

Pressure-support Ventilation in the Operating Room

To the Editor:—I read with interest the study by Jaber *et al.*¹ and the accompanying editorial by Tantawy and Ehrenwerth² regarding pressure-support ventilation (PSV). The Jaber study is noteworthy for documenting that the performance of PSV using modern anesthesia ventilators approaches the performance of an intensive care unit ventilator. The editorial correctly indicates that the testing was not performed under conditions of varying lung compliance and airway resistance that influence the ventilation result obtained when using PSV. Nevertheless, PSV is most likely to find application in the operating room for patients who can be allowed to breathe spontaneously rather than for patients who present a significant ventilation challenge. The question of whether we need PSV in the operating room is germane to clinical practice and needs to be addressed from the perspective of the clinical indications and potential advantages for the anesthetized patient.

Pressure-support ventilation was developed in the intensive care unit to allow patients to breathe spontaneously while intubated for long periods of time and for patients who are in the process of weaning from ventilator support. The clinical indications for PSV in the intensive care unit are not relevant to the operating room. Indeed, for many years, spontaneous ventilation was not used commonly in the operating room because of the work of breathing imposed by the airway and circuit, and the potential for respiratory compromise. The introduction of the laryngeal mask airway reintroduced spontaneous ventilation to anesthesia practice, and we have used this technique despite having learned in the intensive care unit that the work of breathing imposed by an artificial airway and breathing circuit limits the advantage of spontaneous ventilation. Fortunately, studies indicate that PSV can improve oxygenation and ventilation, and even reduce the work of breathing for anesthetized adult and pediatric patients when using a laryngeal mask airway.^{3,4} Using PSV in conjunction with a laryngeal mask airway may well extend the use of laryngeal mask airways to longer procedures as effective ventilation can be achieved.

The potential clinical impact of PSV in the operating room extends well beyond supporting patients with a laryngeal mask airway. During emergence from anesthesia, establishing consistent spontaneous ventilation is useful to help ensure that a patient will continue to breathe effectively after extubation. Concern for hypoventilation and slow elimination of anesthetic agents has been an impediment to using spontaneous ventilation during emergence. PSV will facilitate the use of spontaneous ventilation during emergence by reducing the work of breathing and improving minute ventilation and may lead to more rapid elimination of anesthetic vapors. Certainly, establishing a consistent pattern of regular spontaneous ventilation before extubation is desirable before removing an artificial airway and ventilatory support.

Spontaneous ventilation has other advantages over controlled ventilation that may be realized now that PSV is available in the operating room. The ability to assess anesthetic depth is enhanced when the rate,

rhythm, and depth of breathing can be observed. Titration of anesthetic agents, most notably opioids, is also facilitated. The abnormal ventilation/perfusion ratios that can occur during controlled ventilation may be less likely to occur when supported spontaneous ventilation is used rather than controlled mechanical ventilation. There is even evidence to suggest that PSV set to provide continuous positive airway pressure or bilevel positive airway pressure can be used in awake patients to prevent atelectasis during the preoxygenation process.⁵ Finally, spontaneous ventilation offers the safety advantage of knowing that the patient will likely continue to breathe even if an artificial airway should become dislodged.

Pressure-support ventilation has the potential to significantly influence anesthetic practice in many ways. The Jaber study provides data to allow clinicians to use PSV with the confidence of knowing that it will perform similarly to PSV used in the intensive care unit. We should begin to learn about this new modality, selecting patients who are easy to ventilate, where the risk of using PSV is not significant. As we gain experience, the clinical indications and advantages in the operating room will become more obvious. I welcome this new tool and believe it will become widely used in anesthetic practice to facilitate emergence, titrate anesthetic drug administration, improve intraoperative gas exchange, and potentially enhance patient safety by making patients less reliant on an artificial airway and mechanical ventilator. The question of whether we need PSV in the operating room will only be answered definitively by using it. The Jaber study provides the information needed to use PSV in the operating room with confidence.

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References

1. Jaber S, Tassaux D, Sebbane M, Pouzeratte Y, Battisti A, Capdevila X, Eledjam JJ, Jolliet P. Performance characteristics of five new anesthesia ventilators and four intensive care ventilators in pressure-support mode: A comparative bench study. *ANESTHESIOLOGY* 2006; 105:944-52
2. Tantawy H, Ehrenwerth J: Pressure-support ventilation in the operating room: Do we need it? *ANESTHESIOLOGY* 2006; 105:872-3
3. Brimacombe J, Keller C, Hormann C: Pressure support ventilation *versus* continuous positive airway pressure with the laryngeal mask airway: A randomized crossover study of anesthetized adult patients. *ANESTHESIOLOGY* 2000; 92:1621-3
4. von Goedecke A, Brimacombe J, Hörmann C, Jeske H, Kleinsasser A, Keller C: Pressure support ventilation *versus* continuous positive airway pressure ventilation with the ProSeal™ laryngeal mask airway: A randomized crossover study of anesthetized pediatric patients. *Anesth Analg* 2005; 100:357-60
5. Coussa M, Proietti S, Schnyder P, Frascarolo P, Suter M, Spahn D, Magnusson L: Prevention of atelectasis formation during the induction of general anesthesia in morbidly obese patients. *Anesth Analg* 2004; 98:1491-5

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In Reply:—We appreciate Dr. Feldman's comments on our editorial.¹ Before extubating patients in the operating room, the anesthesiologist typically evaluates the patient's respiratory effort, tidal volume, and respiratory rate, as well as the patient's oxygen saturation and carbon dioxide elimination. To compensate for the difficulties of breathing through an endotracheal tube and the breathing circuit, we frequently apply continuous positive airway pressure using the adjust-

able pressure-limiting valve on the anesthesia machine. Knowing that continuous positive airway pressure is functionally a combination of pressure-support ventilation and positive end-expiratory pressure, the level of support is typically minimal. If the level of support were significant, the patient could be falsely judged as ready for extubation. At the conclusion of the procedure, the adjustable pressure-limiting valve is usually fully opened so that the patient's respiratory perfor-

mance can be evaluated with zero support. If the pressure-support ventilation mode is used until the patient is extubated, we think that the anesthesiologist may get a false sense of security regarding the patient's readiness for extubation. Although this is a common practice in the intensive care unit, we are not sure whether the same practice applies to the operating room. Patients in the operating room temporarily have an acute change in their respiratory status, whereas intensive care unit patients have a more prolonged weaning period before extubation.

Although using the pressure-support ventilation mode with the ventilator in the operating room may be new for some anesthesiologists, anesthesiology residents are familiar with it from their training in the intensive care unit. We think that it is important to emphasize to our residents the need to first look at the patient and do a clinical assess-

ment before relying on mechanical devices. Therefore, the question is still whether there is enough benefit to the patient to justify the increase in cost to add the pressure-support ventilation mode.

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Reference

1. Tantawy H, Ehrenwerth J: Pressure-support ventilation in the operating room: Do we need it? *ANESTHESIOLOGY* 2006; 105:872-3

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In Reply:—We thank Dr. Feldman for his interesting remarks regarding our recent contribution to *ANESTHESIOLOGY*, which showed that for the five tested anesthesia ventilators, pressure-support ventilation (PSV) functioned correctly.¹ Indeed, our laboratory study¹ showed that regarding trigger sensitivity and the system's ability to meet inspiratory flow during PSV, the most recent anesthesia ventilators have performances comparable to those of the modern intensive care unit ventilators. We agree with Dr. Feldman that PSV will facilitate the use of spontaneous breathing with both a laryngeal mask airway and an endotracheal tube. As stated in the discussion of our article¹ and in the accompanying editorial by Tantawy and Ehrenwerth,² the PSV mode may be used in the operating room in spontaneously breathing patients who are undergoing peripheral surgery more often during local-regional anesthesia combined with light sedation with a laryngeal mask airway³ or an endotracheal tube. However, our study¹ only provides the information needed to use PSV in the operating room with confidence, and further clinical studies should now be conducted to better

define the indications and settings of PSV during both local-regional and general anesthesia.

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References

1. Jaber S, Tassaux D, Sebbane M, Pouzeratte Y, Battisti A, Capdevila X, Eledjam JJ, Joliet P: Performance characteristics of five new anesthesia ventilators and four intensive care ventilators in pressure-support mode: A comparative bench study. *ANESTHESIOLOGY* 2006; 105:5944-52
2. Tantawy H, Ehrenwerth J: Pressure-support ventilation in the operating room: Do we need it? *ANESTHESIOLOGY* 2006; 105:872-3
3. Brimacombe J, Keller C, Hormann C: Pressure support ventilation versus continuous positive airway pressure with the laryngeal mask airway: A randomized crossover study of anesthetized adult patients. *ANESTHESIOLOGY* 2000; 92:1621-3

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Awareness in a Community-based Anesthesia Practice

To the Editor:—I read with interest the recent report by Pollard *et al.*¹ on the incidence of awareness in a regional medical system in the United States. The incidence of awareness in their study was comparatively low at approximately 1 in 15,000. This is an order of magnitude less than numerous other large studies conducted in the United States and around the world (incidence around 1 in 1,000).²⁻⁵ The authors attribute this difference to “the anesthesia providers involved, the types of anesthetics chosen, and/or investigational bias.” I believe that their result may have been due, in part, to investigational biases of their own.

