REPORT OF A SCIENTIFIC MEETING

Carol A. Hirshman, M.D., Editor

Society of Neurosurgical Anesthesia and Critical Care. Washington, D.C. October 8, 1993.

The 21st annual meeting of the Society of Neurosurgical Anesthesia and Critical Care was held at the Renaissance Hotel, Washington, D.C., on October 8, 1993. Among the topics discussed were current concepts in brain tumor biology and therapy, new techniques in brain imaging, and neurointensive care. Oral and poster presentations focused on control of the cerebral circulation, pharmacologic agents affecting the central nervous system, methods of protection against cerebral ischemia, and monitoring methods used in neuroanesthesia.

Robert L. Martuza, M.D., chairman of Georgetown University Medical Center's Department of Neurosurgery (Washington, D.C.), outlined recent advances in descriptions of brain tumor biology and prospective therapies. As the Janssen Distinguished Lecturer, Martuza discussed the use of subrenal capsules in nude mice to grow tumors, including as meningiomas, schwannomas, and acoustic neuromas. DNA analysis from such tumors can identify genetic loci associated with tumorigenesis. Using these techniques, the gene for neurofibromatosis type 2 has been cloned, and numerous other loci for central nervous system tumors have been identified.

While discussing therapeutic strategies for patients with brain tumors, Martuza mentioned that genetically engineered retroviruses can deliver genes to dividing cells. Ongoing laboratory work involves the use of vector retroviruses or Herpes simplex virus combinations to insert a thymidine kinase gene, sensitive to both acyclovir and gangliocyclovir, into dividing brain tumor cells and thus allow treatment with chemotherapeutic agents. An additional promising new agent for the treatment of brain tumor patients is the angiogenesis blocker, AGM-1470. This fungal-derived drug has successfully suppressed neovascularization and growth of several human brain tumor cell lines.

As discussed by Martuza, radiation therapy has long been a standard in the treatment of brain tumor patients. Recent advances employing "stealth technology" linear accelerators permit the delivery of specific doses of radiation to a tumor without the necessity of a static field. This type of radiation will be particularly useful in children, as it will be unnecessary that they remain motionless during treatment.

Aaron Fenster, M.D. (London, Ontario), delivered an invited lecture titled "New Horizons in Brain Imaging." Fenster emphasized new applications that are available with modifications of current technology, *e.g.*, computed tomography and magnetic resonance imaging. Magnetic resonance imaging can be refined using a four-tesla magnetic field to produce functional maps of brain tissue. This mapping relies on the paramagnetic characteristics of the oxy-/deoxyhemoglobin relationship. With modification, a computed tomography scanner can provide functional and three-dimensional imaging with superimposed digital subtraction and angiography. Such characteristics as blood-brain barrier permeability and changes in capillary permeability related to the administration of steroids soon may be mapped on computed tomography.

A panel discussion on neurointensive care covered the topics of outcome prediction, status epilepticus, and the choice of sedatives and muscle relaxants in the intensive care settings. Keith H. Berge, M.D. (Mayo Clinic, Rochester, MN), outlined the APACHE (Acute Physiology, Age, Chronic Health Evaluation) III outcome prediction method. The APACHE III method is based on prospectively collected data on 17,444 unselected adult medical/surgical intensive care unit (ICU) admissions at 40 U.S. hospitals (Washington, D.C.). This sample provides a nationally representative standard for measuring several important aspects of ICU performance. An automated information system has been developed to provide real-time information about expected ICU patient outcome, length of stay, cost projections, and ICU performance.

W. Andrew Kofke, M.D. (Pittsburgh, PA), provided an update on the treatment of status epilepticus. According to Kofke, animal studies reveal that, when seizures are unrelenting, animals experience cell loss from the hippocampus. He discussed a series of 10 cases in which isoflurane was administered to achieve burst suppression levels on the electroencephalogram and to control seizures. The administration of isoflurane in the ICU setting requires an enormous commitment of anesthesia service, and the agent fails to reverse the underlying cause of refractory seizures. In Kofke's experience, isoflurane is effective and rapidly titratable but should be used only when intravenous agents in anesthetic doses have proved to be ineffective.

