

Prolonged Wear of Antichemical Protective Gear: The Hazards and Difficulties of Wearing Chemical Warfare Gear

To the Editor:—The interesting article by Flaishon *et al.*¹ included prospective data on the difficulties of performing anesthetic and critical care duties in mass casualty situations. An additional factor to consider is the challenge of continuing to perform one's duties while wearing full antichemical protective gear.

As a member of the Air National Guard, I am obligated to perform chemical warfare training. Wearing the full MOPP 4 antichemical warfare ensemble is uncomfortable, especially in warm environments such as the Middle East. The clinician must contend with the intrinsic difficulties of wearing the suit and be mindful of preventing his own severe dehydration and the need to be resuscitated himself.

Most United States civilians do not appreciate the need to maintain adequate hydration. In the Middle East, constant hydration is a way of life. Military personnel have become familiar with disaster management concepts. In the future, such training will be mandatory for civilians as well. The Society of Critical Care Medicine (Des Plaines, IL)

sponsored its first course on disaster medicine at its annual meeting this year to provide civilian clinicians with the basic concepts of disaster management. The course will heighten awareness of the challenges of airway management as well as the challenges and hazards of extended wear of chemical warfare gear.

Eric L. Bloomfield, M.D., M.S., F.C.C.M. Mayo Clinic, Jacksonville, Florida. bloomfield.eric@mayo.edu

Reference

1. Flaishon R, Sotman A, Ben-Abraham R, Rudick V, Varssano D, Weinbroum AA: Antichemical protective gear prolongs time to successful airway management: A randomized, crossover study in humans. *ANESTHESIOLOGY* 2004; 100: 260–6

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In Reply:—We thank Dr. Bloomfield for his comments. We share his concern regarding the troublesome antichemical gear and discussed it in our article.¹ The psychological and performance effects of the protective gear have also been previously addressed.² Stressful exercise causes fluid shifts, dehydration, and heat stroke, which must be prevented or treated if encountered.^{3,4} The antichemical suit further hampers adequate temperature regulation and is recognized as a cause of dehydration.

In the Middle East, especially during the summer, dehydration and heat stroke are common, especially in the elderly and in civilians or army corps involved in outdoor strenuous exercise.¹

We agree with Dr. Bloomfield that the first step in preventing dehydration and heat stroke is training and education.

It is important to note that according to chemical attack protocols, civilians are expected to wear only an antichemical facemask rather than the full protective gear. The problems mentioned are of major concern for those wearing the full protective suit, namely trained personnel, military and medical, who are required to treat and evacuate attack victims as well as perform other military operations while under such an attack.

Ron Flaishon, M.D., Alexander Sotman, M.D., Ron Ben-Abraham, M.D., Valery Rudick, M.D., David Varssano, M.D., Avi A. Weinbroum, M.D.* * Tel Aviv Sourasky Medical Center, Tel Aviv, Israel. draviv@tasmc.health.gov.il

References

1. Flaishon R, Sotman A, Ben-Abraham R, Rudick V, Varssano D, Weinbroum AA: Antichemical protective gear prolongs time to successful airway management: A randomized, crossover study in humans. *ANESTHESIOLOGY* 2004; 100: 260–6
2. Krueger GP: Psychological and performance effects of chemical-biological protective clothing and equipment. *Mil Med* 2001; 166(12 Suppl):41–3
3. Reardon M, Fraser B, Omer J: Physiological effects of thermal stress on aviators flying a UH-60 helicopter simulator. *Mil Med* 1998; 163:298–303
4. Mudambo SM, Reynolds N: Body fluid shifts in soldiers after a jogging/walking exercise in the heat: Effects of water and electrolyte solution on rehydration. *Cent Afr J Med* 2001; 47:220–5

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Cardiac Arrest, a Preventable yet a Possible Risk of Dexmedetomidine: Fact or Fiction?

To the Editor:—We read with interest the well-written case report “Dexmedetomidine and Cardiac Arrest.”¹ The inference of the authors seems to be simple, but a closer look reveals the omission of many implicating factors that would have contributed to the morbidity attributed to dexmedetomidine. Therefore, we dispute the conclusions. We believe that the patient received an excessive dose of dexmedetomidine after significant doses of other anesthetics and there was delay in treating the bradycardia. We believe that the progression to cardiac arrest could have been potentially prevented.

Dosing of 10 mg of midazolam during the placement of epidural catheter, 250 μg of fentanyl, and 200 mg of propofol for induction and maintenance at 0.9% isoflurane after a loading dose of dexmedetomidine at 1 $\mu\text{g}/\text{kg}$, followed by 0.2 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ by infusion, seems to be excessive.² Even with normal dosing hypotension and bradycardia are the most common side effects of dexmedetomidine.² The concomitant use of anesthetics, sedatives, hypnotics, and opioids has synergistic effects and may worsen bradycardia and hypotension. There may also have been increased vagal activity as a result of pyridostigmine and a

history of vigorous exercise. An unrecognized hypovolemic state was also present. The undiagnosed decrease in preload, even in the presence of acceptable vital signs, is at times overlooked.⁵ Excess dexmedetomidine, nonintervention of bradycardia at an appropriate time, and inadequate hydration sets the stage for unintentional cardiac arrest.²⁻⁴ The implications for the factors we mentioned are well substantiated in the literature.²⁻⁷ Also, the episode seemed to have evolved at a faster pace against a background of what seemed to be benign. Later, cardiac arrest ensued. On hindsight, a stricter insight into potential and unintentional risks would have prevented the development of cardiac arrest.

In short, a close scrutiny of the case that resulted in bradycardia and cardiac arrest seems to stem from multiple factors rather than from dexmedetomidine alone. The authors' direct implication of dexmedetomidine is questionable. Dexmedetomidine probably would have added to the sequence of events that followed but by itself it is an unlikely culprit in this particular case. In other words, dexmedetomidine can cause cardiac arrest if given in too great a dose after relatively large doses of other anesthetics. Bradycardia, if allowed unabated by noninterference in the presence of other risk factors, can also progress to cardiac arrest. The episode would have been thwarted by a judicious insight into the complex series of events that one often recognizes only after the incident has occurred. In this particular case sternotomy with resultant cascade of reflexes, namely vasovagal and Bezold-Jarisch would have aided to the rapidity of cardiac arrest.⁸⁻¹⁰

Although we differ with the authors' observations and the issue may be contentious because of its interwoven complexity, they must be complemented for their deft handling of a difficult case.

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Dexmedetomidine and Asystole

To the Editor:—We read with great interest the report of a cardiac arrest during dexmedetomidine use in a patient with myasthenia gravis.¹ In this case the interaction of pyridostigmine and epidural anesthesia was cited as possible contributors to this complication.

We would like to add our own experience with dexmedetomidine. We began to use it in 20-40-yr-old healthy patients scheduled for laparoscopic gynecological procedures under sevoflurane and fentanyl anesthesia plus cisatracurium for neuromuscular blockade. Dexmedetomidine was infused by the "sufentanil" program of an Anne@ intravenous infusion pump (Abbott Laboratories, North Chicago, IL) with an initial infusion of $4 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ for 15 min followed by $0.3 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$. After 40 patients were anesthetized using this technique, there was one case of severe bradycardia (32 beats/min) and one case of asystole. No patient received pyridostigmine or had epidural anesthesia instituted.

