 2000 to November 2002). All procedures were performed by single endosonographer in the presence of a cytopathologist. Reference standard for classification of final disease included: surgical resection, death from disease progression and repeat radiologic and/or clinical follow-up. Major complications were defined as over sedation, and those that resulted in a physician or emergency department visits, hospitalization, or death.

Results: 540 patients (median age 63 years, 77% white) underwent EUS-FNAs of 656 lesions. These included lymph nodes (LNs, n = 56), solid pancreatic masses (SPMs, n = 229), cystic pancreatic masses (CPM, n = 57), mural lesions (41), bile duct/gallbladder (n = 28), liver (n = 17), mediastinum/lung (n = 17), adrenal (n = 15), spleen (n = 3) and kidney (n = 1). SPMs and bile duct/gall bladder as a group significantly required more passes to achieve a tissue diagnosis as compared to other lesions (p < 0.001) and more likely to have suspicious/atypical masses as compared to all other lesions (8.7% vs. 4.6%); p = 0.04). Final diagnosis could be determined in 641 lesions (97.7%). The overall sensitivity, specificity, PPV, NPV and accuracy of EUS-FNA was 91.7%, 97.1%, 98.1%, 87.7%, and 93.8% (95% CI: 91.9–94.8) respectively. Out of the 540 patients, six patients (1.1%) (95% CI: 0.4–2.4) experienced a major complication. These included severe pain (n = 1), pancreatitis (n = 1), and need of reversal medications (n = 4); EUS-FNA related pancreatitis occurred in 1 (0.35%) out of 286 procedures (95% CI: 0.01 – 1.93). One patient died shortly after the procedure due to pre-existing pulmonary embolus (0.18%).

Conclusions: EUS-FNA is highly accurate and safe in sampling a variety of peri-intestinal organs, pancreas and lymph nodes. With adequate third tier training, a newly developed program can produce results similar to those from expert EUS centers.

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Adjunctive Use of Diphenhydramine for Conscious Sedation during Colonoscopy: Help or Hindrance

Matthew M. Baichi, M.D., Razi M. Arifuddin, M.D., Parvez S. Mantry, M.D.∗ Digestive and Liver Disease Unit, University of Rochester, Rochester, NY.

Purpose: Diphenhydramine has been used anecdotally as an adjunctive agent for conscious sedation during colonoscopy in an effort to reduce standard sedatives and narcotics. Very little literature exists to justify this practice. The purpose of this study was to clarify the utility and safety of diphenhydramine during conscious sedation for colonoscopy.

Methods: We retrospectively reviewed the medical records of outpatient colonoscopies performed at our institution between July and September 2003. Consecutive patients who received adjunctive diphenhydramine were chosen as the study group. An equal number of consecutive patients not receiving diphenhydramine were selected as the control group. Data from the procedure note and the nursing flow sheet was reviewed for the following: indication for procedure, procedure findings, dose of meperidine/ midazolam/diphenhydramine, hypotensive episodes (systolic blood pressure < 90 mmHg), hypoxic episodes (arterial oxygen saturation < 90%), sedation score, reactivity score, baseline and post-procedural recovery scores, time to baseline recovery score, total time from end of procedure to discharge, and details of any adverse events that required intervention (reversal agents, artificial ventilation, cardiac support).

Results: A total of 113 patients were selected (diphenhydramine n = 56, control n = 57). The was no difference between the two group with regard to age, gender, and indication (diagnostic vs. investigational). Average diphenhydramine dose was 48.2 mg. There was no statistical difference in standard sedative dose, hypotensive episodes, hypoxic episodes, or time to baseline recovery score between the two groups. There was a statistical difference in total time to discharge. The diphenhydramine patients’ total time to discharge was longer by 12 minutes compared to the control group (p < 0.05).

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>diphenhydramine group (n = 56)</th>
<th>control group (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>diphenhydramine dose (mg)</td>
<td>48.2</td>
<td>0</td>
</tr>
<tr>
<td>meperidine dose (mg)</td>
<td>61.6</td>
<td>67.1</td>
</tr>
<tr>
<td>midazolam dose (mg)</td>
<td>3.3</td>
<td>3.7</td>
</tr>
<tr>
<td>hypotensive episodes (#)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>hypoxic episodes (#)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>time to baseline recovery score (min)</td>
<td>35.1</td>
<td>33.2</td>
</tr>
<tr>
<td>time to discharge from procedure end (min)</td>
<td>88.5</td>
<td>76.3</td>
</tr>
<tr>
<td>adverse events requiring intervention (#)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: Adjunctive use of diphenhydramine for routine outpatient colonoscopy prolongs time to discharge. Diphenhydramine is safe but does not affect the dose of standard sedatives/narcotics used. The utility of diphenhydramine in patients with prolonged procedures requiring higher sedation (ERCP/EUS) needs to be investigated.

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Frequency and Clinical Outcomes of Capsule Retention during Capsule Endoscopy

Douglas D. Dalke, M.D.,∗ Sachin Wani, M.D., Clark W. Antonsson, M.D., James Sorrell, M.D., Gary W. Vartiak, M.D. Research, Gastroenterology Specialties, PC, Lincoln, NE and Internal Medicine, Bryan LGH, Lincoln, NE.

Purpose: The aim of this study was to retrospectively evaluate the frequency, risk factors, and clinical outcomes of capsule retention (CR).

Methods: All patients that underwent capsule endoscopy (CE) from January,2003 to May,2005 were retrospectively analyzed for procedure indications, findings, and complications. 104 patients underwent 107 CE attempts with 104 completed studies (1 battery failure, 2 inadequate preps). All images were reviewed by experienced endoscopists (CWA, JS, GWV, DDD). All patients had a previous diagnostic work-up including upper endoscopy, colonoscopy, and barium small bowel series. Crohn’s disease (CD) was diagnosed based upon typical CE findings. If the cecum was not visualized on images, and if the patient could not confirm capsule passage, an abdominal X-ray was done to confirm CR.

Results: The main indications were iron deficiency anemia (n = 62,58%) and obscure-overt GI bleeding (n = 40,37%). Other indications were suspected or diagnosed CD (n = 2,2%), abdominal pain (n = 2, 2%), and anemia not classified (n = 1). The cecum was identified in 90 patients. Diagnosis included CD in 7 (7%) patients, suspected NSAID related ulcerations in 10 (10%), vascular lesions in 67 (64%), and small bowel neoplasms in 2 (2%) patients. Non-specific erosions, clinically insignificant, were seen in 7 (6%) and 11 (10%) patients had a normal study. The diagnostic yield of significant positive findings with CE was 83%.
CR occurred in 4 (4%) of patients. 1 patient had a NSAID related stricture and underwent surgical exploration and bowel resection 4 days following CE. The other 3 patients had CR associated with newly diagnosed CD. Of these, 1 patient experienced abdominal pain and required surgical exploration and bowel resection 11 days following CE, 1 has remained asymptomatic at 4 months of follow up, and 1 passed the capsule 4 weeks post initiation of oral budesonide (9mg/day) treatment, 7 weeks after CE.

Thus, approximately 4% of patients in our study demonstrated CR. 43% patients with CD experienced CR.

Conclusions: This study demonstrates an overall CR rate of 4% which is comparable to literature reports. Crohn’s disease was a significant risk factor for CR (43% in patients with CD vs. 1% without CD, p < 0.001). Patients with CD are at a considerably higher risk for CR and should be so informed. If a patient with CR is asymptomatic, observation alone is reasonable, and in patients with CD, a trial of budesonide should be considered.

Aggressive Marketing of Advanced Endoscopic Procedures for Reflux:
A Precautionary Tale
Scott Oosterveen, M.D., Michael D. Brown, M.D.* Gastroenterology & Nutrition, Rush University Medical Center, Chicago, IL.

Purpose: In 2004, our institution launched a multi-media advertising campaign to promote endoscopic therapies for gastroesophageal reflux disease (GERD). This involved television, newspaper, telephone and internet promotions. All of these media promotions offered information regarding indications and methods of endoscopic anti-reflux procedures (EARP). We looked retrospectively at the patients referred to us during this promotional period. Whether patients were referred by gastroenterologists, primary care physicians (PCP), or self-referred was examined in reference to the appropriateness of EARP.

Methods: From 12/04 to 5/05, 86 patients were referred for treatment with EARP. Patient histories involved questions about the nature, duration, and treatments for GERD. Further testing and/or referral were done if the diagnosis was in question. How each patient was referred to the clinic was also noted. The eventual appropriateness of an EARP was compared to sources of referral. Proportions were compared using chi square.

Results: The source of referral of the 42 patients considered appropriate for EARP (PCP (2), GI (12), newspaper (1), television (22), phone (1), hospital website (0), Boston Scientific website (4) varied compared to those 43 patients not considered appropriate (1, 0, 1, 34, 0, 2). The reasons EARP were considered inappropriate included non-adherence (2), inadequate treatment (27), contraindications (5), and alternate diagnosis (9). Alternative diagnoses included achalasia (2), asthma/COPD (3), coronary artery disease (1), collagen vascular disease (1), and fibromyalgia (1). Of the 9 patients with alternative diagnoses, 8 were self-referred (television ads 7, website 1) and 1 was referred by the PCP. EARP was considered inappropriate in only 1 of the 15 patients referred by a physician, as compared to 42 out of the 70 patients self-referred (6.0% versus 60%, p = 0.0002)

Conclusions: Our clinic’s referral experience after a multi-media campaign to promote EARP serves as a precautionary tale. Almost one half of patients referred by gastroenterologists were inappropriate for EARP. Those patients self-referred from a promotion were far more likely to be inappropriate. In a small percentage of patients an inappropriate referral was made as a precautionary tale. Almost one half of patients referred by primary-care physicians were inappropriate for EARP. Those patients self-referred from a promotion were far more likely to be inappropriate.

The Impact of Endoscopic Ultrasound in the Management of Pancreatic Cystic Lesions
D. Brian Jones, M.D., F.A.C.G., Yu Kwan, M.B.B.S., Ian D. Norton, M.B.B.S., Ph.D.* Department of Gastroenterology, Concord Hospital, Sydney, NSW, Australia.

Purpose: Pancreatic cystic lesions (PCLs) are encountered with increasing frequency due to the escalating use of abdominal imaging. Lesions range from benign cysts without malignant potential to overt malignancies. We aim to assess the utility of EUS in differentiation of PCLs according to malignant potential.

Methods: All consecutive patients referred for EUS assessment of a PCL were identified from a prospectve endoscopic database. Follow-up information was collected via contact with referring practitioners, review of medical records and results of surgical pathology and/or subsequent imaging where available.

Results: Between 2002 and 2005, 89 patients with PCLs underwent EUS (8.3% of total EUS case load, 17% of 2004 case load). Median age = 63 (range 29–86), males = 35. Fine-needle aspiration was performed in 38. For the FNA group, one case of intra-cystic haemorrhage was encountered and no cases of pancreatitis or sepsis occurred. Cytology was positive in 16% (adenocarcinoma = 3, mucin = 1 and acid-fast bacilli and M. tuberculosis PCR positive = 2). All positive results were concordant with subsequent surgical and/or clinical findings. No cases with negative cytology have exhibited malignancy at surgery or in clinical follow-up. On univariate analysis no biochemical marker was able to differentiate benign from malignant disease. Of the overall group, 15 patients have undergone surgery. Eleven had lesions deemed malignant by EUS and concordant pathology was found in 7. Four lesions were deemed benign at EUS and concordant pathology was found.
in all. Non-surgical tissue diagnosis was available for 5 patients and EUS diagnosis was correct in all. Of 70 patients managed non-surgically without tissue diagnosis, 15 have undergone repeat EUS with median follow-up = 15 months (8–36). Mean size change was 3.6 mm/year and no malignant transformation has occurred. Of 54 patients who have undergone neither surgery nor repeat EUS follow-up is available for 48, median follow-up = 12 months. 23 patients have undergone repeat imaging and all lesions remain stable. In the remaining patients no unexpected clinical malignant disease has occurred. For the diagnosis of malignant potential (within above clinical follow-up), EUS has sensitivity = 100%, specificity = 94%, PPV = 63%, NPV = 100% and accuracy = 95%.

Conclusions: EUS accurately stratifies PCLs according to malignant potential. EUS assessment results in appropriate decisions regarding need for surgery and good outcomes for patients managed conservatively.

Comparison of Propofol and Midazolam on Driving Ability after Diagnostic EGD
Akira Horiuchi, M.D.*, Yoshiko Nakayama, M.D., Douglas K. Rex, M.D. Department of Gastroenterology, Showa Inan General Hospital, Konnagare, Nagano, Japan and Department of Medicine, Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, IN.

Purpose: Recently the administration of sedative medications has been increasing for endoscopic procedures in Japan. However, most patients want to drive to work or home shortly after EGD. We hypothesized that driving ability as measured by a driving simulator (DS-10, Mitsubishi Precision, Tokyo, Japan) would be a more sensitive indicator of drug effect after sedation than other tests. The purpose of this study was to evaluate and compare the residual effect of propofol and midazolam on driving ability as determined with the driving simulator. In addition, the relation between driving ability and the blood concentration of propofol was evaluated.

Methods: Sixty patients undergoing the diagnostic EGD were randomized to receive a bolus injection of 40 mg of propofol (n = 30) or 4 mg of midazolam (n = 30). Administration of sedation was performed by a registered nurse and supervised by the endoscopist. Patient satisfaction, recovery time, and complications were evaluated. Driving ability using the driving simulator and the blood concentration were measured at before and 30, 60, 120, and 180 min after the injection of each drug. A control group of 20 patients who did not receive any sedative drugs had driving ability evaluated during the same time period.

Results: Overall patient satisfaction on a 10-point visual scale was similar between propofol and midazolam (8.3 vs. 8.6; p = 0.68). On average, after the procedure, the propofol patients could stand at the bedside sooner than midazolam (7.3 vs. 31 min; p < 0.01). No major complication occurred in either group. All propofol patients driving ability recovered to the baseline level at 60 min after the injection whereas 53% (16 patients) in the midazolam group had significantly impaired driving ability up to 180 min. Propofol concentrations ranged from 31 to 89 ng/ml (mean 67 ng/ml) at 60 min whereas midazolam ranged from 0.03 to 1.2 mg/L (mean 0.43 mg/L) at 180 min. The driving ability recovered to the baseline when propofol levels were less than 100 ng/ml.

Conclusions: We propose using driving ability measured by the driving simulator as a sensitive measure of a drug’s effect on psychomotor function. 60 min after receiving 40 mg of propofol it is possible to consider driving or operating heavy machinery. However, driving a car should be prohibited for the day the patient receives 4 mg of midazolam.

Prospective Evaluation of Ultrathin Videoendoscope for Unsedated Esophagogastroduodenoscopy (EGD) in the Medical Checkup
Hideaki Kawabata, M.D., Masami Ogawa, M.D., Eisai Cho, M.D.* Kenjiro Tasuda, M.D., Masatugu Nakajima, M.D. Gastroenterology, Kyoto Second Red Cross Hospital, Kyoto, Japan.

Purpose: The aim of this study was to compare the feasibility, tolerance, and safety of ultrathin EGD (UT-EGD) with conventional EGD (C-EGD) as a screening method in the medical checkup.

Methods: Unsedated EGD was performed in 196 patients in the medical checkup from February to May of 2005 using either ultrathin 5 mm (GIF-XP260, Olympus Corp.) or conventional 9.0–10.2 mm diameter endoscopes. At endoscopy, all patients received topical pharyngeal anesthetic spray prior to the procedure. Endoscopy was randomly performed by three endoscopists with experience time of 22 (A), 8 (B), and 1 years (C). After examination, patients were asked to complete a questionnaire regarding their tolerance of the procedure in terms of discomfort during the insertion of the endoscope and then during the remainder of the examination. Patients who had undergone a prior C-EGD were compared with the current examination. The endoscopists assessed the quality of the instruments including operability, time of examination, endoscopic image, and safety.

Results: After randomization, 121 patients (79 men and 42 women with mean age 53.9 years) were allocated to the UT-EGD group, 75 patients (42 men and 33 women with mean age 52.4 years) to C-EGD group. The attending endoscopist A, B, and C performed UT-EGD for 19, 61, and 41 patients, and C-EGD for 8, 34, and 33 patients, respectively. One hundred and nine patients in the UT-EGD group and 60 patients in the C-EGD group had previously undergone C-EGD. Sixty-five of 121 (54%) patients in the UT-EGD group and 21 of 75 (28%) in the C-EGD group reported none/mild discomfort. A P value was 0.00073 and significant in endoscopist B (P = 0.00173). Seventy-nine of 109 (72%) patients with previous C-EGD in the UT-EGD and 17 of 60 (28%) with previous C-EGD in the C-EGD group reported none/mild discomfort. A P value was 0.00055 and significant in endoscopist A (P = 0.0172) and B (P = 0.01842). Both groups lead to no misdiagnosis. The average time of examination of the endoscopist A, B, and C in the UT-EGD group was 4.83, 5.58, and 7.73 minutes and 4.62, 4.75, and 7.05 minutes in the C-EGD with no significance. All patients had complete examinations without any complications.

Conclusions: UT-EGD is well tolerated and useful endoscopic method especially for experienced endoscopists compared with C-EGD in the medical checkup.

The Benefit of Tegaserod in Bowel Preparation for Colonoscopy
Kenneth D. Glazier, M.D., Brian C. Weiner, M.D. Division of Gastroenterology and Hepatology, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ.

Purpose: Colonoscopy has been demonstrated to detect colorectal neoplasms, and, with removal of premalignant adenomatous polyps, can reduce the incidence of colorectal cancer. The quality of bowel cleansing is crucial for endoscopists to be able to detect colonic neoplasms on routine colonoscopy. Miss rates of colonic polyps during colonoscopy have been reported to be between 15 to 24% and suboptimal preparation likely leads to an increase in missed polyps.

In an attempt to improve the quality of bowel cleansing in clinical endoscopic practice, we recently added Tegaserod to our usual bowel preparation of Fleets phosphosoda in patients under 65 without renal or cardiac impairment. Tegaserod has recently been shown to be safe and effective in the treatment of chronic constipation. In over 200 colonoscopies, two doses of Tegaserod (6 mg given bid on the day prior to colonoscopy) were provided in addition to Fleets phosphosoda (45 ml followed by 6 glasses of water at 7 and 9 p.m., the night prior to colonoscopy).

Methods: In an uncontrolled observational study, the quality of preparations in patients who received Tegaserod (6 mg given bid on the day prior to colonoscopy) in addition to the Fleets phosphosoda preparation (45 ml followed by 6 glasses of water at 7 and 9 p.m.) were compared to a historical group of 200 procedures performed with Fleets phosphosoda preparation without Tegaserod.

Results: We have found that the quality of preparation is better in patients who receive Tegaserod in addition to the Fleets phosphosoda preparation as compared to a historical group of 200 procedures performed with Fleets phosphosoda preparation without Tegaserod.

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Significantly, at least 10% of the patients had an increased number of bowel movements after the first dose of Tegaserod. One patient who vomited much of the water that was to accompany the Fleet's phosphosoda was dehydrated and hypokalemic the day of colonoscopy and required admission to the hospital for rehydration and cardiac evaluation for transient electrocardiogram changes related to the hypokalemia. Hypokalemia and dehydration have been reported as consequences of overdosage of the Fleet's phosphosoda preparation. There have been no cases of ischemic colitis or other adverse events to date in the patients studied.

Conclusions: Tegaserod, in addition to Fleet's phosphosoda preparation, improves colonoscopy bowel preparation.

Relationship of Transit Abnormalities on Capsule Endoscopy to the Identification of Underlying Pathology

Rami Abbass, M.D., Steve Kucera, M.D., Gerard Isenberg, M.D., Richard C.K. Wong, M.D., Amitabh Chak, M.D., Michael V. Sivak, M.D. Division of Gastroenterology, Case Western Reserve University, Cleveland, OH.

Purpose: In the past 2 years, there has been claims in the literature that regional transit abnormalities (RTAs) in the small bowel observed on capsule endoscopy (CE) studies may indicate underlying pathology such as masses, ulcers or strictures.

In this study, we seek to evaluate whether observation of regional transit abnormalities on capsule endoscopy may indicate underlying pathology in the small bowel.

Methods: In this study, we retrospectively reviewed 75 CE studies performed between October 2003 and July 2004 at University Hospitals of Cleveland to identify and record areas of temporary or permanent capsule retention and RTAs in the small bowel. RTAs were defined, as in prior definitions in the literature, as slow movement of the capsule (without cessation of movement) for more than 60 continuous minutes with or without obvious mucosal abnormality. CE study review was performed using the Rapid software used for the M2A video capsule (Given Diagnostic Imaging System). Review of images was performed at 10–15 images per second through the small bowel, the generally recommended rate of review when reading CE studies. Chart review was then performed for those 75 patients who underwent CE to establish whether a source of bleeding and/or small bowel pathology (masses, strictures, or ulcerations) was identified with CE or with further evaluations (surgery, push enteroscopy, repeat capsule endoscopy) in the 8 months that followed the initial CE study. Statistical analysis was performed to investigate whether the presence of RTAs or capsule retention more likely predicted underlying pathology in the small bowel.

Results: Of the 75 CE studies performed at our institution between October 2003 and July 2004, RTAs were observed in 9 studies (12%). Underlying pathology (stricture, mass or ulceration) was identified with CE or with further evaluations (surgery, push enteroscopy, repeat capsule endoscopy) in the 8 months that followed the initial CE study. Statistical analysis was performed to investigate whether the presence of RTAs or capsule retention more likely predicted underlying pathology in the small bowel.

Conclusions: Identification of regional transit abnormalities in the small bowel on capsule endoscopy did not result in a significant increase in identification of underlying small bowel pathology.

Incision vs. Non-Incision Technique of PEG Tube Placement: Success Rate and Early Complications

Samuel A. Charukhchian, M.D., Anand Patel, M.D., Eric Ibegbu, M.D., Samir Habashi, M.D., Louis Lambaize, M.D.* DI Division, University of Florida Health Sciences Center, Jacksonville Florida, Jacksonville, FL.

Purpose: Percutaneous endoscopic gastrostomy (PEG) tube placement with and without skin incision were compared with regard to success of technique, ease of placement, and early PEG site complications in a randomized, controlled, double blinded prospective study.

Methods: 50 consecutive patients were randomized to PEG tube placement by pull technique with either 4 mm skin incision (n = 25) or no skin incision (n = 25). Patients were blinded to type of technique used. 92% of patients in each group received antibiotics. Peak pull-forces required to pull PEG through the abdominal wall, bleeding scores and time of procedure were recorded by an operator. All patients received standardized wound care. At days 2 and 7 post-PEG placement an investigator blinded to type of technique assessed patients for PEG site skin infection, bleeding, and pain.

Results: PEG placement was 100% successful in both groups of patients with no differences in procedure time. The mean procedure time for the incision group was 14.6 min; for the non-incision group it was 15.6 min (P > 0.05). Mean bleeding score during procedure was higher in the incision group 0.4 vs. non-incision group 0.12 (P < 0.05), while mean peak pull-forces were higher in the non-incision group 19.04 lb vs. incision group 11.69 lb (P < 0.05). One patient in the incision group required suturing and pressure to control continuing oozing of blood after the procedure. Mean infection scores were 0.16 for the incision group vs. 0 for the non-incision group (P > 0.05) on day 2, and 0.43 for the incision group vs. 1.37 for the
non-incision group (P = 0.055) on day 7. Purulent MRSA PEG site abdominal wall infection in one patient from the non-incision group necessitated early PEG tube withdrawal and additional antimicrobial therapy. Mean bleeding scores were 0.25 for the incision group vs. 0 for the non-incision group (P < 0.05) on day 2, and 0.13 for the incision group vs. 0.08 for the non-incision group (P = 0.05) on day 7. There was no statistically significant difference in pain scores on day 2 or 7. The mean pain score was < 1 in both groups.

Conclusions: PEG tube placement was feasible in all patients with both incision and non-incision techniques. When compared with the incision technique, the non-incision technique required significantly more forces to pull the PEG tube through the abdominal wall, was associated with lower periprocedural bleeding, and had higher mean infection scores on post-procedure day 7.

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A Novel Device for the Prevention of Looping in Colonoscopy
Raman Mathasamy, M.D., Kenneth R. McQuaid, M.D., Jasmine S. Vargas, M.S.* Division of Gastroenterology, Department of Medicine, University of California, San Francisco, San Francisco, CA and EndoNav Inc., Redwood City, CA.

Purpose: Colorectal cancer (CRC) screening is an established part of routine medical care in the United States. Colonoscopy is currently the gold standard screening test for CRC. However, it is usually performed with intravenous sedation in order to minimize the discomfort resulting from mesenteric stretching caused by looping. This routine use of sedation significantly adds to the cost and inconvenience of this procedure. We evaluated a new device intended to reduce looping associated with colonoscopy insertion.

Methods: An innovative, disposable device that works in conjunction with existing colonoscopes has been developed. It is similar to an overtube, and provides support during colonoscope insertion in order to reduce looping. The device control is attached to the colonoscope handle and limits the motion of the overtube along the colonoscope to the length of the distal bending tip. During colonoscope insertion, the scope is advanced through the overtube to expose the distal bending tip in order to navigate the colon. The overtube is then advanced over the colonoscope and adopts the shape of the distal bending tip, stiffening to retain this shape. As the colonoscope is subsequently advanced, the lateral forces associated with scope advancement are contained within the device. The overtube is then relaxed and the process is then repeated until the cecum is reached. Scope insertion is entirely endoscopist-controlled. To date, this device has been tested on artificial colon and in vitro porcine models.

Results: Initial trials with benchtop artificial and porcine tissue models have demonstrated the ability to navigate these models effectively without looping. A standard pediatric colonoscope was not able to achieve these results in the same models. Initial in vivo porcine studies are underway.

Conclusions: Initial pre-clinical testing of this device suggests a significant decrease in looping. Larger porcine-model trials and a human clinical trial are planned. If these preliminary findings are borne out, colonoscopy with little or no sedation may be possible. This has the potential to enhance patient safety and comfort, endoscopy unit efficiency, and reduce health care costs associated with screening colonoscopy.

1003

Quality Measures for Colonoscopy in a Community Hospital
Eugene J. Burbige, M.D.*, Kris Barr, R.N., Eugene M. Burbige Medicine, Mount Diablo Medical Center, Concord, CA.

Purpose: Colonoscopy and polypectomy, important in the diagnosis and treatment of colorectal cancer, is a complex technical procedure requiring not only basic training, but also continued experience to maximize its usefulness. While initial certification requirements for obtaining endoscopic privileges have been well defined, recredentialing requirements have not been and are frequently based on the number of procedures performed within a specified period of time. This study looked at not only the number of procedures performed, but also the success of cecal intubation among endoscopists with various levels of expertise.

Methods: Dictated colonoscopy reports and the nurse’s records from the same procedures were reviewed for the period between 1/1/04 and 12/31/04. All records were reviewed for cecal intubation, quality of preparation, presence of acute colitis, and to determine if the indication for the procedure was screening vs. medical necessity. Success was recorded as cecal intubation. Those procedures not entering the cecum were recorded as failures unless the procedure was discontinued because of poor preparation or the presence of acute colitis. Success rate for each individual was recorded as percentage of cases, excluding poor preparation and acute colitis cases.

