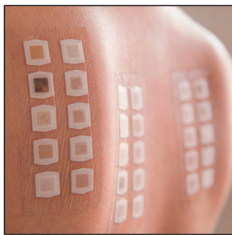


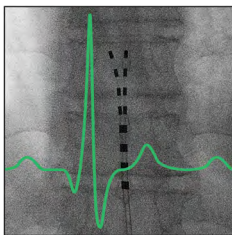
## 354 Postoperative Pulmonary Complications in the ENIGMA II Trial: A *Post Hoc* Analysis

Respiratory complications remain among the most common and serious adverse outcomes of major surgery. The hypothesis that nitrous oxide anesthesia results in a lower rate of postoperative atelectasis compared to an oxygen–air mix at similar fraction inspired oxygen ( $\text{FiO}_2$ ) was tested in a *post hoc* collection of data on postoperative pulmonary complications for 2,328 patients recruited to the Australian cohort of the Evaluation of Nitrous Oxide In the Gas Mixture for Anesthesia (ENIGMA) II trial between 2007 and 2013. The ENIGMA II trial compared the incidence of perioperative cardiovascular and septic complications in high-risk patients undergoing major surgery randomly assigned to receive general anesthesia including a gas mixture containing an  $\text{FiO}_2$  of 0.3 in either nitrogen or nitrous oxide. The incidence of atelectasis in the nitrous oxide group was 14.6% (171 of 1,169 patients) and that in the nitrous oxide–free group was 18.1% (210 of 1,159 patients) for an odds ratio (95% CI) of 0.77 (0.62 to 0.97). The 19.3% lower relative risk of atelectasis with nitrous oxide in the ENIGMA II trial stands in sharp contrast to the 73% higher risk in the earlier ENIGMA trial, the control group of which was administered an  $\text{FiO}_2$  of 0.8. See the accompanying Editorial on [page 345](#). (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals Studio.)



## 364 Immediate Hypersensitivity to Chlorhexidine: Experience from an Allergy Center in China

Chlorhexidine is a topical disinfectant and antiseptic that has a good safety profile but can cause allergic reactions. The experience of a Chinese allergy center with chlorhexidine allergy testing was summarized after retrospective evaluation of the records of all patients who underwent such testing between February 2018 and May 2022. In the center, chlorhexidine allergy testing is routinely performed in all patients with perioperative allergic reactions and who suffered allergic reactions to more than two kinds of infusion drugs or IV saline or glucose infusion. Ten of the 43 patients tested in the center were diagnosed with the allergy by skin prick and serum-specific immunoglobulin E tests. They had experienced a total of 30 allergic reactions to chlorhexidine. Twenty-three of the allergic reactions to chlorhexidine were attributed to its use for skin disinfection, in 22 of which IV cannulation was the route of exposure. (Summary: M. J. Avram. Image: Adobe Stock.)



## 372 GABAergic Signaling during Spinal Cord Stimulation Reduces Cardiac Arrhythmias in a Porcine Model

Spinal cord stimulation therapy is postulated to reduce sympathetic afferent neural signaling induced in the dorsal horn by myocardial ischemia and stabilize efferent outflows to cardiac tissues, thus reducing ventricular arrhythmias during ischemia. The hypothesis that spinal cord stimulation reduces myocardial ischemia/reperfusion–induced sympathetic excitation and ventricular arrhythmias through  $\gamma$ -aminobutyric acid (GABA)–mediated pathways in the thoracic spinal cord was tested in a randomized study in a porcine model of cardiac ischemia/reperfusion injury. Spinal cord stimulation therapy during cardiac ischemia lessened myocardial sympathetic excitation and ventricular arrhythmias. Intrathecal GABA<sub>A</sub> and GABA<sub>B</sub> receptor blockade during spinal cord stimulation therapy abolished its protective myocardial effects, resulting in sympathetic excitation and arrhythmias similar to that observed in animals without spinal cord stimulation. Intrathecal administration of a GABA transaminase inhibitor alone provided cardiac protection similar to that provided by spinal cord stimulation therapy. Spinal cord stimulation neuromodulation during cardiac ischemia was associated with more GABA<sub>A</sub> receptor expression and no change in GABA<sub>B</sub> receptor expression. See the accompanying Editorial on [page 348](#). (Summary: M. J. Avram. Image: J. P. Rathmell.)



