

Cognitive Impairment due to Surgery or Postoperative Complications?

To the Editor:—We read with interest the investigation by Dr. Wan *et al.*¹ of postoperative impairment of cognitive function in rats. We would like to ask whether the investigators believe there was an adequate control group with which to compare the results of their surgical intervention. In addition to the neuroleptic analgesia group alone, it may have been advantageous to include a sham surgical group that received a similar skin incision to the splenectomized group of rats with postoperative treatment of bupivacaine infiltration. This may have permitted an assessment of the contribution of a surgical incision alone with wound infiltration of 0.25% bupivacaine, because, contrary to the suggestion by the authors, the two groups of rats may not have received identical anesthetic regimens, *i.e.*, there was no assessment of the contribution of the local anesthetic infiltration. Bupivacaine has been shown on its own to suppress systemic cytokine activation when given locally or systemically.²

The investigators suggest the neuroinflammatory changes are related solely to the splenectomy surgical injury and not to other factors, such as the development of postoperative infection, which may or may not have been recognized in these rats. Splenectomized animals would more likely develop postoperative infections, and that by itself may alter neurocytokine levels.³ In addition, surgical healing and its potential impairment of full ambulation in the rats after splenectomy may have also contributed to their difficulty in completing the learning maze, which may or may not have been related to neurocognitive

impairment. A few animals with postoperative infection or impairment in their ambulation may have skewed the results on days 1 and 3 after surgery and may explain the large range of learning abilities seen in the Y-maze testing on those days. It would be interesting to note whether there were individual animal correlates of increased neuroinflammation with increased learning times in the maze.

We appreciate the work presented by Dr. Wan *et al.* because they raise important issues with regard to postoperative cognitive impairment and the role of inflammatory changes in the central nervous system.

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In Reply:—We thank the Editor for giving us the opportunity to respond to the questions about our work¹ raised by Drs. Joana and Moeen Panni. Their suggestion that we should have included an additional group receiving a surgical incision plus bupivacaine infiltration is of interest. Less extensive surgery (*i.e.*, without incising the peritoneal cavity or dissecting around the splenic pedicle) could have resulted in less neuroinflammatory response and hence a shorter (or no) period of postoperative cognitive dysfunction; this contention is supported by clinical data showing that the incidence of postoperative cognitive dysfunction is lower after minor than after major surgical procedures.²

The possibility that removal of the spleen predisposes to infection is an important consideration because this organ can modulate the organism's immune function, albeit much less in adults³; interestingly, removal of an injured spleen does not enhance infectious complications in multiorgan-injury patients.⁴ Rats, in common with other rodents, are quite resistant to infective processes even after splenectomy complicated by fecal contamination.⁵ During our study, we also did not observe clinical evidence of postoperative infection. Last, we do not believe that surgery-induced immobility could have contributed to the splenectomized rats' inability to learn because it was their choice of arm entry and not the speed or distance traveled that was assessed.

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Prevention of Vascular Air Embolism

To the Editor:—We were interested in the recent review from Minski *et al.* on diagnosis and treatment of vascular air embolism.¹ These authors should be commended for a nice review of the existing literature on this specific problem. However, we would like to suggest some minor corrections.

First, regarding the incidence of venous air embolism (VAE) during craniostomy repair reported by Faberowski *et al.*² and Tobias *et al.*³ in this journal, the two citations have been reversed. Faberowski using precordial Doppler detection found a high (82.6%) incidence of VAE, contrasting with an incidence of only 8% for Tobias *et al.* This difference has been, in part, explained by the fact that a less invasive surgical method was used in the report of Tobias *et al.*, but the sensitivity of the detection method used in the former study could also be questioned.

Second, and more concerning for us, our method for preventing VAE in sitting neurosurgical children seems to be incompletely reported in the review by Minski *et al.* In our original article published in the *British Journal of Anaesthesia* some years ago, we described the combined use of Military Anti-Shock Trousers (MAST) suit and positive end-expiratory pressure (PEEP) with a 0% incidence of VAE compared with a 30% incidence in the control group.⁴ We found that this method could be reliable and effective to prevent clinically significant VAE without deleterious side effects. Since that time, we have routinely used this method of prevention in 30–40 procedures performed in sitting children each year.

In our experience, MAST suit inflation and PEEP induce a reliable and sustained increase in right atrial pressure, sufficient to increase jugular bulb venous pressure above atmospheric level in children, and to prevent clinically significant VAE. We do agree with Minski *et al.* that PEEP alone cannot be recommended as a routine prevention method, because hemodynamic disturbances related to its use balance negatively its potentially beneficial effect on intrathoracic and right atrial pressures, especially in seated anesthetized patients. Preventive low levels of PEEP are so only used to amplify the increase in right atrial pressure, and to restore adequate ventilation in lower lung compartments that could be compressed with MAST suit inflation.

Considering the potential hazards of this method, with “venous” pressure inflation, namely 40 mmHg in the abdominal compartment and 30 mmHg in the lower limbs compartment, we never observed the described potential risks of hypoperfusion to intraabdominal organs, and compart-

ment syndromes. In our experience, urine output, which could be very sensitive to hypoperfusion of the kidneys during abdominal compression, never decrease under $1 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Moreover, we demonstrated that plasma creatine phosphate kinase level, which could reliably reflect muscular hypoperfusion and ischemia during MAST inflation, was not significantly increased in children with prolonged MAST inflation.

When comparing the incidence of VAE occurrence during procedures performed in the prone or sitting position with PEEP and MAST suit inflation in children, we did not find a significant difference, with only one episode of VAE related to a major surgical vascular effraction during dural closure occurring in a sitting patient.⁵ This could be an additional argument to maintain the use of the sitting position in selected patients, provided that detection and prevention of VAE could be as efficiently secured in both situations. We therefore recommend consideration of the use of a MAST suit and moderate PEEP levels in children when surgical conditions require positioning of the patient in the sitting position.

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Gas Embolisms Revisited

To the Editor:—We read with great interest the comprehensive work on vascular embolism by Dr. Mirski *et al.*¹ but would like to elaborate on some clinically important points. In some situations, this must include an active therapeutic role for the physician.