Results: During the study period, 2621 colonoscopies were performed by 11 colonoscopists (8 gastroenterologists, 3 colorectal surgeons), ranging from 32 to 526, with a mean of 238 per individual. Success rates ranged from 90% to 100%, with an average of 96%. The average gastroenterologist’s success rate was 96% and the colorectal surgeon success rate was 94%. The lowest scoring individual, a gastroenterologist, was 90%, having performed 438 cases (18% of the total cases). If that individual was eliminated as an outlier the percentages changed slightly to 97% and 94%. Eliminating the lowest scoring colorectal surgeon did not change the success rate. The success rate for those procedures with screening as an indication, did not differ significantly from the overall rate.

Conclusions: In the past, rates of cecal intubation above 90% have been the goal of training programs and considered adequate in clinical practice. This study suggests that cecal intubation rates of 95% for all examinations is achievable and should be recommended. Also, recredentialing of endoscopic privileges should include not only the number of procedures performed, but also quality measures such as cecal intubation. Monitoring of this type can help identify individuals requiring improvement of their technical skills.

1004

Modifications of the Expandable Polyester Stent Can Prevent Early Stent Migration for Treatment of Refractory Benign Esophageal Anastomotic Strictures
John H. Sun, D.O., Eric H. Shen, M.D., Taimir Ben-Menachem, M.D.* Gastroenterology and Hepatology, Robert Wood Johnson Medical School, New Brunswick, NJ.

Purpose: Esophago-gastric anastomotic strictures refractory to periodic balloon dilation represent a therapeutic challenge. Placement of removable expandable stents may be a good alternative to repeat dilation. Data supporting the use of an expandable polyester silicone-covered (Polyflex) stent for the treatment of these strictures is limited. We have recently encountered early Polyflex stent migration in several patients with refractory benign anastomotic strictures. We describe a modification of the Polyflex stent which may prevent early migration.

Methods: Three males presented with dysphagia 4–18 months after transhiatal esophagectomy due to severe anastomotic strictures and failed prior endoscopic dilation. One had a Polyflex stent placed unsuccessfully. Indications for surgery were Barrett’s metaplasia with high grade dysplasia for two patients, and squamous esophageal carcinoma for one. The anastomoses were located at 19–22 cm from the incisors. All then underwent a series of aggressive endoscopic balloon dilation to reach a diameter of 20 mm. The strictures recur in all patients within 3–4 weeks. A Polyflex stent (22 mm wide, 90 mm long) was then placed but migrated within 1–3 weeks in all patients, and the strictures promptly recurred. An attempt to anchor the stent to the esophagus with Hemoclips for one patient failed. In order to allow better anchoring of the stent we modified the stents as follows: the silicone cover of the stent was punctured with scissors every other diamond circumferentially, on two rows above and below the middle marker band.

Results: The modified Polyflex stents were placed successfully in the three patients. The stents remained in place for two patients and were removed after 5 weeks. One remains symptom free after 4 months. The other did well for
Conclusions: Modification of the Polytex stent to allow slight tissue protrusion through the silicone covering may prevent early migration without impeding safe stent removal.

Periendoscopic Management and Complication Rates in Patients Taking Nonaspirin Antiplatelet Agents Undergoing Elective Endoscopic Evaluation at MCS: A Retrospective Chart Review

Lillian Choi, M.D., Linda Kral, R.N.; Cuong Nguyen, M.D.*
Gastroenterology and Hepatology, Mayo Clinic Scottsdale, Scottsdale, AZ.

Purpose: To determine the periendoscopic management practices of physicians towards patients taking nonaspirin antiplatelet agents and the complication rates in such patients undergoing endoscopic procedures.

Methods: Retrospective chart review of 205 patients taking at least one nonaspirin antiplatelet agent prior to any elective endoscopic evaluation in 2004 at MCS. Data collected included the specific agent used, whether the agent was stopped, how long the agent was stopped prior to endoscopy and when it was resumed, specialty of the physician who was managing the patient’s case, and complication rates.

Results: The majority (52%) were on both aspirin and plavix or on plavix alone (32%). Of the 119 patients who were taking aspirin plus plavix, pletal, or persantine, 34 (29%) stopped aspirin alone. The mean time of discontinuing the agent pre-endoscopy was 6 days (range: 2–14). 11 (9%) stopped plavix/pletal/persantine when taking a combination of agents. The mean time of discontinuing the agent pre-endoscopy was 4.3 days (range: 2–8). 38 (32%) stopped both agents. The mean time of discontinuing the agent was 5 days prior (range: 1–30). In the 66 patients where plavix was the single agent, plavix was discontinued in 15 cases (23%). The mean time of discontinuing the agent prior to endoscopy was 11 days (range: 2–30). In the remaining cases, the medications were continued. In the majority of cases (73%), the referring primary care physician (PCP) managed the patient’s nonaspirin antiplatelet agents periendoscopically. In the cases where a gastroenterologist was managing the patient’s nonaspirin antiplatelet agents, the management followed the 2005 ASGE guidelines in 61.8% of the cases. The 2005 ASGE guidelines were followed 55% of the time by PCPs. There were only two complications in the 30 day period following one of the endoscopic procedures. There were two thrombotic and one bleeding complication noted outside the 30 day period (30–90 days post procedure).

Conclusions: There is wide variation in the periendoscopic management of nonaspirin antiplatelet agents, both among gastroenterologists and primary care physicians. Despite the wide variation in the periendoscopic management, very few complications were noted overall. Further studies will be needed to determine if periendoscopic management will change with the publication of the 2005 ASGE guidelines and whether there will be a resultant change in patient complication outcomes.

Capsule Endoscopy: One-Year Experience

Mari Hirata, M.D., Gienichi Koyama, Toyo Ihei, Shin’ichi Takahashi.*
Third Department Internal Medicine, Kyorin University, Mitaka, Tokyo, Japan.

Purpose: Capsule endoscopy is the first diagnostic tool of small bowel disease. The aim of this study was to evaluate the ability of capsule endoscopy for small bowel disease in Japanese patients.

Methods: Between March 2004 and April 2005, 32 cases (16 female, 9 male; mean age 55.5yo) underwent capsule endoscopy.Eight of these were outpatients, and 24 were inpatients. The indication for capsule endoscopy were 24 obscure GI bleeding, 3 polypsis surveillance, 1 malabsorption, 1 suspected Crohn’s disease, 1 abdominal pain, 1 anemia, 1 Behcet’s disease. Prior to capsule endoscopy, all patients had undergone at least one upper endoscopy and one colonoscopy. The recording were read independently by two gastroenterologists.

Results: The capsule was easily swallowed by all patients. Mean recording time of images was 488 min (range: 323–527 min). The Mean gastric and small bowel transit times were 43 min (range: 3–146 min), and 323 min (range: 157–499 min). In 11 patients (34%), the capsule did not reach the colon by the end of recording time. Of the 24 patients with obscure GI bleeding, capsule endoscopy findings were positive in 32% (2 small bowel ulcers, 1 multiple erosion in small bowel, 4 active bleeding in small intestine), suspicious lesion in 18% (3 erosions in small bowel, 1 duodenal ulcer) and 50% had no finding. About 3 patients with active bleeding in small intestine, double-balloon endoscopy were performed after capsule endoscopy. Double-balloon endoscopy detected 2 ileum ulcers, 1 angiodysplasia. The case of angiodysplasia was treated by APC using double-balloon endoscopy. The patients with polyposis syndrome (2 Cowden disease, 1 Peutz-Jeghers syndrome) had detectable polyps by capsule endoscopy. In the patients with Peutz-Jeghers syndrome, endoscopic polyeoctomy was performed by double-balloon endoscopy. There were no complications observed in any patients.

Conclusions: Capsule endoscopy is a non-invasive and useful tool for diagnosis of small bowel disease. The combination of capsule endoscopy and double-balloon endoscopy is not only useful for diagnosis of small bowel disease but also its treatment.

Endoscopic Mucosal Resection of Flat & Depressed Colorectal Neoplasms in a North American Population

Andrew Ross, M.D., Erica Rodriguez-Wulff, M.D., Alberto Larghi, M.D.∗
Charles Dye, M.D., Irving Waxman, M.D. Department of Medicine, Section of Endoscopy and Therapeutics, The University of Chicago Hospitals, Chicago, IL.

Purpose: Flat and depressed (F&D) neoplasms of the colon are typically smaller than their polypoid counterparts and may be associated with a more aggressive biological behavior. Endoscopic mucosal resection (EMR) allows for histopathologic staging of resected lesions. Although it has been studied extensively in Japan, data with regard to the utility this technique for the treatment of F&D colonic neoplasms in the West are lacking. The aim of this study was to review the experience at our center with EMR for F&D colonic neoplasms.

Methods: A retrospective review of a prospectively collected database of all patients referred to our institution for EMR of flat or depressed colonic neoplasms was performed. The selection of EMR technique was based on the lesion size, location and morphology. Submucosal injection of saline or a 1:10,000 solution of epinephrine was performed at the discretion of the endoscopist. Lesions were sprayed with a 0.5% indigo carmine solution when further examination of the mucosal surface pattern was required. Argon plasma coagulation was applied to the resection margins. Follow-up intervals were determined based on histopathologic examination of the resected lesion.

Results: EMR was performed in a total of 32 patients (15M 17F); 39 lesions were resected. Lesions were located in the right colon (n = 24), transverse colon (n = 6), descending colon (n = 1) and rectum (n = 8) with sizes ranging from less than 1 cm to 4 cm. 15 of the lesions were resected in a single step whereas 24 were removed piecemeal; submucosal injection was performed for 16 (41%) of the lesions. Histopathology revealed tubular adenoma (n = 18), villous adenoma (n = 2), tubulovillous adenoma (n = 10), hyperplastic (n = 3), serrated adenoma (n = 4), and adenocarcinoma (n = 2). Complications included delayed bleeding in 1 patient which was endoscopically controlled. To date, 12 patients have undergone follow-up colonoscopy with a median duration of follow-up of 6 months (range 3–12). Only 1 patient had residual adenomatous tissue at endoscopic follow-up.
Conclusions: These data add to the growing body of evidence which suggests that EMR is a safe and effective treatment option for patients with F&D colorectal neoplasms. EMR should be considered prior to surgical resection in patients found to harbor such lesions. Prospective studies are required to determine the appropriate endoscopic follow-up intervals following EMR of F&D colorectal neoplasms.

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Economic Impact of Anesthetist-Administered Sedation in Outpatient Gastrointestinal Endoscopy

Thomas J. Bramley, Ph.D.,∗, Kellie L. Meyer, Pharm.D., Amy L. Grogg, Pharm.D., Douglas K. Rex, M.D. Outcomes Research, Applied Health Outcomes, Palm Harbor, FL and Medicine, Indiana University School of Medicine, Indianapolis, IN.

Purpose: Almost all gastrointestinal endoscopic procedures performed with propofol sedation (92%) use an anesthesiologist or a certified registered nurse anesthetist (CRNA) (Cohen 2005) and the economic impact of anesthetist-administered sedation in gastrointestinal endoscopy has not been economically quantified.

Methods: A model was developed to quantify the economic impact of anesthetist-administered sedation in patients undergoing outpatient gastrointestinal endoscopic procedures in a hospital outpatient clinic, physician office, and ambulatory surgical center (ASC). The model was created from the perspective of the U.S. healthcare system. Reimbursement inputs for anesthesia professional services were obtained from published literature (Aisenberg 2005). As these rates vary by payer, a weighted average was calculated based on the distribution of payer type for endoscopic procedures (CDC 2001). The number of gastrointestinal endoscopic procedures performed in the U.S. was estimated using NDCHealth, Solucient, and Versipan data. To measure the robustness of model results to changes in base case inputs, sensitivity analyses were performed. Using a Monte Carlo simulation, the inputs were varied simultaneously and randomly for 1,000 iterations to determine a range of cost estimates.

Results: The total number of outpatient gastrointestinal endoscopic procedures performed in the U.S. is projected to be between 20.4 and 22.3 million in 2005. Approximately 5.1 to 5.6 million of these gastrointestinal endoscopic procedures are performed with propofol sedation. The anesthetist costs associated with gastrointestinal endoscopic procedures using propofol sedation are projected to range from $1.3 to $1.4 billion in 2005. Sensitivity analyses indicated that estimated annual costs of anesthetist-administered sedation for gastrointestinal endoscopy were most influenced by anesthetist professional fees and the percent of procedures using propofol sedation.

Conclusions: Anesthetist-administered sedation for gastrointestinal endoscopy results in a significant economic burden to the U.S. healthcare system. This burden is likely to increase due to population growth, potential increases in colorectal cancer screening compliance, and the increased use of propofol for gastrointestinal endoscopy. As the dynamics of reimbursement change frequently, further research is warranted to determine the entities financially responsible for this burden.

1009

EUS-FNA for the Diagnosis of Cholangiocarcinoma after Unsuccessful ERCP

Bankim Bhatt, M.D., Pankaj Singh, M.D., M.S.∗ Gastroenterology, Central Texas Veterans Health Care System, Temple, TX.

Purpose: ERCP with brush cytology is considered test of choice for the diagnosis of cholangiocarcinoma. However, in 60% of cases ERCP is non-diagnostic. We describe two cases where EUS-FNA helped in the tissue diagnosis when ERCP was unsuccessful.

Methods: Case 1: 87 year old male with weakness, loss of weight and progressively worsening jaundice was referred to gastroenterology for further evaluation. Patient alkaline phosphatase was 483, total bilirubin 9.7, and direct bilirubin of 6.2. His CT of abdomen showed intra-hepatic bile duct dilation with an ill-defined low attenuation area in the anterior segment of the right lobe of liver. Patient underwent ERCP which showed dilated pancreatic duct. Repeated unsuccessful attempts were made to cannulate the common bile duct. Provisional diagnosis was jaundice, most likely secondary to extra-hepatic bile duct obstruction. Linear array endosonography showed dilated intra-hepatic bile ducts and single, round hypoechoic lesion measuring 18.5 mm in diameter in the right lobe of the liver. FNA was performed. Preliminary report on the first pass showed few cells that were suspicious for malignancy. EUS guided contrast was injected in the common bile duct and the intra-hepatic bile ducts (EUS-cholangiography). Dilated intra-hepatic ducts were visualized with obstruction to the flow of the contrast into the distal common bile duct, most likely secondary to the cholangiocarcinoma. Second attempt at ERCP was successful to access the common bile duct. Cholangiogram showed obstruction in the proximal bile duct. Plastic stenting (10 Fr. x 12 cms) was placed in the common bile duct. Malignant cells were identified. Cells were CK-7 positive and CK-20 negative, a pattern typically seen with primary biliary carcinoma.

Case 2: 78 year old male with elevated alkaline phosphatase and total bilirubin had an unsuccessful attempt at ERCP in an outside hospital. Patient was referred for second opinion. Linear array endosonography was performed which showed an ill defined hyperechoic lesion in the right lobe of the liver. FNA of the lesion in the liver was performed. Two passes were made. The final cytological diagnosis was cholangiocarcinoma. Repeat ERCP was performed which was successful and showed normal cholangiogram.

Results: EUS-FNA successfully diagnosed cholangiocarcinoma in both the cases.

Conclusions: EUS-FNA should be considered for the tissue diagnosis and staging in a suspected cholangiocarcinoma, particularly when ERCP is unsuccessful.

1010

Relationship of INR Levels to Rates of Post-Polypectomy Bleeding

Kevin C. Ruff, M.D., Gavin C. Hartwood, M.D., Darrell S. Pardi, M.D.∗ Internal Medicine, Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, MN.

Purpose: To determine whether there is an increased risk of post-polypectomy bleeding in the setting of elevated INR levels, and at what INR level this risk increases. This information will facilitate evidence based guidelines for polypectomies in patients with coagulopathy.

Methods: A retrospective review using the institutional database of all colonoscopies performed from 01/01/04 through 06/30/04 was used to identify all colonic polypectomies over this period. This list was cross-referenced with the laboratory database to identify those procedures for which both
platelet and INR levels were available within one month of the procedure performance. Analysis was confined to those patients in whom platelet levels >100,000. The medical records related to these procedures were reviewed to identify post-procedure bleeding. Post-polypectomy bleeding was characterized by hematochezia within 1 week of the procedure.

**Results:** 464 polypectomies performed in 437 patients meeting the above criteria were identified. Bleeding rates according to varying INR levels are illustrated in figure 1. For INR <1.3 no significant differences in bleeding rates were identified; for INR =1.4 bleeding rates increased (10.7% for INR <1.4 vs. 20.8% for INR >1.4).[figure1]

**Conclusions:** An INR level of 1.3 appears to be the upper limit for safe performance of colon polypectomy.

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**1011**

**ERCP in Post-Whipple Patients**

Prabhleen Chahal, M.D., Todd H. Baron, M.D.* Gastroenterology and Hepatology, Mayo Graduate School of Medicine, Rochester, MN.

**Purpose:** ERCP is an established modality for diagnostic and therapeutic maneuvers in pancreaticobiliary disorders. However, it is technically more challenging in patients with post-surgical anatomy. The effectiveness of ERCP in patients with prior pancreatoduodenectomy (Whipple resection) has not been addressed. We sought to assess the efficacy and safety of ERCP in this patient population.

**Methods:** Post- pancreatoduodenectomy patients who underwent ERCP from 1/02 to 5/05 were identified through a computerized medical index system.

**Results:** Fifty-one patients (27 women, 24 men) post-pancreatoduodenectomy underwent 88 ERCPs. The median age was 64 years (range 27–80 years) and the median follow up was 179 days (range 0–1116 days). The indication was assessment of pancreaticojejunostomy in 27 patients with abdominal pain, stenotinia, pancreatic duct dilatation on radiological imaging and pancreatitis, requiring 44 ERCPs. The indication in 24 was evaluation and management of biliary obstruction, requiring 51 ERCPs. Successful cannulation based upon the duct of interest was achieved in 8 of the 44 (18%) pancreatic indications and was achieved in 43 of 51 (85%) biliary indications including choledocholithiasis and biliary stricture. In seven procedures cannulation of both pancreatic and biliary anastomosis was indicated. The overall success rate of ERCP based on the intention of procedure was 58% (51 of the 88 procedures). Seventy-six of the 88 (86%) ERCPs were successful in advancing to the level of biliary or pancreatic anastomosis. There were five mild procedure related complications including a small self-contained perforation managed conservatively, two patients with post procedure pain requiring oral and intravenous analgesia respectively, and a case each of vasovagal episode and a Mallory Weiss tear with complete hemostasis achieved during procedure.

**Conclusions:** This is the largest experience of ERCP in patients with prior pancreatoduodenectomy. The success rate for biliary indications is good, however, the success rate for pancreatic duct cannulation is low. Alternative and more invasive methods for diagnosis and management of pancreatic duct obstruction are required in these patients. When performed by experienced endoscopists, the procedure is safe in this patient population.

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**1012**

**A Survey of Clinical Experience of Video-Capsule Endoscopy in a University Hospital**

Kuldip S. Banwait, M.D., Kuntal M. Thaker, M.D., Ricardo Lafleur, M.D., Stephanie McConnell, R.M.D., Karl Koo, M.D., Mitchell Conn, M.D., Anthony DiMarino, M.D., Anthony Infantiolito, M.D., Sidney Cohen, M.D.* Division of Gastroenterology and Hepatology, Thomas Jefferson University, Philadelphia, PA.

**Purpose:** Wireless video capsule endoscopy (VCE) is a new technology that enables us to visualize the entire small bowel mucosa. It involves swallowing a video capsule endoscope, which is painless and relatively safe. Its use has been established for suspected small bowel bleeding, and the role of capsule endoscopy in the investigation of inflammatory bowel disease, iatrogenic disease, polyposis syndromes and celiac disease is evolving.

**Aim:** To describe the overall experience of video capsule endoscopy in a large tertiary care center.

**Methods:** All charts of patient who underwent VCE between 2001 and 2005 were retrospectively reviewed. There were 466 charts available with the complete VCE reports.

**Results:** There were 466 patients who underwent VCE. The mean age was 59.5 years (range 7–90). There were 265 female patients and 201 male patients. The most common indication for the procedure was obscure gastrointestinal bleeding (84.9%), followed by abdominal pain (8.8%), Crohn’s (7.1%), diarrhea (5.4%) and abnormal imaging (3.2%). A possible cause of obscure gastrointestinal bleeding was identified in 76.8% of patients. VCE identified a possible cause of abdominal pain and diarrhea in 41.8% and 28% respectively. 16% of patients with diarrhea were found to have newly diagnosed Crohn’s. 57.6% of patients with colonic Crohn’s disease were found to have small bowel involvement. The etiology of abnormal imaging was found in 60% of patients. Small intestinal mass was identified in 3.6% of patients and 88.3% of these patients presented with obscure gastrointestinal bleeding.

**Conclusions:** VCE is a clear choice for evaluation of obscure gastrointestinal bleeding.

VCE is an important tool in diagnosing previously unrecognized Crohn’s disease.

VCE is an important tool in diagnosing upper gastrointestinal involvement in established colonic Crohn’s disease.

VCE is an important supplementary diagnostic tool in investigating not only obscure gastrointestinal bleeding but also Crohn’s disease.

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**1013**

**An Instrument To Guide Sedation Method and Improve Tolerance to Endoscopic Procedures: A Randomized-Controlled Study**

Houssem E. Mardini, M.D., Luis R. Pena, M.D.,* Nicholas Nickl, M.D. Division of Gastroenterology, Hepatology and Nutrition, University of Kentucky, Lexington, KY.

**Purpose:** Despite conscious sedation, up to a quarter of patients may be dissatisfied with sedation during endoscopy. Our group has developed a questionnaire that aims to reliably identify patients who will experience endoscopy adversely. The major predictors of poor tolerance are the level of nervousness before the procedure and chronic use of alcohol, SSRIs and benzodiazepines. The aim of this study is to report the preliminary results of a randomized controlled study that tested the developed questionnaire in guiding sedation method.

**Methods:** Subjects presenting for routine endoscopy were recruited and randomized to receive either conventional conscious sedation with Versed and Fentanyl (control group) or to undergo an evaluation based on the instrument we developed and then assigned to either conscious sedation or sedation using propofol based on the risk of dissatisfaction assessed by the questionnaire. Tolerance was measured using a post-procedure questionnaire. Variables assessed included: nervousness, pain and distress during procedure, the extent to which physical and emotional needs were met and overall satisfaction. A visual analogue scale was used with higher scores corresponding to worse outcomes. Mann Whitney U test was used to assess the differences in scores.

**Results:** 298 subjects (112 males and 186 females) completed the study. 46 subjects (16%) were younger than 40 year old. 196 (66%) were 41–60 year old and 54 (18%) were older than 60 year old. Females had higher levels of nervousness (4.1 vs 3.2; p = 0.007). Nervousness levels were higher among patients younger than 60 years old and among patients with educational level of high school or less (3.9 vs 2.7; p = 0.012 & 4.5 vs 3.4; p = 0.015). Furthermore, chronic narcotic use was associated with higher level of nervousness before procedure (3.3 vs 2.6; p = .023). Fear of pain during...
procedure as reflected by higher levels of expected pain strongly correlated with nervousness before procedure (r = 0.59, p = 0.001).

Conclusions: The preliminary results of our study suggest that the instrument we developed is useful in identifying subjects at risk to experience aversive experience during endoscopy. These subjects are candidate for propofol-based sedation with improved outcomes.

1014
Understanding and Utilization of Endoscopic Ultrasound-Guided Fine Needle Aspiration by Thoracic Surgeons in the Staging of Lung Cancer
Young S. Oh, M.D., Naim Aoun, M.D., Bryan F Meyers, M.D., Mohamad A. Eloubeidi, M.D., Steven A. Edmundo-Wicz, M.D., Dayna S. Early, M.D., Riad R. Azar, M.D.∗ Division of Gastroenterology, Washington University School of Medicine, Saint Louis, MO; Division of Pulmonary, Critical Care and Sleep Medicine, Caritas St. Elizabeth’s Medical Center, Boston, MA; Division of Cardiothoracic Surgery, Washington University School of Medicine, Saint Louis, MO and Division of Gastroenterology and Hepatology, University of Alabama School of Medicine, Birmingham, AL.

Purpose: Our aim was to investigate the understanding and utilization of endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) by thoracic surgeons.

Methods: Thoracic surgeons were contacted by electronic mail and asked to participate in an internet-based survey. Demographic information, availability of EUS-FNA, as well as opinions regarding accessible nodal stations and perceived value of EUS-FNA were solicited from each respondent. Case scenarios were presented to selected respondents.

Results: 130 thoracic surgeons completed the survey. EUS-FNA was available to 68% of respondents. 38% to 64% of respondents correctly identified the mediastinal lymph nodes accessible by EUS-FNA, while 8% to 18% incorrectly answered that nodal stations 3 and 6 could be sampled with EUS-FNA. 29% of thoracic surgeons surveyed were unaware which areas EUS-FNA could access, and inability to perform the procedure. 29% of thoracic surgeons surveyed were unaware which areas EUS-FNA could access. 82% felt that EUS-FNA is the least invasive lung cancer staging modality available. When presented with a sample patient in whom non-small cell lung cancer is suspected but no tissue diagnosis is available, and has anterior and posterior mediastinal lymphadenopathy on positron emission tomography scan, 59% of respondents would perform mediastinoscopy first while only 33% would utilize EUS-FNA first followed by mediastinoscopy if the EUS-FNA was negative. 57% of respondents would increase their use of EUS-FNA if they were personally able to perform the procedure. 97% of thoracic surgeons surveyed felt that EUS-FNA played some role in lung cancer staging.

Conclusions: Although 82% of respondents acknowledged that EUS-FNA is the least invasive means to stage the mediastinum and 97% felt that it had a role in lung cancer staging, EUS-FNA would be utilized as the initial staging modality in a suitable patient by only 33% of thoracic surgeons surveyed. Potential reasons identified for underutilization of EUS-FNA included lack of availability, lack of understanding or misunderstanding of the areas that EUS-FNA can access, and inability to perform the procedure.

1016
Should Percutaneous Endoscopic Gastrostomy (PEG) Be Used in Intensive Care Unit Patients?
G. Koshy, M.D., I. Donepudi, M.D., H. Massoumi, M.D., E. Norkus, Ph.D., N. Kiyici, M.D., H. Hertan, F.A.C.G.∗ Gastroenterology, Our Lady of Mercy Medical Center, Bronx, NY.

Purpose: With rising health care costs, a current trend is to use PEG to shorten hospital length of stay (LOS) and to expedite discharge to the nursing home (NH). Because of this trend, gastroenterologists increasingly are being asked to perform PEGs in acutely ill patients with multiple comorbidities. To determine mortality in patients from medical intensive care units (MICU) versus the medical floors on whom PEG consults had been requested?

Methods: A sample of 191 consecutive patients [mean age of 81 (range 49–105 yrs), 58% female and 81% from NH] referred for PEG placement were included. Patient age, gender, BMI, race, community vs. NH, new PEG vs. replacement, reason for PEG, MICU vs. floor, LOS, clinical lab values, comorbidity, nutritional status classification score and outcome (discharge vs. death) were collected. The data was examined using Student t-tests, chi-square analysis and logistic regression analysis.

