ANESTHESIOLOGY

## Maternal and offspring pools of osteocalcin influence brain development and functions. Cell 2013; 155:228-41.

*Cell* is the most prestigious scientific journal in the world. Some readers may find the inclusion of this article out of their usual scope, too far from the clinician's perspective. The purpose of including this article was to draw readers' attention to how outstanding basic research in a seemingly unrelated field can inform our own approach. This study is based on a pertinent and clinically relevant hypothesis that led to the design of a translational strategy that led to original and robust findings that may serve as the cornerstone for future experimental and clinical studies. The topic is of major interest for our specialty: this study demonstrated that osteocalcin (an osteoblast-derived hormone) exerts multiple postnatal influences on the maternal brain, including alteration of neurotransmitter synthesis, prevention of anxiety and depression, and promotion of learning and memory. Osteocalcin crosses the placenta and exerts neuroprotective effects before the fetus is able to synthesize this hormone. Anesthesiologists, particularly those practicing in obstetrics, pediatrics, and neonatal critical care, should read further about this ground-breaking research.

## Long-term cognitive impairment after critical illness. N Engl J Med 2013; 369:1306-16.

Long-term cognitive impairment after admission to the intensive care unit (ICU) remains poorly characterized. This cohort study enrolled 821 ICU patients with respiratory failure or shock who were evaluated for delirium and global cognition and executive function 3 and 12 months after discharge using the Repeatable Battery for the Assessment of Neuropsychological status. A follow-up cohort included 467 patients. At baseline 6% of the patients had cognitive impairment. Delirium (measured by the CAM-ICU) developed in 74% of patients during the hospital stay. Deficits occurred in both younger and older patients with cognitive status at 12 months close to that of patients with moderate trauma brain injury (34%) and to that of patients with mild Alzheimer disease (24%). A longer duration of delirium was an independent predictor of worse global cognition and executive function at 3 and 12 months, while use of sedative and analgesics were not. These very interesting data support that medical and surgical ICU patients are at high risk of long-term cognitive impairment regardless of age. These data may also temper a possible detrimental role of sedatives on long-term cognitive impairment, which does not mean that avoiding oversedation should not be considered as a cornerstone principle of ICU sedation any longer.

## Chronic use of opioid medications before and after bariatric surgery. JAMA 2013; 310:1369-76.

Morbid obesity is associated with chronic noncancer pain and with chronic opioid use. Whether bariatric surgery reduces the requirements for postoperative pain medications remains unknown. In this retrospective multicenter cohort study, 11,719 patients who had undergone bariatric surgery between 2005 and 2009 were assessed 1 yr before and after surgery for opioid use. Of the 8% of patients that were chronic opioid users before surgery 933 patients (77%) continued chronic use of opioids in the year after surgery. Chronic opioid use was significantly higher postoperatively ($P < 0.01$). These findings suggest the need for better pain management in these patients after surgery.

## Association of national initiatives to improve cardiac arrest management with rates of bystander intervention and patient survival after out-of-hospital cardiac arrest. JAMA 2013; 310:1377-84.

Despite intense research activity dedicated to improve outcomes of patients having experienced out-of-hospital cardiac arrest, long-term survival remains low. Assistance of bystanders in managing early cardiopulmonary resuscitation (CPR) may reduce the duration of the "no flow" period and subsequently improve long-term survival by acting at the first step of the survival chain. This retrospective Danish cohort study used the national registry of cardiac arrests (2001–2010) to examine trends in survival following out-of-hospital cardiac arrest from cardiac causes (at 30 days and 1 yr), and temporal trends in bystander CPR and bystander defibrillation in 19,468 patients. Bystander CPR significantly increased during the study period, while the rate of bystander defibrillation remained low. Bystander CPR was positively associated with 30-day survival, independent from witnessed status. This association was still higher for witnessed cardiac arrest. While a causal relationship cannot be established between rates of bystander intervention and survival, these results strongly encourage the development of national health policies in educating people to provide on-scene CPR in patients with out-of-hospital cardiac arrest, whether or not they witnessed the event.

## Benzodiazepine *versus* nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: A systematic review and meta-analysis of randomized trials. Crit Care Med 2013; 41:830-8.

The use of dexmedetomidine or propofol rather than a benzodiazepine for sedation may improve outcomes. Nonetheless, benzodiazepines are still largely used as sedative drugs for patients in the intensive care unit (ICU). This systematic review and meta-analysis reviewed randomized trials that compared benzodiazepine and non-benzodiazepine regimens in mechanically ventilated adult ICU patients to determine if differences exist between these sedation strategies with respect to ICU length of stay, time on the ventilator, delirium prevalence, and short-term mortality. Six trials enrolling 1,235 patients were included in this review: midazolam *versus* dexmedetomidine (n = 3), lorazepam *versus* dexmedetomidine (n = 1), midazolam *versus* propofol (n = 1), and lorazepam *versus* propofol (n = 1). Compared to a benzodiazepine sedative strategy, a non-benzodiazepine sedative strategy was associated with shorter ICU length of stay and duration of mechanical ventilation but similar prevalence of delirium and short-term mortality rate. Current data suggest that use of dexmedetomidine- or propofol-based sedation rather than benzodiazepine-based sedation in critically ill adults may reduce ICU length of stay and duration of mechanical ventilation. Larger controlled studies are needed to further define the impact of non-benzodiazepine sedative regimens on delirium and short-term mortality.

