◇ This Month in

ANESTHESIOLOGY

■ Is Preoperative Antiendotoxin Immunity Associated with Postsurgical Outcome? Bennett-Guerrero *et al.* (page 992)

Bennett-Guerrero *et al.* enrolled 1,056 patients scheduled to undergo routine noncardiac surgery (general, orthopedic, urological, vascular, and gynecologic procedures) in a prospective, observational study to determine whether preoperative antiendotoxin immunity might confer protection against perioperative inflammatory response. Using serum samples obtained 72 h before surgery, the team conducted assays for patients' concentrations of immunoglobulin (Ig) M antiendotoxin core antibody (EndoCAb), IgG, EndoCAb, total IgM, and total IgG. In addition, patients were assessed using the POSSUM physiologic scoring system, including 12 preoperative factors: age, signs of symptoms of heart failure, abnormal electrocardiogram, respiratory function, blood pressure, heart rate, mental status, hemoglobin level, leukocyte count, blood urea concentration, blood sodium concentration, and blood potassium concentration.

For purposes of this study, the authors defined adverse postoperative outcome either as in-hospital death or as hospital stay greater than 10 days. (Patients enrolled in the study included only those scheduled to undergo procedures that targeted their discharge from the hospital before the 10th postoperative day.)

Most patients in this study were discharged within 1 week of their surgeries. A total of 22 patients died, from multiple system organ failure (15), pulmonary failure (4), bowel necrosis (1), pulmonary embolus (1), or myocardial infarction (1). Concentrations of IgM EndoCAb ranged from 9 to 4,946, with a median of 139. The POSSUM preoperative risk scores ranged from 12 to 42, with a median of 18. Lower IgM EndoCAb concentrations predicted increased risk of postoperative complication, independent of POSSUM risk scores, in these patients. Although the study was not designed to show a causal relation between endogenous antiendotoxin antibody concentrations and postoperative morbidity, the findings suggest that endotoxemia may play a role in the development of postoperative complications.

■ Smoking Cessation and Its Effects on Alveolar Macrophage Function. Kotani *et al.* (page 999)

How long after smoking cessation does recovery of alveolar macrophage function occur? To evaluate the effects of nonsmoking duration on both antimicrobial and inflammatory function of alveolar macrophages during anesthesia and surgery, Kotani *et al.* recruited 71 patients scheduled to undergo general anesthesia for more than 4 h. Of these patients, 15 had never smoked, 15 currently smoked, and 41 were former smokers. The former smokers were further divided into one of three groups determined by how long they had been smoke-free: 2 months (n = 13), 3–5 months (n = 13), or 6–12 months (n = 15).

Immediately after induction of anesthesia (with propofol, fentanyl, and vecuronium), alveolar immune cells were harvested by bronchoalveolar lavage. Cells were also harvested 2 and 4 h after induction and at the end of surgery. To assess alveolar macrophage function, the authors evaluated opsonized and nonopsonized phagocytosis, microbicidal activity, macrophage aggregation, neutrophil influx to the distal airway, and gene expression for proinflammatory cytokines and tumor necrosis factor α (TNF-α). The concentrations and total numbers of alveolar cells were 4–5 times greater in smoking than in nonsmoking patients at each measurement interval. Starting at 4 h after induction of anesthesia, the decreases in antimicrobial functions were 1.5–3 times greater in current and former smokers with 2 months' abstinence than in patients who had never smoked. Also at 4 h after induction, the increase in expression of all cytokines (except interleukin 8) was 2–5 times less in current and former smokers than in the nonsmoking group.

The authors found that the concentration and total number of alveolar macrophages normalized in patients who had been smoke-free for 6 months and that intraoperative increases in gene expression for antiinflammatory cytokines were reduced far more in smokers than in nonsmoking patients. Additionally, phagocytosis and bactericidal activity, key elements of pulmonary defense, were markedly impaired in current smokers and those who had quit smoking only 2 months before surgery. Although cytokine expression does not necessarily correlate with cytokine production, these results suggest that former smokers may have a limited ability to mount an effective pulmonary immune defense for at least 6 months after smoking cessation.

