

ANESTHESIOLOGY

■ Effects of Sevoflurane Preconditioning on Human Myocardium Investigated. Yvon *et al.* (page 27)

To examine the effects of sevoflurane preconditioning on isolated human myocardium challenged with simulated ischemia-reperfusion, Yvon *et al.* obtained 69 samples of right atrial trabeculae from 59 patients who underwent routine coronary artery bypass surgery or aortic valve replacement. For purposes of the experiments, the muscle tissues were suspended between an isometric force transducer and a stationary stainless clip in a 200-ml jacketed reservoir filled with Tyrode modified solution maintained at 34°C. Trabeculae were stimulated at a frequency of 1 Hz and were equilibrated for 60–90 min to allow stabilization of their optimal mechanical performance.

In all groups, a 30-min hypoxic period was followed by 60 min of reoxygenation. One group was exposed to hypoxic preconditioning, accomplished by inducing a 4-min hypoxic period, followed by a 7-min reoxygenation period before the simulated ischemia challenge. In the sevoflurane treatment groups, preconditioning was achieved by delivering 1%, 2%, or 3% sevoflurane *via* vaporizer to the tissue bath for 15 min. Following a 7-min washout period, the muscles were then subjected to ischemic-reperfusion challenge. Time to recovery of force contractions was then compared between groups.

In other experiments, the team exposed tissue to preconditioning with 2% sevoflurane for 15 min following 10 min of pretreatment with several selective antagonists: 10 mM HMR 1098, a sarcolemmal adenosine triphosphate-sensitive potassium channel antagonist; 800 mM 5-hydroxy-decanoate, a mitochondrial adenosine triphosphate-sensitive potassium channel antagonist; and 100 mM 8-cyclopentyl-1,3-depropylxanthine, the adenosine A1 receptor antagonist.

The authors found that both hypoxic preconditioning and brief exposure of the muscles to 1%, 2%, and 3% of sevoflurane enhanced recovery of isometric contractions after 60 min of reoxygenation. This effect was abolished in the presence of 5-hydroxy-decanoate and 8-cyclopentyl-1,3-depropylxanthine, but it was attenuated in the presence of HMR 1098. The results suggest that a 5-hydroxy-decanoate-dependent mechanism (such as opening of Katp channels and stimulation of adenosine A1 receptors) may be involved in the sevoflurane-induced preconditioning of human heart muscle against ischemic insult.

■ Anatomic Changes Associated with Application of Cricoid Pressure. Smith *et al.* (page 60)

In 22 healthy volunteers, Smith *et al.* obtained baseline sagittal and axial views of the neck using magnetic resonance imaging. A single investigator applied cricoid pressure (CP), and additional magnetic resonance scans were taken of the subjects' necks. The applied force was standardized. With each subject's head positioned neutrally in the cervical, thoracic, and lumbar spine coil on the magnetic resonance imaging table, spatial limitations necessitated using a two-handed technique to apply CP.

All magnetic resonance images were presented to two radiologists blinded as to the CP technique used. Measurements were taken from the most cephalad image in which the esophagus was seen clearly. Each radiologist read all images independently. A 25% disagreement occurred on images with CP, and 50% disagreement between radiologists occurred on the images taken before CP was applied. The esophagus was displaced relative to the midline of the vertebral body in 10 of 19 subjects without CP and in 19 of 21 with CP. The airway was displaced relative to the midline of the vertebral body in 7 of 21 subjects without CP and in 14 of 21 with CP.

Although the two-handed technique does not represent standard clinical practice, it should have theoretically resulted in less lateral displacement than with a single-handed technique, according to the investigators. That is because symmetrical pressure was confirmed with the study subjects, who were awake, prior to imaging. Despite these measures, CP was asymmetrically applied with greater pressure on the right in 50% of subjects. These results suggest that CP is unreliable at producing midline esophageal compression without distorting airway anatomy.

■ Do Caspase Inhibitors Provide Neuronal Protection after Cardiac Arrest and Cerebral Ischemia? Vogel *et al.* (page 112)

Might inhibition of caspases and/or apoptosis constitute viable neuroprotective strategies during cerebral ischemia? Vogel *et al.* generated a line of transgenic rats expressing baculovirus p35 (a broad-spectrum caspase inhibitor). During experimental protocols, the team then subjected both the transgenic rats ($n = 13$) and their nontransgenic littermates ($n = 25$) to cardiac arrest induced by electrical stimulation.

At 6 min after cardiac arrest, cardiopulmonary resuscitation procedures (comprised of mechanical ventilation, closed chest cardiac massage, and administration of epinephrine) were instituted by an investigator blinded to experimental group assignment. After restoration of spontaneous circulation, the animals were monitored for 7 days. Neurologic deficit scores were obtained on days 1, 3, and 7 after cardiac arrest. The neurologic deficit scores included five parameters: general behavior, cranial nerve function, motor function, sensory function, and coordination. At the end of the monitoring period, the animals were killed and their brains were removed for later histologic evaluation.

More of the transgenic rats survived after cardiac arrest, suggesting a role of the antiapoptotic protein p35 in posts ischemic recovery. Interestingly, neither histopathologic evidence (number of *in situ* DNA nick end labeling-positive cells or viable neurons in cornu Ammonis 1) nor neurologic deficit scores demonstrated any differences in response to cardiac arrest between transgenic and nontransgenic littermates. These findings suggest that another cascade of apoptotic events different from the activation of caspases is activated after global cerebral ischemia.

■ Morphine Requirements Studied in Elderly Patients following Total Hip Replacement. Aubrun *et al.* (page 160)

Should dosages of postoperative opioids be decreased in elderly patients because of age-related changes in pharmacodynamics and pharmacokinetics? To address this question, Aubrun *et al.* prospectively studied two groups of patients undergoing total hip replacement at their institution. Of the 329 patients included in the study,

224 (68%) were considered young (≤ 69 yr old) and 105 (32%) were elderly (≥ 70 yr old). On extubation in the PACU, all patients were questioned about the presence of pain and were asked to rate their pain intensity using a visual analogue scale (VAS; 0 to 100, hand slide-rule type). When pain increased to a VAS score greater than 30, intravenous morphine was titrated every 5 min by 3-mg increments until pain relief (≤ 30) was attained. According to pain management protocol at the authors' institution, morphine titration was stopped if the patient had a respiratory rate less than 12 breaths per min, and/or a value of oxygen saturation measured by pulse oximetry lower than 95%, and/or a serious adverse reaction to the morphine. Subcutaneous morphine could be started 2 h after the end of intravenous morphine titration, either in the PACU or the ward, and was administered every 4 h, with doses adjusted according to the patient's weight and VAS score.

The team tracked the intravenous boluses of morphine, interval between boluses, patients' VAS score, and doses of subcutaneous morphine administered, if any. They found that acute administration of morphine, *i.e.*, postoperative titration of intravenous morphine in the PACU, did not significantly differ between the young and elderly patients. However, in the subacute setting, patients with more severe pain (VAS score ≥ 70) and a higher duration of surgery required more subcutaneous administration of morphine. The authors note that the PACU nurses were not blinded to patient age, and that the elderly patients might have been using other analgesics before surgery that interacted with the study drugs. Further study in this area will be needed to understand differences in pain requirements.

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