Letters to the Editor

Asleep at the Wheel?

To the Editor:

“Few, if any, issues in anesthetic practice have inspired such divergent opinions as placement of epidural catheters, particularly thoracic catheters, in anesthetized patients” (1).

Dr. Drasner (1) suggests that, “in a situation where one must dispense with evidence-based practice (i.e., lack of solid evidence supporting a particular practice) one must revert to logic-based practice.” (1) We are asked to believe that logic suggests, in adult patients, that thoracic epidurals should be performed, with few exceptions, in conscious patients. Logic is the science of reasoning or inference that results in a conclusion following a given premise. If the premise is invalid, the conclusion will be flawed. The premise that an awake patient consistently provides information that will prevent or mitigate damage done by an improperly placed needle or catheter or that prevents our primary concern of conscious patient may allow technical skill and intervention, thereby minimizing the extent of any harm done, is unproven and simply represent “wishful thinking” (2,3). The recommendation to place thoracic epidural catheters in awake patients is, therefore, best deemed “intuition-based” practice, but nonetheless may be useful when taken in context.

Even if a patient reports procedural pain or paresthesia, it is not clear how we should proceed, as it is not an uncommon phenomenon, is rarely associated with clinical sequelae, and altering or abandoning the procedure may not affect outcome. The unstated corollary assumes that the needle itself causes minimal injury, and serious injury is caused predominantly by injection through the needle, or by insertion of and injection via a catheter (i.e., primarily mechanical disruption that may be compounded by toxicity, ischemia, and inflammation). A series of case reports on spinal cord injury in obstetrical patients seems to support an alternative point of view (3). Most of the cases described were examples of regional anesthesia techniques (spinal, epidural, or CSE) performed in conscious obstetrical patients, some of whom reported procedural paresthesia or discomfort (3). The author concluded that “needle injury alone might be sufficient to cause irreversible damage” (3). If this is true, paresthesia may simply “herald” injury; damage will occur whether the patient is awake or asleep.

There does not seem to be any disagreement among enthusiasts of awake thoracic epidural catheterization in adult patients that, in exceptional circumstances, exceptions can be made (1,4–5). The nature of these “exceptional” circumstances have yet to be fully delineated. In these situations, we are advised to ensure that informed consent is obtained (1,5). Can such enlightenment of the patient actually be accomplished? Who has the time? Can it be facilitated in light of the realities of “production pressure” (6)? Do our professional institutions have some responsibility in assisting individual practitioners to develop better methods of obtaining informed consent in the face of controversy (7)?

If a tragic complication occurs, it will be no less tragic for the patient and their family even if everyone can agree that a proper informed consent was obtained, although it may be less spiritually damaging and result in a more “favorable” medicolegal outcome for the caregivers. Consent is important but will not, in itself, prevent complications. Perhaps our primary focus should be on developing technology and techniques that allow us to provide safer care while we await more information and better and safer substitutes for the way we currently practice—our primary objective should be the safe positioning of the needle and catheter, regardless of whether the patient is awake or asleep (8).

As an interim and continuing measure, I agree that we should enhance vigilance in the “hope” that morbidity can be mitigated by early diagnosis and intervention as pointed out by Dr. Drasner (1,7). Furthermore, I suggest that system processes that facilitate vigilance be applied to all forms of regional anesthesia-anaesthesia, even those procedures felt to be devoid of substantial risk (e.g., intercostal or paravertebral nerve blocks).

It is my opinion that we should divest ourselves, as a profession, of the emotionally laden divergent opinions of advocates and proponents and seek middle ground. Rather than suggest that a recommendation to prohibit placement of thoracic epidural catheters in anesthetized patients is supported by science to the exclusion of alternate points of view, let us be honest with our patients about the facts as we know them. The recommendation really represents an attempt to be perceived as responsible physicians in the face of the unknown. As Dr. Drasner emphasizes, placement of thoracic epidural catheters in awake adult patients is not difficult to accomplish (1). If this is acknowledged, it is reasonable to recommend that, because of the potential for rare but tragic consequences and a “perceived but questionable” benefit of performing the task in awake patients, it may be preferable to perform thoracic epidural catheterization while patients are conscious, thus avoiding discussion about right and wrong while still hoping for benefit.

Finally, consent forms that outline the presence and precise nature of the controversy, provide a recommendation, as well as details of alternative approaches, should be developed.

