2008 in Review

Advancing Medicine in Anesthesiology


WELCOME to the 2008 year in review, highlighting articles that the Editorial Board believes exemplify the mission of ANESTHESIOLOGY, “to advance the science and practice of perioperative, critical care, and pain medicine through the promotion of seminal discovery.” Our goals are to remind you of articles that may change your clinical practice today, to help you better understand the scientific basis of current practice, and to provide glimpses into the future. We recognize how busy you are and hope these brief synopses guide you to new and relevant information.

The full-text on-line articles are a click away at our newly redesigned Web site—www.anesthesiology.org—described more fully in an editorial in this issue.¹ In addition to the synopses chronicled in this review, the ANESTHESIOLOGY Web site now offers new functionality, such as “most viewed” or “most in the press,” that will also help you to determine the most relevant and important content for your practice and research. Two thousand eight is the first full calendar year during which content is regularly highlighted through the American Society of Anesthesiologists Press Release office, and the press release program has met with remarkable success. Throughout the year, several news releases were picked up by more than 1,000 news outlets, including nearly all the major news media entities. As Editors, we are very excited about the public interest in research and other content published in the Journal because press interest stresses the critically important medical advances in our specialty and offers well-deserved recognition to the outstanding authors who publish with us.

This year saw the reorganization of our Table of Contents into the three major medical branches of our specialty: perioperative, critical care, and pain medicine. Although we could have organized these synopses into these three areas, we chose to provide a more clinically focused approach. As such, the first six articles address preoperative assessment; the next eight articles address intraoperative care, and the final four articles address postoperative and critical care.


Recent case reports have highlighted the dramatic increased risk of death in patients with drug-eluting stents in whom antiplatelet agents are withdrawn prematurely. These two retrospective analyses are the largest conducted to date that address the relation between major adverse cardiovascular events during noncardiac surgery and time since bare-metal or drug-eluting stent implantation. Adverse events were investigated in 899 patients with bare-metal stents undergoing noncardiac surgery over a period of 15 yr. Time since percutaneous coronary intervention (PCI) and surgery was significantly related to the occurrence of major cardiovascular complications in patients with bare-metal stents (10.5% when PCI occurred up to 30 days, compared with 2.8% when PCI was performed greater than 90 days, before surgery). In contrast, the risk of cardiac events did not decrease substantially over time in patients receiving drug-eluting stents (fig. 1). Events occurred in 6.4% of 520 patients when PCI occurred up to 90 days, compared with 3.3% when PCI was performed more than

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Postoperative cognitive dysfunction (POCD), most widely described and investigated after cardiac surgery, occurs more commonly in the elderly. Monk et al. advanced our understanding of POCD in this study by extending previous observations to noncardiac surgery and examining mortality as well as morbidity. One thousand sixty-four patients undergoing mostly intraabdominal, thoracic, or orthopedic surgery (and also a small percentage with minimally invasive procedures) underwent neuropsychological testing before surgery, at hospital discharge, and again 3 months later. The results of these two investigations illuminate the ongoing debate regarding the timing of noncardiac surgery, the continuation or discontinuation of antplatelet agents, and the short- and long-term risks of stent thrombosis in patients after PCI. As noted in an accompanying editorial, when it comes to coronary stents and surgery, timing is everything.


Postoperative cognitive dysfunction (POCD) is a problem across ages, and particularly the reasons why POCD becomes chronic in the elderly. In addition, although other population studies show an association between cognitive decline after surgery and mortality in the elderly, the landmark study published in Anesthesiology is the first to demonstrate this in a prospective fashion. With the global increase in the prevalence of major surgery2 and the increasing age of the surgical population, understanding the root causes and the potential methods to prevent and treat this cause of major morbidity and mortality is of the utmost priority to advance our medical care of these patients.


