Editor’s Comment:

Two of the articles highlighted in the This Month in Anesthesiology column (Liem et al. and Xing et al.) deal with the burgeoning field of pharmacogenomics—the influence of patient genetics on the response to drugs. While we are a long way from obtaining personalized ‘genetic maps’ from each patient, and tailoring our choice/dose of drugs to that map, it is clear that genetic differences between patients are responsible for a substantial amount of the variability that we encounter every day in the operating room or intensive care unit or clinic.

I call our readers’ attention to the Journal Symposium, which will be held on Tuesday, October 26, 2004, during the Annual Meeting of the American Society of Anesthesiologists, in Las Vegas, Nevada. The topic of the Symposium will be ‘Pharmacogenomics,’ and it will consist of both posters and lectures, all dealing with this issue.

If you want to gain some insights into one of the most exciting frontiers of our specialty, I urge you to read the articles in this month’s issue—and to attend the Symposium in Las Vegas.

Is There a Scientific Basis for Observations That Redheads Require Increased Anesthetics? Liem et al. (page 279)

To explore the impression shared by many anesthesiologists—that redheads require more anesthesia—Liem et al. recruited 10 women with naturally red hair and 10 with dark hair for their study. Blood samples were obtained from all subjects for later phenotype analysis. Experimental sessions were conducted during the morning of each study day, to control for the influence of circadian rhythms on anesthetic requirements.

Anesthesia was induced with sevoflurane, and then desflurane maintenance levels were randomly set at an end-tidal concentration between 5.5 and 7.5%. After a 45-min equilibration period, the investigators applied a noxious electrical stimulation to the anterior thigh of each subject. If the volunteer moved in response to the stimulation, desflurane was increased by 0.5%. No movement warranted a 0.5% decrease in desflurane. An independent investigator blinded to desflurane concentration (but not to hair color) evaluated movement in response to each stimulus.

The researchers found that the redheaded volunteers required significantly more desflurane than did the dark-haired women (6.2 volume-percent versus 5.2 volume-percent, respectively). Genetic analysis revealed that 9 of the 10 redheads in the study were either homozygous or compound heterozygotes for mutations of the melanocortin-1 receptor. The investigators were able to confirm anecdotal reports that redheads do indeed require increased inhalational anesthetics.

Interested readers should also see the Laboratory Report by Xing et al. (page 544) of this month’s journal. A summary of the Xing et al. report can also be found below.

Reducing Inflammatory Response in Patients Undergoing Cardiopulmonary Bypass Graft. Oliver et al. (page 327)

Pulmonary dysfunction, caused in part by activation of the inflammatory cascade, is common following cardiopulmonary bypass grafting. Oliver et al. studied 192 patients scheduled for elective cardiopulmonary bypass grafting and/or valvular replacement or repair to compare the ability of perioperative steroids or hemofiltration to attenuate inflammation and thus reduce the duration of mechanical ventilation after cardiac surgery.

The study participants were divided into three groups: the control group, who received saline at induction and at 6-h intervals for four doses; the Hemofil group, which received saline and hemofiltration to obtain 27 ml/kg of hemofiltrate; and the Steroid group, which received 1 g methylprednisolone before anesthesia induction and then 4 mg of dexamethasone at 6-h periods for four doses. All patients underwent normothermic cardiopulmonary bypass grafting and received propofol for postoperative sedation. Blood samples, obtained 10 min after initiation of cardiopulmonary bypass, immediately after removal of aortic cross-clamp, 20 min after protamine administration, and 3 h after separation from cardiopulmonary bypass, were analyzed later to determine complement activation (levels of C3a and C5b-9).

All patients remained intubated for at least 2 h after arrival in the intensive care unit. Approximately 10–15% of patients in all three groups remained intubated for 16–24 h, although the median time to reach an intermit-
tent mandatory ventilation of 4/min and extubation was significantly reduced for those in the HemoFil group. However, in this investigation, hemofiltration was not associated with a reduction in complement levels, and the investigators were unable to elucidate the mechanism to account for their results. The investigators did find, unexpectedly, that perioperative blood loss and transfusion requirements were significantly reduced in those patients who received perioperative steroids. Both perioperative steroids and hemofiltration, therefore, require further study in patients undergoing cardiopulmonary bypass grafting.