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References

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Regional Anesthesia Under General Anesthesia and Spinal Cord Injury

To the Editor:

Dr. Drasner’s editorial entitled “Thoracic Epidural Anesthesia: Asleep at the Wheal?” was both balanced and thoughtful (1). In particular, I concur with his statement that “it is inevitable that needles (or catheters) will inadvertantly violate the cord” (especially when the needle must necessarily be near the cord and the patient is under general anesthesia). The same considerations raised by Dr. Drasner regarding thoracic epidural anesthesia under general anesthesia apply to interscalene block under general anesthesia; catastrophic cervical spinal cord outcomes have occurred in the past and will inevitably occur in the future (2).

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References

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In Response:
I appreciate the interest and comments of Drs. Lang and Benuomof. The purpose of the editorial (1) was to highlight the potential, albeit undefined, additional risk associated with thoracic epidural placement in the anesthetized patient. In the absence of exceptional circumstances (e.g., the pediatric or uncooperative patient) such risk argues that patients should be awake during catheter placement. Dr. Lang’s letter questions the logic advanced in the editorial to support this view, noting, “Logic is the science of reasoning or inference that results in a conclusion following a given premise.” and that “If the premise is invalid, the conclusion will be flawed.” Somewhat ironically, I agree with Dr Lang’s conclusions, though the premise on which he bases his arguments are not quite correct—it was not stated in the editorial, nor is it my belief, that an “awake patient consistently provides information that will prevent or mitigate damage.” Clinical experience tells us that needles (or catheters) may impinge upon the spinal cord without evoking a response from the patient. However, sometimes they will. And when they do, both logic and experience (2,3) tell us that injury is likely to occur, or to be enhanced by injection of anesthetic solution.

As Dr. Lang notes, the consent process may be more challenging when risk is ill-defined, but neither uncertainties nor the pressure of time or production, provide reasonable justification for its omission. Perhaps his suggestion to develop consent forms for such circumstances might facilitate this process. That performing epidural anesthesia in an awake patient still carries risk justifies his emphasis on developing safer techniques and technology for catheter placement.

Drs. Lang and Benuomof both raise an important point that cannot be overemphasized. The considerations discussed in the editorial regarding the benefits of performing regional anesthesia in a responsive patient are not restricted to central neuraxial blockade.

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References

Cerebrospinal Lavage Seems to Be Safe and Effective in the Reversal of Inadvertent Spinal Anesthetic Injection

To the Editor:
I read with interest Dr. Tsui’s article (1) regarding the use of cerebrospinal lavage to reverse the inadvertent spinal anesthetic injection. I had a similar case in 2001 with a 26-year-old parturient who was in active labor. A lumber epidural catheter was placed without technical difficulty, with no aspiration and test dose response. After initial loading dose of 0.25% bupivacaine 9 mL (incremental dosing of 3 mL times three), the patient did not develop a spinal block. The sensory blockade level (SBL) was T8 bilaterally, and the 0.2% Naropin infusion started at the rate of 14 mL/h. About 45 min later, the patient developed hypotension and weakness in both upper extremities. Physical examination revealed SBL at C6 bilaterally. Aspiration of the “epidural” catheter obtained free flow CSF. The “epidural” catheter is believed to be intrathecal. Patient remained conscious and spontaneously breathing. To prevent further increase of SBL and impending paralysis of the diaphragm, we decided to perform cerebrospinal lavage by aspirating CSF 20 mL slowly and replacing with normal saline (preservative free) 20 mL. The process was repeated once, and we closely monitored the SBL changes. About 30 min later, SBL was C7-T1. Another 30 min later, the patient developed late decelerations. Immediate cesarean section was performed with no additional local anesthetic given. SBL was T2 just before incision. The motor function recovered about 75 min after the 45-min cesarean section. The patient was discharged the next day, and the follow-up examination did not find any complications. Dr. Malinow of the University of Maryland mentioned a similar obstetric case and that patient also did well. Cerebrospinal lavage seems to be safe and effective if performed appropriately.

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In Response:
Thank you for your comments and for sharing your clinical experience with this technique. We agree that cerebrospinal lavage seems to be safe and effective if performed appropriately. Intuitively, it does not seem this technique has any major drawbacks in a clinically indicated emergency situation. However, a large proper randomized clinical trial (RCT) should be performed to address the effectiveness and safety of this technique. Unfortunately, given the situation in which this technique is used, a proper RCT would be very difficult to perform. Therefore, in light of the limited experiences and information on cerebrospinal lavage, we urge clinicians to carefully consider the possible risks and potential benefits on a case-by-case basis before using this technique.

