

## Anesthesia-compatible Magnetic Resonance Imaging

*To the Editor:*—We read with interest the correspondence by Zimmer *et al.*<sup>1</sup> Although we agree with their conclusion that human error related to magnetic resonance imaging (MRI) use can only be minimized by adequate training, we believe lessening the risks of MRI technology itself is of equal importance. We feel it is time to stress the importance of “anesthesia-compatible” MRI, rather than putting all the emphasis on anesthesiologists adapting to the needs of the MRI machine. Anesthesiologists and patients are now forced into working under conditions that are far less than optimal in MRI suites that are cold and dark, have noisy equipment and facilities, and are often located far away from the main operating area.

There are three aspects of MRI that are important to the anesthesiologist: 1) avoidance of materials and equipment that will be attracted to the MRI machine, 2) avoidance of anesthetic devices that interfere with the function of the MRI machine, and 3) avoidance of MRI interference with the patient and the functioning of materials and devices used for anesthesia. This third aspect is often neglected: most MRI machines are not “anesthesia compatible.”

The first point is obvious, well known, and scary but can be handled with a little experience.<sup>2</sup> It is, however, extremely important for everyone to realize that complete elimination of the use of ferromagnetic materials in devices used in MRI suites is not feasible and is sometimes impossible, as was made clear in the letter by Zimmer *et al.*,<sup>1</sup> among others.<sup>3</sup> We have successfully dealt with this problem by anchoring all devices that have ferrous materials in them to a movable ceiling pendant system with a predetermined limited range of movement. Installation of metal detectors (similar to those used in airports) at the entrance to MRI suites can help to some degree.

The second point involves the use of equipment such as ventilators and infusion pumps for treatment and various patient monitors, personal computer-related devices, and local area network connections for medical information. MRI technology now frequently forces the anesthesiologist to discontinue the use of these devices during MRI activity despite their importance for patient safety.<sup>4</sup> Alternative “MRI-compatible” devices are not always available, functional, or suited for critically ill patients, causing anesthesiologists to make an uncomfortable choice between the continuity of safety of treatment and MRI diagnosis.

The third aspect is the most difficult to resolve. We think more attention should be focused on alleviating this problem although some MRI properties, such as magnetic attraction, electric shock, or heating as a result of radiofrequency pulsing, seem to be inevitable.<sup>4</sup> Anesthesiologists have been forced to adapt to MRI technology, raising a never-ending list of incompatibility issues. While working to build a

new MRI suite, we realized that although there were few technical difficulties to overcome, lack of awareness of the issues involved with traditional MRI was playing a key role in holding back the development of more patient-friendly MRI technology. Companies we attempted to work with that already make both MRI and anesthesia-related equipment did not seem to find safety for patients under anesthesia during MRI a compelling enough reason to consider revising their MRI devices. It would be much more cost effective and safe to improve MRI machines and their installation, including the architectural design of MRI suites, than it would be to carry out patchwork renovation of numerous patient care devices.

The demand for anesthesia care in MRI suites continues to increase as interventional procedures using MRI continue to increase in frequency.<sup>5-6</sup> Time spent in MRI suites will only become longer. Anesthesiologists, as advocates for patients, should actively voice their concern to improve MRI technology not only in terms of radiologic diagnostic function but also in terms of working environment, duration of examination, and, most importantly, patient safety. We must seek solutions for safer anesthesia delivery. We should stop being cursed by the need for “MRI-compatibility” and start actively implementing an “anesthesia-compatible” MRI environment. To achieve this goal, anesthesiologists should be involved from the beginning of the conceptual design of MRI suites.

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*In Reply:*—We appreciate the interest of Miyasaka *et al.* in our recent letter<sup>1</sup> and applaud them for their comments.

Miyasaka *et al.* demand the development of anesthesia-compatible magnetic resonance imaging (MRI) suites and monitoring techniques because conditions to provide anesthesia for patients in MRI suites are often far from optimal and provoke mistakes.

In particular, the authors address difficulties achieving adequate monitoring within the MRI suite, especially in critically ill patients. Clearly, the problem is that monitors, ventilators, and infusion pumps either interfere with the MRI (evoking low quality images or artifacts)

or the equipment contains ferromagnetic parts and may not work correctly in the presence of a strong magnetic field (which results in danger for the patient). At the same time demand for MRI diagnostic procedures in critically ill patients is increasing steeply. Thus, with present equipment the anesthesiologist often faces a “catch-22” situation.

Accordingly, Miyasaka *et al.*'s points that MRI manufacturers should take anesthesiologists' comments regarding more comfortable and safe MRI suites seriously and that anesthesiologists should be involved in conceptual designs of MRI suites from the beginning are well

taken. However, even if MRI suites become more anesthesia-compatible in the future, the main risk, *i.e.*, the presence of a very strong magnetic field with all its hazards, as reported in our letter, is inescapable.

Furthermore, their well-taken comments do not only apply to MRI suites. In the near future, some operating rooms and advanced shock/trauma patient admission units will contain MRI equipment. Thus, the need for more high-tech MRI-safe ventilators and monitors in the future is obvious, and, as always, anesthesiologists should take part in developing and shaping their future work environment.