The search for strategies to reduce perioperative bleeding, particularly during cardiac surgery, has focused on medications that interfere with fibrinolysis. However, the effectiveness of these antifibrinolytics to attenuate blood loss in a variety of studies and applications has yielded mixed results. This has in turn led many to question the role of antifibrinolytics in the perioperative period. One hypothesis to explain these discrepant
findings is genetic polymorphisms of plasminogen activator inhibitor 1 (PAI-1), which is the enzyme responsible for converting plasminogen to plasmin, thereby blocking fibrinolysis. Of the known polymorphisms of PAI-1, the 4G allele has been associated with increased levels of PAI-1, and the 5G allele has been associated with reduced levels of PAI-1. Hence, patients with the 4G allele may bleed less and not benefit from antifibrinolytics, whereas those with the 5G allele may bleed more and benefit from antifibrinolytics. The authors effectively assert that without knowing the distribution of PAI-1 polymorphisms in patients enrolled in a study of the effectiveness of antifibrinolytics to attenuate blood loss, it may be difficult, if not impossible, to interpret the outcome. Accordingly, Iribarren et al. recruited 50 adults undergoing cardiac surgery, characterized their PAI-1 genotype, and randomly assigned them to tranexamic acid or placebo. Outcome measures included blood loss and transfusion requirements during the first 24-h postoperative period (fig. 3). Their results demonstrated that tranexamic acid, compared with placebo, significantly decreased bleeding in those who were 5G homozygotes, but it had no effect in those who were 4G homozygotes. The 4G/5G heterozygotes were intermediate responders. The activity of PAI-1 in the three polymorphisms followed the order 4G/4G > 4G/5G > 5G/5G. This investigation is an excellent example of the role of translational research to bridge basic science (genetics) and clinical research (blood loss during cardiac surgery). That some patients respond to tranexamic acid with decreased bleeding and others do not can now be explained, at least in part, by a genetic susceptibility in the form of polymorphisms of PAI-1. Perhaps these data will prompt others to search for similar explanations in other clinical conundrums.


The prevalence of obstructive sleep apnea (OSA) in the general population is as great as 26% and, in patients who present for specific types of surgery, i.e., bariatrics, as great as 70%. OSA has been associated with a number of diseases, including cardiovascular, cerebrovascular, and gastroesophageal diseases; an increased incidence of perioperative complications; and a 20-yr shortened life span compared with the general population. Yet, for most patients who present for surgery and who may be at risk for OSA, polysomnography has not been performed, and there are no other validated metrics to assess the risk of OSA. In the study by Chung et al., the authors developed and validated a questionnaire that rapidly, simply, and reliably screens for OSA in patients who present for surgery. In the initial questionnaire development, 4 potential yes–no questions combined with 10 from the Berlin questionnaire were answered by 254 patients. Using factor analysis, 4 questions (comprising the acronym STOP: S for snoring loud enough to be heard through closed doors; T for tired, fatigued, or sleepy during the daytime; O for observed apnea during sleep; and P for treatment for high blood pressure) were identified. The STOP questionnaire was then internally validated. The STOP questionnaire itself, and then combined with the four Bang factors (body mass index, age,
neck circumference, and gender), was validated against the results of polysomnography through a testing algorithm that included threshold criteria for OSA (apnea hypopnea index, receiver operating characteristics, and factor analysis). The authors determined that the positive predictive value of STOP when combined with male gender, age greater than 50 yr, and a body mass index greater than 35 kg/m² was 100%. To further refine both the sensitivity and the negative predictive value of the questionnaire, the authors combined the STOP questionnaire with the Bang factors (appendix): B for body mass index greater than 35 kg/m², A for age older than 50 yr, N for neck circumference greater than 40 cm, and G for male gender. For patients with moderate to severe OSA, the STOP-Bang questionnaire yielded a very high sensitivity and positive predictive value. The clinical importance of this questionnaire for the perioperative care of patients cannot be overstated. The STOP-Bang questionnaire is a landmark screening tool for OSA in patients in the perioperative period. We should also recognize that the publication of this article generated widespread interest not only from our readers, but also in the lay press. When this article was released to the press, it had the widest pickup of any article to date, in more than 1,200 separate news outlets.