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Exacerbation of Carpal Tunnel Syndrome Under Treatment with Valdecoxib

To the Editor:
Multiple studies in patients with osteoarthritis, rheumatoid arthritis, and acute pain have now confirmed that the clinical efficacy of COX-2-specific inhibitors is similar to that of conventional NSAIDs (1–3). We treated a 40-year-old patient with knee contusion with 40 mg valdecoxib once a day. Twenty-four hours after beginning therapy, the patient developed a massive exacerbation of a preexisting carpal tunnel syndrome (CTS) with the typical signs (4) previously known by the patient.

Because of suspicion of developing a valdecoxib-associated edema in the carpal arch, the therapy was replaced with ibuprofen 400 mg three times a day. No conservative management with splinting was initiated. Within another 12 hours the CTS signs and symptoms disappeared and the patient’s knee remained pain free.

This case raises the suspicion that a COX-2 inhibitor (valdecoxib) treatment- associated edema may have aggravated a preexisting condition of CTS. The withdrawal of the COX-2 inhibitor was probably relevant for the relief of the CTS.

The effect of nonsteroidal antiinflammatory medications on carpal tunnel syndrome have not been well studied (5), but a trial of these drugs is suggested.

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References
Reflex Vagal Withdrawal After Sympathetic Blockade

To the Editor:
We would like to thank Tanaka et al. for their interesting report (1). The authors referred to a previous study by our group (2) as having results that were conflicting with theirs. Instead, we believe that our work not only was consistent with that of the authors but that we also provided a likely explanation of their findings (2). The initial hypothesis of our groups, that anesthetic induced blockade of the sympathetic nervous system would result in evidence of parasympathetic nervous system dominance, was wrong. Instead, sympathetic blockade either by high spinal anesthesia (2) or cervical epidural anesthesia (1), while leaving the parasympathetic pathways intact, resulted in decreased activity from both neural systems. In our report (2), we discussed why these results actually made physiologic sense. Although both sympathetic and parasympathetic systems are generally opposed to each other, these two systems are also dependent on the continuous interactions between their two neural systems (3). Thus the parasympathetic nervous system activity seems to be inhibited centrally in the absence of an opposing sympathetic outflow. This may explain why cardiovascular collapse, after neuroaxial blockade, is so rare. We believe there is an as yet unnamed “reflex” that protects against an unopposed vagal response. As the saying goes, “it is always better to be lucky than good.”

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References

Intravascular Catheter-Associated Infection

To the Editor:
As physicians involved in the care of critically ill patients, we are always aware of the risk of nosocomial infections, particularly central venous catheter (CVC)-related sepsis. We read with great anticipation the recent paper by Zurcher et al. (1) on colonization and bloodstream infection with CVC. The authors have said the conclusions are based on limited data and suggested use of single-lumen catheters whenever feasible. However, our recent audit (Table 1) of 38 multilumen catheters in 31 critically ill patients carried out prospectively over 30 days shows that it may not be feasible to use single-lumen catheters in patients who are admitted to level 3 critical care facilities in a typical acute district general hospital in the United Kingdom.

The three most common reasons (95% of total) for insertion of CVC in our audit are listed in Table 2. In all of these situations, multilumen catheters are indicated. In 5%, CVC was primarily inserted for CVP monitoring. In 35%, CVC was inserted for CVP monitoring and IO access. In the recent paper by Zurcher et al. (1) on colonization and bloodstream infection with CVC, the authors have said the conclusions are based on limited data and suggested use of single-lumen catheters whenever feasible. However, our recent audit (Table 1) of 38 multilumen catheters in 31 critically ill patients carried out prospectively over 30 days shows that it may not be feasible to use single-lumen catheters in patients who are admitted to level 3 critical care facilities in a typical acute district general hospital in the United Kingdom.

