

ENTERAL VERSUS PARENTERAL NUTRITION AFTER SEVERE CLOSED HEAD INJURY

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We measured energy expenditure (MREE) and nitrogen excretion (UUN) in patients with severe head injury randomized to early parenteral (TPN, $n = 21$) or jejunal (ENT, $n = 27$) feeding with identical formulations. The MREE rose to 2400 ± 531 kcal/day in both groups and remained at $135\% \pm 26\%$ to $146\% \pm 42\%$ of predicted energy expenditure over 4 weeks. Nitrogen excretion peaked the second week at 33.4 ± 10 (TPN) and 31.2 ± 7.5 (ENT) g N/day. Both routes were equally effective at meeting nutritional goals ($1.2 \times$ MREE, 2.5 g protein/kg/day intake, stabilized albumin and transferrin levels). Infections were equally frequent: 1.86 episodes/TPN patient versus 1.89 episodes/ENT patient. While patient charges were much greater for TPN, the hospital costs were similar for TPN and ENT support regimens. These findings show that patients with head injuries are hypermetabolic for weeks, that only 27% are capable of spontaneously eating nutritional requirements by discharge, and that either TPN or ENT support is equally effective when prescribed according to individual measurements of MREE and nitrogen excretion.

PATIENTS WITH severe brain injuries require nutritional support because of an accelerated metabolism and prolonged inability to eat. Several reports describe the hypermetabolic state present after traumatic brain injury, in which energy requirements increase 135% to 200% above normal.¹⁻³ Nitrogen excretion is also significantly increased, and these elevations persist for up to 4 weeks.⁴ There is very large variability in individual energy requirements and nitrogen excretion not reliably predicted by clinical formulas.^{5,6}

The parenteral route is usually recommended because of early gastric feeding intolerance due to atony.⁷⁻⁹ New methods of endoscopic access to the jeju-

num have proved that enteral nutrition may be used successfully early after head injury.^{10,11} An additional advantage ascribed to enteral (ENT) compared with parenteral nutrition (TPN) is a reduction in infectious morbidity, especially among patients with multiple trauma.^{12,13} The advantages of enteral nutrition over parenteral nutrition include better maintenance of gut mucosal integrity, decreased bacterial translocation, equivalent repletion or maintenance of nutrient needs, and less expense. For these reasons, we sought the answers to three questions: (1) What is the comparative nutritional efficacy of TPN versus ENT in patients with severe brain injuries. (2) What is the total complication rate of either route, including all procedural complications, mechanical problems, and infection? (3) What is the cost versus charge performance of nutritional support over an entire hospitalization? Our methodology is unique in its use of individually tailored nutritional support prescriptions rather than a standardized mixture applied uniformly.

CLINICAL METHODS AND MATERIALS

Study Design

The study was a prospective, randomized, nonblinded clinical comparison conducted at Legacy Emanuel Hospital and Health Center, a level 1 trauma center in Portland, Oregon. The main purpose of the study was to investigate the effect of route of nutritional support; start-up formulations, rates of advancement, monitoring, and nutritional refinements were standardized for both groups. Enrollment, randomization, and initiation of feeding occurred within 72 hours of injury,

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Further assistance was provided by the Emanuel Foundation, Emanuel Hospital and Health Center; and by the Research Advisory Committee of Emanuel Hospital.

An analysis of the Western Neurosensory Stimulation Profile was presented by Ms. Parrott and Ms. Bledsoe at the 7th Annual Conference, Cognitive Rehabilitation: Community Integration after Brain Injury September 30–October 3, 1993, Washington, DC.

The effects of parenteral versus enteral nutritional support on rates of cognitive recovery was presented at the Surgical Forum, in San Francisco, October 1993. It is abstracted in the *Surgical Forum* 44:29-31, 1993. The nutritional comparison portion of the project was presented at the Twenty-fourth Annual Session of the Western Trauma Association, February 27–March 4, 1994, Crested Butte, Colorado.

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allowing time for resuscitation to stabilize the patient, families to give informed consent, and those expected to die imminently to declare themselves. The study was approved by the Investigational Review Board (human studies committee) and the Research Advisory Committee of our institution. Fasting controls (no food or dextrose in water solutions) were unacceptable.

Patient Population

All adult (18 to 60 years) patients with head injuries with Glasgow Coma Scale scores of 8 or less and coma persisting over 24 hours were considered. Patients with multiple injuries were included. Exclusion criteria were spinal cord injury, pre-existing metabolic disorders, renal failure, inflammatory bowel disease, status more than 72 hours post-injury, or a neurologic prognosis of rapidly fatal injury. Randomization was done using a computer-generated random number table. APACHE II scores and Injury Severity Scores (ISSs) were determined. Within 24 hours of randomization, all feeding-related procedures were completed and support begun.

Nutritional Regimens

Target rates of calorie support were calculated at enrollment using the Harris-Benedict equations plus an additional 50%. Parenteral nutrition was administered via multi-lumen Vitacuff (Arrow International Inc; Reading, Penn) protected central venous catheters. Interpretation of chest x-ray films confirmed placement. Parenteral nutrition was started at full strength and advanced as follows: 40% of target rate for 24 hours; 60% for 12 hours; 80% for 12 hours, then target rate. Nasogastric sump tubes (18F) drained the stomach.

On postenrollment day 5, efforts were begun to convert the TPN group to gastric feedings. With the nasogastric sump tubes clamped and once gastric residuals were less than 100 mL over 4 hours for three consecutive intervals, full strength Isotein HN (Sandoz Nutrition Corp; Minneapolis, Minn) was begun as a continuous infusion at 25 mL/hour, and advanced every 12 hours to target rate. The sump tubes were then replaced by soft 10F nasogastric feeding tubes. Feedings were held if gastric residuals were higher than 150 mL. Residuals were then re-checked hourly before feeding was resumed. Parenteral nutrition was tapered as gastric feedings progressed.

