



765 Poor Performance on a Preoperative Cognitive Screening Test Predicts Postoperative Complications in Older Orthopedic Surgical Patients

Using the MiniCog, a structured cognitive screening tool, 25 to 33% of elective surgical patients 65 yr old and older score in a range consistent with probable cognitive impairment preoperatively. To test the hypothesis that poor preoperative cognition is associated with suboptimal surgical outcomes, the relationship of a low preoperative MiniCog score to postoperative outcomes was examined in 211 patients aged 65 yr old and older, without a diagnosis of dementia, scheduled for elective lower extremity joint replacement surgery. Fifty (24%) patients scored 2 or less on the preoperative MiniCog, suggesting probable cognitive impairment. On age-adjusted multivariate analysis, patients with a MiniCog score less than or equal to 2 were more likely to be discharged to a place other than home (67% vs. 34%; odds ratio = 3.88), develop postoperative delirium diagnosed by the Confusion Assessment Method (18% vs. 4%; odds ratio = 4.52), and have a longer hospital length of stay (3 vs. 2.5 days). (Summary: M. J. Avram. Illustration: S. Jarret, C.M.I. Photo: ©ThinkStock.)



754 Implementing a Health System-wide Patient Blood Management Program with a Clinical Community Approach

Because blood is a valuable and often scarce resource, avoiding unnecessary transfusions will increase blood availability for patients who truly need this life-saving therapy. Methods for implementing a comprehensive patient blood management program across five hospitals in a healthcare system using a clinical community approach are described. By working together collaboratively across disciplines, sharing best practices, and using high-quality data collection and feedback to promote evidence-based practice, unnecessary transfusions and associated risks were reduced and costs were decreased. Comparing the most recent year (2017) to the baseline time period before patient blood management (2014), the percentage of patients transfused decreased from 11.3% to 10.4% for red blood cells, from 2.9% to 2.2% for plasma, and from 3.1% to 2.7% for platelets. Compared to the baseline year, the annualized blood acquisition cost savings for 2017 was \$2,129,273/yr. See the accompanying Editorial View on [page 738](#). (Summary: M. J. Avram. Photo: J. P. Rathmell.)



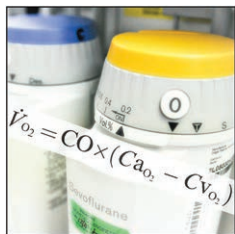
775 Clinical Effectiveness of Intravenous Exenatide Infusion in Perioperative Glycemic Control after Coronary Artery Bypass Graft Surgery: A Phase II/III Randomized Trial

Exenatide is a glucagon-like peptide-1 analog that has the same glucose-dependent antihyperglycemic effect by acting as a glucagon-like peptide-1 receptor agonist but has a longer duration of action by resisting degradation by dipeptidyl peptidase. The hypothesis that intravenous exenatide has a higher clinical effectiveness than a validated intravenous insulin protocol for perioperative glycemic control after coronary artery bypass graft surgery was tested in a randomized superiority trial of 104 patients. Seventy-two percent of the patients in the exenatide group and 80% of those in the control group spent at least half of the first 48 postoperative hours within the blood glucose target range of 100 to 139 mg/dl, the primary endpoint (odds ratio [95% CI], 0.85 [0.34 to 2.11]). Exenatide reduced the time to initiation of intravenous insulin, total dose of insulin infused, and mean number of insulin infusion rate adjustments per patient. (Summary: M. J. Avram. Photo: J. P. Rathmell.)



788 Are Anesthesia and Surgery during Infancy Associated with Decreased White Matter Integrity and Volume during Childhood?

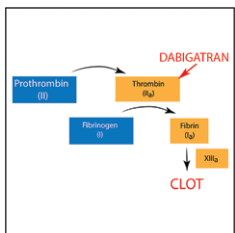
The hypothesis that early anesthesia and surgery might be associated with decreased total and regional white and gray matter volumes was tested in 17 males who had anesthesia for one of four commonly performed operations during infancy and 17 comparable nonexposed controls. Subjects underwent structural magnetic resonance imaging between the ages of 12 and 15 yr. Global and regional measures of brain tissue composition and volume were analyzed. Total white matter volume in patients who had undergone anesthesia and surgery in their infancy, as a percentage of total intracranial volume, was 1.5% (95% CI, 0.3 to 2.8%) less than that in controls. There were no differences between groups in total intracranial, gray matter, and cerebrospinal fluid volumes. Causal relationships of white matter volume to anesthesia and surgery could not be demonstrated nor could the influence of anesthesia be distinguished from that of surgery. (Summary: M. J. Avram. Photo: J. P. Rathmell.)