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*Invited Commentary:*—Observations and conversations have convinced me that anesthesiologists are involved in many more “near miss” magnetic resonance imaging (MRI) safety incidents than are reported, with some having the potential to be as lethal as the highly publicized pediatric death that occurred from head injury after an anesthesiologist inadvertently carried a ferromagnetic oxygen tank into an MRI suite.<sup>1</sup> The letter by Miyasaka *et al.* is highly relevant to such incidents because of the very important points it makes regarding setting up MRI suites and their procedures to prevent unintended safety violations during clinical anesthesia in the magnet room. Miyasaka *et al.* note that in many instances, input from anesthesiologists is sought only after an MRI suite has been constructed and procedures have been streamlined for use by patients who are neither sedated nor anesthetized. Strong support is appropriate for Miyasaka *et al.*'s call for early involvement by anesthesiologists, both in establishing hospital procedures for anesthesia care in MRI suites and for orienting (reorienting?) industry thinking such that there is harmony and balance in the form of asking manufacturers to be anesthesia-compatible at the same time that anesthesiologists are asked to be MRI-compatible. Particularly worthy of attention is Miyasaka *et al.*'s point that hospital managers, contractors, and equipment managers have no professional guidelines or standards regarding the design and construction of anesthesia facilities inside the magnet room of an MRI suite. The American Society of Anesthesiologists has produced *The Operating Room Design Manual* and a booklet on setting up safe office-based anesthesia, but these do not address key MRI safety issues.\* Advances in magnet technologies and medical imaging are likely to require that anesthesiologists function in environments having stronger magnetic field gradients (which exert mechanical force) and more intense radiofrequency power (an energy source with the potential for burns) than

\* <http://asahq.org/publicationsAndServices/physician.htm>. Accessed August 23, 2004.

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## Proponents of Liberalized Fasting Guidelines

*To the Editor:*—We read with interest the case report by Kawabata *et al.*<sup>1</sup> of pulmonary aspiration on induction of anesthesia in an infant fed formula 4.5 h before surgery. We have long been proponents of liberalized fasting guidelines for clear liquids and, more recently, for infant formula.<sup>2,3</sup> For infants younger than 6 months of age, expert opinion has been equally divided as to 4 h or 6 h formula fast requirements.<sup>4,5</sup> The liberalization of formula fasting to 4 h, as outlined by Dr. Coté<sup>6</sup> and at least temporarily adopted by Dr. Kawabata's institution, is a practice we continue to support in healthy infants younger than 6 months old. We recognize that there are very limited data to support either the safety or the hazard of such a practice.

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one currently encounters. Anesthesiologists undergo training and make considerable efforts to learn about MRI-related dangers, and they and the patients deserve anesthesia-friendly, patient-safe systems in MRI suites. But there is truth in the title of Chester L. Karrass' widely known book “You Don't Get What You Deserve, You Get What You Negotiate.” In pointing out the need for MRI suite anesthesia standards Miyasaka *et al.* are really calling for help in negotiating what is deserved. What should be the form? One solution would be a comprehensive statement sanctioned by the appropriate American Society of Anesthesiologists committees, possibly involving other relevant professional groups. If there are manufacturers who do not find anesthesia safety issues to be “compelling,” then anesthesiologists need to provide better, more persuasive arguments, as there can be no compromise on safety. I am impressed by the altruism I have seen in the technical people I have met who are associated with medical manufacturers. Many, in choosing their profession, have shown that they are as highly motivated by seeing patients helped by optimum imaging technologies as surgeons and anesthesiologists are about seeing patients helped by the best invasive procedures. Altruism, however, was not something that the late Senator Everett Dirksen relied on almost half a century ago in a saying he was fond of: “When I feel the heat, I see the light.” It seems appropriate that there be follow-up to the letter by Miyasaka *et al.* in the form of anesthesiologists getting together to provide some heat and light for themselves, hospital colleagues, and equipment manufacturers.

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The bases of our position are both theoretical and experiential. Gastric fluid volume (GFV), used as a surrogate marker for pulmonary aspiration risk, is small and not significantly different if measured in infants fasted for either 4 h or 6 h.<sup>3</sup> Since July 2001 we have employed a preoperative fasting directive at The Children's Hospital of Philadelphia permitting healthy infants formula feeds 4 h before surgery. Using the CompuRecord anesthesia record system (Phillips Medical Systems, Andover, MA) to search for events of “pulmonary aspiration related to anesthesia care,” one of our mandatory quality assurance markers, we reviewed all pediatric cases conducted at our institution from 9/01/98 to 5/31/04. Within this period we compared pulmonary aspiration

**Table 1. Pulmonary Aspiration Over Time**

Time Period	Aspiration Events	Total Cases	Aspiration Incidence
9/1/98–6/30/01 Preliberalization	16	53598	3/10000
7/1/01–5/31/04 Postliberalization	2	64547	3/100000
9/1/98–5/31/04 Overall	18	118145	1.5/10000
9/1/98–5/31/04 In infants <6 months old	0	9266	0

events in two 34-month epochs, one before and one after the liberalization of infant formula fasting from 6 h to 4 h, and found no increased incidence (table 1). In fact, for reasons that remain unclear, there was a 10-fold reduction in overall incidence of pulmonary aspiration from the first epoch to the second (Fisher exact test  $P = 0.0002$ .) With regard to patients <6 months of age, however, there were no documented aspiration events in any of the 9,266 infants cared for in the past 6 yr. Our experience is consonant with that of others.<sup>7</sup> It is important to note that although we allowed healthy infants formula at 4 h before procedures from July 2001 on, we have no data as to how many infants actually fed between 4 h and 6 h before induction of anesthesia. Lastly, from a more global perspective, if we were to assume that the 50% of North American and European practitioners surveyed by Emerson *et al.*<sup>4</sup> and Ferrari *et al.*<sup>5</sup> allow a 4-h fast and have not found an increased incidence of pulmonary aspiration, then the evidence for the safety of this practice may be growing.

