

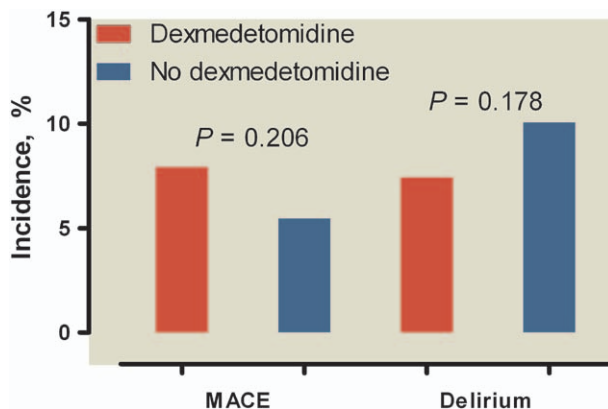
## Perioperative Medicine

### Phylogeny, ontogeny, and emergence from general anesthesia. PNAS 2013; 110:10357–64

In this outstanding review, the authors used a scientific approach based on the different steps of emergence from anesthesia and related investigational tools to address the phylogeny of consciousness. They concluded that the neurophysiologic mechanisms supporting consciousness are evolutionary ancient and highly preserved across species. They emphasized that a review of modern scientific data on the mechanisms of consciousness derived in part from the area of anesthesia supports that differences between species in the ability to experience the world is one of degree and not kind. This conclusion matches with that of the recent Cambridge declaration on consciousness of nonhuman animals as well as Darwin insight.

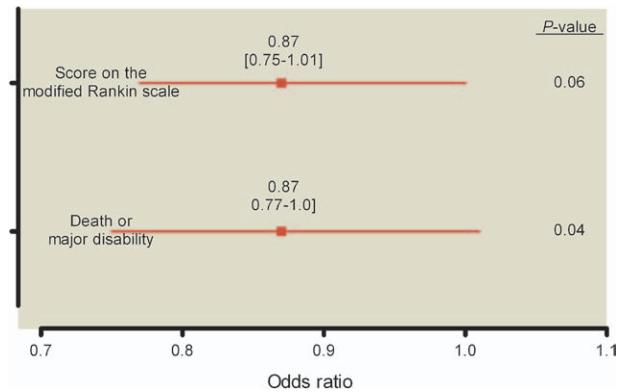
### Perioperative dexmedetomidine improves outcomes of cardiac surgery outcomes. Circulation 2013; 127:1576–84

Approximately 7 million cardiac surgical procedures are performed each year in the world. This single-center, retrospective cohort of 1,134 consecutive patients (half of them receiving perioperative dexmedetomidine, a selective agonist of the  $\alpha_2$ -adrenoceptors) indicates that the use of dexmedetomidine perioperatively was associated with improved 1-yr mortality and a lower rate of major complications. The risk of delirium was also significantly reduced in the dexmedetomidine group (fig. 1). This is the first study showing a benefit of dexmedetomidine on major outcome endpoints such as mortality. Nevertheless, the retrospective nature of this cohort study calls for confirmatory prospective trials.



**Fig. 1.** Effects of dexmedetomidine on postoperative complications and mortality in patients undergoing cardiac surgery. *P* values based on univariate odds ratios (not shown). MACE = major adverse cardiocerebral events.

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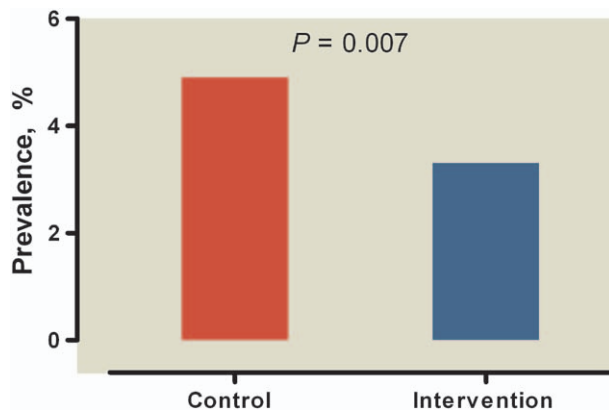
**Fig. 2.** Primary and secondary outcomes at 90 days based on unadjusted odds ratios.

### Rapid blood pressure lowering in patients with acute intracerebral hemorrhage (INTERACT 2). N Engl J Med 2013; 368:2355–65

It is unknown whether rapid lowering of blood pressure at the initial phase of intracerebral acute hemorrhage would improve outcomes. In this randomized, controlled trial, 2,839 patients presenting with acute intracerebral hemorrhage within the previous 6 h were allocated to receive either intensive treatment to lower blood pressure (target blood pressure: 140 mmHg within 1 h) or guideline-recommended treatment (target blood pressure: 180 mmHg). The primary outcome was death or major disabilities (corresponding to a score between 3 and 6 on the modified Rankin scale). No significant difference in mortality was observed between groups (11.9% in the intervention group *vs.* 12% in the guideline-recommended one). However, the ordinal analysis showed significantly lower modified Rankin scores in the intervention group (odds ratio for greater disability: 0.87; 95% CI, 0.77–1; *P* = 0.04; fig. 2). These data suggest the potential safety of intensive treatment to lower blood pressure at the early phase of intracerebral acute hemorrhage.