Although recent maternal mortality reviews published in the Journal suggest that there is a shift from anesthetic deaths in obstetrics from those due to inability to intubate and ventilate to airway disasters and respiratory depression after surgery, we are appropriately concerned about the unexpected difficult airway in this subspecialty. These authors complemented the Samsoon modification of the Mallampati assessment of the airway with an acoustic reflectometry measurement of airway volumes in the upper airway, oral region, and pharyngeal region in women at the onset and at the end of labor. Patients with initial class 4 airways were excluded. The key finding by both techniques was the worsening assessment during the labor process. Airway class increased by one grade or higher in one third of parturients and by two grades or higher in 5% of parturients by the end of labor. Nearly twice as many airways were rated as class 3 or 4 at the end of labor than at the beginning. In the quantitative assessment of airway volume, completion of labor was associated with a significant reduction in oral volume, pharyngeal volume, and mean pharyngeal area. These data extend in several important ways previous observations that anticipated and unanticipated difficult tracheal intubation is increased during pregnancy. Based on previous work, the increase in visual inspection of the airway from grade 2 to grade 4 in some of these women in labor would predict an increase in relative risk of encountering a difficult intubation from 3-fold to 11-fold over a grade 1 airway assessment. The reduction in airway caliber noted in this study complements these observations and most likely reflects increased edema from fluid administration and possibly from straining and pushing. The results indicate that it is not just in the case of facial trauma that airway characteristics important to tracheal intubation can rapidly deteriorate and underscore the importance of reevaluation of the airway in laboring women when an airway intervention is anticipated, rather than relying on an evaluation performed just a few hours before.


Much of what we do during the delivery of anesthesia has no evidence to support it; rather, tradition and bias support our actions. The use of a mask over the mouth and nose seems logical and efficient, but what are the data that support the use of such a mask compared with a mask that covers only the nose? In fact, now there are data indicating that nasal mask ventilation is more effective than using a mask that combines oral–nasal mask ventilation during induction. Although only a small study, this recent investigation documents the significant efficiency of nasal ventilation (fig. 4). Fifteen adult patients who could breathe through their nose and mouths and had an adequate mask seal were recruited. The patients were monitored for anesthetic depth (using a Bispectral Index monitor), noninvasive cardiac output (using a Noninvasive Cardiopulmonary Management System [NICO] monitor), and exhaled carbon dioxide and flow (using a Novametrix monitor), and all ventilation parameters, including respiratory rate, tidal volume, flow waveforms, flow rates, peak inspiratory airway pressures, end-tidal carbon dioxide waveforms, vital signs, and evaluations, occurred with the patient’s head in neutral position, while they were apneic and nonparalyzed. The significant findings included a significantly lower peak inspiratory pressure and a significantly larger expired volume through the nasal mask compared with the combined oral–nasal mask; the peak inspiratory pressure with nasal mask ventilation was 16.7 cm H₂O compared with 24.5 cm H₂O with combined oral–nasal mask ventilation. The expired tidal volume with nasal mask ventilation was a median of 264.5 ml, compared with a median of 65.6 ml from the combined oral–nasal mask ventilation. The volume of carbon dioxide removed with the nasal mask ventilation was a median of 5.0 ml, compared with a median of 0 ml for the combined oral–nasal mask ventilation. So nasal mask ventilation removed more carbon dioxide with lower peak inspira-
tory pressures and generated higher tidal volumes than using a mask over the mouth and nose. The authors suggest the results are due to soft tissue obstruction in the oral pharynx, obstructions that do not affect ventilation via the nose. Future studies should be performed with the head in the sniffing position, but perhaps mask ventilation of the nose will become our evidence-based approach in the future.


Nitrous oxide has been reported to worsen, improve, or be inert with respect to impact on outcome from an ischemic brain insult. Two articles fueled this controversy but also offered insights into potential dilemmas in translational neuroprotection research. Taninishi et al. subjected halothane-anesthetized normothermic gerbils to a severe forebrain ischemic insult in the presence of 70% nitrous oxide or 70% nitrogen in oxygen. Brain injury was measured 5 days later. Their unique finding was that the effect of nitrous oxide on outcome was a function of the ischemic insult duration. Only an intermediate duration of ischemia revealed an effect of nitrous oxide, and that effect was adverse (fig. 5). This study is unique in the anesthetic neuroprotection literature. Instead of comparing a single or different drug doses in the context of a standardized insult, Taninishi et al. studied a fixed drug dose in the context of varying ischemia durations. Consistent with the likely explanation for previous apparently discordant reports, the authors found that the effect of nitrous oxide is dependent on the ischemic conditions, implicating subsets of ischemic conditions in which nitrous oxide might be injurious, protective, or inert. This article is juxtaposed with that of McGregor et al. A database derived from the Intraoperative Hypothermia Aneurysm Surgery Trial (IHAST) was analyzed to discern any substantial effect of nitrous oxide on ischemic outcome. IHAST measured functional outcome from cerebral aneurysm surgery in 1,000 patients 3 months postoperatively. Use of intraoperative nitrous oxide during the study was at the anesthesiologists’ discretion. Therefore, although nitrous oxide use was not randomized, detailed functional outcome data were available allowing comparison between a large number of patients who did (n = 373) and did not (n = 627) receive intraoperative nitrous oxide. In brief, no effect of nitrous oxide on outcome was evident. Given the rigor of the IHAST conduct and the large number of patients studied, if nitrous oxide caused