Results: MICU and medical floor patients had similar age (P = .0736) and gender distribution (P = .278). Significantly more MICU patients came from the community vs. NH (41% vs. 15%, P = .002). Also, a significantly higher proportion of MICU patients died compared to the medical floor patients (59% vs. 18%, P < .0005). Deaths were similar in new PEG and replacement PEG patients (P = .859). MICU patients had significantly longer LOS (mean of 56 vs. 18 days, P = .0240) but similar mean BMI (P = .5123) and nutritional risk assessment scores (P = .457) when compared with medical floor patients. Logistic regression analysis determined that deaths were 93%
more likely to occur in MICU patients (P < .0005), independent of the 10% decreased risk of death for every 1-unit increase in BMI (≥11), and independent of the >15 million-fold likelihood of death in patients with moderately compromised (P < .0005) or severely compromised (P < .0005) nutritional status classification. Further, age, gender, race, place of residence (community vs. NH) and LOS were not risk factors for death in this sample of PEG consult patients.

Conclusions: MICU patients are more severely ill than patients on the floors and may not survive long enough to benefit from PEG. It may be more reasonable to use nasogastric tubes for feeding and allow a “cool off” period between getting a consult for PEG and actually inserting a PEG. Future studies should work to identify both positive and negative factors associated with death in MICU patients to aid gastroenterologists in their decisions regarding PEG insertions.

1017
Radiofrequency (RF) Ablation of Barrett Esophagus (BE) with High Grade Dysplasia (HGD)

Virender K. Sharma, M.D., Bergein Overholt, M.D., Jae Kim, M.D., Roxanne McLaughlin, R.N., Michelle Moirano, Michael David Crowell, Ph.D., David F. Fleischer, M.D.* Department of Medicine/Division of GI, Mayo Clinic Scottsdale, Scottsdale, AZ and Gastrointestinal Associates, Knoxville, TN.

Purpose: To evaluate the safety, tolerability & histological clearance of HGD & BE after RF ablation in patients with BE & HGD.

Methods: Patients with biopsy-proven HGD on 2 EGD & confirmed by 2 independent pathologists without evidence of advanced disease on EUS or chest CT who refused esophagectomy or PDT were offered RF ablation for their HGD. The BARRX System was used for all treatments, which includes an esophageal balloon covered by radial RF electrodes. All patients received treatment at 300 W and 12 J/cm2. During a treatment session, ablation was delivered at least twice to the entire length of BE (intentional overlap). All patients received PPI bid post-ablation. Patients had their standard of care delivered at least twice to the entire length of BE (intentional overlap). All patients received lansoprazole 30 mg bid post-ablation in a 2 yrs confirmed by 2 independent pathologists enrolled. The BARRX RF ablation system consists of radial electrodes encircling an esophageal balloon. All patients received treatment at 300 W; 12 J/cm2 settings. During a treatment session, ablation was delivered twice to the entire length of BE (intentional overlap). All patients received lansoprazole 30 mg bid post-ablation. Procedural tolerability was assessed using 0–100 VAS on peri & 2 hours post procedure discomfort, & a 14-day symptom diary (chest, throat & abdominal pain, odynophagia & dysphagia). Patients had EGD with 4-quadrant, q 1 cm biopsies at 1, 3 & 6 mo post-ablation from the treated segment. Biopsies were interpreted by a blinded pathologist. The primary endpoint was clearance of HGD & secondary endpoint was clearance of BE. Complete Response (CR) = all biopsies negative for the outcome (LGD or IM) at a given time interval. Patients with CR at 3 month, proceeded to 6 mo EGD with biopsy. Patients with persistent BE or LGD at 3 month were re-treated at 4 month & continued the standard follow-up schedule.

Results: Ten patients (9 men, mean age 56 yrs, range 26–79) with BE and LGD (median length 5cm, range 2–6) treated. Median procedure time was 26 min (range 19–37). One patient had mild self-limiting GI bleed. No buried glands in over 450 follow-up biopsies. At follow-up of 3–9 months, 70% of patients are free of IM and dysplasia, while the remaining have only focal non-dysplastic IM remaining. Dysplasia response is 100%.

Conclusions: The RF ablation creates a circumferential ablation of BE with LGD without significant complications. The CR of LGD after 1 or 2 treatments is 100%. Unlike other ablative techniques, buried BE glands have not been observed with this procedure. [figure1]

PEDIATRICS

1019
Wireless Capsule Endoscopy: Initial Pediatric Experience
Francisca Mohr, M.D., Marshya Kay, M.D., Robert Wyllie, M.D., Lori Mahajan, M.D. Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH.

Purpose: Wireless capsule endoscopy (WCE) allows painless imaging of the small bowel without radiation and aids in the diagnosis of obscure small bowel disease in adults. To date there is only very limited data available regarding the use of WCE in pediatric patients and endoscopic deployment has not been reported in children. The aim of our study was to determine the indications, feasibility, outcome and complications of WCE in children.

Methods: An IRB approved retrospective chart review of 17 patients (11 F: 6 M) with a mean age of 14.8yrs (7.6 – 19.2yrs) and mean weight of 49.2 kg (24 – 84.2 kg) undergoing WCE was performed. Indications included possible Crohn’s (CD) disease in 13 patients, assessment of degree of involvement in 2 known IBD patients and occult bleeding in 2 patients. 13 patients swallowed the capsule without difficulty. Endoscopic deployment was performed in the remaining 4 patients using a through-the-channel WCE deployment device.

Results: All studies were successfully completed. Mean small bowel transit time was 266 min. (76 – 510 min.). The capsule was positioned at the IC valve at the end of the study in 2 patients and passed without complication in all. No complications were encountered during or after the procedure. 7 studies (41.2%) showed abnormalities: small bowel lesions consistent with Crohn’s disease in 5 patients (29%), enterobiasis in 1 patient (5.8%) and
gastritis in 1 (5.8%) patient. In addition a small 2 mm polypl was identified in one of the patients with CD. The findings on capsule endoscopy altered the management in 5 patients (29%) by either establishing a new diagnosis or initiating a change of therapy and eliminated additional testing in 5 additional patients (29%)

Conclusions: WCE is a valuable diagnostic tool in children with suspected small bowel disease particularly in Crohn’s disease not confirmed by conventional testing. WCE can be performed safely in young or small pediatric patients. The capsule can be endoscopically deployed in those patients unable to swallow the device because of patient age, size or impaired swallowing.

1020
Lighten up for Kids: A Program for Overweight Children. Does It Work?
Allan J. Rosenberg, M.D., F.A.C.G.,* Lance Green, Ph.D., Amy Abraham, Ph.D., Danielle Gandolpho, R.D., Lisa Daigle, R.N. Pediatrics, Tulane University School of Medicine, New Orleans, LA and Exercise and Sports Science, Tulane University, New Orleans, LA.

Purpose: To assess whether the recommended approach to evaluate and treat overweight children with a weight control/lifestyle change program including medical and psychosocial assessment, dietary management, exercise, and behavior modification works.

Methods: Lighten Up For Kids at Tulane a multidisciplinary team includes a pediatric gastroenterologist, exercise physiologist, psychologist, and diettian. Fifty children ages 8–15, 22 girls and 28 boys, 45 African American and 5 white all greater than 95% BMI started an eight week program. Meetings were biweekly, each included a family and individual behavioral, and dietary counseling and education, and physical exercises for the children. Each child underwent medical evaluation including labs, nutritional assessment, psychosocial and fitness testing. Lab tests included, CBC, CMPl lipid profile, HgbA1C, and fasting Insulin. Behavioral tests were the Child Depression Index (CDI), with Self Esteem subscore and Parenting Stress Index. A parent was required to attend all sessions. Parent and child signed a contract to attend and comply including followup labs, behavioral, and fitness testing and to return for followup in one, three, six and twelve months. There was no cost to participate.

Results: There was no significant weight change after 8 weeks. Two children had hypertension. Initial lab results; 7 elevated ALT, 13 elevated cholesterol 20(40%)and LDL 26(6%), HgbA1C elevated 13(26%). Insulin values at different labs difficult to interpret. Although ordered fasting many lab obtained nonfasting. No child had an elevated CDI score, 4 had elevated scores for Self Esteem. All parents had high Stress Indexes. After eight weeks fitness testing showed improvement in cardiovascular efficiency and lower body strength. No change in flexibility. Upper body strength increased for one group and showed no change in a second. T wenty three(46%) completed an eight week program. Two returned for the one month followup, none after. Behavioral and laboratory reassessments could not be analyzed poor compliance with insufficient data.

Conclusions: Limited outcome data exists for weight control to programs for children. Our attempt to make short term lifestyle changes for overweight children with a weight control/lifestyle change program including medical and psychosocial assessment, dietary management, exercise, and behavior modification works.

2012
The Value of Repeat Anorectal Manometry in Infants
Rita Steffen, M.D.,* Wylie Robert, M.D., Kaplan Barbara, M.D., Mahajan Lori, M.D., Feinberg Lisa, M.D., Mahajan Lori, M.D. Pediatric Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH.

Purpose: Neonates and infants with constipation or history of delay in passage of meconium are often seen for anorectal manometry to screen for short segment Hirschsprung disease. Anorectal manometry is also difficult to perform in this age group, which also includes premature infants, due to motion artifact and the small size of the anal sphincter complex within the anal canal. Performing these motility tests in infants may be time consuming and requires patience, but repeating the manometry has been shown to be of value to us in our clinical practice. Serial manometry will obviate the need to perform suction rectal biopsies in many infants.

Methods: We looked at the previous 100 consecutive anorectal manometry reports of infants less than one year of age done to rule out Hirschsprung disease. Repeating the manometry was recommended in 18 infants, as the RAIR was deemed equivocal.

Results: In all but one infant who went on to have a diagnosis of Hirschsprung disease by rectal biopsy, the second manometric screening showed the development of a normal RAIR in 16, and a third manometry in a premature infant was needed to show the normal RAIR in one infant.

Conclusions: The presence of a normal RAIR rules out Hirschsprung disease and makes suction rectal biopsy unnecessary to perform. Although bleeding which is usually minimal is the most frequent complication of rectal biopsy, obtaining inadequate submucosal tissue to make or exclude a diagnosis of Hirschsprung disease is also common, requiring a second suction rectal biopsy or a referral for a full thickness rectal biopsy by a pediatric surgeon. Other complications, which are serious, have been reported, including hemorrhage requiring transfusion. These may be avoided entirely in the clinical situation of an infant with the equivocal RAIR is restudied and is later found to have a normal RAIR.

1021
Outcomes of Recurrent Abdominal Pain (RAP) in Children and Responses to a Multidimensional Measure for RAP (MM-RAP): A Follow-Up Study
Hoda M. Malaty, M.D., Ph.D.,* David Y. Graham, M.D., Mark A. Gilger, M.D., Sahab Abdassyeh, M.D., Kimberly O’Malley, Ph.D. Medicine, Baylor College of Medicine, Houston, TX and Pediatrics, Baylor College of Medicine, Houston, TX.

Purpose: 1) to characterize the course of children with recurrent abdominal pain (RAP 2) to evaluate the diagnostic outcomes of (RAP), 3) to compare responses of a newly developed measure for RAP across the different diagnostic categories of RAP.

Methods: We conducted a prospective 2 year study of children diagnosed with RAP during their first visit to the Pediatric Gastroenterology Clinic at Texas Children’s Hospital and who were followed-up. At their initial visit, the eligible child/parent completed a multi-dimensional measure for RAP (MM-RAP) consisting of 4 scales (pain intensity scale, symptoms scale, disability scale, and satisfaction scale). The final diagnosis was defined as the diagnosis at their last visit. Outcomes were classified into 3 categories: functional RAP, organic RAP, and Gastrosophgeal Reflux Disease (GERD). The responses of the MM-RAP were analyzed by One-Way ANOVA analysis among the 3 RAP outcome groups.

Results: One hundred and forty one children ages 4 to 18 years (44% boys) participated. The follow-up ranged from 4–130 weeks (mean = 50 weeks). The final diagnoses were functional RAP in 46%, organic RAP in 24% and GERD in 30%. Neither age nor sex predicted the outcome. The total scores for the pain intensity scale were significantly higher among children with functional RAP than organic RAP or GERD (19.7 ±3.5 vs. 14.2 ±4.7 and 13.1 ±4.2); respectively, p = 001). Although the non-pain symptoms total score did not differ between the three outcome groups, independent items within the scale, i.e. diarrhea, vomiting, and heartburn were significantly higher among children with organic RAP and GERD compared to functional RAP. The scores for pain disability and health satisfaction scales were similar among the three outcome groups.

Conclusions: The MM-RAP discriminated between functional and organic RAP across the studied population. Children with functional RAP report more intense pain than children with organic RAP or GERD. Neither the disability scale nor the satisfaction scale differentiated between the functional and organic RAP.
When the morphology of the rectoanal inhibitory reflex is equivocal, we recommend repeating the anorectal manometry within the next one or two weeks. In some cases, anorectal manometry may be done weekly or bi-weekly until the mature and fully reproducible rectoanal inhibitory reflex is established.

1023
Pharmacokinetics of Intravenous Pantoprazole in Children Ages 1 to 16 Years
Gail M. Comer, M.D.,* Brinda Tammara, Ph.D., Kim Adcock, M.D., Stephen Schenayder, M.D., Phyllis Bishop, M.D., Laura P. James, M.D., Michael Hoy, M.S., Jeff Paul, Ph.D., Xu Meng, Ph.D. Clinical Research, Wyeth Pharmaceuticals, Collegeville, PA; University of Mississippi Medical Center Children’s Hospital, Pediatric Gastroenterology, Jackson, MS and Arkansas Children’s Hospital Research Institute, Little Rock, AR.

Purpose: To determine the pharmacokinetics (PK) of a single dose of intravenous (IV) pantoprazole in hospitalized pediatric patients 1 to 16 years of age.

Methods: This was an open-label, single-dose, randomized, parallel group extension of a similar study in 2 to16 year old children(1) study in hospitalized pediatric patients 1 to 2 years of age who could benefit from acid suppression therapy. Patients were randomly assigned to receive either 0.8 mg/kg or 1.6 mg/kg IV pantoprazole infused over 15 minutes. Blood samples were drawn at pre-determined time points and analyzed for plasma pantoprazole concentration using validated assay methods. The plasma data was analyzed using noncompartmental methods. Patients were monitored for signs and symptoms of adverse events in addition to physical examinations and laboratory evaluations.

Results: The mean ± SD dose-independent PK parameters normalized by body weight are shown below in comparison with those obtained previously from other age groups (1). No subjects were poor metabolizers.

<table>
<thead>
<tr>
<th>Age</th>
<th>N</th>
<th>1*</th>
<th>1*</th>
<th>1*</th>
<th>CL(L/hr/kg)</th>
<th>t1/2 (hrs)</th>
<th>Vss (L/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td></td>
<td>0.35 ± 0.10</td>
<td>1.2</td>
<td>0.24 ± 0.10</td>
</tr>
<tr>
<td>2-4</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td></td>
<td>0.17 ± 0.12</td>
<td>0.9</td>
<td>0.20 ± 0.08</td>
</tr>
<tr>
<td>5-10</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td></td>
<td>0.13 ± 0.08</td>
<td>2.0</td>
<td>0.22 ± 0.11</td>
</tr>
<tr>
<td>11-16</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td></td>
<td>0.28 ± 0.34</td>
<td>1.1</td>
<td>0.24 ± 0.20</td>
</tr>
</tbody>
</table>

*median value; †1*1 extensive metabolizer; †1*2 heterozygote

No trends toward a change with age were observed in the dose-independent PK parameters normalized by body weight in pediatric patients ages 2 to 16 years but there appeared to be a slight increase in the clearance of pantoprazole in 1 year old children. The mean peak plasma concentration (Cmax) and total area under the plasma concentration-time curve (AUC) increased with dose from 0.8 mg/kg to 1.6 mg/kg.

Conclusions: The clearance in children ages 1 to 2 years was higher than that in 2 to 4 and 5 to 10 year olds while the t 1/2 remained the same. The CL in the 2–16 year olds, with 1*2 were not significantly different from 1*, (Mean ± SD: 0.11 ± 0.06 and 0.18 ± 0.10) except the range in CL was narrower (0.03–0.13 vs 0.06–0.35). The high variability in CL is consistent with data in children with other PPI’s.


1024
Proton Pump Inhibitors in Infants
Thomas P. Iarocci, M.D.,* Hiangkiat Tan, M.S., Joseph Singer, M.D., Barron John, Pharm.D., Edith Pelzer, M.D., Dinesh Patel, M.D., Alan Bakst, Pharm.D. HQ HealthCare, Inc, Wilmington, DE; Children’s Center for Digestive Healthcare, Atlanta, GA and TAP Pharmaceuticals, Inc., Lake Forest, IL.

Purpose: Pediatric gastroesophageal reflux (GER) practice guidelines include acid suppression therapy for infants meeting certain criteria. This study investigated the off-label use of proton pump inhibitors (PPI) in infants aged < 12 months; findings, however, are not intended to support off-label use.

Methods: This retrospective observational study used data from 1999–2004 from 4 US health plans. Identified infants were < 12 months old with ≥1 index claim for a PPI and were eligible in the health plan for ≥1 month post-index. Pre-index diagnoses were observed and duration of therapy was estimated using a claims-derived algorithm as a proxy. Charts were abstracted in a subset to collect data on dose and treatment patterns occurring during the first year of life.

Results: Identified infants (N = 2,469, 58% male, 19% pre-term) commonly had difficulty feeding, colic, and respiratory infections prior to the index PPI. Of provider specialties captured at index, [pediatric] gastroenterology (39%) and pediatrics (48%) were most common. General practice, pulmonology, neonatology, and other pediatric subspecialties were also observed. Lansoprazole (52%) and omeprazole (46%) accounted for most PPI use. Estimated PPI course averaged 2–3 months, with longer median duration when gastrointestinal infections, food allergies, or URI/asthma variants were present in the peri-index period. Well over 50% had begun PPIs while aged ≤6 months; 16% continued beyond 12 months of age. The chart subset (n = 405) yielded 520 visits with dose documentation; mean dose (mg/kg/day) was 1.89 (lansoprazole) and 1.42 (omeprazole). Documented rationale for dose titration included upward adjustments for weight and/or to achieve adequate therapeutic response.

Conclusions: PPI use in this population was preceded by a variety of diagnoses, many of which could be secondary to or independent of GER.
Duration of therapy exhibited wide variation. Per-weight doses in this population exceeded common adult ranges. Clinical trials would help evaluate safety, efficacy and therapeutic endpoints.[Figure1]

1025

Protein – Energy Malnutrition of Children Less Than Five Years Based on Nutritional Classification in Rural Zone of Central Part of Iran
Naghmeh Jafarinia, M.D., Abolhasan Faraz, M.D., Shahreek Beheshiti, M.D., Zali, M.D., F.A.C.G.∗ Foodborne Disease, Research Center for Gastroenterology and Liver Disease, Shahreek Beheshiti University of Medical Sciences, Tehran, Islamic Republic of Iran and Epidemiology, Arak University of Medical Sciences, Arak, Markazi, Islamic Republic of Iran.

Purpose: To determine the risk factors of protein-energy malnourishment (PEM) among 0–5 year old in rural zone, central part of Iran.

Methods: This analytical cross-sectional study was carried out on all 811 children under five years old, living in 28 rural zone of Arak. This study was conducted between April 2003 and September 2003. Each child was visited by a physician. Weight, height, age, sex, past medical history, birth weight, birth order, breast feeding and supplemental feeding status, immunization status, history of hospitalization, literacy status of parents, rate of respiratory infection, birth interval and complication of pregnancy period was collected. The prevalence of malnutrition was assessed by using tree indicators including Waterlow (stunting and wasting), Welcome and Gomez. Height-for-age, weight-for-age, and weight-for-age Z-scores below 2.00 SD the reference NCHS standard was used to define stunting, wasting, Gomez and Welcome.

Results: The study revealed a prevalence of Wellcome of 7.5%, Waterlow – Stunting of 33.5%, Waterlow–Wasting of 23.0% and Gomez of 30.94%: the most prevalent of mild and severe PEM was 23.05% and 2.71% for Stunting and moderate PEM was 7.39% for Gomez. There was statistically difference between malnutrition and respiratory infection rate, low birth weight, breast feeding and supplemental feeding status (p < 0.05).

There were no significant association between malnutrition and age, sex, parent’s poor education and birth order.

Conclusions: Considering the results, the most rate of malnutrition in each classification was mild. Interventions to improve socioeconomic and environmental situations and family awareness are recommended to prevent the next damage and additional treatment costs and reduce the already low level of PEM further.

1026

Birth Order and Maternal IBS Status Affect Parental Response to GI Symptoms
Shelby L. Langer, Ph.D., Sarah McDonald, B.A, Lynn S. Walker, Ph.D., William E. Whitehead, Ph.D., Lauren Feld, Rona L. Levy, Ph.D.∗ School of Social Work, University of Washington, Seattle, WA; Division of Adolescent Medicine and Behavioral Science, Vanderbilt University Medical Center, Nashville, TN and Center for Functional GI & Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill, NC.

Purpose: While some research has been conducted on the relationship between child birth order and parent-child interactions, no data exist on the relationship between child birth order and parental response to GI symptoms. Aims: Determine if (1) parents respond differently to child GI symptoms as a function of the child’s birth order and (2) this relationship differs by maternal functional GI disorder status.

Methods: Data from 342 children of 228 mothers were examined (112 of the mothers had a diagnosis of IBS; 116 did not). Children ranged in age from 8 to 17 (mean = 12). Gender composition was split (51% male). Respondents completed the child-report version of the Adult Responses to Children’s Symptoms scale (Van Slyke & Walker, 2004). This measure is designed to assess parental solicitousness. Subscales include protection, distraction and minimization. We focus here on the former. Items such as “When you have a stomachache, how often do your parents let you stay home from school?” are rated on a 0–4 (never to always) scale.

Results: Child perceptions of parental protection differed as a function of birth order, p = .039 (Means and SDs = 1.49 ± .65 for only children, 1.65 ± .58 for first born children, 1.72 ± .67 for second born children and 1.91 ± .91 for third born children). Post-hoc comparisons revealed that second and third born children perceived greater parental protection than did only children, p < .05. These analyses were re-run separately for children of mothers with and without IBS. The effect described above was marginally significant for children of mothers with IBS (p = .058) but not significant for children of mothers without IBS (p = .411).

Conclusions: Given the established relationship between parental solicitousness and child disability (Levy et al., 2004), later born children may be at increased risk for such negative outcomes, particularly later born children of IBS mothers. Future research is needed to examine the mechanisms by which these children are responded to in a more “protective” but potentially maladaptive manner.

1027

Fructose Intolerance in Children Presenting with Abdominal Pain

Purpose: Fructose consumed as high fructose corn syrup in soda, fruit juices, or candy is also present in many fruits. While glucose is completely absorbed by active transport, fructose is absorbed by facilitated diffusion which is capacity limited. In small quantities, most dietary fructose is completely absorbed. Unabsorbed fructose may serve as an osmotic load and may be fermented by anaerobic bacteria producing hydrogen, methane, carbon dioxide and short chain fatty acids resulting in abdominal pain, bloating, flatus and diarrhea. The effects of fructose ingestion in children have not been described. We therefore determined the prevalence of fructose intolerance in children with unexplained chronic GI symptoms, to establish whether results of the fructose breath test are influenced by the amount of fructose.

Methods: We administered a Fructose Breath Test to children presenting with persistent, unexplained abdominal pain. Subjects randomly received a 1, 15 or 45 gram challenge of fructose and breath hydrogen was measured with a Quintron 12i GasAnalyzer for 3 hours following ingestion. Breath test results were considered positive when breath hydrogen was 20 ppm greater than baseline and fructose ingestion was accompanied by symptoms of gas, abdominal pain or diarrhea.

Results: To date 27 subjects have been enrolled with an average age of 13.1 ± 3.85 years; 45% male and 55% female. None of the subjects who received 1 gram were positive; 20% who received 15 grams and 50% who received 45 grams were positive (7 of 27 were positive). All subjects regardless of the breath test results were asked to restrict subsequent dietary fructose intake. Among the group that had a positive test, 60% reported improvement of their GI symptoms within 2 weeks while the group that tested negative did not.

Conclusions: Fructose malabsorption may be a significant problem in children and management of dietary intake can be effective in reducing symptoms of abdominal pain, bloating, flatus and diarrhea.

1028

Outcome of Infliximab Therapy in Children with Refractory Crohn’s Disease
David A. Gremse, M.D., F.A.C.G., Zonia I. Fleming, M.D., Karen D. Crissinger, M.D., Ph.D.∗ Pediatrics, University of Nevada School of Medicine, Las Vegas, NV and Pediatrics, University of South Alabama College of Medicine, Mobile, AL.
Purpose: Crohn’s disease (CD) is a chronic inflammatory bowel disorder that can affect children and adults. Treatments include anti-inflammatory and immunomodulator drugs. Due to the potential side effects of impaired growth and osteoporosis due to chronic corticosteroid therapy, steroid-sparing agents are often utilized for treatment of refractory CD. Infliximab, a monoclonal antibody to TNFα, has been increasingly used for treatment of CD refractory to treatment with other medications.

Methods: The medical records of pediatric patients with Crohn’s disease treated with infliximab were reviewed. Demographic characteristics, concomitant medication use, Pediatric Crohn’s Disease Activity Index (PCDAI), and the presence/absence of extraintestinal manifestations were analyzed. All patients received induction therapy with intravenous infliximab 5 mg/kg over 2 hours at 0, 2, and 6 weeks. Treatment efficacy was determined by the change in PCDAI, where < 10 is in remission and > 30 is moderate to severe disease.

Results: The medical records of fifteen patients, age 13.8 ± 2.8 yr, x ± SD, range 8–18 yr, 40% male) with CD who were treated with infliximab were reviewed. There were nine patients with inflammatory disease and six with fistulizing disease with a distribution of 12 with ileocolonic, 2 ileal, and 1 jejunal disease. Concomitant medications at baseline included antibiotics (n = 13), azathioprine (n = 11), 5-aminosalicylates (5-ASA, n = 10), methotrexate (n = 2), and nonsteroidal anti-inflammatory drugs (n = 5). The PCDAI score significantly decreased after infliximab therapy (40.1 ± 13.3 vs. 10.9 ± 8.2, p < 0.000025). The PCDAI score decreased in all patients and 10 of 15 patients were in remission as defined by a PCDAI of < 10. Corticosteroids were used an average of 11.5 months prior to infliximab therapy and were able to be discontinued in 13 of 15 patients. Eleven patients continue to receive infliximab every 8 weeks for maintenance therapy (duration of therapy 26.7 ± 8.7 months, range 15 – 44 mo.) while infliximab was discontinued in 4 patients after fistula closure was achieved. Four patients underwent surgery (2 for fistulae, 2 for resection).

Conclusions: Infliximab significantly reduced the PCDAI and improved symptoms of CD in children with refractory disease. Infliximab can be effective therapy for pediatric patients with refractory Crohn’s disease.

1029

Molecular Epidemiology and Clinical Features of Rotavirus Infection in Iranian Children

Mahnaz Taremi, M.D.,∗ Firouzeh Farahraj, DMT, Latif Gaebkar, M.D., Elham Mazaheri Tehrani, M.S., Haleh Edalatkhah, B.S., Koorosh Zolfagharian, B.S., Mohammad Reza Zali, M.D., F.A.C.G. National Research Department of Foodborne Diseases, Research Center for Gastroenterology and Liver Diseases, Shaheed Beheshti University of Medical Sciences, Tehran, Islamic Republic of Iran and Virology Department, Institute Pasteur, Tehran, Islamic Republic of Iran.

