Anesthesiology 2003; 99:752

Safety of Low-flow Sevoflurane Anesthesia in Patients with Chronically Impaired Renal Function is not Proven

To the Editor:—The recent report by Conzen *et al.* concluding ". . . that low dose sevoflurane anesthesia is safe in patients with chronically impaired renal function"[1] raises some interesting issues both regarding its specific design and conduct (and the resultant conclusions) and the use of sevoflurane in research in human subjects that was outside the recommendations in the package insert.

First, it is not clear that the authors' data support their conclusions. On the basis of existing literature, the authors acknowledged that renal injury is most likely related to Compound A exposure. Accordingly, they took measures to "increase compound A exposure . . . to produce as high compound A concentrations as possible during routine clinical low-flow conditions." The resulting average compound A dose was 44 ± 31 ppm-h. However, previous work suggests that the threshold for injury is approximately fourfold greater, 150–200 ppm-h.[2–5] Some patients received minimal doses of compound A; one patient had a reported inspired dose of zero (0) ppm-h (see table 7 of the article). In addition, the data for compound A dose are skewed, and two thirds of the 55 patients for whom compound A data are available had values less than 44 ppm-h. Only four patients had compound A doses exceeding 100 ppm-h, and for these four the highest dose was 138 ppm-h. Although the authors saw no evidence of renal injury, the relatively low Compound A exposures were not adequate to test their thesis.

In addition, variability in the measured concentrations of the various markers of renal injury was very large. For example, the SD for glucose was four times the mean value. This, again, suggests that the results are skewed, and the variability might obscure a modest nephrotoxic effect of compound A.

Second, the study raises some questions about the use of sevoflurane in patients when there was a possibility of injury but no benefit. Specifically, the sevoflurane package insert approved by the U. S. Food and Drug Administration limits the exposure at low flows, and the authors did not adhere to this directive. We would therefore like to ask the following questions:

1. Were the patients enrolled from American institutions informed in writing of the Food and Drug Administration mandated warning in the package insert that "sevoflurane exposure should not exceed 2 MAC-hours at flow rates of 1 to less than 2 l/min. Fresh gas flow rates less than 1 l/min are not recommended"? Were the institutional review boards at those institutions similarly informed?

2. Although the results of many studies attest to the safety of low-dose sevoflurane, were the patients and the respective institutional review boards informed that results from three studies suggest that prolonged exposure to high concentrations of compound A causes changes suggestive of renal injury, albeit transiently, in humans without renal dysfunction?[2–4]

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(Accepted for publication April 28, 2003)

Dr. Saidman is a member of the Board of Directors of Gentiae Clinical Research Inc. Dr. Eger is a paid consultant to Baxter Healthcare Corp.

Anesthesiology 2003; 99:752–4

In Reply:—We appreciate the interest of Drs. Saidman and Eger in the safety of sevoflurane and the protection of human research participants. Although we disagree with their contentions, we completely share their safety concerns. Indeed, our own concern for patient safety is why we performed the investigation. We assessed the renal effects of low-flow (≤ l/min) sevoflurane in patients at greatest risk for postoperative renal dysfunction: those with preexisting renal insufficiency. Even in such susceptible patients, the renal effects of low-flow sevoflurane and isoflurane were the same.[1] Our conclusions were specific: "Low-flow sevoflurane is as safe as low-flow isoflurane and does not alter renal function in patients with preexisting renal disease." These results amplify previous studies in patients with renal insufficiency, conducted at higher flow rates, which showed no significant differences in the renal effects of sevoflurane and other volatile anesthetics.[2–6]

This investigation helps to resolve any outstanding questions about the renal effects of sevoflurane. These have concerned sevoflurane defluorination, patients with renal insufficiency, low flows and compound A formation, and low-flows in renal insufficiency patients. What has emerged from prospective studies and from postapproval pharmacovigilance is a remarkably consistent picture. Postoperative sevoflurane renal effects are not different from those of other anesthetics. After more than 120 million sevoflurane anesthetics given, there is not a single case report of sevoflurane-related renal dysfunction. Considering together all of the studies published to date in patients or volunteers, and even using proteinuria as a so-called "sensitive" (albeit unvalidated and experimental) marker of renal dysfunction, there is no difference between the renal effects of low-flow sevoflurane and other anesthetics (Fig. 1).

Drs. Saidman and Eger assert that the compound A exposure in our investigation was "too small." The patients received the compound A exposure they did because the average low-flow duration was 3.2 h, and compound A concentrations typically average 10–15 ppm. Clinical research is captive to the patient population at hand. Nevertheless, we

Dr. Kharasch previously served as a consultant to Abbott Laboratories.

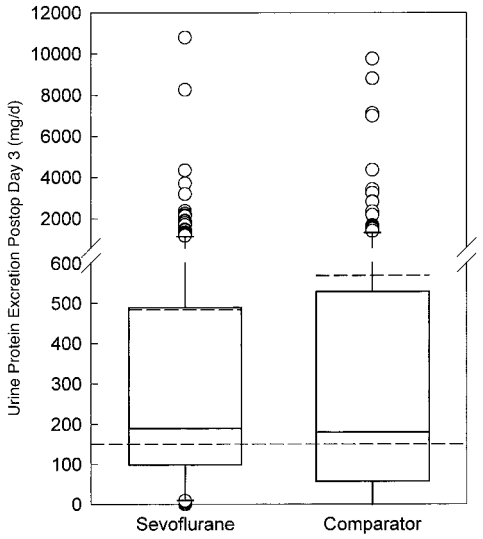

Fig. 1. Effect of anesthesia on urine protein excretion. Results are from postoperative day 3, which is typically the time of maximum proteinuria. Low-flow (< 2 l/min) sevoflurane data are from surgical patients (n = 120),[15–20] surgical patients with chronic renal insufficiency (n = 56),[1] and normal volunteers (n = 71).[7–10,21] Data from Eger and from Goldberg are redrawn from figure 3 of Goldberg, multiplying albumin excretion by 1.25 to estimate protein concentration.[10] Comparator data are from low-flow isoflurane in patients with normal renal function (n = 83),[15,17–19] patients with renal insufficiency (n = 53),[1] and volunteers (n = 4)[8,9]; high-flow sevoflurane patients (n = 40)[15,16,19]; low-flow desflurane patients (n = 18)[20]; and propofol patients (n = 10).[20] Box plots show the median, mean (*dashed lines*), 25th and 75th percentiles (*box boundaries*), 10th and 90th percentiles (*whiskers*), and outliers outside the 10th and 90th percentiles. The reference range based on data from healthy nonsurgical subjects is shown by the dotted line. There were no significant differences between the groups (*P* = 0.25, Mann–Whitney Rank Sum test).