The authors did not define awareness in their report (awareness is often defined as “postoperative recall of intraoperative events”⁴). They imply that the definition was “recall or possible recall” but later mention that cases of dreaming may have been missed by their data collection method. Dreaming during anesthesia is a remarkably common phenomenon that is rarely indicative of awareness and should not be confused with it.⁶ In studies of incidence, the primary endpoint needs to be prospectively and precisely defined.

In addition, the authors did not ask their patients a direct question

about awareness. They omitted the question used by researchers in all of the large studies with which they wish to compare their work²⁻⁵: “Can you remember anything in between these two periods (that is, between going to sleep and waking up)?” Would a study on postoperative vomiting be valid if the patients were not asked “Did you vomit?” Moerman *et al.*⁷ documented that patients are reluctant to report awareness without being questioned directly. In addition, in my routine use of this question in research and clinical practice, I have not found that it alarms patients.^{6,8} The omission of this question is a potent reason for the lower incidence of awareness reported in this study.

The authors comment on possible investigational bias in previous studies, without discussing it any further or addressing the potential for investigational bias of their own. One could make the case that the aim of previous studies was to detect every case of awareness that had occurred. One could also make the case that an internal quality assurance program such as the one described in this study may be designed to *minimize* the incidence of adverse events such as awareness. The authors did not describe the procedures for adjudication of awareness reports, impanel an independent endpoint adjudication committee (with members from outside their practice group), or provide a description or count of awareness reports that were rejected.⁸ Readers therefore cannot interpret for themselves the subjective reports of awareness. These factors together throw doubt on the accuracy of their awareness incidence.

In the past 10 yr, Dr. Leslie has received support from Aspect Medical, Inc., Natick, Massachusetts, in the form of grants for research and travel; she has also received support from the American Society of Anesthesiologists for presentations at state society meetings.

A lower incidence of awareness may be expected in a community-based setting with relatively few patients at high risk of awareness, relatively few anesthesiologists or nurse-anesthetists in training, a relative abundance of patients who were not given neuromuscular blockers, and a protocolized anesthesia care plan that may have promoted more-than-adequate general anesthesia. Unfortunately, Pollard *et al.* did not provide data about any of these potential confounding factors, and their methods cast doubt on their conclusion that the incidence of awareness is 1 in 15,000 in their practice.

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References

1. Pollard R, Coyle J, Gilbert R, Beck J: Intraoperative awareness in a regional medical system: A review of 3 years' data. *ANESTHESIOLOGY* 2007; 106:269-74

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Don't Ask, Don't Tell

To the Editor:—We read with interest the study by Pollard *et al.*¹ suggesting that the incidence of awareness during anesthesia is less than one tenth of that which has been previously described. We are concerned about the implications of these results and wish to comment on the methodology used in this study.

There are several prospective studies in the literature^{2,3} that suggest the incidence of awareness during general anesthesia is approximately 1 in 1,000. The common features of all of these studies are that they used the same brief questionnaire and that they interview patients on a second occasion approximately 1 week after surgery.

The data gathered by Pollard *et al.*¹ was not designed to elucidate the incidence of awareness. Rather, it is a quality improvement database. We have some concerns about the robustness of the data. It is our general impression that quality assurance databases are not collected with the same rigor as research databases. From the article, it seems that there were more than 175,000 completed interviews (2 interviews per patient), which means more than 350,000 data points. Were the answers to all questions recorded in every case? Or are there missing data? If so, how much is missing and how were missing data treated? Another cause for concern is the failure to capture approximately 17% of the total database for unknown reasons. This may also have led to an underestimation of the incidence of awareness.

The authors used for detection of awareness a modification of the interview described by Liu *et al.*⁴ (who modified the questionnaire of Brice *et al.*⁵), which has been the standard for years. Instead of asking the patients the crucial question "Do you remember anything between going to sleep and waking up?" they asked, "Did you have any dreams while you were asleep for surgery?" thus confusing dreaming and awareness. A further possible confusion may have been created by adding what seems like irrelevant questions, *e.g.*, "Were you put to sleep gently?" The argument that no one has proved that one set of questions is better than the other is factual but superfluous. The Liu *et al.*⁴ modification of the interview described by Brice *et al.*⁵ has been used by several independent investigators over the years who have demonstrated its reliability, robustness, and absence of suggestibility. It is difficult to think of a further modification for the better.

Dr. Sebel is a paid consultant for Aspect Medical Systems, Inc., Norwood, Massachusetts.

2. Myles P, Williams D, Hendrata M, Anderson H, Weeks A: Patient satisfaction after anaesthesia and surgery: Results of a prospective survey of 10,811 patients. *Br J Anaesth* 2000; 84:6-10

3. Sandin R, Enlund G, Samuelsson P, Lennmarken C: Awareness during anaesthesia: A prospective case study. *Lancet* 2000; 355:707-11

4. Sebel P, Bowdle T, Ghoneim M, Rampil I, Padilla R, Gan T, Domino K: The incidence of awareness during anesthesia: A multicenter United States study. *Anesth Analg* 2004; 99:833-9

5. Liu W, Thorp T, Graham S, Aitkenhead A: Incidence of awareness with recall during general anaesthesia. *Anaesthesia* 1991; 46:435-7

6. Leslie K, Skrzypek H, Paech M, Kuroski I, Whybrow T: Dreaming during anesthesia and anesthetic depth in elective surgery patients: A prospective cohort study. *ANESTHESIOLOGY* 2007; 106:33-42

7. Moerman N, Van Dam F, Oosting J: Recollections of general anaesthesia: A survey of anaesthesiological practice. *Acta Anaesthesiol Scand* 1992; 36:767-71

8. Myles P, Leslie K, McNeil J, Forbes A, Chan M, Group B-AT: A randomised controlled trial of BIS monitoring to prevent awareness during anaesthesia: The B-Aware Trial. *Lancet* 2004; 363:1757-63

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Other studies report an incidence of dreaming around 6%. The authors specifically asked about dreaming but presented no data related to this question. How many patients dreamed? Were these dreams ever disturbing?

The other, prospective, studies on the incidence of awareness conducted the second interview later than in the study of Pollard *et al.*,¹ where the second interview was conducted at 48 h. Sandin *et al.*² found that only 65% of cases of awareness are elucidated on the first interview. The other 35% of cases are reported on the second interview a week (or more) later. This may have contributed to a substantial underestimation of the incidence of awareness.

In our opinion, the elimination of the "crucial" question from the modified Brice interview^{4,5} means that the data from this study cannot be compared directly with the prospective data reported elsewhere. It is well known⁶ that patients do not spontaneously report episodes of awareness to their anesthesiologist. If you don't ask about awareness, patients are not going to tell you about it.

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References

1. Pollard RJ, Coyle JP, Gilbert RL, Bech JE: Intraoperative awareness in a regional medical system: A review of 3 years' data. *ANESTHESIOLOGY* 2007; 106:269-74

2. Sandin RH, Enlund G, Samuelsson P, Lennmarken C: Awareness during anaesthesia: A prospective case study. *Lancet* 2000; 355:707-11

3. Sebel PS, Bowdle TA, Ghoneim MM, Rampil IJ, Padilla RE, Gan TJ, Domino KB: The incidence of awareness during anesthesia: A multicenter United States study. *Anesth Analg* 2004; 99:833-9

4. Liu WH, Thorp TAS, Graham SG, Aitkenhead AR: Incidence of awareness with recall during general anaesthesia. *Anaesthesia* 1991; 46:435-7

5. Brice DD, Hetherington RR, Utting JE: A simple study of awareness and dreaming during anaesthesia. *Br J Anaesth* 1970; 42:535-41

6. Moerman N, Bonke B, Oosting J: Awareness and recall during general anesthesia: Facts and feelings. *ANESTHESIOLOGY* 1993; 79:454-64

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In Reply:—Thank you for the opportunity to respond to the letters by Dr. Leslie and by Dr. Sebel *et al.* We welcome the opportunity to clear up some misconceptions about our study¹ that are put forward in those letters.

Dr. Leslie expressed concern that we had not defined awareness in our study. Dr. Brice *et al.*² offered this definition: “awareness has been taken to mean the ability to recall, with or without prompting, any events which occurred during the period at which it was thought the patient was fully unconscious.” This has been an accepted definition for several decades and we, perhaps mistakenly, did not think it needed to be repeated.