As for the case presented by Kawabata *et al.*, she appeared to be a healthy infant who came for elective surgery of the lip. Height and weight appeared normal, consistent with normal gastrointestinal function and nutritional status. Nevertheless, undiagnosed chronic and subclinical acute disorders may have caused gastrointestinal dysmotility that could have contributed to the aspiration described. Both total feed volume (260 ml within 1 h) and formula characteristics (formula derived from cow milk) may have contributed to the event as well. A 120-ml feed might be more typical and appropriate 4 h before anesthesia and surgery in a young infant. In our fasting study, feed volumes averaged 120–150 ml.<sup>3</sup> Human milk and whey-based formula are emptied faster than casein-based formula and cow's milk.<sup>8</sup> There is insufficient data to state with certainty that one formula is safer than another, but given the slower emptying times for the latter, a case can be made for either avoiding them or prolonging the fast.

Kawabata *et al.* misquoted our GFV study<sup>3</sup> by stating "...9% of formula-fed infants who fasted for 4 h had undigested traces of formula in their gastric content."<sup>1</sup> In fact, 9% (9/97) of all of our subjects had traces of residual formula. Evidence of formula was found in 13% of subjects fasted for <6 h and in 3% of those fasted for ≥6 h. Interestingly, one 8.5-month-old infant who fasted for 10 h still had a white

tinge to the recovered gastric aspirate. We believe that these white-tinged residua associated with small GFV and pH not different from traditional fasts do not significantly increase pulmonary aspiration risk. Given the limited data, however, practitioners who wish to reduce the risk of even trace amounts of formula in the stomach may feel more comfortable recommending a 6-h fast. Finally, GFV remains an imperfect surrogate marker for pulmonary aspiration.<sup>9</sup> Small GFVs do not preclude vomiting and aspiration of upper small bowel contents *via* retrograde giant contractions and no study has examined small bowel emptying time as it relates to formula feeds.

The central issue is that pulmonary aspiration of gastric contents is a rare event.<sup>7</sup> Mortality or significant morbidity associated with pulmonary aspiration is exceedingly rare. To carefully measure the impact of various fasting regimens on even uncomplicated pulmonary aspiration, randomized, controlled trials would require sample sizes in excess of 30,000.<sup>3</sup> In the past 6 yr, overall patient volume at The Children's Hospital of Philadelphia exceeds this number but not in the infant subpopulation of interest. No matter how fasting guidelines are designed, the risk of pulmonary aspiration of gastrointestinal contents, even in fasted healthy infants, will never be zero. None of this diminishes the importance of the case report. When events are rare, the case report may be the only way of tracking emerging patterns and trends that will enhance our understanding and permit best practice to continue to evolve.

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## Adequate Preoperative Fasting and Aspiration: Factors Affecting Regurgitation

*To the Editor:*—Kawabata *et al.*<sup>1</sup> reported a case of unanticipated vomiting and pulmonary aspiration after induction of anesthesia in a formula-fed 4-month-old female infant who weighed 6.26 kg scheduled for elective cheiloplasty. Anesthesia was induced with sevoflurane and nitrous oxide in 33% oxygen. The anesthesiologist tried to maintain spontaneous respirations but, abruptly, mask ventilation could not be performed. Arterial oxygen saturation decreased to 28% and formula was found in the patient's mouth. The authors argue that despite surveys and the American Society of Anesthesiologists practice guide-

lines' recommended 4-h fasting time,<sup>2–4</sup> the risk of aspiration remains and suggested that further studies and discussions are needed for a consensus on fasting time for formula-fed infants. Several comments related to the case appear warranted.

First, this case demonstrates that despite more than 4 h of fasting, residual formula can still be present in some infants. Not surprisingly, studies have shown that a completely empty stomach is often not achieved after the recommended fasting time.<sup>5,6</sup>

Second, although the authors claim that their patient vomited, it

appears from their own description that the action was regurgitation rather than vomiting. Various factors can play a role in inducing regurgitation in infants.<sup>7</sup> Airway obstruction during spontaneous breathing during anesthetic induction may cause regurgitation by increasing pleuroperitoneal pressure differences (thus increasing the intragastric-esophageal pressure difference) and by raising the intragastric pressure as a result of the "over action" of the diaphragm.<sup>7,8</sup> Positive airway pressure (in excess of 20 cm H<sub>2</sub>O) may result in intermittent opening of the cricopharyngeal sphincter and the gastroesophageal junction with a subsequent increase in intragastric pressure.<sup>7,8</sup> The resting intragastric pressure can be higher in infants<sup>9</sup> (as compared with adults) because of the relatively small size of the stomach, encroachment of some abdominal organs, previous air swallowing during crying, and strenuous diaphragmatic breathing.<sup>7,9</sup> In addition, a mild form of relaxation of the gastroesophageal junction may exist in the first 6 months of age. Once gastric contents are forced up into the esophagus, they may readily find their way into the pharynx because of the short esophagus in the infant.<sup>7,9,10</sup>

