

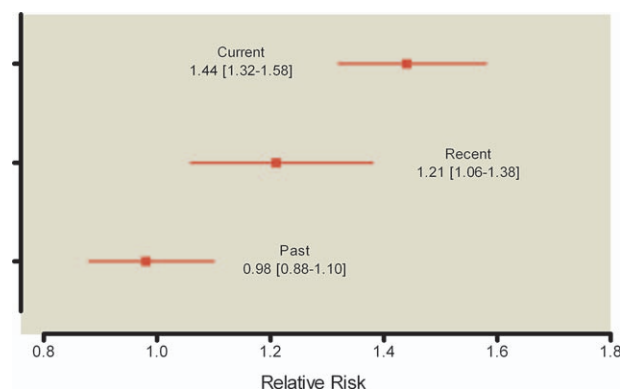
## Perioperative Medicine

**Surge of neurophysiological coherence and connectivity in the dying brain.** *Proc Natl Acad Sci USA* 2013; 110:14432–7

This top-level experimental study shows, using a model of intracardiac injection of potassium chloride in the rat, that cardiac arrest stimulates a marked surge of global coherence of electroencephalography signals. Particularly, gamma oscillations during cardiac arrest were global and highly coherent. This unexpected highly organized brain activity at near death provides a scientific rationale to begin to explain mental experiences reported by cardiac arrest survivors.

**Use of antidepressants near delivery and risk of postpartum hemorrhage: Cohort study of low income women in the United States.** *BMJ* 2013; 347:f4877

In this cohort study, data from the 2000 to 2007 nationwide Medicaid data set including 106,000 pregnant women aged 12–55 yr were analyzed with respect to the use of serotonin or nonserotonin reuptake inhibitors. Subjects were categorized into four mutually exclusive groups according to the pharmacy-dispensing data: current (delivery date), recent (1–30 days before delivery date), past (1–5 months before delivery date), and no exposure (reference group). Exposure to serotonin and nonserotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors, and tricyclics close to the time of delivery was associated with a 1.4- to 1.9-fold increase in postpartum hemorrhage (fig. 1). These findings suggest that patients treated with antidepressant drugs during late pregnancy are more likely to experience postpartum hemorrhage.



**Fig. 1.** Fully adjusted relative risks and 95% CIs comparing risk for postpartum hemorrhage in pregnant women with exposure to antidepressants by alternative exposure groups.

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**Adora2b-elicited Per2 stabilization promotes a HIF-dependent metabolic switch crucial for myocardial adaptation to ischemia.** *Nat Med* 2012; 18: 774–82

Studies have shown that extracellular adenosine signaling may play a role in metabolic adaptation to limited oxygen availability in cardiac tissue. This elegant study identified the circadian protein period 2 (PER2) as a target for adenosine receptor A2b (Adora2b), which is responsible for cardioadaptive responses. Mice lacking the gene encoding for Per-2 had larger infarct sizes, loss of cardioprotection during preconditioning, and limited availability of the heart to use carbohydrate for oxygen-efficient glycolysis compared with wild-type control mice. These data provide an interesting example of the potential importance of proteins involved in circadian rhythm-regulated processes in major adaptive responses.

**Vascular and upper gastrointestinal effects of non-steroidal anti-inflammatory drugs: Meta-analyses of individual participant data from randomized trials.** *Lancet* 2013; 382:769–79

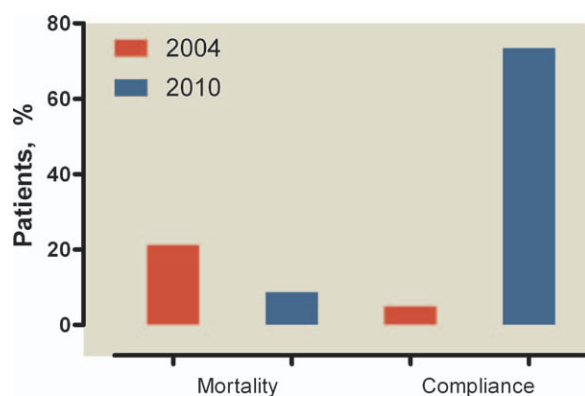
The vascular and gastrointestinal effects of nonsteroidal antiinflammatory drugs (NSAIDs) in patients at increased risk for vascular disease are not well understood. This meta-analysis examined 280 randomized, controlled trials of NSAIDs *versus* placebo and 474 randomized, controlled trials of one NSAID *versus* another were examined. The main outcome measures were major vascular and coronary adverse events (vascular or coronary death, nonfatal myocardial infarction, stroke, cardiac failure, and upper gastrointestinal complications such as bleeding, perforation, and obstruction). It was found that NSAIDs increased vascular and gastrointestinal risks in a predictable manner, and that the vascular risk of high-dose diclofenac, and possibly ibuprofen, is comparable with coxibs, whereas high-dose naproxen is associated with fewer vascular risks than other NSAIDs. These data provide useful information for clinicians which may help to guide the decision-making process.

