REPORTS OF SCIENTIFIC MEETINGS

Richard I. Mazze, M.D., Editor

Gull Harbour Toxicity Symposium

The need for investigators in anesthesiology to meet in a Gordon Research Conference format was demonstrated by the lively discussion generated at the Anesthetic Toxicity Symposium held at Gull Harbour, Manitoba, Canada, June 25–27, 1982. Twenty investigative anesthesiologists, basic scientists, and representatives of industry, representing three countries, met in an informal manner for an exchange of information and future project planning in this vital area of anesthesia research. Dr. William Pope, University of Manitoba, Winnipeg, was the seminar organizer.

Dr. Raymond Fink (University of Washington, Seattle) presented work in progress concerning the problem of cytotoxicity of 2-chloroprocaine. There have been anecdotal reports that high concentrations of this local anesthetic can produce spinal cord neural toxicity in humans. Employing a rabbit model, Dr. Fink lavaged the carotid sheath with various commercial preparations of local anesthetics. Of several local anesthetics tested, only 2-chloroprocaine produced characteristic punctate hemorrhages in the carotid sheath. Microscopic examination confirmed that there was considerable damage of the vagus nerve at this anatomic site produced by 2-chloroprocaine, but not by the other local anesthetics. Dr. Ross Terrell, a representative of industry, commented that if this bioassay for local anesthetic neurotoxicity turns out to be valid, it possesses precisely the ease of performance which would make it rapidly adaptable to large volume drug screening.

Hepatotoxicity of anesthetics and the validity of animal models was discussed by Drs. Marilyn Harper and Edmond Eger from the University of California, San Francisco. Standardization of the so-called reductive model of "halothane hepatitis" by various investigative groups has not been ideal. Because of the variability of experimental conditions in different laboratories, there has been considerable misunderstanding. At inspired oxygen concentrations of 10% or less, the mere state of anesthesia with drugs such as fentanyl has been observed to produce hepatic necrosis in phenobarbital-pretreated rats. Of the inhalation anesthetics studied, only halothane produced hepatic necrosis at an inspired oxygen concentration of 14%. Thus, it was concluded that these animal models are extremely complex and a number of variables contribute to the expression of hepatic injury. Dr. Jay Gandolfi (University of Arizona, Tucson) described another factor which potentiates the phenobarbital-pretreated–mild hypoxia animal model of halothane liver damage: endotoxin. The presence of this lipomucopolysaccharide appears to promote the disruption of hepatocytes once they have been damaged by free radical intermediates produced by reductive halothane biotransformation. Dr. William Ross (University of Virginia, Charlottesville) contributed important observations of hepatic artery and portal vein blood flow in the rat animal model using radioactive microsphere techniques. Impressive reductions in total hepatic blood flow were produced by mild hypoxia in his experimental animals. Lively and informative discussion ensued concerning the meaning, variability, and adaptability of this model to the human situation. In summary, Drs. Leo Strunin (University of Calgary) and Nicholas Greene (Yale University, New Haven) agreed that the several groups working in this area, conceptually, are not far apart. It was agreed that work should be directed to the clinical situation to prove or disprove the thesis that abnormal biotransformation is the vector of hepatic damage.

A session concerning the effects of anesthetics on reproduction was the contribution of Dr. Paul Land (Rush Medical School, Chicago), Dr. Michael Halsey (Clinical Research Center, Northwick Park, U. K.), and Dr. Geoffrey Lane (University of Michigan, Ann Arbor). Alterations of reproduction seem real at anesthetic concentrations, but not at trace levels. The consensus was that studying trace concentrations is rather unrewarding in this area. Dr. Peter Duncan (University of Manitoba, Winnipeg) discussed his epidemiologic study of the outcome of pregnancy of patients anesthetized during gestation. This is a major undertaking which will survey all patients receiving an anesthetic during pregnancy in the entire province of Winnipeg, which has a population of over one million. At present, the work is not completed so that statistical evaluation of the data was not available.

Dr. William Welch (University of California, Irvine) discussed his recent studies which demonstrate marked bacteriophage inhibition produced by inhalation anesthetics on polymorphonuclear cells. Using chemoluminescence techniques, he is attempting to pinpoint the mechanism by which bacterial killing ability is lost by these cells. This work is of clinical importance as it may help to delineate altered host responses to post-anesthetic infection.

Dr. Susan Rice (Stanford University, Palo Alto) presented work concerning the delineation of two populations of isoniazid-treated patients. When these individuals are given enflurane anesthesia, one group produces only the usual amount of plasma fluoride from biotransformation of the anesthetic while the other group produces very high concentrations which can be near renal toxic levels. Obviously, clinical identification of the latter group is important.

The adequate time for discussion afforded by this format led to considerable exchange of information. Consensus among participants was that such anesthesia scientific meetings should continue and be encouraged.

BURNELL R. BROWN, JR., M.D., PH.D.
Professor and Head
Department of Anesthesiology
University of Arizona
College of Medicine
Tucson, Arizona 85724