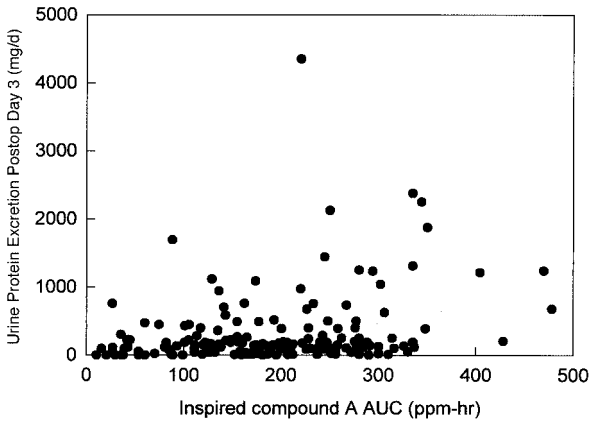

Fig. 2. Relationship between protein excretion and compound A exposure (area under the curve of inspired compound A concentration *vs.* time) during low-flow sevoflurane anesthesia. Results are from postoperative day 3, which is typically the time of maximum proteinuria. Data are from surgical patients (n = 94),[15–20] and normal volunteers (n = 68).[7–10,21] Data from Eger and from Goldberg are redrawn from figure 3 of Goldberg, multiplying albumin excretion by 1.25 to estimate protein concentration.[10]

used all available means to maximize compound A concentrations. The only way to increase compound A exposures even more would have been to prolong the anesthetic far beyond that needed for surgery, purely for research purposes. We would argue against the ethics of this approach. The study conditions reflected typical clinical care. This is a meaningful test of the hypothesis. Under relevant clinical conditions, low-flow sevoflurane and isoflurane effects were the same.

Our colleagues also assert that the compound A exposure was "too small" because it was below the "threshold for renal injury" of 150–200 ppm-hr. We believe that this premise is false. The results of Eger *et al.*[7] in volunteers, on which the purported human "threshold" is based, have never been replicated despite all best efforts.[8–10] Results in patients similarly show no threshold (published studies, and as summarized in Fig. 2).

Drs. Saidman and Eger also complain that the data were "skewed." From a statistical perspective, this is correct—the data were not normally distributed. However, the "skewness" occurred in both anesthetic groups and in this case indicates no inadequacy in study design or conduct. It simply represents a pattern of interindividual variability that is often seen in clinical studies. Nature does not require biologic variability to follow a Gaussian distribution. This variability obscured no "modest nephrotoxicity," and, most specifically, it did not obscure the result that creatinine concentrations (the definitive standard of renal function) were increased in 12% of sevoflurane patients and 14% of patients anesthetized with isoflurane (despite the absence of compound A or meaningful increases in plasma fluoride). Clearly, it is neither the choice of anesthetic nor the flow rate at which it is delivered that determines postoperative renal function.

The hypothesis that sevoflurane has adverse clinical renal effects has been tested and rejected. Nevertheless, Drs. Saidman and Eger continue to suggest that a "controversy" exists (termed a "crusade" by one editorialist[11]). It does not.

Let us provide some additional perspective: The anesthesia community knew of methoxyflurane nephrotoxicity within a year after the drug was introduced.[12] The problem of "halothane hepatitis" became abundantly clear after a few million halothane anesthetics.[13] It has now been nearly a decade and more than 120 million patients since the introduction of sevoflurane. There is still no evidence that sevoflurane causes nephrotoxicity.

We would next like to address the use of sevoflurane at low-flow durations beyond those recommended by the Food and Drug Administration, which Drs. Saidman and Eger question. The study was performed specifically in response to the Food and Drug Administration, which requested further evaluation of sevoflurane safety under low-flow conditions and in patients with renal insufficiency (beyond studies submitted for initial regulatory approval). Furthermore, our study in renal insufficiency patients was performed only after several well-controlled, randomized, monitored, multicenter studies of low-flow sevoflurane in healthy volunteers and in patients with *normal* kidney function showed no difference in renal effects compared to other volatile anesthetics. The phase IV protocol in our study, including design and safety aspects, was reviewed and specifically approved by the Food and Drug Administration. It was also independently monitored, and an interim analysis was performed to ensure patient safety.

Drs. Eger and Saidman also question the informed consent used in our study. They ask what information was provided to the U. S. Institutional Review Boards and to the patients. The applications to the respective Review Boards described the published literature on sevoflurane renal effects and contained the sevoflurane and isoflurane package inserts. Good Clinical Practice requires that the informed consent process, and the consent document that patients read and sign, plainly describe the *relevant and reasonably foreseeable* risks to subjects. The consent document should not itemize the results of individual and controversial scientific articles, debate the literature, or

replicate verbatim the package insert. In our study, the relevant and reasonably foreseeable risks were plainly described in the informed consent documents, which were signed by the research subjects. All of the multiple institutional Review Boards that approved the investigation also approved the informed consent document.

Many years ago, a concern was raised about low-flows and the degradation of another anesthetic, halothane. An author responded: "No new evidence indicates that a risk accrues to the degradation of halothane. When previous experiments have been thorough and the nature of the compound and its metabolites investigated and no toxicity found, isn't this a reasonable working definition of nontoxicity? [This is] the problem of discovering nonexistence. Obviously, when what you're searching for doesn't exist, you'll have trouble finding it even with an infinite number of experiments. Although halothane (or enflurane or diazepam or Innovar) may not be toxic, you cannot construct a study that will conclusively document nontoxicity. Long ago my father warned me that I could not disprove the existence of dragons." That eloquent defender of low-flow halothane was Dr. Eger.[14]

Now, substitute sevoflurane for halothane in the above paragraph. Previous sevoflurane experiments have been very thorough. Over 120 million patients have safely received sevoflurane at both high and low gas-flow rates. There is still no evidence of sevoflurane renal toxicity in surgical patients or in volunteers (other than that reported by Dr. Eger). The nature of sevoflurane and its metabolites and degradation products are more thoroughly understood than any other volatile anesthetic in history. Isn't this a reasonable working definition of nontoxicity? Science and medicine still cannot disprove the existence of dragons.

It is time to discard the unfounded concerns of sevoflurane nephrotoxicity.

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(Accepted for publication April 28, 2003)

Anesthesiology 2003; 99:754–5

Can We Explain the High Incidence of Cardiac Arrest during Spinal Anesthesia for Hip Surgery?

To the Editor:—Auroy *et al.* should be congratulated on their second large study of major complications of regional anesthesia.[1] Because three of the four deaths followed cardiac arrest during spinal anesthesia, it would be helpful if the authors could provide a little more detail about the patients who suffered cardiac arrest in this setting. The authors noted that all of the arrests during spinal anesthesia were preceded by bradycardia, and they mentioned that three deaths occurred over 40 min after spinal injection in elderly patients undergoing hip surgery. Biboulet *et al.* also reported cardiac arrest and death in three elderly patients during spinal anesthesia for hip arthroplasty and noted severe postinduction hypotension and relatively high block levels (T2–T4) in two of the patients who died.[2] The third patient experienced cardiac arrest 5 min after insertion of the cemented femoral component and could not be resuscitated. This may not be a rare event, because Sauer and Nolte reported nine cardiac arrests during 3,260 spinal anesthetics that were all temporally related to cementing the prosthesis.[3] The authors noted that elderly patients are particularly at risk following induction of spinal anesthesia and with application of the cement. They recommended special attention to the circulatory status of the patient and dosing strategies to limit the block

level to less than T6 to reduce the morbidity and mortality of the procedure. Because elderly patients typically have higher sensory levels for a given dose of local anesthetic, it would be helpful to know the doses of local anesthetic agents that were used and the peak block levels obtained. If known, the authors could also comment about the volume status of these patients and how many of the arrests coincided with cementing the prosthesis. Any additional information that the authors can give in response to these questions may help others avoid the same fate.

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(Accepted for publication April 28, 2003)

Anesthesiology 2003; 99:755

In Reply:—We thank Dr. Pollard for his interest in our work. Cardiac arrest was defined as requiring cardiac massage and/or epinephrine. We are happy to provide the following information, which will partly respond to his questions. Because of the uncontrolled nature of the study, it is obvious that information may have been incomplete or may not have been precisely recorded at the time the events occurred, so it might not exactly represent the patients' situation at the time of cardiac arrest. Analysis of the details contained in table 1 should thus be made with caution.