The ability of a patient to tolerate gas embolism is critically dependent not only on the volume and rate of accumulation, but also on the type of gas injected. Carbon dioxide, for example, is 25 times more soluble in blood than nitrogen, the primary constituent of air. Carbon dioxide can be carried in the blood not just in the dissolved form, but also takes advantage of bicarbonate buffering and combination with hemoglobin and plasma proteins. Increased solubility and rapid elimination explain why the lethal dose of carbon dioxide is approximately 5 times greater than that of air.² For these reasons, carbon dioxide is often chosen over air for laparoscopy, and because of carbon dioxide's relative safety, it is used as an intravascular contrast agent for angiog-

raphy. Radiologists commonly inject carbon dioxide intraarterially and do so safely, although inadvertent contamination of the carbon dioxide with air may lead to embolic complications.³

In addition, the clinician should be aware of the distinction between arterial and venous gas embolism. Even relatively small amounts of intraarterial air can cause bubble obstruction and resultant distal ischemia in at-risk brain or myocardial tissue, leading to stroke or myocardial infarction. Intracardiac air leading to potential arterial air embolism is a common event in open-heart procedures, prompting many surgeons to instill the more soluble carbon dioxide into the chest cavity to displace air before separation from cardiopulmonary bypass.⁴ Venous gas, as well described by Dr. Mirski, often passes into the left heart through a patent foramen ovale and then becomes arterial gas as well. In the supine patient, aortic root gas preferentially flows into the nondependent right coronary artery, eventually leading to the Bezold-

Jarisch reflex, bradyarrhythmias, hypotension, and inferior myocardial infarction. Inferior ischemia from this cause can be difficult to manage, although when caused by arterial gas embolism, precordial thumps (or vigorous coughing) have been shown to be effective. The precordial thump physically disrupts large gas bubbles and empties the left heart of these bubbles. Otherwise, the ventricle serves as a gas reservoir, prolonging right coronary artery obstruction as gas exits the left ventricle in small amounts. Precordial thumps lead to nearly complete resolution within two cardiac cycles in the case of carbon dioxide embolism in a pig model.⁵

Finally, transesophageal echocardiography (TEE) can play a vital role not only in detecting air embolism, but also in managing patients at high risk for embolism. TEE is considered minimally invasive in contrast to the pulmonary artery catheter and has a long track record of safety.⁶ It is the study of choice to determine right-to-left shunt through the atrial septum, which increases the chance of a venous embolism reaching the arterial tree. It can also be used in real time to properly position a central venous catheter. Further, evaluating and treating patients with hemodynamic instability is a class I indication for its use. We agree that TEE requires training to be used effectively; however, more and more anesthesiologists are developing this skill and are routinely using it for cardiac and other complex cases.

Gas embolism should be recognized quickly in the appropriate setting, especially if TEE is ongoing in an operative patient, and prompt therapy should be applied. If aortic root gas is probable or known

through the use of TEE or another definitive method, several prompt precordial thumps are justified if symptoms are severe.

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Externally Pressurizing Salvaged Blood Reinfusion Bags: Predictable, Preventable Cause of Fatal Air Embolism

To the Editor:—Eight years ago I wrote a letter to the editor¹ in response to a Medical Intelligence Article published in *ANESTHESIOLOGY* on air embolism (AE).² My letter said, "one totally preventable and recurring cause of potentially fatal venous air embolism that was not mentioned in the article . . . is externally pressurizing a reinfusion blood bag that has been filled with blood from a surgical field scavenging-blood processing system." I was dismayed and astounded that the recent review article published in *ANESTHESIOLOGY* on AE³ also did not mention the predictable, preventable, often fatal AE that occurs from externally pressurizing reinfusion bags filled with surgical field-scavenged/processed/salvaged blood. In the majority of multiple models made by multiple manufacturers (*e.g.*, Cobe Cardiovascular Inc. [Arvada, CO] and Hemonetics [Braintree, MA]), the processing unit (centrifuge bowl wherein the scavenged cells are washed) *must* send a 70- to 80-ml column of air into the reinfusion bag before any blood from the processing unit can enter the reinfusion bag. In addition, there are a number of processing blood circumstances that will cause the reinfusion bag to contain multiples of 70-80 ml of air. If the dead space volume of the infusion line to the patient is less than 70-80 ml, venous AE due to external pressurization of a scavenged/processed/salvaged blood reinfusion bag is a 100% physical certainty. Because the AE bolus is introduced into a sizable vein over 1-2 s, there is a significant probability that significant compromise of the circulation will ensue.

Indeed, Linden reported five cases of fatal AE due to administration of recovered blood under pressure in New York State alone from January 1990 to June 1995,⁴ and the American Society of Anesthesiologists Closed Claims database contains "several" fatalities "from air in the blood from the cell saver."⁵ In my own medical-legal experience, I have reviewed two

fatalities in the past 3 yr and six fatalities in the past 10-12 yr due to pressurizing recovered blood. All of the cases I reviewed had the same horrific story: Multiple bowls of salvaged blood were processed without purging the air from the reinfusion bag, the reinfusion bag was externally pressurized, there was a sudden cardiac arrest within 1 min of the reinfusion bag being emptied of blood, there was a failed resuscitation (including aspiration of air from central veins), and then the autopsy showed a heart filled with air. The obvious, but lifesaving take-home message of these considerations is that reinfusion blood bags that have been filled with blood that has been scavenged and processed by an autotransfusion system should never be externally pressurized.

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Hair Splitting, Air Embolism, and Transesophageal Echocardiography

To the Editor:—The continuing medical education–accredited article “Diagnosis and Treatment of Vascular Air Embolism” by Dr. Mirski *et al.*¹ in the January 2007 issue of this journal merits some comments. The term *vascular air embolism* was new to me, and the PubMed search with the search term *vascular air embolism* yielded 7 results. The search term *venous air embolism*, however, with which I am more familiar, yielded 432 hits. In Dr. Mirski’s article, there are 150 references, but in only one of the cited articles, which is a radiologic article, is the term *vascular air embolism* used.² The Merriam-Webster Online Dictionary defines embolism as “sudden obstruction of a blood vessel.”³ Therefore, by definition, there is no embolism other than vascular. The abbreviation VAE that Dr. Mirski uses for *vascular air embolism* in the literature is generally attributed to *venous air embolism*.

This is no semantic hair splitting. It has rather a fundamental clinical impact as a consequence of various pathophysiologic mechanisms and distinct clinical sequelae. The term *venous air embolism* (VAE) describes the entrainment of air into the venous blood system leading to right ventricular constraint, elevation of pulmonary pressure and an increase in pulmonary vascular resistance, and it eventually ends in right heart failure and death. The sudden increase of right ventricular pressure might cause an reopening of the foramen ovale with consecutive transition of air bubbles from the right to left ventricle, leading to an obstruction of cerebral vessels, coronary arteries, the ophthalmic artery, or other branches of the arterial system, resulting in cerebral infarction, myocardial ischemia, blindness, or other symptoms of hypoperfusion or nonperfusion. In contrast to VAE, the entrainment of air into the arterial system, either directly or secondary through a persistent or a reopened foramen ovale, is termed *arterial* or *paradoxical air embolism* (PAE).

These considerations and the fact that VAE occurs in up to 100% all of operations in the sitting position^{3,4} lead to question which preoperative tests are necessary to identify patients with an increased risk to experience VAE and PAE intraoperatively. The persistent permanent foramen ovale, which is found in an unselected population with a prevalence of approximately 25%,⁵ is as such a major risk factor for PAE. Transesophageal echocardiography (TEE) and transcranial Doppler ultrasound are equally effective in the detection of a permanent foramen ovale before surgery in the sitting position.⁶ There is broad consensus that patients with a permanent foramen ovale should be excluded from surgery in the sitting position; at least the advantages of the sitting position should be carefully weighed against the risk of the potentially hazardous consequences of massive VAE and PAE in the sitting position.

