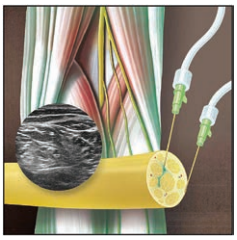
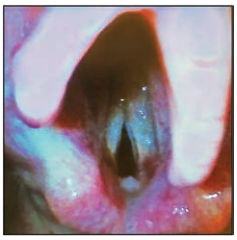
THIS MONTH IN

ANESTHESIOLOGY



241 Intraneural Ultrasound-guided Sciatic Nerve Block: Minimum Effective Volume and Electrophysiologic Effects

If axonal nerve damage produced by both intraneural and extraneural sciatic nerve local anesthetic injection is due to the ischemia caused by the high local anesthetic volume deposited around the nerve fascicles, a significant reduction of the local anesthetic volume possible with the intraneural technique may reduce axonal damage. A prospective, biased-coin up-and-down sequential design study of 47 patients determined the minimum effective volume of ropivacaine 1% to achieve a complete sensory-motor sciatic nerve block in 90% of patients, using an ultrasound-guided intraneural popliteal approach, to be 6.6 ml (95% CI, 6.4 to 6.7), with an onset time of 19 ± 12 min. Electrophysiologic tests in 43 of the patients 5 weeks after surgery and again in 23 patients at 6 months found a significant reduction of the amplitude of action potentials compared with the baseline, while latency and velocity did not differ from the baseline. *See the accompanying Editorial View on* **page 221.** *(Summary: M. J. Avram. Illustration: A. Johnson, Vivo Visuals.)*

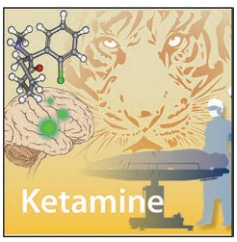


321 Comparison of Tracheal Intubation Conditions in Operating Room and Intensive Care Unit: A Prospective, Observational Study

The hypothesis that tracheal intubation using direct laryngoscopy would be associated with worse intubation conditions and more complications in the intensive care unit than in the operating room was tested prospectively in 208 patients admitted to the intensive care unit who had been intubated in the previous month in the operating room. Patients were intubated by anesthesiologists with similar levels of experience. The primary outcome, glottic visualization assessed using the modified classification of Cormack and Lehane, worsened in 69 patients (33%) in the intensive care unit and improved in 14 patients (7%). The proportion of successful first intubation attempts was 97% in the operating room and 89% in the intensive care unit. The incidence of moderate and difficult intubation was higher in the intensive care unit (16%) than in the operating room (9%), and complications were more common during tracheal intubations in the intensive care unit (37%) than in the operating room (6%). *(Summary: M. J. Avram. Image: M. Tilquist, Brigham and Women's Hospital.)*

249 Cost-benefit Analysis of Maintaining a Fully Stocked Malignant Hyperthermia Cart *versus* an Initial Dantrolene Treatment Dose for Maternity Units

The Malignant Hyperthermia Association of the United States recommends that dantrolene be made immediately available (for administration within 10 min) in operating room areas. A cost-benefit analysis was conducted to evaluate whether, at the population level, the benefits of maintaining a malignant hyperthermia cart in or near maternity units in the United States instead of relying on malignant hyperthermia carts available in other areas of the hospital exceed the costs associated with this practice. Using conservative assumptions of costs, rates of general anesthesia, incidence of malignant hyperthermia, and expected mortality and morbidity from malignant hyperthermia, the cost of a life saved was found to be significantly greater than what is considered of cost-benefit. Only by assuming an unreasonably high case fatality rate, general anesthetic incidences, or cesarean delivery rates does it become of cost-benefit to maintain a fully stocked malignant hyperthermia cart on a maternity unit. *See the accompanying Editorial View on* **page 225.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



260 Combined Recirculatory-compartmental Population Pharmacokinetic Modeling of Arterial and Venous Plasma S(+) and R(–) Ketamine Concentrations

The oscillations of arterial and venous drug concentrations in the moments after drug administration as a rapid intravenous bolus have been characterized by recirculatory pharmacokinetic models that describe intravascular mixing by incorporating cardiac output and its distribution. Using arterial and venous plasma concentrations in blood samples collected simultaneously during and after a 30-min ketamine enantiomer infusion on two occasions in a previous study, an intravascular mixing model was developed to reconcile the divergent arterial and venous ketamine concentration *versus* time curves during and after the infusion. The higher arterial ketamine concentrations during infusion result from the contribution of both unmixed drug from the upstream infusion and fully mixed recirculating drug, an "infusion artifact" that is proportional to the ratio of drug infusion rate and cardiac output. Postinfusion venous ketamine concentrations were systematically slightly higher than the corresponding arterial concentrations due to a contribution of higher drug concentrations eluting from arm tissue. *(Summary: M. J. Avram. Illustration: A. Johnson, Vivo Visuals.)*

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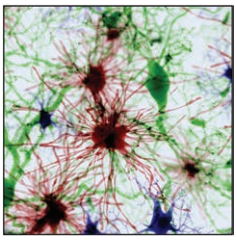


