Abstracts

Work in Progress

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The following are abstracts of papers presented at the WORK IN PROGRESS program of the Annual Meeting of The American Society of Anesthesiologists, Chicago, November 4 and 5, 1963.

The Contractile and Cell Membrane Effects of Halothane. C. H. AWALT, M.D., and E. L. FREDERICKSON, M.D., *University of Kansas Medical Center, Kansas City, Kansas.* While local anesthetics are thought to act by stabilizing the cell membrane, thus preventing depolarization and the formation of a propagated impulse, the site of action of general anesthetics is not known. One possibility would be that they also interfere in some way with the formation of cellular action potential. The microelectrode technique of transmembrane recording, introduced by Ling and Gerard (J. Cell Comp. Physiol. *34:* 383, 1949), makes possible the observation of instantaneous electrical changes across the membrane of individual cells. *Method:* In the present study, the effect of halothane was observed using rabbit atria as the excitable tissue. Contraction of the entire atrial preparation and transmembrane action potentials from individual cells were simultaneously recorded in a manner essentially as described by Levy, Ichiyanagi, and Frederickson (ANESTHESIOLOGY *24*: 185). A comparison was made between those recordings made under stable control conditions and those made with the preparation exposed to approximately 1.0 per cent and 1.5 per cent halothane by means of a Fluotec vaporizer connected in series with the oxygenation line. *Results:* Tabulation and analysis of measurements made on transmembrane action potential amplitude and duration did not demonstrate any significant difference between records made under control conditions and those made when halothane was administered. On the other hand, contraction was notably depressed by the 1.0 per cent concentration and almost completely abolished at the 1.5 per cent level. *Conclusions:* From the data it is inferred that the effects of halothane on excitable tissue are not the result of primary alterations at the level of the cell membrane. Further, since marked changes are produced in contraction which is an intracellular activity, while cyclic electrical events at the surface membrane continue without apparent alteration, it would appear that halothane penetrates the membrane and exerts its depressant effect on contraction at some point within the cell. These conclusions are substantially in agreement with those made by Levy *et al.* (*loc. cit.*) as a result of their studies on cyclopropane, and one is tempted to speculate that similar conditions would prevail with other gaseous hydrocarbon anesthetic agents. (This work was done during the tenure of a postdoctoral fellowship granted to Dr. Awalt by the National Heart Institute. Dr. Awalt is now at the University of Texas Medical Branch, Galveston, Texas.)

Effect of Mephentermine Upon Venous Circulation During Spinal Anesthesia. KALMAN J. BERENYI, M.D., SHIRO SHIMOSATO, M.D., and BENJAMIN E. ETSTEN, M.D., *Department of Anesthesia, Tufts University School of Medicine and Pratt Clinic, New England Center Hospital, Boston, Massachusetts.* Peripheral blood flow and vascular distensibility, by means of venous occlusion plethysmography, using the temperature compensated mercury-in-rubber strain gauge, as described by Whitney (J. Physiol. vol. 121, p. 1), were simultaneously obtained in the upper and lower extremities of human volunteers and surgical patients prior to operation. Eighty-three simultaneous determinations of forearm blood flow were obtained by means of water plethysmography in one arm and the mercury-in-rubber strain gauge in the other arm in 6 volunteer subjects. There was a

positive correlation coefficient of +0.9 between the two methods. Eight non-medicated subjects were studied before and after intravenous infusion of mephentermine, 5 of them with continuous spinal anesthesia (third to eighth thoracic levels) and 3 subjects without anesthesia. *Results:* In the normotensive unanesthetized subjects, the intravenous administration of mephentermine (0.1 per cent solution in 5 per cent dextrose, average dose: 24.4 mg.) caused an increase of forearm blood flow; 47 per cent in five minutes, 32 per cent in thirty minutes and 32 per cent in sixty minutes after infusion of the drug was completed. There was a concomitant increase in calf blood flow. Calculated forearm and calf vascular resistance decreased. Vascular distensibility (change of volume per unit of effective venous pressure) obtained from the initial linear portion of the volume pressure curve, decreased in each of the three non-anesthetized subjects. The maximal change in forearm distensibility was 39 per cent and 14.6 per cent in calf distensibility. Spinal anesthesia resulted in 160 per cent increase of calf blood flow, 70 per cent decrease of calf vascular resistance, slight increase in calf venous distensibility. There was 18 per cent decrease in forearm blood flow, 20 per cent increase in forearm vascular resistance and there was no appreciable change in forearm venous distensibility. There was a further decrease of blood flow with an increase in vascular resistance in the forearm segment when mephentermine was administered during spinal anesthesia. Calf blood flow, however, increased significantly in the presence of decreased vascular resistance. *Conclusion:* In view of these findings, it seems reasonable that mephentermine exerts an action on the capacitance vessels, probably mediated through the autonomic nervous system. (Supported by Research Grant HE-06069 from U.S.P.H.S.)

Distribution and Site of Action of Extradural Analgesic Drugs Using C^{14} Labelled Lidocaine and Mepivicaine in Dogs. P. R. Bromage, M.B., F.F.A.R.C.S., D.A., and M. F. Burfoot, M.A., B.M., D.A., *Royal Victoria Hospital, Montreal, Canada.* A pilot study (Bromage, P. R., Joyal, A. C., and Binney, J. C.: Science *140:* 392, 1963) revealed that the assay of radioactivity in the neuraxis and its coverings, following the injection of local analgesic drugs tagged with C^{14}, is accurately specific for unchanged drug. This work has been continued along lines indicated by trends in this study. *Method:* Mongrel dogs weighing between 15–30 kg. were anesthetized and the subarachnoid and extradural spaces were catheterized. Following injections of the drug, serial samples of cerebrospinal fluid were taken and the spinal cord and its coverings were dissected to yield samples of the extradural and intradural nerve roots, the dura and pia mater and the cord. *Results:* Preliminary results showed a high level of drug in both the extradural and intradural parts of the nerve roots with much smaller amounts in the dura. The level in the pia was also high and the cord contained significant amounts. We postulate that one route of entry into the neuraxis is the passage of drug out of the spinal foramina, by diffusion into the subperineural space and centripetal flow into the cord and cerebrospinal fluid. Cheng has shown (Thesis, McGill University, 1945) as have Brierly and Field (J. Neurol. Neurosurg. Psychiat. *12:* 89, 1949) that a free communication exists between the peripheral nerve and the neuraxis in the subperineural space. Shanthaveerappa and Bourne have described (J. Anat. [Lond.] *96:* 527, 1962) the continuation of the epithelial layer of the pia-arachnoid peripherally as a complete epithelial cell layer that surrounds each fasiculus and nerve fiber to its termination. In addition, they describe this layer as being rich in enzymes. We, therefore, sought evidence to establish whether or not these enzyme systems actively aided or hindered transport of drugs across the membrane. Solutions of dinitrophenol and sodium iodoacetate were injected into the extradural space one hour prior to the injection of the drug under test. The results are as yet indecisive, but in both cases markedly lower levels of drugs were found in both the cerebrospinal fluid and the tissues of the neuraxis and its coverings. Controversy still exists over the respective roles of the epineurineum and perineurium as diffusion barriers. We believe that confusion is due to the postulation of the perineural epithelium described by