Further comments that can be added are that (1) the factors involved in cardiac arrest were several, and (2) the risk probably increases from the start of the procedure to its end as the number of factors causing hemodynamic instability superimpose on those previously present. Cardiac arrest may occur early because a large dose of local anesthetic can be aggressive enough to trigger the unwanted event in a previously hypovolemic patient (due to a combination of denutrition, preoperative fasting, and antihypertensive treatment in most cases), and several patients noted in table 1 clearly received "large" doses of local anesthetic. In other patients, cardiac arrest occurs more "lately" when the patient becomes unable to cope with the additional factor that is inflicted: hemorrhage, cementing, or position change. The patient's underlying hemodynamic reserve delays or accelerates the occurrence of the complication. As it is often clinically difficult to precisely evaluate both the degree of preoperative hypovolemia and the patient's hemodynamic reserve, it is suggested that special attention should be given to correct rapidly all factors that might lead by themselves to decompensation or which may reduce the safety margin and "make the bed" for a complication to occur at the time an additional aggression is being given. Limited or incremental dosing of the spinal anesthesia, intraoperative measurement of hemoglobin concentration, and monitoring of cardiovascular function are among the clinically available means to decrease the incidence of mortality or significant complications after spinal anesthesia.

Yves Auroy, M.D.,* Dan Benhamou, M.D., on behalf of the SOS-RA Hotline Service *Hôpital Percy, Clamart, France. yves.auroy@wanadoo.fr

(Accepted for publication April 28, 2003)

Table 1. Patients' Characteristics at the Time of Cardiac Arrest Occurring during Spinal Anesthesia

Patient	Sex (M/F)	Age (yr)	ASA, Comorbidity	Surgery	Drugs Injected Intrathecally	Fluid or Vasopressors Used from Induction to Cardiac Arrest	Upper Sensory Level to Cold or Pinprick	Onset Time of Cardiac Arrest	Outcome
1	F	85	ASA2, Arterial hypertension	Femoral neck fracture, hip prosthesis	HB bupivacaine 12.5 mg + morphine 150 μg	1,500 ml crystalloids + 30 mg ephedrine	T9	Cardiac arrest 1 min after cement application	Death
2	F	87	ASA2, Arterial hypertension, history of transient ischemic attack	Femoral neck fracture, hip prosthesis	HB bupivacaine 10 mg + clonidine 75 μg	1,000 ml crystalloids + 30 mg ephedrine	T6	Cardiac arrest during transfer from operating table to the patient's bed	Death
3	F	86	ASA3, Arterial hypertension, A-V block, ischemic heart disease	Femoral neck fracture, hip prosthesis	HB bupivacaine 17.5 mg	Crystalloids, ephedrine	T8	Cardiac arrest during position change at end of surgery	Death
4	F	93	ASA2, Arterial hypertension	Femoral neck fracture, hip prosthesis	HB bupivacaine 20 mg	1,000 ml crystalloids + 40 mg ephedrine	T4	Cardiac arrest during cement application	Alive
5	M	70	ASA2, Arterial hypertension	Knee arthroscopy	HB bupivacaine 15 mg		T12	Cardiac arrest before surgery	Alive
6	M	70	ASA2	Transuretral resection of the prostate	HB bupivacaine 15 mg	Crystalloids + 30 mg ephedrine	?	Cardiac arrest 45 min after injection of spinal anesthesia	Alive
7	M	68	ASA1	Ureteroscopy	HB lidocaine 100 mg	?	T10	Cardiac arrest 30 min after injection of spinal anesthesia	Alive
8	M	67	ASA2, laryngeal cancer and tracheostomy	Cystoscopic procedure	HB bupivacaine 12.5 mg	Crystalloids + 12 mg ephedrine	T8	Cardiac arrest 10 min after arrival in PACU	Alive
9	M	35	ASA1	Orthopedic surgery	HB bupivacaine 12 mg	?	T10	Cardiac arrest 40 min after injection of spinal anesthesia	Alive
10	F	32	ASA2, BMI 33	Cesarean delivery	HB bupivacaine 15 mg + sufentanil 10 μg	?	T7	Cardiac arrest 20 min after injection of spinal anesthesia and before surgery	Alive

ASA = American Society of Anesthesiologists; HB = hyperbaric; PACU = postanesthesia care unit.

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New Atrial Fibrillation and Elective Surgery

To the Editor:—I read with interest Dr. Amar's[1] Clinical Concepts and Commentary article on perioperative atrial tachyarrhythmias. I believe, however, that caution must be exercised when proceeding with elective surgery in a patient with newly diagnosed atrial fibrillation, a controlled ventricular response, and no evidence of structural heart disease.

Current practice is to anticoagulate such patients if atrial fibrillation persists longer than 48 h. If the surgery to be embarked on precludes such a strategy, it would be prudent to consider delaying surgery until either sinus rhythm can be restored, or it is decided that atrial fibrillation is entrenched.

Clearly, if the surgery is urgent or emergent, one must proceed recognizing the added risk.

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(Accepted for publication April 28, 2003)

Richard B. Weiskopf, M.D., was acting Editor-in-Chief for this exchange.

Anesthesiology 2003; 99:756

Disagreement with Conclusions

To the Editor:—I read with interest the review by Dr. Amar[1] on perioperative atrial tachyarrhythmias. I disagree with his conclusion that an initial "rate control strategy" in the management of postoperative atrial fibrillation is reasonable. If 50% of patients managed in this fashion will convert within 24 h, it goes without saying that 50% will not convert within this period of time. According to Amar, after this point in time, the patient runs a 1.7% risk of stroke. Further, anticoagulation will be contraindicated for a period of time in postoperative patients. Therefore, it is my practice and recommendation to try to convert all new onset postoperative atrial fibrillation as early as possible using intravenous amiodarone, or, if possible, oral propafenone or flecainide. My personal experience with amiodarone has been excellent, with a high conversion rate (usually within 6 h using a regimen of a 150-mg bolus followed by a 1-mg/min infusion for 6 h, then 0.5 mg per minute) and virtually no adverse effects.

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(Accepted for publication April 28, 2003)

Anesthesiology 2003; 99:756

Amiodarone for Conversion of Atrial Fibrillation

To the Editor:—I would like to thank Dr. Amar for his comprehensive and informative review of atrial tachyarrhythmias.[1] It was stated that amiodarone was not superior to placebo for conversion of recent onset atrial fibrillation (AF) unrelated to surgery. It is true that a few studies did not find a significant difference in conversion rates compared to placebo.[2] However, others have shown a significant increase in conversion rates with respect to placebo, and studies comparing amiodarone to Vaughn Williams class 1c drugs have shown comparable rates of conversion.[3–7] Reviews of the management of AF and of amiodarone use have concluded that it is effective for pharmacologic conversion of recent onset AF.[8,9] It has been recommended as a second-line agent after β-blockers in the conversion of adrenergically mediated AF, which may represent a substantial proportion of postoperative AF without other underlying pathology. Although it may not be a first-line agent for the conversion of AF, amiodarone is increasingly used because of its low cardiotoxicity and is used by many electrophysiologists for AF conversion.