This event of asystole occurred while the patient was in Trendelenburg position with the peritoneal cavity insufflated with carbon dioxide (12 cmH₂O), and it lasted less than 2 min, responding to abdominal deflation, horizontal positioning, intravenous atropine 1 mg, and a

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In Reply:—We appreciate and agree, for the most part, with the comments of Drs. Muntazar and Kumar and those of Drs. Videira and Ferreira. Our purpose in presenting this case was to bring to light the potentially disastrous results from a particular combination of negative chronotropic influences.¹ We have used an anesthetic combination similar to this many times for thymectomy (minus the dexmedetomidine) and never experienced a case of asystole. Thus, we believe it

Muhammad Muntazar, M.D.,* Francis C. Kumar, M.D. * University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma. muhammad-muntazar@ouhsc.edu

References

- Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. *ANESTHESIOLOGY* 2004; 100:738-9
- Precedex [package insert]. North Chicago, IL: Abbott Laboratories; 2001
- Caplan RA, Ward RJ, Posner K, Cheney FW: Unexpected cardiac arrest during spinal anesthesia: A closed claim analysis of predisposing factors. *ANESTHESIOLOGY* 1988;68 5-114
- Gefin B, Shapiro L: Sinus bradycardia and asystole during spinal and epidural anesthesia: A report of 13 cases. *J Clin Anesth* 1998; 10:278-85
- Pollard JB: Cardiac arrest during spinal anesthesia: Common mechanism and strategies for prevention. *Anesth Analg* 2001; 92:252-6
- Dyck JB, Shafer SL: Dexmedetomidine pharmacokinetics and pharmacodynamics. *Anaesth Pharm Rev* 1993; 1:238-45
- Maze M: Autonomic nervous system, physiology and pharmacology: Alpha adrenergic receptors. *Clinical Anesthesia*, 2nd ed. Barash PG, ed. Philadelphia: Lippincott-Raven, 1992, pp 333-4
- Kennedy WF, Bonica JJ, Akamatsu TJ: Cardiovascular and respiratory effects of subarachnoid block in the presence of acute blood loss. *ANESTHESIOLOGY* 1968; 9:29-35
- Mackey DC, Carpenter RL, Thompson GE: Bradycardia and asystole during spinal anesthesia: A report of three cases without morbidity. *ANESTHESIOLOGY* 1989; 70:866-8
- Kinsella SM, Tuckey JP: Perioperative bradycardia and asystole: relationship to vasovagal syncope and the Bezold-Jarisch reflex. *Br J Anaesth* 2001; 86:859-68

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brief period of thoracic compressions. End-tidal carbon dioxide and capnographic curve were normal before and after the asystole.

We wonder if the incidence of asystole with dexmedetomidine is different from that with other anesthetic drugs. A study to verify the safety and not only the efficacy of this new drug should be undertaken while more subtype-selective α -2 receptor agonists with decreased side effects are awaited for clinical practice.²

Rogério L. R. Videira, M.D.,* Roberto Manara V. Ferreira, M.D. * Hospital das Clínicas da Universidade de São Paulo and Universidade Federal do Estado de São Paulo, São Paulo, Brazil. rovid@uol.com.br

References

- Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. *ANESTHESIOLOGY* 2004; 100:738-9
- Kanto J: The place of alpha-2-agonists in anaesthesiology of today. *Acta Anaesthesiol Scand* 1997; 41:4-5

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beyond coincidence that, with the addition of dexmedetomidine, cardiac standstill occurred. We did not state, and did not intend to imply, that dexmedetomidine was the sole cause for this event. Rather, we believe dexmedetomidine was a significant contributor among a number of factors, as summarized by Drs. Muntazar and Kumar and in the discussion section of the case report. Drs. Muntazar and Kumar stated they believe the dose of dexmedetomidine was "excessive." Such may

be the case, but the loading dose (1 $\mu\text{g}/\text{kg}$ over 10 min) was exactly as recommended by the manufacturer in the package insert and the infusion rate (0.2 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) was at the low end of the recommended range. Whether or not our dosing was excessive, it was in line with the recommendations of the manufacturer.

We agree there were multiple factors involved; this was a main point of the article. Also, the assertion that the asystole could have been avoided if the bradycardia had been treated earlier is well taken. The bradycardia in question, however, was an easily explained (by the dexmedetomidine loading dose) decrease in heart rate to 46–50 beats/min with stable blood pressure. Treating this in a patient with good cardiovascular health would ordinarily seem unnecessary. We now believe that even mild, hemodynamically stable bradycardia in the presence of dexmedetomidine and other negative chronotropic influences should be treated. The view through our “retrospectroscope” confirms this.

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Treatment of Rebound Pulmonary Hypertension: Why Not Sildenafil?

To the Editor:—I read with great interest the case report by Augoustides *et al.*¹ published in the April issue of ANESTHESIOLOGY. They highlight the important issue of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin and make a case for the use of inhaled iloprost. They propose that inhaled iloprost may allow gradual controlled withdrawal of perioperative inhaled selective pulmonary vasodilation, probably as a result of its favorable pharmacokinetics. Hence, in their opinion it has great promise in the management of perioperative pulmonary hypertension after cardiac surgery. However, I think that if the authors had highlighted the advantages of using sildenafil, instead of iloprost, in this scenario their case report would have made a more lasting and useful contribution to the existing literature on the topic of management of rebound pulmonary hypertension.

Pulmonary hypertension remains a major complication after surgical correction of congenital and long-standing valvular heart disease. Inhaled nitric oxide has been shown to reduce, but not eliminate, potentially life-threatening episodic pulmonary hypertensive crises.² Nitric oxide increases intracellular cyclic guanosine monophosphate, resulting in smooth muscle vasodilation. Phosphodiesterase type 5 is responsible for cyclic guanosine monophosphate breakdown in lung tissue. Abrupt discontinuation of nitric oxide may be complicated by life-threatening events, and phosphodiesterase activity may play a role in this phenomenon.³ Sildenafil (Viagra; Pfizer Laboratories, New York, NY), a selective and potent inhibitor of phosphodiesterase type 5, augments pulmonary vasodilation with nitric oxide and reduces the risk of pulmonary hypertensive crises in an at-risk postoperative patient.⁴ Furthermore, it ameliorates the rebound pulmonary hypertension caused by withdrawal of inhaled pulmonary vasodilators.⁵

Compared with the standard treatment, inhaled nitric oxide, sildenafil is superior in decreasing the mean pulmonary artery pressure and equally effective and selective in reducing pulmonary vascular resistance.⁶ It also causes a significant increase in the cardiac index.⁶ Its availability in oral, inhaled and intravenous forms, longer half-life of 4 h,⁴ and proven efficacy in randomized controlled trials^{7–9} are some of

We appreciate Drs. Videira and Ferreira sharing their experiences and agree that a large-scale safety study of the drug should be considered. We believe that when used appropriately, dexmedetomidine is very safe and useful. Perhaps by performing such a study and sharing our experiences with the drug, we, as a community, can avoid future closed claims analyses and unnecessary “black box” Food and Drug Administration warnings.

Gerard R. Manecke Jr., M.D.,* Esperanza Ingersoll-Weng, M.D., and Patricia A. Thistlethwaite, M.D., Ph.D. * Thornton Hospital, La Jolla, California. gmanecke@ucsd.edu

Reference

1. Ingersoll-Weng E, Manecke GR, Thistlethwaite PA: Dexmedetomidine and cardiac arrest. ANESTHESIOLOGY 2004; 100:738–9

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the distinguishing features which make sildenafil first-choice agent for managing rebound pulmonary hypertension.

Thus, my question for Augoustides *et al.* is “Why inhaled iloprost and not sildenafil?”