Purpose: Group A rotaviruses are a major cause of acute gastroenteritis in infant and young children worldwide. In this study, the molecular epidemiology and clinical features of rotavirus infection in Iranian children were investigated.

Methods: Between February 2003 and January 2004, thirty hundred and seventy two stool specimens from children under 5 years old with acute diarrhoea who attended the biggest pediatric hospital in Tehran (Iran), were analyzed using ELISA, reverse transcription - polymerase chain reaction (RT-PCR), and electrophoretotyping.

Results: Ninety- four samples (25.3%) were positive for the presence of rotavirus either by polyacrylamide gel electrophoresis (PAGE), ELISA, or both. According to PAGE, the predominant electrophoretic pattern detected was the long electropherotype 62 of 67 (92.5%) followed by the short electropherotype five of 67 (7.5%). Out of the positive specimens, 49 strains were further characterized by RT-PCR typing assay for identification of G types, resulting in 29 strains of G1 genotype while 20 samples could not be assigned a G type. All of G1 genotypes had a long RNA electropherotype. Among the patients with rotavirus infection, 23 (24.5%) patients required hospitalization and the remaining 71 (75.5%) were treated as outpatients. Rotavirus infection mostly affected children under 2 years of age with a peak incidence of 40% in children 1 to 2 years of age and it occurs year round with a seasonal pattern; more frequently during the rainy season (55%). No significant difference was seen between rotavirus-positive and –negative patients with respect to sex and breast-feeding. Watery diarrhea (85%), vomiting (74%) and Fever (65%) were significantly more frequent in children suffering from rotavirus gastroenteritis (P < 0.0001).

Conclusions: This study revealed that rotavirus is an important etiological agent of acute gastroenteritis in Tehran. We found that a major proportion of the specimens were untypeable. Improved detection and characterization of incompletely typed strains will help to develop a comprehensive strain information that may be required for tailoring effective rotavirus vaccines.

Adhesion Molecule and Nonopsonic Oxidative Burst Response in Children with Helicobacter pylori (Hp) Gastritis to 2 Strains of Hp

Vasundhara Tolii, M.D.,∗ Sharada D. Yangigurum, Ph.D., Michael Long, Ph.D., Ron Thomas, Ph.D., Raymond Podzorski, Ph.D. Pediatrics, Children’s Hospital of Michigan, Detroit, MI; Immunology, Children’s Hospital of Michigan, Detroit, MI and Pathology, Wayne State University, Detroit, MI.

Purpose: This study determined the β2 integrin (CD11a, CD11b, CD11c, and CD18) and non-opsonic oxidative burst response of peripheral blood neutrophils from children in different stages of Hp gastritis, and from control children, after stimulation by Hp extracts.

Methods: Peripheral blood was obtained from children with newly diagnosed Hp gastritis (Group 1, n = 25), children with Hp after treatment but non-eradication (Group 2, n = 12), children with Hp after treatment with successful eradication (Group 3, n = 4), and from non-infected controls (Group 4, n = 23). Aliquots from fresh EDTA blood specimens were stimulated for 30-minutes with extracts from a higher virulence strain of Hp (HV, genotype vacA s1a m1, cagA, cagE, and iceA1) and from a lower virulence strain (LV, genotype vacA s2 m2, iceA2). The response and the percentage changes in the mean channel fluorescence between stimulated and unstimulated cells was determined by flow cytometry.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD 18 LV</td>
<td>42 ± 36</td>
<td>51 ± 26</td>
<td>36 ± 15</td>
<td>15 ± 21</td>
</tr>
<tr>
<td>CD 18 HV</td>
<td>67 ± 46</td>
<td>62 ± 58</td>
<td>70 ± 30</td>
<td>41 ± 36</td>
</tr>
<tr>
<td>CD 11b LV</td>
<td>121 ± 158</td>
<td>94 ± 83</td>
<td>95 ± 60</td>
<td>26 ± 30</td>
</tr>
<tr>
<td>CD 11b HV</td>
<td>144 ± 166</td>
<td>89 ± 90</td>
<td>158 ± 74</td>
<td>66 ± 62</td>
</tr>
<tr>
<td>CD 11c LV</td>
<td>67 ± 100</td>
<td>45 ± 17</td>
<td>61 ± 755</td>
<td>20 ± 23</td>
</tr>
<tr>
<td>CD 11c HV</td>
<td>91 ± 97</td>
<td>67 ± 35</td>
<td>167 ± 197</td>
<td>53 ± 46</td>
</tr>
<tr>
<td>Neutrophil Burst LV</td>
<td>30 ± 68</td>
<td>14 ± 35</td>
<td>32 ± 25</td>
<td>23 ± 53</td>
</tr>
<tr>
<td>Neutrophil Burst HV</td>
<td>72 ± 231</td>
<td>16 ± 33</td>
<td>14 ± 49</td>
<td>16 ± 31</td>
</tr>
</tbody>
</table>

Conclusions: CD18 and CD11b were significantly upregulated in treated, untreated and newly diagnosed Hp patients compared to controls. Such induction was higher with HV than with LV strains. Highest induction was observed in patients with successful eradication of Hp. Induction of CD11a (data not shown) and CD11c was unremarkable.

Newly diagnosed Hp patients had higher nonopsonic oxidative burst response to HV strain while Hp eradicated patients had higher response to LV strain. Considering the previously established role of CD18/CD11b in induction of apoptosis such response from newly diagnosed Hp patients can be expected. However, in patients who had successful eradication of Hp, despite higher CD18/CD11b response to HV strain, the nonopsonic oxidative burst response was higher with LV strain suggesting a possibility of the involvement of a novel pathway in the oxidative burst response. Further studies are needed to elucidate this further.
Characterization of Gastroesophageal Reflux after Fundoplication in Children Using Impedance Technology

Ajay Kaul, M.D.,* John A. Krause, B.S.N. Gastroenterology, Hepatology and Nutrition, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH and Aerodigestive and Sleep Center, Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

Purpose: To characterize gastroesophageal reflux after fundoplication in children with aerodigestive disorders.

Methods: Retrograde bolus movement in the esophagus was recorded in children who had had a fundoplication, as part of evaluation prior to airway surgery, using the multichannel intraluminal impedance catheter. There were 24 studies that had a minimum of 14 hours of analyzable data (after deleting the post prandial and continuous feeding periods). 18 subjects were males and 14 had a history of prematurity. The age range was 10 months to 11.5 years. Studies were performed 2 months to 9.5 years after the fundoplication. Catheter was placed after endoscopy under general anesthesia and placement verified by a chest x-ray in all. Recording began after complete recovery.

Catheter was placed after endoscopy under general anesthesia and placement verified by a chest x-ray in all. Recording began after complete recovery from anesthesia. All children were admitted to the hospital overnight and verified by a chest x-ray in all. Recording began after complete recovery from anesthesia. All children were admitted to the hospital overnight and no other medical procedures were conducted during the study. Neither the primary mode of feeding (oral, bolus and continuous gastrostomy feeds or a combination) nor the acid suppression therapy was altered during the study.

Results: 1. After fundoplication the total reflux episodes ranged from 1 to 183 per study with a mean of 31 for the group.
2. Air reflux was as or more frequent than liquid reflux (acid and non acid).
3. A trend towards a decrease in the total number of reflux episodes was noted over time after fundoplication.
4. Endoscopy did not show evidence of esophagitis in any, but microscopic examination of distal esophageal biopsies revealed mild inflammation in 8.

Conclusions: This study indicates that even though fundoplication does not completely prevent gastroesophageal reflux episodes, the incidence of esophagitis is very low. Contrary to current dogma, there was a decrease over time after fundoplication. This may reflect growth and developmental alterations of the upper GI tract in children.

Lymphocytic Gastritis in Celiac Disease: A Database Revision

Francesca Poli, M.D., Nunzio C.M. Salfi, M.D., Giuseppe N. Martinelli, M.D., Angela Collina, M.D., Massimo Masi, M.D., M. Luisa Forchelli, M.D.* Department of Pathology Professor Martini, S.Orsola-Malpighi Hospital, Bologna, Italy and Department of Paediatrics Director Prof. Martini, S.Orsola-Malpighi Hospital, Bologna, Italy.

Purpose: Lymphocytic gastritis (LG) has been associated to celiac disease (CD). The LG diagnosis is based on a histologic cut-off point of 25 intraepithelial lymphocytes (IEL). This cut-off point however, has been criticized. Our aims are as follows: 1. to check the degree of association between LG and CD, and 2. to verify the feasibility of the cut-off point.

Methods: All the children who had a CD diagnosis during 2003 were identified from the Pathology database. Their hematoxylin-eosin-stained gastric and duodenal biopsies were blindly reviewed by two independent pathologists. To clarify the infiltration type, new additional paraffin sections were immunostained with T-cell markers and, again, compared by the same two pathologists. Clinical and laboratory data were taken into consideration as well as the possibility of a Helicobacter pylori infection.

Results: Thirty-three children (23 females, 10 males, mean age 5.5 years range 1.5–12.6) were identified. Overall 36 gastric specimens were available, as three children had double specimens. These were the summarizing results:

- 10 cases with isolated increased IEL without any findings of gastritis (3%)
- 1 case with Helicobacter pylori gastritis with increased IEL (3%)
- 5 cases of mild IEL increase (upper limit of normal range) (15%)

Immunohistochemical and hematoxylin-eosin stained specimens did not show differences. Inter-individual findings were similar (no significance was reached).

Conclusions: The association between LG and CD is confirmed although our percentage was lower than the one described in the literature. However, given the overall presence of increased IEL in CD, although below the cut-off point of 25 IEL, we believe that combined gastric and duodenal biopsies should be performed to help formulating a definite CD diagnosis. Perhaps this would also clarify the cut-off level.

Controlled Clinical Trial of Gatorade or Pedialyte for Viral Gastroenteritis in Children

Satish S.C. Rao, R. W. Summers, B. M. Zimmerman, S. G. R. Rao, S. Ramana, U. Devi, B. Pratap Internal Medicine, University of Iowa, Iowa City, IA and Gastroenterology & Infectious Diseases, Osmania Medical College, Hyderabad, India.

Purpose: Oral rehydration solutions (ORS) are frequently used for treating dehydration in acute viral gastroenteritis. Whether a sports drink-Gatorade (G) can be as efficacious as ORS-Pedialyte (P) is not known. In a randomized double blind trial, we examined the efficacy, safety and palatability of these solutions, and tested the efficacy of a new solution (NS) that contained 4% carbohydrate, 35 mEq/L sodium and 25 mEq/L potassium.

Methods: 73 children admitted with viral gastroenteritis were randomized to receive G, P or NS for 48 hours. A yogurt/rice diet was allowed ad libitum. Stool&urine output, electrolytes, fluid intake, body weight&hematocrit were recorded. Oral rehydration solutions (ORS) are frequently used for treating dehydration in acute viral gastroenteritis. Whether a sports drink-Gatorade (G) can be as efficacious as ORS-Pedialyte (P) is not known. In a randomized double blind trial, we examined the efficacy, safety and palatability of these solutions, and tested the efficacy of a new solution (NS) that contained 4% carbohydrate, 35 mEq/L sodium and 25 mEq/L potassium.

Conclusions: Gatorade was as effective as Pedialyte in correcting dehydration and in improving bowel symptoms. All 3 were safe. Unlike other solutions except palability score = 7.1#.

Body Wt (Kg) 21.8 22.7 23.1 19.8 20.7 21
S. Frequency 7.1 4.8* 2.8* 7.3 4.6* 2.8*
% Stool unformed 100 89 11* 100 90 17*
Taste-VAS 8.4# 5.4
Vol. ingested (ml) 4000 3000 4000 3000
Stool Wt (g) 592 430* 570 463*

Gatorade, n = 20 Pedialyte, n = 19
Admit 24 h 48 h Admit 24 h 48 h

Conclusions: Gatorade was as effective as Pedialyte in correcting dehydration and in improving bowel symptoms. All 3 were safe. Unlike other solutions except palability score = 7.1#.
Pharmacokinetic (PK) Profile of Rabeprazole in Patients Aged 12–16 Years with Gastroesophageal Reflux Disease (GERD)

Kathleen Lomax, M.D., Laura James, M.D.,* Philip Walson, M.D., Shanti Varughese, M.S., Josephine Reyes, DVM Eisai Inc., Teaneck, NJ; Pediatrics, Arkansas Children’s Hospital, Little Rock, AR; Clinical Pharmacology, Cincinnati Children’s Hospital, Cincinnati, OH and Eisai Medical Research Inc., Ridgefield Park, NJ.

Purpose: To characterize the PK profile of single and repeat doses of rabeprazole sodium (RAB) 10 mg or 20 mg tablets in children with GERD.

Methods: This multicenter, open-label, dose-ranging PK and safety trial stratified patients with GERD symptoms into 2 groups (aged 12–< 14 and 14–16 yr) then randomized them to RAB 10 mg or 20 mg. Following enrollment and safety evaluation of the 10-mg group, patients were enrolled in the 20-mg group. Study medication was given in the morning after overnight fasts for 5 or 7 days at the study site (required days 1, 2, and 5/7) or at home. On day 1 and 5/7 (final day of dose administration), patients had clear liquids 2 h and lunch 4 h after dosing. Blood samples were obtained as follows: day 1 and 5/7: baseline (predose), every half hour up to 6 h postdose, and 8 and 12 h postdose; days 2, 3, 4: predose; day 6/8: 24 h postdose day 5/7.

Results: 24 patients were enrolled (male, n = 11; mean weight, 65.66 kg; 12–< 14 yr, n = 8; 14–16 yr, n = 16); 12 patients were randomized in each group. Preliminary results show that on day 1 and 5/7, RAB 20 mg significantly increased AUC and Cmax vs RAB 10 mg. Mean AUC for RAB 20 mg was 557.8 ng·h/mL (day 1) and 828.4 ng·h/mL (day 5/7) vs 305.0 ng·h/mL and 249.8 ng·h/mL, respectively, for RAB 10 mg. Mean Cmax for RAB 20 mg was 319.0 ng/mL (day 1) and 460.4 ng/mL (day 5/7) vs 186.6 ng/mL and 184.1 ng/mL, respectively, for RAB 10 mg. Within-dose group comparisons (ANOVA) showed AUC and Cmax were similar on day 1 and 5/7. The apparent increase in mean AUC on day 5/7 may be due to variable patient response; all plasma concentrations were unquantifiable 12 h postdose. Tmax and t1/2 were relatively unchanged between the 2 groups with multiple dosing. Clearance and t1/2 were within the range for adults. RAB thioether metabolite values followed the same pattern as parent compound values.

Conclusions: Within-group comparisons showed that AUC and Cmax for RAB 10 and 20 mg were similar on day 1 and 5/7, indicating no accumulation of RAB or its thioether metabolite with multiple dosing. Overall, PK profiles were similar on day 1 compared with day 5/7 for both groups. On behalf of the Study 119 Pediatric Trial Investigators. Research supported by Eisai Medical Research Inc., Ridgefield Park, New Jersey, USA.

Safely Profile of Rabeprazole in Patients Aged 12–16 Years with Gastroesophageal Reflux Disease (GERD)

Kathleen Lomax, M.D., Laura James, M.D.,* Philip Walson, M.D., Shanti Varughese, M.S., Josephine Reyes, DVM Eisai Inc., Teaneck, NJ; Pediatrics, Arkansas Children’s Hospital, Little Rock, AR; Clinical Pharmacology, Cincinnati Children’s Hospital, Cincinnati, OH and Eisai Medical Research Inc., Ridgefield Park, NJ.

Purpose: To establish the safety profile of single and repeat doses of rabeprazole sodium (RAB) 10 mg or 20 mg tablets in children with GERD.

Methods: This multicenter, open-label trial stratified 24 patients with GERD symptoms into 2 groups (aged 12–< 14 and 14–16 yr) then randomized them to a single morning dose of RAB 10 mg or 20 mg for 5 or 7 days. Following enrollment and safety evaluation of 10-mg group patients, patients were enrolled in the 20-mg group. All patients underwent complete physical examinations at screening and discharge. Blood pressure, pulse, and temperature were recorded at baseline and throughout the study. ECGs and lab tests were performed predose and 12 h postdose on day 1 and at discharge. Safety variables assessed included adverse events (AEs), serious AEs (SAEs), and treatment-emergent signs and symptoms (TESS). Treatment-emergent ab-

normal (lab) values (TEAVs) were summarized. Clinical evaluations and safety and AE monitoring were reviewed throughout the study.

Results: 24 patients (male, n = 11; mean weight, 65.66 kg) were enrolled (12–< 14 yr, n = 8; 14–16 yr, n = 16); 12 patients were randomized in each RAB group. Preliminary results showed no statistically significant differences between treatments in N patients with AEs. Almost all AEs were mild: 10 patients (41.7%) reported mild AEs; 1 patient (4.2%) reported a moderate AE (dysmenorrhea). 5 patients (20.8%) had AEs considered possibly study-drug related (0 probably related). No deaths or SAEs were reported. No patient discontinued due to AEs. Incidence of TESS was 45.8%, with headache most frequently reported (4 patients, 16.7%), followed by nausea (2 patients, 8.3%). 6 patients (25.0%) had TEAVs (RAB 10 mg: elevated potassium [2] and low calcium [1]; RAB 20 mg: elevated potassium [1] and cosinophils [1] and neutrophils [1]). No TEAV was considered clinically significant by the investigator. There were no clinically significant changes from baseline to discharge in ECGs, hematology, chemistry, or urinalysis.

Conclusions: RAB 10 and 20 mg was well tolerated in patients with GERD aged 12–16 yr with no notable differences in overall safety between treatment groups. On behalf of the Study 119 Pediatric Trial Investigators. Research supported by Eisai Medical Research Inc., Ridgefield Park, New Jersey, USA.

The Etiology of Diarrheal Illness in a Sub-Saharan African Country

Tiffany G. Johnson, M.D.,* Nicholas J. Shaheen, M.D., M.P.H. Department of Gastroenterology, UNC-Chapel Hill, Chapel Hill, NC.

Purpose: Diarrheal illness is a major cause of mortality for children in Africa; however, the epidemiology is understudied and varies from country to country. The purpose is to describe the etiology of diarrheal diseases at an outpatient facility and an inpatient ward in Malawi, Africa.

Methods: We performed a retrospective study of consecutive subjects from ages 4 to 60 months admitted to Kamazu Central Hospital in Lilongwe, Malawi, with the principle diagnosis of diarrhea seen during a one-month period. A second cohort of consecutive subjects of the same ages presenting to MARS Clinic, an outpatient clinic in Lilongwe, Malawi, with a chief complaint of diarrhea was also assessed. Charts were reviewed for demographic information, mode of work-up, and any pathogens isolated. Comparisons were made between inpatients and outpatients using Student’s t-tests and X2 analysis.

Results: Thirty children (mean age 15.3 months) were admitted to the ward, and 28 (mean age 33.0 months) were assessed at the outpatient clinic during the study period (p = 0.0006). Less than half of patients had stool cultures. Blood smears for malaria were performed on 21 (70%) inpatients vs. 22 (79%) outpatients (p = NS). In 19/30 (63.3%) inpatients and 11/28 (39.3%) outpatients, at least one diarrhea-causing pathogen was isolated. Of those patients, the most common etiology was malaria, affecting 19/19 (100%) inpatients and 3/10 (30.0%) outpatients. Other etiologies of infectious diarrhea included bacterial gastroenteritis [2/30 (6.6%) inpatients and 7/28 (25.0%) outpatients]; viral gastroenteritis [1/30 (3%) inpatients and 10/28 (35.7%) outpatients]; and Giardia lamblia [1/30 (3%) inpatients and 3/28 (10.7%) outpatients]. In 11/30 (36.6%) inpatients and 18/28 (64.3%) outpatients, no etiology of the diarrhea was identified. Eleven of 30 (36.6%) inpatients and 17 of 28 (60.7%) outpatients were treated empirically. The most common medications for empiric treatment were oral rehydration salts (15/58, 25.9%), cotrimoxazole (11/58, 19.0%) and paracetamol (13/58, 22.4%). Of the 30 subjects admitted to the hospital with diarrheal illness, 4 (13%) died of their disease.

Conclusions: Pediatric diarrheal illness is a common cause of both inpatient admission and outpatient consultation in Malawi. A significant proportion of patients presenting with diarrhea have minimal work-up and undergo empiric therapy. Of those subjects in whom a pathogen is isolated, malaria is the most common diarrhea-inducing pathogen. Death from diarrheal disease occurred in more than 10% of the inpatient population.
An Unusual Cause for Neonatal Cholestasis
Kara J. Gross, M.D.,* Leslie M. Higuchi, M.D., Denesh K. Chitkara, M.D., John B. Watkins, M.D. Gastroenterology, Children's Hospital Boston, Boston, MA.

Purpose: Babesiosis is an illness caused by malaria-like parasites. Tick bites are the most common form of transmission. Infection is rarely transmitted through blood transfusions. We describe the first known case of Babesiosis acquired by transfusion and manifesting as neonatal cholestasis.

Methods: A 101-day-old ex-27 week female was transferred for progressive hyperbilirubinemia. The patient was found to have a direct bilirubin of 1.6 on day of life (dol) 26, increasing to 6.8 by dol 90 and to 14.3 by dol 100, the day of transfer. There were no signs of illness or liver disease. Past medical history was significant for several blood transfusions during infections.

Pertinent labs were AST/ALT 240/144. CBC (7.2 < 31.4 > 152) was normal. Work-up for common causes of neonatal cholestasis was nondiagnostic. Exam revealed a nontoxic, afebrile, jaundiced female with scleral icterus. CBC decreased to 5.5 < 24.1 > 66. Blood culture was negative. Blood smear revealed multiple intraerythrocytic ring forms diagnostic of Babesiosis. The patient was treated with Quinine and Clindamycin. Lab values normalized in two weeks. Other neonates from the same Cape Cod Hospital had also acquired the infection from blood transfusions.

Results: Babesiosis is the second most common blood parasite worldwide and the most common transfusion-transmitted tick-borne infection. It occurs predominantly on the northeast coast of the U.S. where seroprevalence rates reach 21%. There is a 0.17% transmission risk per unit of packed erythrocytes in endemic areas. Common presentation includes an unconjugated hyperbilirubinemia secondary to hemolysis. It is thought that cholestasis is caused by inflammatory cytokines inhibiting hepatobiliary transporter gene expression, thus down-regulating bile transport. Clinical manifestations vary widely. Definitive diagnosis is made by PCR or blood smear showing intraerythrocytic parasites. Pediatric cases are treated with Quinine and Clindamycin. Mortality from undiagnosed or ineffectively treated infection is as high as 5% in the United States. [figure1]

Long Term Follow-Up in Paediatric-Juvenile Patient with Inflammatory Bowel Disease
Barbara Bizzarri, M.D., Valentina Maffini, M.D., Fabiola Fornaroli, M.D., Nicola de’ Angelis, M.D., Barbara Magieteri, M.D., Benedetta Ghidini, M.D., Francesca Guatelli, M.D., Francesca Vincenzi, M.D., Gian Luigi de’ Angelis, Prof° Paediatric, Paediatric Gastroenterology and Endoscopic Unit, Parma, Italy.

Purpose: Aim of the study: to evaluate incidence, indications, complications and long term follow-up after surgical treatment in paediatric-juvenile patients with inflammatory bowel disease (IBD).

Methods: January 1984-December 2004: 173 new diagnosis (mean age 15 7/12 yrs, range 14–24 yrs) of IBD at Paediatric Gastroenterology and Endoscopic Unit, University of Parma: 77 Crohn’s disease (CD) (42 M, 35 F), 74 Ulcerative Colitis (UC) (32 M, 42 F) e 2 Indeterminate Colitis (IC) (2 F). All patients have been farmacologically treated first to induce remission (corticosteroid, metronidazole, metotrexate or azatioprine, mesalazine), later with a maintenance therapy (immunosopressor and Infliximab), clinically and endoscopically followed-up (range 1–18 years). Fortyone patients (24%) underwent surgery: 29 CD (38%), 10 UC (14%), 2 IC (100%). All patients, after surgery, underwent periodically follow-up: blood test, ultrasound every 3 months, endoscopy every 6 months for the first year, then once a year. Mesalazine, azatioprine, probiotics were used in CD after surgery; probiotics, loperamide, cholestyramine were used in UC.

Results: In CD patients: 22 operations were elective ileal or ileal-cecal resection (16 stenosis, 4 perforations, 2 haemorrhages), 7 in emergency: 3 perforations, in 4 patients diagnosis was made during surgery (1 ileal perforation, 1 hemorrhage, 1 occlusion, 1 appendicitis). All RCU patients underwent elective total colectomy (5 ileal-anal anastomosis, 2 ileal rectum anastomosis, 3 ileal pouch) because of corticosteroid dependence. In IC patients a elective total colectomy was performed for corticosteroidal dependence. Two CD patients underwent re-surgery (ileal-cecal stenosis, multiple entero-cutaneus fistulas). Short term complications occurred in 2 patients with CD (1 enterocutaneus fistula, 1 anastomosis failure), in 1 IC (back-wash ileitis), never in UC. Long term complications occurred in 4 CD (4 anastomosis stenosis), in 2 UC (1 ileal perforation, 1 pouchitis), never in IC. The 4 patients with stenosis underwent perendoscopic dilatation without needling resurgery.

Conclusions: RCU patients usually underwent surgery at a younger age since in RCU surgery can be definitive. CD patients had a low incidence of re-surgery probably due to an improvement of nutritional and pharmacological therapy. IC patients presented a disease with important biological aggressiveness.

Internal Granulation Tissue of Gastrostomies: A Treatable Cause for GI Hemorrhage in Children with Short Bowel Syndrome and Portal Hypertension

Purpose: Children with short bowel syndrome (SBS) who have gastrostomies and are on TPN may develop cholestasis and its complications including portal hypertension. However, in this group, upper GI (UGI) hemorrhage is only rarely due to esophageal varices. Instead, peri-gastrostomy varices preferentially form. We have observed yet another cause of bleeding—namely, granulation tissue at the gastrostomy site. We conducted this study to ascertain the frequency, clinical characteristics, and outcome of this problem in our SBS population.

Methods: We conducted a chart review of all children with SBS in our institution who experienced UGI bleeding between 1/2001 and 6/2005. We tabulated the number of patients who bled, the number who bled from granulation tissue, clinical characteristics, avg. blood loss, and results of endoscopic therapy.

Results: Twenty seven patients had persistent cholestasis, and 15 of them underwent upper endoscopy for bleeding. Causes of bleeding were ulcers in 3, portal hypertensive gastropathy/peristomal varices in 8, and granulation tissue adjacent to the gastrostomy in 4. The granulation tissue was evident only upon deflation of the gastrostomy tube balloon during inspection of the gastrostomy site. All of those with granulation tissue had jaundice and portal hypertension when endoscoped. None of them had synthetic liver dysfunction. Average blood loss prior to endoscopy for those with granulation tissue was 10 ml/kg/wk. All four underwent argon plasma coagulation of the granulation tissue. Bleeding ceased permanently in one of them after a single ablation. Two of the others with granulation tissue required two ablations for resolution of their bleeding. The 4th has required 3 sessions to halve the frequency of transfusions. No complications resulted from therapy. As gut adaptation took place, cholestasis and portal hypertension have resolved or are resolving in all of the group with granulation tissue.