Third, although inhalation induction using 30–35% oxygen is commonly practiced in infants and children, it is time to seriously consider "preoxygenation" to increase oxygen reserves and thereby delay the onset of arterial oxygen desaturation in case airway obstruction occurs.<sup>11–14</sup> Infants are at an increased risk of hypoxemia because of their small functional residual capacity and increased oxygen consumption.<sup>15</sup> The value of preoxygenation in pediatric patients has been recently discussed in a number of reports<sup>15–17</sup> and certainly can be easily achieved.<sup>11–17</sup>

In conclusion, despite what appears to be an adequate preoperative fasting, the anesthesiologist should proceed with the assumption that the stomach is not completely empty. It behooves the anesthesiologist to take into consideration the factors that may induce regurgitation during induction and specifically avoiding and immediately correcting airway obstruction. Finally, preoxygenation before induction should be practiced.

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*In Reply:*—First of all, we would like to convey our appreciation to Dr. Cook-Sather and Dr. Salem for their scientific and detailed responses to our Letter to the Editor.<sup>1</sup>

As Dr. Cook-Sather rightly pointed out, although studies have been conducted, and scientific data accumulated before establishing the guidelines for fasting periods, there is very limited data to definitively support a 4-h *versus* a 6-h fasting period. We are of the opinion that the presence of guidelines for two different fasting times could prove problematic. After encountering this case, we changed our fasting time policy from 4 h for formula milk to 6 h, as we thought that it provided a greater safety margin for the risk of aspiration while not causing any serious disadvantage to the patients and their parents.

Dr. Salem commented that despite an adequate fasting period, infants, owing to their anatomical and physiologic differences from adults, are predisposed to regurgitation of gastric contents. Hence, they should be treated as potential risks for regurgitation and all precautionary measures to minimize this risk should be undertaken. We are in complete concurrence with this opinion.

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Finally, although established guidelines cannot guarantee safety, we believe that our case report contributes to further elucidating the practical implications of these guidelines, making the induction of anesthesia even safer by further reducing the risk of regurgitation and aspiration.

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## Pacemaker and Electrocardiographic Monitor Pseudomalfuction during Extracardiac Radiofrequency Ablation

*To the Editor:*—In their article about pacemakers and extracardiac radiofrequency ablation, Tong *et al.* describe some appropriate precautions; *i.e.*, have temporary equipment available for backup pacing and check the pacemaker with a programmer both before and after the radiofrequency ablation event.<sup>1</sup> However, the authors should have included a statement about the placement of the current return pads, which should be as close as possible to the radiofrequency ablation delivery electrodes to prevent or minimize radiofrequency ablation current travel across the generator and lead system (they did not specify the location of these pads). In addition, this article has a number of inaccuracies.

First, the authors have misinterpreted electrical artifacts displayed by their digital monitor (and marked with upward arrows in strips *D* and *E* [fig. 1]) as pacemaker output pulses, making an incorrect diagnosis of “intermittent temporary runaway pacing.” None of these pulses appears to “capture” the ventricle and pace the heart, and other pacing pulses exist in an appropriate fashion that do depolarize the ventricle. In fact, these are pacemaker “pseudospikes,” which result from inappropriate digital processing of the electrical noise from the radiofrequency ablation by the electrocardiographic monitor. This phenomenon has been well described.<sup>2,3</sup> Additional pseudospikes can be seen in strip *D* after complexes 5 and 8 and in strip *E* after complexes 2, 6, and 7. Also, the term “runaway pacing” refers to continuous, high-rate pacing resulting from internal component failure within a generator. Correction is always by pacemaker replacement.<sup>4,5</sup> Further, the pseudospikes appear at rate of 375 bpm (strip *E*, 160 ms), arguing against runaway pacing, as the Guidant Meridian pacemaker (Guidant Corporation, St. Paul, MN) has a runaway limit of 205 bpm.<sup>6</sup>

Next, the authors report that their patient had “complete atrioventricular block.” Complete atrioventricular block is not demonstrated by

any of the five strips that accompany the text. Strip *C* and strip *E* (complexes 4–7) show narrow complex QRS complexes, suggesting that the patient had intact atrioventricular nodal conduction. The rhythm might be sinus at approximately 70 bpm with a P-R interval of 300 ms. It is not clear if the atrial events are paced, as operating room monitors do a poor job of detecting and showing atrial pacing events. Because the authors did not describe the programmed P-R interval, we have no way to know whether atrial events are paced or native. The atrioventricular delay in strip *D* and possible paced atrial events in strip *A*, complexes 8–10 (*open downward arrows*), do appear to be less than 200 ms. However, without knowing the atrioventricular delay programming and without real-time data from the pacemaker, limited conclusions can be made about the longer atrioventricular delays seen throughout the five strips.

The authors state that the patient’s heart rate immediately changed from 63 to 96 bpm with the onset of radiofrequency ablation delivery, seen in strip *A* complexes 4–7. Yet, there is the suggestion of P waves (*open downward arrows*, added) at these complexes. The possible atrial pacing artifacts at complexes 8–10 (strip *A*) might have resulted from rate smoothing, which will limit any decreasing rate in this pacemaker, if programmed. Thus, without knowledge of the pacemaker settings as well as real-time data from the pacemaker (telemetry), no conclusion can be reached about the etiology of this increased heart rate.

