

## 6 A Dose-finding Study of Sugammadex for Reversal of Rocuronium in Cardiac Surgery Patients and Postoperative Monitoring for Recurrent Paralysis

Sugammadex is effective for reversing neuromuscular blockade produced by rocuronium or vecuronium. The manufacturer has recommended that a sugammadex dose of 2 mg/kg be administered if at least two twitches are present in response to a train-of-four stimulus, or 4 mg/kg if there are less than two twitches but a posttetanic count of more than 0. The hypothesis that many patients would require less than the recommended dose of sugammadex, but that some would require more, and that recurrent paralysis would not occur was tested in a prospective dose-finding study of 97 cardiac surgery patients administered rocuronium in whom neuromuscular blockade was monitored using an electromyography-based twitch monitor. The sugammadex dose required for an individual patient could not be predicted with certainty based on the train-of-four twitch response immediately prior to reversal. Two patients had recurrent paralysis during the postoperative monitoring period. Quantitative twitch monitoring is essential to evaluate the effectiveness of reversal with sugammadex. See the accompanying Editorial on [page 1](#). (Summary: M. J. Avram. Image: A Johnson, Vivo Visuals Studio.)



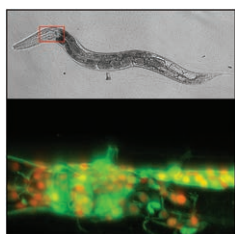
## 16 Morphine and Hydromorphone Effects, Side Effects, and Variability: A Crossover Study in Human Volunteers

Opioids remain the most efficacious systemic analgesics available to treat moderate to severe pain, and morphine and hydromorphone are the opioids most used to treat acute pain in the United States. However, it is unclear whether morphine or hydromorphone is inherently safer or clinically advantageous. The hypothesis that intravenously administered morphine and hydromorphone differ in onset and in the magnitude, duration, and variability of analgesic and ventilatory effects was tested in 42 healthy volunteers who received 2-h infusions of 0.2 mg/kg morphine and 0.05 mg/kg hydromorphone, each on separate occasions, in a randomized crossover study. At the doses studied, hydromorphone had faster onset of analgesic, respiratory, and miotic effects than morphine, and analgesia relative to respiratory depression was 3- to 4-fold greater for hydromorphone than morphine. The magnitude of interindividual variability in clinical effects of the opioids was similar. The authors conclude that hydromorphone may have clinical advantages compared with morphine for treating acute pain in perioperative, emergency department, and other acute care settings. (Summary: M. J. Avram. Image: Adobe Stock.)



## 35 Patient and Process Outcomes among Pediatric Patients Undergoing Appendectomy during the COVID-19 Pandemic: An International Retrospective Cohort Study

The COVID-19 pandemic has forced healthcare systems to change clinical care pathways and processes to accommodate changes in patient volumes and to protect healthcare professionals. The hypothesis that the COVID-19 period was associated with prolonged length of stay in pediatric patients with acute appendicitis undergoing primary appendectomy compared to a prepandemic period was tested in a retrospective study using matched cohorts from 28 participating institutions. The difference in hospital length of stay was determined between 1,618 pediatric patients undergoing primary appendectomy during a 2-month period early during the COVID-19 pandemic (April to May 2020) and 1,684 matched patients during the same 2-month period the previous year. Hospital length of stay, the primary outcome, was chosen as a surrogate measure that encompasses the effect of timely access to care, perioperative processes, and patient-centered outcomes. The median (interquartile range) hospital length of stay was 29 h (18 to 79 h) in the pandemic cohort and 28 h (18 to 67 h) in the prepandemic cohort, a difference that is not clinically significant. (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 49 Measures of Information Content during Anesthesia and Emergence in the *Caenorhabditis elegans* Nervous System

General anesthesia in humans is characterized by transitions between distinct brain states using electroencephalography and functional magnetic resonance imaging to assess communication in the central nervous system on a region-to-region basis rather than on a neuron-to-neuron basis. The hypothesis tested in this study was that application of a novel generalized model of time-dependent information transfer to multineuron activity recordings taken from *Caenorhabditis elegans* head ganglia during isoflurane anesthesia and emergence will discriminate between awake and anesthetized states and characterize recovery to the awake state. Averaging the proportional entropy (a measure of the amount of information present in each signal) content in each information region across all neuron pairs across all animals within each isoflurane exposure level (0%, 4%, 8%) revealed that exposure to isoflurane altered the distribution of entropy. New metrics were empirically constructed from these results by grouping information regions observed to exhibit altered entropy content in anesthetized animals. These novel, empirically derived entropy metrics better distinguish the awake and anesthetized states compared to existing metrics and reveal meaningful differences in information transfer characteristics between states. See the accompanying Editorial on [page 4](#). (Summary: M. J. Avram. Image: From the authors of the study.)