Table 1. Central Venous Catheter-Related Sepsis Snap-Shot

<table>
<thead>
<tr>
<th>Setting</th>
<th>Mixed adult general critical care unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age</td>
<td>62 yr</td>
</tr>
<tr>
<td>Median APACHE II</td>
<td>19</td>
</tr>
<tr>
<td>Median insertion time (days)</td>
<td>9</td>
</tr>
<tr>
<td>Male (%)</td>
<td>19 (50%)</td>
</tr>
<tr>
<td>Antibiotic coated lines (%)</td>
<td>19 (50%)</td>
</tr>
<tr>
<td>Colonized (%)</td>
<td>7 (18%)</td>
</tr>
<tr>
<td>Bacteraemia (%)</td>
<td>6 (15.7%)</td>
</tr>
<tr>
<td>Catheter-related bacteraemia (%)</td>
<td>3 (7.8%)</td>
</tr>
<tr>
<td>Inadequate data capture (%)</td>
<td>3 (7.8%)</td>
</tr>
<tr>
<td>Loss to follow-up (%)</td>
<td>1 (2.6%)</td>
</tr>
</tbody>
</table>

In Table 2, we list the indications for CVC insertion (n = 38).

Table 2. Indications for CVC Insertion (n = 38)

<table>
<thead>
<tr>
<th>Indication</th>
<th>CVP + drugs infusion/TPN</th>
<th>CVP + vasoactive</th>
<th>CRRT*</th>
<th>CVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>18</td>
<td>11</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>47</td>
<td>29</td>
<td>18</td>
<td></td>
</tr>
</tbody>
</table>

* Continuous renal replacement therapy.
References


Brachyconstriction Induced by Carotid Sinus Stimulation During Radical Neck Dissection

To the Editor:

Anesthesiologists are aware that surgical manipulation affecting the carotid sinus potentially induces bradycardia and hypotension, that is, carotid sinus reflex. The specific neuronal pathway of the events involves the carotid sinus nerve afferents through the glossopharyngeal nerve and the vagal cardiac efferents (1, 2). The term “carotid sinus reflex” generally means solely baroreceptor-mediated hemodynamic suppression and little attention has been paid to the possible airway involvement in this reflex. However, we recently encountered a case of significant bronchoconstriction associated with bradycardia that seemed to be evoked by direct stimulation of the carotid sinus. These events occurred suddenly in a 25-year-old nonasthmatic woman when the surgical manipulation reached to the carotid sinus during radical neck dissection for her tongue cancer. Fortunately, the patient’s adverse symptoms were transient, and she recovered with no sequelae. The involvement of the glossopharyngeal afferents in the vagomimetic bronchoconstriction has been identified in a very limited experimental condition in guinea pigs (3), but not in humans. Clinical relevance of this phenomenon, therefore, has been quite controversial in the pathophysiology of asthma (4). However, our case may bring attention to the possibility that the airway constriction can occur in the context of the carotid baroreceptor-mediated autonomic reflex.

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An Unusual Case of Guidewire Impaction During Internal Jugular Venous Cannulation

To the Editor:

Central venous cannulation is a commonly performed procedure both in the operation theater and in the wards. Apart from catheter-related infections, technical difficulties encountered during insertion still remain a cause of concern for the clinician performing the procedure (1). A number of causes have been speculated for failure to advance the
guidewire while using the Seldinger technique (1–3). We report an unusual cause of failure to advance the guidewire.

Following antiseptic skin preparation and draping, we identified the standard landmarks for cannulating internal jugular vein (IJV). We used a 22-gauge finder needle to ascertain the exact location and the depth of IJV. This was followed by successful cannulation of the IJV with a 18-gauge thin walled introducer (Seldinger) needle with a free flow of venous blood, and then a J-tipped guidewire was advanced gently. The guidewire got stuck after passing about 5 cm or so from the distal end of the needle. It was neither advancing forward, nor could we afford to withdraw it for the fear of severing the guidewire tip, which would result in an embolization of a severed fragment. Arya et al. (1) have advocated a technique for the retrieval of a J-tip guidewire without the withdrawing introducer needle during central venous cannulation by twisting the J-tip guidewire by 90–180 degrees through the needle. This maneuver also failed to produce any results. Similarly, replacing the thin walled metal needle with a plastic cannula (without the inner needle) over the guidewire was jammed with the guidewire (Fig. 1). Thus, there was no option left for us other than simultaneous withdrawal of the former was jammed with the guidewire (Fig. 1). There was no option left for us other than simultaneous withdrawal of the needle-guidewire assembly (4). With great difficulty we disengaged the guidewire from the needle ex vivo. A piece of tissue was recovered from inside the introducer needle. Histopathology revealed that the tissue was of vascular origin.