At most, these strips might demonstrate atrial and ventricular oversensing, which should be expected during radiofrequency ablation, according to the Meridian Physician’s Manual.<sup>6</sup> In a DDD-programmed pacemaker, the occurrence of atrial oversensing, without ventricular oversensing, will result in higher rates of ventricular pacing than expected; usually, these events take place at the upper limit for tracking. With the presumed upper limit for tracking in this case of 120 bpm, atrial oversensing could have taken place at A4–6 and B5–6. Ventricular oversensing is difficult to prove with these strips, as the longest R-R interval occurs at A9–10 and represents a heart rate of 70 bpm. In the setting of ventricular oversensing, the pacemaker will fail to pace the ventricle and an inappropriately long R-R interval will occur. No such intervals are demonstrated.

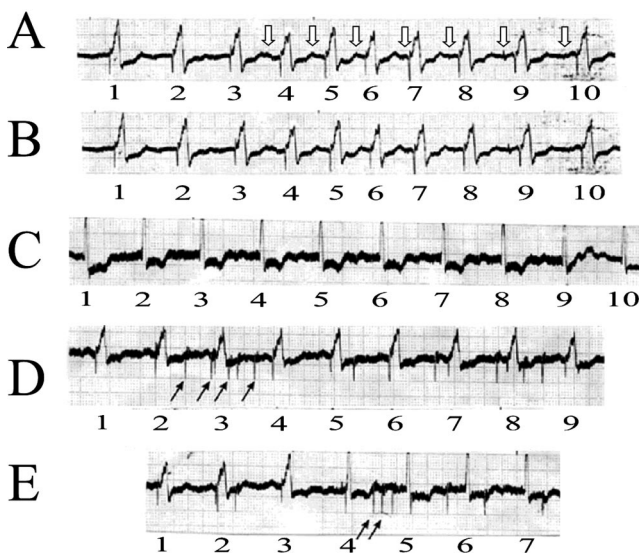
In summary, Tong *et al.* remind us that extracardiac radiofrequency ablation in a patient with a cardiac generator should be approached with caution owing to possible electromagnetic interference with the generator and potential misinterpretation of electrocardiographic behavior.

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**Fig. 1.** The original fig. 1 from Tong *et al.* was copied from the electronic document. No changes were made to any electrocardiographic tracing that would alter the apparent strip recorder rate, and all five strips appear to have been recorded at 25 mm/s. The *up-arrows* appearing in strips *D* and *E* were placed by the original authors. Annotations (*letters*, *numbers*, and *down-arrows*) were added for reference within the text. Reprinted with permission from *ANESTHESIOLOGY*.

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*In Reply:*—In our letter, we only noted that the radiofrequency current interfered with the function of the pacemaker but that there was no damage to the pacemaker itself.<sup>1</sup> Actually, we described this effect as “falsely inhibited,” which was very similar to what was first described by Chin *et al.*<sup>2</sup> Chin *et al.* noted that intracardiac radiofrequency current may produce a number of potentially serious pacing systems malfunctions. When such ablation was performed in close proximity to a pacing lead, false inhibition was observed, even when devices were programmed to the asynchronous mode. Several devices paced at abnormal rates during current flow, producing extremely rapid pacemaker runaway. Some pacers reverted to a noise mode of operation during the ablation procedures. Despite these effects, none of the devices was spuriously reprogrammed by the ablation, with the exception of revision to reset mode. Nor were any of the pulse generators permanently damaged. In our case, the situation was similar and that is why we described the device as “falsely inhibited” rather than “true inhibition” in our first submission. However, some reviewers had different opinions and were uncomfortable with the term “falsely inhibited.” They insisted that the generator is either inhibited or it is not. Finally we omitted the word “falsely.”

Second, a statement is needed regarding the placement of the current returns pads, which should be as close as possible to the radio-

frequency ablation delivery electrodes to prevent or minimize radiofrequency ablation current travel across the generator and lead systems. In this case, two grounding pads were applied to the posterior aspects of the patient's thighs as close as possible to the ablation electrodes. This comment was deleted during the revision of the work.

Third, complete supra-Hisian Atrio-ventricular block was diagnosed by a cardiologist *via* a formal electrophysiological study.

**Ng Yuet Tong, M.D., Hsieh Jing Ru, M.D., Hui Yu Ling, M.D., FICA, Yu Chun Cheung, M.D., Lau Wai Meng, M.D., Peter Chi Ho Chung, M.D.\*** \*Chang Gung Memorial Hospital at Keelung, Keelung, Taiwan, ROC. p654084@cgmh.org.tw

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## Amitriptyline Neurotoxicity

*To the Editor:*—The July 2004 issue of *ANESTHESIOLOGY* contained a report by Estebe and Myers<sup>1</sup> demonstrating neurotoxic effects of amitriptyline when injected in high doses immediately adjacent to the rat sciatic nerve. Local anesthetic properties have been demonstrated with high doses of amitriptyline,<sup>2,3</sup> and local anesthetics also have been shown to produce neurotoxicity after similar methods of administration.<sup>4</sup> The demonstration of neurotoxic effects following local administration is an important reminder of the need for careful assessment of novel routes of drug administration.