Shahzad G. Raja, M.R.C.S. Alder Hey Hospital, Liverpool, United Kingdom. drrajashahzad@hotmail.com

References

1. Augoustides JG, Culp K, Smith S: Rebound pulmonary hypertension and cardiogenic shock after withdrawal of inhaled prostacyclin. ANESTHESIOLOGY 2004; 100:1023–5
2. Miller OI, Tang SF, Keech A, Pigott NB, Beller E, Celermajer DS: Inhaled nitric oxide and prevention of pulmonary hypertension after congenital heart surgery: A randomized double-blind study. Lancet 2000; 356:1464–9
3. Ivy DD, Kinsella JP, Ziegler JW, Abman SH: Dipyridamole attenuates rebound pulmonary hypertension after inhaled nitric oxide withdrawal in postoperative congenital heart disease. J Thorac Cardiovasc Surg 1998; 115:875–82
4. Atz AM, Lefler AK, Fairbrother DL, Uber WE, Bradley SM: Sildenafil augments the effect of inhaled nitric oxide for postoperative pulmonary hypertensive crises. J Thorac Cardiovasc Surg 2002; 124:628–9
5. Atz AM, Wessel DL: Sildenafil ameliorates effects of inhaled nitric oxide withdrawal. ANESTHESIOLOGY 1999; 91:307–10
6. Michelakis E, Tymchak W, Lien D, Webster L, Hashimoto K, Archer S: Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension: comparison with inhaled nitric oxide. Circulation 2002; 105:2398–403
7. Stocker C, Penny DJ, Brizard CP, Cochrane AD, Soto R, Shekerdemian LS: Intravenous sildenafil and inhaled nitric oxide: A randomised trial in infants after cardiac surgery. Intensive Care Med 2003; 29:1996–2003
8. Bharani A, Mathew V, Sahu A, Lunia B: The efficacy and tolerability of sildenafil in patients with moderate-to-severe pulmonary hypertension. Indian Heart J 2003; 55:55–9
9. Ghofrani HA, Wiedemann R, Rose F, Schermuly RT, Olschewski H, Weissmann N, Gunther A, Walrath D, Seeger W, Grimminger F: Sildenafil for treatment of lung fibrosis and pulmonary hypertension: A randomised controlled trial. Lancet 2002; 360:895–900

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In Reply:—I thank Dr. Raja for an excellent appraisal of the role of sildenafil (Viagra; Pfizer Laboratories, New York, NY) in the management of rebound pulmonary hypertension after withdrawal of inhaled prostacyclin, as highlighted in our recent case report.¹ Dr. Raja has correctly highlighted that sildenafil is an alternative to iloprost in this setting.²⁻⁷ Our discussion of iloprost in the case report focused on its advantages over inhaled prostacyclin in the withdrawal of inhaled pulmonary vasodilator therapy. The pharmacokinetics of iloprost highlight a limitation of inhaled prostacyclin, namely its short half-life, that may facilitate serious rebound pulmonary hypertension.

However, this discussion was by no means intended to minimize the role of alternative approaches to the management of rebound pulmonary hypertension. As emphasized, a tiered multimodal therapeutic approach to pulmonary hypertension is essential for successful management.^{1,8,9} Indeed, this multimodal therapeutic approach to this clinical scenario not only includes sildenafil but also extends beyond this agent. The withdrawal of inhaled pulmonary vasodilators with a short half-life (nitric oxide, prostacyclin) should be managed in the setting of optimized ventilation, and where required, sufficient supplemental pulmonary vasodilator, whether inhaled, intravenous, or oral. There is a wide selection of possible agents that may be administered alone or in synergistic combination.^{8,10} The choice of regimen should also take into account drug availability, drug familiarity, and patient idiosyncrasies.

In summary, rebound pulmonary hypertension with withdrawal of nitric oxide or prostacyclin should be approached in a tiered multimodal fashion. Although sildenafil is eminently suitable, it is but one of a possible menu of pharmacologic choices.

John G. Augoustides, M.D. Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania. yiandoc@hotmail.com

References

1. Augoustides JG, Culp K, Smith S: Rebound pulmonary hypertension and cardiogenic shock after withdrawal of inhaled prostacyclin. *ANESTHESIOLOGY* 2004; 100:1023-5
2. Atz AM, Lefler AK, Fairbrother DL, Uber WE, Bradley SM: Sildenafil augments the effect of inhaled nitric oxide for postoperative pulmonary hypertensive crises. *J Thorac Cardiovasc Surg* 2002; 124:628-9
3. Atz AM, Wessel DL: Sildenafil ameliorates effects of inhaled nitric oxide withdrawal. *ANESTHESIOLOGY* 1999; 91:307-10
4. Michelakis E, Tymchak W, Lien D, Webster L, Hashimoto K, Archer S: Oral sildenafil is an effective and specific pulmonary vasodilator in patients with pulmonary arterial hypertension: Comparison with inhaled nitric oxide. *Circulation* 2002; 105:2398-403
5. Stocker C, Penny DJ, Brizard CP, Cochrane AD, Soto R, Shekerdemian IS: Intravenous sildenafil and inhaled nitric oxide: A randomised trial in infants after cardiac surgery. *Intensive Care Med* 2003; 29:1996-2003
6. Bharani A, Mathew V, Sahu A, Lunia B: The efficacy and tolerability of sildenafil in patients with moderate-to-severe pulmonary hypertension. *Indian Heart J* 2003; 55:55-9
7. Ghofrani HA, Wiedemann R, Rose F, Schermuly RT, Olschewski H, Weissmann N, Gunther A, Walrmath D, Seeger W, Grimminger F: Sildenafil for treatment of lung fibrosis and pulmonary hypertension: a randomised controlled trial. *Lancet* 2002; 360:895-900
8. Augoustides JG, Ochroch EA: Perioperative use of nitric oxide in cardiothoracic anesthesia and intensive care, *Progress in Anesthesiology*. Vol XV. Chapter 7. San Antonio, Texas, Dannemiller Foundation, 2001, pp 115-24
9. Augoustides JG, Mancini DJ: Postoperative care of the adult cardiac surgical patient, *Progress in Anesthesiology*. Vol XVI. Chapter 7. San Antonio, Texas, Dannemiller Foundation, 2002, pp 99-112
10. Lowson S: Inhaled alternatives to nitric oxide. *ANESTHESIOLOGY* 2002; 96:1504-13

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Frequent Utilization of Fluoroscopy Is Essential for Precise Needle Placement in Interventional Pain Procedure

To the Editor:—I read with interest the article recently published by Haspelslagh *et al.*¹ concerning an inadvertent lumbar disc injection which occurred during unilateral diagnostic infiltration of lumbar L3 nerve root.

Although the authors did mention the importance of fluoroscopy, they did not extensively discuss the reasons for the complication. This event must have been caused by a failure to note the depth of needle insertion during the procedure. The needle tip on the lateral view should be in the posterior aspect of the foramen when the transforaminal epidural injection is performed.² The authors' figure suggests that the needle had been inserted too far; the tip of the needle was beyond the dura, therefore no epidurogram was demonstrated in the fluoroscopic images.

As the authors indicated, "meticulous care should be taken when a transforaminal epidural injection . . . is performed." In addition, frequent utilization of fluoroscopy in different planes during the needle

insertion (not just at the time of dye injection) is essential for precise needle placement.

Jeffrey Huang, M.D. Anesthesiologists of Greater Orlando, Orlando, Florida. jeffrey_j_huang@hotmail.com

References

1. Haspelslagh S, Van Zundert J, Puylaert M, Heylen R, van Kleef M, Vissers K: Unilateral diagnostic infiltration of lumbar L3 nerve root resulting in an inadvertent discogram: the importance of fluoroscopic guidance in interventional pain therapy. *ANESTHESIOLOGY* 2004; 100:1019-21
2. Raj P, Lou L, Erdine S, Staats P: Decompressive neuroplasty, *Radiographic Imaging for Regional Anesthesia and Pain Management*, 1st ed. Raj P, Lou L, Erdine S, Staats P, eds. Philadelphia, Churchill Livingstone, 2003, pp 254-71

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In Reply:—We thank Dr. Huang for his interesting comments. We agree that frequent control of the correct needle position by the use of fluoroscopy is important during interventional pain procedures.¹

The depth of the needle position on a lateral view is important because antiinflammatory agents must be injected as close as possible to the site of pathology; *i.e.*, in the anterior plane of the epidural space.² With respect to the presented anteroposterior view (Fig. 2a in our article)¹ and in accordance with another review,³ the insertion of the needle no further medial than the six o'clock position in the anteroposterior view reduces the risk of dural puncture.³ Moreover, when our needle had been positioned intradurally at this level, a discogram could not have been explained.

