

## Reports of Scientific Meetings

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### Canadian Anaesthetists' Society

The 1971 Annual Meeting of the Canadian Anaesthetists' Society took place June 27 through July 2 in the scenically arresting setting of the Chateau Frontenac Hotel, Quebec City. Although there were a number of stimulating papers of clinical interest, this report focuses mainly on those of an investigational nature. The aim is to direct attention to scientific work now in progress in our neighboring country. I trust that the meeting's participants, as well as the reader, will forgive inaccuracies, in the interest of over-all reporting. It is not easy to catch all the details while listening, viewing slide projections and following translations from the French.

On Sunday, before the opening of the scientific sessions, an all-day symposium on Anesthesia and the Endocrines was held. Aably directed by R. Déry of Quebec, participants included: L. D. Vandam of Boston, J. Genest of Montreal, T. Oyama of Japan, P. Huguenard of Paris, A. B. Dobkin of Syracuse, R. G. Merin of Rochester, N. Y., and R. Déry. On Monday, C.-H. Sirois reported on investigations relative to muscle pains following succinylcholine administration. Prior treatment with meperidine or diazepam failed to affect the severity or incidence of pain, likewise having little influence on plasma levels of  $K^+$  and CPK, two substances reputed to be related to pain. C. S. Fox noted that lumbar epidural anesthesia was now used in 85 per cent of anesthetics for labor and delivery in the department at McGill. Following repeated 50–60-mg doses of 1 per cent lidocaine with epinephrine plus terminal perineal injection for an average dose of 4.7 mg/kg, blood levels of anesthetic taken from fetal scalp veins before delivery hardly exceeded 0.65  $\mu\text{g/ml}$ , half the maternal level—both well below toxic concentrations. The latter figures were much lower than those reported for paracervical block. G. L. Houle from the same department reported on the use of carbonated lido-

caine, 2 per cent, with freshly added epinephrine, total average dose about 290 mg of local anesthetic, for cesarean section. Although time for complete anesthesia was reduced by 33 per cent compared with the time for 2 per cent lidocaine hydrochloride and epinephrine, Apgar scores were not so good, spread of anesthesia was more extensive, and greater maternal hypotension was encountered. Though maternal and fetal blood levels of anesthetic were higher with the carbonate than with hydrochloride, the former did not approach the toxic range. To conclude the first morning, a panel discussion on Medical-Legal Aspects of Anesthesia was led by S. L. Vandewater of Kingston, in a closed session.

C. A. Gronert of Rochester, Minnesota, studied over a six-week period the effects of succinylcholine administered to thermally-injured swine otherwise maintained in good general condition. A second group of animals had undergone denervation of an extremity via sciatic-nerve section. The swine burned full-thickness without muscle injury showed no excessive increase of serum  $K^+$ , but levels in venous blood from the denervated legs showed considerable increases of  $K^+$ , 4.0 mEq/l. A. E. Johnston reported preliminarily on the biochemical effects of a hemodilution technique using ACD blood prime in pediatric patients undergoing bypass open-heart operations. Final results are awaited, but a notable feature of the work was the utilization of a seemingly reliable analytic method for determining ionized and total calcium in plasma. L. G. Cruickshank found that self-administration of methoxyflurane for pain relief during labor and delivery was safe in the presence of adequate nursing supervision. His contention was supported by data on Apgar scores and fetal and maternal blood gases, as well as respiratory and blood levels of anesthetic. Others, however, condemned the procedure on the basis of had experience. P. C. Duke employed the pulse-slowing effect of a vasopressor stimu-

lus to judge the effect of age as well as halothane and methoxyflurane anesthesia on baroreceptor activity in man. Although the components of this complex reflex were not dissected out, baroreceptor activity was found to diminish with advancing age and with halothane, but not methoxyflurane.

On Tuesday, there were papers on the Guillain-Barré Syndrome (H. Desmeules), Familial Dysautonomia (H. Meridy), and the Clinical Use of Pancuronium Bromide (A. B. Dobkin and J. P. Dechene).