Enteral nutrition was given via surgically placed jejunal tubes (needle catheter jejunostomies were preferred but some surgeons used red rubber tubes); gastrostomy tubes drained the stomach. Full strength tube feeding was begun immediately after surgery and advanced as follows: 20% of target rate for 12 hours; 40% for 12 hours; 60% for 12 hours; 80% for 12 hours, then target rate.

Table 1 lists the nutrient formulations, which were isonitrogenous and isocaloric. Vivonex TEN (Norwich Eaton Pharmaceuticals, Inc., Norwich, NY) contained 4.90 g glutamine per liter, the modified 10% Travasol (Baxter Healthcare Corp., Deerfield, Ill.) mixture contained 3.21 g/L. The branched chain amino acid contents were ENT 12.6 g/L; TPN 12.5 g/L. In anticipation of wide intersubject variability in calorie and nitrogen needs, we chose not to prescribe nutritional therapy based only on admission weight, but altered nutritional prescriptions according to individually measured needs. After the third study day, urine urea nitrogen (UUN) measurements guided protein replacement, up to a maximum nitrogen intake of 2.5 g nitrogen per kilogram of body weight per day. When extra protein was needed above that supplied by either of the 150 nonprotein calorie per gram nitrogen formulas, it was given as Travasol 10% added to the intravenous TPN solution or to the tube feeding for ENT patients. Calorie

Table 1
Nutrient formulation analyses per liter

	Vivonex TEN	Parenteral
Calories (kcal)	1000	1162
Nonprotein Cal:N	149:1	134:1
Carbohydrate (g)	205.6	240
Fat (g)	2.8	5.6
Amino Acids (g)	38.19	38.44
Percentage BCAA	33.1	32.5
Percentage AAA	6.0	6.24
EAA (g)	20.0	19.56
Non-EAA (g)	18.19	18.88
MVI-12 (mL/day)	10 mL	10 mL
Sodium (mEq)	20	
Potassium (mEq)	20	
Iodine (μ g)	75	0
Zinc (mg)	10	4
Manganese (mg)	0.9	0.4
Selenium (μ g)	50	0
Molybdenum (μ g)	50	0
Chromium (μ g)	16.7	150

supplementation determined by indirect calorimetry was supplied as microlipid emulsion in the ENT feeding or as 20% lipid emulsion in TPN solutions.

Based on earlier reports showing that gastric feedings were reliably tolerated by day 9 to 11, we converted the ENT group from Vivonex TEN to Isotein HN via jejunal tube on postenrollment day 12, thus keeping both groups identical except for route. All TPN patients were converted to gastric feedings, and all ENT patients continued to receive jejunal feedings. Tube feedings continued until a speech pathologist, a regular member of our brain injury team, determined that patients could swallow liquids or food without aspirating. Usually, pureed foods were the first safe source of oral nutrients. The day these foods were recommended by the speech pathologist was called the first day of oral feedings. Oral intake was encouraged until tube feedings were needed only at night (i.e., >50% of needs taken orally) or not needed at all (>80% taken orally). The study was concluded when patients took all nutrition orally or until the time of discharge.

Metabolic Studies

Daily 24-hour UUN studies were done for 11 days to establish cumulative nitrogen balance and then at least weekly thereafter to guide therapy. Three grams of nitrogen was added to UUN to estimate daily nitrogen needs. When patients exhibited extraordinary levels of protein wasting, we set a maximum repletion of 2.5 g protein/kg/day.

Indirect calorimetry was done every 3 days for the duration of the study. The instrument used was the Sormedics 2900, an open circuit calorimeter using infrared sensors for CO₂ content and zirconium oxide sensors for oxygen content of respired gases (Sormedics 2900, Sormedics Corp., Yorba Linda, Calif.) Calibration and validation tests were performed before each patient session.¹⁴ Mechanically ventilated patients and those with tracheotomies were studied via endotracheal tubes. Spontaneously respiring patients were studied under a rigid plastic canopy. Studies lasted 30 to 75 minutes in resting patients until 10 minutes of stable (<10% variation) energy values were obtained. Agitated or unusually sedated patients were restudied. Observations about activity during study (sedated, calm, agitated, posturing) were reported to the dietitians, who also conferred with nursing staff to extrapolate the measured resting energy expenditure (MREE) values to 24-hour activity and caloric needs. Deliv-

Table 2
Study population characteristics

	TPN	ENT
Number enrolled	23	36
Number studied	21	28
Age (years) (range)	28.9 ± 10 (18–54)	26.2 ± 10.4 (16–58)
Male-to-female ratio	19:2	21:7
APACHE II	14.9 ± 3.9 (n = 17)	15.7 ± 3.5 (n = 14)
ISS	33.4 ± 9.51	32.5 ± 10.1
Deaths (%)	1 (4.4)	5 (13.9)
Admission GCS score	5.4 ± 1.9	5.2 ± 1.6
Length of Stay (days)	36.9 ± 14	39.1 ± 23.1
Number (%) of CT findings		
Epidural	2 (9.5)	1 (3.6)
Subdural	8 (38.1)	8 (28.6)
Intraventricular	2 (9.5)	3 (10.7)
Contusion/shear	10 (47.6)	16 (57.1)
Fractures	9 (42.9)	12 (42.9)
Normal	1 (4.8)	1 (3.6)
Number (%) of Associated Injuries		
Chest	8 (38.1)	9 (32.1)
Abdomen	2 (9.5)	4 (14.3)
Orthopedic	10 (47.6)	13 (46.4)
Soft tissue/face	5 (23.8)	3 (10.7)
Number (%) of Operations		
Craniotomy	10 (47.6)	9 (32.1)
Laparotomy	1 (4.8)	3 (10.7)
Orthopedic	3 (14.3)	5 (17.8)
Gastrostomy/ jejunostomy	3 (14.3)	25 (89.3)
PEG-J	13 (61.9)	3 (10.7)
Tracheostomy	17 (81.0)	23 (82.1)

ered energy goals were set at 120% of MREE to help compensate for expected interruptions in tube feeding. Respiratory quotients were measured, and together with UUN values were used to compute individual substrate contributions in percentage of protein, carbohydrate, and lipid.