With respect to intraoperative monitoring, TEE is considered to be the accepted standard in detecting VAE, with an indisputable high sensitivity and specificity. Moreover, it is the only monitor to intraoperatively detect PAE, persistent foramen ovale, and pulmonary passage of air bubbles during massive VAE.⁷ There is no intraoperative monitoring device other than TEE to reliably and quickly clarify the cause of sudden hypotension

and acute hemodynamic instability, which can be due to VAE, hypovolemia, and left or right ventricular failure of any other cause.

Transesophageal echocardiography requires some expertise and, for various reasons, it is not readily available everywhere. Nobody, however, would seriously have doubted the usefulness of intraoperative pulse oximetry, even in the early years after its introduction in clinical practice when it was not on hand in every operating room on the planet. Of course, anesthesiologists strongly advocate the use of pulse oximetry because it is a highly useful and an even life-saving monitoring device even if the incidence of intraoperative hypoxia is definitely not as high as VAE during operations in the sitting position. At least for procedures where one has to face potential life-threatening complications such as VAE and PAE with an incidence of up to 100%, the use of a monitor, such as TEE, with a nearly 100% specificity, sensitivity, and accuracy, has to be strongly recommended.

Recently, a task force of expert neuroanesthesiologists has been entrusted by the Scientific Neuroanesthesia Subcommittee of the German Society of Anesthesiology and Intensive Care Medicine to update the recommendations regarding neurosurgical operations in the sitting and semisitting positions. Preoperative assessment and intraoperative monitoring in patients scheduled to undergo operations in the sitting or semisitting position is of paramount importance. For the task force, the usefulness of TEE in this setting is beyond any doubt, even if there are no prospective, controlled studies to answer the questions whether and how far the use of TEE has a positive impact on clinical outcome parameters such as reduction in complications and mortality.

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* Available at: www.m-w.com/dictionary/embolism. Accessed January 25, 2007.

Vascular Air Embolism: Lung Injury and Its Pathophysiology Also Need to Be Considered

To the Editor:—In their review of vascular air embolism, Mirski *et al.*¹ define the condition as the entrainment of gas into the venous or arterial vasculature, but virtually the entire review is about venous air embolism (VAE), and arterial air embolism is described solely as secondary to VAE. Although blast injury and thoracentesis are included in a comprehensive list consisting mainly of VAE causes, no explanation of etiology is given for these two conditions, and readers may be led to believe that their pathophysiology is the same as that of VAE. Two case reports that actually describe arterial air embolism are also cited among the many VAE causes, and the explanation is simply excessive ventilatory pressure.

Arterial air embolism is a far more dangerous condition, requiring little air to inflict serious damage, even fatality, and deserves a better explanation. One of the most important causes of arterial air embolism is lung trauma (occurring in 4% of major thoracic trauma²), as the following case illustrates: A 20-yr-old jockey fell off a horse in the middle of a race. The jockey was trampled by several horses and sustained severe injuries, including those involving the chest. By the time the patient arrived at the hospital, there were few signs of life. The trachea had been intubated, and assisted ventilation had already begun. A radial artery line was started during cardiopulmonary resuscitation. Copious amount of gas bubbles were aspirated from the arterial line. The jockey died from the injuries.

If the pulmonary parenchyma has been damaged, direct communication between the pulmonary vasculature and bronchial tree becomes possible. Whereas this injury may manifest in a spontaneously breathing patient as hemoptysis (pulmonary vascular pressures > airway pressure), arterial air embolism may occur when positive-pressure ventilation reverses this pressure gradient and facilitates air entry into the pulmonary veins, from whence air bubbles travel in particular to the brain and the coronary arteries, with devastating results.³ Through this mechanism, arterial air embolism has been reported following external chest compression,⁴ lung biopsy,⁵ rapid decompression or rapid ascent from deep sea diving with a closed glottis,⁶ and rupture of an intrapulmonary bronchogenic cyst.⁷ Single contralateral lung ventilation and immediate thoracotomy for hilar clamping (if the injury is unilateral), avoidance of high airway pressure, and maintenance of adequate pulmonary venous pressure, where appropriate, are remedies that have been suggested.^{5,8,9} Without understanding the underlying pathophysiology, however, one might wrongly assume that venous air has traveled to the arterial side *via* a cardiac defect or an overwhelmed lung vasculature,¹ and the above measures would make no sense (and hence would not be considered).

Some important causes of VAE are also missing from the review. In coronary artery bypass grafting, the saphenous vein grafts are sometimes harvested endoscopically using carbon dioxide insufflation. The purported advantages include reduced hematoma, pain, wound complications, hospital stay, and vein trauma.¹⁰ Using transesophageal echocardiography, carbon dioxide VAE may be detected in more than 17% of patients, some of them severe and necessitating emergency cardiopulmonary bypass.¹⁰ Cardiovascular collapse has also been described.¹¹ Decreasing the carbon

dioxide pressure reduces the problem, and continuous transesophageal echocardiography monitoring of the inferior vena cava has been recommended.¹²

Venous air embolism has also been reported during hepatic resection using the Cavitron Ultrasonic Surgical Aspirator[®].^{13,14} Minimization of the duration of using the Cavitron Ultrasonic Surgical Aspirator[®] device (Valleylab Inc., Boulder, CO) has been suggested.¹⁴

Even in a comprehensive review, lists often cannot be totally exhaustive. Nevertheless, we thought the above causes have sufficient relevance that they should have been included.

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In Reply:—We very much appreciate the comments from our esteemed anesthesia colleagues. We must immediately apologize to Drs.

David C. Warltier, M.D., Ph.D., served as Handling Editor for this exchange.

Faberowski and Tobias in our error in referencing their published data in table 1 of our review.¹ Indeed, as Drs. Meyer *et al.* point out, the percent of vascular air embolism (VAE) detected in their studies was reversed; an 82.6% incidence of VAE was recorded in the study by Faberowski *et al.*,² whereas an incidence of 8% (4 of 50 patients) was

noted by Tobias *et al.*³ As Dr. Tobias suggests, the method of craniostylosis repair likely accounts for much of the reduced incidence of VAE. With respect to the use of the Military Anti-Shock Trousers (MAST) suit with or without positive end-expiratory pressure, we acknowledge the limited discussion that was presented in the review. It is reassuring to review the data from Drs. Meyer *et al.* regarding their experience and lack of any significant untoward effects from MAST suit use in sitting pediatric neurosurgery cases. Undoubtedly, the action of the suit aids in maintaining thoracic venous pressure and thus should reduce the incidence of VAE as their studies have shown.⁴ On review of the many studies on VAE (> 1,200 upon our last appraisal of the literature), few clinical centers have reported routine use of a MAST suit for VAE prevention in pediatric neurosurgery. Reviewing some of the largest series to date, such as that of Harrison *et al.*⁵ involving 407 pediatric sitting craniotomies or that of Leslie *et al.*⁶ involving 100 patients, MAST suits were not used, and the authors of both studies thought that less provocative maneuvers were adequate in the surveillance and prevention of VAE. Both reported approximately a 9% detection rate of VAE, with no untoward clinical circumstances. Unfortunately, no study to date has been published that supports MAST suit use over other technologies with regard to patient outcome benefit. Therefore, the conclusion should be that each center should use such methods in preventing clinically significant VAE as they are comfortable with them and can routinely train and monitor their cases for both benefits and risk.