### Natriuretic peptide-based screening and collaborative care for heart failure: The STOP-HF randomized trial. JAMA 2013; 310:66–74

The increasing prevalence of heart failure is a major health problem calling for efficient preventive strategies. In this randomized, multicenter, controlled trial, patients with cardiovascular risk factors were randomly assigned to undergo either usual primary care (*n* = 677, control conditions) or screening with brain-type natriuretic peptide testing (*n* = 697). Patients with brain-type natriuretic peptide levels of 50 pg/ml or higher underwent echocardiography and collaborative care between their primary care physician and specialist cardiovascular service. The primary endpoint was the prevalence of asymptomatic left ventricular dysfunction with or without newly diagnosed heart failure. There was a significant reduction in the primary



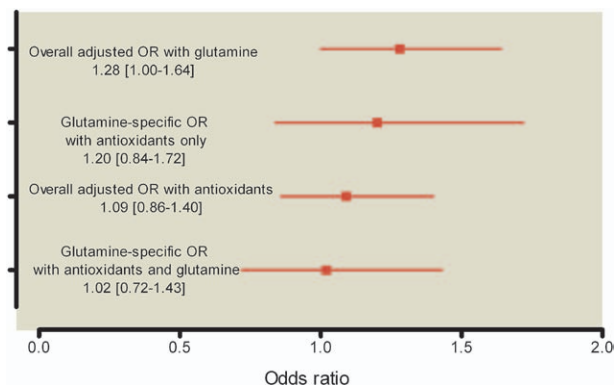
**Fig. 3.** Prevalence of heart failure or left ventricular systolic dysfunction.

endpoint as well as in asymptomatic left ventricular dysfunction in the intervention group *versus* control (fig. 3). The incidence of heart failure was not significantly different between groups. This study emphasizes the efficiency of systematic strategies based on cardiac biomarkers and collaborative physician networks to slow the development of heart failure.

### Critical Care Medicine

#### A randomized trial of glutamine and antioxidants in critically ill patients. *N Engl J Med* 2013; 368:1489–97

Critically ill patients experience considerable oxidative stress. Glutamine and antioxidant supplementation may offer therapeutic benefit, although current data are conflicting. Thus the Canadian Critical Care Trial Group performed a two-by-two factorial trial to assign 1,223 critically ill adult patients with multiorgan failure and who were mechanically ventilated to receive supplements of glutamine, antioxidants, both, or placebo. The primary outcome was 28-day mortality. Supplements were started 24 h after admission to the intensive care unit and were given both intravenously and enterally. The results showed that the early provision of glutamine or antioxidants did not improve clinical outcomes, and glutamine was associated with an increase in mortality among critically ill patients with multiorgan failure (fig. 4). Although previous studies have already shown that antioxidants given after the onset of multiorgan failure do not ameliorate clinical outcomes, the increase in in-hospital mortality at 6 months was somehow surprising. There are several explanations for this result. First, the assumption that there is a need to replenish low plasma levels of glutamine observed in critically ill patients might be erroneous. Second, glutamine was given early after intensive care unit admission and at a higher dose than in previous clinical studies that may have caused toxicity mediated by direct or indirect effects of the amino acid or its metabolites. Third, multiple preclinical and small clinical studies have shown that glutamine induces a heat shock response. There is strong mechanistic evidence



**Fig. 4.** Odds ratio for death according to the study agent. The overall adjusted odds ratios are the estimates of the pooled effect of each study agent, controlled for other study agents; this is the primary outcome. The specific odds ratios are estimates of the effect of each study agent separately with or without the other study agent. All odds ratios have been adjusted for the presence or absence of shock. An odds ratio of more than 1 indicates an increased mortality associated with the study agent.  $P = 0.49$  for the test of interaction between antioxidants and glutamine. OR = odds ratio.

that the activation of the heat shock response is protective in sterile inflammation by inhibiting major cellular pathways that participate to that immune response. However, it is possible that the inhibition of the innate immunity caused by the glutamine-induced heat shock response may be deleterious for critically ill patients admitted to the intensive care unit with serious infection and septic shock (65–70% of the patients included in the current study). These patients are already at high risk for the development of an endogenous immunosuppression to control the overwhelming inflammatory response associated with septic shock.