Biochemical measurements included blood chemistry profile, albumin, and transferrin, and were repeated weekly. Blood glucose level was monitored every 6 hours during TPN, twice daily during tube feedings.

Patient Management

Patients were intubated, hyperventilated, and nursed in a head-up position. Neurosurgeons determined the use of steroids, barbiturates, mannitol, intracranial pressure monitoring, craniotomy, and diagnostic management. Resuscitation, pulmonary artery catheter, torso and extremity injuries, fever, and infections were managed by the trauma team. Following central venous cannulation in the TPN group, further timing and choice of tube feeding access (nasogastric, nasoduodenal, endoscopic, or surgical gastrostomy) was at the discretion of the trauma surgeon, and not determined by study protocol. All TPN patients had initial efforts at gastric feeding with 8–10F nasogastric feeding tubes.

Complications

Complications were pre-defined by the study protocol and grouped into two categories, infections and nutrition-related. A subset of problems related to the route of nutritional support included patient discontinuance of feeding tubes, wound infection/dehiscence, tube dysfunction, and intolerance of feeding. Bronchitis was defined by fever, leukocytosis, leukorrhea, and predominant bacteria on gram staining; pneumonia as bronchitis with the addition of an infiltrate on chest

films; and sinusitis by nasal discharge, fluid on CT scan, and culture-positive sinus aspirates. Urinary tract infections required $>10^5$ organisms per milliliter. Hyperglycemia was defined as a blood glucose level >180 mg/dL. Elevations were treated with insulin. Diarrhea was treated first with Lomotil or decreased tube feeding rates if antidiarrheals were not effective.

Statistics

Data gathered over time were graphed and Student's unpaired *t* test was used to define differences. Categorical data points were compared using Chi-square analysis with Yates' correction for small numbers.

RESULTS

The study was conducted from July 1990 through December 1991. Twenty-three subjects were randomized to TPN; one died on postinjury day 4, one was dropped as a protocol violation when onset of feeding was delayed. Thirty-six subjects were randomized to ENT; four died of brain injury, one died on day 18 of multiple organ failure, and three were dropped because of an inaccurate low GCS score (1), delay in feeding (1), and quadriplegia (1). One ENT patient with peritonitis was a treatment failure because jejunal feedings massively refluxed into the stomach and his surgeon began parenteral nutrition. Sample population characteristics listed in Table 2 show that the two groups were comparable with no significant differences by chi-square analysis (including male-to-female

Table 3
Post hoc analyses of nutritional response in patients with isolated head injury and in those with associated major injury

	Isolated Head Injury		Closed Head Injury & Associated Injury	
	ENT	TPN	ENT	TPN
Age (mean \pm SD) (years)	26.2 \pm 12.2	25.4 \pm 8.8	26.2 \pm 8.3	32.3 \pm 10.1
Sex (F:M)	3:12	1:8	4:9	1:11
Number	15	9	13	12
LOS (days)	40.9 \pm 24.8(15)*	37.6 \pm 16.7(9)	38.5 \pm 21.8(12)	38.7 \pm 13.9 (11)
ISS	26.1 \pm 6.4(15)	29.3 \pm 6.7(9)	40.4 \pm 8.0(12)	36.5 \pm 10.4 (12)
MREE (mean \pm SD)(kcal/d)				
1 week	2416 \pm 672 (14)	2210 \pm 423 (9)	2404 \pm 505 (13)	2524 \pm 598 (11)
2 week	2486 \pm 657 (8)	2408 \pm 465 (6)	2621 \pm 742 (8)	2443 \pm 632 (9)
3 week	2708 \pm 1251 (8)	2136 \pm 809 (5)	2126 \pm 610 (4)	2797 \pm 771 (5)
4 week	2690 \pm 1590 (4)	1710 (1)	2139 \pm 556 (5)	2599 \pm 158 (3)
Nitrogen excretion (mean \pm SD)(UUN + 3)				
1 week	25.0 \pm 5.3 (15)	21.8 \pm 4.2 (9)	23.6 \pm 7.8 (13)	29.3 \pm 11.6 (12)
2 week	31.8 \pm 10.9 (12)	29.1 \pm 9.5 (9)	30.6 \pm 8.2 (12)	36.6 \pm 9.6 (12)
3 week	29.3 \pm 9.6 (11)	26.2 \pm 10.6 (6)	24.5 \pm 8.3 (9)	31.8 \pm 6.9 (8)
4 week	27.3 \pm 9.1 (7)	20.6 \pm 4.1 (6)	24.1 \pm 4.4 (5)	25.3 \pm 4.0 (7)

* Numbers in parentheses are numbers of patients at each time interval.

ratio: $\chi^2 = 1.023$, $p > 0.1$). The ISSs reflect the serious nature of CNS and associated injuries. Craniotomy and intracranial pressure monitoring rates were similar. Six TPN and six ENT patients received barbiturates for 1 to 7 days. Patients 27 (TPN), 2, 28, and 39 (ENT) each received four to six 4-mg doses of dexamethasone in the first 24 to 48 hours post-injury. A slight, statistically nonsignificant increase in daily nitrogen excretion lasting 2 days followed steroid use; therefore, these patients were included in the total group analyses.

A post hoc analysis was done on the subset of patients with isolated head injury with or without facial injuries, foot (1) or finger (1) injuries and that group with head and torso or long bone injuries. Table 3 contains data on ISS, which is significantly greater when major injuries occur with head injury. However, age, sex, MREE over time, and nitrogen excretion over time are not significantly different in either subset or either nutritional support arm. Although the trend in the subset of multiple injury patients receiving early TPN was for elevated nitrogen excretion, it did not reach significance except in week 1; isolated CHI versus CHI with associated injuries: 21.8 ± 4.2 g/day vs. 29.3 ± 11.6 g/day, $p < 0.05$. The conclusion was that severe head injury was the predominate factor in accelerated metabolism. Therefore, all patients in each nutritional support group were analyzed together, without regard to the presence or absence of associated injuries.