Finally, low back pain and sciatica resulting from migrated disc herniations are an indication for transforaminal epidural infiltrations.⁴ By placing the needle in a correct fluoroscopic position, the needle can accidentally encounter a rostrally displaced disc herniation, which possibly explains this unexpected event. Our finding emphasizes the use of fluoroscopy in interventional pain procedures.

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Regimens for Patient-controlled Epidural Analgesia during Labor

To the Editor:—Boselli *et al.* are to be congratulated on their excellent study of patient-controlled epidural analgesia in labor.¹ The merit of a background infusion in addition to boluses of epidural solution on patient demand has been contested for many years.^{2,3} The finding by Ferrante *et al.* that some rates of infusion appeared to reduce the requirement for additional supplementary boluses⁴ may have influenced North American practice, where continuous infusion techniques are popular and physician workload is an important issue.⁵ In contrast, demand-only patient-controlled epidural analgesia is also associated with good efficacy and high maternal satisfaction. Even in countries where midwife-administered supplementation is not permitted, such as Belgium, patient-controlled epidural analgesia is usually delivered without a background infusion (verbal communication, May, 2004, Marc Van de Velde, M.D., Ph.D., Professor, Department of Anesthesiology, U.Z. Gasthuisberg, Leuven, Belgium).

Boselli *et al.* are incorrect, however, in stating that only two studies have previously compared the efficacy and local anesthetic consumption of patient-controlled epidural analgesia with or without background infusion. I conducted the first of such studies in 1991 and no benefit from a background infusion was found, albeit in a small sample ($n = 52$) and with only one rate of background infusion (4 ml/h).⁶

Although it is an oversimplification to suggest that "one regimen fits

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In Reply:—We would like to thank Dr. Paech for his comment on our study, and to apologize for not having cited his previous study devoted to the role of background infusion during labor patient-controlled analgesia performed more than 10 yr before ours.^{1,2} Although a smaller sample size, a different anesthetic solution (0.125% bupivacaine and fentanyl 3 μ g/ml) and only one rate of background infusion were studied, Paech had shown no benefit of using a background infusion in combination with self-administered boluses with equivalent analgesia and satisfaction in both groups, low rates of bupivacaine usage, and similar maternal and neonatal outcomes. No differences

Sara Haspelslagh, M.D., F.I.P.P., Jan Van Zundert, M.D., F.I.P.P., Kris Vissers, M.D., Ph.D.* * Multidisciplinary Pain Center, Genk, Belgium. kris.vissers@skynet.be

References

1. Haspelslagh S, Van Zundert J, Puylaert M, Heylen R, van Kleef M, Vissers K: Unilateral diagnostic infiltration of lumbar L3 nerve root resulting in an inadvertent discogram: the importance of fluoroscopic guidance in interventional pain therapy. *ANESTHESIOLOGY* 2004; 100:1019-21
2. Derby R, Bogduk N, Kine G: Precision percutaneous blocking procedures for localizing spinal pain: Part 2. The lumbar neuroaxial compartment. *Pain Digest* 1993; 3:62-75
3. Noor MG: Selective nerve root blocks for low back pain and radiculopathy. *Reg Anesth and Pain Med* 2004; 29:234-56
4. Vad VB, Bhat AL, Lutz GE, Cammisia F: Transforaminal epidural steroid injections in lumbosacral radiculopathy: a prospective randomized study. *Spine* 2002; 27:11-6

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all" for patient-controlled epidural analgesia during labor, Boselli *et al.* provide more compelling evidence that the routine use of a background infusion is not beneficial; indeed that it increases drug consumption and cost without improving maternal comfort or satisfaction.

Michael Paech, D.M., F.A.N.Z.C.A. University of Western Australia and King Edward Memorial Hospital for Women, Perth, Australia. michael.paech@health.wa.gov.au

References

1. Boselli E, Debon R, Cimino Y, Rimmele T, Allaouchiche B, Chassard D: Background infusion is not beneficial during labor patient-controlled analgesia with 0.1% ropivacaine plus 0.5 μ g/ml sufentanil. *ANESTHESIOLOGY* 2004;100:968-72
2. Paech MJ: Patient controlled epidural analgesia for labor (letter). *Anesth Analg* 1995; 80:1064
3. White PF, Gambling DR, Parker RK: Role of continuous background infusion with patient-controlled analgesia (letter). *Anesth Analg* 1995; 80:646
4. Ferrante FM, Rosinia FA, Gordon C, Datta S: The role of continuous background infusions in patient-controlled epidural analgesia for labor and delivery. *Anesth Analg* 1994; 79:80-4
5. D'Angelo R: Epidural PCA during labor. *ASA Newsletter* 2001; 65:116-8
6. Paech MJ: Patient-controlled epidural analgesia in labour: Is a continuous infusion of benefit? *Anaesth Intensive Care* 1992; 20:15-20

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were observed in the mean \pm SD hourly bupivacaine doses (11 \pm 5 mg in the bolus groups and 13 \pm 7 mg in the bolus plus 4-ml/h background infusion group, not significant), which was similar to our study, where no differences were observed in the hourly consumption of anesthetic solution between the 0-ml/h and 3-ml/h groups. This might be explained by insufficient power of both studies to detect small differences in the hourly requirements. However, the results from both studies and from the two previous studies devoted to this subject provide evidence that background infusion may not be routinely used during labor patient-controlled analgesia.^{3,4}

Emmanuel Boselli, M.D., Dominique Chassard, M.D., Ph.D.*

* Hôtel-Dieu Hospital, Lyon, France. dominique.chassard@chu-lyon.fr

References

1. Boselli E, Debon R, Cimino Y, Rimmelé T, Allaouchiche B, Chassard D: Background infusion is not beneficial during labor patient-controlled analgesia with 0.1% ropivacaine plus 0.5 microg/ml sufentanil. *ANESTHESIOLOGY* 2004; 100: 968-72

2. Paech MJ: Patient-controlled epidural analgesia in labour: Is a continuous infusion of benefit? *Anaesth Intensive Care* 1992; 20:15-20

3. Petry J, Vercauteren M, Van Mol I, Van Houwe P, Adriaensen HA: Epidural PCA with bupivacaine 0.125%, sufentanil 0.75 µg and epinephrine 1/800,000 for labor analgesia: is a background infusion beneficial? *Acta Anaesthesiol Belg* 2000; 51:163-6

4. Ferrante FM, Rosinia FA, Gordon C, Datta S: The role of continuous background infusions in patient-controlled epidural analgesia for labor and delivery. *Anesth Analg* 1994; 79:80-4

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Cholinesterase Inhibitors, Neuromuscular Blocking Drugs and Perioperative Memory Enhancement

To the Editor:—I read the fascinating review by Dr. Ghoneim¹ with great interest, especially the section on memory-enhancing or memory-impairing drugs. Anesthetics impair memory function in perisurgical periods, whereas cholinesterase inhibitors enhance memory¹ and act at central muscarinic cholinergic receptors involved in the process of memory consolidation.² Cholinesterase inhibitors donepezil, galanthamine, and rivastigmine, currently in clinical use,^{1,3} represent the first line of treatment in Alzheimer disease and the only drugs of proven benefit.^{4,5} Other cholinesterase inhibitors (*i.e.*, physostigmine) are under clinical evaluation.³