Conclusions: Granulation tissue of the gastrostomy site is a common, treatable cause of UGI bleeding in children with SBS and portal hypertension. The lesions can be visualized best if the gastrostomy balloon is deflated during inspection of the gastric body. Therapy with argon plasma coagulation appears to be safe and effective.
**Modulation of Plasma Cholesterol by Mast Cells**


**Purpose:** Plasma cholesterol is derived from two main sources: dietary intake and *de novo* synthesis. Most cholesterol synthesis occurs in the peripheral tissues such as liver, intestine, muscle, and skin. The relative contribution of cholesterol from any of these sources is dependent upon genetic predisposition, diet, and other factors. Fakuda M et al. (Hypertens Res. 2002) reported that HDL cholesterol level was significantly higher among carriers of the G3255A polymorphism in the male cell chymase gene. We therefore hypothesized that mast cells influence HDL cholesterol levels.

**Methods:** We initially measured the plasma total and HDL cholesterol levels in normal (+/+), and mast cell-deficient *Kit*+/Kit−/− (Kit mutant) mice on a normal chow diet (Phase I). The mice were then fed a high fat diet (Western diet containing 42% calories from fat) for 5 weeks and plasma total and HDL cholesterol were measured (Phase II).

**Results:** There was significant increase (~30%) in the level of total plasma cholesterol level in *Kit* mutant mice compared with normal/+/+ mice on a regular (Phase I) diet. This increase in total cholesterol was mainly due to an increase in the level of HDL cholesterol (see Table). On the phase II diet, while there was a 2–2.8 fold increase in the levels of total cholesterol in the mice, there was now no significant difference in either total cholesterol or HDL cholesterol comparing +/+ with *Kit* mutant mice (see Table).

**Plasma cholesterol levels**

<table>
<thead>
<tr>
<th>Phase I (regular diet)</th>
<th>Plasma Cholesterol (mg/dl)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Normal +/+ Mice</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>82.8 ± 7.4</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>53.2 ± 9.2</td>
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<tr>
<td>LDL Cholesterol</td>
<td>29.6 ± 11.9</td>
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<tr>
<th>Phase II (after 5 wks. high cholesterol diet)</th>
<th>Plasma Cholesterol (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>227.9 ± 11.3</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>187.9 ± 16.1</td>
</tr>
<tr>
<td>LDL Cholesterol</td>
<td>40 ± 20.8</td>
</tr>
</tbody>
</table>

**Conclusions:** These results suggest that mast cells influence total cholesterol levels specifically by raising HDL cholesterol. However, this effect of mast cells was not seen when the mice were fed a high fat diet. These results suggest that inhibiting mast cell activity may be a novel clinical approach to raise HDL levels.

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**Survey of Pediatric Health Care Providers on Their Knowledge of Celiac Disease Confirms the Need for Educational Initiatives**

Martha H. Dirks, M.D., Stefano Guandalini, M.D.*. Department of Pediatrics, University of Montreal, Montreal, QC, Canada and Department of Pediatrics, University of Chicago, Chicago, IL.

**Purpose:** In 2005, guidelines and consensus statements on celiac disease (CD) were published by NASPGHAN, the NIH and the CDHNF. Aims: To conduct a survey of pediatric health care providers and endocrinologists in order to assess their level of knowledge of CD prior to the publication of these educational initiatives.

**Methods:** A 17 item peer-reviewed questionnaire was designed by the authors to assess the understanding of appropriate screening tools and the populations that should be screened for CD. The survey was administered via the internet to 207 US physicians (87 family practitioners, 90 pediatricians and 30 endocrinologists) via Epocrates. Response rates were 100%.

**Results:** Only 31% of respondents chose either IgA anti-human tissue transglutaminase or anti-endomysial antibody as the most appropriate first line-screening test for CD. A majority (51%) chose either IgA or IgGt antigliadin antibody. Only 48% recommended an intestinal biopsy be performed in those with positive serology to confirm the diagnosis prior to starting the gluten-free diet. Only 23% identified 4 conditions associated with CD among a list of 5. Iron deficiency was the most commonly recognized sign (85%) of CD. 41% responded that type 1 diabetics should be screened, while 29% felt that they should not. The principal rationale against screening diabetics in this subgroup was unknown (45%). Only 8% chose the recommended strategy for re-screening diabetic patients. Just 6% correctly identified HLA DQ2 and DQ8 heterodimer as useful to rule out the diagnosis of CD if negative. Although hereditary factors were known to be a risk for development of CD in the majority (88%), only 18% were aware of statistics to counsel patient’s families. Finally, 61% recognized the need for a strict, life long gluten-free diet in affected patients. A Doc Alert email summary of the findings was sent to 35,000 Epocrates subscribers.

**Conclusions:** The recent educational initiatives on CD were much needed. Improved awareness of the appropriate serological testing for CD, the utility of HLA testing, requirement to confirm the diagnosis with an intestinal biopsy, and treatment by life long gluten free diet should continue to be the focus of physician education programs. The reasons for non-referral for biopsy require elucidation. A repeat survey is planned to assess the impact of recent initiatives on physician knowledge of celiac disease.

1042

**Laser Photothermolysis in the Treatment of Pilonidal Disease in Children**

Jeff R. Lukish, M.D.,* Chris Norwood, M.D., Arthur Delorimier, M.D. Pediatric Surgery, Uniformed Services University, Bethesda, MD; Dermatology, The National Naval Medical Center, Bethesda, MD and Pediatric Gastroenterology, Walter Reed Army Medical Center, Washington, DC.

**Purpose:** Pilonidal disease (PD) is a frustrating condition due to recurrence rate as high as 30%. Hair removal with shaving or depilatories is a part of many postoperative regimens. These methods are resource intensive and adversely impact the lifestyle of both child and family. Therefore we investigated the use of laser photothermolysis (LP) of the intergluteal hair in adolescents with PD as a method of permanent hair removal.

**Methods:** As part of an IRB trial, all children with PD who presented to the pediatric surgery division were offered LP. Children who presented with PD abscess or infection were initially managed with a combination of drainage, debridement, excision and antibiotics. Following resolution of the acute process, LP of the intergluteal hair with a 1064 nm Nd:YAG laser at a standard fluence (J/cm2), pulse duration and repetition rate based on skin phototype was performed. The children were observed for hair re-growth and recurrence.

**Results:** Ten adolescents (mean age 16.5 ± 2.0 years) underwent LP. LP was well-tolerated and without complication in all children. At outpatient follow up, intergluteal hair was completely removed in all children with 3 ten minute treatment sessions. To date, no child has developed recurrence. (Mean follow up 12.2 ± 3.3 months).

**Conclusions:** In this pilot study, laser photothermolysis is a safe and effective method to permanently remove intergluteal hair in adolescent children with pilonidal disease. At early follow-up, laser photothermolysis appears to reduce pilonidal recurrence.

1043

**Fecal Calprotectin Level Predicts Clinical Relapse in Clinically Quiescent Crohn’s Disease**

Dorota Walkiewicz, M.D., Steven L. Werlin, M.D.,* Matthew C. Scanlon, M.D., Jingnan N. Mao, M.S., Partick J. Hanaway, M.D., Subra Kugathasan, M.D., Daryl Fish, D.O. Pediatrics, Medical College of Wisconsin, Milwaukee, WI and Genova Diagnostics, Asheville, NC.
Purpose: Measurement of fecal calprotectin (FC) has been proposed as a non-invasive test to determine the degree of intestinal inflammation in patients with inflammatory bowel disease (IBD). FC levels may fluctuate in relation to disease activity. Adult studies have shown that FC level > 250 µg/g predicts relapse for both ulcerative colitis (UC) and Crohn’s disease (CD) patients. The purpose of the study was to assess role of FC in identifying risk for clinical relapse in asymptomatic pediatric CD patients.

Methods: Retrospective analysis of 25 stool samples from 18 CD patients in clinical remission was done. Disease activity was defined by a physician global assessment within 2 weeks of sample submission. Clinical relapses were recorded up to 9 months post-stool sample. Relapse was defined by a physician during clinic visits, based on symptoms and physical examination. FC levels were measured by ELISA. Descriptive statistics, Chi-square and Kaplan-Meier analyses were performed.

Results: 12 episodes of clinical relapse were documented during the study time frame. 16 encounters were observed with FC levels > 400 µg/g and 9 with FC levels < 400 µg/g. Using the Kaplan-Meier method and log rank test, an FC level of 400 µg/g was significantly associated with a clinical relapse in asymptomatic CD patients within 9 months of stool sample collection (p = 0.03). Using the identified FC level of 400 µg/g as a threshold, the Chi-square analysis showed that 56.2% of clinical encounters with FC levels >400 µg/g had clinical relapse within 9 months (95% CI 30%-80%), and 90% of clinical encounters resulting in clinical relapse had FC levels > 400 µg/g (95% CI 55.5%-99.8%). Among clinical encounters of CD patients with FC levels < 400 µg/g, 89% had no clinical relapse within 9 months (95% CI 51.8%-99.7%).

Conclusions: FC level obtained in pediatric CD patients while in clinical remission may have potential utility in determining the risk for clinical relapse. In contrast to the published adult threshold (>250 µg/g), FC level in predicting clinical relapse was found to be much higher in our CD pediatric group (400µg/g). These findings suggest a need for a large, prospective clinical trial in pediatric population that will further define statistically significant FC level in predicting clinical relapse in those who are in clinical remission.

1044

Fecal Lactoferrin in Children with Gastrointestinal Symptoms

Marion D. Pfefferkorn, M.D.∗ James Boone, M.S., Steven J. Steiner, M.D., Gail M. Waltz, R.N., J. Sue Lee, M.S., Krista Tygrett, B.S. Pediatric Gastroenterology, Hepatology and Nutrition, Indiana University School of Medicine, Indianapolis, IN and TechLab, Inc., Blacksburg, VA.

Purpose: Lactoferrin is a glycoprotein found in neutrophils and mucosal secretions. The aim of this study is to compare fecal lactoferrin levels in children with symptomatic inflammatory bowel disease (IBD) versus non-IBD who are undergoing colonoscopy ± esophagogastroduodenoscopy.

Methods: Fresh stool samples from outpatients undergoing colonoscopy were collected and frozen within 72 hours prior to the bowel cleansing regimen. Fecal lactoferrin was determined using a polyclonal antibody-based enzyme-linked immunoassay. An elevated value is ≥7.25 mg/g fecal wet weight.

Results: Thirty-seven patients (3–16 years old, 24 males) participated: 5 had active IBD (Crohn’s disease = 3, ulcerative colitis = 2) and 32 had non-IBD diagnoses (irritable bowel syndrome = 8, polyposis = 6, functional abdominal pain = 4, constipation = 4, hemorrhoids = 2, others = 8). The mean fecal lactoferrin was significantly elevated at 659 ± 250 mg/g in IBD compared to 73.9 ± 197 mg/g in non-IBD patients (p < 0.001). Fecal lactoferrin was elevated in 4/5 IBD (80% sensitivity) and normal in 18/32 non-IBD patients (56% specificity).

Conclusions: Fecal lactoferrin is a sensitive test for detecting active IBD and may be a useful screening test in differentiating IBD versus non-IBD patients.

1045

Liver Transplantation for alpha-One-Antitrypsin Deficiency

Aleeta A. Somers-DeHaney, M.D.∗ Elizabeth Lyden, Sandeep Mukherjee, M.D. Internal Medicine, Creighton University Medical Center, Omaha, NE and Gastroenterology, University of Nebraska Medical Center, Omaha, NE.

Purpose: We report the outcomes of liver transplantation (LT) for alpha-1-antitrypsin deficiency from a single transplant program.

Methods: A retrospective review of the Organ Transplant Database at the University of Nebraska Medical Center was performed to identify all patients (pts) transplanted for AAT deficiency between 1990–2005. Pts were diagnosed with AAT deficiency if 3 of the following 4 criteria were present: depressed serum levels of AA; ZZ phenotype; liver biopsy and/or explant histopathology confirming the presence of diastase resistant AAT globules. The following outcomes were recorded: age; sex; prevalence of hepatoma; hepatic artery thrombosis (HAT); biliary complications; episodes of rejection and infection; post transplant lymphoproliferative disease (PTLD); graft and patient survival.

Results: 35 pts were transplanted for AAT deficiency with a median age of 8 mths. The majority of AAT pts were male (77%) under the age of 18 yrs (76%) and received a cadaver liver (74%). Incidental hepatoma was present in 2 explants and occurred in 1 pt. HAT developed in 4 pts (8.3%) and biliary complications (leaks, strictures and/or necrosis) occurred in 9 pts (26%). Acute rejection occurred in 21 pts (60%) and chronic rejection occurred in 7 pts (20%). PTLD occurred in 7 pts (20%). Eight pts died, with sepsis accounting for cause of death in 6 pts (75%). Infection was seen in 77% of pts. Mean follow up was 7.5 years. Estimates of overall survival were based on the Kaplan Meier Method. Cumulative incidence methods were used to estimate the incidence of graft failure (GF). Outcome information was available for 32 of 35 patients. 1 year Overall Survival (OAS) was 77% (95% CI 57–88%), 3 year OAS is 72% (95% CI 52–85%). There was no difference in OAS when the patients were categorized by the number of complications (p = 0.7). Pts < 18 years tend to have improved estimates of OAS compared to pts > than 18 yrs (p = 0.087). Estimated cumulative incidence of GF at 1 year is 6% (95% CI 0–17%) and at 7 years 13% (95% CI 0–34%).

Conclusions: In this predominantly male, pediatric cohort of LT pts with AAT, long term survival is approximately 72%. Pediatric pts tend to have a better OAS than adult pts. The number of post transplant complications does not appear to be a predictor of outcome. Sepsis was the most common cause of death. Long term results of LT for AAT deficiency are otherwise encouraging with outcomes comparable to pts undergoing LT for other indications.

1046

Indications, Findings and Complications of ERCP in Children

James D. Panetta, D.O., Paul J. Berggreen, M.D.∗ Department of Gastroenterology, Phoenix Children’s Hospital, Phoenix, AZ.

Purpose: Endoscopic retrograde cholangiopancreatography (ERCP) is an effective and widely employed endoscopic procedure in adult populations with pancreaticobiliary disease; however less is known about the usefulness and safety of this procedure in children. The goal of this study is to describe our clinical experience in performing ERCP in the pediatric population.

Methods: Retrospective chart review was performed on pediatric patients undergoing ERCP between May 1991 and March 2005. The following data were recorded: 1) Patient age, 2) Indication for procedure, 3) Method of anesthesia used, 4) Any therapeutic or diagnostic procedure performed, and 5) Intraoperative complications.

Results: Eighty pediatric ERCPs were performed during the study period. The average patient age was 11.8 years (range 5 months to 18 years). Table 1 shows the number of procedures performed for each indication with recurrent pancreatitis and suspected biliary obstruction being the most common.

Number of ERCPs by Indication

<table>
<thead>
<tr>
<th>Procedure Description</th>
<th>Number of ERCPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent pancreatitis</td>
<td>33</td>
</tr>
<tr>
<td>Suspected choledocholithiasis/gallstone pancreatitis</td>
<td>32</td>
</tr>
<tr>
<td>Suspected sclerosing cholangitis</td>
<td>6</td>
</tr>
<tr>
<td>Bile leak</td>
<td>2</td>
</tr>
<tr>
<td>Suspected pancreatic trauma</td>
<td>3</td>
</tr>
<tr>
<td>Known duct strictures</td>
<td>3</td>
</tr>
<tr>
<td>Choledochal cyst</td>
<td>1</td>
</tr>
</tbody>
</table>

∗Department of Gastroenterology, Phoenix Children’s Hospital, Phoenix, AZ.
in a peds GI clinical setting. and may not perform as well in the clinical setting. The purpose of this study serologic tests have been derived from studies conducted in a research setting 8mo period were reviewed. Those with any of the above CD Ab’s, an IgA Purpose: Most of the sensitivity (sens) and specificity (spec) data for CD

methods have been performed from studies conducted in a research setting and may not perform as well in the clinical setting. The purpose of this study was to assess the performance of AGA-G and A Ab’s, TTG-A Ab, and AEA in a peds GI clinical setting. Methods: The charts of 515 pts. (9mo-19y) who underwent UED in a recent 8mo period were reviewed. Those with any of the above CD Ab’s, an IgA level and SBBx were tabulated. Those with sub-normal IgA levels or known CD were excluded. The sens, spec, PPV and NPV were calculated for the four Ab’s and for the combinations of AGA-A/TTG-A, and TTG-A/AEA (+/+ = + test; ±, −/+, or −/− = − test). Positive TTG-A tests were expressed as multiples above normal and divided into groups with and without CD. Results: There were 132 pts. with 25 having an initial dx of CD. There were 130 AGA-G tests(sens.87,spec.38, PPV23, NPV93). There were 131 AGA-A tests(sens.56, spec.74, PPV33, NPV88). There were 117 TTG-A tests(sens.96, spec.89, PPV70, NPV99). There were 32 AEA tests (sens.78, spec.1.0, PPV1.0, NPV92). There were 110 combination values for AGA-A/TTG-A (sens.57, spec.98, PPV86, NPV91). There were 17 values for TTG-A/AEA (sens.86, spec.1.0, PPV1.0, NPV91). Of 31 positive TTG-

In contrast to adult ERCPs, which are usually performed under conscious sedation, most pediatric ERCPs in this study were carried out under general endotracheal anesthesia (n = 46) administered by an anesthesiologist, with only 9 procedures performed under conscious sedation managed by the endoscopist. The success rate of ERCP, as defined by imaging of ducts of interest or success of intended therapy, was 98.8% (in one procedure duodenal intubation could not be achieved). There were no intraoperative complications noted in any of the 80 procedures. Conclusions: ERCP is a valuable tool in the evaluation of suspected pancreaticobiliary disorders in children. ERCP in the pediatric population was highly successful (98.8%), intraoperatively safe, and associated with a high rate of therapeutic interventions.

Table 2. Shows the Number of Each Type of Therapeutic or Diagnostic Intervention with Sphincterotomy being the Most Common

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sphincterotomy</td>
<td>26</td>
</tr>
<tr>
<td>Needle knife</td>
<td>2</td>
</tr>
<tr>
<td>Stone extraction</td>
<td>10</td>
</tr>
<tr>
<td>Stent placement</td>
<td>10</td>
</tr>
<tr>
<td>Bile aspiration</td>
<td>12</td>
</tr>
</tbody>
</table>
Methods: A prospective pilot study was conducted by administering the newly developed 11 page GERD Q to patients with endoscopy proven GERD and controls to assess demographics, symptoms and quality of life (QOL) issues in patient and parents. The survey consists of symptoms grouped into 5 different categories: 1. Gastrointestinal 2. Ears, nose, throat, 3. Respiratory, 4. Neurological and 5. Allergy. To develop scales for these symptoms, internal consistency of these symptoms groups were assessing Cronbach's Alpha for each group.

For those who returned the original one, a second GERD Q was mailed after 2 weeks to assess test-retest validity. SAS software was used for data analysis.

Results: 180 patients were given the questionnaire and 88 were returned. The patients were between 2 – 18 years of age, 35 M, 53 F. The ethnic distribution was 58 Caucasians, 20 African Americans and 10 others. 50 patients were mailed the questionnaire again and 19 returned. The Cronbach's Alpha for Each set of symptoms with k items are: 1. Gastrointestinal = 0.86, k = 23, 2. Ears, nose, throat = 0.84, k = 11.3. Respiratory = 0.70, k = 5, 4. Neurology = 0.78, k = 6 and 5. Allergy = 0.63, k = 3. Alpha was also computed for the set of negative Quality of Life (QOL) questions for the child (Alpha = 0.95, k = 29). In addition, there were 17 completed second surveys returned between 2 – 10 months after the first survey for which we assessed test-retest related reliability. The test = retest reliabilities were: Gastrointestinal = 0.86, Ears, nose, throat = 0.72, Respiratory = 0.80, Neurology = 0.80, Allergy = 0.93, child’s QOL = 0.84. All were significant at the 0.05 level. We also correlated the child’s and parents QOL scales with the symptom scales for the 70 children. The correlations of the child’s QOL scale with the Gastrointestinal, Ears, nose throat, Respiratory, Neurological and Allergy scales were 0.54, 0.52, 0.50, 0.52 and 0.40 respectively and with the parents QOL scale were 0.43, 0.44, 0.43, 0.44 and 0.45 (all 0.05)

Conclusions: Child’s and parents’ life were negatively affected by GERD. Further studies are needed to understand the role of GERD in children’s and their parents’ lifestyle.

1050
Anemia from Ileocolonic and Jejunocolonic Anastamotic Site
Ulceration in 2 Pediatric Patients
Shabana Shahnavaz, Stephen Nanton, Radha Nathan, Kapil Gupta, Stanley Fisher Pediatrics, SUNY Downstate Medical Center, Brooklyn, NY.

Purpose: CASE 1 - A 5 yr old female with short gut syndrome and iron deficiency anemia. She had resection of ileum and ileocecal valve with ileocolonic anastamosis in the neonatal period due to gastroschisis. She presented at 3.5 yrs with abdominal pain, anemia and guiac positive stools. She has had multiple transfusions and received parenteral iron therapy after failing to respond to oral iron. 

Bleeding scan - was positive for low rate of bleeding. 

CASE 2 - Patient H presented at 6 yrs of age with guiac positive stool and severe microcytic hypochromic anemia, refractory to oral and intravenous iron therapy. She had resection of ileum and ileocecal valve with jejunocolonic anastamosis at 3 days of life due to volvulus and necrotising enterocolitis. 

Bleeding scan - findings of intermittent small amount of active intestinal bleeding in the right lower quadrant.

Upper GI series - Small bowel colonic anastomosis without evidence of ulceration or obstruction.

Upper Endoscopy - Normal.

Colonoscopy – Single anastamotic site ulcer.

Clinical Features of Our Patients with Anastamotic Ulcers
<table>
<thead>
<tr>
<th>Case</th>
<th>Indication of surgery</th>
<th>Age at surgery</th>
<th>Age at presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Gastrochisis</td>
<td>infancy</td>
<td>3.5yrs</td>
</tr>
<tr>
<td>Case 2</td>
<td>volvulus</td>
<td>3 days of life</td>
<td>6 yrs</td>
</tr>
</tbody>
</table>

Significant lab values

<table>
<thead>
<tr>
<th></th>
<th>Pretransfusion Hb (mg/dl)</th>
<th>Pretransfusion HCT (%)</th>
<th>Pretransfusion MCV (fl)</th>
<th>Pretransfusion TiRGN</th>
<th>Pretransfusion Ferritin (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CASE 1</td>
<td>3.1</td>
<td>95.5</td>
<td>70.9</td>
<td>15</td>
<td>150</td>
</tr>
<tr>
<td>CASE 2</td>
<td>3.7</td>
<td>12.9</td>
<td>70.3</td>
<td>15</td>
<td>176</td>
</tr>
</tbody>
</table>

Conclusions: Ileocolonic and jejunocolonic anastamotic site ulcers are rare causes of iron deficiency anemia refractory to standard iron therapy. The most common presentation is iron deficiency anemia from chronic blood loss. This rare entity must be considered in symptomatic children with history of ileocolonic or jejunocolonic anastomases. [figure1]

1051
Utilization Trends and Outcomes for Endoscopic Retrograde Cholangiopancreatography (ERCP) in the Pediatric Population
Eileen M. Janec, M.D., Steven A. Edmundowicz, M.D., Kevin J. Peifer, M.D., Riad Azar, M.D., Young S. Oh, M.D., Elizabeth A. Brinkmann, R.N., Feng Gao, Ph.D., Phillip Tarr, M.D., Ross Shepherd, M.D., Sreenivasa Jomnalagadda, M.D.* Gastroenterology and Hepatology, Washington University in St. Louis, St. Louis, MO.

Purpose: To analyze technical success, complication rates, and high risk patients in relation to patient characteristics such as age, diagnosis, and co-morbid conditions when experienced interventional endoscopists perform ERCP in the pediatric population.

Methods: Retrospective case review of 115 cases in 72 pediatric patients who underwent ERCP from December 1998 to December 2002. Inclusion criteria include all consecutive children (< 18 years) who had undergone an ERCP. Patients were identified from the endoscopy data base at our institution. Data collected includes demographics (zip code, county, date of birth, age, gender, ethnicity, height, and weight), co-morbid conditions, indications, final diagnosis, technical outcomes, and complications. Demographic and clinical characteristics of the sample were summarized with descriptive statistics. The association between outcomes (complications or failures) and patient characteristics were tested by Fisher's exact test.
Results: 115 ERCPs in 72 patients were performed ERCP in the pediatric population. The ERCPs were all performed by experienced interventional endoscopist at a tertiary referral center. The mean age was 13. The age was subcategorized into groups: age 2–10 (24.3%); age 11–15 (34.8%); age 16–19 (47%). The average BMI of our study population was 24.2. The BMI was subcategorized as < 20 (38%), 20–30 (38%), > 30 (22%). The indication for the procedures included biliary 31.3%, pancreatic 34.78%, or both/either 33.9%. The post procedure diagnosis included: chronic pancreatitis 37 (35.4%), gallstone disease manifested as cholecodolithiasis and biliary sludge was 31 (27.4%), normal 18 (15.9%), biliary strictures 9 (7.9%), pancreas divisum 5 (4.4%), primary sclerosing cholangitis 3 (2.7%), pancreatic duct stenosis 3 (2.7%), bile leak 2 (1.8%) cholecdochal cyst 1 (0.88%). Therapeutic intervention was performed on 79.1% of the cases presenting for evaluation. The success rate at our institution was 96.5% with and an overall complication rate of 5.2% (6 patients). The complications included mild pancreatitis in five patients (4.3%) and post sphincterotomy bleeding in one patient (0.87%).

Conclusions: ERCP in the pediatric population can be performed safely by experienced endoscopists. Age, gender, ethnicity, BMI, and co-morbidities do not increase the risk in children.

COLORECTAL CANCER PREVENTION

1052

The Finding of Hematochezia Should Prompt Investigation, Despite Prior Normal Colonoscopy

Jonathan D. Siegel, M.D., D. Shane Pendley, M.D., Jack A. DiPalma, M.D.* Internal Medicine: Division of Gastroenterology, University of South Alabama, Mobile, AL.

Purpose: Current ACG guidelines recommend screening colonoscopies (CS) in average risk people every 10 years beginning at age 50. However, no guidelines or data address the most appropriate evaluation of patients who had normal baseline CS but subsequently presented for the evaluation of hemocult positive stool (HPS).

Methods: Retrospective chart review of patients who had previously undergone CS with normal findings and were then re-evaluated because of a HPS prior to scheduled screening CS date.

Results: Of the 3184 CS performed at our facility between August 2002 and November 2004, 651 were normal. Seventy four of these were repeated before their scheduled screening interval because of the finding of a HPS. The study population included 4874 (65%) men, 3674 (49%) Caucasians, 3374 (45%) African Americans. The average age at index CS was 54 years. The average interval between procedures was 47 months. Findings at subsequent CS done for HPS were: 60/74 (81%) normal, 8/74 (11%) adenomas < 1.0cm, 4/74 (5%) advanced adenomas, and 2/74 (3%) had invasive adenocarcinoma. For those with advanced polyps, the procedure intervals were 18, 24, 33, and 56 months, and only one of these had a FH of colon cancer. For the two subjects with cancer, the intervals were 64 and 84 months, with only the former having a FH of colon polyps.