## Evolution of mortality over time in patients receiving mechanical ventilation. Am J Respir Crit Care Med 2013; 188:220–30.

The characteristics and management of patients requiring mechanical ventilation have changed over time; the impact of these changes on patient outcomes is unclear. This study aimed to estimate whether mortality in mechanically ventilated patients has changed over time. This analysis included prospective cohort studies conducted in 1998, 2004, and 2010, including patients receiving mechanical ventilation for more than 12 h in a 1-month period, from 927 units in 40 countries including 18,302 patients. The reasons for initiating mechanical ventilation varied significantly among cohorts. Ventilatory management changed over time, with increased use of noninvasive positive-pressure ventilation (5% in 1998 to 14% in 2010), a decrease in tidal volume (mean 8.8 ml/kg actual body weight in 1998 to 6.9 ml/kg in 2010), and an increase in applied positive end-expiratory pressure (mean 4.2 cm $H_2O$ in 1998 to 7.0 cm $H_2O$ in 2010). Crude mortality in the intensive care unit decreased in 2010 when compared with 1998 (28 *vs.* 31%; odds ratio, 0.87; 95% confidence interval, 0.80–0.94), despite a similar complication rate. Hospital mortality decreased in parallel. After adjusting for baseline and management variables, this difference remained significant (odds ratio, 0.78; 95% confidence interval, 0.67–0.92). This demonstrates that the use of low tidal volume and an open lung strategy decreases mortality in ventilated intensive care unit patients independent from the original indication for the institution of mechanical ventilation.

## Neonatal pain-related stress, functional cortical activity and visual-perceptual abilities in school-age children born at extremely low gestational age. PAIN 2013; 154:1946-52. Accompanying editorial: PAIN 2013; 154:1899-901.

The past several years have seen a rapid growth in studies related to the long-term neurocognitive consequences of prematurity. Extremely low gestational age (ELGA; <28 weeks) infants may be at particular risk for complications. Anesthesiologists have long been concerned about the effects of anesthesia and surgery in this population. In their recent publication, Doesburg *et al.* provide evidence suggesting a relationship between neonatal pain in ELGA infants and long-term neurocognitive deficits. The authors evaluated 54 preterm children and 25 age-matched full-term controls. Cumulative neonatal pain, defined using the number of skin-breaking procedures, was correlated with the results of magnetoencephalography, a sophisticated technique allowing the investigators to estimate cortical oscillatory levels. The results suggest that cumulative pain was associated with abnormal oscillatory levels even when results were adjusted for confounders. The abnormal magnetoencephalography results predicted lower visual-perceptual abilities at school age. A relationship between pain and longer term neurocognitive deficits has been suspected for some time; this study may be the first to provide results linking pain in premature infants to abnormalities in brain functional activity and later age cognitive abilities. The authors explain in their paper that the premature brain may be especially vulnerable to pain-related input during this critical developmental period. The results suggest that we should reexamine the use of analgesia during painful procedures in neonates.

**Ethnography in qualitative educational research: AMEE Guide No. 80. Medical Teacher 2013; 35:e1365-79.**

Physicians, as scientists, often think of research in terms of the double-blind, randomized, controlled trial. This approach is not so easily applied to investigations about medical education. Education occurs in a setting where people interact with each other and are influenced by real-life circumstances. Is there a research methodology that lends itself to the study of the social setting of medical education? Ethnography is a research approach unfamiliar to many physicians, which is applicable to the study of social interactions like those that occur in the course of medical education. Utilizing the ethnographic construct, actions are investigated in real-life settings through direct observation of social interactions (see Box 1 of the manuscript). This is bolstered by review and analysis of interviews of the participants. Relevance and validity of ethnography is provided through a process of triangulation. There are three aspects involved in this data analysis: description, analysis, and interpretation. Description refers to the recounting and describing of data. Analysis refers to the process of examining relationships, factors, and linkages across the data points. Interpretation of data builds an understanding or explanation of the data beyond the data, description, and analysis. If we are to assure that students and society are reaping the benefits of the best educational programs, ethnography provides a methodology to assess this benefit. The article by Reeves *et al*. provides a broad overview of ethnography and includes resources to assist us in its use in quasi-experimental research on medical education.