Drugs affecting central cholinergic activity also influence the anesthetic effect. Increasing central cholinergic tone with physostigmine antagonizes the hypnotic effect of propofol, shown by the return of consciousness (defined as responsiveness to commands) or wakefulness (appearance of being awake with open eyes but without cognitive content).⁶ Plourde *et al.*,⁷ measuring the action of physostigmine on the hypnotic effect of inhaled volatile anesthetics, conclude that physostigmine can, at least partially, antagonize the hypnotic effect of sevoflurane (subanesthetic concentrations) and that the resulting arousal is reflected by an increase in the amplitude of auditory steady-state response and, to a lesser extent, of the bispectral index. An interesting possibility is the antagonism of the anesthetic effect with physostigmine that results from potentiation of 40 Hz oscillations *via* increased muscarinic tone,⁸ whereas anesthetic-induced unconsciousness is associated with a reduction of gamma or 40 Hz oscillations in thalamocortical systems.⁷ These rhythms constitute background activity reflecting depolarization of thalamic and cortical neurons, a physiologic condition required for consciousness.⁹ In addition, Hill *et al.*¹⁰ demonstrated that physostigmine decreased the time for return of consciousness after halothane anesthesia.

These data, taken together, suggest not only that if reversal of the neuromuscular blockade occurs during anesthesia using cholinesterase inhibitors patients could be at risk of intraoperative awareness, as we recently underlined,¹¹ but also that these drugs may promote an enhancement of implicit memory for any awareness event that occurs. It may occur above all during light levels of anesthesia, common during the final period of anesthesia. During this period, cholinesterase inhibitors are given by anesthesiologists to reverse neuromuscular block. In other words, patients may better recall memories of the awareness experienced intraoperatively.

It was also reported that inhibition of central nicotinic acetylcholine receptors contributes to secondary effects attributed to anesthesia such as impairment in memory and cognitive performance,¹² whereas nicotinic acetylcholine receptors agonists improve memory.¹³ Other

drugs used in anesthesia, as well as the neuromuscular blocking drugs atracurium and the atracurium and cisatracurium metabolite laudanosine, activate nicotinic acetylcholine receptors at concentrations comparable to those measured in the central nervous system during, and for several hours after, general anesthesia.^{14,15} Administration of these neuromuscular blocking drugs, resulting in laudanosine production, has been suggested to improve postoperative cognitive functions,^{16,17} with the clinical relevance that they could have a potentially therapeutic effect in patients with Parkinson's disease.¹⁸ We ask if atracurium, cisatracurium, and their metabolite laudanosine should be included in the list of drugs acting at the cholinergic receptors and therefore potentially enhancing memory, with advantages and disadvantages mentioned above, and if these data merit, as do the anticholinergic agents, more detailed exploration by laboratory and clinical studies.

Vincenzo Fodale, M.D.,* Marco Tescione, M.D., Caterina Praticò, M.D. * University of Messina, Messina, Italy. vfodale@unime.it

References

1. Ghoneim MM: Drugs and human memory (part 2). Clinical, theoretical, and methodologic issues. *ANESTHESIOLOGY* 2004; 100:1277-97

2. Boccia MM, Acosta GB, Baratti CM: Memory improving actions of gabapentin in mice: Possible involvement of central muscarinic cholinergic mechanism. *Neurosci Lett* 2001; 311:153-6

3. Nordberg A, Svensson AL: Cholinesterase inhibitors in the treatment of Alzheimer's disease: A comparison of tolerability and pharmacology. *Drug Saf* 1998; 19:465-80

4. Doody RS, Stevens JC, Beck C, Dubinsky RM, Kaye JA, Gwyther L, Mohs RC, Thal LJ, Whitehouse PJ, DeKosky ST, Cummings JL: Practice parameter: Management of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001; 56: 1154-66

5. Knopman DS, Morris JC: An update on primary drug therapies for Alzheimer disease. *Arch Neurol* 1997; 54:1406-9

6. Meuret P, Backman SB, Bonhomme V, Plourde G, Fiset P: Physostigmine reverses propofol-induced unconsciousness and attenuation of the auditory steady state response and bispectral index in human volunteers. *ANESTHESIOLOGY* 2000; 93:708-17

7. Plourde G, Chartrand D, Fiset P, Font S, Backman SB: Antagonism of sevoflurane anaesthesia by physostigmine: Effects on the auditory steady-state response and bispectral index. *Br J Anaesth* 2003; 91:583-6

8. Metherate R, Cox CL, Ashe JH: Cellular bases of neocortical activation: Modulation of neural oscillations by the nucleus basalis and endogenous acetylcholine. *J Neurosci* 1992; 12:4701-11

9. Llinas RR, Pare D: Commentary of dreaming and wakefulness. *Neuroscience* 1991; 44:521-35

10. Hill GE, Stanley TH, Sentker CR: Physostigmine reversal of postoperative somnolence. *Can Anaesth Soc J* 1977; 24:707-11

11. Fodale V, Santamaria LB: Different actions of sevoflurane and propofol on central nicotinic receptors may explain differences in hypnotic antagonism by cholinesterase inhibitors. *Br J Anaesth* 2004; 92:773-4

12. Andoh T: Effects of general anesthetics on neuronal nicotinic acetylcholine receptors and their roles in the mechanism of anesthesia. *Masui* 2001; 50:1072-84

The above letter was sent to the author of the referenced article. The author did not feel that a response was required.—David C. Wartier, Editor.

13. Addy NA, Nakijima A, Levin ED: Nicotinic mechanisms of memory: effects of acute local DHBetaE and MLA infusions in the basolateral amygdala. *Brain Res Cogn Brain Res* 2003; 16:51-7

14. Fodale V, Santamaria LB: Laudanosine, an atracurium and cisatracurium metabolite. *Eur J Anaesth* 2002; 19:466-73

15. Tassonyi E, Fathi M, Hughes J, Chiodini F, Bertrand D, Muller D, Fuchs-Buder T: Cerebrospinal fluid concentrations of atracurium, laudanosine and vecuronium following clinical subarachnoid hemorrhage. *Acta Anaesthesiol Scand* 2002; 46:1236-41

16. Fodale V, Santamaria LB: Drugs of anesthesia, central nicotinic receptors and post-operative cognitive dysfunction. *Acta Anaesthesiol Scand* 2003; 47:1180

17. Fodale V, Santamaria LB: The inhibition of central nicotinic nACh receptors is the possible cause of prolonged cognitive impairment after anesthesia. *Anesth Analg* 2003; 97:1207

18. Fodale V, Praticò C, Santamaria LB: Drugs of anesthesia, central nicotinic receptors and Parkinson's disease. *Parkinsonism Relat Disord* 2004; 10:189-90

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Is It the Validation or Invalidation of the Airway Management Algorithm?

To the Editor:—The authors must be congratulated for undertaking the study attempting to answer the question of protocol-based airway management in the event of unanticipated difficult intubation.¹ However, this raises some serious questions about the content and conclusions of the study.