We agree with Drs. Culp that carbon dioxide would be the preferred gas over nitrogen or other inert gas. Although there is no direct literature that we could find regarding the specific evaluation of nitrogen, there are several investigations comparing carbon dioxide *versus* helium demonstrating more serious sequelae from helium-derived VAE.^{7,8} It is probably safe to presume that nitrogen would exert similar effects, and several authors of review articles on insufflation gases have made this assumption. The comments of Drs. Culp regarding the risk of morbidity stemming from arterial air embolism and the clinical utility of transesophageal echocardiography are certainly seconded by us, and we appreciate the additional voices of support for vigilant monitoring to prevent VAE-associated patient injury.

The authors certainly agree with Dr. Benumof regarding the risk of autotransfusion and VAE. We did find the report by Linden *et al.*⁹ in 1997 chronicling the incidence of fatal gas embolism after transfusion of salvaged blood, but it was after final submission of our manuscript. They indeed found from a database of 127,000 autotransfusion cases a 1:30,000 risk of mortality from insufficiently purged blood bags.⁹ They also reviewed routine banked blood transfusion and recorded no cases of fatal VAE from among almost 3,000,000 transfusions. We certainly recommend attentive removal of all air from the autotransfusion bag and lines before administering the blood to the patient.

We also appreciate the thoughtful comments by Dr. Fritz. It is indeed accurate to state that the majority of instances of perioperative and line-associated air emboli are venous in origin. While we were organizing the contents for the review article, however, it became apparent that with the arrival of laparoscopic procedures, interventional radiologic interventions, and so forth, new avenues for entraining air into the vascular system were becoming commonplace. *Paradoxical air embolus* typically refers to entrainment of venous air that

subsequently passes to the arterial vascular network rather than sequestering in the right ventricle or pulmonary tree. Therefore, Dr. Fritz is correct in stating that the combination of both venous and arterial air embolus embodies the umbrella term *vascular air embolus* that was used in the review. We also concur that transesophageal echocardiography is the most sensitive tool for the diagnosis of VAE and in documenting the exact passage through the cardiac chambers. Its widespread use is precluded by virtue of the expense and availability of trained personnel, but we again agree that in preparation for procedures at high risk for VAE, transesophageal echocardiography warrants serious consideration.

Dr. Ho *et al.* remind us that chest trauma is often complicated by systemic air embolism. Dr. Ho's important review article published in 1999 on the occurrence of systemic air embolism after lung trauma remains quite relevant today.¹⁰ Certainly the physical disruption of either the pulmonary venous or arterial vasculature, coupled with increases in thoracic pressure, creates an excellent scenario for arterial embolism to occur. We also concur with Dr. Ho *et al.* that there are indeed many possible clinical scenarios inviting risk for VAE, and we thank them for including additional mention of pulmonary procedures, endoscopic saphenous vein harvesting, and Cavitron ultrasound aspiration. It should be clear to the readers of ANESTHESIOLOGY that any circumstance that affords a pressure gradient promoting air into the vasculature may result in clinically significant air embolism.

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Sevoflurane and Epileptiform Extrapolation?

To the Editor:—In a recently published article, Julliac *et al.*¹ describe risk factors for the occurrence of electroencephalographic abnormalities with sevoflurane anesthesia. Although it is appropriate to state that “induction with high sevoflurane concentrations may trigger epileptiform electroencephalographic activity” and “only electroencephalographic monitoring allowed the diagnosis,” the final sentence of the

article seems to extrapolate electroencephalographic findings to clinical safety. Did the patients with epileptiform activity demonstrate a postictal state? Was recovery prolonged? The decision to perform an inhalation induction with sevoflurane, as with all clinical decisions, should indeed undergo “careful consideration,” but the risk-benefit analysis should be based on evidence-based trials of clinical outcomes.

No studies to date have demonstrated that intraoperative epileptiform activity during induction of anesthesia translates into adverse clinical outcomes, postoperative seizure activity, or other perioperative morbidity, and findings of this well-done study should not be extrapolated to inappropriate clinical conclusions.

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In Reply:—We thank Dr. Soto for raising this important point and appreciate the opportunity to reply.

Sevoflurane can be proconvulsive at high alveolar concentrations.^{1,2} Our study demonstrated that rapid inhalation induction may result in the occurrence of epileptiform discharge. The important question is whether these epileptiform discharges result in deleterious brain effects.

The postoperative clinical outcome of the patients included in our study was outside the scope of our article. However, we did not observe any especially prolonged recovery or postoperative clinical seizure, although we did not do any systematic postoperative assessment. The question of the deleterious clinical effects of nonconvulsive seizure remains a matter of debate.³ For this reason, although we cannot demonstrate that nonconvulsive epileptiform discharges are damaging for the brain, we cannot demonstrate the opposite, either.

We agree that it would be interesting to study perioperative morbidity associated with sevoflurane-related epileptiform action. However, for evident ethical reasons, we cannot schedule a new study where we purposely use epileptogenic sevoflurane concentrations to answer these questions.

However, sevoflurane remains a safe anesthetic agent because of its

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Nasotracheal Intubation in Children

To the Editor:—We were interested in the recent study by Watt *et al.*¹ to reduce epistaxis during nasotracheal intubation in children by telescoping the tip of the endotracheal tube into the funnel end of the red rubber urethral catheter. However, we have a few points to make.

The results of using a prewarmed tube for nasotracheal intubation are variable.¹⁻³ Although studies in adults suggest reduced bleeding, its efficacy in pediatric patients seems to be poor.¹⁻⁴ In the control group in the study by Watt *et al.*,¹ where tracheal intubation was achieved by using a tube at room temperature, the incidence of bleeding was 56%, significantly higher than in the control group of Elwood *et al.*,⁴ wherein a thermosoftened tube was used and the incidence of bleeding was only 29%. Further, although Watt *et al.*¹ report that a 39% incidence of epistaxis in patients in whom the nasotracheal tube was carried with a thermosoftened uncuffed tube is consistent with that reported by Elwood *et al.*⁴ in their thermosoftening group (29%), it is still higher in the study of Watt *et al.* Considering these facts, in the study by Watt *et al.*, the higher incidence of bleeding in patients in whom a prewarmed tube was used can be attributed to the use of a larger tube (selected by Cole's formula, *i.e.*, ID (mm) = (age/4) + 4) rather than lack of efficacy of thermosoftening and topical vasoconstriction, especially when no direct comparison of epistaxis, with and without a nasal topical vasoconstrictor, was made by the authors. For nasotracheal intubation, it is strongly recommended to use an endotracheal tube with an ID 0.5-1.0 mm less than that used for an oral tube, to allow for smooth and atraumatic passage of the nasal tube.⁵ This is evident in various adult and pediatric studies of nasotracheal