## Critical Care Medicine

**Multicenter implementation of a severe sepsis and septic shock treatment bundle.** *Am J Respir Crit Care Med* 2013; 188:77–82

Timely recognition and management of patients with sepsis/septic shock are of paramount importance, particularly with the increasing incidence, costs, and burden of morbidity and mortality associated with mismanagement of these

patients. Although bundled recommendations for treating severe sepsis/septic shock have been published by multiple professional societies since 2004, the overall all-or-none compliance with best-practice recommendations remains poor. The current multicenter study reports the results of a quality improvement (QI) project that demonstrates that it is possible to significantly improve overall compliance with the resuscitation bundle elements in treatment of patients with severe sepsis/septic shock. The QI intervention consisted of a large-scale education of healthcare workers on the intent of the sepsis bundle elements. The first three bundle elements consisted of measuring plasma lactate, performing blood cultures, and administering broad-spectrum antibiotics within 3 h of admission of the patients to the emergency department. The remaining four resuscitation bundle elements, administration of intravenous fluids (20–40 ml/kg) for arterial hypotension of lactate greater than 4 mm, administration of vasopressors for arterial hypotension despite adequate fluid resuscitation, obtaining a central venous pressure of greater than 8 cm H<sub>2</sub>O, and a central venous oxygen saturation of greater than 70% (including the administration of vasopressors to achieve these goals and/or the packed red cells if the hematocrit was less than 30%), had to be achieved within 6 h after admission to emergency department. Among 4,329 adult subjects with severe sepsis/septic shock admitted from the emergency department to intensive care units between January 2004 and December 2010 hospital mortality declined from 21.2% in 2004 to 8.7% in 2010 (fig. 2). All-or-none total bundle compliance increased from 4.9 to 73.4% simultaneously. Regression models adjusting for age, severity of illness, and comorbidities identified an association between mortality and compliance with each of inotropes and red cell transfusions, glucocorticoids, and lung-protective ventilation. Finally, compliance with early resuscitation elements during the first 3 h after admission to emergency department caused ineligibility, because of lower subsequent severity of illness, for these later bundle elements. These results indicate that severe sepsis/septic



**Fig. 2.** Temporal association between mortality rates and compliance with quality improvement measurements.

shock bundle compliance increased substantially after the implementation of a QI project, and this was associated with a marked reduction in hospital mortality after adjustment for age, severity of illness, and comorbidities in a multicenter intensive care unit cohort. Early resuscitation bundle element compliance predicted the decrease for the need of subsequent bundle elements. Although this study included a QI project for patients admitted to the intensive care unit from the emergency department, this QI approach could easily be applied to patients who develop a severe sepsis/septic shock in the operating room during a surgical procedure.

*(This article was suggested and commented  
by Jean-François Pittet.)*

### Early acute lung injury: Criteria for identifying lung injury prior to the need for positive pressure ventilation. *Crit Care Med* 2013; 41:1929–37

Acute lung injury (ALI) is associated with high mortality rates despite extensive investigation and lung-protective strategies for mechanical ventilation remain the only disease-specific therapy shown to improve survival. In this prospective study, the authors sought to empirically derive clinical criteria for a pragmatic definition of early ALI to identify patients before the need for positive pressure ventilation. Two hundred fifty-six patients admitted with bilateral opacities on chest radiograph without isolated left atrial hypertension were enrolled in the study. From this cohort, 62 patients (25%) progressed to ALI requiring positive pressure ventilation. Oxygen requirement, maximal respiratory rate, and baseline immune suppression were independent predictors of progression to ALI. A simple three-component early ALI score (1 point for oxygen requirement greater than 2–6 l/min or 2 points for greater than 6 l/min; 1 point each for a respiratory rate of 30 or greater and immune suppression) accurately identified patients who progressed to ALI requiring positive pressure ventilation (area under the receiver-operator characteristic curve, 0.86). An early ALI score of 2 or greater identified patients who progressed to ALI with 89% sensitivity and 75% specificity. Median time of progression from early ALI criteria to ALI requiring positive pressure ventilation was 20 h. This pragmatic definition of early ALI accurately identified patients who progressed to ALI before requiring positive pressure ventilation. Pending further validation, these simple criteria could be useful to select patients who may require high level of monitoring after their admission to the hospital and to determine which patients should be included in future clinical trials targeting early treatment of ALI.

