Unexpected Gender Difference in Time to Recovery from Anesthesia Revealed. Gan et al. (page 1283)

During a multicenter study originally designed to measure effects of the bispectral index (BIS) on intraoperative anesthetic management and patient recovery, Gan et al. unexpectedly found gender to be a highly significant independent predictor for time to emergence from general anesthesia.

Ninety six men and 178 women in four separate institutions completed the study. Scheduled for various procedures from general surgical to urologic and orthopedic, participants received similar premedication of midazolam. 1 to 2 mg intravenously, followed by induction regimens consisting of propofol, 1 to 2 mg/kg, and alfentanil, less than 30 μg/kg. After loss of consciousness, infusions of propofol at 140 μg·kg⁻¹·min⁻¹ and alfentanil at 0.5 μg·kg⁻¹·min⁻¹ with 50% nitrous oxide were started. Neuromuscular blocking agents were administered to facilitate placement of endotracheal tubes, and when surgically necessary.

Recovery data from 35 patients receiving propofol/ alfentanil/nitrous oxide anesthesia were collected to study preexisting clinical practice and comprised the historical control group. In addition to standard monitoring, each patient’s level of consciousness was monitored using the BIS. Patients were randomly assigned to one of two groups: (1) those in whom the propofol component of the anesthetic was titrated to keep BIS between 45–60, and (2) those for whom propofol was adjusted based on usual signs of inadequate anesthesia. Anesthesia was reduced in both groups 15 min before the end of surgery to facilitate rapid recovery.

During data analysis, the researchers discovered that women recovered significantly faster than did the men. The time from end of anesthesia to eye opening was 7.05 (women) versus 11.22 min (men). Response to verbal command was 8.12 (women) versus 11.67 min (men). Differences were significant at all four study sites and in each treatment group. These findings may help to explain the greater reported incidence of intraoperative awareness in women, and support inclusion of gender as a variable in pharmacokinetic and pharmacodynamic studies of anesthetic drugs.

Effects of Ketamine and Its Isomers on Human Myocardium Assessed. Kunst et al. (page 1363)

From patients undergoing open heart surgery for bypass or valve replacement, Kunst et al. obtained right auricular myocardium. The group exposed muscle strips to increasing concentrations of racemic ketamine, S(+)-ketamine or R(-)-ketamine, and then assessed isometric force, isotonic shortening, contractility, relaxation, and time to maximal isotonic and isometric force in all samples. Ten muscle strips in each group were loaded with the calcium-sensitive fluorescent dye FURA-2/AM for simultaneous measurements of calcium transients.

With S(+)-ketamine at the concentration of 73 μM, the researchers observed an increase between 12.5 and 22.4% in maximal isotonic shortening amplitude, contractility, and relaxation. No such changes were seen after adding 75 μM R(-)ketamine. At the highest concentration (750 μM), the team recorded a direct negative inotropic action: ketamine and its isomers decreased maximal isometric developed force, maximal shortening amplitude, contractility, and relaxation by 26.8 ± 57.4%. This decrease was accompanied by a significant decrease of the intracellular calcium transient.

The positive inotropic effect of racemic ketamine, the authors note, can be blocked by the addition of esmolol. The negative inotropic effect of high doses of racemic ketamine and its isomers, associated with decreases in intracellular calcium transient, can be reversed by dobutamine. Despite certain limitations, including the fact that the tissue specimens originated from patients with potentially diseased myocardium, the use of such a human model has the potential to contribute more understanding about the pharmacodynamics of ketamine and its isomers.

Effects of Sevoflurane on Regional Myocardial Blood Flow in Dogs and Humans. Kitahata et al. (page 1436)

Using myocardial contrast echocardiography, Kitahata et al. investigated the effects of sevoflurane on myocardial blood distribution in humans and dogs. The team assigned six mongrel dogs to a group to receive dipyrindamole and nine to receive sevoflurane. Anesthesia was induced with 20 mg/kg thiamylal intravenously and maintained with an initial bolus and then continuous infusion of fentanyl. Hemodynamic and myocardial con-
trast echocardiographic data were simultaneously obtained at four intervals: (1) at baseline; (2) 30 min after producing stenosis of the left circumflex coronary artery (CX) (reducing blood flow by approximately 40%); (3) 5 min after intravenous administration of dipyridamole (1 mg/kg) or 20 min after inhalation of 1 minimum alveolar concentration (MAC) sevoflurane during CX stenosis; and (4) after restoration of arterial blood pressure (with administration of phenylephrine) to levels before administration of study drugs.

