# ANESTHESIOLOGY

## ■ Genetic Testing of Pediatric Patients To Assess Risk of Capillary Leak Syndrome. Zhang *et al.* (page 1387)

The activation of complement plays an important role in the inflammatory changes that occur following cardiopulmonary bypass. Zhang et al. hypothesized that polymorphism of the gene coding the fourth complement component (C4) might be involved in development of postoperative capillary leak syndrome related to cardiopulmonary bypass (CPB) in pediatric patients. To test their hypothesis, they recruited 154 children (aged 2-10 yr) scheduled for elective cardiac surgery with CPB to repair ventricular or atrial septal defects. C4 isotype studies (using gel immunoelectrophoresis) were performed on plasma samples obtained before surgery. Null alleles were inferred by the reduction in the density of corresponding C4A or C4B bands. The patients were assigned to one of five possible C4 phenotype groups based on test results: AABB (no detectable null alleles, 80 patients); A0BB (a heterozygous single null allele at the C4 locus, 28 patients); 00BB (a homozygous C4A null allele, 7 patients); AAB0 (a heterozygous single null allele at the C4B locus, 31 patients); and AA00 (a homozygous C4B null allele, 10 patients).

Just before and 1 h after CPB, plasma protein was measured using a biuret test kit. Plasma colloid osmotic pressure was determined using a membrane osmometer. Evans blue dye was used to measure plasma volume, serum protein, intravenous protein pool, and transvascular escape rate. One hour after CPB, serum protein averaged 3.6  $\pm$  0.4 g/dl in patients with the 00BB C4 phenotype, a value significantly lower than in patients with all other C4 phenotypes. At the same point following CPB, the transvascular escape of Evans blue dye averaged 11.5  $\pm$  -1.3%/h in the same group of patients. On the basis of these results, the authors concluded that patients with homozygous C4 null phenotype are likely to develop capillary leak syndrome following CPB, whereas patients with the other phenotypes are not. Although the primary cause of capillary leak syndrome appears to be the C4A null gene, CPB is just one of the inducing factors. Detection of C4 phenotypes before cardiac surgery might serve as a warning that some patients could incur a serious systemic inflammatory response, and develop capillary leak syndrome secondary to CPB.

### ■ A Closed Claims Analysis of Injuries Related to Central Catheters. Domino *et al.* (page 1411)

Domino *et al.* reviewed the American Society of Anesthesiologists Closed Claims Project database to identify injuries related to central vascular catheter complications. Of a total 6,449 closed claims included in the database (from 1978–1999), 110 claims, or 1.7%, were for injuries related to central catheters. Compared to other types of claims in the database, central catheter claims involved a higher proportion of inpatients and patients with American Society of Anesthesiologists status 3–5. These claims were also associated with higher severity of injury, and a higher proportion of death (47%), compared to other claims.

In the majority of central catheter-related claims, an anesthesiologist alone or an anesthesiologist in tandem with a surgeon (93 and 6, respectively) had inserted the catheter. A nonanesthesia provider was involved in 68% of complications associated with catheter use/maintenance. The most common complications were wire/ catheter embolus (n = 20), cardiac tamponade (n = 16), carotid artery puncture/cannulation (n = 16), hemothorax (n = 15), and pneumothorax (n = 14). Cardiac tamponade, hemothorax, and pulmonary artery rupture led to more patient deaths than did the other types of central catheter-related injuries. The proportion of claims for vascular access injury increased and use/maintenance injury decreased in the period from 1994-1999 compared to the period 1978-1983. During their review of the closed claims database, the authors also indicated which injuries could have been prevented. On the basis of these judgments, they recommend that patient safety may be improved by using ultrasound guidance with cases of difficult placement; using pressure waveform monitoring to prevent accidental arterial cannulation; and checking and acting on chest radiographs after catheters are placed.