*(This article was suggested and commented  
by Jean-François Pittet.)*

## Pain Medicine

The State of US Health, 1990–2010. Burden of diseases, injuries, and risk factors. *JAMA* 2013; 310:591–08

Estimating the burden of disease helps us to understand the causes and consequences of medical conditions on a population level. One recent innovation in this area has been the global burden of disease framework comprised a set of definitions and methods allowing healthcare comparisons between cities, states, and nations (Lancet 2007; 370:109–10). The current study used the global burden of disease framework to compare several major facets of U.S. health care between 1990 and 2010. Although this carefully conducted and very accessible study provides an excellent overview of the challenges facing U.S. medical care, it is remarkable for specific findings related to our efforts to control chronic pain and the associated disability. The study provides statistics quantifying the years lived with disability and years of life lost. Although diseases including cardiovascular disease, lung cancer, and stroke were prominent in the list of causes for years of life lost, the top five contributors to living with disability were low back pain, major depression, musculoskeletal disease, neck pain, and anxiety disorders. This list of conditions is very familiar to any practitioner practicing chronic pain management and includes some of the most common diagnoses and most problematic comorbidities seen in our pain clinics. Thus in the year 2010, more than 3 million patient-years were lost to disability from low back pain and more than 2 million patient-years were lost to neck pain in the United States. These staggering rates of time-spent suffering from common painful conditions emphasize the importance of our pain management efforts and the lack of control over these conditions we currently have. Finally, the authors point out that a very small amount of National Institutes of Health and other federal funding is directed at the major causes of disability; this includes those specifically related to pain, when compared with those conditions such as cardiovascular disease and cancer, two of the major causes of death in the United States. An accompanying editorial suggests that the principal causes of disability including those conditions related to pain and psychological disease enhanced attention in both policy and funding priority discussions (*JAMA* 2013; 310:585–6).

*(This article was suggested and commented by David Clark.)*

## Education

Effects of modelling examples in complex procedural skills training: A randomized study. *Med Educ* 2013; 47:888–98

### Show Me What You Want Me To Learn-That Will Guide Me!

Simulation is fast becoming the most desirable initial method to teach procedural skills, as it is an effective way to provide this education with no risk to patients and lower stress to students than when they learn in real patient care settings. When the task to be learned is complex requiring multiple steps be performed in correct sequence, the novice is faced with assimilating a large cognitive load (*Med Educ* 2010; 44:85–93). It would be desirable if another teaching method could augment the educational experience and moderate/focus the cognitive load, rather than relying solely upon simulation's trial and error-practicing to effect the most efficient and lasting learning for the novice.

Bjerrum and colleagues investigated the benefit of adding teacher-modeled procedural skills to simulation using bronchoscopy as a complex task to learn. Forty-eight medical students served as the study population. One half learned by participating in eight simulated bronchoscopies. The other half participated in the same simulations and additionally observed three model bronchoscopies, one each performed by experienced instructors before the first two, second two, and third two simulations. The learning effectiveness was measured by how swift and with what degree of accuracy (number of segmental bronchi entered and how frequently bronchial wall collisions occurred and/or the tip of the bronchoscope was against the wall mucosa) simulated bronchoscopy was ultimately preformed.

The authors demonstrated that simulation alone and when augmented with instructor modeling resulted in a positive-learning experience. When modeling was used with simulation, the educational impact was enhanced; segment entry was 46% higher during the immediate posttest period and maintained at 43% higher during the 3-week retention evaluation.

This educational research demonstrates two valuable principles: (1) combining educational methodologies may result in greater learning than using single strategies and (2) understanding the psychology of learning (*e.g.*, the effect of cognitive load) will assist in the selection of the most effective teaching methods.

*(This article was suggested and commented by Alan Jay Schwartz.)*