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pharmacologic and clinical properties. Our purpose is not to contraindicate inhalation induction with sevoflurane, especially when the risk-benefit ratio is in favor of this technique. To decrease the risk of the occurrence of epileptiform discharges, incremental induction might be used.⁴

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intubation. Elwood *et al.* selected the uncuffed tube for nasotracheal intubation by the formula of Motoyama⁶ (*i.e.*, ID (mm) = (age/4) + 3.5) and, as aforementioned, had better results in the thermosoftening group than achieved by Watt *et al.*, who used endotracheal tubes at room temperature and after thermosoftening.^{4,7,8} Although we wholeheartedly agree with Watt *et al.*'s report of better results than Elwood *et al.* in regard to clinically relevant bleeding (5% *vs.* 9.4%) in patients in whom a red rubber catheter was used, we believe that selection of the tube by the formula of Motoyama or Khine (*i.e.*, ID (mm) = (age/4) + 3.0) by Watt *et al.* could have further reduced the incidence of clinically significant nasal bleeding in all three groups.^{5,6}

Regarding the intubation attempts, Watt *et al.* did not mention the number of times each naris was entered or the navigability (smooth or impinged) of the endotracheal tube. No data were provided regarding postoperative nasal complications such as nasal pain, persistent discharge or bleeding, difficult breathing, or crusting, which are important secondary outcomes in patients undergoing nasotracheal intubation and are likely to be significantly affected by the size of tube used, thermosoftening, and whether topical nasal vasoconstrictor drops were used.^{5,7,8} Including these sequelae in their trial could have better delineated the role of the vasoconstrictor in delayed outcomes of pediatric nasotracheal intubation.

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More about Telescoping for Nasotracheal Intubation in Children

To the Editor:—I read with interest the study by Watt *et al.*¹ of telescoping tracheal tubes into catheters to minimize epistaxis during nasotracheal intubation in children.

The authors selected uncuffed tracheal tubes (nasal RAE; Mallinckrodt, St. Louis, MO) for their 2- to 10-yr-old study patients using the formula (age of the patient in years divided by 4) + 4. Khine *et al.*² demonstrated that 23% of their patients, full term to 8 yr old, needed reintubation to obtain an appropriate fit using the same modified Cole formula for uncuffed Mallinckrodt tubes. I have had air leaks often with the uncuffed Mallinckrodt tracheal tubes selected by the same formula; sometimes the proper size tube was two sizes larger. The authors chose not to investigate this relevant sequela. As a result, readers are left pondering how the authors managed the rest of the anesthetics. In a previous study about telescoping by Elwood *et al.*,³ the nasal RAE uncuffed tubes, selected using the formula (age/4) + 3.5, were even smaller. In 1 of 103 study patients, the leak around the tube was large, necessitating a change of tube. Could there be a regional difference of larynx size in the United States?

The OD of the funnel end of a 10- or a 12-French Davol® urethral catheter (Davol Inc., Cranston, RI) is approximately 9–10 mm. The end is made to accept a connector from a urine-collecting bag. When an ID 4.0 endotracheal tube is telescoped into the funnel end, the combination is bulky. It is difficult to visualize how this combination, without any modification, can pass the naris or choana easily.

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In Reply:—We thank the authors of both letters for their thought-provoking comments. In the first letter, Dr. Mahajan *et al.* refer to the incidence of nasopharyngeal bleeding after native tubes in our study¹ (56%) and the incidence after warmed tubes and a vasoconstrictor in the study by Elwood *et al.*² (29%). Although these were both “control” groups, the two treatments have no common basis for comparison. Considering the incidence of bleeding associated with warmed tubes in the two studies,^{1,2} Dr. Mahajan *et al.* posit that the 0.5-mm-larger tube diameter in our study contributed to the greater incidence of bleeding. This is a possibility that we did not test. Whether the larger tube diameters in our study contributed to the incidence of bleeding with native and warm tubes is a moot point because the incidence of bleeding with a larger diameter tube telescoped into a soft rubber catheter seems to be trivial (5%).¹ Further direct comparisons between the results of the two studies should be limited because we did not test the effect of oxymetazoline in our study. Although the larger-diameter uncuffed tubes may have contributed to the incidence of bleeding in our study, this was

Telescoping a cuffed pediatric endotracheal tube, instead of an uncuffed tube, may be the better approach to minimize epistaxis and avoid nasal reintubation to achieve an appropriate air leak. Although no cuffed RAE-type nasal tubes are currently available in sizes smaller than ID 5.0, cuffed pediatric oral tracheal tubes are available down to ID 3.0. The cuffed oral endotracheal tube can be cut proximally to the proper length, and a standard 90° endotracheal connector can be inserted to lower the profile.

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a compromise rooted in our other concern to minimize the magnitude of the endotracheal tube leak. The authors correctly point out that we did not report complications from nasotracheal intubation that occurred in the postanesthesia care unit and thereafter. We can state categorically, though, that whereas surrogate markers for complications may have occurred, neither ear, nose, and throat consultation nor admission to or delayed discharge from the hospital occurred as a result of nasopharyngeal bleeding.

Dr. Wu also questions the sizes of the tubes that we used and the magnitude of the endotracheal tube leak. We did not change any of the tubes because the tracheal leak was too large. This is not to suggest that such a situation cannot occur. However, during dental surgery, we minimize the clinical impact of a small endotracheal tube leak by maintaining spontaneous ventilation and by packing the throat with gauze. There is no evidence that the size of the larynx in children in the United States varies geographically. Dr. Wu describes a modification to the proximal end of a cuffed straight nasal tube to facilitate its use in dental surgery, which is analogous to using the old-fashioned metal

“nasal” connectors. However, we urge caution when considering the use of “homemade” modifications to airway devices that have not been tested under rigorous conditions to identify the risks of failure and disconnect during anesthesia.

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Electroconvulsive Therapy: Compassion in Care and Risk–Benefits of Discomfort

To the Editor:—The recent case report by Litt and Li raises several unmentioned issues.¹ Anesthesia for electroconvulsive therapy (ECT) typically involves the administration of the lowest effective dose of induction agent (affording amnesia and minimizing drug-induced seizure inhibition) and liberal administration of muscle relaxant to prevent injury, especially in patients with severe osteoporosis (demographically, elderly women predominate). It is not uncommon for the relaxant to outlast the amnestic agent (in which case, liberal use of postseizure amnestic agents is recommended to prevent awake paralysis). ECT is frankly a situation inviting awareness and requiring close clinical observation and communication *via* isolated limb responses to ensure amnesia in patients able to communicate (many cannot because of psychiatric illness). Repeated ECT raises seizure thresholds, reducing duration and effectiveness, often requiring changes from methohexital to induction agents less inhibitory, including etomidate to ketamine. Meticulous vigilance to ensure effective amnesia is important, because anesthetic dosage varies widely and changes in injection technique and cardiac output can influence induction characteristics of minimally effective, empiric doses.