In many respects, the Residents' Competition that followed was a highlight of the meeting, the presentations well-founded, crisp and punctual. E. Binns spoke of the effects of albumin-saline and saline preloading on renal function during halothane anesthesia, based on classical clearance techniques. Although well-designed, conclusions were not forthcoming on the basis of so few studies. Circulating plasma renin levels were little affected by the anesthetic. R. K. Claverley was awarded First Prize for studies of anesthetic applications of measurement of serum digoxin levels by means of radioimmunoassay. Toxic levels seem to be clearly defined, and the implications for prophylactic digitalization, interpretation of the therapeutic effect, and toxicity seem clear. In treated patients, digoxin levels changed little during the course of anesthesia. Disadvantages of the technique are the expense, ten dollars per analysis, and a lapse of eight hours for a definitive reading. Using a lung model, D. W. Davies tested the effect of a positive-expiratory-pressure plateau on functioning of the Bird MK 7 and MK 8 ventilators. As might have been anticipated in a pressure-cycled unit, tidal volume decreased, inspiratory time decreased and expiratory time was prolonged, often to the point of nonfunctioning of the ventilator. Similarly, Venturi flow ceased. B. J. Green, noting the desirability of humidifying gases in anesthesia circuits, observed the effects of humidification on concentrations of halothane and methoxyflurane delivered from standard vaporizers. Unfortunately, the humidifier employed was the ether bottle of a Boyle's machine, not a reliable device, and results of the experiments were equivocal. In an effort to study muscular hyperactivity occurring after general anesthesia,

M. G. Soliman, by means of visual observation, characterized movements as either hypertonicity or shivering. A number of physiologic variables were measured, and it turned out that hyperactivity was common after all anesthetics, with an incidence of 85 to 90 per cent; less after nitrous oxide and *d*-tubocurarine, all at a time when the patient was beginning to awaken. When response to verbal stimuli was adequate, hypertonicity disappeared. Shivering was related to heat loss. H. Samulski, awarded Second Prize, presented a nice study of the persistence of halothane vapor in several types of anesthetic breathing systems. The greater the surface area exposed, including canister and conduits, the longer the persistence of trace amounts of anesthetic. Every patient, then, is exposed to trace amounts of halothane, at least initially, unless the system is completely changed for each anesthetic given. Awarded Third Prize, C. Margaria tested the response in volunteers of elastic loads imposed during epidural anesthesia to the fourth thoracic dermatome. Apparently, mechanical properties of the thorax are not affected by motor block, the gamma system seemingly uninvolved. Finally, W. A. Tweed measured the cardiovascular effects of phenylethylamine given to patients with minimal or no demonstrable cardiovascular disease, during the course of cardiac catheterization. In the presence of several complicating factors, including prior injection of radiodiagnostic contrast medium, cardiac index rose, stroke volume index was unchanged, and pulse rate and blood pressure were elevated. Changes in peripheral vascular resistance varied markedly. The judges for this competition were the fourteen chairmen, University Departments of Anaesthesia, Canadian Universities.

On Wednesday, L. D. Vandam of Boston delivered a lecture on Drug Interactions in Anaesthetic Practice. In the afternoon, papers on the Hyperbaric Treatment of Cerebral Air Embolism (R. K. Claverley), Therapeutic Lung Lavage for Alveolar Proteinosis (G. A. Benzere), and Anaesthesia for Simultaneous Bilateral Nephrectomy (L. C. Jenkins) were presented. E. M. Kavan of Los Angeles presented preliminary data on the effects of volatile anesthetics on EEG activity recorded in

limbic and sensory systems. There was little doubt of the seizure patterns produced by *Ethrane* in these cats with chronically-implanted electrodes.

On Thursday, July 1, following a presentation on General Anaesthesia for Pacemaker Implantation (A. McClish), J. Couture presented data on airway closure and A-a oxygen gradients in two groups of individuals distinguished one from the other by obesity but approximately the same in age ranges and smoking habits. Measurements made in sitting and supine positions produced the best correlation when expiratory reserve volumes minus closing volumes expressed as percentages of vital capacity were plotted against A-a gradients. Here, the adverse effects of obesity were clearly demonstrated. H. I. A. Nisbet assessed cardiorespiratory reserves in the dog anesthetized with halothane, methoxyflurane or trichloroethylene at multiples of MAC, then submitted to hypoxia. Results were given in terms of available oxygen transport (cardiac output times oxygen content), but venous oxygen content was not measured and no effort was made to assess changes in hemoglobin affinity for oxygen. In general, despite elevations in cardiac output and pulse, the transport system failed below a  $P_{O_2}$  of 25 torr. To study the neurologic effects of phenacyclidine, L. Authier attempted to distinguish between extrapyramidal and cataleptic components, theorizing that atropine or procyclidine might make this distinction possible. With the aid of a rabbit head-lift assay, differences between the effects of atropine and procyclidine were detected, but they were not enough to permit drawing conclusions. Later that day, presentations on Ketamine Anaesthesia for Cardiac Catheterization in Children and Infants (A. McClish's group), Routine Computer Surveillance of Physiologic Changes in Patients under Intensive Care (L. Fournier), and Mechanical Ventilation during Laparoscopy (P.-R. Tremblay) were made.