Dr. Leslie and Dr. Sebel *et al.* expressed concerns over the questions used in the study. We used the questions designed to elicit awareness as defined by Dr. Brice in 1970.² As was described in the article, we substituted two nonawareness questions with two anesthesia-related ones to increase sensitivity. Despite the correspondents’ assertions, it is nonsensical to suggest that this substitution would cause a greater than 10-fold decrease in the incidence of anesthesia recall. Dr. Sebel *et al.* themselves admit that there is no evidence that differing modifications of the Brice questions are any more or less effective at detecting awareness. We also believe that the correspondents are mistaken in their belief that direct questions are required to elicit recall. The use of nonthreatening questions has been previously advocated as a valid technique of eliciting the incidence of recall in patients,³ thus obviating the need for the “crucial” question. It is our clinical experience that patients respond more openly to indirect and nonthreatening questions. We would also like to mention that with two interviews, a follow-up survey on anesthesia experience, and heightened public awareness of this problem, we still have not heard of any other cases.

Dr. Leslie and Dr. Sebel *et al.* expressed some confusion with regard to the mention of dreaming in the study. It was not our intention to discuss the incidence or categorization of dreams in the article. The issue was only mentioned because an in-depth analysis of dreaming during anesthesia was not undertaken in the postoperative period.

Dr. Leslie and Dr. Sebel *et al.* expressed concern about our use of a quality assurance program to collect data on patients. This process attempts to collect data on all patients undergoing anesthesia. The continuous quality improvement team completes this evaluation tool and ensures that all questions are answered and documented at several points during the patients’ hospital stay. As was mentioned in the article, the validity of the quality assurance data are confirmed by an independent audit performed retrospectively, using a statistically significant sample size to ensure the accuracy of collected data. The article reports all cases and suspected cases uncovered for the study period. Readers can therefore examine the reported cases and make their own assessment as to whether possible cases of recall should have been included in this study. The article emphasizes that the purpose of such a program is to identify and remedy the causes of such instances through education and system process modification, not through obfuscation. Dr. Leslie is therefore correct in that a quality assurance program is designed to minimize the incidence of adverse events.

Dr. Sebel *et al.* question the robustness of the data. We would like to reiterate that the purpose of a quality assurance process is to identify and monitor adverse outcomes to decrease these incidences through education and systems processes modification. This study illustrates the ongoing institution of a quality assurance process in a hospital system where new locations are added as the anesthesia group expands its practice. The majority of the patients included in the study were from the level I trauma and tertiary referral hospital where the

system originated. Here, the quality assurance system failed to capture less than 10% of all cases. This compares favorably with the study of Dr. Sebel *et al.*,⁴ where they were unable to complete 33% of their interviews on enrolled patients. If the correspondents are concerned about the loss of comparatively few data points in our study, what must this say about their own? After all, a quality assurance database strives to collect information on all patients, whereas a research database is under no such constraint. The general impression that we are left with is that the use of a passive research database using recruited patients does a disservice to those same patients we are charged to protect.

Dr. Leslie suggests that the lower incidence of intraoperative awareness demonstrated in this study is due to lower risk patients in a community-based setting. This assertion conveniently overlooks the fact that the primary site in the study is a level I trauma center and tertiary referral hospital serving a population of several million. It is possible, but very unlikely, that this is one of the nation’s busiest hospitals serving “not really sick” patients. The article discussed the fact that this hospital has a similar acuity, but a higher volume, than the three other teaching hospitals in North Carolina.

Dr. Leslie finishes by alleging that the study in question may have been influenced by investigational biases. Unlike the correspondents, none of the authors work for, or are compensated in any fashion by, a corporation that stands to make money from the data. Nor is there any intent or ability to sell or profit from the study. There have been multiple articles on the use of corporate funds to conduct research.^{5,6} Lexchin *et al.*⁷ goes as far as to state that systemic bias favors products that are made by the company funding the research. One could rephrase one of Dr. Leslie’s comments by saying that the aim of previous studies was to inflate the incidences of intraoperative awareness.

In summary, we understand that Dr. Leslie and Dr. Sebel *et al.* are concerned about the implications of the study; however, we believe that these data represent a true picture of anesthesia awareness in clinical practice. The use of an independently audited quality assurance program allows practitioners to rapidly identify flaws in anesthetic techniques and practices, and to make the appropriate changes to decrease their incidence.

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References

1. Pollard R, Coyle J, Gilbert R, Beck J: Intraoperative awareness in a regional medical system: A review of 3 years’ data. *ANESTHESIOLOGY* 2007; 106:269–74
2. Brice DD, Hetherington RR, Utting JE: A simple study of awareness and dreaming during anaesthesia. *Br J Anaesth* 1970; 42:535–41
3. Fleischer LH, Glass PSA: Can we prevent recall during anesthesia? Evidence Based Practice of Anesthesiology. Edited by Fleisher LA. Philadelphia, WB Saunders, 2004, pp 223–7
4. Sebel PS, Bowdle TA, Ghoneim MM, Rampil JJ, Padilla RE, Gan TJ, Domino KB: The incidence of awareness during anesthesia: A multi-center United States study. *Anesth Analg* 2004; 99:833–9
5. Tallon D, Chard J, Dieppe P: Relation between agendas of the research community and the research consumer. *Lancet* 2000; 355:2037–40
6. Bekelman JE, Yan L, Gross CP: Scope and impact of financial conflicts of interest in biomedical research. *JAMA* 2003; 289:454–65
7. Lexchin J, Bero LA, Djulbegovic B, Clark O: Pharmaceutical industry sponsorship and research outcome and quality: Systemic review. *BMJ* 2003; 326:1167–70

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Use of the Airtraq[®] Laryngoscope

To the Editor:—I read with interest the case report by Dhonneur *et al.*¹ describing their use of the Airtraq[®] laryngoscope (AL; Prodol Meditec S.A., Vizcaya, Spain) in morbidly obese patients undergoing emergency cesarean delivery. I congratulate these authors on the incorporation of this recently introduced intubating device into their practice. However, there is surprisingly little discussion of the actual AL in their article.

The AL is a disposable laryngoscope that allows viewing of the vocal cords without a straight line of sight from outside of the patient to the vocal cords. The AL light should be turned on approximately 1 min before use, to allow heating of the lens and to avoid fogging. The neck of the patient can be positioned in a neutral position. The curved blade is inserted in the center of the tongue. While looking through the viewer (or optional video), it is advanced further such that the epiglottis is identified, and the tip is placed into the vallecula. The handle is then lifted straight up to expose the vocal cords. The AL has a channel that is used to direct the tube through the vocal cords once visualization has been achieved. I have successfully used the AL, and one important difficulty that was not stated in the letter is that the tube may pass posteriorly as it leaves its guide, and further manipulation of the handle of the AL may be needed to allow the endotracheal tube to be successfully passed through the vocal cords.

An important issue not discussed by the authors is the challenge of obtaining proficiency while at the same time controlling cost. The manufacturer recommends two to four uses before use in a patient with a difficult intubation. As in all techniques for intubation, there is a learning curve. ALs cost approximately \$80 each and cannot be reused. This could pose a large expense to train an entire department and then maintain skills. It could also be a major ongoing expense if used frequently. If skills could be obtained in a simulator, the AL could be an important asset if kept on the difficult airway cart as a backup technique, but not used regularly. Obtaining the AL was discussed by our equipment committee but was not thought to be cost-effective for

training an entire department, which has more than 100 members. Dhonneur *et al.*¹ stated that the anesthesiologists had “performed the clinical learning process with the AL” but did not describe what this was; this information would have been helpful.

The authors state that “There are only two validated airway devices allowing visualization of the glottis without alignment of oral and pharyngeal axes: the LMA CT_rach (SEBAC, Pantin, France) and the AL.” This is not true; there are multiple such laryngoscopes now available. The Glide scope (Saturn Biomedical, Burnaby, British Columbia, Canada) is a nondisposable video laryngoscope that is easy to use and allows visualization of the vocal cords without alignment of the axes. The endotracheal tube is held in the right hand and can be manipulated independently from the laryngoscope. The first laryngoscope developed, which combined fiberoptic viewing with a curved rigid blade, was the Bullard laryngoscope (Circon ACMI, Stamford, CT).

The authors also stated that the Sellick maneuver was applied before induction; this would potentially be uncomfortable for the patient. The cricoid should be palpated before induction, but the actual cricoid pressure should not be applied until the patient is starting to fall asleep. It has been recommended to apply 10 N (1 kg) of pressure as the patient is falling asleep and increase to 30 N after the patient becomes unconscious.²

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References

1. Dhonneur G, Ndoko S, Amathieu R, Housseini LE, Poncelet C, Tual L: Tracheal intubation using the Airtraq[®] in morbidly obese patients undergoing emergency cesarean delivery. *ANESTHESIOLOGY* 2007; 106:629–30
2. Landsman I: Cricoid pressure: Indications and complications. *Pediatr Anesth* 2004; 14:43–7

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Conquering the Management of the Difficult Airway in Obstetric Cases

To the Editor:—We are intrigued by the report of Dhonneur *et al.*¹ and would like to congratulate them for successfully intubating the trachea with an Airtraq[®] laryngoscope (AL; Guangzhou Intmed Medical Appliance Co., Tianhe, Guangdong, China) in two morbidly obese parturients undergoing “emergency” cesarean delivery.

