

clamping the trachea. Brain, liver, kidney, blood, muscle and fat specimens were analyzed. The total body anesthetic concentration was determined in other animals by homogenizing the entire carcass in a sealed jar of known volume. In separate experiments animals were exposed to the same anesthetic concentration in test tubes. Tail blood samples were analyzed every 1-2 minutes using 1  $\mu$ l. of blood for analysis. The water-gas, blood-gas, and tissue-gas partition coefficients of each anesthetic in each species were determined by microtonometry. The percentage of organ weight to whole body weight of numerous animals was recorded. The measured tissue weight, anesthetic solubility and anesthetic concentration after various periods of exposure were utilized to calculate organ blood flow as well as the contribution of each tissue to the total anesthetic uptake. **Results:** The rates of uptake and tissue distribution of diethyl ether, fluroxene, halothane, chloroform and methoxyflurane were not significantly altered by exposure to equivalent anesthetic tension at 3 atmospheres. The initial rates of uptake of these agents (ml./minute/kg./%) in mice, rats and man were almost directly proportional to the metabolic rate of the species. The rate of elimination of ether and fluroxene following complete saturation of the animals were identical with the rate of uptake. When saturation was not complete, the rate of elimination was proportional to the fractional whole body saturation. **Summary:** The rates of uptake and distribution of inhalation anesthetics are not altered to any degree by exposure to equivalent anesthetic tensions under hyperbaric conditions.

**A Study of Dural Penetration of Local Analgesic Agents Following Peridural Injection and the Influence of Epinephrine.** P. C. LUND, M.D., and J. C. Cwik, M.D., *Conemaugh Valley Memorial Hospital, Johnstown, Pennsylvania.* It was postulated that the spinal fluid concentration curve which follows peridural administration of a local anesthetic agent is an index of its permeability. **Method:** The spinal fluid concentration of lidocaine, mepivacaine and prilocaine with and without epinephrine following the peridural administration of 300 mgs. of each of these agents in various combinations were deter-

mined by the gas chromatographic technique. **Results:** The results indicated a marked similarity in the spinal fluid concentration curves of lidocaine and prilocaine following simultaneous peridural administration. There was also a marked similarity in the spinal fluid concentration curves of lidocaine and mepivacaine following simultaneous peridural administration. A statistical analysis indicated that the addition of epinephrine did not significantly affect the maximum spinal fluid levels of the above agents. In a previous study, however, following the individual peridural administration of lidocaine, prilocaine and mepivacaine a considerable difference in respective spinal fluid concentration curves was found. **Discussion:** The mechanism of spread of local analgesic solution in the peridural space across the dura *in vivo* is a complicated physiochemical problem which is not well understood. The simultaneous peridural administration of two local anesthetic agents may equalize certain variables which influenced their respective spinal fluid concentrations, for example, the respective vasodilator properties of each analgesic agent will probably influence the caliber of the dural blood vessels and consequently also dural penetration. **Summary and Conclusions:** This study suggests that if all physiological factors are equal the dural penetration of lidocaine, propitocaine and mepivacaine are very similar and probably clinically insignificant. It is further suggested that the vasodilator properties of each of these agents affect their respective dural penetration. It also suggests that because of the considerable variation in spinal fluid concentrations of local anesthetic agent from patient to patient, at specific time intervals, a much larger series of cases is required to determine the significance of dural penetration or to determine whether or not dural penetration is an index of the respective permeability or diffusion characteristics of a local anesthetic agent.

