concentration (flow constant). The apparatus (disc oxygenator, roller pump, and heat exchanger) was primed with fresh heparinized blood. Bypass of heart and lungs was accomplished by right atrial and femoral artery cannulations. Temperatures (esophageal and blood), pressures (right atrial and arterial), and blood gas levels were followed. Halothane in desired concentrations was added to the gas mixture introduced into the oxygenator. O_2 uptake was determined by the Fick principle (flow $\times$ $(A\text{-}V)_{O_2}$). *Results:* At fixed halothane concentrations of either 0.8 per cent of 3.2 per cent, O_2 uptake was unchanged as flow was reduced from 3.5 to 2.0 liters/minute/m.^{2} At flow rates below 2.0 liters/minute/m.^{2}, O_2 uptake fell as flow was reduced. At fixed flow rates (2.3 to 3.0 liters/minute/m.^{2}), O_2 uptake fell successively as halothane was increased from 0.8 to 3.2 per cent and from 3.2 to 10.0 per cent. At 10 per cent halothane, O_2 uptake was approximately 60 per cent of that observed at 0.8 per cent and an increased concentration of fixed acids was present in arterial blood. The administration of Arfonad (0.5 to 1.5 g.) in this circumstance (10 per cent halothane) was associated with a prompt increase in O_2 uptake (3 dogs). After a variable degree of "overshooting," O_2 uptake (10 per cent halothane plus Arfonad) returned to and stabilized at the level previously observed at 0.8 per cent. The administration of epinephrine (1–5 mg.) at this point was associated with a return toward the lower levels of 0_2 uptake previously observed at 10 per cent halothane without Arfonad. These observations suggests several possibilities. Clearly, the changes in O_2 uptake in perfused animals at 10 per cent halothane were not necessarily appropriate indices of changes in *tissue metabolic rate.* Accordingly, a reduction in O_2 uptake is not necessarily evidence of depression of metabolism. The explanation for these incongruities would necessarily include altered distribution of blood flow through the true capillaries—a microcirculatory phenomenon. *Conclusion:* A direct metabolic depressant effect of halothane was not demonstrated in the present studies.

Rate of Appearance and Disappearance of Meperidine in Fetal Blood After Administration of Narcotic to the Mother. Sol M. Shnider, M.D., E. Leong Way, Ph.D., and Merrilyn J. Lord, B.A., *Departments of Anesthesia, Obstetrics and Gynecology, and Pharmacology, University of California Medical Center, San Francisco, California.* Although it has long been established that meperidine crosses the placental barrier, the time of appearance of the drug and rate of increase of blood level in the fetus has not been determined. This information is pertinent in view of recent findings that there is an apparent delay in the clinical depression found in the newborn following administration of the narcotic to the mother (Shnider, S. M., and Moya, F.: Amer. J. Obstet. Gynec. *89:* 1009, 1964). *Method:* A group of 30 healthy full-term pregnant women received single intravenous injections of meperidine, 50 mg., at various intervals from 30 seconds to 4 hours before delivery. At delivery, samples of blood were drawn simultaneously from a maternal artery and the umbilical vein and artery. The latter vessels were considered representative of fetal blood. The concentration of meperidine in these samples was determined according to the indicator-dye (methyl orange) and spectrophotometric method of Burns, as modified by Way. The clinical condition of the newborn at birth, as determined by the Apgar score, was correlated with the fetal plasma levels of meperidine. *Results:* For the first few minutes after administration of meperidine the maternal plasma levels declined rapidly from an average of 2.0 μg./ml. at 2 minutes to 0.46 μg./ml. at 6 minutes. After this time the decline became slower, and by 30 minutes the maternal plasma levels were beyond the limits of sensitivity of the method (less than 0.20 μg./ml.). The placenta appeared to offer little barrier to the transmission of meperidine. The narcotic was present in the umbilical vein 90 seconds after administration to the mother in levels approaching 70 per cent of the maternal values. This ratio of umbilical venous to maternal arterial concentration was maintained for approximately 6 to 10 minutes. Following this time there was a decrease in the difference in concentration between maternal and umbilical venous blood. The umbilical vein had considerably higher concentrations than the umbilical ar-

tery for the first 3 minutes following administration of the narcotic. Thereafter the mean plasma levels of both umbilical vein and artery were essentially the same. There was no correlation between Apgar scores and levels of meperidine in fetal plasma: all infants in this series were vigorous, with scores of 8, 9, or 10, irrespective of narcotic concentration. *Conclusions:* Meperidine reaches the fetal circulation in concentrations approaching those in the maternal circulation within 90 seconds after intravenous administration of 50 mg. to the mother. Equilibrium between maternal and fetal blood occurs at approximately 6 minutes. No meperidine is assayable in either maternal or fetal blood after 30 minutes. There was no clinical depression with 50-mg. doses of any of the infants at birth.