Fig. 4. Illustration of the oral mask, nasal mask, and application of both masks and their interface with the two noninvasive cardiac output monitors. One noninvasive cardiac output monitor was placed between the nasal mask and the breathing circuit (flowmeter 1), and the other was placed between the oral mask and the breathing circuit (flowmeter 2). A and B are the photos of the oral and nasal masks, respectively. C shows the application of the nasal and oral masks held by two separate straps. Reprinted with permission from Liang Y et al., ANESTHESIOLOGY 2008; 108:998–1003.
The mechanisms for development of ION are still poorly understood. Lee et al. undertook the task to set up an experimental model in piglets for investigating intracranial and extracranial factors in the development of ION. The model is not suitable for the investigation of all pathophysiologic aspects of ION but can be considered an important first step to elucidate the role of changes in hemodynamics and oxygen supply in the development of ION. Blood flow and oxygen delivery to the optic nerve and the brain were studied under various conditions, such as euvolemia, hypovolemia, hypotension, anemia, venous congestion, and combinations thereof. A major finding was that during euvolemic anemia, cerebral blood flow was significantly increased, resulting in no change in cerebral oxygen delivery. In contrast, optic nerve blood flow was almost unchanged. Consequently, optic nerve oxygen delivery was reduced during euvolemic anemia when compared with controls. When euvolemic anemia was combined with deliberate hypotension, cerebral blood flow was not significantly increased in response to anemia, resulting in a significant decrease in cerebral oxygen delivery. Under this condition, optic nerve oxygen delivery was also significantly decreased when compared with control animals.

With all limitations given by the differences in cerebrovascular structures and blood supply between different species and the difficulties to simulate a prone position in animals that can mimic the physiologic changes seen in humans, the authors were able to elucidate some factors that are probably involved in the development of ION. They were able to demonstrate that in piglets, the optic nerve is even more susceptible to physiologic perturbations than the brain. Based on their findings, the authors speculate that in situations when oxygen delivery is compromised, an increase in collateral blood flow to the brain would explain why the majority of cases of ION are seen in the absence of cerebral or cardiac ischemia.

These findings contribute invaluable information about the pathophysiology of ION, and they may help to identify mechanisms and risk factors and to guide further research in the areas involved in the development of this rare but devastating complication.
opioids after either preconditioning or postconditioning. Postconditioning can be induced by repetitive ischemic episodes applied before coronary reperfusion.

Jang et al. demonstrated that morphine, a mixed opioid agonist, produced postconditioning that was abolished by δ-opioid receptor antagonist or pharmacologic opening of the mPTP. The authors concluded that postconditioning protects the heart by targeting the mPTP via activation of δ-opioid receptors, which in turn activate the nitric oxide–cyclic guanosine monophosphate–protein kinase G pathway (fig. 6). The role of nitric oxide and reactive oxygen species in postconditioning is interesting because overproduction of nitric oxide, and especially reactive oxygen species along with calcium overload, leads to an opening of mPTP, mitochondrial membrane depolarization and swelling, inhibition of adenosine triphosphate production, and a complete mitochondrial dysfunction. However, low concentrations of nitric oxide and reactive oxygen species are necessary to initiate the preservation of mitochondrial integrity and myocardium during ischemia and reperfusion injury.

The work by Jang et al. points to a possible role for δ opioids in the modulation of mPTP, most likely the final end effector in cardiac myocyte protection and an important therapeutic target for cardiac-protective strategies.