Conclusions: The finding of a subsequent HPS after a prior normal CS should prompt re-evaluation, regardless of the interval since the prior normal procedure.

1053

Attending a Pre-Procedural Education Session Does Not Improve Compliance with Screening Colonoscopy


Purpose: Patient-initiated procedure cancellation on “short-notice” and failure to present for scheduled procedures are not infrequent occurrences. This prospective study was designed to determine whether attending a pre-procedural education session impacts patients’ compliance with subsequently presenting for “direct-access” screening colonoscopy.

Methods: Outpatients scheduled (between 4/26/04 and 4/26/05) to undergo “direct access” screening colonoscopy (patients asymptomatic/average-risk) who either cancelled the procedure on “short-notice” (within 48 hours prior) or failed to present as scheduled (“no-show”), were prospectively identified and comprised the study group. Procedures were scheduled at either a hospital or office-based ambulatory endoscopy unit. All patients were offered an opportunity to attend an educational session, during which an instructional video and pre-procedural preparation were reviewed in detail. Results were analyzed after accrual of a total of 80 patient cancellations or “no-shows.” A similar number of patients who presented contemporaneously for “direct access” screening colonoscopy comprised the comparison group. The rate of attendance at an education session was compared between the groups.

Results: Over the study period, 80 outpatients who were scheduled to undergo “direct access” screening colonoscopy and cancelled on short-notice or “no-showed” were identified in this prospective study (Group A). Over the same study period, 80 patients who were similarly scheduled for “direct access” screening colonoscopy, and presented for the procedure, comprised the comparison group (Group B). The rate of attendance at a pre-procedural education session was not statistically significant between the groups (6/80 = 7.5% in Group A and 7/80 = 8.8% in Group B (p = 1.0 by Fisher’s exact test)).

Conclusions: This prospective study suggests that patients who present for “direct-access” screening colonoscopy are not significantly more likely to have attended a pre-procedural education session, than patients who cancelled on short-notice, or “no-showed” for the appointment. Such education sessions are likely of benefit, but other strategies will require consideration if the goal is to improve patient compliance with previously scheduled screening colonoscopic procedures.

1054

Patients Scheduled for Screening Colonoscopy Are Not More Likely To Cancel or “No-Show” Than Are Patients Scheduled To Undergo GI Endoscopy for “Other” Indications


Purpose: Patient-initiated procedure cancellation on “short-notice” and failure to present (“no-show”) for previously scheduled GI endoscopic procedures is not an infrequent occurrence. One wonders whether asymptomatic persons scheduled for screening colonoscopy are more likely to cancel or “no-show” for their procedure than patients scheduled to have GI endoscopy for evaluation of “other” problems. This prospective study was designed to identify whether patients scheduled for screening colonoscopy are more likely to cancel or “no-show” than patients scheduled to have GI endoscopic procedures for “other” indications.

Methods: All outpatients who either cancelled an endoscopic procedure on “short-notice” (within 48 hours prior to the anticipated procedure) or failed to present as scheduled (“no-show”), were identified in this prospective study. All patients had their procedures scheduled at either a local hospital or office-based ambulatory endoscopy unit. Rates of cancellation “no-show” were then compared between patients who were scheduled to undergo screening colonoscopy and patients scheduled to undergo GI endoscopic procedures for “other” indications.

Results: Over the study period (4/26/04 through 4/26/05), 6871 scheduled outpatients were eligible for inclusion in this prospective study. Of 6871 total outpatients, 322 were contacted after either cancellation or “no-
Conclusions: The results from this prospective study suggest that asymptomatic/average-risk patients who are scheduled for screening colonoscopy are not more likely to cancel on "short notice" or "no-show" than are patients scheduled to undergo EGD or colonoscopy for "other" indications.

1055
Average Risk Screening Colonoscopy in the Elderly: Outcome of Screening at Age 75 Years and Above
Aaron Walfish, M.D., Sabino Augello, M.D., Gopal Narasimhan, D.O., Pauline Sawandhi, M.D., Christopher Lee, M.D., Babak Danesh, M.D., Alan Gingold, D.O., Min Albert, M.D., Christopher Lee, M.D., Babak Danesh, M.D., Alan Gingold, D.O., Min Albert, M.D.* Division of Digestive Disease, Beth Israel Medical Center, New York, NY.

Purpose: Most guidelines recommend that screening for colorectal cancer should begin at age 50 for average risk individuals. However, there is no consensus regarding the age at which screening should be discontinued. Since the elderly often have comorbidities that increase the risk of undergoing endoscopy, more evidence regarding the utility of screening in this population is required. This study compares the rate of detection of pathology at colonoscopy in patients aged ≥75 years to that in patients between 65 and 69 years.

Methods: We reviewed all colonoscopy reports from patients ≥65 years of age, performed at Beth Israel Medical Center between 1999 and 2003, with the indication of average-risk screening colonoscopy (ARSC). Patient age, gender, endoscopic findings, and pathology were recorded.

Results: The reports of 178 patients undergoing ARSC who were ≥75 years old and 318 patients aged 65–69 years were retrospectively analyzed. A mass or polyp was found in 77 patients (43%) ≥75 years vs. 133 patients (42%) between 65–69 years (p = 0.86). Of the patients ≥75 years with positive findings on ARSC, 17 (22%) had a polyp or mass ≥1 cm vs. 25 (18%) in patients aged 65–69 years (p = 0.73). The most common pathology finding in each group was tubular adenoma, accounting for 38 polyps (49%) found in patients ≥75 years vs. 75 polyps (58.6%) in patients between 65–69 years. There were no complications reported in either group (See table).

<table>
<thead>
<tr>
<th></th>
<th>≥75 years</th>
<th>65–69 years of age</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>178</td>
<td>318</td>
</tr>
<tr>
<td>Mean Age</td>
<td>77.5 ± 3.5</td>
<td>66.5 ± 0.7</td>
</tr>
<tr>
<td># of patients with polyp or mass found</td>
<td>77 (43.25%)</td>
<td>133 (41.8%) p = 0.8641</td>
</tr>
<tr>
<td># of patients with polyp or mass ≥1 cm</td>
<td>17 (22%)</td>
<td>25 (18.8%) p = 0.7271</td>
</tr>
<tr>
<td>Pathology found:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubular adenoma</td>
<td>38 (49%)</td>
<td>75 (58.6%)</td>
</tr>
<tr>
<td>Tubulovillous adenoma</td>
<td>9 (12.5%)</td>
<td>8 (6.25%)</td>
</tr>
<tr>
<td>Villous adenoma</td>
<td>5 (6.9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hyperplastic polyp</td>
<td>22 (30.5%)</td>
<td>47 (36.7%)</td>
</tr>
<tr>
<td>Inflammatory</td>
<td>6 (8.3%)</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Normal</td>
<td>6 (8.3%)</td>
<td>11 (8.6%)</td>
</tr>
</tbody>
</table>

Conclusions: Our data support continued screening of elderly patients. There was no significant difference in the rate of pathology detection or complications with advanced age.

1056
Screening Colonoscopy – Are We Starting Too Late?
Suryakanth R. Gurudu, M.D., Jonathan A. Leighton, M.D., David E. Fleischer, M.D., Russel I. Heigh, M.D., Ananya Das, M.D.* Department of Medicine, Division of Gastroenterology, Mayo Clinic Scottsdale, Scottsdale, AZ.

Purpose: Although screening colonoscopy in average risk adults is recommended to start at the age of 50 years, very limited information exists on the prevalence of neoplastic colorectal lesions in persons below the age of 50.

Objective: To assess the prevalence of colorectal neoplasia in average-risk persons between the ages of 40 to 49 years.

Methods: We retrospectively analyzed the prevalence of colorectal neoplasia in a cohort of average-risk adults aged 40 to 49 years who underwent screening colonoscopy as part of an executive health care program offered at our institution in 2003 and 2004. For this analysis, an advanced neoplasm was defined as an adenoma ≥10 mm in diameter, villous histology or high-grade dysplasia/cancer. The proximal colon was defined as the portion of the splenic flexure to the cecum as determined by the endoscopist. The numbers needed to screen with confidence intervals were derived from the inverse of the point prevalence of the type of the lesion and 95% confidence intervals were calculated using the exact binomial method.

Results: A total of 116 average-risk patients [81% men, mean age 46 (2.8) years] in the age group of 40 to 49 years underwent screening colonoscopy during the study period. Nineteen (16%) patients had 31 adenomatous polyps removed endoscopically and confirmed by pathology. Polyps ranged from 2 mm to 18 mm [median 4 (3–6)] in size. Seventeen adenomas were seen in 9 patients in the proximal colon but none of these patients had proximal adenomas in the absence of distal adenomas. Seven patients had advanced neoplasia, none of which were cancer. Four of the 7 advanced neoplasms were located distally, potentially within reach of a flexible sigmoidoscope. The estimated numbers of screening colonoscopy needed to screen for detection of any adenoma and a proximal adenoma in this population were 6 (95% CI, 4–9) and 13 (95% CI, 7–28), respectively. For detection of advanced neoplasms anywhere in the colon, the number needed to screen was 17 (95% CI, 8–41).

Conclusions: A significant proportion of average-risk patients in the age group of 40 to 49 years undergoing screening colonoscopy appears to have neoplastic lesions. Current recommendations of initiating colorectal cancer screening at the age of 50 may be too restrictive. Prospective studies in a larger cohort are needed to assess the prevalence of colorectal neoplasia in this age group and also to identify specific risk factors.

1057
Colonoscopy Surveillance after Polypectomy: A National Survey Study of Primary Care Physicians
Vikram Boolchand, M.D., Joseph Singh, M.D., Gregory Olds, M.D., Pankaj Singh, M.D., Amitabh Chak, M.D., Gregory S. Cooper, M.D.* Department of Medicine, University Hospitals of Cleveland, Cleveland, OH.

Purpose: Previous surveys suggest that gastroenterologists often recommend and perform surveillance colonoscopies in excess of guidelines, following polypectomy. However, decisions about surveillance colonoscopy in both open and non-open access systems, are often made in the primary care setting. The purpose of this study was to determine the surveillance practices of primary care physicians.

Methods: After content validation, a two page survey which included 6 clinical vignettes was mailed to a random sample of 500 members of the American College of Physicians-Society of Internal Medicine and 500 members of the American Academy of Family Practice. A repeat mailing with a token financial incentive was sent to those that did not respond. Each vignette described an asymptomatic 55 year old male with no family history who had a polyp on a well prepped colonoscopy. Findings included a hyperplastic polyp (HP), single 6 mm tubular adenoma (TA), two 6 mm TA’s, 12 mm TA...
with focal high grade (HGD) or a negative exam in a patient with a prior TA. Physicians were asked when they would recommend a repeat colonoscopy.

**Results:** The overall response rate was 50.7% (n = 507) response rate. Of the respondents 48% were internists and 52% were family practitioners. Eighty-six percent of the respondents were male and 67% indicated that they refer patients for open access endoscopy. Findings are shown in the table. In addition, females more than males (p = 0.01), family practitioners more than internists (p = 0.0001), and those who have been in practice less than 20 years (p = 0.05) are more likely to survey a HP in less than 10 years. No consistent differences were observed according to physician gender, number of years in practice, practice volume and use of open access endoscopy.

**Conclusions:** Primary care physicians recommend post-polypectomy colonoscopy surveillance more frequently than published guidelines, especially with a hyperplastic polyp and a single small adenoma. More intensive surveillance may compromise the capacity for primary screening and the evaluation of symptomatic patients.

### 1058

**Implementing Screening Colonoscopy at a VAMC: A 1 Year Experience**

**Sorin Petre, M.D., Francisco C. Ramirez, M.D.* Gastroenterology, Carl T Hayden VA Medical Center, Phoenix, AZ.**

**Purpose:** Implementing colonoscopy for CRC screening may be challenging when the demand exceeds the supply creating significant backlogs that may be perceived as detrimental.

**Aim:** (1) To report the results of a rapid and progressive implementation of screening colonoscopy at a VAMC. (2) To determine whether a delay in performing the procedure, negatively influences the findings at colonoscopy.

**Methods:** Endoscopic, medical and pathology records of patients undergoing screening colonoscopy (1/04–12/04). Demographics, presence/absence of polyps, size and location were noted. Cecal intubation rate was calculated. Proximal location = proximal to splenic flexure. Advanced neoplasia = adenoma ≥ 10 mm, villous component, HGD, or invasive carcinoma. The delay between the date of performance and date of request was calculated.

**Results:** Of 2617 colonoscopies, 915 were for CRC screening; mean age: 61 yrs. The screening colonoscopy: flexible sigmoidoscopy ratio was 74%: 26% during the 1st QTR and 98%: 2% during the 4th QTR. The overall waiting time for colonoscopy was 141 days. By the 4th QTR, the time delay (169.1 ± 7.3 days) was significantly longer than the 1st QTR (135.6 ± 3.6 days) (p < 0.05). The cecal intubation rate was 97.4%. The no show up rate for outpatients colonoscopy was 8%. There was 1 post-polypectomy bleeding. 643 patients (71%) had no adenomas/advanced neoplasia; 9 had: leiomyomas (3), carcinoids (2), lipoma, lipogranuloma, ganglioneuroma and juvenile polyps, 1 each. 212 (23.2%) had adenomas < 10 mm and 51 (5.6%) advanced neoplasias.

Of the 6 advanced neoplasias found proximally only, 4 were adenomas ≥ 10 mm and 2 villous adenomas. During the 1st QTR, 29.9% of colonoscopies yielded adenomas and advanced neoplasia whereas in the 4th QTR, the yield was 20.7% (p = 0.05).

For advanced neoplasia only however, the yield was 6.6% and 5.5%, respectively (NS)

**Conclusions:** Implementation of a screening colonoscopy program at a VAMC is challenging and is associated with time delays due to a progressive backlog. The prevalence of adenoma and advanced neoplasia was 28.7%. Proximal adenomas and advanced neoplasia without any other adenoma(s) distally were found in 24.7%.

### Location Distribution of Adenomas < 10 mm and Advanced Neoplasias

<table>
<thead>
<tr>
<th>Location</th>
<th>Adenoma &lt; 10 mm</th>
<th>Advanced Neoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 212)</td>
<td>(n = 51)</td>
<td></td>
</tr>
<tr>
<td>Proximal only</td>
<td>59/212 (27.8%)</td>
<td>6/51 (11.8%)</td>
</tr>
<tr>
<td>Distal only</td>
<td>85/212 (40%)</td>
<td>20/51 (39.2%)</td>
</tr>
<tr>
<td>Proximal &amp; Distal</td>
<td>68/212 (32.2%)</td>
<td>25/51 (49%)</td>
</tr>
</tbody>
</table>

Proximal advanced neoplasia was found in 11.8% (0.7% of total number of screening colonoscopies). The time delay did not negatively affect the yield for advanced neoplasia.

**1059

**Recognition of Patients at Increased Risk for Colorectal Cancer: Data from the Second National Colorectal Cancer Roundtable (NCCRT) Trainee Survey**

A. S. Oxentenko, M.D., R. A. Vierkant, D. S. Pardi, M.D., D. R. Farley, M.D., E. J. Dozios, M.D., T. E. Hartman, M.D., M. D. Hough, M.D., W. O. Petersen, Ph.D., C. Klabunde, Ph.D., K. Sharpe, MTS, J. H. Bond, M.D., R. A. Smith, Ph.D., B. Levin, M.D., J. B. Pope, M.D., P. C. Schroy, M.D., P. J. Limburg, M.D.* Mayo Clinic College of Medicine, Rochester, MN; NCI, Bethesda, MD; ACS, Atlanta, GA; VA Medical Center, Minneapolis, MN; MD Anderson, Houston, TX; LSU, Shreveport, LA and BMC, Boston, MA.

**Purpose:** Guidelines endorsed by the U.S. Multisociety Task Force on Colorectal Cancer identify several patient groups for whom earlier and/or more frequent colorectal cancer (CRC) screening tests are recommended (Gastroenterology 2003;124:544-60). Since long-term practice patterns may be established during postgraduate training, we sought to determine whether trainees appropriately recognize patient groups with increased CRC risk.

**Methods:** Between 4/14/04–6/25/04, program directors/administrators (PDs/PAs) from 646 gastroenterology (GI), surgery and radiology training programs were asked to forward our survey announcement to their trainees. Willing trainees then completed an anonymous online questionnaire. Participants were asked to select patient groups that required more intensive CRC screening or surveillance, compared to average-risk patients. Six different patient groups were defined. Proportions and exact 95% confidence intervals (CI) were calculated based on the binomial distribution.

**Results:** PDs/PAs from 130 programs (20%) forwarded our survey, which was completed by 478 trainees. Data are provided in the Table. Although endorsed guidelines stipulate groups 1–5 should be classified as higher risk, most respondents only identified groups 1, 2, and 3 as such. Conversely, group 6 was incorrectly classified as higher risk by 9% of respondents.

### Results

<table>
<thead>
<tr>
<th>Patient Groups</th>
<th>Classified as Higher Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>%</td>
</tr>
<tr>
<td>1 History ulcerative colitis (&gt; 10 years)</td>
<td>456</td>
</tr>
<tr>
<td>2 or more FDRs with CRC, any age</td>
<td>437</td>
</tr>
<tr>
<td>3 1 FDR with CRC or adenomatous polyps, age &lt; 60</td>
<td>424</td>
</tr>
<tr>
<td>4 1 FDR with CRC or adenomatous polyps, age &gt; 60</td>
<td>197</td>
</tr>
<tr>
<td>5 2 SDRs with CRC, any age</td>
<td>148</td>
</tr>
<tr>
<td>6 1 SDR or TDR with CRC</td>
<td>41</td>
</tr>
</tbody>
</table>

FDR: First degree relative; SDR: Second degree relative; TDR: Third degree relative.

**Conclusions:** In this large national survey of GI, surgery and radiology trainees, recognition of patient groups at increased CRC risk was suboptimal. Further instruction regarding familial predisposition to CRC may facilitate enhanced application of current early detection guidelines.
Follow-Up of Positive Colorectal Cancer Screening Tests: Data from the Second National Colorectal Cancer Roundtable (NCCRT) Trainee Survey

A. S. Oxentenko, M.D., R. A. Vierkant, D. S. Parodi, M.D., D. R. Farley, M.D., E. J. Dozois, M.D., T. E. Hartman, M.D., D. M. Hough, M.D., W. O. Petersen, Ph.D., C. Klahunde, Ph.D., K. Sharpe, MTS, J. H. Bond, M.D., R. A. Smith, Ph.D., B. Levin, M.D., J. B. Pope, M.D., P. C. Schroy, M.D., P. J. Limburg, M.D.† Mayo Clinic College of Medicine, Rochester, MN; NCI, Bethesda, MD; ACS, Atlanta, GA; VA Medical Center, Minneapolis, MN; MD Anderson, Houston, TX; LSU, Shreveport, LA and BMC, Boston, MA.

Purpose: Multiple tests can be used for colorectal cancer (CRC) screening. However, colonoscopy (CS) has been endorsed as the preferred option for diagnostic follow-up of a positive CRC screening test (Gastroenterology 2003;124:544–60). In the present study, we sought to assess trainee recommendations for diagnostic follow-up of several CRC screening options: fecal occult blood test (FOBT), double-contrast barium enema (DCBE), or CT colonography (CTC). Because controversy remains regarding the definition of a positive flexible sigmoidoscopy (FS), we did not analyze follow-up recommendations for FS or FS plus FOBT.

Methods: Between 4/14/04–6/25/04, program directors/administrators (PDs/PAs) from 646 gastroenterology (GI), surgery and radiology training programs were asked to forward our survey announcement to their trainees. Willing trainees then completed an anonymous online questionnaire. Three separate questions were asked to identify recommendations for diagnostic follow-up of a positive FOBT, BE, or CTC. Response options for each question included (alone or in combination): FOBT, FS, DCBE, CTC, or CS.

Results: PDs/PAs from 130 programs (20%) forwarded our survey announcement, which was completed by 478 trainees. Nearly all trainees selected CS alone as the preferred option for follow-up of a positive DCBE or CTC. However, 34% of trainees selected an option other than CS alone for diagnostic follow-up of a positive FOBT (see table), including 19% who recommended follow-up testing that did not include CS and 18% who recommended > 1 follow-up test.

Diagnostic Follow-Up Tests, N (%)  

<table>
<thead>
<tr>
<th>Test</th>
<th>FOBT</th>
<th>FS</th>
<th>DCBE</th>
<th>CTC</th>
<th>CS</th>
<th>&gt; 1 Test</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOBT</td>
<td>29 (6)</td>
<td>27 (6)</td>
<td>11 (2)</td>
<td>8 (2)</td>
<td>314 (66)</td>
<td>87 (18)</td>
<td>2 (&lt; 1)</td>
</tr>
<tr>
<td>DCBE</td>
<td>0 (0)</td>
<td>6 (1)</td>
<td>0 (0)</td>
<td>5 (1)</td>
<td>436 (91)</td>
<td>23 (5)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>CTC</td>
<td>0 (0)</td>
<td>1 (&lt; 1)</td>
<td>1 (&lt; 1)</td>
<td>3 (1)</td>
<td>456 (96)</td>
<td>6 (1)</td>
<td>11 (2)</td>
</tr>
</tbody>
</table>

Conclusions: In this large national survey of GI, surgery and radiology trainees, one-third of respondents chose inappropriate follow-up testing for a positive FOBT. Further efforts are needed to insure that trainees are familiar with current CRC screening guidelines, including proper diagnostic evaluation for abnormal screening test results.

Colonoscopy Screening of Average-Risk Patients for Colorectal Cancer in a Large Staff Model HMO

David H. Winston, M.D., FACP,* Charles Baughman, M.D., Rodger Siddoway, M.D., F.A.C.G., Donna C. Winston, Ph.D. Gastroenterology, Cigna Medical Group, Sun City, AZ.

Purpose: Prevailing ACG guidelines recommend colonoscopy as the preferred screening strategy for colorectal cancer in average-risk adults starting at age 50 every 10 years. Our large staff model HMO began a screening colonoscopy program based on these guidelines in 2003. The study objective was to evaluate the results of screening colonoscopy in the first 1,000 average-risk patients referred for colonoscopy at a single multispecialty center (CIGNA Medical Group Sun City).

Methods: The first 1,000 patients referred for screening colonoscopy whose only risk-factor was age 50 or above underwent colonoscopy by either of 2 experienced colonoscopists. Nominal data consisting of age, sex, number, location, and types of polyps and cancers was collected prospectively.

Results: Complete colonoscopy to the cecum was achieved in 100% of patients and there were no complications. Ages ranged from 50–86 (median 68 years). There were 432 men (43%) and 568 (57%) women. Colonie lesions were found in 497 (50%): 207 patients (21%) had hyperplastic polyps; 282 (28%) had adenomas, 150 of the men (35%) and 132 of the women (23%), 7 had an adenocarcinoma (0.7%), 4 of the men (0.9%) and 3 of the women (0.5%). 16 patients with adenomas (6%) had a villous component and 99 patients with adenomas (35%) had more than 1. 182 patients had adenomas (65%) beyond the sigmoid colon, 105 of the men (70%) and 77 of the women (58%). 159 patients had adenomas (56%) beyond the splenic flexure, 95 of the men (63%) and 64 of the women (49%). 121 adenomas (43%) were < 5 mm, 64 (23%) were 5 mm-9 mm, 61 (21%) were 1 cm-1.4 cm, and 36 (13%) were 1.5 cm or larger. 97 patients (10%) had an adenoma >9 mm (34% of all adenomas), 59 of the men (14%) and 38 of the women (7%). 76 adenomas (27%) had mild dysplasia, 16 (6%) had moderate dysplasia, and 9 (3%) had severe dysplasia. 4 adenomas with severe dysplasia (45%) were beyond the splenic flexure. In polyps with villous histology 2 were 5 mm-9 mm (13%), 14 were > 1 cm (88%) and 9 (56%) were beyond the splenic flexure. 4 carcinomas (57%) were in the rectum, 2 (29%) in the right colon, and 1 (14%) was in the sigmoid.

Conclusions: Our cohort of average-risk community based patients > 50 years undergoing screening colonoscopy has a yield of neoplastic lesions similar to previous studies. The overall prevalence of advanced neoplasia (cancer, adenomas with severe dysplasia, size > 9 mm, or villous histology) was 11% with a prevalence of 15% in men and 7% in women.

Angiotensin Converting Enzyme (ACE) Inhibitors Reduce the Incidence of Colon Cancer: A Study of Half a Million US Veterans

Vikas Khurana, M.D., F.A.C.G.,* Gloria Caldito, Ph.D., Hannamth Beljanki, M.D. Gastroenterology/Internal Medicine, Overton Brooks VA Medical Center, Shreveport, LA and Biometry, LSUHSC, Shreveport, LA.

Purpose: To investigate the effect of ACE (Angiotensin Converting Enzyme) Inhibitors’ use in reducing the incidence of colon cancer in the US veteran population.

Background: ACE Inhibitors are commonly used antihypertensive and nephroprotective agents that are noted to suppress tumor growth by inhibiting tumor angiogenesis in several animal and experimental models.

Methods: The VISN 16 database contains clinical and demographic information about all veterans (>1.4 million patients) cared for in the South Central VA Health Care Network. The data was queried from Oct 1998 to June 2004, using a retrospective case control design. Statistical analysis was performed using SAS software version 9.0 (Chicago, IL). Multiple logistic regression analysis was used with calculation of odds ratios and 95% confidence intervals. The data was adjusted for age, race, gender, BMI, smoking, alcohol use and diabetes.

Results: A total of 483,733 patients were included in the analysis. 185,898 (38.43%) of those were using ACE inhibitors. Colon and rectal cancer (ICD-9 codes 153 and 154) was seen in 6697 (0.14%). ACE inhibitor users were 59% less likely to develop colon cancer (Odds ratio 0.41; 95% CI 0.39–0.44, p < 0.0001). The protective effect of ACE inhibitors was significant even when the data was adjusted for statin use.

Discussion: Vascular Endothelial Growth Factor (VEGF) is believed to play a major role in angiogenesis in human tumors. Blocking the VEGF inhibits angiogenesis and suppresses tumor growth. ACE inhibitors cause suppression of VEGF in experimental models, leading to their anticancer effect. Our study should be evaluated with caution, given the limitations of the population, the database and the fact that this is a case control study. Patients were placed in the ACE inhibitor user group if they were using ACE inhibitors prior to the diagnosis of colon cancer. The dose, duration and type of ACE
inhibitor used were not factored into the analysis. Some factors known to increase the risk of colon cancer like family history was not incorporated into the study.

**Conclusions:** ACE inhibitors are associated with a 59% reduced incidence of colon cancer after controlling for age, race, gender, BMI, smoking, alcohol use and diabetes.

### 1063

**Does Waiting 5 Years after Polypectomy Increase the Risk of Detecting Clinically Significant Neoplasia? Direct Evidence for a 5 Year Post-Polypectomy Interval**

*Mihir R. Bakhru, M.D., Carol A. Burke, M.D.,* *Rocio Lopez* Department of Gastroenterology, Cleveland Clinic Foundation, Cleveland, OH.