Cumulative nitrogen balance over the first eleven study days was equally negative: TPN, -70.8 ± 49.0 ; ENT -67.9 ± 36.2 g. Nitrogen excretion rose throughout the first two post-injury weeks (Fig. 1), peaking at 0.46 ± 0.12 g N/kg/day by about the ninth day, ranging from 0.30 to 0.74 g N/kg/day. This was slightly above the planned maximum protein delivery rate of 2.5 g N/kg/day, or 0.4 g N/kg/day. These high levels of nitro-

gen excretion persisted over 5 weeks (Table 4). No significant differences existed between the groups at any interval for nitrogen excretion, intake, or balance.

Measured resting energy expenditures were increased but not quite to the degree expected. The data in Figure 2 are for TPN and ENT combined as no significant differences existed between the two groups. The efficiency of feeding, computed as the ratio of calories delivered to MREE (target 120% MREE), showed a TPN advantage on day 3 (106.2% versus 90.5%), that was lost thereafter (Fig. 3). Energy needs increased in patients with agitated recovery, infections, or persistent hypertonicity. The combined groups' mean respiratory quotient was 0.91 ± 0.08 the first week, and remained unchanged over the next several weeks.

Serum transferrin (Fig. 4A) levels were sustained in the normal range throughout hospitalization, and serum albumin (Figure 4B) was well maintained at mild levels of "depletion." No exogenous albumin was used. Liver function was monitored using serum bilirubin, GOT, GGT, and alkaline phosphatase values. Elevated bilirubin levels fell to normal by the second week (Fig. 5A), but the enzymes peaked at that time and mean values had not returned to normal by the fourth week. A significantly lower mean GGT value in the third week in the ENT group (181 ± 106 vs. 366 ± 325 Units/L, TPN) was probably not clinically important (Fig. 5B).

Complications are listed in Tables 5 and 6. Catheter sepsis (greater than 15 colony-forming units on a catheter tip from a febrile patient with leukocytosis) occurred in 9.5% of TPN and 11.1% of ENT patients. Hyperglycemia was significantly more common among TPN ($\chi^2 = 10.4898$, $p < 0.05$) than ENT patients, despite identical methods of measuring energy needs and rates of delivery. The number of patients with diarrhea (three or more loose stools in one day and/or the use of antidiarrheals) was significantly greater in the TPN group ($\chi^2 = 5.00$, $p < 0.05$), as was the num-

Urine Urea Nitrogen Excretion

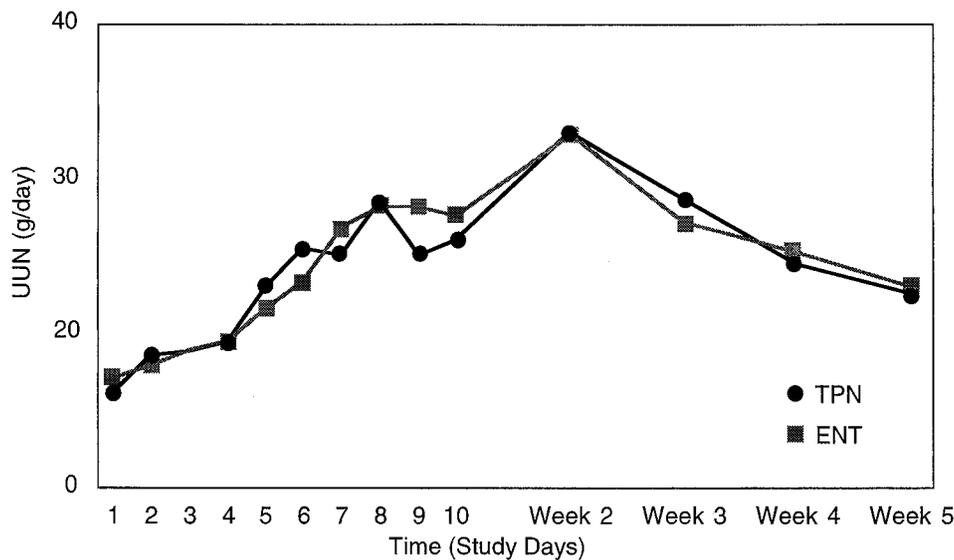


Figure 1. Nitrogen excretion rises steadily during the first week post-injury, peaks in the second week, and remains highly elevated for many weeks.

ber of patient-days with diarrhea, (68, TPN versus 37, ENT). Diarrhea was most common during the first two weeks for ENT and weeks 2, 3, and 4 for TPN. Most episodes were associated with systemic antibiotic therapy, and there were six *Clostridium difficile* infections. Aspiration during hospitalization was infrequent, occurring twice in ENT patient number 48; none led to pneumonia. This low incidence may be the result of jejunal versus gastric feedings in most patients, the use of gastric residual volumes of only 150 mL before withholding tube feedings, the use of cuffed tracheostomy tubes, and supervised advance of oral diets by speech pathologists.

Of note is a problem frequently encountered with indwelling feeding tubes in patients with closed head injury. Dislodgement of tubes by the patients (even nasal septal bridles were broken) was a major impediment to feeding, especially when nasogastric (NG) tubes were used. Ten TPN patients fed via NG tubes pulled out 51 tubes before the physicians resorted to percutaneous endoscopic gastrostomies (PEG) or surgical gastrostomy devices. Each replacement required

a chest film to confirm placement before feeding resumed. Sixteen gastric (1 TPN, 5 ENT) or jejunal (1 TPN, 9 ENT) tubes were pulled out. Dislodged needle catheter jejunostomies could not be replaced: feeding was transferred to gastrostomy tubes. Dislodged rubber tube jejunostomies or gastrostomies were replaced whenever possible. No intraperitoneal feeding complications occurred. Tube dislodgements usually occurred as cognitive recovery entered the confused/agitated stage in strong, young patients who could not comprehend or remember instructions and for whom restraints provided limited protection for tubes, especially those in the face.

