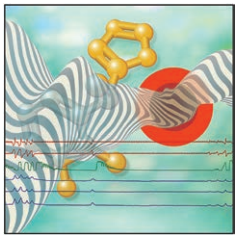
THIS MONTH IN ANESTHESIOLOGY



962 Upper Airway Collapsibility during Dexmedetomidine and Propofol Sedation in Healthy Volunteers: A Nonblinded Randomized Crossover Study

Dexmedetomidine is used for sedation in both children and adults, with and without obstructive sleep apnea, in the belief that both upper airway patency and ventilatory drive are less compromised with dexmedetomidine than they are with other sedatives. This belief has been challenged by findings from several recent studies. The hypothesis that dexmedetomidine sedation would have less effect on upper airway collapsibility than propofol sedation was tested in a randomized crossover study of nine volunteers. Pharyngeal critical pressure, which assesses the intraluminal pressure at which airway closure occurs, was used as a measure of collapsibility. Apnea episodes occurred during sedation with both drugs. Pharyngeal critical pressure values indicative of total obstruction at atmospheric pressure (*i.e.*, values of 0 cm H_2O or higher) were observed in five of the nine subjects during dexmedetomidine infusion at low and/or moderate infusion rates. There was no difference in pharyngeal critical pressure value thresholds during sedation with dexmedetomidine or propofol at either low or moderate infusion rates. *See the accompanying Editorial View on* **page 953.** *(Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals.)*

1004 Pharmacodynamic Interaction of Remifentanil and Dexmedetomidine on Depth of Sedation and Tolerance of Laryngoscopy

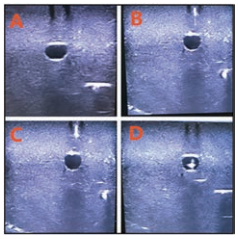
Patients sedated with standard clinical doses of dexmedetomidine can be readily aroused. Dexmedetomidine doses producing mild to deep sedation lack significant analgesic effect. Although remifentanil is an opioid analgesic with only modest sedative properties, addition of remifentanil to propofol sedation reduces the propofol concentration required to reach tolerance of shaking the patient while shouting their name and tolerance of laryngoscopy. This three-phase crossover trial was designed to study the pharmacodynamic interaction between remifentanil and dexmedetomidine and quantify their expected synergy in 30 age- and sex-stratified healthy volunteers on two occasions. On day one volunteers were administered stepwise increasing target-controlled infusions of dexmedetomidine while on day two they were administered target-controlled infusions of remifentanil alone and remifentanil with a fixed background dexmedetomidine concentration. Despite falling asleep, most subjects remained arousable by calling their name, shaking them while shouting their name, or a trapezius squeeze, even after reaching supraclinical dexmedetomidine concentrations. The addition of remifentanil to dexmedetomidine sedation did not affect the likelihood of subject response to graded stimuli. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

983 An Assessment of Penetrance and Clinical Expression of Malignant Hyperthermia in Individuals Carrying Diagnostic Ryanodine Receptor 1 Gene Mutations

Malignant hyperthermia is a rare life-threatening disorder triggered in genetically predisposed individuals by exposure to certain anesthetics. The ryanodine receptor 1 (*RYR1*) gene, which encodes the Ca^{2+} release channel of skeletal muscle sarcoplasmic reticulum, is the major malignant hyperthermia-associated locus. Malignant hyperthermia diagnostic mutations are more prevalent than the reported incidence of clinical malignant hyperthermia episodes because many mutation carriers are never exposed to anesthetic triggers and some may have several uneventful anesthetics before developing malignant hyperthermia. In a multicenter case-control study of 229 genotype-positive subjects with previous recorded exposure to trigger anesthetics, there were 93 malignant hyperthermia cases, for an overall penetrance for the analyzed *RYR1* mutations of 41%. The probability of developing malignant hyperthermia on exposure to triggers was 0.25 among all *RYR1* mutation carriers and 0.76 in survivors of malignant hyperthermia reactions (95% CI of the difference, 0.41 to 0.59). Young age, male sex, and the use of succinylcholine were major nongenetic risk factors influencing expression of the *RYR1* genotypes conferring malignant hyperthermia susceptibility. *See the accompanying Editorial View on* **page 957.** *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

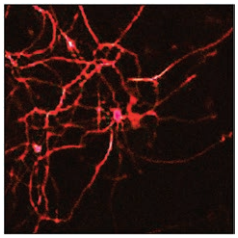
974 Genetic Analysis of Patients Who Experienced Awareness with Recall while under General Anesthesia

The incidence of explicit recall of intraoperative events, or awareness with recall, is less than 0.2%. Anesthetic dosing is apparently adequate in 10 to 25% of patients with awareness with recall. The awareness with recall phenotype only reveals itself when patients are exposed to anesthesia; typically, awareness with recall patients display no other identified phenotypic disturbance in day-to-day life. A preliminary study in 12 patients who had suffered awareness with recall in the presence of apparently adequate anesthesia sought to determine whether there is evidence that awareness with recall is caused by a few rare genetic variants with high penetrance. Whole exome sequencing was conducted and identified variants were filtered and prioritized to identify a candidate list that might be suitable for further investigation of causes of awareness with recall. No candidate gene(s) suggestive of a monogenic etiology were identified, possibly because of the application of a filtering strategy, the small sample size, or use of exome sequencing, which does not interrogate potentially important regulatory noncoding sequences. *See the accompanying Editorial View on* **page 955.** *(Summary: M. J. Avram. Image: ©gettyimages.)*