The vascular tissue might have been punched in at the time of venipuncture and somehow been jammed between the introducer needle and the guidewire, thus preventing the advancement of guidewire through the needle. The best option for prevention of this occurrence is to use cannula with an inner needle for IJV cannulation. Any tissue that is impacted would most likely get impacted in the inner needle. This would result in the removal of any impacted tissue when the needle is removed and the J-tipped guidewire is passed through the cannula. However, if one wishes to use an introducer needle for cannulation, then we recommend the use of an introducer needle with an inner needle for aspiration. Until such introducer needle becomes commercially available, one can use the guidewire as a stylet for the introducer needle while advancing its tip to a depth already determined by the finder needle. Once the approximate depth is reached, the guidewire can be withdrawn to allow for aspiration of venous blood on puncturing the IJV. This might prevent tissues from the skin and subcutaneous and adjoining areas (except the vascular tissues) from getting trapped in the introducer needle. Following venipuncture, we suggest that one should aspirate 5 mL of blood through the introducer needle. This should increase the likelihood of any punched tissue being aspirated out of the needle and thus minimize the chances of its getting lodged between the needle and the guidewire.

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Identification of the Epidural Space

To the Editor:

We read with interest the article by Evron et al. (1). Unfortunately, there are some ambiguities in the tables that cast doubt on the main conclusions. In particular, it is not possible, in Table 2 of their article, to determine how the P values were derived. Using a two-tailed Fisher’s exact test and comparing the “air” to the “lidocaine” groups the P value for the incidence of accidental dural puncture is 0.2, vs <0.02. If the two lidocaine groups are combined, the P value becomes 0.035, favoring the combined group. This does not make clinical sense, since the needle in the “air + lidocaine” group is placed using loss of resistance to air. Also, the P value for the incidence of unblocked segments is 0.06 when the “air” group is compared to the “lidocaine” group and 0.03 when air is compared to the “air + lidocaine” group. While the latter value is statistically significant, it may be due to either the increase in volume of 2% lidocaine in the “air + lidocaine” group (3 vs 6 mL), or statistical error (multiple testing).

When reporting P values, it is important to state exactly how they were derived in order to aid in interpretation.

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In Response:

Drs. Halpern and Angle are correct that we erred in reporting the P value for the comparison of accidental dural puncture across all treatment groups. Using the Fisher’s exact test, the significance for a comparison of the incidence of accidental dural puncture across all treatment groups simultaneously is 0.046. While 0.046 does not equal our reported 0.02 (our mistake, for which we are sorry), it does not change the outcome of our findings. It appears that the P value reported by the authors of the comments were obtained by making pairwise comparisons, which is not the appropriate approach.

As to the second question, all patients in all groups received the same total volume of epidural test dose of lidocaine, i.e., 3 mL.

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Lightwand-Assisted Intubation of Patients in the Lateral Decubitus Position

To the Editor:

Cheng et al. (1) showed that lightwand-assisted intubation was equally successful in the supine and lateral positions, a finding similar to our recent study using lightwand-assisted intubation via the intubating laryngeal mask airway (ILMA) (2). However, we would like to challenge the suggestion that their technique is superior to ours.

First, they state that their technique “directly saves intubation time.” However, the saving of only 15 seconds was primarily related to different definitions for intubation time. Second, they state that our technique “presented complications to clinical personnel who needed to promptly intubate certain patients who were not lying in the supine position.” In fact, there were no such instances.

Finally, they state that “adequate ventilation via the ILMA and LMA techniques without involvement of tracheal intubation have been reported to be only 77% and 56%, respectively (3).” This figure is for inexperienced personnel and represents one of the lowest ventilatory success rates ever reported in the literature. More representative figures would be 99% for the ILMA (4) and 98% for the LMA (5).

We therefore consider these are equivalent intubation techniques; however, the ILMA may be better for airway rescue, as it allows ventilation before intubation.

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In Response:

Using lightwand-assisted intubation via the intubating laryngeal mask airway (ILMA) or lightwand-assisted intubation directly has been demonstrated to successfully establish patient airway patency under supine or lateral position (1,2).

Dimitriou et al.’s (1) description of the technique of lightwand-assisted intubation via the ILMA did incorporate two separate aspects: the initial insertion of the ILMA apparatus, followed by the subsequent lightwand-guided intubation. Here, we are trying to use lightwand-assisted intubation directly, eliminating the procedure of insertion of the ILMA apparatus, and we were successful. In addition, there is no obvious difference of intubating-related data in comparison with ours.