Hemodynamic Effects of Metabolic Acidosis in Dogs. N. Ty Smith, M.D., *Department of Anesthesia, Stanford University, School of Medicine, Stanford, California,* and Aldo N. Corbascio, M.D., *Department of Pharmacology, College of Physicians and Surgeons, School of Dentistry, University of the Pacific, San Francisco.* Some of the cardiovascular problems observed during shock, massive transfusions, and the post-cardiac arrest period have been attributed to the myocardial depressant effects of the attendant metabolic acidosis. To evaluate the extent and importance of decreased *p*H, the cardiovascular effects of metabolic acidosis were studied in 13 dogs in which anesthesia was induced with thiopental and maintained with nitrous oxide-oxygen-succinylcholine. Arterial *p*H was lowered in five steps from 7.40–7.42 to 6.90–7.05 with graded infusions of 0.3 *M* lactic acid. Thirteen parameters, chosen to reflect various cardiovascular functions, were recorded. Simultaneously, arterial *p*H was measured. Regression equations were computed for each parameter against the *p*H values. *Results:* The parameters were divided into groups, according to the magnitude of change. The number given after each parameter represents the percentage change for each 0.10 decline in *p*H from control: *Group I, marked changes* —total peripheral resistance, 19.2; mean transit time, 19.9; cardiac output (dye-dilution), −10.6; left ventricular work, −10.4. *Group II, slight changes*—stroke volume, −4.8; heart rate, −3.6; left ventricular pressure, −3.2; first derivative of left ventricular pressure, −3.2; first derivative of right ventricular pressure, −4.7; first derivative of central aortic pressure, −4.1. *Group III,* no statistically *significant change*—mean aortic pressure, 0.7; systolic aortic pressure, −0.6; right ventricular pressure, 2.6. *Discussion:* Group I involved mainly those parameters reflecting changes in resistance and flow; Group II, changes in "contractility," particularly the derivatives of the pressures; and Group III, changes in pressures. In intact dogs, then, metabolic acidosis has a more profound effect on the peripheral portion of the cardiovascular system, the effects on "contractility" being relatively small. This disagrees with the classic concept of marked myocardial depression with a decreased *p*H (Price, H. L., and Helrich, M.: J. Pharmacol. Exper. Therap. *115:* 206, 1965), but agrees with more recent studies which show little myocardial effect with decreased *p*H in intact hearts (Baue, A. E., and McClerkin, W. W.: Ann. Surg. *161:* 41, 1965) or in isolated hearts (LeVeen, H. H., Falk, G., Lustrin, I., and Helft, A. E.: Surgery *51:* 360, 1962). The release of catecholamines partially compensates for the myocardial depression which occurs with decreased *p*H. Isolated guinea pig atria show little depression with metabolic acidosis unless catecholamines are depleted by reserpine, or blocked with a beta-blocking agent (Smith, N. Ty, and Corbascio, A. N., unpublished data). The decrease in total peripheral resistance with a metabolic acidosis is also at variance with studies on isolated segments of vessels showing vasodilation (Carrier, O., Jr., Cowsert, M., Hancock, J., and Guyton, A. C.: Amer. J. Physiol. *207:* 169, 1964). However, recent studies by Kittle *et al.* (Surgery *57:* 139, 1965) show an increase in carotid, coronary, renal, and systemic resistance with metabolic acidosis in dogs. Again, the release of catecholamines may play an important role. Should the physician continue to correct metabolic acidosis during cardiac arrest, shock, transfusion, or hypothermia? Prevention of the acidosis which follows declamping of the aorta did not prevent a drop in pressure (Baue, A. E., and McClerkin, W. W.: Ann. Surg. *161:* 41, 1965). Correction of acidosis