Ontario, Canada. Clinical observation has suggested the tolerance to cerebral ischemia to be approximately three minutes. In the operating room it has been suggested that patients are more tolerant of cerebral ischemia under general anesthesia. It has been shown experimentally that halothane can increase this tolerance but the methods used require extensive surgery.

The advantage of the following method, modified from a technique used in Germany, is that no surgical procedure is involved. Cerebral ischemia can be produced in the rabbit by inflating a tourniquet around the neck. Apart from observation of the electroencephalograph we have confirmed this with radioactive isotopic studies. *Method:* After induction with a halothane-oxygen mixture in a plastic box, rabbits were intubated under direct vision and succinylcholine paralysis. For a period of 45 minutes the animals were maintained on the selected anesthetic mixture, were paralyzed and ventilated with a small animal respirator. Electroencephalogram and electrocardiogram electrodes were positioned and the femoral artery cannulated. Blood pressure was monitored throughout. Arterial blood samples were taken at selected intervals for blood gas and *p*H determinations. At the end of this period a cuff was placed around the animal's neck and instantaneously inflated to 600 mm. of mercury pressure. The EEG potentials disappeared within thirty seconds and an isoelectric line was maintained throughout the period of occlusion. One minute before the release of the cuff the anesthetic agents were discontinued and the rabbits ventilated with oxygen for twenty minutes and then with room air. Artificial ventilation was discontinued and the endotracheal tube removed on the return of adequate respiratory function. Animals alive after 24 hours were considered as survivors. *Results:* Forty-seven rabbits were subjected to three minutes of cerebral ischemia. Twenty eight were anesthetized with nitrous oxide and oxygen (3:1) and 10 survived; 19 were anesthetized with nitrous oxide–oxygen and halothane 1.5 per cent and 18 survived. Seventeen rabbits, in two similar groups, were subjected to six minutes of cerebral ischemia. Without halothane one out of 11 survived, while all 6 rabbits anesthetized with 1.5 per cent halothane recovered completely. Three groups of 6 rabbits each underwent nine minutes of ischemia; halothane 1.5 per cent with nitrous oxide and oxygen gave a survival of 2 animals out of 6, halothane 1.5 per cent with oxygen only, a survival of 4 out of 6; and halothane 3 per cent with nitrous oxide and oxygen, a survival of 3 out of 6. No significant differences between the survivors and non-survivors was found in relation to sex, weight, temperature (rectal), *p*H and P_{CO_2}. *Conclusions:* The addition of halothane to a 3:1 nitrous oxide-oxygen mixture markedly increased the tolerance of the rabbit brain to ischemia at normothermia. Nitrous oxide possibly could have reduced this tolerance. The blood pressure at the time of release of the cuff was not, *per se,* a critical factor in survival. Neither in the survivors nor in the animals anesthetized with halothane was there any prolongation of the EEG potentials after vascular occlusion, indicating a different cortical response than that of hypothermia. Oxygen consumption measurements were not made in these experiments. (Dr. Cox was a fellow of the Medical Research Council of Canada, and the work was supported by a grant from the Council.)

Kinetics of Distribution of C^{14}-Dimethyl-d-Tubocurarine. GIANFRANCO DAL SANTO, M.D., *Professor and Chairman Department of Anesthesiology, Wayne State University, School of Medicine, Detroit, Michigan.* Several aspects pertinent to the distribution of curarine in the organism remain to be fully understood. Using the radioisotopic trace technique, the turnover of C^{14}-dimethyl-*d*-tubocurarine in plasma, its urinary elimination, metabolism, passage into the cerebrospinal fluid (CSF) and transport by plasma protein were studied. (Parallel studies with C^{14}-succinylcholine are under way.) *Method:* A trace of C^{14}-labeled dimethyl-*d*-tubocurarine was administered intravenously to 26 control dogs anesthetized with pentobarbital (20 mg./kg.) and to 26 dogs under hypoxia, hypercapnia, hemorrhagic shock, arterial hypotension and hypothermia. C^{14}-labeled-*d*-tubocurarine was determined with a liquid scintillation counter. ECG, EEG, arterial P_{O_2}, P_{CO_2} and *p*H were monitored. *Results and Conclusions:* In *control animals* a