■ Spinal Anesthesia and Tumor-promoting Effects of Surgery. Bar-Yosef *et al.* (page 1066)

Bar-Yosef *et al.* wanted to determine whether spinal blockade, which attenuates the neuroendocrine stress

response, might lessen perioperative immunosuppression and thus reduce the tumor-promoting response observed in animal studies after surgery. The group used an animal model that was used previously to study the influence of surgical stress on metastatic development. After laparotomy under halothane anesthesia, Fischer-344 male rats were intravenously inoculated with DNA-radiolabeled MADB106 adenocarcinoma cells. This selected variant cell line is obtained from pulmonary metastasis of a mammary adenocarcinoma chemically induced in inbred F344 Fischer rats. The cells are retained, and metastases develop only in the lung.

The researchers assigned animals to one of 7 groups: a control group, which remained undisturbed in their cages; one of three subgroups undergoing anesthesia without surgery; or one of three subgroups undergoing anesthesia with surgery. Anesthetic regimens included halothane only, halothane with systemic morphine, or halothane with spinal block. Analgesic effects of morphine and spinal block had been previously validated in a pilot study. Animals were used for only one experiment each. In the first experiment, MADB106 cells were injected 4–5 h after induction of anesthesia, and the animals' lungs were removed 24 h after tumor inoculation for assessment of lung tumor retention. Animals' lungs were removed 3 weeks after tumor inoculation for the second experiment. In the third, researchers drew blood 4–5 h after induction of anesthesia and assessed the number and activity of natural killer cells *in vitro*.

In this study, laparotomy produced a 17-fold increase in lung tumor retention, and addition of spinal block to halothane anesthesia reduced this effect by 70%. Systemic morphine also reduced the tumor-promoting effects of surgery but to a lesser extent. Activity of natural killer cells was suppressed by surgery and by anesthesia alone. The clinical significance of attenuating postoperative immunosuppression by regional anesthesia is unclear, and the authors urge consideration of a controlled clinical study to assess whether metastatic development could be decreased during the susceptible postoperative period, when immunosuppression reduces the activity of natural killer cells.

■ Transgenic Mice Used to Test Nitric Oxide as Therapy for Sickle Cell Disease. Martinez-Ruiz *et al.* (page 1113)

Although carbon monoxide and cyanate have been used to increase the affinity of sickle hemoglobin for oxygen (thus reducing sickling) *in vitro*, the therapy is too toxic to be used *in vivo*. Because low-dose inhaled nitric oxide (NO) has been shown to increase the oxygen affinity of sickle hemoglobin erythrocytes *in vitro* and *in vivo*, Martinez-Ruiz *et al.* studied the effects of NO breathing at various doses and time regimens in the presence of severe hypoxia (6% oxygen) using the transgenic SAD mouse model.

Fifty-nine SAD mice were divided into two groups and exposed to either hypoxia or no hypoxia plus NO gas (in doses from 9 to 60 parts per million [ppm]). Their survival was recorded for up to 1 h or until death. Tail blood samples were collected before and after hypoxia to study erythrocyte structure. The percent of erythrocytes that were sickled, deformed, or normal were compared between prehypoxic and posthypoxic samples with and without NO exposure. Oxygen hemoglobin dissociation curves were determined in an additional five mice before and after 60 minutes' exposure to 20 ppm NO breathing at 21% oxygen.

The SAD mice had improved survival rates when they breathed 20 ppm NO gas in air for 30 min before and during severe hypoxic gas exposure. The beneficial, protective effects of NO seemed to be rapid and dose dependent. Pretreatment alone or breathing lower doses of NO were not protective. Changes in hemoglobin SAD oxygen affinity were not detected with NO breathing, and methemoglobinemia levels were low in all mice. Multiple mechanisms and sites, such as hemoglobin interactions and vascular and blood cell components, may be involved in the beneficial effects of inhaled NO. Further studies may delineate and define mechanisms and illuminate the possible role of NO as a therapeutic intervention for sickle cell disease.

Gretchen Henkel