Although it is an interesting case report, in our opinion, it raises issues regarding use of equipment for difficult airways in emergency cesarean delivery. The authors¹ seem to have had training on a manikin and to have performed the clinical learning process, and they suggest that the AL was efficient in cases of difficult intubation. It is not clear whether the clinical learning process included the use of the AL in straightforward nonobstetric cases or elective cesarean delivery or/and nonemergency difficult airway scenarios. Somehow, they managed to

include the AL in their algorithm for the emergency difficult airway in obstetrics.

The only published literature for use of the AL in the difficult airway is by Maharaj *et al.*² Maharaj *et al.*² compared the AL's performance with that of the Macintosh laryngoscope in five simulated scenarios of difficulty of tracheal intubation on a manikin (SimMan; Laerdal, Kent, United Kingdom). Although they concluded that the AL was superior to the Macintosh laryngoscope in difficult airway scenarios, the only scenario in which the AL was superior to the Macintosh laryngoscope was the manikin with tongue edema. But even in that scenario, 2 of 25 anesthesiologists could not intubate the trachea with the AL. In our opinion, this study alone does not validate using the AL for difficult airway scenarios in obstetric emergencies.

There seems to be an urgency to conquer the management of the difficult airway in obstetric cases, but is there a danger of losing the conventional and tested skills (e.g., use of a McCoy laryngoscope for the first case¹) while rushing to find a magic bullet?

The conclusion of Dhonneur *et al.*¹ to consider the AL as a primary airway management device for the difficult airway in emergency caesarean delivery is, in our opinion, premature and daring.

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Comparing the Airtraq[®] with the LMA CTrach[™]

To the Editor:—I read with great interest the case report by Dhonneur *et al.*¹ using the Airtraq[®] (King Systems, Noblesville, IN) optical laryngoscope after failed direct laryngoscopy in two patients requiring emergency caesarean delivery. Placing an Airtraq[®] (or any of the new video-laryngoscopes, e.g., GlideScope[®] [Verathon, Bothell, WA], McGrath[®] [LMA North America, San Diego, CA]) as a brief plan B after a failed direct laryngoscopy in obstetrics may be an evolving new standard of practice for an emergency caesarean delivery. However, comparing the Airtraq[®] intubation time with the LMA CTrach[™] (LMA North America, San Diego, CA) intubation time (<1 min *vs.* 3 min) is not an entirely appropriate comparison.¹ The CTrach time of 3 min includes establishing ventilation and removing the CTrach airway after intubation is confirmed.² The ventilatory capacity of the CTrach is arguably equally important to its effectiveness as an intubation conduit during airway resuscitation.³ It is well known how quickly a term parturient can desaturate during laryngoscopy. The CTrach (like the intubating laryngeal mask airway) is an effective ventilatory device with ventilatory success rates of greater than 99%.^{2,4} If intubation is not successful, the presence of an effective airway can be lifesaving. The CTrach gives the operator time to optimize the laryngeal view and the

References

1. Dhonneur G, Ndoko S, Amathieu R, Housseini LE, Poncelet C, Tual L: Tracheal intubation using the Airtraq[®] in morbid obese patients undergoing emergency caesarean delivery. *ANESTHESIOLOGY* 2007; 106:629–30
2. Maharaj CH, Higgins BD, Harte BH, Laffey JG: Evaluation of intubation using the Airtraq or Macintosh laryngoscope by anaesthetists in easy and simulated difficult laryngoscopy: A manikin study. *Anaesthesia* 2006; 61:469–77

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In Reply:—We read with interest the letters to the Editor regarding our case reports, published recently in *ANESTHESIOLOGY*, describing the use of the Airtraq[®] laryngoscope (AL) in morbidly obese parturients undergoing emergency caesarean delivery.¹ We think that it is a privilege to have our reports reviewed by such experts in the field of airway management.

In regard to Dr. Neustein's comments, positioning the AL in a difficult airway management algorithm is the result of a long educational and clinical process conducted through an airway management teaching program begun almost 5 yr ago with the validation of a predefined algorithm for the unexpected difficult airway in the operating room² and then in prehospital conditions.³ We have been conducting for 3 yr in France the first national University Diploma of Airway Management program, and now this French teaching program has evolved into a European diploma, the EXCLAM (Excellence Level in Airway Management). In 2005, with the arrival on the French market of the LMA CTrach[™] (CT; SEBAC, Pantin, France), we have implemented our algorithm built in case of the unexpected difficult airway, and finally 1 yr ago we incorporated one of the new generation of tracheal intubation devices that we call the "glottiscopes," such as the

patient's physiologic parameters before attempting intubation.^{3,5} Liu *et al.*² report a 99% first-pass intubation success in the 84% of patients whose larynx was seen on the CTrach monitor. In the remaining 16%, the CTrach functioned as an intubating laryngeal mask airway would, with corresponding intubation/ventilation success rates. Ventilation and oxygenation, not solely intubation, are the primary goals of effective airway resuscitation.

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References

1. Dhonneur G, Ndoko S, Amathieu R, Housseini L, Poncelet C, Tual L: Tracheal intubation using the Airtraq[®] in morbid obese patients undergoing caesarean delivery. *ANESTHESIOLOGY* 2007; 106:629–30
2. Liu E, Goy R, Chen F: The LMA CTrach[™], a new laryngeal mask for endotracheal intubation under vision: Evaluation of 100 patients. *Br J Anaesth* 2006; 96:396–400
3. Goldman A, Rosenblatt W: The LMA CTrach[™] in Airway Resuscitation: Six case reports. *Anaesthesia* 2006; 61:975–7
4. Goldman A, Wender R, Goldman J: The LMA CTrach[™]: A prospective evaluation of 100 cases (abstract). *ANESTHESIOLOGY* 2006; 105:A521
5. Goldman A, Rosenblatt W: Use of the fiberoptic intubating LMA CTrach[™] in two patients with difficult airways. *Anaesthesia* 2006; 61:601–3

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AL (VYGON, Ecoen, France). Since we submitted our case report to *ANESTHESIOLOGY*, a third "glottiscope," the AirwayScope (PENTAX, Argenteuil, France), has become available, and we had the opportunity of testing it. These "glottiscopes" are equipped with both video-endoscopic resources and a built-in channel (or tube) driving the endotracheal tube in regard to glottis aperture into the trachea. The AL and, more generally, the other "glottiscopes" are really different from the basic, although sexy-looking, video-laryngoscopes, such as the GlideScope[®] (VERATHON Medical, Strasbourg, France) or the McGrath[®] (LMA North America, San Diego, CA), that are efficient at improving the Cormack and Lehane score but do not systematically facilitate and shorten tracheal intubation in case of a difficult airway.

Of course, we are concerned with cost-effectiveness, and we agree that \$80 is certainly too expensive for a single-use primary airway management device. However, we are sure that if the AL were sold for less than 10% of its actual price, we would not use the Macintosh laryngoscope anymore in potentially difficult airway patients such as morbidly obese patients. Almost all of the anesthesiologists in our department have completed their learning curve with the AL. All are experts in airway management, and our university hospital is now

considered as an Excellence Center for teaching airway management. In addition to cadaver training and manikin workshops, physicians become involved in regularly updated programs on new techniques in airway management. Teaching clinical use of new airway devices to residents or visiting physicians is systematically supervised and filmed. Our teaching program has been funded mainly by the university and private sources coming from attendees participating in our diploma program. Because his English is of better quality than ours, we thank Dr. Neustein for his nice description of the AL and its use. Moreover, we accept his advice on how to apply the Sellick maneuver.