Unfortunately, there is a significant error in the calculation of the total dose administered in the Estebe and Myers<sup>1</sup> study. Thus, they inject 0.2 ml of 25 mg/ml or 79.6 mM amitriptyline as their highest dose and compute this to correspond to a dose of 16 nmol. However, this dose actually corresponds to a dose of 16  $\mu$ mol; therefore their dose computation is in error by a factor of 1000 (table 1, section A).<sup>1</sup> The doses administered are comparable to those administered in demonstrating local anesthetic properties of amitriptyline (table 1, sections B1, B2)<sup>2,3</sup> but are significantly higher than those administered in producing antinociception (table 1, section C).<sup>5,6</sup> Much of their discussion regarding amitriptyline systematically perpetuates the thousand-fold error in calculations, and this results in some very misleading considerations.

After peripheral administration, by injection locally into the dorsal or plantar surface of the hindpaw, amitriptyline produces antinociception in rat models of ongoing (formalin test) or neuropathic pain (spinal nerve ligation model).<sup>5,6</sup> Efficacy of locally administered amitriptyline has also been demonstrated in a rat model of diabetic neuropathy.<sup>7</sup> In each of those studies, doses of 100 nmol amitriptyline produced antinociception against spontaneous (formalin) and evoked (thermal, mechanical) behaviors. This dose, however, had no effect on thermal latencies in the uninjured state<sup>8</sup> and did not produce tissue edema.<sup>9</sup> Increasing the dose of amitriptyline to 300 and 1000 nmol leads to increases in thermal thresholds in the uninjured state, which may reflect involvement of local anesthetic properties.<sup>9</sup> These higher doses

**Table 1. Doses of Amitriptyline Administered Locally Immediately Adjacent to the Sciatic Nerve (A,B1) or Locally into Tissue (B2,C) to Determine Local Anesthetic Properties or Antinociceptive Actions**

Dose amitriptyline hydrochloride	Total dose administered
<b>A. Estebe and Myers (2004)<sup>1</sup></b>	
5 mg; 0.2 ml of 25 mg/ml, 79.6 mM	16 $\mu$ mol or 16,000 nmol
2.5 mg; 0.2 ml of 12.5 mg/ml, 39.8 mM	8 $\mu$ mol or 8,000 nmol
1.25 mg; 0.2 ml of 6.25 mg/ml, 19.9 mM	4 $\mu$ mol or 4,000 nmol
0.625 mg; 0.2 ml of 3.125 mg/ml, 10.0 mM	2 $\mu$ mol or 2,000 nmol
<b>B1. Gerner et al (2001)<sup>2</sup></b>	
0.2 ml of 5 mM	1 $\mu$ mol or 1,000 nmol
0.2 ml of 10 mM	2 $\mu$ mol or 2,000 nmol
<b>B2. Khan et al (2002)<sup>3</sup></b>	
0.6 ml of 0.05%	0.96 $\mu$ mol or 960 nmol
0.6 ml of 0.25%	4.8 $\mu$ mol or 4,800 nmol
0.6 ml of 0.5%	9.6 $\mu$ mol or 9,600 nmol
<b>C. Sawynok et al (1999)<sup>5</sup>; Esser and Sawynok (1999)<sup>6</sup></b>	
50 $\mu$ l of 2 mM	0.1 $\mu$ mol or 100 nmol

also cause tissue edema that, at the 1000 nmol dose, persists to some degree at 24 h, but mechanisms involved in edema are unclear.<sup>9</sup>

The Estebe and Myers<sup>1</sup> study evaluates doses of 2,000–16,000 nmol amitriptyline injected immediately adjacent to the sciatic nerve in rats. When amitriptyline up to 100 nmol is administered locally into the hindpaw of rats in models of antinociception, it is administered at a much lower total concentration and into tissue that is not necessarily in the immediate vicinity of the nerve. There is no data to suggest that neurotoxic or overt local anesthetic properties are involved in antinociception at doses up to 100 nmol. Indeed, the actions of amitriptyline at these doses are substantially blocked by methylxanthine adenosine receptor antagonists,<sup>5-7</sup> and it is very unlikely that such antagonists would block neurotoxic or local anesthetic actions. This issue is raised in the context of implicating a receptor-operated mechanism in the action of amitriptyline rather than in the context of implicating any

single particular mechanism in its action. Thus, amitriptyline is a complex drug with a range of pharmacological actions (given acutely it blocks noradrenaline, 5-HT, and adenosine uptake, inhibits  $\alpha$ -adrenergic, histamine H<sub>1</sub>, 5-HT<sub>2</sub>, and *N*-methyl-D-aspartate receptors, and blocks Na<sup>+</sup>, Ca<sup>2+</sup>, and even K<sup>+</sup> channels), and many of these effects could contribute to peripheral antinociception. Clearly, any form of topical application of amitriptyline to the skin in humans will need to proceed with due caution regarding the potential for local toxicity.

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*In Reply:*—We thank Dr. Sawynok for the interest in our study<sup>1</sup> and for correcting an error in the conversion of our doses from mM to nmol. Fortunately, the experimental protocol, preparation and dosing of drug, and results and conclusions of our article remain unchanged, as this error was only one of unit conversion for the reader. The error does not affect the experimental paradigm or significance of the results. We also thank Dr. Sawynok for comparing the dose used in several studies of amitriptyline in their table, as this helps place our experiments in context. The range of dose evaluated in our study was in accordance with the doses previously used in studies that reported a prolongation of sciatic nerve blockade<sup>2</sup> (*i.e.*, 5–0.625 mg or 16,000–2,000 nmol; each dose administered in a 0.2-ml volume adjacent to rat sciatic nerve). Our data clearly demonstrate that amitriptyline causes a dose-related neuropathologic change if it is administered in the immediate vicinity of a nerve, and suggests that it should not be used as a local anesthetic agent. This conclusion remains unchanged. Moreover, it has recently been reported in a volunteer study that amitriptyline (25.2 mg to 6.3 mg) did not provide better ulnar nerve blockade at the wrist level than current local anesthetics.<sup>3</sup> Indeed, amitriptyline has a reduced margin of safety and an increased potential for neurotoxic injury.