In the presentations on the final day, L. Fournier measured the effects on production of methemoglobinemia of alpha-prolanest, a preparation of prilocaine in polyvinylpyrrolidone with a reputed prolonged action. Used for peridural and caudal anesthesia in 30 patients in a dosage of 900 mg and compared

with prilocaine in the same amounts, the preparation produced the same pattern of formation of methemoglobin. S. Stubbs gave methoxyflurane to dogs in the range of 1 MAC for five hours under carefully controlled conditions. In contrast to halothane, which produced little change, methoxyflurane in ten dogs studied over a six-day period led to increased urinary output, progressive weight loss, and a significant decrease in urinary osmolality, peak effects reached in 24-48 hours. There were no changes in glomerular filtration or renal blood flow, while both light and electronmicroscopy failed to reveal a tubular lesion. In renal cortical slices from methoxyflurane-treated animals, uptake of PAH was diminished, suggesting tubular dysfunction. Last, M. Minuck found, in a moderately well-controlled study of postoperative pain, that methotrimeprazine, 10 mg, produced relief approximately the equivalent of 75 mg meperidine, with greater hypotension and less emesis.

There was little doubt about the educational value of this meeting, fostered by the intimate exchange of ideas that comes from having a congenial, relatively small Anaesthesia Society such as exists in Canada. The work presented covered adequately subjects of current concern, further clarified by assigned discussion and audience participation. All this fitted well into the context of the admirable traditions of Canadian Anaesthesia, made all the more enjoyable by the superb hospitality of our hosts in Quebec.

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#### Conference of Adverse Reaction Reporting Systems

An international Conference of Adverse Reaction Reporting Systems was held in Washington, D. C., October 22-25, 1970, sponsored by the National Research Council Committee on Clinical Pharmacology. It brought together world authorities on adverse drug reaction reporting systems and epidemiology to review existing detection systems.

Dr. Derrick Dunlop (the keynote speaker) pointed out that during the last 30 years ill health caused by drugs has become a new factor of unknown dimensions in the etiology of disease. He further indicated that international linkage of the national drug monitoring systems would be beneficial, in that evidence of adverse reactions might be obtained earlier; the body of information available would be greater; and any country in which use of a particular drug is limited could gain information from more extensive experience elsewhere.

The first session dealt with spontaneous reporting systems. Dr. D. J. Finney stressed that such monitoring of adverse reactions to drugs should be one of the mandatory phases in the development and management of drug therapy. In this regard, Dr. Arthur Ruskin noted that the Center for Drug Information was established in July 1970 as a reorganization of the Bureau of Drugs in order to investigate the epidemiologic problems in the development of new and already marketed drugs.

Dr. W. H. W. Inman cautioned that many years' experience has shown that neither laboratory testing in animals nor human clinical trials is a dependable means of predicting the nature or incidence of adverse reactions. Despite its many defects, in particular under-reporting, the current spontaneous system of reporting suspected adverse reactions has brought to light many previously unrecognized hazards.

The second reporting system examined was intensive drug surveillance in which a defined population subjected to drugs is continuously monitored. Intensive drug surveillance programs are currently being used for "hypothesis generation" and "hypothesis testing." Dr. Hershel Jick expressed an urgent need for effective intensive drug surveillance systems which, though very costly, detect major serious unanticipated adverse drug reactions sooner. In order to follow all classes of drugs,

both inpatient and outpatient surveillance is necessary.

In addition to spontaneous reporting and intensive surveillance, there are the prospective and retrospective approaches to the study of adverse reactions. The latter two approaches were used by Drs. John Bunker, Daniel Seigel, and U. C. Dubach, who reported their successful studies of toxic effects of halothane, oral contraceptives and phenacetin, respectively.

Various factors which should be taken into account in all surveillance systems were discussed by Drs. Bert La Du, John Oates and Bernard Levine. These investigators suggested that the use of pharmacogenetic markers and an understanding of the species variation in uptake and distribution were important. Dr. John Oates noted that failure of drug response may be an adverse effect.

Next, the role of the WHO in developing spontaneous reporting and extensive monitoring systems was discussed by Dr. B. W. Royall. Ten countries have established national drug monitoring centers which report to the WHO headquarters in Virginia. WHO's international data-linkage problems were discussed by Dr. Natalie Hurwitz. Dr. David Rall then noted the "vexing problems inherent in the dissemination of information to the public of an unproved adverse reaction."

Drs. James Long and John Adriani noted that the information already available on drug hazards and toxicity is so voluminous and scattered that it almost defies intelligent organization and presentation. The Drug Research Board, in collaboration with other national health organizations, is, however, attempting to develop a prototype system along with prototype publications for the dissemination of drug adverse reaction information on a national scale.

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