In response to Drs. Chandan and Sadashivaiah, early and recent reviews have identified airway management complications such as aspiration of gastric contents, failed tracheal intubation, esophageal intubation, and airway obstruction as associated with anesthesia-related maternal mortality in Western countries. Moreover, some reports have recognized morbid obesity as a worsening factor of airway management difficulty. We believe that airway protection against aspiration of gastric contents requires insertion of a cuffed tube into the trachea as quickly as possible. Any device improving the laryngoscopic view (specifically in morbidly obese patients) and allowing visual control of the endotracheal tube passing through the vocal cords may eliminate the risk of esophageal intubation and fatal airway obstruction. Therefore, the AL, which combines the abilities to (1) facilitate the glottis view, (2) control the transglottic passage of the tube, and (3) dramatically reduce the time (elapsing between loss of consciousness to inflation of the cuff) to securing the airway, is of major interest for emergency and particularly obstetric anesthesia. For these reasons, we placed the AL as a brief plan B after failed direct laryngoscopy in emergency cesarean delivery patients and proposed it as a primary airway management device when parturients showed predictable criteria for difficult intubation. Moreover, we observed that video-controlled emergency tracheal intubation with the AL helped the operator performing the Sellick maneuver to adapt external manipulations over the cricoid area to facilitate glottis access without releasing cricoid pressure intensity. This interesting adaptation of the Sellick maneuver is not possible with the Macintosh laryngoscope when the glottis view is poor. As already stated, almost all of the anesthesiologists in our department have completed their learning curve with the AL. We have placed more than 250 ALs. We are conducting a randomized study in the intensive care unit, and we have recently been involved in clinical trials evaluating the AL in anticipated difficult airway patients, including elective cesarean deliveries. Accepted manuscripts are ready to be edited. We are sure (if this response to the Editor fails) that our data (and those of others coming from different teams) will convince Drs. Chandan and Sadashivaiah that our positioning of the AL in a difficult airway algorithm is not "premature and daring" but rather results from a long maturation (almost 2 yr of training and practice) and rational reflection on the optimal airway management strategy to apply in emergency obstetric situations. We believe that the AL is not a "magic bullet" but just an efficient airway device to facilitate tracheal intubation of difficult airway parturients. We did not aim to conquer any market but rather propose a reasonable and efficient alternative to the Macintosh laryngoscope, which was proposed almost 50 yr ago. We are sure that Drs. Chandan and Sadashivaiah will find on PubMed (May through August 2007) some interesting articles describing the use of the AL in difficult airway patients.

We are aware of the magnificent works performed by Dr. Goldman

et al.,⁴⁻⁶ and we share similar opinions with Liu *et al.*⁷ We have been involved in the first clinical trials with the CT,^{8,9} and we are still working on the evolution of this wonderful device. More than 300 CTs have been placed at our University Hospital of Paris, and not only for clinical trials. We confirm that the CT is the most effective ventilatory device, and we have also demonstrated great tracheal intubation performance of the CT in normal⁸ and difficult airway patients.⁹ Unfortunately, we are not certain that emergency tracheal intubation with the CT may prevent the risk of aspiration in case of true gastric content, as in our emergency cesarean delivery patients. Indeed, time to securing the airway with the CT requires, in expert hands, 1.5-2 min without real protection of the airway. First, the Sellick maneuver must be resumed during CT insertion. Second, maneuvers performed just after CT insertion to adjust ventilation (requested in 30-40% of cases) augment the risk of gastric inflation and increase pressure and regurgitation. Finally, the most risky period during CT manipulations occurs when maneuvers performed to optimize the view (requested in 30-50% of cases) require large-amplitude up-and-down movements of the mask. During these maneuvers, the distal tip of the mask is necessarily removed from its "protective" place in the hypopharynx and exposes the airway to possible regurgitated contents from the stomach. For all of these reasons, we placed the CT in plan C for emergency situations in case of failure of the AL to intubate within 1 min and in plan B in case of poor oxygenation during airway management for any elective or emergency cases. Finally, we believe that the AL is the airway of choice in the situation of difficult direct laryngoscopy when there is urgency to secure the airway with a cuffed endotracheal tube, as in emergency obstetric situations.

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References

1. Dhonneur G, Ndoko S, Amathieu R, Housseini LE, Poncet C, Tual L: Tracheal intubation using the Airtraq[®] in morbid obese patients undergoing emergency cesarean delivery. *ANESTHESIOLOGY* 2007; 106:629-30
2. Combes X, Jabre P, Jbeili C, Leroux B, Bastuji-Garin S, Margenet A, Adnet F, Dhonneur G: Prehospital standardization of medical airway management: Incidence and risk factors of difficult airway. *Acad Emerg Med* 2006; 13: 828-34
3. 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
4. Goldman A, Rosenblatt W: The LMA CTrach[™] in airway resuscitation: Six case reports. *Anaesthesia* 2006; 61:975-7
5. Goldman A, Wender R, Goldtaz J: The LMA CTrach[™]: A prospective evaluation of 100 cases (abstract). *ANESTHESIOLOGY* 2006; 105:A521
6. Goldman A, Rosenblatt W: Use of the fiberoptic intubating LMA CTrach[™] in two patients with difficult airways. *Anaesthesia* 2006; 61:601-3
7. Liu E, Goy R, Chen F: The LMA CTrach[™], a new laryngeal mask for endotracheal intubation under vision: Evaluation of 100 patients. *Br J Anaesth* 2006; 96:396-400
8. Dhonneur G, Ndoko SK: Tracheal intubation with the LMA CTrach or direct laryngoscopy. *Anesth Analg* 2007; 104:227
9. Dhonneur G, Ndoko SK, Yavchitz A, Foucher A, Fessenmeyer C, Pollian C, Combes X, Tual L: Tracheal intubation of morbidly obese patients: LMA CTrach *versus* direct laryngoscopy. *Br J Anaesth* 2006; 97:742-5

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Decreased Alveolar Fibrinolysis in Patients with Ventilator-associated Pneumonia: A Species-specific Event

To the Editor:—In a recent issue of ANESTHESIOLOGY, Song *et al.*¹ examined the relation between plasminogen activator inhibitor 1 (PAI-1) in bronchoalveolar fluid and mortality in patients with ventilator-associated pneumonia (VAP) caused by *Pseudomonas aeruginosa*. Although the authors found no difference in the concentration of PAI-1 levels between patients with VAP and those without VAP, there was a positive correlation between the levels of PAI-1 and the risk of mortality. Whether *P. aeruginosa* was responsible for more severe derangement in the fibrinolytic system compared with other VAP-responsible pathogens was hitherto unknown.

In a recent investigation, we demonstrated a bacteria-specific activation of the tissue factor-dependent procoagulant system.² Our observations paralleled those of Song *et al.* in documenting a profound shift toward procoagulant activity when *P. aeruginosa* was the culprit. Infection with methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *S. aureus*, and *Escherichia coli* induced similar coagulation imbalance, but the derangement was less severe in terms of intraalveolar fibrin deposition. More importantly, the restoration of the hemostatic balance was delayed in cases of *P. aeruginosa* VAP despite adequate antimicrobial therapy. However, the study did not assess the role of PAI-1 as a function of bacterial pathogens. Therefore, to evaluate whether the observed coagulation derangement may be due to species-specific inhibition of fibrinolysis, we tested our bronchoalveolar samples collected at the onset of VAP and at day 4 and day 8 after treatment for PAI-1 levels. Figure 1 shows that PAI-1 levels were elevated for all pathogens at the onset of VAP compared with controls ($P < 0.001$). However, the concentrations of PAI-1 levels in bronchoalveolar fluid were more pronounced in those patients infected with *P. aeruginosa* than in those observed in the other infectious categories and continued to be elevated for the duration of the study. The PAI-1 levels did not correlate with the bacterial burden at any specific time point, but there was a correlation between the total bacterial load and the concentrations of PAI-1 for each of the organisms over the study period ($r = 0.76$, $P < 0.001$). This finding confirms the hypothesis that the extent of local disturbance in alveolar hemostasis is species specific and is attributed not only to the activation of the tissue factor-dependent pathway but also to down-regulation of fibrinolysis *via* increased PAI-1 levels.

It is clear that the derangement of the local alveolar coagulation system seems to be a universal reaction to invading pathogens, but

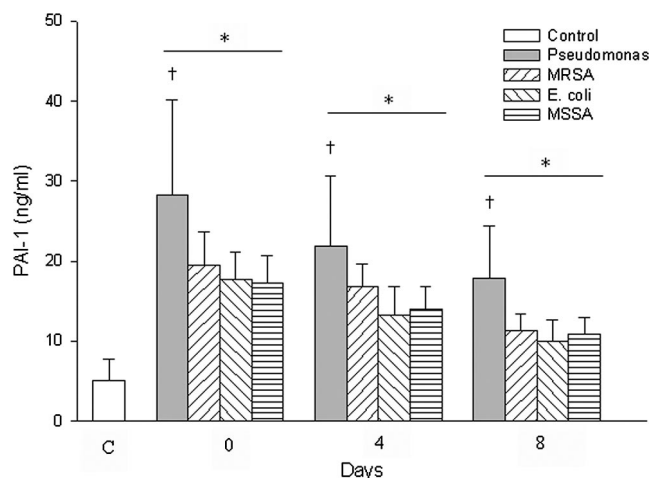


Fig. 1. Serial bronchoalveolar lavage fluid of plasminogen activator inhibitor 1 (PAI-1) at onset of ventilator-associated pneumonia and at day 4 and day 8 after onset of ventilator-associated pneumonia caused by *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli*, and methicillin-sensitive *S. aureus* (MSSA) compared with controls (C). * $P < 0.05$ compared with controls. † $P < 0.05$ compared with MRSA. Analysis of variance results among the four groups for days 0, 4, and 8 are 0.04, 0.02, and 0.002, respectively.

whether local and/or systemic intervention aiming at preventing local alveolar fibrin deposition can translate into improved outcome remains an unanswered question.