We did not test the neurotoxic effect of a 100 nmol dose used by Sawynok *et al.*<sup>4</sup> and Esser and Sawynok<sup>5</sup> because that dose is not associated with neural blockade of major nerve bundles. A 100-nmol dose produces an analgesic effect of uncertain mechanism, as Dr. Sawynok notes. However, the point should be made that local neurotoxic injury is concentration-dependent and that there may be subclinical neurotoxic injury with even small doses of high concentration solutions. Although the analgesic effect of amitriptyline is of considerable interest, it should also be noted that adverse effects were reported

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*To the Editor:*—Burkle *et al.*<sup>1</sup> perpetuate the belief held by younger practitioners of the specialty that Robert Macintosh added the curve to his laryngoscope blade to “lessen the chance of damage to the patient’s upper teeth.” Although Sir Robert indicated that exposing the larynx

This Letter was sent to the authors of the referenced report. The authors did not feel that a response was required.—Michael M. Todd, Editor-in-Chief

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when slightly higher doses (0.3 ml of 500 mM) were administered transdermally<sup>6</sup> or by subcutaneous injection (300 to 1000 nmol).<sup>7</sup>

Thus, we believe there is consensus that the use of amitriptyline as a local agent in clinical situations for analgesia or anesthesia requires additional experimental study that includes a neuropathologic and a behavioral or electrophysiologic endpoint. We support these studies and regret that our conversion error may have introduced some confusion in the literature.

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## The Macintosh Laryngoscope Blade

with a long straight blade “occasionally jeopardizes the patient’s upper teeth or takes a minor divot out of the posterior pharyngeal wall,”<sup>2</sup> his primary purpose was to facilitate exposure of the vocal cords. Avoidance of damage to the teeth or soft tissue was not his primary purpose. Having observed a pediatric anesthetist use a straight blade in much the same manner as we now use the Macintosh blade, he modified the blade to allow the tip to “fit into the angle made by the epiglottis and the base of the tongue.” Elevation of the laryngoscope pushes the base

of the tongue upward whereas the epiglottis, because of its attachment to the tongue, is drawn upward, providing a clear view of the larynx.

Of greatest import, however, was Macintosh's observation, confirmed 2 months later by Rowbotham,<sup>3</sup> that it was possible to easily expose the larynx at a lighter plane of anesthesia than with any of the standard blades. Before the ubiquitous use of neuromuscular blocking agents to facilitate intubation and of intravenous agents and halogenated hydrocarbons to induce and maintain anesthesia, relatively deep anesthesia was required to avoid laryngospasm when the epiglottis was elevated because the glottis and the inferior surface of the epiglottis are innervated by the vagus nerve. When the use of cyclopropane became commonplace, bradycardia and hypotension, attributed to a vagal-vagal reflex when the epiglottis was lifted with a straight blade, was said to occur with alarming frequency. This untoward event, too, could be avoided with the use of Macintosh's blade because the superior surface of the epiglottis and the vallecula are innervated by the glossopharyngeal nerve.

Over the years, there have been a number of modifications of the Macintosh blade<sup>4</sup> that purportedly reduced the danger of damage to

the upper incisors and facilitated exposure of the larynx. None have met with even a modicum of success. Although Sir Robert's blade is still one of the most popular, contemporary anesthetic techniques have eliminated its original purpose—intubation of the trachea under light anesthesia.

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## Macintosh's Laryngoscope

*To the Editor:*—We have read the paper of Burkle *et al.* regarding the history of the laryngoscope in anesthesia<sup>1</sup> with great interest. The authors give a very good historical perspective of the different types of laryngoscope. Nevertheless we would like to highlight the laryngoscope designed by Robert Macintosh in 1943 because of its importance and significance.<sup>2</sup> In our opinion, the Macintosh blade is much more than a variant of the models previously mentioned, as it allowed a better view of the vocal cords, making the tracheal intubation easier.

Sir Robert Reynolds Macintosh was the first professor of Anesthesia at Oxford University, which was the first chair of anesthesia in Europe.<sup>3,4</sup> The laryngoscope designed by Macintosh is probably the most successful and lasting instrument in the history of anesthesia; it has survived plastic translation and the adoption of fiber light. The laryngoscope was designed to lessen the difficulty of exposing the larynx by direct elevation of the epiglottis, as the blades existing at that time did not allow correct visualization of the vocal cords.<sup>2</sup> This becomes evident in a letter that Sir Robert Macintosh wrote to Jephcott in which he also explained how he got the idea to design a new laryngoscope:<sup>5</sup> "The ability to pass the endotracheal tube under direct vision was the hallmark of the successful anesthetist. Magill was outstanding in this respect. I described a new approach in 1941 but it was not much of an improvement.<sup>6</sup> The difficulty was to expose the cords. Then, one morning during a tonsillectomy list, I had a bit of luck and the nous to take advantage of it. On opening a patient's mouth with a Boyle-Davis gag, I found the cord perfectly displayed. Richard Salt (a really excellent chap) was in the theater with me; before the morning had finished he has gone out and soldered a Davis blade on to the laryngoscope

handle and this functioned quite adequately as a laryngoscope. The important point being that the tip finishes up proximal to the epiglottis. The curve, although convenient when intubating with naturally curved tubes, is not of primary importance as I emphasized subsequently."