First, we are unclear as to how the investigators have concluded that their local protocol-based approach to airway management in the event of unanticipated difficult intubation after induction is efficacious. In an 18-month interval, 100 patients who were anticipated to be easy to intubate on preoperative work-up were subsequently found to be difficult to intubate. Sixteen percent of these patients suffered severe hypoxemia. Although the authors have not provided any data regarding the incidence of hypoxemia at induction among the true positive participants, it is unlikely that the incidence in that population could be as high as 16%. One patient suffered significant dental trauma and one ended up aspirating gastric contents. In addition, 89 patients were subjected to multiple attempts at direct laryngoscopy. The authors fail to acknowledge that these adverse events could very well be the result of the sticking with the proposed airway algorithm. It appears that most of the patients suffered hypoxemia as a result of multiple attempts at laryngoscopy. Hypoxemia, as we understand, is a clear sign of ventilatory failure under these situations unless it is attributable to other causes. Failure to keep a substantial number of patients oxygenated highlights the inefficiency of the proposed algorithm. Unless the study was designed to evaluate the efficacy of the *Intubating Laryngeal Mask Airway*TM (LMA North America, Inc., San Diego, CA) as a tool for rescue ventilation, the conclusion that 100 percent of the patients were successfully ventilated underestimates the significant problems at ventilation encountered by the anesthesiologists while following the algorithm.

We are also unclear on what basis the authors claim that the study has validated the local protocol-based approach to airway management. The study has neither the design nor the power to answer this question, as we do not know what would happen if the anesthesiologist were not restricted by the protocol to the use of direct laryngoscopy, gum elastic bougie, *Intubating Laryngeal Mask Airway*TM, or the transtracheal jet ventilation. Whether anticipated or unanticipated,

the approach to airway management in the event of failed intubation at induction depends on multiple factors. The result of preliminary laryngoscopy, the view of the glottis, the primary reason for intubation failure (is it the poor laryngoscopic view or the failure to pass the tube?), ease of ventilation with the mask, the muscle relaxant used, emergency or elective surgery, state of oxygenation of the patient, presence or absence of risk factors for aspiration, the condition of upper dentition, and, above all, the skill and expertise of the anesthesiologist all must be taken into account before defining the next step. A protocol-based approach like the one proposed by the investigators may limit anesthesia providers from applying individual problem-based solutions in the event of inadvertent difficult intubation. The end result: the patient with the poor dentition suffers dental trauma, the patient with full stomach may wind up aspirating gastric contents; failure of the *Intubating Laryngeal Mask Airway*TM regardless of the cause (morbid obesity/limited mouth opening) commits the anesthesia provider to expose the patient to the risk of transtracheal jet ventilation although switching to simple a laryngeal mask airway or laryngeal tube might have solved that problem. A broad-based protocol that incorporates all the fundamental goals and objectives of airway management, e.g., the American Society of Anesthesiologists airway protocol, allowing for stepwise evaluation based interventions while taking into account factors specific to operator skill and experience, available resources, and patient continues to be the most prudent approach to management of inadvertent difficult intubation.²

Govind R. Rajan, M.D. Veterans Affairs Medical Center and Saint Louis University, St. Louis, Missouri. govind_r@hotmail.com

References

1. Combes X, Le Roux B, Suen P, Dumerat M, Motamed C, Sauvat S, Duvaldestin P, Dhonneur G: Unanticipated difficult airway in anesthetized patients: Prospective validation of a management algorithm. *ANESTHESIOLOGY* 2004; 100:1146-50

2. Benumof JL: Laryngeal mask airway and the ASA difficult airway algorithm. *ANESTHESIOLOGY* 1996; 84:686-99

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Unanticipated Difficult Airway: What about Emergency Cases?

To the Editor:—We read with great interest the recent report on unanticipated difficult airway in anesthetized patients by Combes *et al.*¹ The article confirms that by strictly adhering to a simple pre-defined algorithm most problems occurring during management of an unexpected airway can be solved. This has already been

proven in two other large prospective studies.^{2,3} Using the gum elastic bougie as the first choice in a “can ventilate” but “cannot intubate” situation is a well-established technique, especially in Great Britain, and, of course, is much cheaper than, for example, a fiberoptic bronchoscope.⁴

However, the study raises several questions. The algorithm was only applied in elective cases. It would be very informative whether this airway algorithm was also used in emergency situations (out of the study) and how they succeeded.

The authors did not mention the distribution of intubations across surgical disciplines in detail although it is well known that many difficulties occur in Ear, Nose and Throat departments.

The authors correctly pointed out that the results are not transposable to patients with an anticipated difficult airway. Nevertheless, it would be very interesting how they managed these scenarios and how they decided what is an anticipated difficult airway and consequently excluded them from the study.

Thomas Heidegger, M.D.,* Hans J. Gerig, M.D. * Cantonal Hospital St. Gallen, St. Gallen, Switzerland. thomas.heidegger@kssg.ch

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In Reply:—We read with interest the letters of Drs. Rajan and Heidegger. Dr. Rajan asks if our study was a validation or an invalidation of the Airway Management Algorithm. Clearly, our study was designed to assess a difficult Airway Management Algorithm and not *The* Airway Management Algorithm because we do not think that there is only one way to manage the unanticipated airway.¹

We do not agree with Dr. Rajan that the 16 patients who experienced transient hypoxemia prove the inefficiency of the algorithm assessed. Indeed, most of these patients experienced arterial desaturation at the end of gum elastic bougie challenge only a few seconds before effective tracheal intubation. On the other hand, the *Intubating Laryngeal Mask Airway*TM (LMA North America, Inc., San Diego, CA) was used as a first step alternative technique in patients demonstrating a difficult ventilation scenario whenever arterial desaturation occurred. We agree with Dr. Rajan that several factors must be taken into account before defining the different steps of the algorithm. Obviously, in our algorithm, difficulties with face mask ventilation and oxygenation have been taken into account. Last, our study was not a comparative study assessing different management strategies of unanticipated difficult airway, but we are convinced of the great interest of such studies. It is possible that, as stated by Dr. Rajan, a broad-based protocol taking into account several factors could be the most prudent and effective approach in case of unanticipated difficult airway. Nevertheless, to our knowledge, large, prospective or retrospective, descriptive or comparative studies assessing the efficiency of such kind of protocol are still lacking.

To answer Dr. Heidegger, among our 100 patients with unanticipated difficult airway, 15 were anesthetized in emergency situations and considered at risk of pulmonary aspiration. We agree with Dr. Heidegger that difficult intubation distribution is not the same across

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Use of a Fogarty Catheter Sheath as an Endotracheal Tube Changer

To the Editor:—We recently encountered a case that required extubation strategy for difficult airway as recommended by American Society of Anesthesiologists task force.¹ A 50-yr-old lady underwent segmental mandibulectomy and radical neck dissection with deltopectoral flap for

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

References

1. Combes X, Le Roux B, Suen P, Dumerat M, Motamed C, Sauvat S, Duvaldestin P, Dhonneur G: Unanticipated difficult airway in anesthetized patients: Prospective validation of a management algorithm. *ANESTHESIOLOGY* 2004; 100:1146-50
2. Parmet JL, Colonna Romano P, Horrow JC, Miller F, Gonzales J, Rosenberg H: The laryngeal mask airway reliably provides rescue ventilation in cases of unanticipated difficult tracheal intubation along with difficult mask ventilation. *Anesth Analg* 1998; 87:661-5
3. Heidegger T, Gerig HJ, Ulrich B, Kreienbühl G: Validation of a simple algorithm for tracheal intubation: Daily practice is the key to success in emergencies: analysis of 13,248 intubations. *Anesth Analg* 2001; 92:517-22
4. Latto IP, Stacey M, Mecklenburg J, Vaughan RS: Survey of the gum elastic bougie in clinical practice. *Anaesthesia* 2002; 57:379-84

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surgical disciplines. Nevertheless, in our experience the difficulties of airway management encountered in the Ear, Nose, and Throat department are most often expected and strategies other than the one proposed in our study are applied.