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(Accepted for publication April 28, 2003)

Anesthesiology 2003; 99:757

In Reply:—I thank Drs. Oxorn, Liebowitz, and Botelho for their comments. Dr. Oxorn addresses the controversial issue of when to start anticoagulating a patient with newly diagnosed atrial fibrillation (AF). The statement that "current practice is to anticoagulate such patients if AF persists longer than 48 h" is not supported by the most recent practice American College of Cardiology/American Heart Association/European Society of Cardiology guidelines for the management of patients with atrial fibrillation.[1] These guidelines clearly state that for patients with newly discovered or first episode of AF: "Whether these individuals require long-term or even short-term anticoagulation is not clear, and the decision must be individualized for each patient based on the intrinsic risk for thromboembolism." In figure 1 of my review,[2] the list of published risk factors for thromboembolism related to AF is presented, and in table 14 of the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines,[1] recommendations are made regarding initiation of antithrombotic therapy and which agents to use. Therapy may range from none (age $<$ 60 yr and no heart disease) to aspirin alone (age $<$ 60 yr with heart disease but no other risk factors, or age $\geq$ 60 yr with no risk factors), anticoagulation alone (age $\geq$ 60 yr with diabetes mellitus or coronary artery disease, age $\geq$ 75 yr, heart failure, left ventricular ejection fraction $<$ 35%, thyrotoxicosis, hypertension, rheumatic heart disease with mitral stenosis, prosthetic heart valves, prior thromboembolism, and persistent atrial thrombus on transesophageal echocardiography), or their combination, depending on the patient's risk.[1] The risks of anticoagulation and/or antiarrhythmic drugs must be weighed against the 0–48% of patients with acute AF who convert to sinus rhythm spontaneously.[1–3] In patients with multiple risk factors for thromboembolism who are not candidates for, or do not wish to receive, systemic anticoagulation, the "fast-track" approach to conversion of AF using transesophageal echocardiography is an acceptable and frequently used approach in settings where such services are available.[1,2]

Dr. Liebowitz offers anecdotal experience, whereas Dr. Botelho refers to published data on the use of amiodarone for acute conversion of acute AF. In reference 9 provided by Dr. Botelho, the author accurately stresses the importance of having a placebo-controlled arm in trials examining the conversion efficacy of antiarrhythmics on acute AF, because almost 50% may convert without treatment.[4] A recent meta-analysis in nonsurgical patients showed that the efficacy of amiodarone therapy for recent-onset AF was 56% at 6–8 h and 82% at 24 h compared to 43% and 56% with placebo, respectively.[5] Efficacy studies of amiodarone *versus* placebo for the treatment (not prophylaxis) of acute postoperative AF are sparse. Furthermore, a randomized, open-label study that compared rate control *versus* rhythm control (amiodarone was one of five drugs used) strategies for the management of acute AF after cardiac surgery, showed no significant difference in time to conversion to sinus rhythm between the groups or in the proportion of patients free of AF at 48 h.[6] Although amiodarone is widely used and has a good overall safety record compared to other antiarrhythmic drugs, it is not without cardiovascular or noncardiac toxicity.[1,4] There is controversy on whether perioperative amiodarone causes severe pulmonary toxicity after cardiothoracic surgery.[7–9] Considering that intravenous amiodarone therapy for 48 h costs approximately $750 per patient[10] and the lack of well-designed efficacy trials in postoperative patients, I would agree with Dr. Botelho that amiodarone may be considered after a rate-control strategy has failed 24 h after onset of AF.[1] Until better outcome data are available on how to manage postoperative patients who develop AF with respect to antiarrhythmic or antithrombotic therapy, the algorithms presented in my review can serve as guidelines to the individualized management of complex patients while keeping one's own institutional practices in mind.[2]

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(Accepted for publication April 28, 2003)

Anesthesiology 2003; 99:757–8

Anatomic and Physiologic Discrepancies in Perioperative Hearing Impairment

To the Editor:—I want to commend the authors on writing an excellent article on a topic that has not been discussed much in anesthesia circles and meetings.[1] I did come across some deficiencies in the section labeled Brief Overview of Anatomy and Physiology. In figure 2 of the article, the structure labeled as the outer hair cell is actually the inner hair cell, and the structure labeled as the inner hair cell is not the inner hair cell. Please refer to the current Figure 1 for the correct labeling of the outer and inner hair cells.

The inner hair cells number about 3,500 in each ear and are present

David C. Warltier, M.D., Ph.D., was Acting Editor-in-Chief for this exchange.

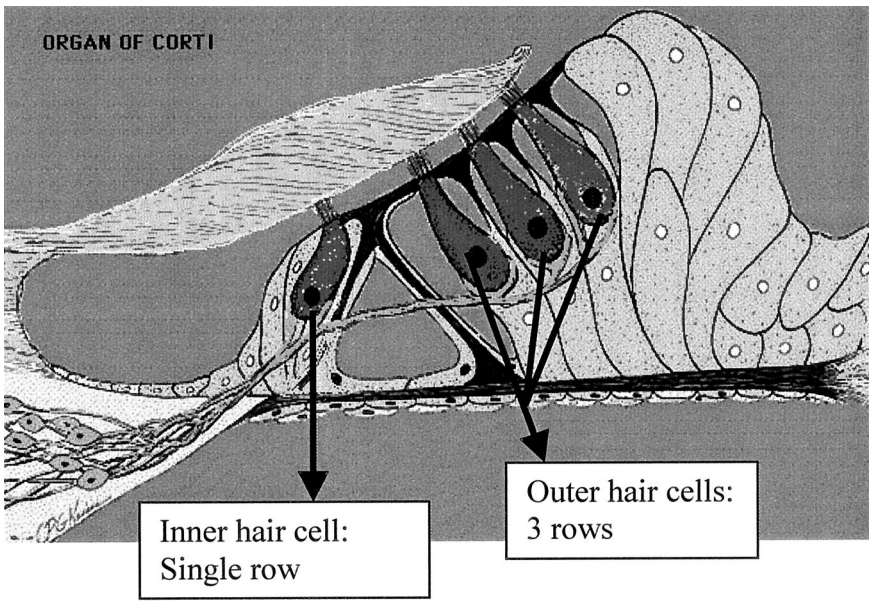

Fig. 1. Magnified cross-section of Organ of Corti. Three rows of outer and single row of inner hair cells as labeled.

in a single row. The outer hair cells number about 20,000 in each ear and are present in three rows. Ninety to 95% of afferent innervation in the cochlear nerve comes from the inner hair cells, versus 5–10% from the outer hair cells.[2] The inner hair cells are mainly responsible for transforming the acoustic signal to neural signal, whereas the role of the outer hair cells is secondary and supportive.

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Anesthesiology 2003; 99:758

In Reply:—Dr. Singh is correct. Our figure 2 was mislabeled. We thank him for his interest in the article and for correcting the error. Apparently, in the multiple revisions, the labels were moved slightly, and we failed to notice it.

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(Accepted for publication April 28, 2003)

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(Accepted for publication April 28, 2003)

Anesthesiology 2003; 99:758

Baclofen, Hemodynamic Instability and Delayed Emergence: Our Perspective

To the Editor:—We read with interest the case report of Lyew *et al.*[1] concerning hemodynamic instability and delayed emergence for general anesthesia following intrathecal baclofen overdose. We would like to call the authors' attention to the report of Anderson *et al.*[2] concerning anesthesia and intrathecal baclofen. We have also experienced three cases of hemodynamic instability in patients following the placement of pumps and intraoperative dosing with baclofen. All of our patients were awake and alert in the PACU and had received intravenous morphine for pain control. Their vitals signs were stable on discharge from the unit, but after a few hours on the ward we were called because of the patients' increased somnolence and hemodynamic instability. They were given a trial of Narcan because morphine had been used with no response, and all were given fluid boluses, atropine, and oxygen. All baclofen infusions were stopped. One patient required dopamine for a short period when he did not respond to the fluid boluses. Each of our patients made an uneventful recovery.

