

## ANESTHESIOLOGY

### ■ Does Rate of Propofol Infusion Independently Influence Sedation Endpoints? Doufas *et al.* (page 1112)

To determine whether rates of infusion influence plasma-effect site equilibration of intravenous anesthetics, Doufas *et al.* recruited 18 healthy volunteers to receive five consecutive target-controlled propofol infusions. The authors also tested the performance of an automated responsiveness measure, consisting of computerized voice commands asking the participant to press the button on a handheld vibrating device. Participants were familiarized with the device immediately before the first sedation trial. During each infusion, the target-controlled drug delivery system produced a constant ramp in the effect site concentrations (0.1, 0.3, 0.5, 0.7, or 0.0  $\mu\text{g} \cdot \text{ml}^{-1} \cdot \text{min}^{-1}$ ). Each ramp was continued until loss of responsiveness (defined by an Observer's Assessment Alertness/Sedation score equal to 1). After loss of responsiveness, the infusion was stopped and Observer's Assessment Alertness/Sedation was determined every 15 s until recovery of responsiveness (an Observer's Assessment Alertness/Sedation score of 2). The study protocol included standard anesthetic monitoring (arterial pressure, electroencephalogram, end-tidal partial pressure of carbon dioxide, oxygen saturation, and bispectral index values).

After conclusion of the infusion protocol, the authors combined results from the automated responsiveness measure with pharmacokinetic/pharmacodynamic modeling. They found that effect site concentrations associated with clinical measures were not affected by the rate of infusion, once the correct rate of plasma-effect site equilibration was determined for each individual. Study participants stopped responding to the automated responsiveness measure at lower effect site propofol concentrations than those associated with loss of responsiveness. From the results of this study, the authors surmise that it may be possible to combine population-based pharmacokinetics with real-time electroencephalogram measures of drug effect to individualize pharmacodynamic modeling during target-controlled drug delivery.

### ■ Effects of Catecholamines on Intravascular Volume Expansion during Fluid Therapy in Sheep. Vane *et al.* (page 1136)

Inotropic and vasoactive catecholamines are commonly administered with fluid infusion to improve hemodynamic and cardiovascular function. To further explore

the interactions between fluid infusions and catecholamine infusions, Vane *et al.* designed a study to measure volume expansion and hemodynamics during and after a 0.9% NaCl bolus in conscious, splenectomized, normovolemic sheep.

In six sheep, the authors performed splenectomies and surgical instrumentation in preparation for the experiments. After a 1-week recovery period, four different protocols were performed randomly in each sheep, with a minimum 2-day recovery period between each experiment. Responses to a 0.9% NaCl bolus of 24-ml/kg infused over 20 min were evaluated during a continuous infusion of three different catecholamines (50  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  dopamine, 0.1  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  isoproterenol, 3  $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  phenylephrine) or control protocol. Heart rate, mean arterial blood pressure, mean pulmonary arterial pressure, central venous pressure, left atrial pressure, and cardiac output were continuously monitored. Hematocrit, hemoglobin, and urinary output were recorded during baseline and at specific points before and after administration of the 0.9% NaCl bolus. Blood volume (BV) changes over time were calculated from the estimated baseline BV of 65 ml/kg for normal sheep.

Results revealed that 2 h post-NaCl bolus, sustained BV expansion was greatest in the isoproterenol protocol, whereas the dopamine protocol remained similar to control protocol and the phenylephrine protocol had a net BV loss. The authors attributed some BV expansion differences to changes in renal function: phenylephrine infusion increased urinary output, whereas isoproterenol was associated with antidiuresis. Dopamine, however, caused both diuresis and a sustained augmentation of BV. Multiple mechanisms for augmented BV expansion seen with dopamine and isoproterenol are possible. The most likely mechanisms are reduced capillary pressure secondary to increased microvascular surface area or augmented lymphatic pumping.

### ■ Acute and Delayed Preconditioning against Myocardial Infarction in Rabbits. Chiari *et al.* (page 1160)

Chiari *et al.* randomly assigned rabbits to receive one of five intravenous solutions in acute preconditioning experiments. Their aim was to test whether acute myocardial preconditioning with inhaled halogenated anesthetics could be extended to intravenous administration 24 h

preceding ischemia. In the first set of acute preconditioning experiments, rabbits received either 0.9% intravenous saline, lipid vehicle, or emulsified isoflurane (6.9%), enflurane (7.1%), or sevoflurane (7.5%) during 30-min infusions. Arterial blood samples were collected before and during the infusions and immediately before occlusion of the left anterior coronary artery. Occlusion of the left coronary artery lasted 30 min, followed by 3 h of reperfusion.

Additional experiments designed to examine delayed preconditioning consisted of randomly assigning conscious rabbits to receive saline, lipid vehicle, or emulsified sevoflurane 24 h before ischemia. At the completion of each experiment, the left anterior coronary artery was reoccluded and blue dye was injected so that authors could determine size of myocardial infarct. The infarct size was expressed as a percentage of the area at risk. Although lipid vehicle produced transient increases in heart rate, it did not affect infarct size. Emulsified isoflurane, enflurane, and sevoflurane reduced infarct size in the acute preconditioning experiments, and emulsified sevoflurane reduced infarct size as compared to control in delayed preconditioning experiments.

### ■ Researchers Analyze Impact of Anesthesia Resident Training on Operating Room Efficiency. Eappen *et al.* (page 1210)

Eappen *et al.* collected all operating room data for three 2-week periods over the course of 1 academic year at their institution. Their goal was to measure what, if any, impact is produced on anesthesia-related time measures of operating room efficiency when initiating new anesthesia resident trainees to the operating room. The three time periods were: the first 2 weeks of July, when most operating rooms are staffed by attending physicians working alone; 2 weeks in September when new anes-

thesia residents work in a 2:1 ratio with staff; and 2 weeks in May, when residents have presumably acquired more experience.

The authors extracted data for all procedures performed in their institution's 38 operating rooms for each of the three time periods. All patient identifiers were stripped from the operating room case data, in compliance with the Health Insurance Portability and Accountability Act. The data captured for analysis included endpoints defined by the American Association of Clinical Directors (*e.g.*, patient in the room; induction complete; incision is made; wound closure; patient ready for transfer to stretcher; patient out of room).

A total of 3,004 surgical procedures were performed during the three selected time periods, 1,996 of which met the study's inclusion criteria. The mean anesthesia induction times for the attending physicians working alone, the new anesthesia residents working in a 2:1 ratio with staff, and the anesthesia residents after more experience were 17.3, 19.0, and 20.8 min/case. The corresponding mean anesthesia emergence times were 8.7, 9.7, and 10.0 min, respectively. The difference in mean induction times between July and September was statistically significant, but the difference between July–May and May–September was not statistically different. There was no difference in room turnover between the three groups. All told, it appeared that initiation of new anesthesia residents added about 9 min to an 8-h day. This time was gradually attenuated as residents gained proficiency throughout their academic year. Although the authors did not control for difficulty of surgical cases, their study does provide some initial evidence for assessing the effect of anesthesia trainees on anesthesia-controlled times in the operating room, and suggests that their training may not have adverse effects on operating room efficiency.

Gretchen Henkel