Christian K. Spiss, M.D. (Vienna, Austria), discussed the use of sedatives and muscle relaxants, particularly related to neurosurgical intensive care. Currently, Spiss maintains a regimen of intermittent bolus muscle relaxant use when tracheal suctioning is necessary in patients with Glasgow coma scale scores of 7 or lower.

Control of the Cerebral Circulation

Relationships of the various components of the cerebral circulation and pharmacologic manipulations of the intracranial contents were discussed in many presentations. Roger A. Craen, M.D., *et al.* (London, Ontario) described results of a study in a rabbit model in which regional cerebral blood volume was measured using dynamic contrast-enhanced computed tomography. Under isoflurane anesthesia, changes in cerebral blood flow (CBF) measured by radiolabeled microspheres failed to result in changes in cerebral blood volume of similar magnitude. Isoflurane may induce a lower responsiveness of the venous system relative to the arterial system explaining these findings. Heidi M. Koenig, M.D., *et al.* (Chicago, IL) used nitro-L-arginine methylester (L-NAME), a competitive inhibitor of nitric oxide synthetase, and D-NAME, the inactive enantiomer of L-NAME, to examine the role of nitric oxide in pial vessel dilatation. Mercury light/fluorescein dye endothelial ablation also was performed to examine the role of the endothelium in isoflurane-induced vasodilatation. In this study, the cerebromicrovascular dilatory response to isoflurane was attenuated or blocked when the rat vessels were exposed to isoflurane following the inhibition of nitric oxide synthetase with L-NAME and endothelial destruction. Isoflurane caused an endothelial-dependent, nitric oxide-mediated cerebral microvessel dilatation in this model.

Mazen A. Maktabi, M.D., and Michael M. Todd, M.D., (Iowa City, IA) studied the response of cerebral blood vessels to hypoxia in rabbits anesthetized with either pentobarbital or isoflurane. In each group, the anesthetic was titrated to achieve burst suppression on the electroencephalogram, and CBF was measured using radiolabeled microspheres. Measurements were made at normoxia and at three levels of increasingly severe hypoxia. Despite higher control levels of tissue

oxygen in the rabbits anesthetized with isoflurane, CBF increased by a similar magnitude in both groups. This suggests that the trigger for increasing CBF during hypoxia is not tissue oxygen but may be arterial oxygen tension. Anesthetics may reset the hypoxic-CBF dose response.

Pharmacology in Neuroanesthesia

An interesting presentation by Gary Thal, M.D., *et al.* (Boston, MA) focused on the unmasking of focal neurologic deficits by the sedative medication midazolam. In this study, following baseline neurologic examination, 1–4 mg midazolam was administered intravenously, and a neurologic examination was performed 5 min later. In 29 neurosurgical patients who were easily arousable and cooperative, 10 subjects demonstrated midazolam-induced focal-motor deficits. These patients were all members of a subgroup of 13 patients who had a history of preexisting motor deficits on the baseline examination or a history of a focal motor deficit that had resolved preoperatively. Only patients with a history of motor weakness developed a focal deficit during sedation, and pulse oximetry oxygen saturation and blood pressure were stable in all patients. Proposed mechanisms might include altered drug distribution in abnormal brain or increased neuronal sensitivity to sedatives.

Cerebral Ischemia

Steve R. Wagner IV, M.D. (Rochester, MN), was awarded the Anaquest New Investigator Award for his study, coauthored by William L. Lanier, M.D., of the metabolism of glucose, glycogen, and high-energy phosphates during complete cerebral ischemia in hyperglycemic and normoglycemic rats. Although increases in brain glucose will worsen outcome following cerebral ischemia, there is evidence that, in equally hyperglycemic subjects, chronic hyperglycemic patients may have better postischemic outcomes than would acute hyperglycemic patients. To determine whether metabolic differences could be identified to account for alterations in postischemic outcome, 90 pentobarbital-anesthetized Sprague-Dawley rats were divided into three groups: normoglycemic, chronically hyperglycemic diabetic, and nondiabetic, acutely hyperglycemic rats. Similar ischemic injuries were induced in all animals, brains harvested, and brain metabolites measured using enzymatic fluorometric techniques. The rate of brain glycogen metabolism was inversely proportional to preischemic brain glucose concentrations. Despite greater lactate production in hyperglycemic rats, chronically hyperglycemic diabetic and nondiabetic, acutely hyperglycemic rats had greater intraischemic ATP concentrations and energy charges of the adenylate pool than did normoglycemic rats. Further, energy status was more favorable in nondiabetic, acutely hyperglycemic rats than in chronically hyperglycemic diabetic rats. No difference was found in the intra-ischemic carbohydrate consumption between chronically hyperglycemic diabetic and nondiabetic, acutely hyperglycemic rats. The data suggest not that energy failure is the origin of the more severe ischemic neurologic injury in hyperglycemic subjects but that failure of total brain carbohydrate mobilization may contribute to energy failure in hyperglycemic patients.