Interindividual variabilities in pharmacokinetics and pharmacodynamics (PK/PD) regarding hypnotics and analgescics have been shown to be 20–25% and more than 200%, respectively. In contrast, information dealing with local anesthetics in this context is sparse. For clinicians, it is obvious that the PK/PD of interscalene block is usually different from that of axillary block. Moayeri et al. may have brought new insights into understanding PK/PD variability regarding proximal and distal brachial plexus blocks. The authors hypothesized that differences in neural architecture might shed some light on differences in onset time and local anesthetic volumes that exist in daily practice between proximal and distal brachial plexus block. To provide better insight into the dimensions and location of the various tissues without altering topographic relations, the authors used a sophisticated methodology combining cryomicrotomy with high-resolution photography. Two important findings were demonstrated by this study. First, the ratio of neural to nonneural tissue inside the epineurium decreased from proximal to distal and was 45, 34, and 34% in the interscalene, midinfraclavicular, and subcoracoid regions, respectively. Second, the area of the connective tissue compartment surrounding the brachial plexus increased from proximal to distal (fig. 7). These anatomical findings are important because the ratio of neural to nonneural tissue and the amount of tissue surrounding the epineurium may explain (at least in part) the different PD/PK observed during performance of brachial plexus block at different levels. It would also be interesting to know whether these differences are enhanced or diminished in selected populations (women compared with men, obesity, muscular individuals). The authors also speculated that the ratio of neural to nonneural tissue may play a role in the prevention or occurrence of neurologic complications after regional anesthesia. Although this hypothesis is attractive, it remains speculative, and this issue will need to be addressed in future investigation.

This title pretty much says it all. Despite publication of guidelines and standards regarding asepsis in the insertion of vascular catheters and peripheral nerve blocks, there is little emphasis in education research related to this essential aspect of invasive procedures. This study examined regional anesthesia learning by video-recording second-year residents over a 6-month period as they were being taught and were acquiring the skill of epidural catheter insertion. Recordings were analyzed using checklists for manual skill, aseptic technique, and a global score over this period of time as the residents performed more than 90 epidural insertions. There was a positive and strong correlation between the number of epidurals inserted and the manual skills and global assessment. In the case of manual skills in placing epidural catheters, more than 60% of the interindividual scores in this checklist could be predicted by the number of insertions performed, and a near perfect score was achieved on average after approximately 100 procedures. In contrast, there was no significant relation between the number of epidurals performed and scores on aseptic technique, and the score on aseptic technique remained disappointingly low, at approximately 50% performed correctly. Although some aspects of aseptic technique as applied to regional anesthesia are controversial, this was not the case for nearly all of the items on the checklist (table 1). The study did not detail or control the didactic and hands-on teaching provided for these residents, so it is possible that they simply did not teach aseptic technique. On the other hand, it is understandable that teachers and learners often focus on the mechanics of the ultimate goal in regional anesthesia of inserting a catheter and depositing local anesthetic in the correct location, and it is likely that aseptic technique is inadequately emphasized in many programs. For those of us in academic institutions, the simple checklist used in this assessment, which incorporates many of the suggestions in recent guidelines, should perhaps serve as an important daily reminder when we are teaching these skills. For those beyond training, these data suggest that a quick review of aseptic technique is not a bad idea.


Last year’s review included a discussion of the controversy regarding whether local anesthetic derivatives could produce selective block of only pain fibers, without motor or proprioceptive block, when deposited in combination with capsaicin via a peripheral nerve block. This concept follows from the observation of some of these authors that capsaicin, by stimulating transient receptor potential vanilloid 1 channels, which are only expressed on C fibers, opens transient receptor potential vanilloid 1 pores such that local anesthetic derivatives, which are normally poorly permeate, enter these fibers. Because local anesthetics block sodium channels by actions inside the nerve axon, this means that only fibers that express transient receptor potential vanilloid 1 are blocked with this combination. The current study extended this observation by studying both relatively poorly permeate local anesthetic derivatives and the clinically used local anesthetics, lidocaine and bupivacaine. They confirmed, using different molecules, the observation that the poorly permeate local anesthetics could produce prolonged nociceptive blockade when combined with capsaicin and, more importantly, showed that this occurred also with lidocaine and bupivacaine, especially when the perineural injection of capsaicin followed that of the local anesthetic. There is much work to be done before the clinical utility of these observations can be determined, including preclinical neurotoxicity testing and determining whether capsaicin can be injected without