Awareness is to be regarded as a frequent risk of ECT, mitigated only by close, continual observation. Specifically regarding the case report, I found it unusual that these authors chose to allow the patient to remain conscious after determining awake paralysis and before ECT was delivered, because the judicious injection of additional induction agent rapidly terminates this unpleasant situation. They instead allowed conscious paralysis to persist for several minutes until neuromuscular recovery was complete, determined then that the patient “described being awake and paralyzed and not liking it,”¹ only to start again shortly thereafter. I would suggest, contrary to the title provided, that this indicates recall was present, but retrograde amnesia occurred with the successful subsequent ECT treatment, something quite unpredictable.

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In Reply:—We thank Dr. Kempen for his letter to the editor, which again draws attention to the importance of careful planning when providing anesthesia care for electroconvulsive therapy (ECT). We agree that our case report¹ raised several unmentioned issues. The first key point in Dr. Kempen’s letter is that as soon as we appreciated that the patient was awake and aware, an additional dose of methohexital could have been given to restore unconsciousness. In general, additional doses are appropriate for restoring unconsciousness and are well within standards of care. For example, a typical clinical recommendation for adult methohexital administration is 1–1.5 mg/kg intravenous for induction, and 20–40 mg intravenous every 4–7 min for maintenance.² However, in our case, the patient was completely awake, responsive to complex yes/no questions with toe response, and therefore not treatable by a small additional methohexital dose. A concern

The authors asked the important ethical question: “To what extent should a physician allow discomfort if it is known that there will be no explicit memory of it?” In regard to ECT, a frank informed consent requires discussion of awareness with consideration of the risks and benefits of the anesthetic technique as well as ECT itself. This is no different than for the multiple surgical and diagnostic procedures during minimum alveolar concentration or regional anesthesia (*i.e.*, cesarean delivery during spinal, awake fiberoptic intubations, intensive care unit sedation, surgical procedures or endoscopies during minimum alveolar concentration or no anesthesia), where discomfort is a daily and apparently accepted risk–benefit consideration. We must prevent discomfort as is reasonable and possible, but we cannot ensure complete lack of perioperative discomfort, remembered or forgotten. We would need to abandon regional and sedation techniques (with the inherent pain involved), as well as abandon the use of propofol, methohexital, and especially etomidate *via* peripheral intravenous injection, because of the commonplace extreme, remembered and clearly expressed pain on injection. This is especially true (yet completely impossible) in ECT therapy, where preemptive intravenous lidocaine’s membrane stabilization (seizure inhibition) is specifically avoided.

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there was that additional methohexital doses might lead to a reduction in seizure duration, possibly to a point where the duration was inadequate.

The relation between anesthetic agent and effect on seizure duration is an important issue. In our case, the patient, who may have had a high anesthetic threshold, would have required a second induction dose, not a small additional maintenance dose. Etomidate is a commonly used anesthetic for ECT and has been shown to provide longer seizure durations.³ The same study also found a dose-dependent reduction of seizure duration by methohexital in the dose range 0.75–1.50 mg/kg. Indeed, a 2003 randomized, double-blind, crossover study of middle-aged patients found that using remifentanyl with a reduced methohexital dose of 0.625 mg/kg markedly improved the marginally acceptable seizure duration that results from a methohexital dose of 1.25 mg/kg.⁴

Anecdotally, we have also had excellent experience with a combination of fentanyl and etomidate.

Finally, there was a concern related to Dr. Kempen's second key point: the importance of having properly conducted the informed consent process. Interestingly, the State of California mandates that the psychiatrist's informed consent for ECT include the possibility of amnesia, muscle aches, nausea, headache, and post-ECT confusion. Awareness-recall during anesthesia for the procedure is not listed. Perhaps it would be a good thing to add to the ECT consent, although it certainly is covered in the informed consent discussion with anesthesia providers. As noted in Dr. Kempen's letter as well as in the case report's first citation,⁵ one cannot depend on retrograde amnesia being provided by the electroshock and seizure.

All things considered, it was thought during the case that the preferred course of action would be to wake the patient, review the situation with him, and then, with the patient's informed consent, switch to etomidate. This was done, and the outcome was completely satisfactory, in terms of both anesthesia and ECT response. Dr. Kempen's letter highlights several

important aspects of providing ECT anesthesia care, and we are deeply grateful for his observations and comments.

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A Prospective Study of Pain at Rest: Incidence and Characteristics of an Unrecognized Symptom in Surgical and Trauma versus Medical Intensive Care Unit Patients

To the Editor:—Pain is one of the major stressors experienced by the patients hospitalized in an intensive care unit (ICU).¹ The DOLOREA study has shown that 33% of the ventilated patients experienced pain at rest and 56% experienced pain during a procedure.² Recently, we have reported that a systematic evaluation of pain and agitation at rest in ventilated and nonventilated ICU patients was associated with a better outcome.³ Although literature evaluating procedural pain is consistent,⁴ surprisingly, there are few data available regarding the occurrence of pain at rest in ICU patients.⁵ The objective of the current analysis was to compare the incidence and characteristics of pain at rest in surgical and trauma versus medical ICU patients included in the previous database.³

All consecutive patients aged 18 yr or older and staying in a 12-bed medical-surgical ICU for more than 24 h were eligible. Exclusion criteria were decision to withdraw life support within 48 h after admission, brain injuries that limited communication by the patient, and transfer to another ICU for specialized care. Pain and agitation scores were recorded twice daily by nurses or students in medicine or pharmacy at rest, 30 min after any procedure. The 0- to 10-point numerical rating scale,⁶ enlarged to be easily visible (3.9 × 11.8 inches), was used. The behavioral pain scale score^{7,8} was used for evaluation of pain in intubated or tracheotomized patients if they were not able to perform the numerical rating scale. Only moderate to severe pain events were recorded. Therefore, a pain event was defined by either a behavioral pain scale score greater than 5 according to the study of Payen *et al.*⁷ or a numerical rating scale score greater than 3 according to usual definitions.⁶ The main cause of pain was prospectively documented in communicating patients. Vigilance and agitation had been assessed with the French-translated Richmond Agitation-Sedation Scale.⁹ Data were prospectively recorded as previously described.³ Trauma and surgical patients were grouped together (group ST) and compared with the medical patients (group M). Quantitative data are shown as median [25th-75th percentiles]. Univariate analyses (chi-square, Fisher test, Mann-Whitney U test) between the two groups were used. A *P* value of 0.05 or less was considered statistically significant.