The reports of Lyew and Anderson are important to call our attention to the problems related to intraoperative intrathecal baclofen. Both authors give excellent reviews of the drug baclofen and the intensive postoperative monitoring these patients require.

Timothy W. Martin, M.D., F.A.A.P.P.*, James F. Mayhew, M.D., F.A.A.P. University of Arkansas for Medical Sciences, Arkansas Children's Hospital. martintimothyw@uams.edu or mayhewjamesf@uams.edu

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(Accepted for publication May 8, 2003)

Anesthesiology 2003; 99:759

In Reply:—We were aware of the article by Anderson *et al.*, which appeared in *Pediatric Anaesthesia* at the time our manuscript was accepted with revisions by the Editor of ANESTHESIOLOGY. We noted that there was considerable variation in the intervals between the start of the dead space purge of the pump and catheter and the onset of coma in their patients. Could this be related to the dermatomal level of the spinal catheter tip? This level is described in our report, whereas it is missing in their article. We received no reply to this query after we e-mailed Anderson *et al.* at their address listed for correspondence. Thus, their article was not included in our references, which were limited to those that were strictly relevant to our case description.

Michael A. Lyew, M.D.,* Christina Mondy, M.S., C.R.N.A., Susan Eagle, M.D., Sandra E. Chernich, P.A. *Children's Medical Center, Medical College of Georgia, Augusta, Georgia. mlyew@mail.mcg.edu

(Accepted for publication May 8, 2003)

Anesthesiology 2003; 99:759

Antiemetic Prophylaxis for Office-based Surgery: Methodologic Concerns

To the Editor:—We read with great interest the article by Tang *et al.*[1] regarding the efficacy of adding 5-HT_3 antagonists to a combination of droperidol and dexamethasone in the prevention of postoperative nausea and vomiting (PONV) following office-based surgery. It would seem, however, that the validity of the conclusion should be viewed with some caution because of the following methodologic concerns.

First, the occurrence of PONV after discharge was assessed by a telephone interview 24 h after patient discharge from the private office-based surgical center. This would certainly introduce the potential for *recall bias*, particularly with regard to the number of episodes of nausea at home. It is also conceivable that the observed average age of the study patients would make this type of bias more likely to occur than not. The risk of recall bias would have been avoided had patients been instructed to keep a diary of their postoperative adverse events.

Second, despite the above-mentioned limitation, the authors reported an overall incidence of PONV of 18% in the control group, 11% in the dolasetron group, and 13% in the ondansetron group (see table 3 of the article).[1] Given the number of study participants, an α of 0.05, and the observed results, the study had a power of 15%, at best, to detect differences in the incidence of PONV among the study groups. Although one could argue that the observed 39% reduction in PONV in patients who received dolasetron (compared with those who received saline) was clinically relevant, 396 patients would have had to be recruited per group to make this difference statistically significant, which is clearly neither feasible nor practical.

Finally, although we acknowledge the current contribution of Tang *et al.* to the literature on the role of prophylactic antiemetic therapy in office-based anesthesia, we believe that the posed question of whether the addition of a 5-HT_3 receptor antagonist to a droperidol-dexamethasone combination reduces the occurrence of PONV after office-based surgery remains to be answered.

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(Accepted for publication May 21, 2003)

Anesthesiology 2003; 99:759–60

In Reply:—We appreciate the interest of Alhashemi and Mujallid in our recent article examining the use of drug combinations for antiemetic prophylaxis of outpatients undergoing office-based surgery.[1] However, we think that the authors' methodologic concern is simply invalid.

First, the potential for recall bias was apparently based on an erroneous assumption that patients did not record the episodes of nausea and vomiting that occurred after discharge from the office-based surgery facility. Although the postdischarge information regarding episodes of postoperative nausea and vomiting (PONV) was obtained by a telephone interview at 24 h after discharge, the patients were instructed to record all episodes of PONV at home. It is not clear why this fairly "standard" postdischarge evaluation procedure could be a "methodologic concern." Although "recall bias" may be a valid issue for patients with cerebral impairment, we *excluded* all patients with neurologic disorders.

Second, the authors' suggestion that dolasetron produced "a 39% reduction in PONV" is very misleading. We believe it has no clinical relevance in the interpretation of these findings, because it fails to take into account that this difference was based on a very small number of patients. In our study, only one or two fewer patients in the dolasetron and ondansetron groups developed PONV before or after discharge, respectively, compared to the control group. Are Alhashemi and Mujallid suggesting that this difference could be of "clinical" significance? Inasmuch as only five patients in the control group developed PONV in the 24-h evaluation period, a difference of only one to three patients between groups would represent a 20–60% change! Although this may seem to be a large *percentage* difference, it is clinically insignificant.

As previously discussed in an editorial,[2] the use of a combination of two or more antiemetic drugs for routine antiemetic prophylaxis seems to be warranted for outpatient populations considered to be "at risk" for developing PONV. In this outpatient surgery population (involving a variety of superficial, nongynecologic, and nonotolaryngologic procedures), it would seem that the addition of the 5-HT_3 antagonist to a two-drug regimen consisting of low-dose droperidol and dexamethasone failed to produce either a clinically or statistically significant benefit before or after discharge from the office-based surgery facility. It is entirely possible that we would have obtained a *different* result if we had studied an outpatient population at *higher* risk of developing PONV (*e.g.*, those undergoing laparoscopic or otolaryngologic procedures).

Finally, we encourage Drs. Alhashemi and Mujallid to perform a randomized, double-blind, placebo-controlled study in a *similar* (or higher-risk) patient population using the same anesthetic technique. We would hope they would then be satisfied that the question we posed in our study has indeed been adequately answered!

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(Accepted for publication May 21, 2003)

Anesthesiology 2003; 99:760–1

Droperidol Editorial: Making a Mountain Out of a Mole Hill!

To the Editor:—We would like to address several points raised by Dr. Scuderi in his recent editorial entitled "Droperidol: Many questions, few answers."[1]

Dr. Scuderi rightfully points out that the recent Food and Drug Administration (FDA) "black box" warning on droperidol may "overshadow" many other important issues involving the treatment of postoperative nausea and vomiting (PONV). Indeed, as Dr. Scuderi has suggested, the power of the black box warning is so great that many clinicians are now reluctant to use droperidol because of medicolegal concerns, despite its long and successful track record. The FDA-imposed black box warning on droperidol has rendered the results of numerous, placebo-controlled, comparative clinical trials practically moot.