fraction (0.8 per cent) of the intravenous trace dose of labeled *d*-tubocurarine remained in the circulatory system 15 hours subsequent to the administration. Eighty-five per cent of the drug was eliminated in the urine during a 15-hour period. Fifteen hours following the administration, the extravascular space still contained 14 per cent of the administered C^{14}-dimethyl-*d*-tubocurarine. The possibility that this fraction of the drug remained attached to sites from which it might be liberated was considered. Trace doses administered to previously fully curarized dogs were distributed and eliminated according to a pattern similar to that of noncurarized animals. Radiochromatographic scannings of plasma, urine and CSF suggested that the molecule of C^{14}-dimethyl-*d*-tubocurarine might remain unchanged in the body of the dog. Seventy per cent of a trace dose of C^{14}-dimethyl-*d*-tubocurarine was found to bind to plasma *in vitro*. This was found by the ultrafiltration technique. A very small amount, of the order of 10^{-5} of the amount injected of labeled curarine, crossed the blood-brain barrier, and appeared in the cerebrospinal fluid. However, when injected into the cisterna magna, the labeled drug was detected in a much higher concentration in plasma and urine. An increased passage of the drug from plasma into the cerebrospinal fluid took place during long lasting *shock, hypoxia, hypercapnia* and *hypothermia*. However, in these conditions (similar to what was found in the control animals) the degree of passage was still very limited. This suggests that the possibility of a direct central action of curarine is remote. The distribution and elimination of tagged dimethyl-*d*-tubocurarine during the mentioned abnormal conditions was significantly altered. This was characterized by a remarkably similar pattern: (1) slow disappearance from plasma, (2) impaired urinary elimination, (3) higher and persistent accumulation in the extravascular compartment, and (4) an increased passage into the cerebrospinal fluid. As the same pattern was duplicated in dogs in which the renal vessels were bilaterally ligated, we were inclined to suspect that the marked impairment of the renal elimination was the common denominator responsible for that picture. However, such an explanation is without doubt oversimplified and obviously it disregards many other concomitant factors.

Intravenous Regional Anesthesia with Chloroprocaine. DONALD J. DICKLER, M.D., PAUL L. FRIEDMAN, M.D., and IRVIN C. SUSMAN, M.D., *The Jewish Hospital of St. Louis, St. Louis.* Intravenous injection of local anesthetic, below a tourniquet, for regional anesthesia of extremities, has been reported sporadically since Bier (Arch. Klin. Chir. *86:* 1007, 1908) described the technique in 1908. Widespread acceptance failed due to inconsistent results with safe doses of agents previously available. Holmes' report (Lancet *1:* 245, 1963) stimulated renewed interest. Of eight articles in the English literature in 1964, 7 reported the use of lidocaine, and one of Citanest. Chloroprocaine's low toxicity, rapid action and tissue penetration suggested its study with this technique (Foldes, F. F. & McNall, P. G.: ANESTHESIOLOGY *13:* 287, 1952). *Method:* In our present technique only hospital patients were premedicated, out-patients were not. A vein was cannulated with a plastic needle. One or two tourniquets were applied to the arm or thigh proximal to the cannulation. The extremity was drained of blood by elevation or exsanguinated with an Esmarch's bandage. The tourniquet was properly inflated and 30 ml. 2 per cent chloroprocaine was injected for the upper extremity or 60 ml. for the lower extremity. Dosage varied somewhat with the patient's size. Further injections were made if needed. Total anesthesia and motor paralysis developed within 6 minutes in the arm and 15 minutes in the leg. After the tourniquet was released anesthesia lasted 10–15 minutes. Reactions were minimal to absent if the tourniquet was released intermittently, several times, for 5 seconds. Anesthesia was satisfactory in all cases and was terminated and re-started if desired without cumulative effect of medication. *Results:* Sixty-four cases, 48 upper extremity and 16 lower extremity, are reported. The procedures lasted from 3 minutes to 2¼ hours. The patients' ages ranged from 5 to 70 years. Surgical procedures included ganglion excision, Achilles tendon repair, patella fracture wiring, and hand reconstruction. The main problem was ischemic tourniquet discomfort in longer cases. This was usually