Lightwand-assisted intubation directly provides a rapid and safe technique to establish airway patency for patients lying in a number of different positions including the supine, left, or right lateral positions. In addition, it is not complicated for clinical personnel, whether they are residents or attending medical personnel.

The intubating time was counted from the left hand opening the mouth, insertion of the assembly into trachea, removal of the wand from the tracheal tube following correct placement of the ETT, to connecting the respirator. Both the techniques of lightwand-assisted intubation directly or using lightwand-assisted intubation via the ILMA provide fast intubation in acceptable intubation time. I cannot determine if there are any advantages of saving 15 seconds in this study. In actuality, there are many things to do for resuscitation for these 15 seconds.

There are some conflicting data on spontaneous or mechanical ventilation while patients are in supine position with LMA or ILMA (3–5). There is no adequate data to prove the benefit of ILMA or LMA while patients were ventilated under lateral position (6–8). However, it is true that I stated the results of ventilation via the ILMA and LMA from inexperienced personnel initially. Actually, I want to emphasize the possibility of air leakage. Therefore, we discussed about the novice and attending investigator in the next paragraph.

I cannot agree more with Dimitriou et al. when they stated “the ILMA may be better for airway rescue, as it allows ventilation before intubation.” However, we have to keep in mind that, while using ILMA or LMA, some patients still failed to establish patent airway in the lateral position (6–7). Under such a condition, the simple and easy method using a face mask to maintain airway patency should be used.

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References

Leukocytes with Bright Fluorescence in Rats

To the Editor:

We have a great interest in the recent article by Hayes et al. (1). Because leukocytes act as a major role for the tissue/organ damages, there has been much focus on in vivo visualization of these circulatory leukocytes. Intravital fluorescent microscopy has been established as a versatile technique for the study of cell-cell interaction and blood flow at the level of the microcirculatory unit. While Hayes et al. (1) did not mention how they labeled and detected circulating leukocytes, fluorescent markers such as acridine orange and rhodamine 6G are usually used for direct visualization of leukocytes during these processes. However, there are some pitfalls of these labeling methodologies. It has been mentioned that these fluorescent dyes often induce phototoxic effects and arteriolar vasoconstriction at high concentration levels (2). These dyes are taken up predominantly by leukocytes, but their fluorescent intensity is transient and quickly taken up by hepatocytes 10–20 minutes after IV injection (data not shown). Therefore, this labeling technique does not permit stable identification of individual cell types during observation.

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References
To address this issue, we have established a new method for in vivo visualization of leukocyte trafficking using our ubiquitously expressed GFP transgenic (Tg) rats (3). Characteristically, this Tg rat has two peaks of strong GFP intensity in the mononuclear cells and GFP positive granulocytes. Almost all of the granulocytes are detected separately from lymphocytes according to their size and fluorescent intensities (4). Thus, using fluorescent microscopy and charge-coupled-device (CCD) camera, we could visualize the trafficking of GFP-positive leukocytes in the lung and liver in vivo (Fig. 1) (see supplemental Figure 1 as a video file available at anesthesia-analgesia.org).

Considering the results of our study, we would like to ask how the authors elegantly visualized the activated leukocytes to monitor their dynamics in postcapillary venules using the epifluorescence microscope (1).

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In Response:

We thank Sato et al. for their interest in our article (1) and for inquiring into the method we used to visualize leukocytes in our study. Our experimental preparation used the mesentery of the rat. This established model has been used for years by other researchers (2,3) and is well suited for intravital microscopy because it is readily accessible, easily surgically isolated, thin (<200 μm thick), and transparent, thus allowing for direct transillumination of vessels and cellular morphotic elements.

In the present study (1), we used an upright epifluorescence microscope (Olympus BX51) with water immersion lens (magnification 20× or 40×; numerical aperture = 0.5 or 0.8, respectively) operating in bright field mode. Due to the exceptional clarity of the morphotic elements within the mesenteric microcirculation, no fluorescent dye was needed in our study to observe and quantitate leukocyte-endothelial interactions (adhesion and leukocyte rolling velocities).

Leukocytes, as mentioned in the first paragraph of our study (1), is a general term that we and others (4) use to describe polymorphonuclear leukocytes. However, the distinction between granulocytes and mononuclear cells could not readily be made during real-time flow conditions when employing intravital microscopy; hence we use the general term leukocyte. The off-line analysis system we used to analyze the number of adherent leukocytes, and the velocity of rolling leukocytes as they adhered to or traveled along the endothelium of a postcapillary venule from videotape, generally allowed us to differentiate granulocytes from the smaller lymphocytes (Fig. 1).