**Purpose:** The recommended post-polypectomy (PP) surveillance interval is 3 yrs for "high" risk and 5 yrs for "low" risk individuals. Direct evidence to support the lengthened interval is lacking. We compared the incidence of neoplasia, advanced adenoma (AA) and cancer in individuals who underwent PP surveillance colonoscopy 3 versus 5 years after the clearing exam.

**Methods:** We reviewed prospective data from subjects who underwent PP surveillance 3 and 5 years after adenomas were cleared from their colorectum. 1486 subjects had a 3 yr and 163 subjects had a PP interval of 5 years. We matched the 5 year subjects to 163 of the 3 year subjects by age (± 5 yrs) and gender. The frequency of neoplasia including AA (≥1 cm, TVA, VA, SD) and cancer was compared between cohorts. A multivariable analysis was performed to determine which baseline characteristics (# of adenomas (≥2 or >2), size of adenoma (≥1 cm or ≥1 cm), pathology of adenoma (advanced versus non-advanced) were associated with recurrent neoplasia. Subjects with ≥2, <1 cm, tubular adenomas at baseline were considered "low" risk and those with >2, or AA were considered "high" risk.

**Results:** The median age at baseline colonoscopy was 58.3 years in the 3 yr and 62.4 years in the 5 yr group (p = 0.02). 73.6% were male. 34% of the 3 year and 42.3% of the 5 year subjects were considered "high" risk at baseline. Recurrent neoplasia occurred in 55.8% of the 3 yr and 58.9% of the 5 yr group (p = 0.57). The majority of recurrent neoplasms were tubular adenomas, 79% vs 80.2%. Frequency of recurrent AA was similar in the cohorts, 23.3% versus 19.6% (P = 0.42). No cancers were detected. On multivariable analysis the follow up interval was not associated with recurrent neoplasia [OR 1.04 (0.65, 1.66)] or AA [OR 0.71 (0.40, 1.26)]. Baseline polyp size was not associated with AA recurrence [OR 0.74 (0.47–1.18)]. > 2 adenomas [OR 4.0 (1.8–9.3)] and AA [OR 3.8 (1.6–8.2)] on baseline exam were associated with recurrent neoplasia and AA, respectively. High risk subjects were more likely to have recurrent AA [OR 3.68 (1.65–8.25)].

**Conclusions:** The incidence of colorectal neoplasia including advanced neoplasia is similar in individuals undergoing post-polypectomy surveillance at 3 and 5 year intervals. A 5 year interval between post-polypectomy examinations may be appropriate for both high and low risk adenoma bearing populations.

### 1064

**Non-Invasive Stool DNA Testing Leads to Increased Screening Adherence in an Asymptomatic Population**

Jennifer L. Rosenberg, MPA, Cathy Thompson, Robert B. Rochelle, Paul C. Schroy III, M.D., M.P.H., F.A.C.G.* Marketing, EXACT Sciences Corporation, Marlborough, MA; Marketing Services, Laboratory Corporation of America, Burlington, NC and Department of Medicine, Boston Medical Center, Boston, MA.

**Purpose:** Colorectal cancer (CRC) is the leading cause of cancer deaths in the U.S. among non-smokers, with an estimated 57,000 deaths in 2004. Screening is a cost-effective yet underutilized strategy for reducing both colorectal cancer mortality and incidence due to poor patient acceptance. It was previously shown that non-invasive stool-based DNA screening was perceived by patients to have a number of advantages over fecal occult blood testing (FOBT) and colonoscopy, suggesting that stool-based DNA testing might be a preferred strategy for routine CRC screening (Am J Prev Med 2005; 28 (2)). The primary objective of this study was to assess patient acceptance of stool-based DNA testing in a community-based setting.

**Methods:** Stool-based DNA screening has been commercially available (PreGen-Plus®) in the U.S. since August 2003. The manufacturer, Lab-Corp® requests patient feedback on pre-paid business reply cards (BRCs). Data are tallied centrally.

**Results:** Data from the first 1145 BRCs tallied were as follows: 91–94% found it easy/easy to pick up and drop off sample collection materials, 87% found it easy/easy to collect a stool sample and 92% said they would be likely/very likely to perform the test again if recommended by their physicians. Importantly, 52% of patients screened with stool-based DNA testing had never been screened for CRC in the past. Among those who had been previously screened, 52% reported that they had been screened with FOBT.

**Patient Perceptions of Stool DNA Testing**

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Few Easy/Likely</th>
<th>Neither</th>
<th>Somewhat Difficult/Unlikely</th>
<th>Very Difficult/Unlikely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ease of pick-up</td>
<td>83%</td>
<td>11%</td>
<td>4%</td>
<td>1%</td>
</tr>
<tr>
<td>Ease of collection</td>
<td>64%</td>
<td>23%</td>
<td>10%</td>
<td>2%</td>
</tr>
<tr>
<td>Ease of drop-off</td>
<td>74%</td>
<td>17%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Likely to re-use</td>
<td>81%</td>
<td>11%</td>
<td>5%</td>
<td>1%</td>
</tr>
</tbody>
</table>

**Conclusions:** CRC screening using stool-based DNA testing appears to be very acceptable to patients. Moreover, given that more than half of subjects had never been screened before, stool-based DNA testing may be an effective way to draw more people into the CRC screening system, thereby increasing the likelihood of detecting more CRCs at an earlier, more curable stage. And, given a high likelihood of re-use, stool DNA screening may be an effective way to retain people in an ongoing screening program.

### 1065

**Adherence to Competing Colorectal Cancer Screening Strategies**

John M. Inadomi, M.D., Lataya Kahn, M.P.H., Sandeep Vjian, M.D., A. Mark Fendrick, M.D., Laurence F. McMahon, M.D., Rodney A. Hayward, M.D.* Center for Practice Management and Outcomes Research, Ann Arbor VA Healthcare System, Ann Arbor, MI; Division of Gastroenterology, Department of Medicine, University of Michigan, Ann Arbor, MI and Division of General Medicine, University of Michigan, Ann Arbor, MI.

**Purpose:** Although the U.S. Preventive Services Task Force concluded that screening with either annual fecal occult blood testing plus flexible sigmoidoscopy every 5 years (FOBT/FS), or colonoscopy every 10 years (COL) provide similar decreases in mortality from colorectal cancer (CRC), insufficient data about adherence impairs identification of the optimal strategy. It is hypothesized that adherence between competing screening strategies is heterogeneous, and that providing choice to patients adversely affects adherence. We aimed to compare the proportion of subjects who adhere to FOBT/FS or COL, and compare adherence after counseling for a single versus both strategies.

**Methods:** We conducted a randomized clinical trial of subjects at average-risk for CRC. Patients solicited at their primary providers’ office consented to receive CRC screening counseling and 6-month follow-up. Subjects were randomized to undergo counseling about: (1) FOBT/FS, (2) COL, or 3) both strategies (the Choice arm). A trained research assistant provided counseling and scheduled the CRC screening tests. The primary outcome was adherence to a CRC screening strategy (FOBT/FS: receipt of 3 FOBT cards by the laboratory, documented FS, and COL if either were positive; COL: documented procedure), and was assessed through medical records and subject contact.
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Colonoscopic Screening of a Community-Based Population of Asymptomatic Average-Risk Individuals

Kevin J. Herlihy, M.D., F.A.C.G.* Joseph C. Yarze, M.D., F.A.C.G., Howard P. Fritz, M.D., Michael P. Chase, M.D., William M. Bauer, M.D.
Division of Gastroenterology, Gastroenterology Associates of Northern New York, Glens Falls, NY.

Purpose: Colonoscopy has become the preferred colorectal cancer screening modality. It is widely believed that colonoscopic detection and removal of adenomas will lead to a reduced incidence of colorectal cancer. Cross sectional screening colonoscopy studies indicate that 25–40% of the asymptomatic US population older than 50 years of age have one or more adenomas. Male gender, older age and a positive family history of colorectal neoplasia are associated with an increased risk. In this study, a community-based evaluation was performed which included only asymptomatic, average-risk persons.

Methods: Between 1/1/04 through 12/31/04, 792 consecutive asymptomatic, average-risk individuals between 50 and 79 years of age underwent screening colonoscopy at an ambulatory GI endoscopy facility. The examinations were performed by the 5 board-certified members of a single-specialty group practice. Advanced colorectal neoplasia were defined by the presence of one of the following: adenomas greater than or equal to 10 mm, adenomas with histologic villous features, adenomas with high-grade dysplasia, and invasive colorectal cancer.

Results:

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Number of Pts</th>
<th>No.Pts w/ adenoma</th>
<th>% Pts w/ adenoma</th>
<th>Gender (M/F)</th>
<th>% M/F w/ adenoma</th>
<th>% w/ advanced neoplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–59</td>
<td>528</td>
<td>159</td>
<td>30%</td>
<td>269/259</td>
<td>35%/25%</td>
<td>4%</td>
</tr>
<tr>
<td>60–69</td>
<td>216</td>
<td>80</td>
<td>37%</td>
<td>115/101</td>
<td>40%/34%</td>
<td>4%</td>
</tr>
<tr>
<td>70–79</td>
<td>48</td>
<td>23</td>
<td>48%</td>
<td>17/31</td>
<td>47%/48%</td>
<td>0%</td>
</tr>
<tr>
<td>Total</td>
<td>792</td>
<td>262</td>
<td>33%</td>
<td>401/391</td>
<td>37%/29%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Conclusions: Asymptomatic, average-risk individuals have a significant prevalence of adenomas, which increases with advancing age. Advanced colorectal neoplasia, including invasive colorectal cancer (3 patients), was present in 3% of screened individuals. This information provides prospective patients as well as other interested parties with adenoma/advanced colorectal neoplasia prevalence rates in the community setting.

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Primary Care Physicians Knowledge and Practices Regarding Colorectal Cancer Screening in Alabama

Mohamad A. Eloubeidi, M.D., M.H.S., Michele Shipp, M.D., Dr.PH., Renee Desmond, Ph.D., Tykeysha Boone, M.P.H., Norm Weissman, Ph.D., Marion Nadel, Ph.D., Mona Fouad, M.D., M.P.H.* Division of Gastroenterology and Hepatology, University of Alabama at Birmingham, Birmingham, AL; Division of Preventive Medicine, University of Alabama at Birmingham, Birmingham, AL; The Comprehensive Cancer Center, University of Alabama at Birmingham, Birmingham, AL and Division of Cancer Prevention and Control, Centers for Disease Control and Prevention, Atlanta, GA.

Purpose: Colorectal cancer (CRCa) screening is associated with decreased mortality. Alabama primary care physicians’ (PCPs) knowledge and practices regarding CRCa screening are unknown. Our objectives were (1) to assess Alabama PCPs knowledge and practices regarding CRCa screening, (2) to assess the need for PCPs to a) gain additional training in flexible sigmoidoscopy (FS) and b) to implement it in their offices.

Methods: A Self-administered questionnaires were mailed to 1916 PCPs. Data were sought on personal demographics, practice characteristics, CRCa screening knowledge and practices as they pertained to various screening tests. The questionnaire also addressed issues of PCPs current and previous training in FS, the use of FS within practices, and PCPs willingness and ability to perform FS in their practices once trained.

Results: Out of 1916, 660 (34%) PCPs returned completed questionnaires. Sixty four percent recommended FOBT testing to their patients. In contrast, only 16% of the physicians recommended FS. Sixty-six percent recommended FS; while 8% recommended DCBE. Sixty-three percent of PCPs received prior FS training and the majority of those trained received it while in residency training (76%). Of those, only 21% performed more than 25 FS procedures during training. Only 17% reported actually performing FS in their offices. Patients’ non-compliance, cost to conduct the procedure, lack of practice time, cumbersome regulations related to endoscopic disinfection, and difficulty in finding and training assistants were among the reported obstacles preventing PCPs from performing FS. Thirty-seven percent reported interest in pursuing training. Eighty-seven percent of those interested in training reported that they would perform FS if adequately trained.

Conclusions: Most survey respondents recommend adequate screening tests for CRCa. However, only a minority recommend FS as a screening procedure. Very few PCPs perform FS currently in their office. Whether providing these PCPs with training opportunities in FS will increase FS utilization remains to be seen.

1068
A Retrospective Review of Colonic Polyp Distribution and Pathology in a Minority Population

K. Grover, M.D., M. J. Sterling, M.D.,* V. P. Mehta, M.D., S. Kancherla, D. Kaperschmidt, M.D., M. Brimacombe, Ph.D. Internal Medicine, UMDNJ – New Jersey Medical School, Newark, NJ; Gastroenterology, UMDNJ – New Jersey Medical School, Newark, NJ and Preventative Medicine, UMDNJ – New Jersey Medical School, Newark, NJ.

Purpose: Colon cancer is the second leading cause of cancer deaths in the United States. Previous studies have shown an increase in the proximal distribution of cancerous lesions in African Americans. We retrospectively analyzed colonoscopies done in inner city African Americans (AA) and Hispanics (H) to determine the distribution of polyps with respect to location, age, and pathology.

Methods: 6,845 colonoscopies were performed at the University Hospital in Newark, NJ from 1998–2004. Of these, 1,414 contained polyp biopsies from 926 AA and 488 H patients with available pathology reports for analysis.

Results: The number of polyps in AA (n = 1790) and H (n = 837) found in the proximal colon (proximal to the splenic flexure) was 818 and 596, respectively. Thus 46% of polyps in AA and 47% of polyps in H were in this region. Furthermore, the pathology of these polyps shows that 60% and 56% of polyps found in the proximal colon were of pathological significance (Tubular adenoma, Villous Adenoma, Tubulovillous Adenoma, Adenocarcinoma) in AA and H, respectively. In the AA population, there was a positive association between age and the percentage of pathologically significant proximal colon polyps. Within this population 51% of proximal polyps in patients younger than 50 were pathologically significant, 58% in those aged 50–64, and 67% in those over 64 (Pearson Chi-Square, P-Value = 0.001).
This association was not present in the H population. In AA, there were 63 instances of cancerous lesions in 57 patients. 34 of these lesions were in the proximal colon. Therefore, 6.8% of polyps found in AA were cancerous, with 54% of these being in the proximal colon. In H, there were 20 instances of cancerous lesions found in 17 patients. 8 of these were in the proximal colon. Thus, 4.1% of polyps found in H were cancerous with 40% of these located in the proximal colon.

Conclusions: Our study provides further evidence to support that there is a higher percentage of pathologically significant polyps in the proximal colon in AA and H when compared to the distal colon. In addition, it shows that in the AA population, older patients have a higher percentage of pathologically significant proximal colon lesions when compared to younger age groups. This finding is not true of the H population.

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Results of hMLH1 and hMSH2 Mutation Analysis among Iranian Patients with HNPCC

Purpose: To determine the molecular epidemiology of hMLH1 and hMSH2 mutations among Iranian patients with HNPCC (Lynch Syndrome).

Methods: We screened 41 Iranian patients who fulfilled the Bethesda criteria for HNPCC. Germline mutations for hMLH1 or hMSH2 genes were evaluated in all 41 patients. Mutation analysis was performed by PCR amplification of the 19 exons for hMLH1 and 16 exons of the hMSH2 genes. The amplicons were screened by SSCP for mutations. Samples which showed band shifts on the SSCP were submitted to direct sequencing.

Results: For the hMLH1 gene we found one missense mutation in the exon 11 at c.326T > C(Val – Ala) and two nonsense mutations in the exons 13 and 19 at c.677C > G(Thr – Stop) and c.2146 2147 delGT(Val – Stop), respectively.

For the hMSH2 gene an insertion was found at the nucleotide 3010 InsG causing a frameshift in the exon 13. This mutation was found in four patients. In one of the patients another transversion was also found at c.677C > G(Thr – Arg) in the exon 13 besides the 3010 InsG.

Conclusions: This is the first report of the mutational analysis of patients with HNPCC in Iran. Our results provide further insight into the mutational spectrum of MMR genes in HNPCC families.

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Chemoprevention with Mesalamine – Myth or Reality?
Eric C. Chu, M.D., Jianyuan Chai, Ph.D., Andrzej S. Tarnawski, M.D., Ph.D.* Section of Gastroenterology, Department of Medicine, VA Long Beach Healthcare System, Long Beach, CA and Division of Gastroenterology, Department of Medicine, University of California, Irvine, Orange, CA.

Purpose: Patients with ulcerative colitis face an increased risk of developing colorectal carcinoma, the magnitude of risk varying depending on duration and extent of disease. Based on cohort and case-control studies, mesalamine has emerged as a candidate chemopreventive agent. Mesalamine shares close molecular similarity with aspirin and may share chemopreventive properties comparable to aspirin and NSAIDs. The molecular mechanisms involved in potentially reducing cancer risk remain incompletely understood, but limited studies have suggested that mesalamine promotes apoptosis and inhibits proliferation in addition to controlling inflammation. This study examined the effect of mesalamine on 96 genes of a cancer pathway gene array. The following studies were performed: (1) mRNA expression by gene array, (2) protein expression by Western blot analysis, and (3) subcellular localization by immunohistochemistry.

Results: Two-hour treatment with mesalamine 4 mM and 40 mM downregulated expression of genes encoding transcription factors and signaling transduction molecules such as Akt (∼61% and 138%, respectively), c-Ets2 (∼74% and 77%, respectively), and c-Myc (∼50% and 89%, respectively). In addition, the gene encoding apoptosis regulator Bcl-x was decreased by ∼34% and 39%, respectively. Five-hour treatment with mesalamine 40 mM significantly decreased protein expression of c-Myc ∼ 3 fold (p < 0.05) compared to those cells treated with mesalamine 4 mM or control. Immunohistochemistry demonstrated reduced expression of both Akt and c-Myc.

Conclusions: (1) Mesalamine downregulates genes encoding pro-apoptotic factors, transcription factors, and signaling transduction molecules in human colon cancer cells. (2) The apoptotic and growth inhibitory effects of mesalamine are dose-dependent. (3) Expression of c-Myc protein is significantly reduced by high dose mesalamine, whereas it is not significantly affected by standard maintenance dose of mesalamine. This research was funded in part by an unrestricted grant from Proctor&Gamble Pharmaceuticals, Cincinnati, OH.

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Screening Flexible Sigmoidoscopy Using a Gastroscope Versus a Sigmoidoscope in Primary Care: A Pilot Study
Larissa S. Buccolo, M.D.,* Chris B. Hyun, M.D. Family Medicine, Naval Hospital, Jacksonville, FL and Internal Medicine, Division of Gastroenterology, Naval Hospital, Jacksonville, FL.

Purpose: Studies in the gastroenterology literature and anecdotal evidence suggest that use of a gastroscope may be more effective than a sigmoidoscope for colon cancer screening. In order to address this question further we conducted a pilot study to compare patient tolerability of flexible sigmoidoscopy performed using standard sigmoidoscope versus a gastroscope.

Methods: Thirty patients over age 50 referred for colon cancer screening by flexible sigmoidoscopy in primary care were included. At completion of the procedure, patient tolerability was assessed using a 100 mm visual analog scale (VAS), and a measure of the ease of the procedure was recorded by performing the examination. Physician and supervising gastroenterologist.

Results: Results were analyzed using a one-tailed t-test. Results of 30 patients, 15 in each group, show a mean VAS of 20.3 in the gastroscope group, and 30.4 in the sigmoidoscope group, with a p-value of 0.055. Subjective measures of ease of the procedure significantly favored the gastroscope (p = 0.02).

Conclusions: We plan to perform a randomized controlled study with a total of 60 patients in order to expand on these results. However, these preliminary results tend to favor the gastroscope, both in patient tolerability and ease of procedure, for flexible sigmoidoscopies performed by a family physician in a primary care setting. If this technique is more widely utilized in primary care, patient compliance to receive colorectal cancer screening will improve and will further optimize colorectal cancer screening programs.

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Radiation Toxicity Induces Endothelial Dysfunction in Rat Intestinal Microvessels
Ottama A. Hafoum, M.D., M.S., Mary F. Otterson, M.D., Hiroto Miura, M.D., Ph.D., Brandon T. Larsen, David G. Butson, M.D., David D. Gutterman, M.D.* Medicine, Medical College of Wisconsin, Milwaukee, WI.

Purpose: Endothelial dysfunction and vascular dysregulation further the pathogenesis and complications of radiation toxicity in tissues. This induced endothelial dysfunction is thought to be involved in both early and delayed radiation responses. The objectives of this study are to assess the acute effect of radiation on acetylcholine (Ach)-induced dilation of intestinal arterioles and the potentially therapeutic effect of antioxidants.
Methods: Rats (2 groups; treated with and without tempol, a water soluble superoxide dismutase mimetic [1µM] for 3 weeks during irradiations) were irradiated using 300 kV X-rays with a half-value thickness of 1.2 mm Cu. Rats received 9 equal doses of 250 cGy in 3 fractions per week on alternate days for 3 successive weeks for a total dose of 2250 cGy. Rats without irradiation were used as controls. Submucosal microvessels were dissected, mounted on glass pipettes, and pressurized at 60 mmHg. The dose-dependent dilation of isolated arterioles (diameter 100–200 µm) to Ach was determined. In addition, dihydroethidine and DCF-DA staining of vessels was used to assess superoxide and total reactive oxygen species (ROS) production by fluorescence microscopy.

Results: After constriction (30–50%) with endothelin, dilation to graded doses of Ach (10−9 – 10−4M) was observed in control vessels (max dilation (MD) 90 ± 4% at 10−3M, n = 7). However, Ach dilation was abolished in intestinal microvessels from irradiated rats (MD = 3 ± 1%, n = 7, p = < 0.05 compared to controls). Fluorescence microscopy revealed significant increases in superoxide (350 ± 31, vs. 210 ± 15; arbitrary units; P < 0.05, ANOVA, n = 7) and total ROS (430 ± 12, vs. 230 ± 2; arbitrary units; P < 0.05, ANOVA, n = 5) in irradiated microvessels compared to control. Irradiated rats treated with tempol, along with the radiation, demonstrated < 0.05 compared to controls). Fluorescence microscopy revealed significant 

Conclusions: Injury to endothelium, heralded by vasodilatory dysfunction, could be a key contributor to both acute responses of normal tissue to ionizing radiation and progressive chronic radiation effects (e.g. ischemia, fibrosis). We believe that ROS may be a potential therapeutic target to minimize radiation toxicity.

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Individuals with Diabetes Have an Increased Risk of Colon Cancer: A Cross-Sectional Analysis
Brenda J. Hoffman, M.D., Donald Garrow, M.D., * Joseph Romagnuolo, M.D. Division of Gastroenterology and Hepatology, Medical University of South Carolina, Charleston, SC.

Purpose: To assess the risk of colon cancer among individuals with diabetes within a nationally representative population.

Previous studies have yielded evidence that diabetes mellitus may be a risk factor for colon cancer. Both hyperinsulinemia and hyperglycemia have been noted in vitro to be promoters of colon cancer growth. Furthermore, insulin and insulin-like growth factor-1 (IGF-1) receptors have been found on colon cancer tissue. Also, high levels of circulating IGF-1 are associated with an elevated risk of colorectal adenomas and cancer. This study further considers the relationship between diabetes mellitus and colon cancer.

Methods: Data collected by the 1997–2003 National Health Interview Survey (NHIS) was analyzed to assess the risk of colon cancer among individuals with diabetes. The NHIS is a comprehensive nationally representative survey designed to represent the U.S. adult population. There were 226,953 subjects represented in the combined seven years of the NHIS, of which 161,235 had complete and comparable data which could be evaluated. Multiple logistic regression was performed probing the relationship between diabetes mellitus and colon cancer while controlling for age, race, gender, obesity, alcohol use, tobacco use, and physical activity. SAS statistical software was used to account for the complex survey design of the NHIS.

Results: Among the 161,235 subjects in this study, 16,664 (10.3%) revealed a history of diabetes mellitus. Adjusted for potential confounders, individuals with diabetes were significantly more likely to have colon cancer than persons without diabetes (Odds ratio (OR) = 1.59, 95% Confidence interval (CI) = 1.3 to 1.9). Age > 50 years (OR = 14.48, 95% CI = 10.8 to 19.4), caucasians (OR = 1.91, 95% CI = 1.1 to 3.2) and smokers (OR = 1.55, 95% CI = 1.2 to 2.0) were also revealed to be significant risk factors.

Conclusions: Caution should be taken with interpretation of this analysis, given the cross-sectional nature of this design. Commonly accepted risk factors for colon cancer including inflammatory bowel disease and family history were not clearly defined in the database. Furthermore, methods of treatment or duration of diabetes were not included in this analysis. Nevertheless, the results from this large cross-sectional survey analysis confirm and expand on previous research which indicates that diabetes mellitus is a significant risk factor for colon cancer.

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Histology, Distribution and Incidence of Polyps in Average Risk Patients Undergoing Colorectal Cancer Screening
Charles W. Randall, M.D., * Carlo M. Taboada, M.D., Cesar Garza, M.D., Rogelio Garcia, M.D. Research, Gastroenterology Clinic of San Antonio, San Antonio, TX and GI, Methodist Hospital, San Antonio, TX.

Purpose: Greater flexibility by government & private insurance carriers in regard to colorectal cancer screening has resulted in a steady flow of referrals for colonoscopy. Historically more attention has been directed towards outcomes of screening procedures with regards to high-risk groups. We recently published an abstract detailing our findings in average-risk patients (pts) undergoing screening for colorectal cancer. This paper presents our most recent findings in a long-term study looking at outcomes of average-risk pts undergoing screening colonoscopy.

Methods: From March ‘03 through April ‘05 pts referred to our center for screening colonoscopy were evaluated regarding their risk of developing colorectal cancer in their lifetime. Only those deemed to be average-risk as defined as asymptomatic individuals w/no prior history of colonic neoplasia, family history of colonic neoplasia, or history of gross or occult bleeding, or anemia were considered. Data was gathered regarding history & distribution of polyps found during colonoscopy. A single dedicated GI pathologist reviewed all cases.

Results: 1324 pts were considered to be average-risk. 320 pts (24.2%) had adenomas. Of this 320, 163 had 1 adenoma and 157 had more than one adenoma. 214 pts (16.2%) had hyperplastic polyps. Only 3 pts (0.23%) had adenocarcinoma. Of these pts w/adenomas, 83 (25.94%) had polyps found in the left colon; 124 (38.75%) in the right colon; 19 (5.94%) in the rectum & 94 pts (29.38%) had polyps in all 3 regions of the colon.

Conclusions: 1. The relatively high incidence of adenomatous polyps (24.2%) in the screening population justifies current screening guidelines. 2. Unlike older studies that found the majority of adenomas to be distributed in the left colon & rectum. Our findings revealed the majority of patients to have right-sided lesions (38.75%) compared to 31.88% for left colon & rectal polyps. 3. A large percentage of patients w/adenomas were found to have more than one polyp at their screening examination (49.06%) and 29.38% of the patients had polyps distributed to all 3 regions of the colon.

1075
Gender-Specific Promotion of Colorectal Cancer Risk by Tobacco but Not Alcohol Use
Anna L. Zisman, M.D., Angel Nickolov, MA, Addi Gorchow, M.S., Randall E. Brand, M.D., Hemant K. Roy, M.D.* Department of Internal Medicine, Evanston Northwestern Healthcare, Evanston, IL; Center for Outcomes Research, Evanston Northwestern Healthcare, Evanston, IL and Cancer Registry, Evanston Northwestern Healthcare, Evanston, IL.