Table 1. Examiner’s Checklist for Aseptic Technique

<table>
<thead>
<tr>
<th>No.</th>
<th>Task</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Removes rings and watches</td>
</tr>
<tr>
<td>2</td>
<td>Washes hands and arms upon entering the room</td>
</tr>
<tr>
<td>3</td>
<td>Wears a hat and puts on a fresh facemask</td>
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<tr>
<td>4</td>
<td>Opens the epidural tray in the correct manner and sequence (top flap opened away from operator)</td>
</tr>
<tr>
<td>5</td>
<td>Washes hands with alcohol gel and air dries</td>
</tr>
<tr>
<td>6</td>
<td>Dons gloves in a sterile fashion</td>
</tr>
<tr>
<td>7</td>
<td>Prepares the skin aseptically and waits for the solution to dry</td>
</tr>
<tr>
<td>8</td>
<td>Applies the drape in a cuffed and sterile manner</td>
</tr>
<tr>
<td>9</td>
<td>Works in a manner that minimizes crossing of bare forearms over the sterile field/equipment</td>
</tr>
<tr>
<td>10</td>
<td>Holds the anesthetic receptacle away from the sterile area to allow assistant to pour in required solutions</td>
</tr>
<tr>
<td>11</td>
<td>Keeps all epidural equipment on the sterile tray when not in use</td>
</tr>
<tr>
<td>12</td>
<td>Maintains control over the catheter tip to avoid contamination</td>
</tr>
<tr>
<td>13</td>
<td>Dries the entry site of the epidural catheter and covers it with a sterile dressing while maintaining sterility (this requires keeping one hand sterile over the catheter insertion site, while partially removing the drape with the other hand to allow the nurse to apply the dressing)</td>
</tr>
<tr>
<td>14</td>
<td>Further removal of any residual antiseptic or blood in the surrounding area is completed only after the entry site itself is protected by the sterile dressing</td>
</tr>
<tr>
<td>15</td>
<td>Maintains vigilance over all sterile fields and equipment and notes any potential breaks in technique</td>
</tr>
</tbody>
</table>

0 = did not perform; 1 = inadequately performed; 2 = adequately performed. Reprinted with permission from Friedman Z et al., Anesthesiology 2008; 108:914–20.
causing pain. Nonetheless, these observations may show us a way toward the desired outcome of selective regional analgesia without unwanted motor, sympathetic, and proprioceptive block. This is one of several of the articles in this review that was highlighted on the cover of the Journal this year (fig. 8).


Acute pain from bone fractures is a common and difficult-to-treat problem. Opioids have limited efficacy, and local anesthetic nerve blocks potentially impair assessment of emergent tissue ischemia and acute nerve injury. Depending on surgical preference, the use of nonsteroidal antiinflammatory drugs and cyclooxgenase-2 inhibitors may be prohibited in some fracture patients. The studies of Minville et al. and Freeman et al. used newly developed closed fracture models in mice and rats, respectively, to evaluate the time course and degree of pain-related behaviors after bone injury. Fracture rats exhibited more guarding, an increased number of flinches, and reduced weight bearing compared with naive and pin rats through 14 days. Histologic analyses revealed a relation between pain behaviors and callus formation. Radiographs (figs. 9A and B) and three-dimensional micro–computed tomography images (figs. 9C and D) of the mid-diaphysis reveal calcification of the callus around the fracture site has begun in both female and male rats at day 14 after fracture.

In a similar mouse model, pain behaviors tended to be of similar magnitude and somewhat shorter in duration. Analgesic responses to drugs were also measured. Studies in
bone pain are lacking compared with those in other tissues, such as skin, colon, or dura, because of the inherent problems associated with characterizing sensory nerves in calcified tissues. Studies in fracture models like these should lead to the development of future treatments for patients with traumatic injuries such as hip fractures and rib fractures, injuries associated with significant morbidities. Using these models, the effects of novel analgesic treatments on bone healing can also be assessed.