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References

- Song Y, Lynch SV, Flanagan J, Zhuo H, Tom W, Dotson RH, Baek MS, Rubio-Mills A, Singh G, Kipnis E, Glidden D, Brown R, Garcia O, Wiener-Kronish JP: Increased plasminogen activator inhibitor-1 concentrations in bronchoalveolar lavage fluids are associated with increased mortality in a cohort of patients with *Pseudomonas aeruginosa*. ANESTHESIOLOGY 2007; 106:252-61
- El Solh AA, Choi G, Schultz MJ, Pineda LA, Mankowski C: Clinical and hemostatic responses to treatment in ventilator-associated pneumonia: Role of bacterial pathogens. Crit Care Med 2007; 35:490-6

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Supported by Research for Health in Erie County, Buffalo, New York. The above letter was sent to the authors of the referenced report. The authors did not feel that a response was required. —James C. Eisenach, M.D., Editor-in-Chief.

Possible Mechanisms Underlying the Effects of Inhaled Nitric Oxide

To the Editor:—We read with great interest the recent elegant and important article by Mathru *et al.*,¹ who demonstrated that inhaled nitric oxide attenuates reperfusion injury and inflammatory responses in humans. We would like to add a few comments regarding the

possible mechanisms underlying these exciting effects of inhaled nitric oxide.

First, ischemia-reperfusion injury is characterized, in part, by increased tissue oxidative stress, *i.e.*, the formation of reactive oxygen species, including superoxide.² Nicotine adenine dinucleotide phosphate (NADPH) oxidase has emerged as a major inducible source of superoxide.² In turn, NADPH oxidase expression and activity is rapidly up-regulated by factors associated with ischemia-reperfusion injury. These include hypoxia, cy-

The above letter was sent to the authors of the referenced report. The authors did not feel that a response was required. —James C. Eisenach, M.D., Editor-in-Chief.

tokines, thromboxane A₂, isoprostanes, hydrogen peroxide, and superoxide itself.³ Superoxide elicits a battery of proinflammatory effects, such as increased adhesion molecule expression, activation of proinflammatory protein kinases, and vasoconstriction.²

In contrast, endogenous vasculoprotective factors, nitric oxide and prostacyclin (PGI₂) are potent inhibitors of NADPH oxidase expression and activity.⁴⁻⁶ These effects are mediated by inhibition of Rac1 activation, a key cofactor for activation of NADPH oxidase. However, superoxide negates nitric oxide bioactivity through chemical reactions^{5,6} and reduces PGI₂ by diverting arachidonic acid into isoprostanes,⁴ effectively rendering tissue more susceptible to an increase of NADPH oxidase expression and activity. Nitric oxide donors and iloprost (stable mimetic of PGI₂) are potent inhibitors of NADPH oxidase expression and activity and concomitant superoxide formation in pulmonary artery endothelial and vascular smooth muscle cells.⁴⁻⁶ Both inhalational nitric oxide and PGI₂ have also met with success in treating acute respiratory distress syndrome,⁷ a condition also characterized by aggressive inflammation. This beneficial effect may be due to suppression of NADPH oxidase expression and activity.

It is reasonable to suggest, therefore, that the inhalational nitric oxide may influence the expression and activity of NADPH oxidase within ischemia tissue distal to the lung, which in turn would reduce local superoxide formation. This in turn would conserve the endogenous bioavailability of nitric oxide and PGI₂, which in turn may protect against ischemia-reperfusion injury. It is also reasonable to predict that inhalational PGI₂ may also exert a beneficial effect on peripheral ischemic damage because PGI₂ not only inhibits NADPH oxidase activity but also exerts the same antiinflammatory effects as nitric oxide.

Nilima Shukla, Ph.D., Saima Muzaffar, Ph.D., Gianni D. Angelini, M.D., F.R.C.S., Kai Zacharowski, M.D., Ph.D., F.R.C.A., Jamie Y. Jeremy, Ph.D.* ^aBristol Heart Institute, University of Bristol, Bristol, United Kingdom. j.y.jeremy@bris.ac.uk

References

1. Mathru M, Huda R, Solanski DR, Hays S, Lang JD: Inhaled nitric oxide attenuates reperfusion injury inflammatory responses in humans. *ANESTHESIOLOGY* 2007; 106:275-82
2. Griendling KK, Sorescu D, Lassegue B, Ushio-Fukai M: Modulation of protein kinase activity and gene expression by reactive oxygen species and their role in vascular physiology and pathophysiology. *Arterioscler Thromb Vasc Biol* 2000; 20:2175-83
3. Muzaffar S, Shukla N, Jeremy JY: Nicotinamide adenine dinucleotide phosphate oxidase: A promiscuous therapeutic target for cardiovascular drugs? *Trends Cardiovasc Med* 2005; 15:278-82
4. Muzaffar S, Shukla N, Lobo C, Angelini GD, Jeremy JY: Iloprost inhibits superoxide formation and NADPH oxidase expression induced by the thromboxane A₂ analogue, U46619, and isoprostane F_{2α} in cultured porcine pulmonary artery vascular smooth muscle cells. *Br J Pharmacol* 2004; 141:488-96
5. Muzaffar S, Jeremy JY, Angelini GD, Stuart Smith K, Shukla N: The role of the endothelium and nitric oxide synthases in modulating superoxide formation induced by endotoxin and cytokines in porcine pulmonary arteries. *Thorax* 2003; 58:598-604
6. Muzaffar S, Shukla N, Angelini GD, Jeremy JY: Nitrospirins and SIN-1, but not aspirin, inhibit the expression of endotoxin- and cytokine-induced NADPH oxidase in vascular smooth muscle cells from pig pulmonary arteries. *Circulation* 2004; 110:1140-7
7. Cepkova M, Matthay MA: Pharmacotherapy of acute lung injury and the acute respiratory distress syndrome. *J Intensive Care Med* 2006; 21:119-45

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Cost Effectiveness of Epidural Injection of Steroids and Local Anesthetics for Relief of Zoster-associated Pain

To the Editor:—The Prevention by Epidural Injection of Postherpetic Neuralgia in the Elderly study recently showed that a single epidural injection of local anesthetics and steroids during the acute phase of herpes zoster was not effective for the prevention of long-term postherpetic neuralgia compared with care as usual.¹ However, it was associated with a modest but significant effect in reducing the presence (relative risk, 0.83; 95% confidence interval, 0.71-0.97) and severity of zoster-associated pain at 1 month after inclusion (median visual analog scale score in the epidural injection group, 2 mm [25th-75th percentiles, 0-23] vs. 6 mm [0-32] in the control group). Here, we report the economic analysis of the Prevention by Epidural Injection of Postherpetic Neuralgia in the Elderly study to assess the balance between the additional costs of a single epidural injection and the associated benefits.

The Prevention by Epidural Injection of Postherpetic Neuralgia in the Elderly study included 598 patients older than 50 yr with acute herpes zoster (rash <7 days) below dermatome C6. All patients received the current herpes zoster standard treatment, *i.e.*, analgesics and antiviral medication (if rash <72 h). Patients randomly allocated to the intervention group in addition received an epidural injection of bupivacaine and steroids.

Quality of life was assessed using the EQ-5D at various time points: at inclusion and at 1, 3, and 6 months after inclusion. The EQ-5D is a generic measure that defines health-related quality of life in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.² Cost data about units of resource utilization (including

doctor visits, medication, additional visits to healthcare providers, and hospitalizations) were also collected. All costs were estimated from a societal viewpoint. Costs of the epidural injection were estimated using two approaches: (1) the actual costs (€186) defined by the sum of labor (32 min by an anesthesiologist, 36 min by a nurse, and 20 min by an administrative employee), costs of material and location (€40), and overhead (€46); and (2) the current charges for an epidural injection (€870) as defined by the recent diagnosis-therapy-combination reimbursement scheme adopted by Dutch medical insurance companies. All other costs were estimated using tariffs. Direct non-healthcare costs included costs of paid and unpaid help. Indirect costs of loss of production owing to absenteeism from work or days of inactivity were not included, because most study participants were retired.

All analyses were performed with an intention-to-treat approach. The balance between costs and effects was expressed in terms of additional costs per additional quality-adjusted life year (QALY). One QALY equals 1 yr of full-health life. QALYs were calculated using the York A1 tariff.³ Because the estimate of the costs highly depended on the chosen cost estimate of the epidural injection, we assessed to what extent the results and inferences from our analysis were determined by the chosen cost estimate.