An important question that remains unanswered relates to how the FDA make its assessment that a black box warning—its most serious "indictment"—is merited? To date, we, as well as other experts in the field (personal written communications with Tong J. Gan, M.B, Department of Anesthesiology, Duke University, Durham, North Carolina, and Mehernoor F. Watcha, M.D., Department of Anesthesiology & Critical Care Medicine, Children's Hospital of Philadelphia, Philadephia, Pennsylvania, on May 25, 2003), remain totally unconvinced that the process is objective, adequate, or even rational. Indeed, the database summarizing the "reported" adverse events with droperidol is seriously flawed.[2] Furthermore, it is unclear whether any effort was made by the FDA to validate the "sources" of these alleged adverse events? The attention given the FDA black box warning by anesthesiologists is very surprising in light of the extensive peer-reviewed literature on the safety and efficacy of low-dose droperidol.[3]

Previous experience with other often-used "generic" anesthetic drugs (*e.g.*, succinylcholine) has demonstrated that the FDA black box process is less than perfect.[4] Interestingly, somewhere between 10 and 20% of all FDA-approved drugs eventually receive some sort of black box warning.[5] The popular sedative-anxiolytic drug midazolam (Versed®; Roche Laboratories, Nutley, New Jersey) received a black box warning regarding respiratory depression because a large number of patients died from iatrogenic "overdosing" of the drug by nonanesthesiologists (*e.g.*, gastroenterologists, pulmonary specialists). Did anesthesiologists stop administering midazolam to their patients in the wake of that black box warning? Obviously not. What would be the impact if clinicians believed that they could no longer administer otherwise useful drugs that have received black box warnings (*e.g.*, cyclosporine, atenolol, metoprolol, or ketorolac)? At both of our teaching institutions, droperidol remains approved by the hospital pharmacy and therapeutics committees for the prophylaxis and treatment of PONV. Although droperidol remains in widespread clinical use, Dr. Scuderi's recent editorial will make some anesthesia providers less comfortable about using this cost-effective antiemetic drug in the future.

Dr. Scuderi also implies that in keeping with the notion of *primum non nocere* (first, do no harm), perhaps the benefits of prophylaxis against PONV are outweighed by the risks of these therapies. He further states that we have insufficient data to address this matter and, thus, we cannot make a rational decision. We strongly disagree! First, very good data exist documenting the cost-effectiveness[6,7] and safety of droperidol,[8] as well as the patient concerns regarding PONV[9] and its impact on patient satisfaction.[10] These facts, combined with our knowledge of the mechanisms of PONV and its effective pharmacologic treatment, has led most experts to conclude that low-dose droperidol (0.625–1.25 mg IV) is the most rational choice for prophylaxis in patients at risk of developing PONV. Does Dr. Scuderi really believe that there may be less risk in allowing these patients to vomit compared to administering antiemetic prophylaxis with low-dose droperidol? When our patients express concerns regarding PONV, are we supposed to tell them, "Oh don't worry, a little throwing up won't hurt you!"

As noted by Dr. Scuderi, many different types of drugs prolong the electrocardiographic QT interval (including the popular antiemetic drugs dolasetron [Anzemet®; Abbott Laboratories, Chicago, Illinois] and ondansetron [Zofran®; Glaxo Smith Kline, Research Triangle Park, New Jersey]).There are no data demonstrating that these 5-HT_3 antagonists are any safer than droperidol with respect to adverse cardiac events. The two frequently cited studies of QT prolongation by droperidol involved large (0.1–0.25 mg/kg) doses of the drug.[11,12] The question of QT prolongation with low-dose droperidol is a red herring. As Dr. Scuderi concluded in his recent editorial, questioning the safety of droperidol is about "as productive as arguing about how many angels can dance on the head of a pin." What funding agency would be willing to pay for additional prospective studies involving a generic drug with a well-established safety and efficacy profile? The FDA has already declined! More important, what truly informed patient would consent to participate in a placebo-controlled study involving an antiemetic drug with proven efficacy in preventing this common postoperative side effect?

With patient safety at the top of everyone's list of concerns, we should be devoting our attention to addressing important healthcare issues. It is time for the FDA, along with experts in the field, to resolve that a "mountain has been made of a mole hill" in the case of droperidol's safety when administered in *appropriate* doses for antiemetic prophylaxis and treatment. We maintain that the FDA-mandated black box warning on droperidol is not only undeserved but also detrimental to the provision of cost-effective patient care. The FDA black box warning and the consequences of this dubious act may very well cause more harm than good to our patients!

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(Accepted for publication May 22, 2003)

Anesthesiology 2003; 99:761

In Reply:—The "black box" warning regarding the use of droperidol for antiemetic prophylaxis issued by Food and Drug Administration (FDA) on December 5, 2001, has created tremendous controversy within the anesthesia community. Many anesthesiologists, myself included, believe that the action taken by the FDA was inappropriate because of its basis on limited and scientifically suspect data.[1] This action was thus unwarranted and potentially detrimental to patient care. Many practitioners continue to use low-dose droperidol as a first-line agent for preventing postoperative nausea and vomiting (PONV). Others in our profession have suggested that the FDA warning regarding the use of droperidol should be taken seriously and that practitioners should reconsider the risk/benefit ratio of even low-dose droperidol for managing PONV.[2] Regardless of which position (if either) is correct, the position taken by the FDA has had an undeniable effect. As Drs. Bailey and White note, many clinicians have stopped using droperidol, even in very low doses, because of the perceived medicolegal implications of continued use. My own informal polling also indicates that droperidol has even been removed from many hospital formularies out of the same medicolegal concerns.

Unfortunately, strength of personal convictions may have little to do with scientific fact. Evidence-based medicine continues to be the goal of all thoughtful clinicians. Nevertheless, much of the practice of medicine in general, and anesthesiology in particular, must of necessity be based on experience and judgment, because conclusive scientific data may simply not exist. This does not, however, imply that we should not continually question the premises on which our clinical practice is based. Consequently, I am amazed to think that Drs. Bailey and White would believe my editorial "will make some anesthesia providers less comfortable about using this cost-effective antiemetic drug in the future." I believe it is highly unlikely that thoughtful and conscientious practitioners will be unduly swayed by a balanced presentation.

I stand by my assertion that the risk of serious adverse events (SAEs) associated with the use of low-dose droperidol remains unquantified. Just as important, the risk of SAEs associated with the use of all other antiemetics is also unknown. Similarly, the risk of SAEs from PONV has not been quantified, despite our tacit belief that certain frequently cited complications can occur. To restate this important point: neither the risk of SAEs from low-dose droperidol administration nor from PONV is known. Does this in any way imply that we should not attempt to manage PONV in a responsible fashion? Of course not! Virtually every drug and every therapeutic intervention that can be undertaken in the practice of medicine in general or the specialty of anesthesiology in particular carries some risk. Our duty is to balance the risk with the benefit. Clearly, there are rational strategies for both preventing and treating PONV. Most of these strategies, at least in my opinion, involve the use of low-dose droperidol. To once again restate the obvious, droperidol has a nearly unparalleled safety record coupled with undeniable efficacy. It is a cost-efficient therapeutic option for preventing PONV. The frequency with which this drug has been administered virtually guarantees that some "association" with adverse events will occur. As I pointed out in the editorial, an association of adverse events with drug administration cannot be used to prove cause and effect. So what then is the "point?" The disservice that the FDA's black box warning does is to imply that alternate therapeutic options for managing PONV are somehow "safer" than droperidol. There are not only no data to support this position, but there are also no theoretical reasons to believe that it is so.

The variety of reaction by the anesthesia community to the black box warning on the use of droperidol calls attention to an extremely important philosophical point. It is frequently tempting to confuse the strength of one's beliefs with the weight of scientific evidence. What we believe may not coincide completely with what we know to be true. For instance, it is an incontrovertible fact that a certain percentage of patients undergoing anesthesia and surgery will experience PONV. Nearly as incontrovertible is the fact that low-dose droperidol will prevent a certain percentage of patients from experiencing these symptoms when compared to patients who received no prophylactic therapy. The data on the safety of droperidol is much less conclusive for several reasons. First, how safe is safe? What is an acceptable incidence of adverse effects? Of SAEs up to and including death? Many of us strongly believe that droperidol is in fact "safe" based on the incomplete data that are available. Although it is correct that we can estimate the number of doses of droperidol administered per year,[3] the true incidence of SAEs remains unknown. Retrospective data analysis and voluntary reporting, particularly when event frequency is low, are not likely to yield conclusive results. Could prospective data collection provide the answer? The answer is, of course, yes, though as Drs. Bailey and White note, the task would be daunting and might be neither practical nor economically feasible. And even if the exact incidence of adverse effects could be determined, what would be an acceptable death rate for the use of low-dose droperidol?