800 Effect of Bronchoconstriction-induced Ventilation–Perfusion Mismatch on Uptake and Elimination of Isoflurane and Desflurane

Inhalational anesthetic arterial kinetics depends on not only alveolar ventilation and pulmonary perfusion but also their distribution, agent solubility, and mixed venous kinetics. Methacholine inhalation causes bronchoconstriction, shifts mean ventilation to regions with higher ventilation/perfusion ratios, and broadens perfusion dispersion with increased perfusion in low ventilation/perfusion regions and interpulmonary shunt. Inhaled methacholine delayed desflurane uptake and elimination in a piglet model. The null hypothesis that methacholine inhalation-induced bronchoconstriction affects the pharmacokinetics of isoflurane and desflurane to a similar extent was tested in piglets by comparing the uptake and elimination of these inhalational anesthetics with different blood solubilities. Although the kinetics of

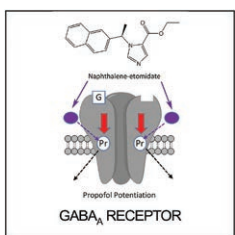
the fairly insoluble desflurane were always faster than those of the more soluble isoflurane, desflurane uptake and elimination were more affected by the alveolar ventilation/perfusion heterogeneity produced by methacholine inhalation. *See the accompanying Editorial View on page 741.* (Summary: M. J. Avram. Photo: J. P. Rathmell.)



852 Reversing Dabigatran Anticoagulation with Prothrombin Complex Concentrate versus Idarucizumab as Part of Multimodal Hemostatic Intervention in an Animal Model of Polytrauma

Prothrombin complex concentrates reverse the anticoagulant effects of the oral anticoagulant dabigatran, a direct thrombin inhibitor, by increasing the amount of prothrombin in the plasma until it exceeds the concentration of dabigatran. Idarucizumab binds and inactivates dabigatran, thereby restoring thrombin generation. The hypothesis that idarucizumab is more effective in reducing blood loss than prothrombin complex concentrate when administered with tranexamic acid and fibrinogen concentrate was tested in a porcine polytrauma model under dabigatran anticoagulation. The mortality rate was 100% in the placebo control and tranexamic acid and fibrinogen concentrate groups, with

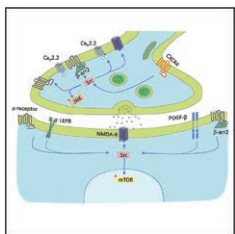
mean survival times of 96 and 109 min and mean blood losses of 3,652 and 3,497 ml, respectively. All animals treated with prothrombin complex concentrate 50 IU/kg or idarucizumab in addition to tranexamic acid and fibrinogen concentrate survived to 240 min with average blood losses of 1,367 and 986 ml, respectively. *See the accompanying Editorial View on page 744.* (Summary: M. J. Avram. Illustration: J. P. Rathmell.)



824 Competitive Antagonism of Anesthetic Action at the γ -Aminobutyric Acid Type A Receptor by a Novel Etomidate Analog with Low Intrinsic Efficacy

The hypothesis that anesthetic analogs that bind selectively to γ -aminobutyric acid type A (GABA_A) receptor transmembrane anesthetic binding sites but possess little or no intrinsic efficacy for positively modulating receptor function would act as competitive anesthetic antagonists capable of selectively reversing the GABA_A receptor actions of more efficacious anesthetic agents was tested in oocyte-expressed $\alpha 1\beta 3\gamma 2L$ GABA_A receptors using voltage clamp electrophysiology and in receptor photoaffinity labeling studies. Naphthalene-etomidate inhibited photoaffinity labeling of the two classes of GABA_A receptor transmembrane anesthetic binding sites with similar affinities, but possessed low

intrinsic efficacy for positively modulating GABA_A receptor function. It reduced the positive modulatory actions of drugs that bind to these receptor sites (propofol > etomidate ~ pentobarbital) but not those of drugs that bind elsewhere on the receptor (γ -aminobutyric acid and diazepam). It also shifted the propofol concentration-response curve for potentiation rightward without affecting the maximal response obtained at high propofol concentrations. (Summary: M. J. Avram. Illustration: Modified from original manuscript.)



878 Src Kinase Inhibition Attenuates Morphine Tolerance without Affecting Reinforcement or Psychomotor Stimulation

μ -Opioid receptors are G protein-coupled receptors that also recruit β -arrestin2, which participates in desensitization, endocytosis, and signaling through various kinases, including extracellular signal-regulated kinase and the nonreceptor tyrosine kinase, c-Src. Inhibition of c-Src causes reductions in μ -receptor endocytosis and opioid-induced desensitization. The hypotheses that c-Src contributes to morphine tolerance as well as the locomotor and reinforcing effects of morphine were tested in wild-type mice, in μ -opioid receptor heterozygous mice, in mice lacking the μ -opioid receptor, and in mice lacking β -arrestin2. The c-Src inhibitor, dasatinib, not only attenuated tolerance but, when administered before morphine, also rapidly restored analgesia that had diminished during the preceding days. These effects

occurred without the altered psychomotor or reinforcing effects of morphine, suggesting that inhibitors of c-Src reduce opioid tolerance without increasing reward. (Summary: M. J. Avram. Illustration: From original manuscript.)