Infectious morbidity is listed in Table 6. A majority of patients received systemic antibiotics triggered by fever, leukocytosis, and clinical suspicion. Many never met criteria for an established diagnosis of infection, but antibiotics were often continued for persistent fever and leukocytosis. A retrospective review of charts, laboratory tests, chest x-ray films, and bacterial cultures was done by two of the authors. No significant differences occurred for all infections combined, which

Table 4
Nitrogen balance studies over 1 month in grams of nitrogen per 24 hours (mean \pm SD)

	Week 1	Week 2	Week 3	Week 4
N_{in}				
TPN	21.4 \pm 5.5 (21)*	26.3 \pm 5.9 (21)	23.4 \pm 7.5 (16)	21.4 \pm 5.9 (14)
ENT	18.3 \pm 4.5 (28)	27.9 \pm 4.8 (24)	27.1 \pm 5.3 (20)	21.6 \pm 5.8 (12)
N_{out}				
TPN	26.1 \pm 9.8 (21)	33.4 \pm 10 (21)	29.4 \pm 8.8 (14)	23.1 \pm 4.6 (13)
ENT	24.3 \pm 6.5 (28)	31.2 \pm 7.5 (24)	27.2 \pm 9.2 (20)	26.0 \pm 7.4 (12)
N_{bal}				
TPN	-4.2 \pm 6.5 (21)	-6.8 \pm 6.0 (21)	-6.2 \pm 7.6 (14)	-2.1 \pm 7.5 (13)
ENT	-6.1 \pm 5.6 (28)	-3.5 \pm 7.7 (24)	-1.2 \pm 8.8 (20)	-2.9 \pm 5.6 (12)

* Number of patients in parentheses.

Energy Profile: ENT and TPN Combined

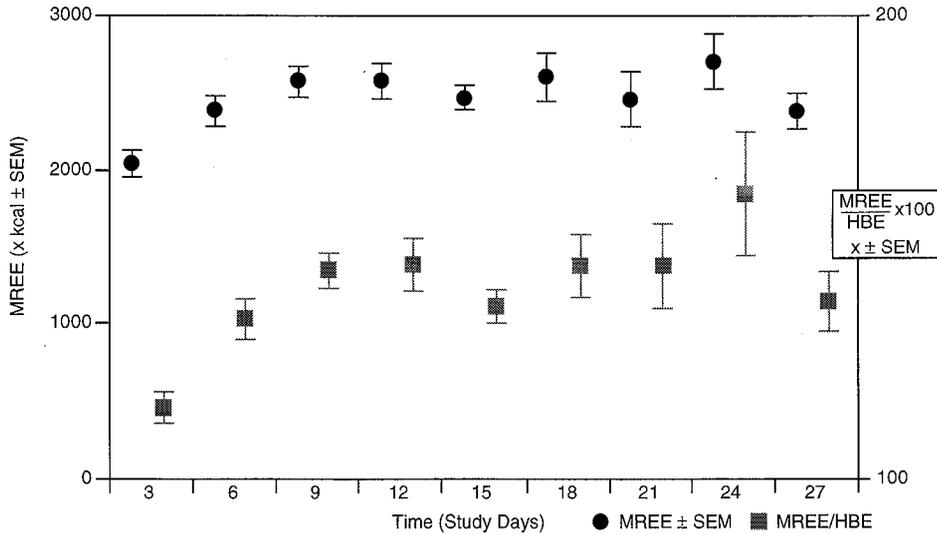


Figure 2. The combined values of MREE for both the TPN and ENT groups are shown by the circles; increased energy expenditure above basal needs persists throughout 4 weeks (squares).

gave an incidence of 1.86 episodes per TPN patient versus 1.89 per ENT patient.

A sample of patients from the TPN (9) and ENT (10) groups had their hospital bills analyzed line by line to extract all nutrition related charges (Table 7). Samples matched groups for length of stay (TPN, 37.9 ± 17.8 days; ENT, 35.9 ± 22.9 days), ISS (TPN, 33.8 ± 8.6 ; ENT, 32.7 ± 11.0), associated injuries, and relative outcomes. Another model of cost analysis was done by identifying actual 1991 hospital purchase prices plus indirect costs assigned to each item (e.g., nasogastric tubes, a chest film, a liter of tube feeding, or central parenteral nutrition) or procedures (operating room time, disposables cost, customary professional fees).

The results were then applied to a "typical" patient with severe head injury, fed either enterally or parenterally for 10 days then converted to gastric feeding (Table 8). As expected, charges for the parenterally fed group greatly exceeded those for the enterally fed patient. While the patient charge disparity remains, hospital costs were remarkably similar for 10 days of central parenteral nutrition and subsequent tube feedings compared with enteral support alone.

DISCUSSION

Brain injury induces a hypermetabolic state marked by elevated energy expenditure to levels usually asso-

Calories Delivered As a % of MREE

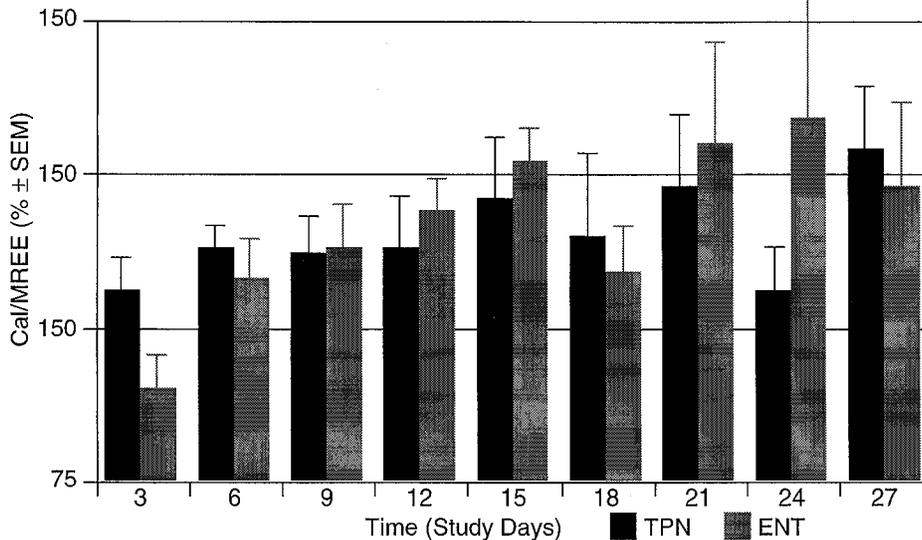


Figure 3. Efficiency in feeding is the ratio of kilocalories delivered to MREE, with a goal of $1.2 \times$ MREE. The only significant difference occurred on day 3.