My personal opinion is that I *know* droperidol works and I *believe* that it is safe. As a clinician, educator, and scientist I still am compelled to ask the difficult questions while knowing full well that the answers may be impossible to obtain. Unquestioning adherence to dogma does a disservice to our profession. Questioning accepted practice does not mean abandoning that practice; rather, it means maintaining an open mind and a willingness to change as new information becomes available.

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(Accepted for publication May 22, 2003)

Anesthesiology 2003; 99:762

Critical Incident with Narkomed 6000 Anesthesia System

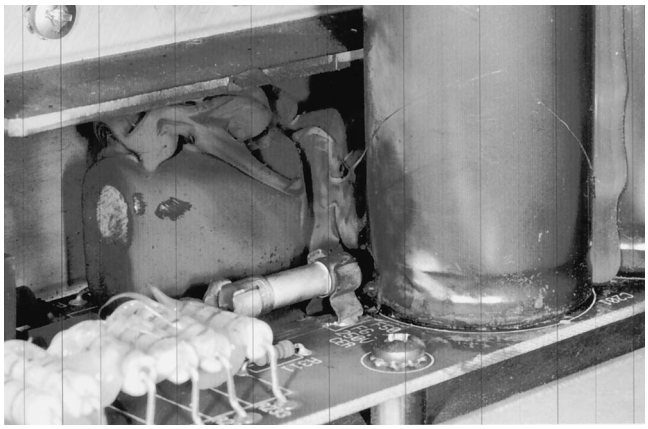

Fig. 1. Power supply circuit board showing location of short circuit.

To the Editor:—We would like to report an incident with a Narkomed 6000 Anesthesia System (Draeger Medical, Inc., Telford, PA). An attendant was cleaning an unoccupied operating room when she witnessed a loud "bang," followed by sparks coming from the bottom of the anesthesia machine. At the time of the noise, the attendant had been adjusting the position of the machine, which was connected to the electrical and gas mains supply but was switched off. The charge nurse, on arrival at the scene, noted smoke in the room. The machine was immediately disconnected from the electrical and gas mains supply, and the problem subsided.

Subsequent analysis showed that a high-impedance short circuit had occurred between the metal can of a capacitor and traces on a printed circuit board in the power supply (Fig. 1). The power supply is located under the main body of the anesthesia machine, and there was minimal flammable material in the immediate area. The engineer's report concluded the incident was due to an intrinsic design fault and was not caused by cleaning solution that had been used to clean the floor prior to the incident. The manufacturer has implemented design changes and replaced the power supplies of all affected machines in Canada and the United States, and the event has been reported to the appropriate health authorities. The manufacturer noted that had the event occurred during use, the anesthesiologist could have disconnected the machine from the main supply with the operation continuing on battery backup, although we would choose to immediately replace the machine, given the unknown status of the internal components.

Until recently, reports of operating room fires and explosions caused by anesthesia equipment were usually attributable to flammable or explosive anesthetic agents[1] or to contamination of pressurized gas systems with dust or oil.[2,3] The development of sophisticated electronics in anesthesia machines has been associated with occasional reports of malfunctions and one previous report of an electrical fire.[4] This event is an important reminder of the risks that modern anesthesia equipment may bring to the operating room. Prompt reporting of critical incidents allows the rapid investigation and implementation of design improvements to this equipment.

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(Accepted for publication April 9, 2003)

Support was provided solely from institutional and/or departmental sources.

Anesthesiology 2003; 99:762

In Reply:—The letter by Usher *et al.* is an accurate representation of our investigations into this event. Draeger Medical, in conjunction with the power supply manufacturer, instigated a recall action in November 2002 for the affected power supplies (154 in total). This action was completed on December 20, 2002 (FDA Recall No. Z-0268–3/Z-0269–3).

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(Accepted for publication April 9, 2003)

Anesthesiology 2003; 99:762–3

Fatal Intraoperative Anaphylaxis Related to Aprotinin after Local Application of Fibrin Glue

To the Editor:—We report a case of intraoperative fatal anaphylaxis. The chronology of the event and the subsequent evaluation strongly point to a role of the aprotinin contained in the fibrin glue locally applied to the operating field.

This letter is accompanied by an Editorial View. Please see: Moss J: Allergic to anesthetics. ANESTHESIOLOGY 2003; 99:521–3.

A 52-yr-old man underwent surgery for a painful lumbar disc herniation. His past medical history included a rhinoplasty, and his only other medical problem was a glaucoma treated with carteolol. After premedication with hydroxyzine 100 mg, anesthesia was induced with midazolam, propofol, and rocuronium and maintained with sufentanil and desflurane. No event occurred for 2 h until application of 0.2 ml of fibrin glue (Tissucol® Kit 500 U/ml; Baxter, Maurepas, France) on a

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Table 1. Allergologic Workup

	Normal Value	Preoperative Stored Plasma	Plasma Sample (2 h after Shock)
Histamine, RIA (Immunotech, France)	<10.8 nmol/l		94 nmol/l
Tryptase, RIA (Pharmacia, Sweden)	<13.5 μg/l		76 μg/l
Antilatex, IgE (RAST, Phadebas, Pharmacia, Sweden)	<0.35 kU/l	Negative	
Antiquaternary ammoniums, IgE (RIA SAQ)		Positive (6.86% of fixation)	
Antiaprotinin IgE (RAST) Allerbio, Varennes en Argonne, France)	<0.5 kU/l	Positive at 3.4 U/ml	

IgE = immunoglobulin E antibodies; RAST = radio-allergosorbent assay; RIA = radioimmunologic assay.

dural tear. Blood pressure decreased immediately (60 mmHg), accompanied by a bronchospasm and a skin rash. The anesthetic agents were discontinued. The patient received hydroxyethyl-starch and intravenous epinephrine, but cardiac arrest developed. Cardiac massage was started and was soon followed by defibrillation. Stabilization of hemodynamic parameters was achieved with epinephrine infusion (epinephrine 3 mg/h). Right heart and pulmonary artery catheterism performed in the intensive care unit showed a low cardiac output with low left and right filling pressure. Despite intensive inotropic support, the patient died 48 h later from multiorgan failure.

The plasma levels of histamine and tryptase were increased 2 h after initial symptoms, confirming anaphylaxis. Antiaprotinin immunoglobulin (Ig) E and antiquaternary ammoniums immunoglobulins were identified in the preoperative serum of the patient (table 1).

No drugs other than those cited above had been given during the 2 h preceding the shock, except for Tissucol®. The chronology does not point to a role of neuromuscular blocking agents, because a 2-h interval had elapsed between the injection of rocuronium and the shock. Our patient had specific IgE against quaternary ammoniums (detected on his preoperative stored plasma), but this has little predictive value because antiquaternary ammoniums IgE are present in 10% of the population without allergic reaction to neuromuscular blocking agents.[1] An allergic reaction to latex may occur at any time during surgery, but the negativity of antilatex IgE in the preoperative serum does not support this hypothesis in our case. The chronology of events and the presence of antiaprotinin IgE in the preoperative serum strongly argue in favor of an allergic mechanism induced by fibrin glue.

