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curves were repeated at weekly intervals during pargyline administration and for 4–5 weeks after pargyline was withdrawn.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 tranylcypromine (Parnate) 4–10 mg./kg., and after withdrawal of these monoamine oxidase inhibitors. Acutely, the dose-response curves of the dogs receiving tranylcypromine 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 Neurological 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 *p*H. *Results:* The O_2 consumption of the normal liver slices exposed to only O_2 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_2 consumption of fatty liver slices exposed to only O_2 averaged 1,143 μl./g./hour. With 2 per cent halothane, the average O_2 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_2 consumption of 1,123 μl./g./hour in 100 per cent O_2, 974 μl./g./hour in 2 per cent halothane, and 929μl./g./hour in 4 per cent halothane. Four per cent

halothane significantly depressed the O_2 consumption of slices from all three groups of rats. Upon removal of the 4 per cent halothane, the normal liver slices increased their O_2 consumption to 1,402 μl./g./hour, closely approaching control values (1,523 μl./g./hour). In contrast, the fatty liver slices, with or without starvation, showed no recovery of O_2 consumption. Liver slices from animals with fatty livers that had been further stressed with 12 hours starvation were the only group whose O_2 consumption was markedly depressed by 2 per cent halothane. These slices, however, did increase their O_2 consumption to near control levels once the halothane was removed. Measurements of glucose, lactate and pyruvate released to the media by the slices indicate there are metabolic differences between liver slices from normal, fatty and starved animals. Halothane, of itself, does not appear to alter glucose release and lactate or pyruvate production in any of the liver slices. *Discussion:* Halothane in anesthetic concentration (2 per cent) depresses the O_2 consumption of liver slices only when the stress of starvation is added to fatty infiltration of the liver. This depression is reversed by removal of the anesthetic. The lack of recovery of both geroups of fatty livers from the effect of 4 per cent halothane could be due to either a direct toxic action of halothane on the liver or simple retention of halothane due to the approximately 300 per cent increase in fat content of the choline-deficient livers. (Supported by Grant GM-090 69-04 and NB 3359 for the National Institutes of Health, U.S.P.H.S.)

Respiratory Threshold in Hypothermia. LUCIEN E. MORRIS, M.D., S. A. ALLAN CARSON, M.D. and P. J. TOMLIN, M.D., *Anesthesia Research Laboratories, Providence Hospital, Seattle, Washington.* It has been accepted that hypothermia depresses respiration to the point of apnea when temperatures are lowered below 28° C. (Virtue, R. W.: Hypothermic Anesthesia. Thomas, 1951, p. 23). In contrast to this belief, we have observed relatively normal respiratory efforts in man, even at 20° C. or below, provided the Pa_{CO_2} is appropriately elevated in accord with the temperature change. Hyperventilation of a normothermic anesthetized man will ordinarily produce apnea by lowering the Pa_{CO_2} below 40 mm. of mercury provided there is not present at the same time hypoxia or response to surgical stimulus. This apneic threshold has been suggested as an index to the adequacy of ventilation during anesthesia (Morris, L. E.: Brit. J. Anaesth. *35:* 1, 35, 1963). More recently a part of this concept has been related to the management of anesthetized patients during hypothermia and cardiopulmonary bypass surgery. *Method:* In order to obtain a preliminary determination of the respiratory threshold to carbon dioxide and hypothermia, past anesthetic records of patients subjected to hypothermia and open-heart surgery were examined and compared with blood gas and *p*H data which had been obtained. Anesthesia used was nitrous oxide-oxygen-halothane, maintained by addition of halothane to the pump oxygenator during the bypass period. Carbon dioxide was added to the pump-oxygenator gases in increasing concentrations as the body temperature was progressively lowered (Carson, S. A. A., and Morris, L. E.: ANESTHESIOLOGY *23:* 5, 618, 1962). *Results:* There were 44 patients in which clinical observation of ventilation or its absence was correlated with an arterial blood gas analysis. In those patients making good spontaneous respiratory effort the corrected *p*H was less than $7.4 - [0.0147(37-T)]$. Apnea was observed when P_{CO_2} was low enough to raise the *p*H 0.01 units or more above this line. The P_{CO_2} values obtained when patients were making spontaneous respiratory effort (in the absence of metabolic acidosis) ranged about or above $Pa_{CO_2} = 10^{(2.460 - 0.0232T)}$. *Summary:* Thus using the respiratory center activity as a measure of normalcy it can be postulated that in acutely hypothermic man the optimum *p*H and P_{CO_2} progressively change with temperature and that *p*H of 7.40 and P_{CO_2} of 40 mm. of mercury are optimum only at normothermia.

Metabolic Effects of Beta-Adrenergic Blockade with Propranolol. R. E. MORRIS, P. R. ROBINSON, T. D. GRAFF and O. KANTT, *The Johns Hopkins University School of Medicine, Baltimore.* Beta-adrenergic blockade with propranolol is effective in preventing