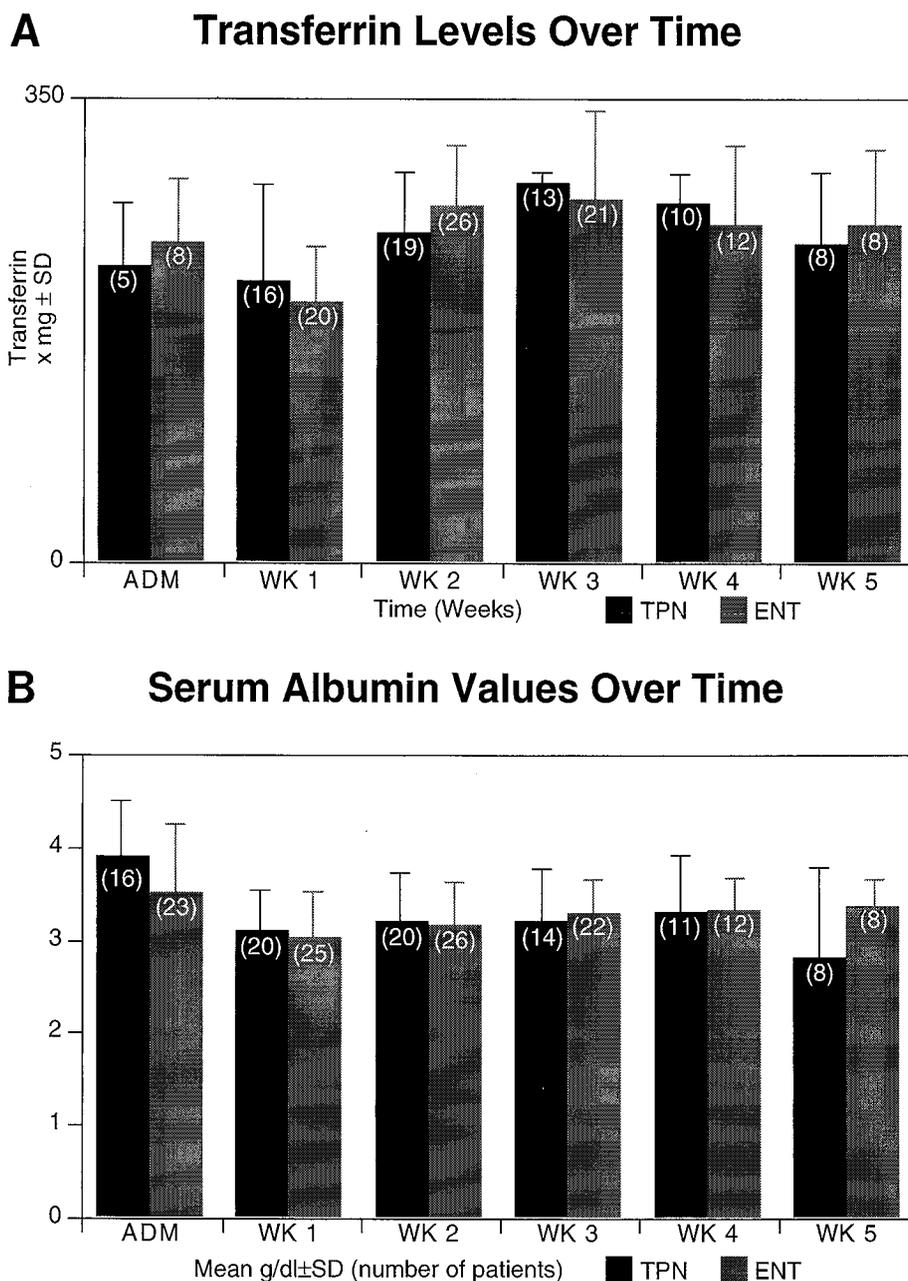


Figure 4. (A) Serum transferrin levels from admission through post-injury week 5 show that both TPN and ENT feeding maintain normal levels (221–394 mg/dL). (B) Serum albumin levels were already slightly lowered on admission but were sustained at a level only slightly below normal (3.5–5.0 g/dL).

ciated with 20% to 40% total body surface area burns.⁴ The elevation persists for several weeks, and in Haid-er's report, increased levels were present one year after brain injury.¹⁵ Although elevation is roughly propor-tionate to the severity of injury, regression analysis of MREE versus GCS score did not show a significant correlation.¹⁶ This study (Fig. 2) showed a relative pla-teau in MREE over 4 weeks, possibly because patient activity increased over time, obviating any reduction in energy expenditure that may be the result of brain healing.

The injured brain itself is the most likely source of the factors altering the body's economy. Although Fell et al.¹⁷ could find no hypermetabolic state in patients

with isolated head injuries compared with patients with multiple trauma or head injury plus multiple traumas, this study continued for only 5 days and nei-ther UUN nor MREE was measured. It did not contin-ue long enough to identify accelerated metabolism from head injury. Numerous other studies have fo-cused on isolated head injuries and routinely show hypermetabolism.^{4,6,7,18} Bouzarth et al.¹⁹ found an ad-renocortical response directly proportional to the se-verity of acute brain injury. Comatose patients with isolated head injury have up to sevenfold increases in norepinephrine levels,²⁰ with higher values in patients with lower Glasgow Coma Scale scores. Experimental brain injury in rats causes interleukin-1 production by