However, on occasions when rolling velocities of a specific cell type is required, or when tracking the movement of leukocytes in tissues or organs is not amiable to transillumination, for example, in parenchymatous or opaque organs of the body such as in the liver, brain and lung, then other techniques, such as using fluorescent markers, may be required to visualize leukocyte dynamics. As pointed out by Sato et al., some fluorescent dyes may induce phototoxic effects especially in leukocytes (7). To avoid these potential problems, many researchers, including ourselves (Fig. 2), use transgenic animal models that express green fluorescent protein (GFP) in certain cell lines, such as the murine lysozyme M GFP mouse (8).

Figure 1. Successful visualization of GFP positive leukocytes in the liver of a GFP Tg rat using fluorescent microscopy with CCD camera. Arrowhead = leukocytes with bright GFP.

Figure 2. Epifluorescence illumination of lys-M GFP mouse showing GFP labeled neutrophils in a cremasteric venule.
These mice express GFP in their mature neutrophils, while other cell lineages are fluorescent negative.

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Use of BIS Monitoring Was Not Associated with a Reduced Incidence of Awareness

To the Editor:

Sebel et al. (1) have prospectively documented the occurrence of awareness during general anesthesia in a large group of patients treated in several hospitals in the United States. They found the incidence of awareness in their study (0.13%) to be comparable with that previously reported in other countries. Roughly 40% of their patients were monitored with the BiPac Index (BIS) and, interestingly, the BIS-monitored group had a higher incidence of awareness (0.18%) than the control cohort (0.10%). The authors state that this trend was not statistically significant without quoting any statistical analysis (a χ2 test on the data in their Table 6 gives a P value of 0.17).

I believe that the authors ought to have given more weight to their finding that BIS monitoring was not associated with a reduction in the incidence of awareness. First, the abstract of the paper does not mention this result; in fact, the use of BIS monitoring is not mentioned at all in the abstract. A future literature search (for example using the terms “awareness” and “bispectral or BIS”) could fail to identify this important data.

Second, in their Discussion the authors downplay the failure of BIS monitoring to reduce the incidence of awareness, noting that the trial was not randomized. Randomized studies are not the only method of testing a hypothesis. The authors correctly describe this study as a cohort study, which is another method of attempting to identify the effect of a variable (e.g., use of BIS monitoring) upon an outcome (e.g., awareness). Cohort studies may be biased by poor matching of control and study groups, but the authors give no information to suggest any difference between the groups with respect to risk factors for awareness.

Another reason why the authors might be minimizing the importance of their result is that the use of BIS monitoring was not standardized, implying it was the way the monitor was used that led to its failure to reduce the incidence of awareness. This is a potentially very important issue, and it may explain the discrepancy between the results of Sebel et al. (1) and those of other two recent studies. A large Scandinavian study (2) found BIS monitoring to be associated with a 77% reduction in the incidence of awareness when compared to historical controls. The BIS monitor was introduced into several institutions and the anesthesiologists were instructed to use it in all cases were muscle relaxants were given and to maintain a BIS score below 60 during intubation and surgery. Around half of the patients in that study had a mean BIS score below 40 during maintenance of anesthesia. Another recent study, the B-Aware trial (3), was a randomized controlled trial confined to patients at high risk of awareness that found BIS monitoring led to an 82% reduction in the incidence of awareness.

The previous two studies suggest that standardized use of BIS monitoring, with the specific aim of reducing the risk of awareness, can indeed be effective. However, the study by Sebel et al. (1) is no exception to the knowledge, the first large-scale documentation of the incidence of awareness when BIS monitoring is used in routine clinical practice, and their data indicate no benefit of the monitor for preventing awareness. There is insufficient information in their report to glean exactly why awareness occurred in 13 patients despite BIS monitoring. It is possible that some cases of awareness occur because the BIS is used to administer a minimum dose of anesthetic agent to each patient (with the intention of minimizing drug usage, emergence times, and drug side-effects), resulting in a reduced safety margin against awareness. Perhaps it is now necessary to review the way BIS monitoring is utilized, with greater emphasis needed on maintaining a low BIS score and less emphasis on using the BIS to reduce the dose of anesthetic agents.