278 Ketamine Alters Hippocampal Cell Proliferation and Improves Learning in Mice after Traumatic Brain Injury

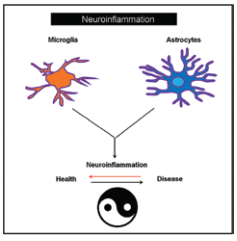
The postinjury response to traumatic brain injury includes increased glial proliferation and activation as well as an increase in hippocampal neurogenesis. *N*-methyl-D-aspartate-type inotropic glutamate receptors potently modulate glial function and proliferation, either directly or indirectly, *via* alterations in neuronal function and signaling. The effects of the administration of ketamine, a noncompetitive *N*-methyl-D-aspartate receptor antagonist, on hippocampal cell proliferation after traumatic brain injury was tested in mice in which traumatic brain injury was modeled using a controlled cortical impact injury. Traumatic brain injury induced robust cellular proliferation in the hippocampus, which included the generation of immature neurons and astrocytes from radial glial-like cells. When ketamine was administered after controlled cortical impact, hippocampal cell proliferation in the dentate granule cell layer was markedly accelerated. These changes in proliferation were associated with an improvement in learning weeks after ketamine cessation, as determined by the Morris Water Maze reversal task. *See the accompanying Editorial View on* **page 232.** *(Summary: M. J. Avram. Image: ©ThinkStock.)*

311 Sphingosine-1-phosphate Receptor 2 Signaling Promotes Caspase-11–dependent Macrophage Pyroptosis and Worsens *Escherichia coli* Sepsis Outcome

Pyroptosis, a proinflammatory programmed cell death, is initiated by at least one type of inflammasome, such as the canonical inflammasome nucleotide-binding oligomerization domain-like receptor 3 (NLRP3) assembled in response to both microbial infection and endogenous "danger signals" or the noncanonical inflammasome caspase-11 formed by cytosolic exposure to endotoxin. Sphingosine-1-phosphate signaling can amplify interleukin-1β secretion in endotoxin-induced inflammation. The hypothesis that signaling through sphingosine-1-phosphate receptor 2 (S1PR2), the predominant sphingosine-1-phosphate receptor in macrophages, increases caspase-11–dependent macrophage pyroptosis and worsens Gram-negative sepsis outcome was tested in S1PR2 knockout and NLRP3 knockout mice using a peritoneal *E. coli*–induced sepsis model. NLRP3 was not involved in S1PR2 signaling-mediated macrophage pyroptosis. Genetic deficiency of S1PR2 significantly improved survival and decreased caspase-11 activation, macrophage pyroptosis, and interleukin-1β secretion both *in vivo* and *in vitro*. S1PR2-overexpression promoted macrophage pyroptosis and subsequent interleukin-1β secretion after *E. coli* stimulation. Inhibition of Ras homolog gene family, member A (RhoA), which plays a role in inflammatory diseases, prevented the enhanced caspase-11 activation in wild type or S1PR2-overexpression macrophages. *See the accompanying Editorial View on* **page 238.** *(Summary: M. J. Avram. Image: ©ThinkStock.)*

335 Presumed β-Lactam Allergy and Cross-reactivity in the Operating Theater: A Practical Approach (Clinical Focus Review)

A β-lactam antibiotic allergy is the most common suspected in-hospital drug allergy. The main β-lactam antibiotic groups are the penicillins, cephalosporins, carbapenems, and monobactams, and the most frequently reported β-lactam antibiotic allergy is a penicillin allergy. The consequence of a presumed β-lactam antibiotic allergy is often that all β-lactam antibiotics are avoided as surgical prophylaxis, because of possible cross-reactivity, and an alternative antibiotic is prescribed. While this may be a short-term risk avoiding strategy during surgery, the long-term consequences of it are overuse of the alternative antibiotics, which may lead to an increase in serious hospital infections. This review provides an evidence-based and practical approach to patients with presumed β-lactam antibiotic allergies admitted to the operating room and gives guidance on the selection of alternative antibiotics based on cross-reactivity patterns. The recommended approach may reduce the likelihood of a perioperative anaphylaxis without fully excluding it. *(Summary: M. J. Avram. Image: ©ThinkStock.)*



343 Neuroinflammation and Central Sensitization in Chronic and Widespread Pain (Review Article)

Chronic pain is maintained in part by central sensitization, a phenomenon of synaptic plasticity and increased neuronal responsiveness in central pain pathways after painful insults. Central sensitization may also be driven by neuroinflammation in the peripheral and central nervous systems, which is characterized by activation of glial cells, leading to the release of proinflammatory cytokines and chemokines. Indeed, cytokines, chemokines, and other glia-produced mediators circulated in the cerebrospinal fluid can induce and maintain central sensitization. Enthusiasm for the development of new treatments that specifically target neuroinflammation and glial activation has been tempered by the somewhat disappointing results of clinical trials, which may point to the need to develop animal models that better reflect the various genetic, sex-dependent, psychologic, and environmental factors and sequelae of the development and maintenance of chronic pain. Alternative approaches that can control excessive neuroinflammation include specialized proresolution mediators, cell therapies, and neuromodulation. *(Summary: M. J. Avram. Illustration: Modified from original article.)*