Although, as manifested in this letter, Sir Robert Macintosh did not consider the shape or curve of the blade of primary importance, the use of a curved blade may often avoid jeopardizing the patient's upper teeth, as it makes it unnecessary to pass the straight blade of the standard laryngoscope beyond the epiglottis.<sup>7</sup>

We consider that in an historical review about laryngoscope, the one designed by Sir Robert Macintosh in 1943, which is still nowadays the most common currently used blade, deserves a bit more mention, as it not only lessens the chance of damage of the patient's upper teeth but also allows a correct visualization of the vocal cords, which was sometimes more difficult with the previously existing models.

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This Letter was sent to the authors of the referenced report. The authors did not feel that a response was required.—Michael M. Todd, Editor-in-Chief



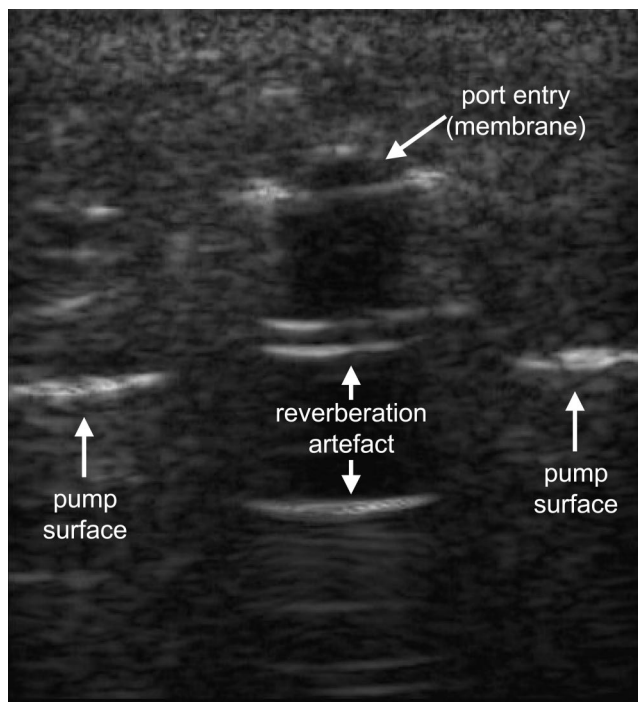
## Sonographic Localization of an Implanted Infusion Pump Injection Port: Another Useful Application of Ultrasound in Pain Medicine

*To the Editor:*—Correct localization of an implanted infusion pump injection port only by palpation can sometimes be cumbersome, especially in obese patients and when there are no visible signs of previous successful punctures. Fluoroscopy, if available, is sometimes used in these difficult cases. We found that ultrasound can be helpful to facilitate puncture and that the method is easily practicable.

A 43-yr-old patient with an implanted intrathecal drug delivery device (Archimedes Implantable Constant-Flow Pump; Codman, Raynham, MA) was suffering from acute breakthrough pain of malignant origin (duodenal carcinoma with lumbar bone metastases). We decided to deliver a bolus through the bolus injection port of the implanted pump. This type of pump has a separate bolus port located on the outer end of the circular symmetrical body, distant from the centrally located port to refill the reservoir chamber. Thus, depending on the orientation of the pump during the implantation, the bolus port can be found anywhere on the circumference and may be difficult to localize depending on the overlying tissue. Moreover, because aspiration through a correctly positioned bolus needle is not consistently feasible, control possibilities after positioning of the needle are limited. In our case, repeated careful palpation of the skin to find the port was inconclusive. Therefore, we decided to use sonography for localization. With a 5–10 MHz linear “hockey-stick” transducer attached to a portable ultrasound device (SonoSite 180; SonoSite, Bothell, WA) we could easily visualize the bolus port (fig. 1). The skin was marked accordingly and a needle was introduced successfully at this point perpendicular to the skin.

Only in one case report by Egerszegi *et al.* in 1990<sup>1</sup> was ultrasound used to facilitate the repeated localization of a soft expander injection port in a pediatric patient. It is important to note that we did not perform real-time guidance of the needle under ultrasound in this case but only used sonography to mark the puncture site before disinfection and insertion of the needle. It seems to be easier for this application, is effective, and avoids sterile wrapping of the transducer.

Ultrasound guidance has gained increasing interest in regional anesthesia and pain medicine in recent years.<sup>2</sup> Many private offices and outpatient pain clinics and most hospitals are equipped with ultrasound devices today. The development of smaller, portable systems has further increased the availability of ultrasound. Compared with fluoroscopy that could also be used to facilitate port localization in difficult cases, ultrasound is portable today, more easily available, and not associated with exposure to ionizing radiation. We believe that with this easy-to-learn method, which is another useful application of ultrasound in pain medicine, multiple puncture attempts can be



**Fig. 1.** Sonographic view of the bolus injection port with a linear transducer at 10 MHz.

avoided when conventional localization of a pump injection port becomes difficult.

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