REPORTS OF SCIENTIFIC MEETINGS

Richard I. Mazze, M.D., Editor

First World Conference on Clinical Pharmacology and Therapeutics

The First World Conference on Clinical Pharmacology and Therapeutics was held at the impressive Wembley Conference Center, London, England, from August 3–8, 1980. The meeting was jointly sponsored by the International Union of Pharmacology and the British Pharmacological Society. The high standard of the opening ceremony, which was heralded by a fanfare from the band of Her Majesty's Welsh Guards, was maintained throughout the meeting. The scientific program consisted of a series of symposia, workshops, sessions on therapeutics, oral and poster presentations, and plenary and update lectures. A wide range of topics was covered in the six-day scientific program including drug metabolism, cardiovascular pharmacology, anti-arrhythmic drugs, clinical trials, pharmacokinetics, beta-adrenoceptor blocking drugs, CNS pharmacology, and general toxicology.

It was gratifying to see that one poster session which attracted a great deal of interest was devoted to anesthetic agents. Highlights of this session included a paper by K. Shukla and colleagues (Lucknow, India) which described a new local anesthetic for use in ophthalmic surgery. The drug, known as centbucridine (4-N-butylamino-1,2,3,4-terahydroacridine hydrochloride), was administered as an 0.25 per cent solution for nerve block or infiltration anesthesia to 147 patients who underwent surgery for cataract (121 cases), glaucoma (6 cases), entropion (9 cases), and other ophthalmic conditions (11 cases). The onset of action as well as degree of anesthesia were reported to be satisfactory in 145 of the 147 cases and there were no side effects. Westra and colleagues (Groningen, the Netherlands) reported results of their study on the kinetics of gallamine in patients with extrahepatic cholestasis. Four severely jaundiced patients undergoing biliary tract surgery received 2.5 mg/kg of gallamine, iv, in 30 s. Five patients having biliary surgery with insertion of a bile duct drain served as controls. Three-compartment analysis of plasma gallamine concentrations revealed similar kinetics in both groups. Renal elimination was also the same, equalling 95 per cent of the total dose within 48 hours after administration, while biliary elimination was negligible (1 per cent). The authors concluded that in patients with cholestatic jaundice without renal failure, gallamine was preferable to pancuronium bromide because unlike pancuronium, it did not produce prolonged neuromuscular blockade. In a companion poster presentation, A. Scaf and colleagues (Groningen, the Netherlands) described the pharmacokinetics of curare-like agents and the distribution and elimination factors which determine their duration of action. The relative contribution of renal and hepatic elimination to the total body clearance of *d*-tubocurarine, metocurine, pancuronium, gallamine, and hexafluorenium was estimated in patients. Biliary elimination was significant, only for hexafluorenium, *d*-tubocurarine and pancuronium (average values 38 per cent, 14 per cent, and 11 per cent of the administered dose, respectively). Except for gallamine (90–100 per cent recovery) no more than 60 per cent of the dose of the other drugs was recovered within 48 hours. Based on these kinetic data, the authors postulated that there was a storage compartment from which muscle relaxants were slowly released. They further suggested that the liver played an important role in the storage of these agents.

Another twist in the search for the ultimate animal model for halothane hepatitis was provided by M. Wood and colleagues (U.S.A.). Using triiodothyronine (T_3) to sensitize male Sprague-Dawley rats, they were able to produce centrilobular necrosis with 1 per cent halothane administered for two hours with 14 per cent, 21 per cent, or 99 per cent oxygen. Liver glutathione concentration were depressed 24 hours after T_3 administration, but fell no further with continued T_3 pretreatment or with administration of halothane. Liver cytochrome P-450 also was reduced by T_3 administration and decreased further following halothane administration to the T_3-treated rats. The authors concluded that hyperthyroidism sensitizes rats to halothane-induced hepatic necrosis, a situation that may have important implications for thyrotoxic patients undergoing surgery. However, the overall relevance of such an animal model to most clinical cases of hepatitis following halothane administration, is still far from clear.

Although not specifically dealing with anesthetic agents, many other sessions had great relevance to the clinical and scientific aspects of anesthetic practice. One particularly lively session was a workshop on clinical trials with C. Maxwell (U. K.), P. Lucchelli (Italy), J. Levin (U. S. A), L. Lasagna (U. S. A.), H. Wulff (Denmark), and D. Vere (U. K.), as participants. The overall flavor of the discussion revolved around the difficulty of conceiving, organizing, and performing worthwhile clinical trials. The discussants pointed out the weaknesses of the statistical analytical methods used in many clinical trials and emphasized that it was often difficult for nonstatisticians to appreciate all of the fine points of statistical methodology. They agreed that it was imperative that the strengths and weaknesses of the statistical methods to be used in a trial be thoroughly explored with a biostatistician before the trial commences. Another frequently encountered problem was obtaining a truly random sample for a study population. In fact, it is virtually impossible to do so because the usual procedure of choosing only hospital patients with a particular disease biases the population considerably. Even normal healthy volunteers are a biased sample. Clearly then, clinical trials must be viewed in light of the biases and difficulties in doing a proper study. Nevertheless, over the years, such trials combined with anecdotal reports and other forms of clinical data have provided the basis for assessment of virtually all new and existing drugs.

The full proceedings of the conference will be published by MacMillan Publishers Ltd., London and Basingstoke, and will cost $12.00 for the paperback edition, and $30.00 for the hardback edition.

JEFFREY M. BADEN, M.D.
Assistant Professor of Anesthesiology
Stanford School of Medicine
Stanford, California 94305
and
VA Medical Center
Palo Alto, California 94304