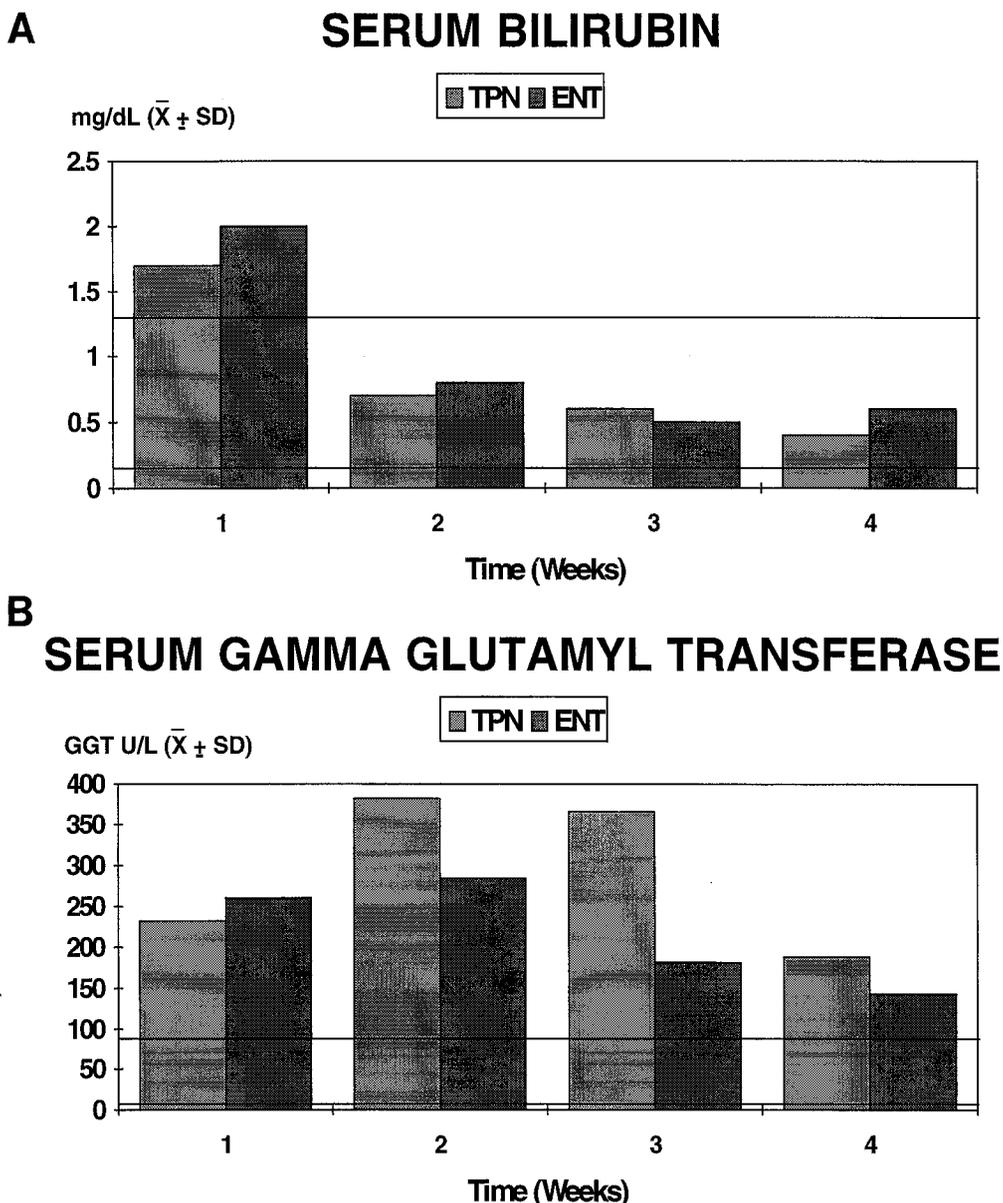


Figure 5. Serum bilirubin levels (A) rapidly returned to normal in both groups, but GGT (B) as well as other liver enzymes rose for several weeks before declining toward normal levels.

the damaged tissues.²¹ Interleukin 1 can stimulate the entire range of hypermetabolic changes seen post-injury.

The increased MREE was probably causally associated with elevated circulating levels of counterregulatory hormones such as cortisol, glucagon, and catecholamines found after brain injury.^{3,19} Tachycardia, fever, and hypertension are almost constant physiologic findings. Energy expenditure is lessened by administration of propranolol,¹⁶ indicating the role of catecholamines in this setting. This physiologic "flow" state is revealed in other ways. When comparing indirect calorimetry with predictive formulas for estimating energy expenditure, Sunderland and Heilbrun's regression analysis showed only heart rate, temperature, and days post-injury to be significant ($R = 0.32$, $p < 0.001$).⁵ Deutschman et al.¹ showed accelerated

physiologic variables peaking on the third post-injury day and remaining well above stressed controls at the end of their seven-day study. In 14 steroid-treated, comatose patients studied for up to 28 days, Clifton et al.⁴ found the MREE was $138\% \pm 37\%$ of normal, and mean urinary nitrogen excretion was 20.2 ± 6.4 g/day. The present report clearly shows that energy needs are increased in almost all patients for more than one month post-injury, even after awakening from coma.

Concern that the catabolic state was a result of steroid therapy itself led Young et al.²² to study metabolic rate, substrate oxidation, and serum protein levels in 16 non-steroid-treated patients. The MREE was $140\% \pm 50\%$ of the predicted level, and negative nitrogen balance persisted even when protein intake exceeded 1.5 g/kg/day. Robertson et al.²³ could find no difference in MREE between a steroid-treated and nontreated

Table 5
Nutritional support and route-related morbidity

	TPN Number (%)	ENT Number (%)
Placement		
Pneumothorax	0	1 (3.7)
Dehiscence	0	2 (7.4)
Maintenance		
Intolerance [patient days]	9 (42.9)[17]	9 (33.3)[23]
Aspiration	2 (9.5)	3 (10.7)
Hyperglycemia	16 (76.2)	12 (44.4)
Diarrhea [patient days]	13 (61.9)[68]	8 (29.6)[37]
<i>Clostridium difficile</i>	4	2
Antibiotic-related	8	5
Feeding/unknown	4	3
Tubes		
NG		
Plugged	3 (14.3)	
Displaced	51*	
Gastric		
Plugged	0	2 (7.4)
Displaced	1 (6.2)	5 (18.5)
Jejunal		
Plugged	0	4 (14.8)
Displaced	1 (8)	9 (33.3)

* In ten patients, or 5.1 ± 2 tubes each.