#### Risks of Epidural Catheter Penetration in a Human Cadaveric Model. Angle *et al.* (page 1491)

To investigate possible factors contributing to unrecognized subarachnoid catheter penetration, Angle *et al.* (page 000) obtained 10 fresh human cadaveric spinal cords with intact dura. Specimens measuring 2 cm square, taken from L1–2 to L4–5, were mounted in order of harvest (cephalad to caudad) over a 1-cm aperture in a cylindrical human dural sac model, thus preserving the anatomic orientation of the tissues. A wet seal was achieved using a customized gasket and hose clamps. The model was pressurized to physiologic levels with artificial cerebrospinal fluid, and the research team then attempted catheter passage and punctures under standardized conditions. First, a 20-g three-port, closed end, nonflexible tip catheter was passed through an epidural needle mounted on a micromanipulator at a 90-degree angle. After five attempts with the three-port catheter, the team then followed with five attempts using a 19-g single-port, flexible tip catheter, according to standard protocol at their institution when clinicians encounter difficulty with catheter insertion. Catheter passage was compared in intact dura; in dura with clinically occult versus obvious epidural needle punctures; and in dura with subjected to uncomplicated combined spinal epidural placement.

The investigators found that neither the three-port, nonflexible tip catheter nor the single-port flexible tip penetrated the intact dura specimens. In dura that had clinically occult epidural needle punctures (evidenced by cerebrospinal fluid leakage around the needle tip but no evidence from the needle hub), the 20-g catheter penetrated one of three specimens in 1 of 14 attempts, with a distinct "pop" felt as the catheter passed through the dura and into the model. In specimens with clinically obvious epidural needle punctures, the 20-g, nonflexible tip catheter passed in 6 of 33 attempts and the 19-g flexible tip catheter passed through a single 25-g spinal needle puncture in the specimens subjected to combined spinal epidural placement.

The findings of this study suggest that subarachnoid catheter passage is unlikely when the dura is intact or following an uncomplicated combined spinal epidural placement with a 25-g Whitacre needle. Unintentional subarachnoid catheter passage would therefore suggest the presence of dural damage with the epidural needle.

Effects of Intrathecal Morphine and Sufentanil On Lower Urinary Tract Function. Kuipers *et al.* (page 1497) In 45 healthy male volunteers recruited for a randomized, double-blind trial, Kuipers *et al.* performed baseline urinary pressure flow and residual volume measurements using two urethral catheters—one for filling the bladder, another for measuring pressure. Detrusor pressure was estimated by subtracting abdominal pressure (measured *via* a rectal catheter) from the intravesical pressure (the measurement of pressure within the bladder). For baseline measurements, subjects' bladders were filled with saline until they had a strong desire to void. While standing, participants voided and pressures and flow were recorded.

After baseline measurements, subjects received 10 or 30  $\mu$ g of sufentanil, or 0.1 or 0.3 mg of morphine, intrathecally. The research team performed another pressure flow study 20 min after administration of the study drug, filling the bladder to its cystometric capacity. Participants were allowed to urinate, and residual bladder volume was also determined. Urodynamic measurements were then repeated every hour until full recovery of normal lower urinary tract function, defined as a residual volume of less than 10% of bladder capacity and maximum flow and voiding time within 10% of initial baseline values, up to a maximum of 24 h. Subjects' heart rate, respiratory rate, blood pressure, and oxygen saturation were also recorded, as were the presence or absence of adverse effects such as itching, nausea, or vomiting.

The administration of both opioids caused dose-dependent suppression of detrusor contractility and decreased sensation of the urge to void. After 10  $\mu$ g of sufentanil, the mean time to recover of lower urinary tract function was 5 h; after 30  $\mu$ g, 8 h; after 0.1 mg morphine, 14 h; and after 0.3 mg morphine, 20 h. Adverse effects included frequent itching; nausea and vomiting were less common. No changes in heart rate, blood pressure, or respiratory rate were observed during the experimental period. One participant had a postdural puncture headache but completely recovered within a week. None of the remaining participants experienced the protocol as unpleasant, according to their reports on a postprocedure questionnaire. Recovery of normal lower urinary tract function is significantly faster after intrathecal sufentanil than morphine, and recovery time is also clearly dose-dependent.

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