

ANESTHESIOLOGY

■ Reducing Children's Preoperative Anxiety. Kain *et al.* (page 65)

A variety of techniques have been studied that are aimed at reducing children's preoperative anxiety, including premedication with antianxiety agents and allowing parents to be present during anesthesia induction. Kain *et al.* developed a family-centered, behavioral preoperative preparation program and compared it to other preoperative interventions in a randomized controlled study.

The team recruited 408 children (aged 2–10 yr old) and their parents, excluding children with a history of chronic illness, prematurity, or diagnosed developmental delay. Families were enrolled 2–7 days before their child's surgery and randomly assigned to one of four groups: the control group, in which children did not receive premedication and their parents were not present during anesthesia induction; the parental presence group; the ADVANCE (Anxiety-reduction, Distraction, Video modeling and education, Adding parents, No excessive reassurance, Coaching, and Exposure/shaping) behavioral preparation group; and the midazolam group, in which children received 0.5 mg/kg oral midazolam before being separated from their parents in the operating room.

Using a variety of psychological assessment instruments, the psychologist on the research team assessed child and parental anxiety, emergence behavior, and parents' baseline coping styles. Postoperative analgesic requirements and time to discharge were recorded. Parents and children who underwent the ADVANCE preparation had significantly lower anxiety in the preoperative holding area compared with the three other groups. Children in the ADVANCE group were also less anxious during induction of anesthesia compared with the control and parental presence groups. The ADVANCE preparation also reduced the incidence of emergence delirium, analgesic requirements, and time to discharge. The ADVANCE preparation program was as effective as midazolam in reducing perioperative anxiety in children. Further research would be helpful to evaluate which components of their combinations in ADVANCE provide benefit and to assess its increased operational costs, due to the time required for preparing families.

■ Milrinone plus Vasopressin: An Improved Combination during Cardiopulmonary Resuscitation? Palmaers *et al.* (page 100)

Although considered a first-line drug for cardiopulmonary resuscitation (CPR), epinephrine carries unwanted

side effects that adversely affect cerebral and myocardial oxygen consumption as well as pulmonary gas exchange. The alternative of using vasopressin has now also been refuted. To investigate whether use of milrinone, a phosphodiesterase III inhibitor, could be advantageous during CPR, Palmaers *et al.* induced ventricular fibrillation and cardiac arrest in 32 male pigs by 9-V direct current and subsequent ligation of the circumflex coronary artery. After a 4-min period, the investigators began CPR. Pigs were randomly assigned to receive CPR with epinephrine (30- μ g/kg bolus); vasopressin (0.4-U/kg bolus); epinephrine-vasopressin (15- μ g/kg epinephrine bolus, 0.2-U/kg vasopressin bolus); or milrinone-vasopressin (0.4-U/kg vasopressin bolus, 50- μ g/kg milrinone bolus over 5 min then a continuous infusion of milrinone). Measurements of heart rate, mean arterial pressure, mean pulmonary arterial pressure, systemic vascular resistance index, maximal rate of change of left ventricular pressure, and coronary perfusion pressure were taken before CPR (baseline) and 4, 8, 15, and 30 min after return of spontaneous circulation. After the 30-min assessment period, the animals were killed with an infusion of 20 mmol potassium chloride.

All animals were successfully resuscitated, although one pig in the epinephrine group and one in the milrinone-vasopressin group died during the 30-min post-CPR observation period. Animals in the group receiving milrinone-vasopressin displayed significantly higher cardiac index values 30 min after return of spontaneous circulation than did animals in the other three groups, without exhibiting a decrease in mean arterial pressure or coronary perfusion pressure. This study supports the use of milrinone and vasopressin in treatment of cardiac arrest, justifying further investigation.

■ Researchers Test Effects of Inhaled Anesthetics on Minimum Alveolar Concentration, Learning, and Righting Reflexes in Knock-in Mice. Sonner *et al.* (page 107)

Widely distributed in the central nervous system, γ -aminobutyric acid type A receptors have been considered prime candidates as targets of inhaled anesthetic action. To test this theory, Sonner *et al.* genetically engineered mice to express two point mutations in the GABRA1 locus: the S270H mutation, which selectively reduces *in vitro* sensitivity to large *versus* small volatile

anesthetics, and the L277A mutation, which normalizes the γ -aminobutyric acid dose-response. They conducted electrophysiologic and behavioral experiments in groups of knock-in and wild-type mice.

In neurons obtained from slices of the hippocampus from the knock-in and wild-type mice, the team recorded miniature inhibitory synaptic currents. The decay in currents was more rapid in interneurons and CA1 pyramidal cells from the knock-in compared with wild-type mice. In behavioral studies, mice were tested for amnesic effects of inhaled anesthetics using a fear conditioning assay. Investigators also determined the minimum alveolar concentration and the concentration at which 50% of animals would lose their righting reflexes.

Results showed that the minimum alveolar concentration for isoflurane, desflurane, and halothane did not differ between knock-in and wild-type mice. The two groups of mice also did not differ in their sensitivity to

isoflurane for Pavlovian fear conditioning. However, in tests of loss of righting reflexes, the homozygous knock-in mice were more resistant than wild-type mice to loss of righting reflexes induced by isoflurane and enflurane (but not to halothane). Results of the study reveal that γ -aminobutyric acid type A receptors containing the α_1 subunit do not mediate the capacity of isoflurane to produce amnesia, as they have been shown to do for the benzodiazepines. Nor do they mediate the capacity of desflurane, isoflurane, or halothane to produce immobility in the face of noxious stimulation. Loss of righting reflex, however, does require these receptors, and more studies of mice with mutations in the α_4 , α_5 , α_6 , and/or δ subunits in these receptors may allow further evaluation of the role of γ -aminobutyric acid type A receptors in anesthetic actions.

Gretchen Henkel