Fibrin glue is effective for hemostasis and sealing of tissue wounds but has been associated with severe anaphylactic reactions.[2] Since 1990, Tissucol® has been composed of human coagulation factors and bovine aprotinin. The aprotinin role is to delay the destruction of the glue by fibrinolysis. None of the allergic cases following exposure to fibrin glue related to human coagulation factors. Bovine aprotinin was therefore held responsible.[3] More than 100 cases of allergy to intravenous aprotinin have been published, essentially after reexposure to the drug.[4,5] In our patient, the antiaprotinin IgE level was moderately positive, indicating previous sensitization. Cases of allergy after local application of the product are rare, and our case is the first related death reported. A case similar to ours was described after neurosurgery with local injection of fibrin glue for closure of a liquor fistula, which resulted only in a generalized skin rash.[6] After further enquiry, we discovered that fibrin glue had been applied during the previous rhinoplasty 5 yr before. It has been demonstrated in cardiovascular surgery that locally given aprotinin results in a 10% 12-month prevalence of IgG antibodies.[7] On the other hand, it has been observed in cardiovascular surgery that even a careful research of exposure history is not very sensitive to identify patients with aprotinin-specific antibodies.[8] In case of known previous exposure to aprotinin, a preoperative allergologic workup is usually performed. However, the predictive value of the tests (prick-test, specific antiaprotinin IgG or IgE) has not been studied for aprotinin local application. Because the prevalence of reactions to aprotinin is higher in patients with a reexposure interval less than 6 months, such a short interval should be considered a relative contraindication to fibrin glue application.[5]

This is the first report of a fatal case of intraoperative anaphylactic shock related to local aprotinin. Because the preoperative questioning to investigate previous exposure to fibrin glue is difficult, and because an allergologic workup cannot be performed in every patient, the liberal use of fibrin glue must be weighed in relation to the risk of allergy.

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(Accepted for publication April 8, 2003)

Anesthesiology 2003; 99:764

Sustained Ventricular Tachycardia in Long QT Syndrome: Is Propofol the Culprit?

To the Editor:—It was indeed very interesting to read the case report by Sakabe *et al.*[1] We have recently come across a similar case, in which a 28-yr-old man weighing 62 kg, suffering from chronic osteomyelitis of the right femur, was scheduled for débridement and gentamicin beading on a daily basis. The patient had no history of syncope, palpitations, or any other cardiac symptoms, and examination was unremarkable. There was no history of sudden death or symptoms suggestive of long electrocardiographic QT syndrome in immediate family members. The patient's blood biochemistry results were normal, but he had not undergone an electrocardiogram. The patient had also undergone surgery uneventfully twice before for the same disease under spinal anesthesia.

Anesthesia was induced with fentanyl 100 μg and propofol 120 mg, followed by *Laryngeal Mask Airway™ #4* insertion and was maintained on spontaneous respiration with O_2/N_2O/isoflurane. At the end of the 1-hr surgery, the patient had a heart rate of 86/min, blood pressure of 126/80 mmHg, respiratory rate of 28/min, and an end-tidal CO_2 concentration of 45 mmHg. Before closure, the wound was irrigated with hydrogen peroxide, at which point the patient became tachypneic with a respiratory rate of 40/min along with a tachycardia of 120/min and a blood pressure reading of 130/90 mmHg. There was no associated sudden decrease in Sa_{O_2} or Et_{CO_2}. Suspecting a light plane of anesthesia, a bolus of propofol 60 mg was given, after which the patient developed ventricular entrasystoles that rapidly converted into a ventricular tachycardia that was polymorphic in nature. The patient was ventilated with 100% O_2; cardiopulmonary resuscitation was instituted and was continued for 30 min, but despite the administration of antiarrhythmic agents such as lidocaine and amiodarone and consecutive cardioversion, the rhythm continued to be a pulseless polymorphic ventricular tachycardia that would intermittently change into ventricular fibrillation. Blood analyzed for electrolytes and ionized calcium was normal. At the end of 30 min, the rhythm suddenly reverted to a normal sinus rhythm. The patient regained spontaneous respiration and consciousness over the next 10 min. He was moved to the intensive care unit, where he was observed for 24 h. The patient recovered completely with no neurologic deficits.

The patient's electrocardiogram revealed a borderline prolonged QTc interval of 460 ms. Echocardiography was normal and he was referred to the cardiology department for follow-up. A repeat electrocardiogram also showed a prolonged QTc interval. On the basis of a prolonged QTc interval and history of torsade de pointes,[2] he was diagnosed as having long QT syndrome and was started on β-blocker therapy. He was recommended to receive an automatic implantable cardioverter defibrillator but was lost to follow-up.

In conclusion, the cause of the sustained ventricular tachycardia in this patient was a long QT syndrome that was unknown before surgery. The factors that could have contributed to the development of the arrhythmia are (1) sympathetic stimulation because of the wound irrigation, and (2) bolus of propofol leading to a further prolongation of the QTc interval. Propofol is known to cause an increase in the QT interval but not as much as thiopentone.[3] In this case, propofol may have possibly triggered the polymorphic sustained ventricular tachycardia. Although the cause-and-effect relationship between propofol and ventricular tachycardia is not established, the immediate appearance of ventricular tachycardia after a bolus of propofol suggests that propofol played at least some role.

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(Accepted for publication April 9, 2003)

Support was provided solely from institutional and/or departmental sources.

Anesthesiology 2003; 99:764

Spinal Anesthesia for Magnetic Resonance Imaging Examination

To the Editor:—A 62-yr-old man who had undergone surgical removal of a T9–T10 neurofibroma a decade previously was referred to the Magnetic Resonance Imaging Institute of our institution for a semi-urgent examination to rule out recurrence of the disease, precipitated by the recent onset of severe back pain. He had severe spastic paraparesis with marked involuntary movements, even when supine. However, despite sedation with midazolam, intravenous propofol, and (subsequently) inhaled nitrous oxide and isoflurane (up to 2% inspired), immobility could not be achieved. The examination was therefore canceled to allow further discussions with the treating physicians.

Given the risk of a worsening neurologic deficit if a lesion were undiagnosed and hence left untreated, it was determined that obtaining a high-quality scan was mandatory. General endotracheal anesthesia with neuromuscular blockade was considered, but given the patient's obesity and smoking history, alternatives were also discussed. A spinal anesthetic was considered and discussed with the patient's neurosurgeon, who was agreeable to this plan as long as the lumbar puncture could be performed below the level of the patient's suspected thoracic lesion. A 22-gauge Quincke spinal needle was inserted in the L3–L4 interspace, with the patient lying on his left side (an atraumatic bloodless tap). Plain bupivacaine was progressively and slowly injected (5 mg and then 2.5 mg; total, 7.5 mg) to achieve a level of T12. The patient stopped moving his legs, and the magnetic resonance imaging examination was easily completed. The patient was stable during the scan and recovered motor function uneventfully 20–30 min after completion of the scan. No complications were noted, and he was sent home 1 h later.

To our knowledge, a spinal anesthesia for a magnetic resonance imaging examination has not been reported previously. This approach may be reasonable in patients with involuntary movements of the legs in whom difficulties in performing a general anesthetic are anticipated.

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(Accepted for publication May 1, 2003)

Support was provided solely from institutional and/or departmental sources.