## Comparison of General versus Regional Anesthesia for Ambulatory Hand Surgery. McCartney et al. (page 461)

In 100 patients undergoing ambulatory hand surgery, McCartney et al. randomized half to receive general anesthesia and half to receive regional anesthesia (via axillary brachial plexus block). Prior to surgery, all study participants were asked to rate their hand pain and pain-related disability, using the Visual Analogue Scale and the Pain–Disability Index, respectively. Anesthesia induction time, total surgical time, total tourniquet time, and total anesthesia time were recorded. Patients were assessed for fast-track eligibility immediately upon termination of surgery and anesthesia. Duration of stay in either the post anesthesia care unit or the day surgery unit was also recorded.

After surgery, patients who reported pain equal to or greater than 40 on the Visual Analogue Scale were given fentanyl in 25 microgram increments every 5 min. When oral fluid intake was initiated, patients received either Tylenol #3 (containing 300 mg acetaminophen, 30 mg codeine, and 15 mg caffeine) or acetaminophen 325 mg/oxydodone HCl 5 mg. Upon hospital discharge, patients received prescriptions for one of these two analgesics and were instructed to take 1–2 tablets every 4 h for pain, up to 12 tablets per day. They also received diaries in which to record their pain scores, daily analgesic consumption, incidence of nausea or vomiting and other side effects, as well as satisfaction with anesthetic care. Study investigators called participants on postoperative days 1, 7, and 14 to remind them to complete their diaries.

Fourteen of the patients assigned to the regional anesthesia group had inadequate anesthesia, with 11 requiring fentanyl supplementation and 7 requiring propofol. Five patients in the regional anesthesia group required conversion to general anesthesia because of block failure. In the regional anesthesia group, pain ratings at 30, 60, 90, and 120 min after surgery were lower than those for the general anesthesia group. Overall, patients in the regional anesthesia group also spent less time in the hospital. More general anesthesia patients had postoperative nausea and vomiting while in the hospital. However, when analyzing the home diaries, the investigators found no difference between the two groups in terms of pain report, opioid consumption, adverse effects, pain-disability levels, or satisfaction. Although regional anesthesia does not seem to reduce pain postoperatively, it does offer the benefits of faster hospital discharge and less nausea.

## Minimum Alveolar Concentrations of Volatile Anesthetics Evaluated in MC1R Knockout Mice. Xing et al. (page 544)

Using melanocortin 1 receptor (MC1-R) knockout mice and wild type mice, Xing et al. determined the minimum alveolar concentration (MAC) values of four different volatile anesthetics. Their goal was to elucidate possible mechanisms for the observed increased anesthetic requirement in redheads. These MC1-R knockout mice, the authors maintain, provide a model of red-haired humans, since natural redheads also have a mutation of the MC1-R.

During the study, all animals for the study were kept in individual gas-tight plastic chambers connected to a circle rebreathing system containing a carbon dioxide absorber and fan. With at least 1 week’s separation between experiments, the team equilibrated each animal with each halothane concentration for 40 min; with desflurane for 20 min; with isoflurane for 30 min; and with sevoflurane for 30 min. After the equilibration period, the team used a tail clamp stimulus (1 Hz for 1 min or until the animal moved, whichever came first. Anesthetic partial pressures were then increased in a stepwise fashion until there was no movement during application of tail-clamp stimulus.

There was no difference in MAC between the mutant and control mice. By combining treatment groups and normalizing results, the authors concluded that MAC across all four anesthetic agents in the mutant mice slightly exceeded MAC in wild type mice, by about 5.5%. The authors hypothesize that the increased MAC might be caused by a change in central a-MSH concentrations in the MC1-R mutant mice. In addition, MAC might also be influenced by the fact that MC1-Rs are also expressed in glial cells and neurons of the ventral periaqueductal gray matter, and thus may affect nociception.

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