A total of 230 patients were included for analysis, 154 in group ST (12 trauma, 142 postoperative patients) and 76 in group M. Among the 142

postoperative patients, 77 were admitted to the ICU after an unplanned surgery, 47 were admitted after a planned surgery, and 18 were admitted after a postoperative complication that occurred at a median time of 3.5 [3.0-5.0] days after surgery. The abdominal site was the site of surgery for 136 of the 142 postoperative patients. Reasons for admission for medical patients were acute respiratory failure (*n* = 24), drug intoxication (*n* = 12), digestive bleeding (*n* = 9), acute pancreatitis (*n* = 8), septic shock (*n* = 8), acute renal failure (*n* = 5), and miscellaneous (*n* = 10).

The incidence of pain in the 230 evaluated patients was 51%, with no significant difference between group ST and group M (52% *vs.* 50%; *P* = 0.78). The number of pain ratings was not significantly different between the two groups (11.0 [5.3-19.0] *vs.* 9.0 [5.0-18.3]; *P* = 0.43). Group ST had a significantly higher rate of intubation (77% *vs.* 55%; *P* < 0.001), a lower Simplified Acute Physiology Score II (29 [20-39] *vs.* 36 [26-49]; *P* < 0.01), and a lower sepsis rate (36% *vs.* 49%; *P* = 0.05) at admission. The use of analgesic drugs before the diagnosis of pain was significantly greater in group ST (64% *vs.* 37%; *P* = 0.0001). Acetaminophen was the main drug used in this situation (86% in the two groups). Fourteen surgical patients had epidural analgesia. No significant difference was shown between group ST and group M for age (58 [50-70] *vs.* 58 [47-73] yr), female sex (33% *vs.* 34%), duration of mechanical ventilation (96 [24-192] *vs.* 132 [36-288] h), use of a continuous infusion of sedatives (57% *vs.* 50%), its duration (54 [24-144] *vs.* 96 [24-204] h), Richmond Agitation-Sedation Scale level of sedation (-4.1 [-2.5 to -4.8] *vs.* -4.2 [-3.6 to -4.3]), duration of stay (8.0 [4.0-13.5] *vs.* 6.0 [3.0-13.7] days), or mortality (12% *vs.* 17%) in the ICU.

Table 1 shows the characteristics of pain in all patients with pain. No significant difference was shown between the two groups except for the median intensity of the numerical rating scale score, which was significantly higher in group M than in group ST (5.6 [5.0-6.7] *vs.* 5.0 [4.3-6.0]; *P* = 0.03). Figure 1 reports the causes of pain in the communicating surgical-trauma (*n* = 71) and medical (*n* = 34) patients. The site of injury responsible for admission is the main cause of pain at rest (49%) for surgical-trauma patients, whereas the back and limbs were the main causes of pain at rest (41%) in medical patients.

The main finding of this analysis is that the incidence of pain in this population of ICU medical patients is not different than that in surgical-trauma patients. Moreover, intensity of pain in ICU medical patients

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Table 1. Characteristics of Pain in All Patients with Pain

	Surgical-trauma Group (n = 80)	Medical Group (n = 38)	P Value
Onset of pain from day of ICU admission, days	2.0 [1.0–4.5]	2.0 [0.0–4.4]	0.48
Tracheal intubation status, n (%)			
Pain exclusively during intubated period	24 (30)	6 (16)	0.23
Pain exclusively during nonintubated period	51 (64)	30 (79)	
Pain during both periods	30 (6)	2 (5)	
Sedative infusion status, n (%)			
Pain exclusively during sedated period	4 (5)	2 (5)	0.70
Pain exclusively during nonsedated period	71 (89)	35 (92)	
Pain during both periods	5 (6)	1 (3)	
Diagnosis of pain, n (%)			
Diagnosis by BPS	9 (11)	4 (11)	0.85
Diagnosis by NRS	63 (79)	31 (86)	
Diagnosis both by BPS and NRS	8 (10)	3 (3)	
Number of ratings per patient with pain, n			
BPS ratings	2.0 [1.0–3.3]	1.5 [1.0–1.8]	0.71
NRS ratings	2.0 [1.0–4.0]	2.0 [1.0–4.8]	0.76
Median intensity of ratings in patients with pain			
BPS ratings	6.8 [6.0–7.1]	7.0 [7.0–7.5]	0.18
NRS ratings	5.0 [4.3–6.0]	5.6 [5.0–6.7]	0.03

Quantitative data are expressed in median [25th–75th percentiles].

BPS = behavioral pain scale (3–12 points); ICU = intensive care unit; NRS = numerical rating scale (0–10 points).

experiencing pain is significantly higher than for surgical-trauma patients. Medical patients received preventive analgesia less frequently. The back and limbs are the main areas of pain in medical patients. This could be explained in part by the fact that medical patients had a



Fig. 1. Causes of all of the episodes of pain at rest in the surgical-trauma group versus the medical group. This figure shows all of the causes of pain for the 105 communicating patients. Causes for the 81 episodes of pain in the 71 surgical-trauma patients and the 39 episodes in the 34 medical patients were pooled together for each group, and the groups were then compared with each other (chi-square test). The site of injury responsible for admission is the main cause of pain at rest for surgical-trauma patients, whereas the back and limbs were the main cause of pain at rest in medical patients. The site of injury responsible for intensive care unit admission was identified for trauma patients, as was the surgical site for surgical patients. In medical patients, the site of injury responsible for intensive care unit admission was defined by the disease-related area (e.g., pancreatitis, esophagitis, pleuritis, myocardial infarction). Abdominal pain, not including surgical-trauma injury or pancreatitis, was defined by a pain that occurred several days after surgery or pancreatitis and differed from the initial injury of the abdominal tissues (e.g., reoccurrence of intestinal transit, intestinal spasm, ileus, peptic ulcerations of the stomach). A pain event in communicating patients was defined by a numerical rating scale score greater than 3.⁶

greater rate of sepsis upon admission than the surgical patients. Myalgia and arthralgia are common clinical features associated with fever, determined in part by inflammation and the muscle hypercatabolism induced by the thermogenesis.¹⁰ Inflammatory cytokines and sympathetic amines have been implicated in the hypernociceptive state associated with inflammation.¹¹ Back and limb pain may be also related to the obligatory immobilization of patients in the ICU bed, often requiring the use of sedatives or physical restraint.¹² Considering that turning of the patient is the most painful procedure in the ICU^{2,4} and that the pain before the procedure is associated with pain during the procedure,^{5,13} efforts to better manage pain at rest should be encouraged. Moreover, decreasing pain at rest and its stress response may be associated with a better outcome in critically ill patients.³ If so, pain at rest should be considered as a major clinical diagnostic symptom.

In conclusion, the incidence and intensity of pain in ICU medical patients are not lower than in surgical-trauma patients in this cohort of ventilated and nonventilated patients.

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A Post Hoc Analysis of Research Study Staffing: Budgetary Effects of the Health Insurance Portability and Accountability Act on Research Staff Work Hours during a Prospective, Randomized Clinical Trial

To the Editor:—This letter is in response to the “wake-up call” issued by Schwinn and Balsler¹ and the 2006 Rovenstine lecture by Reves² regarding research training in academic anesthesiology. Our goal with this letter is to report on research staff hours per month before and after the implementation of the Health Insurance Portability and Accountability Act (HIPAA), which was enacted in April 2003. Training future clinical researchers, we believe, will have significant budgetary implications in the settings of (1) HIPAA and (2) institutional review board interpretations of HIPAA and other escalating regulatory burdens in clinical research contexts.