The EQ-5D scores at 1 month significantly differed between both treatment groups. From 3 months onward, however, these differences lost statistical significance. The number of QALYs in the intervention group was 0.412 (SE = 0.006), and that in the control group was 0.403 (SE = 0.005). This leads to an estimated difference of 0.010 QALYs (95% confidence interval, -0.006 to 0.026). After 6 months, the estimated difference in total costs with and without epidural injection—excluding the cost of the injection—was estimated at €6. When the costs of the injection were estimated at €186 (based on resource

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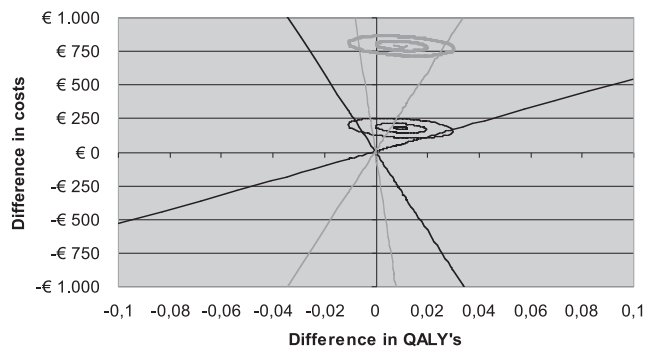


Fig. 1. Cost-effectiveness plane of epidural injection. The outer ellipses define the smallest area containing costs and effects with 95% probability. The inner ellipses do so for 50% and 5%. The lines mark the 95% confidence limits surrounding the central estimates. (Lower ellipses: estimating the costs of for the intervention at €186; upper ellipses: estimating the costs of the procedure at €870.) QALY = quality-adjusted life year.

utilization), the costs per QALY amounted to €17,540. Using the diagnosis-therapy-combination tariff of €870, costs per QALY increased to €79,859.

Figure 1 presents the uncertainty surrounding costs and effects as based on these estimates of costs and effects. The probability density in the two southern quadrants (costs savings of epidural injection compared with standard therapy) was zero, that in the northeast quadrant (higher costs and better clinical effectiveness of injection) was 87.9%, and that in the northwest quadrant (higher costs and less clinical effectiveness) was 12.1%.

Hence, the short-term (<1 month) effectiveness of a single epidural injection was confirmed in terms of quality of life. Within the investigated time horizon of 6 months, the gain in QALYs was estimated at 0.01 QALY, *i.e.*, equivalent of 4 days in perfect health. Because the economic savings of the injection strategy are relatively small compared with the direct costs of the epidural injection, the costs per QALY are equal to approximately 100 times the costs of the injection.

There may be two limitations. Although no participant experienced an adverse event related to the injection, this risk is not absent.^{4,5}

Complications such as meningitis and epidural abscess may induce additional costs and reduction of quality of life. Assuming an adverse event risk of 1:10,000 and estimating the associated costs at €10,000, the costs of the injection increase with €1. Similarly, a major loss of QALYs caused by complications (*e.g.*, 20) may only slightly decrease the gain of effectiveness (*i.e.*, 20/10,000). Therefore, allowing for the small risk of severe complications does not substantially disrupt the estimated balance between costs and effects of the intervention. Second, the results of the Prevention by Epidural Injection of Postherpetic Neuralgia in the Elderly study do not rule out that the observed short-term analgesic effect by the epidural injection could as well be achieved by adequately administered, and possibly less costly, oral analgesics.

In conclusion, an epidural injection with steroids and local anesthetics modestly relieves the acute pain in older zoster patients with an acceptable balance between actual costs and effects as compared with standard treatment. The balance may tip to the other side, however, when the local tariff for epidural injection is much higher than the actual costs.

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References

1. van Wijck AJ, Opstelten W, Moons KG, van Essen GA, Stolker RJ, Kalkman CJ, Verheij TJ: The PINE study of epidural steroids and local anaesthetics to prevent postherpetic neuralgia: A randomised controlled trial. *Lancet* 2006; 367:219-24
2. Brooks R: EuroQol: The current state of play. *Health Policy* 1996; 37:53-72
3. Dolan P: Modeling valuations for EuroQol health states. *Med Care* 1997; 35:1095-108
4. Fitzgibbon DR, Posner KL, Domino KB, Caplan RA, Lee LA, Cheney FW: Chronic pain management: American Society of Anesthesiologists Closed Claims Project. *ANESTHESIOLOGY* 2004; 100:98-105
5. Moen V, Dahlgren N, Irestedt L: Severe neurological complications after central neuraxial blockades in Sweden 1990-1999. *ANESTHESIOLOGY* 2004; 101: 950-9

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Abducens Nerve Palsy after Thyroidectomy with Unilateral Modified Neck Dissection

To the Editor:—A 48-yr-old patient with right-sided thyroid carcinoma underwent subtotal thyroidectomy with right unilateral modified neck dissection (MND). MND involves removal of lymph node groups I-III while preserving all three of the functional structures, *i.e.*, the internal jugular vein (IJV), the spinal accessory nerve, and the sternocleidomastoid muscle. Standard subtotal thyroidectomy was performed by two thyroid specialists. The patient was not reconstructed with any flaps and did not have postoperative radiation treatment or any findings of infection.¹⁻³ On postoperative day (POD) 1, the patient's recovery was unremarkable, and his appetite was good. On POD 2, he developed nausea and lost his appetite. On POD 4, he reported severe headache and nausea. However, the surgeon in charge considered these complications to be induced by cervicogenic factors because of the typical neck-extended position, and prescribed antiemetics and analgesics. The patient was discharged from the hospital. On POD 7, he developed

diplopia, transient visual obscuration, and continuous visual blurring. Cranial computed tomography and magnetic resonance imaging scans were normal. On POD 24, clinical examination revealed binocular papilledema, reduced visual acuity, and left abducens nerve palsy. The patient was hospitalized again, but the etiology could not be diagnosed. Only symptomatic treatment was given. The ophthalmologist consulted me about this case; pseudotumor cerebri was suspected (POD 36). Therapy was started with oral prednisolone (20 mg/day), acetazolamide (500 mg/day), and mecobalamin (1.5 mg/day). On POD 49, the clinical symptoms resolved. Ultrasonography showed that the right-side IJV had no flow, whereas the flow of the left-side IJV was normal (POD 57). In addition, cerebral angiography ruled out left transverse sinus thrombosis. On POD 80, the papilledema improved little by little.

This is the first report of a patient with pseudotumor cerebri undergoing unilateral MND. This case illustrates that severe neurologic complications after unilateral MND may develop, even in the presence

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of a prominent contralateral IJV, if the remaining venous collateral network, comprising the intraspinal and extraspinal vertebral system and the deep neck veins, is inadequate.

It is difficult to distinguish these common symptoms (headache, nausea and vomiting) after thyroid surgery from the almost identical symptoms caused by intracranial hypertension. This delayed a diagnosis of a right IJV thrombosis and subsequently pseudotumor cerebri. The most important and atypical finding in this case was the onset of the clinical symptoms. From January 2004 to February 2007, 354 patients underwent thyroid surgery at our hospital. Forty-eight hours postoperatively, 58% of these patients reported headache and/or head fullness. Postoperative nausea and vomiting (PONV) occurred in 45%. Headache occurred in 95.8% of patients and PONV occurred in 95.6% of patients within 24 h postoperatively, and the severity of these complications was decreased 48 h postoperatively. There were no patients except the current one who reported no symptoms during the first postoperative 24 h followed by onset of severe headache and PONV after 36 h. Retrospectively, the time delay of more than 36 h between surgery and the onset of severe headache and PONV and the more difficult complications 48 h postoperatively were distinctive in this case. The blood loss volume was only 26 ml, the urinary volume was 250 ml, and the total infusion was 1,350 ml during the intraoperative period. For 24 h postoperatively, the patient had no PONV, and his appetite was good. It is therefore difficult to imagine that circulatory changes, including dehydration, were the main cause of thrombosis. The patient was given a percutaneous drain (OD = 3.3 mm) *via* the front of the trachea to the front of the right IJV under the sternocleidomastoid muscle for 24 h postoperatively. The position of the drainage of the thyroid space is important because it is suspected to have induced mechanical compression of the right IJV in the current case.

Serious neurologic complications are extremely rare in patients undergoing unilateral radical neck dissection.⁴ Few patients with pseudotumor cerebri after unilateral radical neck dissection have been reported previously.^{5,6} In all cases, insufficient venous outflow *via* the opposite transverse sinus and IJV was postulated. In the current case, cerebral angiography demonstrated occlusion of the right IJV and the left transverse sinus without extension of the cerebral venous circulation time. Some authors suggest a retrograde thrombosis of the sigmoid sinus with a subsequently compromised collateral flow *via* emissary veins as a possible explanation for pseudotumor cerebri.^{7,8} In patients with cerebral venous outflow obstruction, resistance to venous drainage generates elevated venous back pressure.⁸ Elevated sinus pressure increases the resistance to cerebrospinal fluid absorption. In addition, lower flow is found consistently in the left IJV with little compensatory increase in flow after resection of the right IJV.⁹ In the current case,

ultrasonography demonstrated that the flow in the left IJV remained within the normal range, and there was no compensatory increase in flow. Right IJV thrombosis, left transverse sinus occlusion, and a small compensatory increase in flow of the left IJV are thought to explain the pseudotumor cerebri in the current case. Previously, only intracranial involvement in the pathogenesis of pseudotumor cerebri was reported, but this case provides evidence for the involvement of extracranial vasculature. The restriction of venous outflow in the IJVs was associated with increased intracranial pressure, probably due to cerebral venous congestion. Abducens nerve palsy caused by elevated intracranial pressure is most likely a consequence of prolonged increased extracranial resistance to venous outflow.