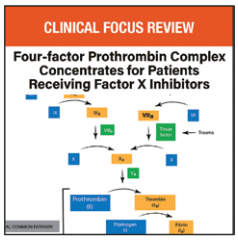
1018 Acoustic Shadowing Facilitates Ultrasound-guided Radial Artery Cannulation in Young Children

The success rate of radial artery puncture has improved with the ultrasound-guided technique but depends on the operator's experience and skills due to the two-dimensional nature of the imaging. The acoustic shadowing ultrasound with double developing lines produced by metal-containing strands taken from x-ray detectable surgical gauze and bound in parallel 2 mm apart to the ultrasound probe helps locate the projection point of the midpoint of the radial artery on the skin surface to enable quick and accurate determination of the puncture point. The hypothesis that ultrasound-guided vascular puncture with double developing lines could help increase the success rate of radial artery puncture was tested in a randomized controlled trial of 79 young children. Radial artery cannulation was successful at the first attempt in 35 of the 39 (90%) patients in the novel ultrasound group and in 24 of the 40 (60%) patients in the traditional ultrasound group (difference 30%; 95% CI, 12 to 48%). *(Summary: M. J. Avram. Image: From original article.)*



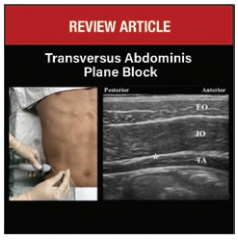
1063 Nitrous Oxide Impairs Axon Regeneration after Nervous System Injury in Male Rats

Methionine is the single carbon donor in mammalian cells. Methionine synthase requires 5-methyl-tetrahydrofolate as its single carbon source and is irreversibly inactivated by nitrous oxide with oxidation of its cobalamin cofactor. The hypothesis that single and serial *in vivo* nitrous oxide exposures impair axon regeneration was tested in four experimental male rat models of nervous system injury. *In vitro* axon regeneration 48 h after a single *in vivo* 70% nitrous oxide exposure was less than half that in the absence of nitrous oxide. One exposure to 80% nitrous oxide fully inhibited the beneficial effects of folic acid on *in vivo* dorsal root ganglion axon regeneration after sharp spinal cord injury. After sharp optic nerve injury, serial 80% nitrous oxide administration reversed the regenerative benefits of folic acid on *in vivo* retinal ganglion cell axon regeneration. The marked beneficial effects of folic acid on *in vivo* scores of behavioral recovery after direct spinal cord contusion were reversed by coadministration of serial 80% nitrous oxide exposure. *(Summary: M. J. Avram. Image: From original article.)*



1153 Four-factor Prothrombin Complex Concentrate for the Management of Patients Receiving Direct Oral Activated Factor X Inhibitors (Clinical Focus Review)

Direct oral anticoagulants, which achieve anticoagulation by inhibiting specific coagulation factors, have been approved for the prevention of stroke and systemic embolism in atrial fibrillation, treatment and secondary prevention of venous thromboembolism, and thromboprophylaxis after major orthopedic surgery. In cases of severe or life-threatening bleeding or for patients undergoing urgent surgery, restoration of hemostasis requires prompt reversal of anticoagulation in addition to a multimodal approach using hemostatic agents. Prothrombin complex concentrates contain factors II, IX, and X, with or without factor VII, and, depending on the formulation, similar proportions of coagulation inhibitors such as protein C, protein S, and low doses of heparin. Current data support the use of prothrombin complex concentrate for the reversal of activated factor X inhibitors in bleeding patients and suggest that prothrombin complex concentrate could become a useful and relatively affordable option for management of direct oral anticoagulant-associated bleeding. Further studies are needed to investigate the optimal dosing of prothrombin complex concentrate to maintain the balance between procoagulant effectiveness and low thrombotic risk. *(Summary: M. J. Avram. Image: J. P. Rathmell.)*



1166 Transversus Abdominis Plane Block: A Narrative Review (Review Article)

Transversus abdominis plane blocks have been used to provide postoperative analgesia for open and laparoscopic abdominal surgery as well as inpatient and outpatient surgical procedures. This review discusses the anatomy, nomenclature, history, approaches (posterior, lateral, and subcostal), techniques, pharmacology, and complications of transversus abdominis plane blocks. It also reviews the evidence supporting their clinical use for common open and laparoscopic surgical procedures and explores possible alternative truncal blocks as well as areas requiring further investigation. Despite contradictory findings, scarcity of evidence, and shortcomings afflicting some randomized controlled trials, certain clinical suggestions can be made. Overall transversus abdominis plane blocks appear most beneficial in the setting of open appendectomy (posterior or lateral approach). Lateral transversus abdominis plane blocks are not suggested for laparoscopic hysterectomy, laparoscopic appendectomy, and open prostatectomy. Transversus abdominis plane blocks could serve as an analgesic option for Cesarean delivery (posterior or lateral approach) and open colorectal surgery (subcostal or lateral approach) if there exist contraindications to intrathecal morphine and thoracic epidural analgesia, respectively. *(Summary: M. J. Avram. Image: From original article.)*