**The Effects of Monoamine Oxidase Inhibitors on the Hypotensive Action of Meperidine and the Pressor Action of Nor-epinephrine.** SHIBLEY MARKEE, M.D., *Department of Anesthesiology, College of Physicians and Surgeons, Presbyterian Hospital, New York City.* Although marked hypotension has been reported in patients receiving

monoamine oxidase inhibitors, little is known of the duration of this phenomenon after monoamine oxidase inhibitor withdrawal, its treatments, or its mechanism of action. In the present experiment dose-response curves of the hypotensive action of intravenously administered meperidine were obtained in cats and dogs anesthetized with pentobarbital. *Methods and Results:* The animals received pargyline (Eutonyl) 20 mg./kg. daily for 1 to 2 months. Dose-response curves were repeated at weekly intervals during pargyline administration and for 4-5 weeks after pargyline was withdrawn. During pargyline administration the dose-response curves were shifted progressively to the left up to 10 fold; after pargyline withdrawal they showed a progressive return to control, reaching the initial values within 2-3 weeks. Control animals, not receiving the drug, showed no shift of the dose-response curve. Dose-response curves of the pressor effect of norepinephrine were also studied in anesthetized dogs before, during acute and chronic administration of pargyline 20 mg./kg., or tranlycypromine (Pamate) 4-10 mg./kg., and after withdrawal of these monoamine oxidase inhibitors. Acutely, the dose-response curves of the dogs receiving tranlycypromine were shifted to the left 2-5 fold. Chronically, the maximum shift to the left occurred with both drugs after 1 week of treatment, whereas after 3 weeks of treatment the dose-response curves had returned to control values. Dose-response curves of the pressor action of phenylephrine were found to be unchanged during acute and chronic monoamine oxidase inhibition. *Conclusion:* The data indicate that increased sensitivity to the hypotensive effect of meperidine, as measured by a shift to the left of the dose-response curve, does occur in the dog and cat, and persists beyond the duration of monoamine oxidase inactivation. It also appears that phenylephrine and norepinephrine can be used safely as vasopressors in the presence of chronic monoamine oxidase inhibition.

**The Effects of Halothane on Oxygen Consumption and Glucose Metabolism in Normal and Fatty Rat Livers.** RICHARD S. MATTEO, M.D., and GEORGE P. HOECH, JR., M.D., *Department of Anesthesiology and Neurologi-*

*cal Clinical Research Center, College of Physicians and Surgeons, Columbia University, New York City.* The biochemical effects of 2 and 4 per cent halothane on normal and fatty rat liver slices were studied in this experiment. *Methods:* Fatty livers were produced in male Sherman rats weighing 100-125 g. by a 72 hour feeding of a standard choline-deficient diet (Nutritional Biochemical Corp.). At the end of a 72 hour period, animals receiving the choline-deficient diet, together with animals receiving a normal diet, were sacrificed and slices prepared from the left lobes of their livers with a Stadie-Riggs tissue slicer. Liver slices from a third group of animals who had been fed a choline-deficient diet for 72 hours and then fasted an additional 12 hours were prepared in a similar manner. All slices were then halved, each half weighed and placed in Warburg vessels containing standard Krebs-Ringer solution with phosphate buffer and glucose (Umbreit: *Manometric Techniques*, 1964, p. 132). One of each paired slice was then gassed with humidified oxygen to serve as a control, the other half slice received humidified halothane in oxygen for 20 minutes. Oxygen consumption was then measured by standard Warburg manometric technique at 37° C. for one hour. After this period, all flasks were gassed for 20 minutes with humidified oxygen. Oxygen consumption of the liver slices was measured for another hour. At the end of the experiment, samples were taken from the incubation media for determination of glucose, lactate, pyruvate and pH. *Results:* The O<sub>2</sub> consumption of the normal liver slices exposed to only O<sub>2</sub> averaged 1,442 μl./g./hour, those exposed to 2 per cent halothane averaged 1,221 μl./g./hour, and those exposed to 4 per cent halothane averaged 922 μl./g./hour. The O<sub>2</sub> consumption of fatty liver slices exposed to only O<sub>2</sub> averaged 1,143 μl./g./hour. With 2 per cent halothane, the average O<sub>2</sub> consumption was 1,107 μl./g./hour, and with 4 per cent halothane 894 μl./g./hour. Liver slices from animals that had been fasted for 12 hours following a 72 hour preparation with a choline deficient diet had an O<sub>2</sub> consumption of 1,123 μl./g./hour in 100 per cent O<sub>2</sub>, 974 μl./g./hour in 2 per cent halothane, and 929 μl./g./hour in 4 per cent halothane. Four per cent