Postamputation is a serious public health concern, with nearly 200,000 amputations occurring annually in the United States alone and with a third or more of these leading to chronic pain. As such, there is considerable research in approaches to prevent and treat this devastating problem. This leading group of researchers used a powerful, three-period, crossover trial design to test the efficacy of morphine and mexiletine to treat established postamputation pain. The group has been instrumental in demonstrating in the past that neuropathic pain does indeed respond to opioids, and they observed that morphine provided better analgesia than either placebo or mexiletine in these patients with at least moderate pain (fig. 10). The numbers needed to treat with morphine to achieve a reduction in pain of 33% and 50% were 4.5 and 5.6, respectively, and these measures of efficacy compare well to other approved treatments for neuropathic pain. These data do not support the routine use of mexiletine to treat pain in this population and demonstrate clearly that morphine provides pain relief. Although the authors are to be congratulated for adding to evidence on which we can base therapy in this difficult situation, they also acknowledge that side effects were more common with morphine than with other treatments and that patients were only exposed to each drug for 8 weeks—4 weeks of titration, only 2 weeks of maintenance, and then 2 weeks of tapering off. In addition, self-reported levels of overall functional activity were not improved despite the pain relief afforded by morphine in this study. These investigators nonetheless provide an essential and important first step in determining who may benefit from chronic morphine treatment for pain.


Mechanical ventilation itself may aggravate pulmonary inflammation when ventilation volumes are excessively large. An important question for anesthesiologists is whether all ventilation volumes should be “smaller” to protect against this injurious effect. The investigation reported in Anesthesiology evaluated the effect of 5 h of mechanical ventilation on pulmonary inflammation and apoptosis on 40 patients undergoing major surgery. The patients were randomly assigned to two different ventilation strategies, a tidal volume of 12 ml/kg with zero end-expiratory pressure or a tidal volume of 6 ml/kg of ideal body weight with 10 cm H2O positive end-expiratory pressure (PEEP). None of the patients had preexisting lung disease. Bronchoalveolar lavage was performed twice on each patient: immediately after the initiation of anesthesia and mechanical ventilation and then again after 5 h of anesthesia and surgery. The results documented that there were no differences in the gas exchange parameters or in postoperative pulmonary complications between the two groups of patients. Both groups of patients had increased values of inflammatory mediators in their fluid obtained by bronchoalveolar lavage, suggesting that inflammation was occurring in their lungs—either due to surgery and the mechanical ventilation or due to mechanical ventilation alone (because all patients underwent surgery, the direct cause cannot be distinguished). There was a trend for higher concentrations of mediators in the bronchoalveolar lavage fluid obtained from the patients who had received the higher tidal volumes and

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**Fig. 10.** Percentage self-reported pain relief between placebo, morphine, and mexiletine. The use of morphine was associated (general estimating equation model) with significantly higher self-reported percentage pain relief error bars compared with mexiletine ($P < 0.0001$) and placebo ($P < 0.0001$). Reprinted with permission from Wu CL et al., Anesthesiology 2008; 109: 289–96.
zero PEEP, and there were significantly higher concentrations of myeloperoxidase levels and nucleosome levels in the bronchoalveolar lavage fluid from the patients who were ventilated with larger tidal volumes compared with the patients who were ventilated with lower tidal volumes and PEEP. Clearly, further studies are needed to distinguish the role of surgery and PEEP in these findings, but smaller tidal volumes and PEEP seem to be associated with less inflammation and may therefore lead to better outcomes in patients at risk for lung injury.

As was the case, we could easily have chosen another 20 articles to highlight, and we recognize that articles chosen for this review may seem arbitrary. The point of this exercise, however, is to underscore the practical importance of the outstanding research performed in our medical specialty as well as to highlight a few of the fundamental and fascinating observations that will drive our specialty forward in the coming year and beyond. We thank these authors for submitting their work to us, and through us, to you.

References

1. Lichtor JL. I can’t take my eyes off this Web site (with apologies to Frankie Valli). ANESTHESIOLOGY 2008; 109:960–1

Appendix: STOP-Bang Scoring Model

1. Snoring
   Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
   Yes  No
2. Tired
   Do you often feel tired, fatigued, or sleepy during the daytime?
   Yes  No
3. Observed
   Has anyone observed you stop breathing during your sleep?
   Yes  No
4. Blood pressure
   Do you have or are you being treated for high blood pressure?
   Yes  No
5. Body mass index (BMI)
   BMI more than 35 kg/m²?
   Yes  No
6. Age
   Age over 50 years old?
   Yes  No
7. Neck circumference
   Neck circumference greater than 40 cm?
   Yes  No
8. Gender
   Gender male?
   Yes  No

High risk of obstructive sleep apnea (OSA): answering yes to three or more items
Low risk of OSA: answering yes to less than three items