

meter, it is now possible to measure blood flow continuously and simultaneously in the cerebral, coronary, renal and hepatic circulation of dogs. Data revealed that each organ possesses its own characteristic response to shock and vasopressor drugs, that the circulation of the intestine as well as that of the kidney plays a vital role in circulatory homeostasis during acute shock and that the use of vasopressor drugs in shock increased the circulation to the brain and the heart while, at the same time, the blood flow to the intestine and kidney was decreased. The concepts of "mesenteric vascular insufficiency" and conclusions of clinical significance are discussed in detail. (*Corday, E., and Williams, J. H., Jr.: Effect of Shock and of Vasopressor Drugs on Regional Circulation of Brain, Heart, Kidney and Liver, Amer. J. Med. 29: 228 (Aug.) 1960.*)

**ATROPINE** The effect of 1.5 mg. of atropine sulfate intramuscularly upon blood pressure, pulse rate, respiration rate, pupil size, power of accommodation and perception was compared with that of the same dose of atropine sulfate given in combination with 5 mg. of metaraminol bitartrate (Aramine). Addition of metaraminol bitartrate resulted in a significantly higher mean systolic blood pressure, a larger pulse pressure and a slower heart rate during the hour following administration. Pupillary dilatation was also less. Visual perception was not significantly influenced. (*Taylor, W., and others: Use of Metaraminol Bitartrate to Reduce Side Effects of Atropine, Canad. M. A. J. 82: 1147 (June 4) 1960.*)

**ATROPINE METABOLISM** Two men were injected with a single 2-mg. dose of isotope labelled atropine. Between 85 and 88 per cent of the radioactivity was excreted in the urine within the first 24 hours. No activity was found in expired air, and only a trace could be extracted from feces. About half the dose appeared in the urine as intact atropine. More than a third was excreted as unknown metabolites, which appeared to be esters of tropic acid; less than 2 per cent appeared as free tropic acid. Neither hydroxylation of the aromatic ring nor glucuronide

formation could be demonstrated. In man the ester bond is largely preserved and most if not all modifications in the molecule occurs in the tropine moiety. (*Gosselin, R. E., Gabourel, J. D., and Willis, J. H.: Fate of Atropine in Man, Clin. Pharmacol. Ther. 1: 597 (Sept.-Oct.) 1960.*)

### NEUROMUSCULAR TRANSMISSION

There are three types of neuromuscular block: depolarization, non-depolarization and dual. Recovery from dual blocks is slow unless aided by anticholinesterase therapy. When there is apnea at the end of an operation, the diagnosis of the cause can be made by using a peripheral nerve stimulator. Muscular paralysis can be differentiated from depression of the respiratory center. Observation of the hand muscles allows distinction between a depolarization and a dual type of neuromuscular block. (*Churchill-Davidson, H. C.: Review of Neuro-Muscular Transmission, Der Anaesthetist 9: 253 (Aug.) 1960.*)

**MUSCLE RELAXANT PAIN** The incidence of muscle pain and stiffness in 100 patients given suxethonium and suxamethonium was found to be the same for both drugs, namely, 25 per cent complained of severe stiffness or pain and an additional 45 per cent of mild stiffness. Stiffness was mostly in the neck, abdomen and chest. Onset of symptoms is from 12-24 hours postoperatively. Duration of symptoms is 4-5 days on the average. The incidence and severity of symptoms appears to vary with the dose of relaxant used. (*Parbrook, G. D., and Pierce, G. F. M.: Comparison of Post-Operative Pain and Stiffness After Use of Suxamethonium and Suxethonium Compounds, Brit. Med. J. 2: 579 (Aug. 20) 1960.*)

**TUBOCURARE** A quantitative study of the antagonism between acetylcholine and tubocurarine was made by taking depolarization of the end-plate skeletal muscle as a measure of drug-action. The results are consistent with the hypothesis that these substances compete on a one to one basis for receptors at the end-plate. Micro-electrodes were employed to show that individual end-plates do not vary greatly in their sensitivity

to tubocurarine as measured by an "affinity constant." The constant was little affected by changes in temperature or by a four-fold increase in the potassium concentration. Values determined in the presence of calcium and magnesium were smaller by about 30 and 40 per cent respectively. (*Jenkinson, D. H.: Antagonism Between Tubocurarine and Substances Which Depolarize the Motor End-Plate, J. Physiol. 152: 309 (July) 1960.*)