In our 12-week prospective study³ from May 2001 to October 2004, patients were followed up daily for 4 days and then at 1, 3, 7, and 12 weeks after surgery. Our study recruitment target was 8 participants per month, to meet sample size requirements ($n = 270$) in 36 months. We queried our data to determine (1) months in which our recruiting target was met and (2) months with evidence of hard-copy communication log updates (or “work logs,” which are a conventional method to track tasks in clinical research). Both (1) and (2) represent important indicators of research team function. We then determined research staff hours (individually and in aggregate), as well as months in which staff overtime was incurred. Finally, we described each study month with the following dichotomous designations: “recruitment target met,” “work log(s) updated,” and “HIPAA implemented.” These three independent, dichotomous variables were inserted into a linear regression equation to determine the continuous dependent variable “number of hours per month of research staff time.”

Our research staff consisted of a full-time monitor-coordinator (June 2001 to November 2003), a part-time recruiter-coordinator at the surgeons’ clinic (author K.A.F., June 2001 to February 2003), and a full-time recruiter-coordinator (author M.T.B., December 2002 to October 2004). There was significant task sharing among research team members.

Nineteen of 40 months met the study recruitment target (table 1). Enrollment continued for 4 months beyond the originally planned finish date of June 2004. Four of the 6 “below-target” months after HIPAA was implemented were May through August 2003, which we attributed to HIPAA-related transitions. We statistically excluded a seasonality component (*i.e.*, “month of the year” factor; data not shown).

There were fewer hard-copy log updates after November 2003 (table 1), which corresponded with the full-time monitor-coordinator leaving the position and not being replaced due to the budgetary impact of HIPAA implementation.

Throughout the study, the research staff worked 205 h (95% confidence interval, 182-228) per month ($n = 41$ months), averaging 146 h per month per full-time equivalent staff member. Four epochs are described in table 1, in which each epoch indicated an appreciable change in the composition of the research team. Over the four epochs, staff hours per full-time equivalent-month increased. There was no relation between meeting the monthly recruiting target and either the full-time monitor-coordinator or the full-time recruiter-coordinator surpassing the “overtime threshold” of hours worked (data not shown).

Of the three independent, dichotomous variables analyzed in the multivariable linear regression equation (recruitment target met, work log(s) updated, and HIPAA implemented), only two of these factors were associated with the continuous dependent variable of monthly staffing hours. The first was evidence of updates of work logs, and second was whether HIPAA had been implemented. In the final linear regression model, the “total hours constant” for general recruitment, follow-up, and case form reporting was 106 h per month (95% confidence interval, 42-169), with work log updates associated with 75 additional hours per month (95% confidence interval, 16-134), and HIPAA implementation associated with 77 additional hours per month (95% confidence interval, 32-121).

Work log updates and HIPAA implementation were each associated with a 70% increase beyond monthly base work hours (of recruiting and follow-up). Meeting recruiting targets (as a dichotomous variable) did not seem to influence work hours per month, nor did numbers of newly recruited study participants. Junior clinical investigators in anesthesiology and their research mentors and department chairs may find these calculations useful for forecasting study budgets and hiring the correct mix of research staff to specifically address patient recruitment and follow-up, work log documentation, and HIPAA and associated regulatory compliance.

This analysis was limited in at least two respects. First, these results may not be uniformly applicable to other clinical research settings. In addition, we did not specifically investigate in detail what aspect of HIPAA actually increased staff hours, primarily because research staff members were simply asked to comply as best as possible with our institution’s specific interpretation of HIPAA and mandates generated therefrom (as opposed to identifying which elements of HIPAA may

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Table 1. Descriptive Statistics Involving Study Research Staff Work Hours, Recruitment Success, Communication Log Updates, and Overtime Occurrences

Months	FTE	Staff Hours per Month and per FTE-Month, Mean (95% Confidence Interval)	Participants Recruited per Month (Range); Months Meeting Recruiting Target (n ≥ 8 Participants/Month)	Months with Work Logs Updated	Overtime Threshold* Exceeded
0–17 (June 2001 to November 2002)	1.15	156 (137–174) per month 136 (119–152) per FTE-month	0–11 participants/month 4/18 months meeting recruiting target	17/18 (94%)	11/18 months (61%)
18–21 (December 2002 to March 2003)	2.15	310 (285–334) per month 144 (132–155) per FTE-month	5–12 participants/month 2/4 months meeting recruiting target	4/4 (100%)	2/8 person-months
HIPAA implemented mid-April 2003					
22–29 (April 2003 to November 2003)	2.0 (1.75 in 1 month)	304 (280–329) per month 154 (144–165) per FTE-month	4–11 participants/month 4/8 months meeting recruiting target	8/8 (100%)	5/16 person-months
30–40 (December 2003 to October 2004)	1.0 (1.25 in 4 months)	176 (151–201) per month 162 (144–177) per FTE-month	7–13 participants/month 9/11 months meeting recruiting target	5/11 (45%)	7/11 months (64%)

Work logs included manual of operating procedures and individual communication logs for the institutional review board, funding sources, and vendors.

* The calculated overtime threshold per month was 159 h, accounting for allowable vacation, conference, and personal time off for research team members.

FTE = full-time equivalents of personnel on the research team; HIPAA = Health Insurance Portability and Accountability Act.

have increased workload). As a retrospective review, our regression equation estimates are likely biased downward.

Whether HIPAA is a help or a hindrance⁴ to clinical research does not warrant specific discussion here, but there have been reports describing the real costs of HIPAA to clinical research enterprises, both at the level of the university⁵ (faculty and staff training requirements, paperwork and administrative burden, and so forth) and at the level of researchers choosing or not choosing to submit new or revised protocols.⁶

In our experience, we had staff budgeting challenges after HIPAA was implemented, in addition to existing complexities of clinical research in anesthesiology related to initial patient encounters for research purposes occurring on the day of surgery.^{7–10} In our study, we do not believe that one person was sufficient to accomplish preoperative recruiting tasks (on-site in several surgeons' outpatient clinics, to satisfy our institution's response to HIPAA), plus day-of-surgery study coordination, plus work log maintenance (such as the manual of operating procedures, communications with the institutional review board, funding sources, and vendors). When we were able to accomplish all of these tasks, one of our coordinators primarily managed surgical office patient recruitment and day-of-surgery study coordination proceedings; while the other coordinator managed postoperative patient follow-up and most work log updates. When we were unable to replace one of the coordinators because of the budgetary drain associated with HIPAA implementation, the work logs were no longer reliably updated. In either case, we consider ourselves fortunate to have been able to complete the described study, given that no additional resources were allocated to compensate for the anticipated workload increases associated with HIPAA implementation.

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