Mild to moderate hypothermia, which attenuates ischemic brain injury, has become the subject of renewed interest in clinical neuroanesthesia care. Kristy Z. Baker, M.D., *et al.* (New York, NY) studied the safety and feasibility of intentional mild hypothermia and rewarming. Two groups of patients were scheduled for elective, supine craniotomies for tumor resection or aneurysm repair. In the normothermic group, temperature was maintained between 36.5°C and 37°C. The hypothermic group was cooled with a water blanket set to 25°C and a convective device circulating room temperature air. Cooling was stopped at 35°C, and rewarming was initiated when the temperature was 34.5°C or at the beginning of dural closure. All patients received a similar narcotic-based anesthetic. Although no one in the normothermic group shivered postoperatively, five of nine patients in the hypothermic group experienced this problem. One patient in each group had postoperative electrocardiogram changes, which were ruled out for myocardial infarction. The authors concluded that intentional mild hypothermia is feasible, but complete rewarming may be difficult to achieve for short procedures. In a related study, Edwin M. Nemoto, Ph.D., (Pittsburgh, PA) examined the effects of hypothermia on the attenuation of active as opposed to basal cerebral metabolic rate for oxygen. This investigation performed in rats failed to support the hypothesis that hypothermia aids cerebral protection because of a differential attenuation of active as opposed to basal cerebral metabolic rate for oxygen, but variable effects on CBF and basal cerebral metabolic rate for oxygen were documented that warrant further investigation.

Daniel J. Cole, M.D., (Loma Linda, CA) reported the results of a study on the effects of etomidate on brain injury during temporary, focal cerebral ischemia. Twenty-eight rats were divided into four groups. Halothane (1.2 MAC) was used during preparation and maintained for the control group. Thiopental was used in one group to achieve burst suppression on the electroencephalogram. Isoflurane also was used in a third group to provide burst suppression on the electroencephalogram, as was etomidate in a fourth group. Middle cerebral artery occlusion was achieved for 180 min, followed by 120 min of reperfusion. Brains were analyzed for ischemic injury by a 2-3-5 triphenyl tetrazolium chloride stain. Brain injury was less severe in the thiopental group than in the control group. In the isoflurane and etomidate groups, however, rate of injury exceeded that observed in either the control or the thiopental group. This study questions the ability of etomidate or isoflurane to protect against brain injury during temporary focal cerebral ischemia.

Monitoring

Jugular venous bulb oxygen saturation measurements have been obtained in groups of head-injury patients to assist with management of intracranial hypertension. B. J. Matta, M.B., *et al.* (Seattle, WA) reported the experience of using this monitor intraoperatively in 95 consecutive patients undergoing neurosurgical procedures. The catheter was placed successfully in 93 patients with a mean insertion time of 98 s. Easily managed carotid artery puncture on four occasions was the only complication. The monitor detected severe desaturation (jugular venous bulb oxygen saturation less than 45%) requiring therapeutic interventions in 17 patients.

Abstracts of the scientific papers presented and the poster presentations are published in the *Journal of Neurosurgical Anesthesiology* (1993, volume 5, number 4).

Patricia H. Petrozza, M.D.
Associate Professor of Anesthesia
Head, Section on Neuroanesthesia
The Bowman Gray School of Medicine
of Wake Forest University
Medical Center Boulevard
Winston-Salem, North Carolina 27157-1009