In summary, the current case illustrates that a critical increase in intracranial hypertension after unilateral MND may develop, even in the presence of a contralateral IJV, if complete IJV thrombosis occurs after MND. The fact that the patency of the IJV cannot always be preserved, even after MND, is important when clinicians find atypical headache and PONV.

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References

1. Harada H, Omura K, Takeuchi Y: Patency and caliber of the internal jugular vein after neck dissection. *Auris Nasus Larynx* 2003; 30:269-72
2. Leontsinis TG, Currie AR, Mannell A: Internal jugular vein thrombosis following functional neck dissection. *Laryngoscope* 1995; 105:169-74
3. Bree R, van den Berg FG, van Schaik CV, Beerens AJF, Manoliu RA, Castelijns JA, Snow GB, Leemans CR: Assessment of patency of the internal jugular vein following neck dissection and microvascular flap reconstruction by power Doppler ultrasound. *J Laryngol Otol* 2002; 116:622-6
4. Qurahashi HA, Wax MK, Granke K, Rodman SM: Internal jugular vein thrombosis after functional and selective neck dissection. *Arch Otolaryngol Head Neck Surg* 1997; 123:969-73
5. Doepp F, Schreiber SJ, Benndore G, Radtke A, Gallinat J, Valdueza JM: Venous drainage patterns in a case of pseudotumor cerebri following unilateral radical neck dissection. *Acta Otolaryngol* 2003; 123:994-7
6. De Varies WAEJ, Balm AJM, Tiwari RM: Intracranial hypertension following neck dissection. *J Laryngol Otol* 1986; 100:1427-31
7. Alperin N, Lee SH, Mazda M, Hushek SG, Roitberg B, Goddwin J, Lichtor T: Evidence for the importance of extracranial venous flow in patients with idiopathic intracranial hypertension (IIH). *Acta Neurochir Suppl* 2005; 95:129-32
8. Karahalios DG, Rekatte HL, Khayata MH, Apostolides PJ: Elevated intracranial venous pressure as a universal mechanism in pseudotumor cerebri of varying etiologies. *Neurology* 1996; 46:198-202
9. Lake GM, Dianro LJ, Demeo JH: Performance of the internal jugular vein after functional neck dissection. *Otolaryngol Head Neck Surg* 1994; 111:201-4

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Successful Use of Succinylcholine for Cesarean Delivery in a Patient with Postpolio Syndrome

To the Editor:—Anesthetic procedures are performed regularly in survivors of the 1930s poliomyelitis epidemic, some of whom may have developed postpolio syndrome.¹ When a patient with postpolio syndrome is scheduled to undergo a procedure requiring anesthesia, anesthesiologists should carefully assess the patient's preoperative status, namely his or her respiratory function, and inquire about swallowing difficulties or history of intolerance to any general or local anesthetic agent. The use of neuromuscular blocking agents in this context remains controversial.¹ Increased potency of nondepolarizing neuromuscular blocking agents occurring in patients with a history of

poliomyelitis has been suggested.² It is also traditionally well accepted that succinylcholine should be avoided in patients with neuromuscular disease to prevent fatal hyperkalemia. Interestingly, however, this assumption has not been based on any specific report regarding the use of succinylcholine in the context of postpolio syndrome.¹ Hence, we report here the first case of successful use of succinylcholine in a patient with postpolio syndrome who underwent elective cesarean delivery during general anesthesia.

A 39-yr-old woman (height, 150 cm; weight, 65 kg) was scheduled to undergo elective cesarean delivery at 38 weeks of amenorrhea. She presented with postpolio syndrome according to all of the criteria of Mulder *et al.*³: a history of paralytic poliomyelitis when she was 1 yr old followed by motoneuron deficit with electromyographic confirma-

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tion. She then had a 20-yr period of recovery and functional stability before experiencing gradual and major peripheral muscular fatigue with muscle atrophy of the limbs starting 5 yr ago, for which no other diagnosis was proved. The patient's motor deficit due to polio at that time was isolated paraplegia without respiratory or bulbar weakness. She presented with atrophy and motor deficit of the limbs. She had no respiratory problems, thoracic deformation, or sleep apnea. Her medical history showed a comprised cholecystectomy performed during general anesthesia 25 yr ago, but no information regarding the type of anesthetic agents used was available. Preoperative evaluation showed the absence of criteria predicting difficult intubation. The blood potassium level was 3.4 mM. General anesthesia, *versus* spinal or epidural anesthesia, was chosen after an extensive risk-benefit discussion focused on either strategy in light of the recent review published in *ANESTHESIOLOGY* in 2005.¹ The patient was carefully informed of this discussion. General anesthesia with awake fiberoptic tracheal intubation was proposed to the patient preferentially to spinal anesthesia because of the possible neurotoxic effects of local anesthetics on the functional motoneurons of the limbs and the lack of symptoms arguing for a central nervous disease, which could have been a relative contraindication to the use of succinylcholine and hence to general anesthesia. However, the patient declined fiberoptic intubation and gave informed consent for general anesthesia with orotracheal intubation. Succinylcholine was therefore chosen because of the lack of absolute contraindication to this agent in the current case¹ and the patient's full stomach. After a 10-h fasting interval and preoperative medication with oral effervescent cimetidine (400 mg), preoxygenation was performed for 5 min. Anesthesia was induced with propofol (150 mg in 30 s); a reference train-of-four ratio was measured showing four motor responses at the adductor pollicis. Succinylcholine (50 mg) was then given, and the trachea was intubated 1 min later under the Sellick maneuver, with excellent conditions of exposure of the larynx and no response to train-of-four stimulation. Tympanic temperature was recorded every 15 min and kept as close as possible to 37°C by keeping the patient covered with a Bair-Hugger warming blanket (Arizant France, La Ciotat, France) throughout the procedure. Anesthesia was maintained with use of isoflurane (0.6% end-tidal), nitrous oxide (50%/50% in oxygen, vol/vol), and 0.15 µg/kg sufentanil after extraction of the newborn to obtain a Bispectral Index value between 40 and 60. The Apgar score was 9 at 1 min and 10 at 5 min after delivery. Because of the long-acting effect of succinylcholine, no additional injection of a nondepolarizing neuromuscular blocking drug was required despite the long duration of surgery (90 min). The train-of-four measured at the adductor pollicis every 5 min showed full recovery of the four motor responses only 35 min after tracheal intubation. The trachea was extubated uneventfully shortly after skin closure. The patient was transferred to the postanesthesia care unit. Postoperative pain was treated with use of paracetamol, nefopam, nonsteroidal antiinflammatory drugs, and intravenous morphine titration. Only 6 mg intravenous

morphine was required on postoperative day 1. Neurologic examination was performed daily from postoperative day 1 to day 5 and did not reveal any abnormal drowsiness, myalgia, or other significant change in comparison with the patient's preoperative status. The full postoperative course was uneventful, and the patient was discharged from the hospital on postoperative day 5.

Our case is the first report demonstrating that succinylcholine may be used safely in patients with postpolio syndrome. In the current case, the choice of general anesthesia with succinylcholine was based on an extensive risk-benefit analysis with discussion of general anesthesia and perimedullary anesthesia. A lack of symptoms suggesting a diagnosis of postpolio-related central disorder syndrome, a normal preoperative blood potassium level (although of limited value in predicting the magnitude of potassium increase due to motor endplate receptor up-regulation), a full stomach with an increased risk of pulmonary aspiration, and a possible harmful effect on residual motoneurons of local anesthetics given by intrathecal injection were the cornerstones to support our decision. One may notice that the dose of succinylcholine that was used (0.8 mg/kg) resulted in a prolonged depressive action on the train-of-four. We do not believe that hypothermia played a role in this case, because great attention was paid to keeping the patient warm during the procedure. We suggest that, more likely, sensitivity to succinylcholine (and probably muscle relaxants) is enhanced in patients with postpolio syndrome, necessitating careful titration and monitoring of muscle relaxants in this context. The prevalence of postpolio syndrome is estimated to be in the hundreds of thousands in the United States.⁴ Overall, we hope that our data will provide useful information for anesthesiologists in their clinical practice.

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References

1. Lambert DA, Giannouli E, Schmidt BJ: Postpolio syndrome and anesthesia. *ANESTHESIOLOGY* 2005; 103:638-44
2. Gyermek L: Increased potency of nondepolarizing muscle relaxants after poliomyelitis. *J Clin Pharmacol* 1990; 30:170-3
3. Mulder DW, Rosenbaum RA, Layton DD Jr: Late progression of poliomyelitis or forme fruste amyotrophic lateral sclerosis? *Mayo Clin Proc* 1972; 47:756-61
4. Jubelt B, Agre JC: Characteristics and management of postpolio syndrome. *JAMA* 2000; 284:412-4

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