ripheral resistance is calculated from blood flow and arterial blood pressure. Of these three parameters, only blood pressure is monitored during clinical anesthesia, and the importance of vascular resistance is often overlooked. Severinghaus and Cullen (ANESTHESIOLOGY *19:* 165, 1958) reported an increase in total peripheral resistance in halothane anesthetized man. Johnstone (Brit. J. Anaesth. *30:* 435, 1958) believed that vasodilation continues as halothane anesthetic depth is lowered. Nunn (Modern Trends in Anaesthesia by Frankis T. Evans and T. Cecil Gray, Butterworth's, 1962, p. 68) believed that respiratory acidosis causes a weakening of ventricular contraction in the dog. Carson (J. Appl. Physiol. *20:* 948, 1965) demonstrated that cardiac output arises logarithmically with Pa_{CO_2} in the dog. Studies were initiated to explore further peripheral resistance and cardiac output relations to halothane and carbon dioxide in the dog. *Methods:* Studies of cardiac output were made with the use of square wave electramagnetic flowmeter probes implanted on the ascending aorta of 7 dogs. A minimum 6-day recovery period was observed before experimentations; 159 cardiac outputs were paired with simultaneous arterial determinations of *p*H, P_{CO_2}, P_{O_2} and arterial and right atrial pressures in 12 experiments. Anesthesia was induced and maintained with halothane and oxygen. End-expiratory halothane concentrations were 0.75, 1.5, and 2.25 per cent. Stepwise production and elimination of respiratory acidosis was accomplished with up to 20 per cent carbon dioxide at each concentration of halothane. Each step occupied not less than 15 minutes. Spontaneous, unassisted respirations were allowed throughout each study. *Results:* At the deeper concentrations of halothane, total peripheral resistance decreased to 80 per cent of baseline values obtained during initial 0.75 per cent halothane anesthesia. Total peripheral resistance decreased along a predictable slop at all three concentrations of halothane when respiratory acidosis was produced. Cardiac output decreased with deeper concentrations of halothane, but increased at each concentration when respiratory acidosis was produced. Heart rate remained stable. Mean arterial blood pressure dropped from higher values or remained at its original low value upon production of respiratory acidosis. *Conclusions:* Blood flow is increased in respiratory acidosis in light or deep halothane anesthesia in dogs because of a decreased vascular resistance. Respiratory acidosis in the intact dog does not produce myocardial depression. (Supported in part by the Hartford Foundation and the Washington State Heart Association.)

Metabolic and Circulatory Aspects of Halothane Anesthesia. ALAN D. SESSLER, M.D., and RICHARD A. THEYE, M.D., *Section of Anesthesia, Mayo Clinic and Mayo Graduate School, Rochester, Minnesota.* Halothane appears to have no effect on O_2 uptake in man when moderate concentrations are employed and when compensatory heat-producing mechanisms are blocked by muscle relaxants (Theye, R. A., & Tuohy, G. F.: ANESTHESIOLOGY *25:* 627, 1964). In an effort to explore further the effect of halothane on O_2 uptake, additional studies have been carried out in the laboratory both in intact and in artificially perfused dogs. *Method:* Intact, unpremedicated, paralyzed dogs (13) were studied at 0.8 and 3.2 per cent halothane inspired concentrations. After induction (halothane-air) and intubation, ventilation was maintained artificially (Harvard pump). O_2 uptake was determined by conventional open-circuit spirometric technique with analysis by gas chromatography (Theye, R. A.: ANESTHESIOLOGY *25:* 75, 1964). Additional measurements included cardiac output (dye-dilution), arterial and right atrial pressures (strain gauge), arterial and pulmonary artery blood gas levels (electrodes and reflection oximeter) and esophageal temperature. At the greater halothane concentration (3.2 per cent), both O_2 uptake and cardiac output were less than at 0.8 per cent halothane. These reductions were, respectively, 10–30 per cent (O_2 uptake) and 30–60 per cent (cardiac output). With a return to 0.8 per cent halothane, both O_2 uptake and cardiac output returned to levels previously observed. Additional hemodynamic and metabolic data are available to complement these major findings. In the perfusion studies (11), O_2 uptake was studied both as a function of flow (halothane constant) and as a function of halothane

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-