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

#### Reduced cortisol metabolism during critical illness. *N Engl J Med* 2013; 368:1477–88

Critical illness elicits a major stress response that activates the hypothalamic–pituitary–adrenal axis associated with hypercortisolemia that is proportionate to the severity of illness. However, this stress response may not be sufficient for a good prognosis in patients with relative adrenal insufficiency. In addition, it has been shown that plasma levels of corticotropin are only transiently increased during critical illness, whereas plasma levels of cortisol remained high during the course of the disease. In a total of 158 patients in the intensive care unit and 64 matched controls, five aspects of cortisol metabolism were tested: daily levels of corticotropin and cortisol; plasma cortisol clearance, metabolism, and production during infusion of deuterium-labeled steroid hormones as tracers; plasma clearance of 100 mg of hydrocortisone; levels of urinary cortisol metabolites; and levels of messenger RNA and protein in liver and adipose tissue, to assess major cortisol-metabolizing enzymes. The results showed that during critical illness,

reduced cortisol breakdown, related to suppressed expression and activity of cortisol-metabolizing enzymes, contributed to hypercortisolemia and hence corticotropin suppression. These findings have clinical implications. The contribution of reduced cortisol breakdown to hypercortisolemia during critical illness changes our understanding of the stress response. Reduced inactivation of cortisol may be important not only to increase circulating levels, but also to potentiate cortisol levels and activity within the vital tissues that express inactivating enzymes. More pragmatically, the data suggest that “stress doses” of hydrocortisone (200 mg/day), which are advocated to replace cortisol production in critically ill patients who are presumed to have adrenal failure, are too high. These data also suggest that a low cortisol response to corticotropin stimulation does not necessarily reflect adrenal failure, because cortisol production in critically ill patients is not subnormal and the suppressed clearance maintains hypercortisolemia. Finally, this study calls for additional work to better determine which critically ill patients have a true adrenal insufficiency and thus require treatment.

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

## Pain Medicine

**The extent of neurocognitive dysfunction in a multidisciplinary pain centre population: Is there a relation between reported and tested neuropsychological functioning?** *Pain* 2013; 154:972–7

The field of chronic pain treatment and research is becoming increasingly aware of associated nonpain complaints. For example, depression, anxiety, and sleep disturbances are now routinely assessed and addressed in multidisciplinary pain clinics. However, it is becoming clear through both controlled evaluations and clinical experience that some chronic pain patients have additional neurocognitive problems including difficulties with memory, attention, and diminished general intelligence. These problems have gone relatively unexplored in part because of the inherent difficulties in implementing formal testing procedures. In a recent study by Landro *et al.*, the authors sought to define the prevalence of such neurocognitive problems in a heterogeneous chronic pain population and determine whether cognitive complaints are associated with objective changes in performance in structured neurocognitive tests. Seventy-two new patients presenting at a multidisciplinary pain center were evaluated. In addition to a battery of neurocognitive tests, information was collected on medication use and the type of pain experienced. The authors concluded that 20% of these patients had clinically significant neurocognitive dysfunction, and that subjective patient complaints correlated with the results of the objective testing. Furthermore, those suffering from neuropathic or more generalized pain suffered from deficits about a third of the time. The

results of the study both confirm the relatively high rates of neurocognitive dysfunction in chronic pain patients and suggest that patients are often able to recognize these problems. More regular testing and the introduction of treatments for these problems in multidisciplinary centers may be indicated.

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

## Education

**The relationship between the American Board of Anesthesiology Part 1 Certification Examination and the United States Medical Licensing Examination.** *J Grad Med Ed* 2013; 5:276–83

Are test scores valid criteria for acceptance into an anesthesiology residency? Information that is reviewed in an application file when a medical school graduate applies for admission to a core anesthesiology residency includes such documents as medical school transcript, letters of recommendation, and scores from standardized tests. The United States Medical Licensing Examination (USMLE) is a standardized test that is commonly used in the residency application and approval process. Little information exists as to whether successful performance of USMLE aids in predicting successful performance in anesthesiology residency education. Dillon *et al.* conducted a retrospective observational study to determine the relationship between USMLE scores and success in core anesthesiology residency education represented by the American Board of Anesthesiology (ABA) Part 1 Certification Examination among more than 7,000 residents taking the ABA Part 1 Examination in 2002–2007. In addition to the total scores on the USMLE and Part 1 Examination, an “expert review” of the content areas of the USMLE was performed to see whether higher scores on the appropriate content areas could predict ABA Part 1 performance. A moderately high and positive correlation was documented between USMLE scores and performance on the ABA Part 1 Examination. This correlation was seen with all Part 1 candidates (International and U.S. Medical Graduates) and for U.S. Graduates only. Scores in specific content areas in the USMLE most appropriate to anesthesiology graduate education as defined by the expert review also correlated well with performance on the ABA Part 1 Examination.

The authors of this investigation note that although USMLE performance correlates well and positively with ABA Part 1 Examination performance and content of anesthesiology core residency education, when USMLE data are used to assist in decisions about acceptability of applicants to anesthesiology residency, it should not stand alone and should be viewed with other criteria that will facilitate understanding a full picture of the future resident.

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