## 63 TREK-1 and TREK-2 Knockout Mice Are Not Resistant to Halothane or Isoflurane

The Trek channels (TREK-1 and TREK-2) belong to the two-pore domain potassium channel superfamily; their activation hyperpolarizes neurons, decreasing neuronal activity. They are widely expressed in the mammalian spinal cord and are activated by volatile anesthetics. Knocking out TREK-1 is reported to render mice resistant to volatile anesthetics. Spinal cord slices from mice, either wild-type or an anesthetic-hypersensitive mutant (*Ndufs4*), have an isoflurane-induced outward potassium leak that correlates with their minimum alveolar concentrations and is blocked by norfluooxetine (a TREK-1 and TREK-2 channel inhibitor). The hypothesis that this outward cation current is carried by TREK-1 and contributes to volatile anesthetic suppression of movement

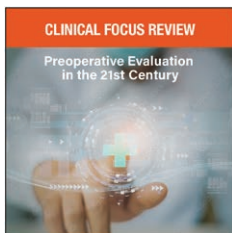
and *Ndufs4* anesthetic hypersensitivity was tested in wild-type mice and mice carrying knockout alleles of *Trek-1* and *Trek-2*, the double knockout *Trek-1;Trek-2*, and *Ndufs4;Trek-1*. Loss of TREK-1 or TREK-2 channels individually or as a double mutant had no effect on either tail clamp or loss of righting reflex response to isoflurane or halothane. An isoflurane-inducible rise in holding current remained with TREK loss in both wild-type and *Ndufs4* cells but it became norfluooxetine insensitive. (Summary: M. J. Avram. Image: Adobe Stock.)



## 77 Hemostatic *In Vitro* Properties of Novel Plasma Supernatants Produced from Late-storage Low-titer Type O Whole Blood

Low-titer group O whole blood is used for trauma resuscitation. It has a 21- to 35-day shelf life, depending on how it is collected, and has the potential for high wastage due to its singular indication for use in hemorrhaging patients. After 14 days of storage, unused low-titer group O whole blood units are converted by some to packed red blood cell units, which have broader indications for use, and the plasma supernatant is discarded. The present study tested the hypothesis that, compared to fresh, never-frozen liquid plasma, supernatant prepared from late-storage low-titer group O whole blood being converted to red blood cells would have enhanced hemostatic activity and coagulation parameters without increasing free hemoglobin due to longer storage in the

presence of platelets and red blood cells. Whole blood supernatant units had improved thrombin generation and viscoelastic parameters compared to never-frozen liquid plasma units of similar storage age. Concentrations of residual platelets and microparticles were increased in whole blood supernatant units without an increase in the free hemoglobin concentration. (Summary: M. J. Avram. Image: J. P. Rathmell.)



## 91 Preoperative Evaluation in the 21st Century (Clinical Focus Review)

The preanesthesia evaluation provides the basis for the creation of the perioperative anesthesia and pain management plan. The preoperative evaluation is a separate and distinct service provided for complex patients that seeks to improve both their perioperative and their long-term health outcomes by identifying and intervening on modifiable risk factors. Common components of the preoperative evaluation include risk assessment and planning for anesthesia and surgery, patient education and shared decision-making, optimizing modifiable conditions that could affect perioperative outcomes, multidisciplinary care coordination, and discharge planning. This Clinical Focus Review provides a conceptual framework for the preoperative evaluation of cardiac risk, pulmonary risk, stroke risk, obstructive sleep apnea, diabetes, anemia, and frailty, among others, using validated perioperative risk

screening tools when they are available. It also discusses focused assessments and interventions for modifiable risk factors when they are indicated. (Summary: M. J. Avram. Image: Adobe Stock.)



## 108 Sugammadex Vial Wastage: Implications for the Cost of Anesthesia Care in Children: Research Letter

Sugammadex is one of many expensive medications for which the minimum vial contains doses larger than those needed by pediatric patients. Sugammadex vials are labeled single-dose or single-use only. The present study estimated the proportion of drug wastage, defined as documented less than or equal to 100 mg administered from a 200 mg/2 mL (the smallest) sugammadex vial among 400,838 sugammadex doses administered to children less than 18 years old across 49 children's hospitals between January 2017 and September 2022. Drug wastage was found to have occurred for 59.2% (237,092 of 400,838) of the administered doses. A budget impact analysis of the amount of wasted drug, calculated as the 2022 inflation-adjusted cost savings,

estimated that \$14,000,000 worth of drug would not have been discarded over the study period had a sugammadex vial size of 100 mg/ml been available at a cost approximately half that of a 200-mg vial or had vials been split. (Summary: M. J. Avram. Image: J. P. Rathmell.)