Finally, it would be interesting if the authors could confirm their statement that “this study was not designed to test the efficacy of BIS monitoring.” Since the study was funded by the manufacturers of the BIS monitor, it would not be surprising if the intention had been to demonstrate the effectiveness of the monitor. The authors mention that a power analysis was performed without specifying the parameters used; the chosen sample size of 20,000 patients would seem to be roughly that required to detect a significant reduction in the incidence of awareness with BIS monitoring (82% reduction from 0.15% to 0.02%). This seems to have been a study designed to test the efficacy of BIS monitoring and, regardless of any flaws in the study, the negative result will have to be taken into account when considering the role of awareness monitoring in routine clinical practice.

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In Response:

We thank Dr. McCulloch for his interest in our paper and his comments. Let us clearly state that the extent of this study was to establish the incidence of awareness in anesthetic practice in the United States. All recent data on the incidence of awareness during anesthesia have come from outside the United States. Due to variations in anesthetic techniques and patient populations, rates of awareness during general anesthesia in the U.S. patient population may be different. We can confirm our statement that “this study was not designed to test the efficacy of BIS monitoring.” Had we wanted to do this, we would have prospectively randomized patients to BIS/no BIS and standardized monitoring practice as well as BIS usage guidelines at all sites.

Dr. McCulloch correctly identifies the reason that the incidence of awareness was not reduced when BIS was used in this study compared with the studies from Myles et al. (1) and Ekman et al. (2) where the incidence of awareness was reduced. It is quite clear that applying a BIS sensor to the forehead by itself will not reduce the incidence of awareness. It is necessary to apply the monitor prior to induction to confirm good quality data from the monitor, and then the anesthetic should be guided to maintain a BIS < 60 in order to reduce the incidence of awareness. This was not done, for example, in Figure 1 in our study, where BIS was above 60 for a prolonged period of time and a case of awareness occurred. Similarly, in the Ekman et al. study (2), Figure 1 demonstrates two cases of awareness during intubation in which the protocol had not been followed and BIS was greater than 60. Had the investigators followed the
protocol, then the incidence of awareness in the Ekman et al. study would probably have been zero, compared with 0.18% in their historical controls (3). The lesson to be learned from these studies is that physician action, in accurately interpreting monitor data and then acting on it, and not a monitor per se is important in determining differences in outcome.

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Subdural Empyema Combined with Paraspinal Abscess After Epidural Catheter Insertion

To the Editor:

Epidural anesthesia and postoperative analgesia (for 3 days) was used in a 64-year-old ASA 1 patient for hip replacement surgery performed with perioperative antibiotic prophylaxis. Sixteen days later, he developed a fever, mild headache, and inconsistent back pain. Initial antibiotic treatment effectively reduced the fever, and 4 days later the patient became afebrile but uncooperative with an extensive acute organic brain disorder (inability to speak, concentration deficit). MRI studies showed a subdural empyema and paraspinal abscess formation (Fig. 1) in the absence of paresis or sensory dysfunction or pain. A light reddish spot could be seen where the epidural puncture site had been (Fig. 2). Surgical intervention at L3/4 showed pus from below the left paraspinal fasciae (Fig. 3) and a 3-mm defect of the posterolateral dura. Postoperatively, his sensory dysphasia quickly improved, and the patient left the hospital with no residual paresis or sensory deficits and was able to walk. A telephone call 5 months later indicated full recovery, apart from a subjective mild concentration deficit.

The clinically prominent symptom of the presented case was an acute sensory dysphasia (he was able to understand questions but could not answer), in the absence of known risk factors (duration of catheter use > 3 days; severe comorbidity and immunosuppression) (1). MRI diagnosis instead of CT myelography without the potential of seeding bacteria in the subarachnoid space was used appropriately. A conservative approach (2) could not be recommended because of the presence of central

Figure 1. Contrast-enhanced MRI scan of the patient’s spine. In A, a sagittal section is shown with the arrow indicating empyema membrane. In B, an axial section shows empyema (upper arrow) and paraspinal abscesses at L3/4 (lower arrow).

Figure 2. Former puncture site immediately before the surgical drainage with only minor residual redness and no pain.

Figure 3. Intraoperative situs showing pus in the left paraspinal area.
deficits. Although rare, abscess formation presenting as an acute brain disorder should always be considered as a complication of epidural anesthesia.

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