Purpose: Understanding interactions between genetic and environmental factors is critical for colorectal cancer (CRC) risk-stratification and hence designing effective screening strategies. Females tend to have more proximal disease (Schoenfeld et al, NEJM 2005) and a higher frequency of microsatellite unstable lesions. Smoking and alcohol are well-established CRC risk factors yet little is known about gender-specific susceptibility. In this study, we performed a retrospective analysis of the gender-specific risks of tobacco/alcohol use with the age of onset of CRC as a surrogate marker.
Methods: We utilized the IMPAC Medical Registry Services Cancer Information Resource file (CIRF) from 1993 -2004. This database includes data from more than 350 teaching and community hospitals. A logistic regression model was constructed using gender, tobacco and alcohol use. Regression coefficients and standard errors were compared among the univariate and multivariable models to assess confounding. Data were analyzed with SAS.

Results: Age of onset was lower in males than females (69.1 vs. 72.5, p < 0.001) in the baseline non-smoking/non-drinking categories. Current smokers had a markedly decreased age of presentation in both males and females (66.0, p < 0.001 and 65.1, respectively, p < 0.001). Similarly, alcohol use was associated with an earlier age of diagnosis in males and females (67.9, p < 0.001 vs. 64.4 p < 0.001). Assessment of differential sensitivity to smoking and alcohol use in men and women showed females to be more sensitive to tobacco but not alcohol (see Table).

Conclusions: Our data demonstrates that while tobacco and alcohol decrease the age of onset of CRC in both men and women, the effect of tobacco is significantly greater in females. Given that age of onset has clear ramifications for screening strategies, our data strongly suggests that gender/environment interactions need to be factored into a comprehensive CRC prevention regimen.

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Colorectal Cancer Screening in Average-Risk Patients: A Comparison of Findings Based on Ethnicity
Charles W. Randall, M.D.*, Carlo M. Taboada, M.D., Cesar Garza, M.D., Rogelio Garcia, M.D. GI, Methodist Hospital, San Antonio, TX and Research, Gastroenterology Clinic of San Antonio, San Antonio, TX.

Purpose: The importance of colorectal cancer screening has slowly but effectively moved from academic circles to the general populace. As more patients become eligible for screening, identifying sub-groups that may require special attention will be necessary. This paper presents data comparing colonoscopic findings with regard to ethnicity.

Methods: 1324 average-risk patients underwent screening colonoscopy between March 2003 & April 2005. Average-risk was defined as no personal or family history of colorectal cancer, anemia, gross or occult blood loss or gastrointestinal symptoms. Comparisons of findings were made based on ethnicity.

Results: 255 patients of Hispanic descent were screened. 30 had hyperplastic polyps (11.76%); 1 had adenocarcinoma (0.39%) and 67 had adenomas (26.27%). 1044 Caucasian patients were screened. 179 (17.15%) had hyperplastic polyps; 2 had adenocarcinoma (0.19%) and 248 (23.75%) had adenomas. 18 Asian Americans had screening with 3 (16.67%) having hyperplastic polyps and 22 (22.22%) with adenomas. None had cancer. African-Americans and patients of Middle-Eastern heritage made up the remaining 7 patients. 5 were African-American with 1 patient (20%) having an adenoma and 2 patients (40%) with hyperplastic polyps. None had cancer. 2 patients of Middle-Eastern descent were screened with no lesions.

Conclusions: 1. Despite variations in sample size among the predominant ethnic groups the incidence of adenomas was similar among patients of Caucasian, Hispanic and Asian heritages (23.75%; 26.27% and 22.22%, respectively).
2. Our metropolitan area has less than 7% African-Americans and even a smaller population of people of Middle-Eastern descent, making statistical conclusions impossible. Future studies looking at these populations would be advisable.

3. The relative frequency of finding adenomas in patients across several ethnic backgrounds supports current practice standards for colorectal cancer screening.

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Outcomes of Screening Colonoscopy in Asian Americans Compared to Other Ethnic Groups
Ruel T. Garcia, M.D., Khhoa D. Lam, B.A., Huy N. Trinh, M.D., Khanh K. Nguyen, M.D., Long Nguyen, Huy A. Nguyen, M.D., Mindie H. Nguyen, M.D., MAS∗ Gastroenterology, San Jose Gastroenterology, San Jose, CA; Human Biology, Stanford University, Stanford, CA; Biology, University of California, Los Angeles, Los Angeles, CA; Medicine, Stanford University, Palo Alto, CA and Research and Education, Pacific Health Foundation, San Jose, CA.

Purpose: Results of several large North American studies have lead to the current U.S. colorectal cancer (CRC) screening guidelines. However, none of these pivotal studies included Asian Americans in significant numbers. Only a few studies from Asia have examined outcomes of CRC screening in Asians and none in the diverse Asian American population.

The purpose is to compare the yield of screening colonoscopy in Asian Americans versus other ethnic groups and to determine predictors of advanced colonic neoplasia.

Methods: We performed a retrospective study of 2083 consecutive elective colonoscopies performed by 5 endoscopists from June 6, 2003 to September 1, 2004 at a community-based practice, serving a large Asian population in the United States. We reviewed patients’ medical, endoscopy, and pathology records and determined the prevalence of advanced colonic neoplasia defined as adenoma ≥10 mm, villous histology, or cancer. Multiple logistic regression inclusive of age, gender, ethnicity, and family history of CRC was used to determine predictors for advanced neoplasia.

Results: We identified a total of 812 colonoscopies that were performed for CRC screening without any other symptoms. The mean age was 60 ± 11, 47% were male, and 84% were Asian. Outcomes of colonoscopy are summarized in Table.

On multivariate analysis, only male gender was an independent predictor for advanced neoplasia (OR 2.1 P = 0.001).

Conclusions: There is no significant difference in the prevalence of advanced colonic neoplasia in Asian Americans and Non-Asians. Male gender is a risk factor for advanced neoplasia. However, compared to Non-Asians, Asians have a significantly higher prevalence of small adenomas.

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Diminutive Colon Polyps in Asians Are More Likely To Be Adenomatous Compared to Non-Asians
Khooa D. Lam, B.A., Mindie H. Nguyen, M.D., M.A.S., Huy N. Trinh, M.D., Long H. Nguyen, Khanh K. Nguyen, M.D., Huy A. Nguyen, M.D., Aijaz Ahmed, M.D., Ruel T. Garcia, M.D.* Gastroenterology, San Jose Gastroenterology, San Jose, CA; Human Biology, Stanford University,
Purpose: Small (5–9 mm) and diminutive (< 5 mm) colon polyps are less likely to be adenomatous and are less likely to receive endoscopic treatment. However, there may be ethnic differences in the histology of colon polyps. The purpose of this study is to determine the prevalence of adenomas in small and diminutive polyps in Asians compared to Non-Asians.

Methods: We performed a cross-sectional study of all colonoscopies performed from June 6, 2003 to September 1, 2004 at a community-based practice, serving a large Asian population in the United States. We reviewed patients’ medical, endoscopy, and pathology records and analyzed the prevalence of adenoma in small polyps in Asians compared to Non-Asians.

Results: Of the 2083 colonoscopies reviewed, polyps were found in 743 (36%). A total of 1308 polyps were removed. Of these, 481 (37%) were small polyps and 554 (42%) were diminutive polyps. Mean age was 58 ± 11; 48% were male; 87% were Asians. The three most common indications for colonoscopy were: CRC screening (39%), abdominal pain (18%) and rectal bleeding (16%). Prevalence of adenomas was summarized in Figure. On multivariate analysis inclusive of age, gender, ethnicity, family history and indications for colonoscopy, significant independent predictors for adenoma in diminutive polyps were proximal (cecum through transverse colon) location (OR = 3.2, p < .0001) and Asian ethnicity (OR = 1.6, p = .048).

Conclusions: Proximal diminutive polyps are more likely to be adenomatous than those found in distal colon. In addition, these diminutive polyps are more likely to be adenomatous in Asians compared to Non-Asians. Therefore, they should be considered for removal especially those found in the proximal colon and in Asians.

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Colorectal Cancer Screening Using Stool DNA Analysis: Colonoscopic Findings in Cases with Abnormal Results

Barry M. Berger, M.D.,* Myla Lai-Goldman, M.D., Trisha Brown, M.S., Robert Rochelle, M.B.A., Marcia Eisenberg, Ph.D., Paul R. Billings, M.D. Laboratory Medicine, EXACT Sciences Corporation, Marlborough, MA and Molecular Diagnostics, Laboratory Corporation of America, Research Triangle Park, NC.

Purpose: Routine colorectal cancer (CRC) screening using stool DNA analysis (PreGen-PlusTM) was recently made available to general clinical practice [Laboratory Corporation of America, Holdings (LabCorp) [LCA]]. We correlated the results of colonoscopies with their antecedent abnormal stool DNA results.

Methods: A physician (PB) or genetic counselor from LCA telephoned the referring physicians to obtain the colonoscopy and biopsy findings. Office staff provided the follow-up information present in the primary care chart to the interviewer. The DNA based CRC screens were performed between August 2003 and July 2004.

Results: Of 1649 stool DNA screens, 159 had positive results (male to female ratio 41:59; age: 13% < 50, 66% 50–64, 22% >64 yrs). Of these, 72 patients completed colonoscopy and 69 had results available. Results included: colorectal cancer 3 (4%), adenomatous polyps, single 14 (20%) or multiple 9 (13%), hyperplastic polyps 3 (4%), colitis or inflammatory bowel disease (IBD) 5 (7%), or negative findings 35 (51%), including 2 cases (3%) with altered BAT-26 microsatellite due to normal polymorphisms. All cases of CRC were associated with abnormal DNA integrity (DIA), a measure of disrupted apoptosis. Two cases also had mutations in p53 (1) and APC and K-ras (1). One CRC was Stage I and two were Stage II. The patients were 63, 53, and 54 years old respectively, all presented for routine screening and though one had a prior history of a chronically bleeding anal fistula/hemorrhoids. Single adenomatous polyps were associated with abnormal DIA (54%), or mutated APC (15%), K-ras (23%) or p53 (8%). Multiple adenomatous polyps were most commonly associated with abnormal DIA (44%) or mutated APC (22%), K-ras (11%) or p53 (11%). DIA alone was abnormal in all cases of colitis/IBD. Based on an estimated prevalence of CRC in a population of this age of 1–3, this approach appears to have identified the majority of CRC’s expected in this population. This approach appears to add significant clinical value to screening programs.

Conclusions: CRC screening by stool DNA analysis identified patients with early stage CRC and single and multiple adenomatous polyps in a screening population. The discovery of three CRC’s, with only half of the follow-ups completed, is consistent with the identification of the vast majority of CRC’s expected in this population. This approach appears to add significant clinical value to screening programs.

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Analysis of the Human Colon Cancer Proteome by Two-Dimensional Gel Electrophoresis and Mass Spectroscopy

Jody W. Houston, M.D., B. McGowan, O. Eidelman, A. Kline-Burgess, X. Zhang, C. Formas Norris, Michael S. Gold, M.D., H. Pollard, Ph.D., David M. Jacobowitz, Ph.D.* Gastroenterology, Washington Hospital Center, Washington, DC and Department of Anatomy, Physiology & Genetics, Uniformed Services University of the Health Sciences, Bethesda, MD.

Purpose: Colorectal cancer ranks second only to lung cancer as a cause of cancer death, and it is third both in frequency and death in men and women. Knowledge of differential protein expression by colonic adenocarcinoma compared to normal colon could be important in determining the molecular mechanisms involved in the development and progression of colorectal cancer. We designed this study to identify proteins differentially expressed by colonic adenocarcinoma compared to normal colon. We used 2D-gel electrophoresis and mass spectroscopy to look for tumor-specific changes in the human colon cancer proteome.

Methods: Samples of human colon adenocarcinoma were freshly harvested from a total of eight patients undergoing resection for treatment of colon cancer. From each patient a sample of adjacent normal colonic mucosa was harvested for use as a control. Thick slices were then cut in a cryostat (300 µm) and placed on glass slides. Adjacent thin sections were also cut and stained with thionin in order to aid in the microdissection of epithelial cells from the villi. Samples were subjected to protein extraction and quantified. Protein (200µg) from each control and tumor pair from each patient was loaded onto pH gradient strips for isoelectric focusing over 24h. This was followed by 2nd dimension SDS-PAGE to separate proteins based on molecular weight. The gels were stained, scanned and difference analysis conducted using Image Master software. Differentially expressed proteins were punched from the gels, digested, and identified by MALDI-TOF tandem mass spectrometers.

Results: Database interrogation resulted in the identification of 45 significant protein differences in colonic adenocarcinoma as compared to normal colonic epithelium.

Conclusions: The identification of tumor-specific changes within the human colon cancer proteome may lead to the production of useful biomarkers or novel drug therapies for colorectal cancer in the future.
Negative Scar Biopsy after Large Polypectomy at 3 Months Predictive of Cure

Michael B. Rasche, M.D., Vidyasree Chadalawada, M.B.B.S., Lorin L. Bratcher, R.N., Douglas K. Rex, M.D.*. Department of Medicine, Indiana University Medical Center, Indianapolis, IN.

Purpose: Adenoma recurrence rates after colonoscopic piecemeal resection of large sessile polyps have ranged from 16–55%. In some studies, half of recurrences occur after a negative follow-up. The need for multiple follow-up exams looking for recurrence increases costs and patients may be lost to follow-up. The aim of this study was to determine whether absence of visible polyp at the scar at short term follow-up plus negative scar biopsy (no dysplasia in biopsies of the flat scar) predicts cure, allowing return to regular screening intervals without additional follow-up.

Methods: 150 consecutive patients underwent piecemeal resection of 166 large (≥ 2 cm) sessile adenomatous colorectal polyps after submucosal injection. The cases were reviewed to determine factors at initial follow-up (2–6 months after initial polypectomy) that predicted cure (absence of polyp in the scar ≥ 1 year after initial polypectomy). Polyps which had both an early follow-up exam and a one year or longer exam were classified based on findings at the first (2–6 month) follow-up: presence of residual polyp, whether scar biopsy was done, and histology on scar biopsy. Recurrence was defined by either visible residual polyp or positive scar biopsy for dysplasia.

Results: A one year or longer follow-up exam was available on 75 patients (50.0%) and 78 polyps (47.0%). Of these 78 polyps, 68 (87.2%) had completed a follow-up exam 2–6 months after the initial polypectomy (average 85 days). While recurrence at early follow-up endoscopy was 19/68 (27.9%), recurrence at one year was low at 2/68 (3%). In the group with residual polyp on early endoscopy (n = 15), all were treated and four had additional recurrences within the one year follow-up period requiring one additional treatment for ablation of recurrent polyp in each case. In the group without residual polyp but with a scar biopsy demonstrating adenomatous tissue (n = 4), all received additional treatment and one had an additional recurrence within the follow-up period which required one treatment. There were no recurrences within the two groups without residual polyp and either no scar biopsy (n = 8) or negative scar biopsy (n = 41) and none received additional treatment.

Conclusions: Colonoscopic resection of large sessile polyps has high 1 year cure rates. Early endoscopy with scar biopsy after resection has prognostic value. Patients without visible residual polyp growth and with negative scar biopsies for dysplasia are cured and could return to regular screening intervals.

Endoscopist Is Comparable to Age and Gender as Predictor of Adenomas at Colonoscopy

Shawn C. Chen, M.D., Douglas K. Rex, M.D.* Department of Medicine, Indiana University Medical Center, Indianapolis, IN.

Purpose: Increasing age and male gender are known predictors of any adenoma and large adenomas. Indication is not an established predictor of adenomas. The relative importance of endoscopist compared to age and gender as a predictor of adenomas is not certain.

Methods: We reviewed database of 11400 consecutive colonoscopies performed by attending gastroenterologists at a university hospital. Patients with IBD or who were referred for polypectomy were excluded, leaving 9912 colonoscopies. There was no difference between endoscopists in the percentage of males, mean age of patient or indication for procedures.

Results: Multivariate analysis showed that males were more likely to have any adenoma (23.7% vs. 16.2%; p < 0.0001) and any adenoma ≥1 cm in size (p = 0.0015). Increasing age predicted any adenoma and any adenoma ≥1 cm (p = 0.0001). One or more adenomas increased from 14.7% at age 30 to 34.7% at age 70. The range between endoscopists for detection of any adenoma (35.1% – 14.1%), at least 1 adenoma ≥1 cm (5.5%-1.4%), at least 2 adenomas (16.2% – 4.2%), at least 3 adenomas (8.6%-0.4%) and adenomas/colonoscopy (0.71–0.21) were as wide or wider than the differences based on gender or age.

Conclusions: Differences between endoscopists in adenoma detection exceed differences based on gender and age. Whether continuous quality improvement can reduce the variation in detection remains uncertain.

A Discriminant DNA Marker Panel for Detection of Colorectal Adenomas

Anthony P. Shuber, M.S.,* Lisa Kann, Ph.D., Theodore R. Levin, M.D., Douglas K. Rex, M.D., David Alhquist, M.D. Applied Research, Exact Sciences, Marlborough, MA; Division of Gastroenterology, Kaiser Permanente Medical Center, Walnut Creek, CA; Division of Gastroenterology, Indiana University School of Medicine, Indianapolis, IN and Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN.

Purpose: On well characterized tissue, to compare adenoma detection rates by a set of DNA markers used in previous clinical studies (Version 1) with a novel panel of markers (Version 2).

Methods: Assays were performed in blinded fashion on Qiagen-extracted DNA from colonoscopy-obtained tissue comprising 50 paraffin-fixed adenomas ≥ 1 cm and control mucosal biopsies from eleven healthy subjects without pathology. Median age was 63 (range 50–80) for patients and 67 (51–72) for controls; patients and controls comprised 60% and 55% men, respectively. Median adenoma size was 1.1 cm (range 1.0–5.0). 22 were proximal to splenic flexure, and 49 had low grade dysplasia only. Version 1 (V1) is made up of a panel of the 22 markers including selected sequence specific mutations within APC, Kras, p53, and Bat-26 genes (N Engl J Med 2004: 351:2704). Version 2 (V2) assays a panel of 7 markers including the detection of de novo mutations within APC-Mutator Cluster Region (APC-MCR), P1K3CA-Exons 9 and 20 (PIK9, PIK20), and B-catenin; point mutation on BRAF; and hypermethylation on vimentin 29 (VI29) and HLTF.

Results: At specificity cut-offs of 100% for all component markers, sensitivity for adenomas by V1 was 62% and by V2 was 94% (p = 0.0003). For V1, component marker yields were APC (38%), Kras (38%), p53 (4%), Bat-26 (4%). For V2, component yields were APC-MCR (74%), VI29 (50%), HLTF (38%), PIK 9 (14%), PIK 20 (4%), BRAF (4%), and B-catenin (4%). Combinations of markers are compared against V1 in Table.

Marker Combinations # Markers Sensitivity (p vs V1)

<table>
<thead>
<tr>
<th>Marker Combinations</th>
<th># Markers</th>
<th>Sensitivity (p vs V1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1 + V2</td>
<td>29</td>
<td>98% (p &lt; 0.0001)</td>
</tr>
<tr>
<td>V2</td>
<td>7</td>
<td>94% (p = 0.0003)</td>
</tr>
<tr>
<td>APC-MCR/VI29/HLTF/P1K9</td>
<td>4</td>
<td>92% (p = 0.0006)</td>
</tr>
<tr>
<td>APC-MCR/VI29/HLTF</td>
<td>3</td>
<td>90% (p = 0.010)</td>
</tr>
<tr>
<td>APC-MCR/VI29</td>
<td>2</td>
<td>88% (p = 0.0029)</td>
</tr>
<tr>
<td>APC-MCR</td>
<td>1</td>
<td>74% (p = 0.0208)</td>
</tr>
</tbody>
</table>

Conclusions: Wit a panel of just a few candidate DNA markers, high tissue sensitivity for adenomas can be achieved with high specificity. APC-MCR is a particularly informative single marker for adenomas. The improved yield over V1 with substantially fewer markers could influence simplicity and cost of an applied screening assay.

The Patient Referred for EGD: An Opportunity for CRC Screening

Stacy Menees, M.D., A. Mark Fendrick, M.D., Ruth Carlos, M.D., James Scheiman, M.D.* GI, Univ. of Michigan, Ann Arbor, MI.

Purpose: Half of Americans fail to undergo colorectal cancer(CRC) screening. Recently, we reported CRC screening rates of 68% among eligible individuals referred for open access esophagogastroduodenoscopy(EGD) representing a key opportunity to enhance screening rates. Similarly, patients referred to
Improving Knowledge of Familial Colorectal Cancer Risk Using the ACG Brochure
David T. Rubin, M.D.,* Rishi Gandhi, B.S., Nicole Yadron, B.S., Gordon Wood, M.D., Dezheng Huo, Ph.D. Medicine, University of Chicago, Chicago, IL; Medicine, UCSF San Francisco, CA and Health Studies, University of Chicago, Chicago, IL.

Purpose: Previously we have shown that only 49% of patients with a history of colorectal cancer (CRC) understood their family members’ increased risk of CRC, and a significant number of these did not know appropriate screening recommendations. In addition, there was a significant disparity between Caucasian and African American patients’ knowledge (DDW 2005). This is a follow-up of our first study, and was performed to test the impact of an educational brochure on the understanding of familial risk and screening recommendations.

Methods: In phase 1 of this study, a 12 question telephone survey was administered to 254 CRC patients in the University of Chicago Cancer Registry. They were subsequently mailed a brochure developed by the American College of Gastroenterology, “Understanding Colorectal Cancer Screening: A Consumer Education Brochure.” In phase 2 of the study, these patients were re-surveyed 6 months later with the same instrument to test the ability of the brochure to improve understanding of family risk and current screening guidelines. Univariate and multivariate logistic regression was performed.

Results: 202 patients (80%) participated in phase 2 of the study. Inter-phase reliability was excellent (τ = 0.95). The perceived CRC risk for FDRs did not change in phase 2 (Wilcoxon rank test, p = 0.22), but knowledge of the correct age of CRC screening (within 5 y) improved after the intervention (43% vs 56%, p = 0.007). The proportion of participants who told family they were at elevated risk increased, but the change was not significant (p = 0.06), but the proportion of participants who told family members about CRC screening increased significantly (p < 0.001). In both univariate analysis and multivariate logistic regression, Caucasians and participants with a younger age at CRC diagnosis were associated with increased familial risk understanding in phase 1 and 2. In addition, age at diagnosis and higher educational attainment were associated with better knowledge of correct screening age for CRC in phase 2.

Conclusions: The ACG CRC Brochure is effective at improving knowledge of age of screening and asking family to be screened, but is not effective at improving general knowledge about familial risk of CRC, and did not improve racial or educational disparities. More effective targeted interventions are needed to address the significant lack of understanding of familial CRC risk.

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Statins and Risk of Colorectal Cancer: Results from a Large Case-Control Study
David T. Rubin, M.D.,* William A. Blumenthal, Ph.D., Richard L. Sheer, B.S., Michael Steinbach, Ph.D., Linda Law, M.D. Department of Medicine, University of Chicago, Chicago, IL and Procter & Gamble Pharmaceuticals, Mason, OH.

Purpose: Recent studies have indicated that statins may reduce the risk of colorectal cancer. In the high-risk IBD population, analysis of the effect of statins has been limited by small sample size. We examined statins and CRC risk in non-IBD and IBD populations using two large administrative claims databases.

Methods: CRC cases were defined as patients ages 18 and older, with newly diagnosed CRC between 1/1/01 and 12/31/03. The CRC diagnosis was validated by examining for evidence of a colonoscopy or bowel surgery ±60 days from the diagnosis date. Extent of statin therapy was measured during a 12-month period prior to the CRC diagnosis date. For each case, 20 control patients who were continuously enrolled between 1/1/00 and 12/31/03 and who had no record of CRC or bowel surgery were randomly selected, and matched by age, gender, and calendar year on the CRC diagnosis date. We matched 20 controls to cases in order to enrich the control group with IBD patients. Odds ratios were computed using conditional logistic regression models and adjusting for age; gender; ever use of NSAIDs, glucocorticosteroids, immunomodulators, and 5-ASAs; hospitalization; physician visits; and colonoscopy 61–365 days before the CRC diagnosis date.

Results: A total of 18,440 CRC cases and 368,800 matched controls were identified. Of these, 364 CRC cases and 1,172 controls were diagnosed with IBD (ulcerative colitis or and Crohn’s disease). Among non-IBD patients, ever use of statins resulted in a modest reduction of CRC (adj OR = 0.92, 95% CI = 0.89–0.96). Nonstatistically significant risk reduction among ever users of statins was observed in the IBD patient population (adj OR = 0.74, 95% CI = 0.52–1.05). Increasing the number of prescriptions for statins in the non-IBD population showed a slight directional benefit compared to non-users of statins (1–2 prescriptions, adj OR = 1.00, 95% CI = 0.93–1.08; 3–4 prescriptions, adj OR = 1.01, 95% CI = 0.98–1.04; and ≥5 prescriptions, adj OR = 0.90, 95% CI = 0.88–0.93; trend p-value = 0.02). Limited sample size precluded our ability to assess trend among IBD patients.

Conclusions: This large case-control study shows a modest reduction in the risk of CRC among non-IBD patients receiving statins, but the association was not confirmed in IBD patients. It is possible that carcinogenic factors present in IBD may be greater or work by a different mechanism than the possible chemopreventive effect of statins.
inadequate support systems to ensure completion of testing contribute to this problem. A prototype stool DNA test was recently shown to be more acceptable to patients than other screening tests (Am J Prev Med 2005; 28(2)); a technically-enhanced test is now commercially available (PreGen-Plus™). The effect of a robust, enrollment-based patient support system on stool DNA screening test adherence was studied.

**Methods:** Individuals receiving an order for a stool DNA test were given the option to enroll, with appropriate informed consent, in a pilot patient support program (PreGen-Cares™ (PGC)), which authorized PGC staff to contact them several days after the office visit to: enhance patient education, reinforce the need for screening, ensure proper at-home stool collection, provide timely feedback to the caregiver and collect outcomes data. Follow-up contacts were attempted 7–10 days after initial contact. Data were compared to a control group for which stool DNA tests were ordered and collection kits received, but to which no support system was offered. Receipt of a stool specimen by the laboratory was the measure of success.

**Results:** In the first four months of the pilot program, 106 enrollees received initial and follow-up contacts. Discussions with enrollees uncovered a widespread lack of disease awareness and a profound under-appreciation of the importance of regular screening, as well as a moderate concern about reimbursement and out-of-pocket expense. Though not all encounters are closed, a substantial number of potential screening failures have been avoided thus far, resulting in an enrollee adherence rate of at least 69% (73/106), significantly better than the adherence rate in the control group (49/171) (p < 0.0001). In addition, five (5) PGC enrollees who ultimately declined testing with the stool DNA test were convinced by the PGC staff to re-contact their caregivers to schedule colonoscopies.

**Conclusions:** Patient adherence with CRC screening recommendations may benefit from a system-wide approach using reminder calls and at-home educational assistance to supplement communication between patient and physician, address any questions that arise before or during testing, and reinforce the importance of regular screening.