◇ This Month in

# ANESTHESIOLOGY

## ■ Trauma Patients' Adrenal Reserves: Correlating Responses to Corticotropin Stimulation to Clinical Outcomes. Hoen *et al*. (page 807)

Hoen *et al.* assessed adrenal reserves in trauma patients to understand the relationship between early inflammatory response and clinical outcomes. All consecutive trauma patients admitted to the surgical ICU between November 1, 2000 and January 31, 2001 were prospectively enrolled in the study. Patients who were pregnant, older than 55 years of age, who had previous acute or chronic diseases or treatment, or who had disrupted hypothalamic-pituitary-adrenal (HPA) axes were excluded from the study.

A total of 34 patients were ultimately included in the study, with severity of injury in the moderate to severe range. A Simplified Acute Physiology Score (SAPS II) was calculated to assess the magnitude of patients' trauma. An Abbreviated Injury Scale for the Head defined the extent of brain injury; a Shock Score rated hemorrhagic shock; and Multiple Organ Dysfunction (MOD) scores were calculated daily. Patients were also monitored daily for presence of nosocomial infections (urinary, bloodstream, and wound). The number of infectious pneumonia episodes was noted for each patient, as was the length of ICU stay and time to discharge.

The research team performed a short corticotropin stimulation test on study patients at the end of the "early phase" and during the "late phase" of their treatment. (The early phase encompassed the resuscitative period as well as surgical procedures immediately after the trauma, while the late phase corresponded to the first post-trauma week.) A cortisol response of less than $+9$ g/dL$^{-1}$ to the intravenous bolus of tetracosactrin indicated impaired adrenal function and the patient was deemed a "nonresponder." The early phase stimulations were done $21.7 \pm 14.3$ h after trauma. There were 19 patients (56%) with a basal cortisol plasma level below 18 $\mu$g/dL$^{-1}$, and 16 patients were classified as nonresponders based on their cortisol responses during the early phase stimulation. In the 16 nonresponders, hemorrhagic shock was more frequent and IL-6 levels were higher. The duration of norepinephrine treatment and the total amount of the infused drug were significantly higher in these early nonresponders. The study confirms that a sustained inflammatory response from either an infective or noninfective source can result in cortisol deficiency related to a primary adrenal insufficiency and/or loss of ACTH secretion. Therefore, using the measurement of ACTH and cortisol levels before and after stimulation by corticotrophin or corticotrophin-releasing hormone may be indicated in trauma patients to help identify the consequences of modified HPA axis activity.

## ■ Addressing Intraoperative Hypovolemia with Goal-Directed Plasma Volume Expansion. Gan *et al*. (page 820)

Because of preoperative fasting, surgical trauma, evaporation, and the use of dry anesthetic gases, many surgical patients experience hypovolemia. The consequences of this condition range from postoperative nausea and vomiting to organ dysfunction and prolonged hospital stays. Using guidance from esophageal Doppler monitors (EDMs), Gan *et al*. investigated whether goal-directed intraoperative plasma volume expansion would improve surgical patients' postoperative outcomes.

One hundred patients scheduled for major elective general, urological, or gynecological procedures, with an anticipated blood loss of greater than 500 mL, were recruited for the study. (Two patients were later excluded when their surgeries were cancelled.) After induction of anesthesia and insertion of EDMs into the mid-esophagus, patients were randomized to the protocol or control group. In the study group, boluses of fluid were administered, guided by an algorithm linked to the EDM estimations of stroke volume and corrected flow time (FTc). A 200 ml aliquot of 6% hydroxyethyl starch in saline (hetastarch) was given when the FTc was less than 0.35 s. If stroke volume was stable or increased with the fluid challenge and the FTc remained below 0.35 s, the fluid challenge was repeated until the upper limit of 20 mL/kg of solution was reached.

All EDM variables were collected by an independent research team member, and EDM monitors for control group patients were obscured from anesthesiologists' view. In control group patients, fluids were given according to standard institutional hemodynamic variables (such as a urinary output of less than 0.5 mL$\cdot$ kg$^{-1}$ $\cdot$ h$^{-1}$ or an increase in HR greater than 20% over baseline).