**SUCCINYLCHOLINE APNEA** If the Hering-Breuer reflex is active, intermittent positive pressure breathing (5 to 25 centimeters of water) causes longer apnea following administration of succinylcholine than positive-negative pressure breathing. In deep ether anesthesia, when the Hering-Breuer reflex is depressed, no difference is seen. (*Koerner, M.: Investigations Concerning Duration of Apnea After Succinylcholine with Intermittent Positive Pressure and Positive-Negative Pressure with Consideration of Hering-Breuer Reflexes, Der Anaesthetist 9: 225 (July) 1960.*)

**NEOMYCIN APNEA** A 47 year old man was anesthetized with thiopental, nitrous oxide, ether and a minimal amount of succinylcholine. The peritoneal cavity was irrigated with 500 cc. of 1 per cent neomycin. Fifteen minutes later the patient became apneic; there was no circulatory disturbance. One hour later 1 mg. of neostigmine was given intravenously in divided doses, without effect. A mechanical respirator was used for 14 hours. Respiratory movements began in the fifteenth hour, and improved for 6 hours. The patient then aspirated coffee-ground vomitus and died. The lessons to be learned: When intraperitoneal neomycin is needed, place catheters in the abdomen, and delay giving the drug until the patient recovers from anesthesia; use 0.5 mg. every 6 hours if renal function is adequate. Pretreatment with neostigmine may be valuable. (*Kownacki, V. P., and Serlin, O.: Intraperitoneal Neomycin as a Cause of Apnea, A. M. A. Arch. Surg. 81: 838 (Nov.) 1960.*) (*Abstractor's Note: A more safe alternative would be to use an antibiotic, such as bacitracin, which does not have potent neuromuscular blocking properties.*)

**INTRAPERITONEAL NEOMYCIN** The Bennett ventilation meter was used to measure respiration of patients during and after laparotomy. Two grams of neomycin were placed in the peritoneal cavities of adults. One half of these patients developed respiratory depression in 1 to 20 minutes. One third of the patients had severe depression or apnea, and required respiratory assistance for as long as 10 hours. The mode of action of neomycin is thought to be neuromuscular blockade. Various anesthetic and relaxant drugs were used; ether is believed to contribute definitely to the neomycin depression. It is pointed out that a similar effect may be caused by streptomycin, dihydrostreptomycin, polymyxin B, and kanamycin. (*Mann, L. S., and Levin, M. J.: Respiratory Depression with Intraperitoneal Neomycin, A. M. A. Arch. Surg. 81: 690 (Nov.) 1960.*)

**NARCOTIC ANTAGONISTS** Morphine injected into rabbits, dogs, and man produces an electroencephalographic pattern resembling that observed in sleep or light anesthesia. Nalorphine, injected alone, produces the same effect, with a smaller dose, but only after a delay of fifteen to thirty minutes. If nalorphine is injected at the peak of action of morphine, an immediate waking reaction occurs. What is the mechanism of action of these two drugs? Does nalorphine change into morphine in the body? Electroencephalographic studies were made in adult male albino rabbits, with the electrodes embedded in the skull. Injection of drugs was intravenously. From these studies it was determined that morphine and nalorphine when administered separately produce changes in the EEG similar to those produced by barbiturates. No data could be obtained to suggest that nalorphine was slowly transformed in the body to morphine. The mechanism of interaction between morphine and nalorphine is conceived to be an extremely complex one. (*Goldstein, L., and Aldunate, J.: Quantitative Electroencephalographic Studies on Effects of Morphine and Nalorphine on Rabbit Brain, J. Pharmacol. Exp. Ther. 130: 204 (Oct.) 1960.*)

**CEREBROSPINAL BARRIER** The importance of lipid-solubility in the dissociation