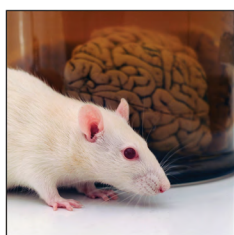
## 420 Lung Injury Is Induced by Abrupt Increase in Respiratory Rate but Prevented by Recruitment Maneuver in Mild Acute Respiratory Distress Syndrome in Rats

A high respiratory rate may cause ventilator-induced lung injury in a mechanically heterogeneous lung. The hypotheses that gradually approaching a higher respiratory rate would produce less ventilator-induced lung injury than abruptly increasing to the same rate and that a recruitment maneuver before abruptly increasing the rate may prevent its injurious effect were tested in mechanically ventilated rats with acute lung injury induced by intratracheal instillation of *Escherichia coli* endotoxin. Compared with an abrupt increase to a given rate for 1 h or 2 h, both short and long increases to the same rate decreased mechanical power, attenuating ventilator-induced lung injury. Cumulative power in the group with abrupt increase of respiratory rate for 1 h was similar to that in control rats without an increased rate, but their diffuse alveolar damage score was higher. The cumulative power of shorter and longer respiratory rate adaptation groups ventilated for 2 h were higher than in animals exposed to the abruptly increased rate for 1 h, but their diffuse alveolar damage score was lower. A recruitment maneuver prevented the injurious biologic effect of abrupt increases in respiratory rate. See the accompanying Editorial on [page 351](#). (Summary: M. J. Avram. Image: Adobe Stock.)



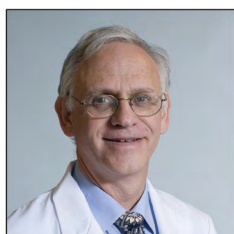
### 403 **Mouse Model of Spinal Cord Hypoperfusion with Immediate Paralysis Caused by Endovascular Repair of Thoracic Aortic Aneurysm**

Thoracic aortic aneurysm disease can be lethal if left untreated, but both traditional open repair and thoracic endovascular aortic repair can cause ischemic spinal cord injury. After a pilot study of varying ligation strategies was conducted, the hypothesis tested was that double-ligating three pairs and single-ligating two pairs of adult mouse intercostal arteries would simulate thoracic endovascular aortic repair–induced ischemic spinal cord hypoperfusion with paralysis severity variability and mortality rates comparable with those observed in human patients. Radiologic, behavioral, and histopathologic studies demonstrated that the model induced spinal cord hypoperfusion and caused spinal cord histopathologic ischemic damage resulting in variable behavioral deficits mimicking human patient findings. Paralysis occurred immediately, with wide behavioral deficit variability (severe to mild). Motor function improved gradually in mildly and moderately paralyzed mice throughout the 2-week follow-up period but was permanently lost in severely paralyzed mice. The mortality rate was higher in severely paralyzed mice (83%) than in moderately paralyzed (33%) and mildly paralyzed mice (24%). (Summary: *M. J. Avram. Image: Adobe Stock.*)



### 388 **Intergenerational Perioperative Neurocognitive Disorder in Young Adult Male Rats with Traumatic Brain Injury**

Perioperative stress, neuroinflammation, and preexisting neurodegenerative diseases may play a role in the development of perioperative neurocognitive disorder. Repeated exposure of young adult rats to sevoflurane not only affects exposed rats but also causes intergenerational neurobehavioral abnormalities. The hypothesis that the effects of sevoflurane anesthesia, surgery, and traumatic brain injury interact to induce neurobehavioral abnormalities in adult male rats and their offspring was tested in a randomized controlled trial that included four treatment groups. In adult male rats, the effects of surgery under sevoflurane anesthesia to induce traumatic brain injury and, to a greater extent, the combined effects of surgery and traumatic brain injury interact with the effects of subsequent repeated sevoflurane exposure to induce abnormalities in hypothalamic–pituitary–adrenal axis functioning, inflammatory markers, and some behavioral tests. Male offspring of the affected rats developed the same types of abnormalities. Epigenetic changes in spermatozoa may play a role in the intergenerational transmission of the adverse effects of paternal sevoflurane exposure, surgery, and traumatic brain injury. (Summary: *M. J. Avram. Image: Adobe Stock.*)



### 436 **Luck, an Inquisitive Mind, and Opportunities: Lessons Learned: A Blinded Study of Pulse Oximetry before It Became a Standard of Care (Classic Paper Revisited)**

In revisiting his Classic Paper, Charles J. Coté, M.D., provides an overview of his rich and rewarding research career devoted to improving pediatric patient safety beginning with a careful observation he made as a medical student that affected patient outcome and stimulated his interest in anesthesiology and critical care. He continued to make clinical observations that led to patient safety studies. Then, at the 1986 Annual Meeting of the American Society of Anesthesiologists, he was introduced to a new device that could provide continuous oxygen saturation monitoring, the pulse oximeter. Recognizing the potential importance of this device, he conducted the first blinded study of pulse oximetry. The Classic Paper that resulted from this study was published in *ANESTHESIOLOGY* in 1988 and concluded that “pulse oximetry, in contrast to changes in vital signs, does provide an early warning of developing hypoxemia in anesthetized children,” something that is now taken for granted. Dr. Coté concludes with advice to those who are or could become interested in pursuing research opportunities: “Never doubt your powers of observation . . .” (Summary: *M. J. Avram. Image: From original article.*)