Results from tracking patients' intraoperative and postoperative hemodynamic indicators revealed that patients in the protocol group had significantly higher stroke volume and cardiac output at the conclusion of surgery than did control group patients. These patients also

experienced shorter hospital stays (5 ± 3 *vs.* 7 ± 3), had less postoperative nausea and vomiting, and tolerated oral intake of solid food earlier than their control group counterparts. For patients undergoing moderate and high-risk surgery, goal-directed fluid administration with 6% hetastarch is associated with improved outcomes and shorter hospital stays.

## ■ Early Effects of pH *versus* α-Stat Management during Acute Focal Cerebral Ischemia in Rats. Kollmar *et al*. (page 868)

Using a middle cerebral artery occlusion (MCAO) model of transient cerebral ischemia in 21 rats, Kollmar *et al*. subjected 10 rats to α-stat ventilatory management during a 5-h reperfusion period with moderate hypothermia (33°C). The respiratory rate was adjusted to an arterial carbon dioxide partial pressure ($Paco_2$) of 40 mmHg and not corrected for the animal's body temperature. The team used pH-stat to manage the remaining 11 rats, adjusting the respiratory rate to a $Paco_2$ of 40 mmHg corrected for body temperature.

Cerebral blood flow (CBF) was analyzed in all animals for 7 h after induction of ischemia by iodo[$^{14}$C] antipyrine autoradiography. Cerebral infarct volume and cerebral edema were measured by high contrast silver infarct staining (SIS) of frozen brain sections after the experimental segment had concluded. Both local and global CBF during hypothermia in the reperfusion period showed a greater increase in the pH-stat management group compared with the α-stat management group (69.5 ± 12.3 ml ·100 $g^{-1} \cdot min^{-1}$ *versus* 54.7 ± 13.3 ml · 100 $g^{-1} \cdot min^{-1}$). The authors also found that this increased CBF in pH-stat management was associated with reduced cerebral infarct volume and cerebral edema.

The authors offer several theories as to why increased CBF during pH-stat management may help to decrease tissue damage: improved oxygen delivery may reduce ischemia; increased CBF may remove neurotoxic metabolites during ischemia; or increased CBF may provide a more homogenous brain cooling profile. Whatever the mechanism, the authors also point out that cerebral infarct volume and cerebral edema can change over time. Because they examined CBF during a relatively short period of reperfusion, a full tissue reaction may not have had time to develop. Further investigation is warranted.

## ■ Does Sleep Deprivation Potentiate the Hypnotic Effects of Anesthetic Agents in Rats? Tung *et al.* (page 906)

To test whether sleep-deprived rats would require less anesthetic than rested rats to achieve loss of responsiveness, Tung *et al.* subjected rats to either sleep deprivation or ad-lib activity for 24 h. Sleep deprivation was achieved by placing rats on a 45 cm diameter disk suspended over a pan of water. Continuous computerized electroencephalographic–electromyographic monitoring, *via* previously implanted electrodes, detected sleep states and then initiated wheel rotation at a rate of 3 revolutions/min to rouse rats in the sleep-deprivation protocol. Once rats awakened and began walking to avoid falling into the water, the rotation stopped.

After the 24 h intervention period, the investigators began an infusion of propofol at a rate of 800 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Infusions were discontinued when rats no longer exhibited righting reflex in response to gentle prodding or placement on their backs or sides. Prodding then took place every 15 s to determine time to recovery from the infusion. Observations of loss of righting reflex and time to recovery were conducted by an investigator blinded to each rat's deprivation history. In a second experiment, rats were exposed to inhaled isoflurane after either sleep deprivation or ad-lib activity. Again, time to loss of righting reflex and time to recovery were measured for each rat.

Two additional control experiments were then conducted, subjecting rats to either ad-lib activity or an equivalent sleep deprivation stimulus. In this case, the rotating wheel was programmed to deliver the same total rotation in a 24 h period, but at the same time each hour.

The disk-over-water protocol reduced the rats' total sleep to 13.9 ± 4.4% of the 24-h period (compared with rats in the ad-lib activity group who slept approximately 52% of the time). Sleep deprivation reduced the time to loss of righting reflex by 40% for propofol and 55% for isoflurane, and also prolonged rats' time to recovery. When wheel rotation occurred in a predictable fashion, sleep was only slightly reduced, and did not significantly alter response to the anesthetics. Results of this study support the hypothesis, say the authors, that neuronal networks active in sleep are also involved in the anesthetized state. They also suggest that sleep deprivation may be responsible for variability in patients' responses to anesthesia, and may also play a role in recovery and requirement for postoperative pain medication.

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