Table 6
Infectious morbidity

	TPN	ENT
Meningitis	0	2
Sinusitis	6	3
Bronchitis	6	6
Pneumonia	9	15
Peritonitis	1	0
Wound Infection	1	6
<i>Clostridium difficile</i>	4	2
UTI	6	6
Intravascular device	2	3
Bacteremia	4	8
Total Infections	39	51
Number per patient	1.86	1.89

group of 20 head injured patients. Urine nitrogen levels were greater in the steroid group for the first week, but the difference disappeared in the second week. These studies show that steroid therapy is not a main determinant of accelerated energy metabolism, although it may transiently increase proteolysis.

Nitrogen excretion sharply increases throughout the weeks postinjury, peaking in the second week, and remaining increased well above normal throughout hospitalization.^{4,16,22} Protein losses are rarely balanced by protein feeding, although nitrogen intake up to 2.2 g/kg/day is more effective than 1.5 g/kg/day.^{18,24} Nitrogen excretion is not diminished by energy intake even up to twice the basal energy expenditure.²⁵ However, the Baylor group did show that administration of 161% to 240% of resting metabolic energy expenditure could help achieve nitrogen balance in severely injured patients.⁴

Table 7
Nutritional support: Actual costs/charges taken directly from hospital bills, 1990-1991

	TPN (n = 9)	ENT (n = 10)
Length of Stay (days)	37.9 \pm 17.8	35.9 \pm 23
Hospital Bill (US \$)	\$112,450	\$121,941
Nutrition		
Cost, daily	\$ 57.17	\$ 40.98
Total	2,020.23	1,202.40
Charges, daily	133.82	134.95
Total	11,375.60	4,015.05

Table 8
Nutritional support costs and charges in dollars (typical severe CHI inpatient for 37 days)

	Costs	Charges
Enteral		
Endoscopic	\$2878	\$ 4815
Surgical	5523	6336
Parenteral		
TPN + NG	\$2159	\$ 9697
TPN + PEG	2635	9707
TPN + both	3116	10,654

Table 9
Chronologic progress in nutritional support after severe closed head injury

	TPN	ENT
Start support (post-injury days)	1.8 \pm 0.7	2.4 \pm 1.0
First NG* Feeding (post-injury days)	9.2 \pm 2.7	NA
TPN to NG transition (days)	3.9 \pm 3.8	NA
First PO† Meal (post-injury days)	19.8 \pm 7.2	23.8 \pm 12.5
TF‡ to PO only transition (post-injury days)	6.2 \pm 2	8 \pm 3
Number (%) on TF at discharge		
None	3 (14.3)	10 (35.7)
Partial	4 (19.0)	6 (21.4)
Full	14 (66.7)	12 (42.9)

* Nasogastric or gastrostomy.

† Per os by self or assisted.

‡ Tube feedings via gastric or jejunal tubes.

Large variations in energy and nitrogen needs occur between individuals with traumatic brain injury and over the course of recovery. In our subjects, variability ranged from 25 to 50 nonprotein calories per kilogram of body weight per day; and from 290 to 730 mg/kg/day nitrogen excretion. Precise values for individual therapy cannot be reliably computed using clinical predictive formulas and are further distorted in individual patients because of treatment with barbiturates, paralytics, sedatives, and the presence or absence of posturing, infection, or fever and the severity of injury/depth of coma. For these reasons, routine repeated monitoring of patient energy and protein needs should be done using indirect calorimetry and urinary urea or total nitrogen measurements. Repeated re-evaluations are needed for weeks.

The time from injury to initiation of oral intake was measured, as was the frequency with which patients could eat all, part, or none of their nutritional needs. Table 9 shows again that it takes almost 10 days to successfully begin intragastric feedings, when acceptable residual volumes are set at 150 mL. We believe that our low incidence of aspiration was related in part to this conservative approach. Vane et al.²⁵ have shown that lower esophageal sphincter pressures exist after head injury and may thus predispose the patient to aspiration. The first eaten meals were taken about 3 weeks after injury, but in less than half the population. At discharge, after 18 to 96 days, over half the patients remained fully dependent on tube feedings.

Several conclusions can be reached from this study. It is again shown that a hypermetabolic state is a consequence of severe brain injury and that it persists for 4 to 6 weeks, even after awakening from coma. The large variability in measured energy and nitrogen requirements shown in Tables 3 and 4 and their dissociation from one another require that nutrition support prescriptions be based upon individual, repeated measurements of MREE and nitrogen excretion (UUN). When a support program is based on such measurements, with energy target fixed at 120% of MREE and protein intake maximized at 2.5 mg/kg/day, then excellent results can be obtained. Infectious morbidity is not reduced by early enteral feeding. Benefits of the jejunal route compared with parenteral feeding included less hyperglycemia, less diarrhea, fewer interruptions in feeding because of operation or tube dislodgement, and significantly lower patient charges.

At this time, we have adopted many of the lessons learned during the project. Enteral feeding begins as early in the first 72 hours post-injury as is practicable, and uses percutaneous endoscopic gastrojejunostomies for simultaneous gastric decompression and jejunal feeding. We begin with a formula having an 80:1 ratio of nonprotein calories to grams of nitrogen, and advance to estimated target rates in 48 hours. Weekly UUN and MREE measurements are used to tailor support to individual needs. Tubes are protected by a Velcro abdominal binder (albeit not absolutely). To prevent obstruction, the jejunal tube is flushed every 3 days with three instillations of a solution of one ounce water, one tablet of Viokase (A. H. Robbins Co., Inc., Philadelphia, Penn) and one tablet of bicarbonate. Oral intake is withheld until speech pathologists demonstrate that the patient can handle secretions and food without aspirating.

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