In our study, we have considered that difficult airway was unanticipated when occurring in a patient who was considered to have normal preanesthetics evaluation of the airway (thyromental distance ≥ 60 mm, mouth opening ≥ 30 mm, Mallampati classification less than III, free from any history of difficult airway management in the past, unknown of ear, nose, and throat pathology, and with a body mass index < 35 kg/m²).

During the study period, 253 patients with anticipated difficult airway were managed in our institution. Ninety-nine underwent primary fiberoptic intubation under topical and locoregional anesthesia. For the other patients, general anesthesia was induced using short-acting anesthetic agents and succinylcholine. With difficult face mask ventilation or class III-IV Cormack laryngeal view, gum elastic bougie was used as first alternative technique (n = 42) and *Intubating Laryngeal Mask Airway*TM as a second step in case of gum elastic bougie failure (n = 3).

Xavier Combes, M.D.,* Gilles Dhonneur, M.D. * Hôpital Henri Mondor, Creteil, France. xavier.combes@hmn.aphp.fr

Reference

1. Combes X, Le Roux B, Suen P, Dumerat M, Motamed C, Sauvat S, Duvaldestin P, Dhonneur G: Unanticipated difficult airway in anesthetized patients: prospective validation of a management algorithm. *ANESTHESIOLOGY* 2004; 100:1146-50

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carcinoma parotid gland. At the end of surgery the oral endotracheal tube was left in place and she was shifted to the intensive care unit.

In the absence of either a jet stylet² or commercially available tube changer³ that is "rigid to facilitate intubation and/or hollow to facilitate ventilation,"¹ we thought of using a readily available tube changer. We were wary of using the previously described tube changers because of their lack of lumen to provide oxygen,⁴ lack of stiffness,⁴⁻⁶ or small

external diameter.^{4,5} Therefore, we decided to test these on mannequins (Ambu International, Copenhagen, Denmark). In the course of our experiments we realized that the sheath provided with Fogarty catheters (Willy Rusch AG, Kerns, Germany) is hollow and stiff and has a length of 80 cm and a varying external diameter (3–5 mm for sheaths of 6-French, 7-French, and 8-French Fogarty), making it a potentially good tube changer. We tested it on mannequins and found that it was successful in guiding the endotracheal tube every time and was adequate for both oxygen insufflation and jet ventilation.

We extubated the trachea of our patient over this tube changer (sheath of Fogarty 8-French), confirmed its correct position by end-tidal carbon dioxide monitoring before and after extubation, and kept it in place for over 2 h, giving oxygen at 4 l/min for the initial 30 min. For monitoring the end-tidal carbon dioxide we connected the sample line of the side-stream capnometer (Capnomac Ultima; Datex Ohmeda Division Instrumentarium Corporation, Helsinki, Finland) to the machine end of the Fogarty sheath (it could be easily screwed into the machine end). On the other hand, for delivering oxygen, we could slide the oxygen delivery tubing from the wall-mounted flowmeter over the machine end of the Fogarty sheath. We also tried keeping both carbon dioxide sampling tube and oxygen delivery tube together after mounting a three-way connector to the machine end of our tube changer (carbon dioxide sampling tube on the side port and oxygen delivery tube on the end port). The problem with this arrangement was that the end-tidal carbon dioxide readings became too low at oxygen flow rates greater than 1.5 l/min. The patient tolerated our tube changer well until it was removed; our patient did not require reintubation.

We feel that in the absence of a commercially available tube changer, this tube changer fulfills all the criteria of rigidity, hollowness, and

length required of such a device.¹ Its two minor limitations are 1) its nonstreamlined tip, which is of little practical consequence if it is used correctly when it passes through an already placed endotracheal tube and remains in mid-trachea and 2) its material is probably not tested for tissue compatibility.

Rakesh Kumar, D.A., M.D.,* Shrawan Mittal, D.A., D.N.B., Sunil Kumar, D.A., Chander Kanta Dua, D.A., M.D. * Maulana Azad Medical College and Associated Hospitals, New Delhi, India. rakeshrampal@hotmail.com

References

1. Caplan RA, Benumof JL, Berry FA, Blitt CD, Bode RH, Cheney FW, Connis RT, Guidry OF, Nickinovich DG, Ovassapian A: Practice guidelines for the management of the difficult airway: An updated report by the American Society of Anesthesiologists Task Force on the management of the difficult airway. *ANESTHESIOLOGY* 2003; 98:1269–77
2. Benumof JL: Additional safety measures when changing endotracheal tubes. *ANESTHESIOLOGY* 1991; 75:921–2
3. Cooper RM: Consider other extubation strategies to maintain difficult airways (letter). *Chest* 1995; 108:1183
4. Stanley GD: Extubating the difficult airway—an unusual role for a Fogarty catheter. *ANESTHESIOLOGY* 1999; 90:341–2
5. Garg S, Mohindra BK, Mittal S, Sodhi GS, Bhambri V, Tiwari A: Use of an unusual nasal guide to change an endotracheal tube in a case of difficult intubation. *J Anaesth Clin Pharmacol* 2002; 18:340–3
6. Suhasini T, Murthy NVVS, Rao SM: Nasogastric tube as a tracheal tube introducer (letter). *Anaesthesia* 1995; 50:270

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Foreign Body in the Airway

To the Editor:—The NIM® electromyographic endotracheal tube (Medtronic Xomed, Jacksonville, FL) is a wire-reinforced endotracheal tube equipped with surface electrodes often used to monitor recurrent laryngeal nerve function during thyroid surgery. Recently, while preparing a new NIM® tube we noticed a kink midway along its shaft. The mechanism of this tube kink was not known but at least one other anesthesiologist in our department has experienced a similar problem with this tube. Closer examination of our tube revealed that the reinforcing metal coil had separated from the internal surface of the tube (fig. 1). To see how the coil had become dislodged we hooked part of the separated metal coil with a flexible stylette and intentionally pulled it out with minimum effort. It is possible to pull out the entire length of the reinforcing wire once a portion of it has been dislodged (fig. 2). The coil in these tubes is normally held in place by a thin plastic layer that keeps it adhered to the internal surface of the tube.

This is in contrast with other reinforced tubes in which the reinforcing wire is embedded within the wall of the tube.

Such a foreign body within the lumen of an endotracheal tube can potentially cause airway management problems, including difficulty suctioning the trachea and advancing a fiberoptic instrument or airway obstruction. From our experience, it is possible for the reinforcing wire to become dislodged during normal use of this tube. For instance, a patient could bite on the tube separating the wire. Anesthesiologists should be aware of this possibility. Clinicians are cautioned not to excessively bend the NIM® tube and to carefully inspect its lumen before each use.

Sundara K. Rengasamy, M.D.,* Rafael A. Ortega, M.D. * Boston University Medical Center, Boston, Massachusetts. sundarakumaran.rengasamy@bmc.org

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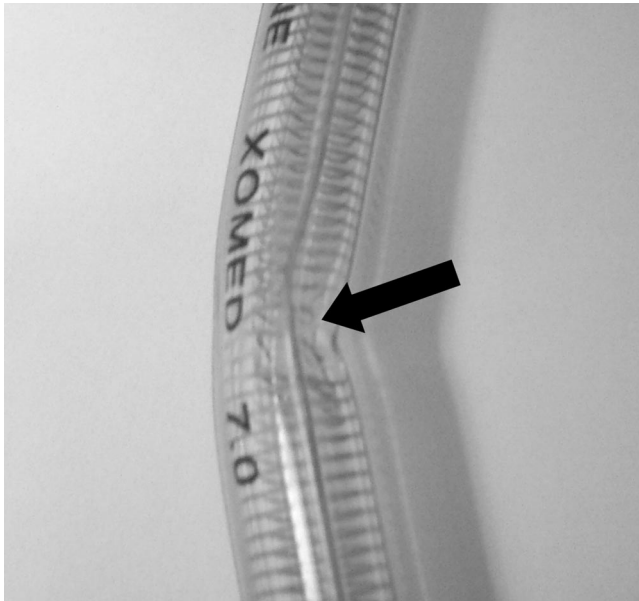


Fig. 1. Metal coil inside the lumen (arrow) of NIM® endotracheal tube at the kinked site.