In the human study, nine patients (60 ± 7 yr of age) scheduled for coronary artery bypass participated. Anesthesia was induced with fentanyl (200–500 μg) and thiopental (25–100 mg) and maintained with continuous intravenous infusion of fentanyl, oxygen and air, or nitric oxide. Inhalation of 1 MAC sevoflurane in oxygen was begun after confirmation of stable hemodynamic and echocardiographic variables. The regional distribution of coronary blood flow was measured by myocardial contrast echocardiography with a transesophageal probe. As in the animal studies, end-diastolic images were transferred to a computer and digitized to quantitate the degree of enhancement of the peak gray level after injection of the contrast medium.

In the animal experiments, the researchers observed that dipyridamole produced a significant decrease in both the inner:outer ratio of the peak gray area in the ischemic area and the ischemic:nonischemic ratio of the peak gray level. After arterial pressure was restored with phenylephrine, neither the inner:outer nor the ischemic:nonischemic ratio improved. However, after sevoflurane, the inner:outer ratio and the ischemic:nonischemic ratios remained unchanged, and increased with the addition of phenylephrine. In the human studies, sevoflurane did not change the inner:outer ratio in the area supplied by the most stenotic coronary artery. (Six of the nine patients had 99 or 100% occlusion in one or two coronary arteries). Sevoflurane did not cause transmural coronary steal or intercoronary steal in either the dog or the human studies. Using myocardial contrast echocardiography was useful in quantitating coronary blood flow and its transmural distribution.

- Does Decreased Hematocrit Affect Arterial Thrombosis Rate and Bleeding Time in Rabbits? Ouaknine-Orlando et al. (page 1454)

Ouaknine-Orlando et al. designed a two-part prospective study to evaluate the role of hematocrit variations in the thrombotic process and in bleeding time. In the first part of the study, the team applied the Folt model of arterial thrombosis, in which a vascular wall injury associated with stenosis induces cyclic flow reductions (CFRs), resulting in endothelial damage, platelet accretion, and formation of a platelet plug that embolizes. First producing a 60% stenosis in the right common carotid artery, the team triggered a series of cyclic episodes of thrombosis and clot lysis by performing a compression injury. The team recorded the number of CFRs in a 20-min period, and then randomly assigned the rabbits to one of three groups: control; hemodilution with rabbit homologous platelet-rich plasma (PRP group); or hemodilution with gelatin solution and then reinfusion of shed blood (GEL group). They recorded the number of CFRs in the successive 20-min period, and followed with car immersing bleeding time experiments. Hematocrit decreased in the PRP group from 36 ± 3% to 23 ± 2%, and from 38 ± 3% to 23 ± 2% in the GEL group. Decreases in hematocrit in the PRP and GEL groups abolished CFRs and significantly lengthened bleeding time. Thrombosis reappeared in the GEL group after blood reinfusion and resultant normalization of hematocrit.

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Comment from the Editor: Merlin D. Larson, M.D., Professor, Department of Anesthesiology, University of California, San Francisco, California, recently wrote and pointed out an ambiguity in the last sentence of the "This Month in Anesthesiology" column from December 1998, dealing with the article by Segawa et al. (Anesthesiology 89: 1407-15). The authors clearly showed that while increasing concentrations of volatile anesthetic blunted the hemodynamic response to a surgical incision, these agents simultaneously augmented the circulating catecholamine response. The authors suggest that the ability of an anesthetic to prevent a hypertensive response to pain is more likely related to the drug's action on vascular response to catecholamines than on the circulating catecholamines per se.