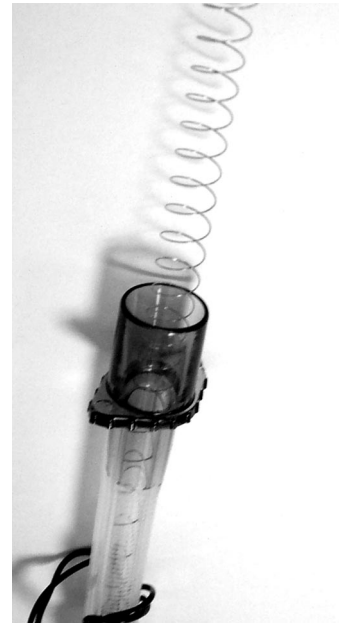


Fig. 2. Reinforcement metal coil pulled out.

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Linezolid-Bupropion Interaction as Possible Etiology of Severe Intermittent Intraoperative Hypertension?

To the Editor:—Linezolid is a valuable drug that is finding increased use in the hospitalized surgical patient for the treatment of infections resulting from resistant, gram-positive organisms. Along with its known efficacy as an antibacterial agent, linezolid is a mild, reversible monoamine oxidase inhibitor.¹ Reviews on the subject of its monoamine oxidase inhibitor-like profile have expressed caution about the use of linezolid in the clinical setting, specifically when combined with sympathomimetic agents,² but there have been few, if any, reported clinical examples of a significant interaction. Recently, however, we observed unexpected intraoperative hemodynamic lability, as well as severe intermittent hypertension, in a psychiatric patient maintained on bupropion who was subsequently placed on linezolid for treatment of an infected vascular graft. We raise the concern that we have seen one of the first examples in the perioperative setting of a potentially dangerous interaction between linezolid and bupropion.

The patient was a 57-yr-old male status post axillary-femoral bypass graft who presented to the emergency room with evidence of a graft infection and was admitted for antibiotics. After a trial of several antibiotics, he was placed on linezolid for treatment of resistant, gram-positive organisms. As an outpatient, he had been stably maintained on bupropion for long-standing depression; this drug was continued throughout his hospital course. After about 24 h of linezolid therapy, the patient was taken to the operating room for graft removal, where he underwent a propofol/succinylcholine induction with standard doses and a maintenance anesthetic of 1.5% isoflurane and fentanyl 250 μ g. His intraoperative course was notable for several episodes of severe hypertension (as high as 260/145 mmHg), despite an otherwise stable anesthetic. The unexpected hemodynamic lability was severe enough to result in an unplanned admission to the intensive

care unit, where the patient had an unremarkable postoperative course.

The possibility of a significant drug interaction between linezolid and bupropion was suspected immediately and is supported by a careful analysis of the underlying pharmacologic mechanisms. Bupropion is an antidepressant that, in concert with its primary metabolite hydroxybupropion, acts as a norepinephrine reuptake inhibitor as well as a mild dopamine reuptake inhibitor.³ Both norepinephrine and dopamine are monoamine compounds metabolized by monoamine oxidase. The use of bupropion with older, more traditional monoamine oxidase inhibitor drugs (such as phenelzine and tranylcypromine) has long been contraindicated in standard psychiatric practice because of the risk of a hypertensive crisis.³ The older monoamine oxidase inhibitors do differ from linezolid in that they are strong, irreversible inhibitors of monoamine oxidase. As linezolid is a weak, reversible monoamine oxidase inhibitor, it had not been appreciated that coadministration with bupropion might cause a similar hypertensive state.

However, linezolid clearly resembles the stronger monoamine oxidase inhibitors in its capacity to interact adversely with certain drugs. Combining the older monoamine oxidase inhibitors with serotonergically active drugs, such as selective serotonin inhibitors,^{4,5} meperidine,⁶ and dextromethorphan,⁷ may lead to a severe central serotonin syndrome.⁸ Similarly, linezolid has been implicated in producing a central serotonin syndrome when combined with either paroxetine⁹ or citalopram¹⁰ (both selective serotonin reuptake inhibitors). Furthermore, it is known that sympathomimetic agents, when administered in combination with the traditional monoamine oxidase inhibitors, may produce severe hypertensive events.¹¹ Again, linezolid mimics the interaction profile of the stronger monoamine oxidase inhibitors by producing statistically significant increases in blood pressure when

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combined with pseudoephedrine and phenylpropanolamine.¹² Based on this information, it is not surprising that linezolid acts like a more traditional monoamine oxidase inhibitor when combined with bupropion, especially in the context of the well-known physiologic stimulation and adrenergic stress of surgery.¹³

It is hoped that this letter will alert clinicians to the monoamine oxidase inhibitor-like profile of linezolid and prevent the combination of linezolid with agents that enhance the function of any of the monamines (serotonin, norepinephrine, epinephrine, and dopamine).

Catherine Marcucci, M.D.,* Neil B. Sandson, M.D., Joyce A. Dunlap, C.R.N.A. * University of Maryland Medical System and Baltimore Veterans Administration Hospital. sandson.marcucci@comcast.net

References

1. Zyvox [package insert]. Kalamazoo, MI: Pharmacia and Upjohn Company, 2001
2. French G: Safety and tolerability of linezolid. *J Antimicrobial Chemother* 2003; 51(Suppl 2):II45-53
3. Wellbutrin [package insert]. Research Triangle Park, NC: GlaxoSmithKline, 2001
4. Graber MA, Hoehns TB, Perry PJ: Sertraline-phenelzine drug interaction: A serotonin syndrome reaction. *Ann Pharmacother* 1994; 28:732-5
5. Beasley CM Jr, Masica DN, Heiligenstein JH, Wheadon D, Zerbe R: Possible monoamine oxidase inhibitor-serotonin uptake inhibitor interaction: Fluoxetine clinical data and preclinical findings. *J Clin Psychopharmacol* 1993; 13:312-20
6. Sporer A: The serotonin syndrome: Implicated drugs, pathophysiology and management. *Drug Saf* 1995; 13:94-104
7. Bem JL, Peck R: Dextromethorphan: An overview of safety issues. *Drug Saf* 1992; 7:190-9
8. Bodner RA, Lynch T, Lewis L, Kahn, D: Serotonin syndrome. *Neurology* 1995; 45:219-23
9. Wiggen CL, Goetz MB: Serotonin syndrome and linezolid. *Clin Infect Dis* 2002; 34:1651-2
10. Bernard L, Stern R, Lew D, Hoffmeyer P: Serotonin syndrome after concomitant treatment with linezolid and citalopram. *Clin Infect Dis* 2003; 36:1197
11. Phenelzine [package insert]. Morris Plains, NJ: Parke-Davis, 1998
12. Hendershot PE, Antal EJ, Welshman IR, Batts D, Hopkins N: Linezolid: Pharmacokinetic and pharmacodynamic evaluation of coadministration with pseudoephedrine HCl, phenylpropanolamine HCl, and dextromethorphan HBr. *J Clin Pharmacol* 2001; 41:563-72
13. Breslow MJ: Clinical implications of the stress response to surgery: Principles and Practice of Anesthesiology, 2nd edition. Edited by Longnecker DE, Tinker JH, Morgan GE. St. Louis, Mosby 1998, pp 117-123

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