expert obstetrician, working closely together as a team. (Supported in part by a China Medical Board Visiting Professorship at Sapporo Medical College.)

Quantitative Programmed Closed-circuit Methoxyflurane Anesthesia. H. T. KYE, M.D., and H. J. LOWE, M.D., *University of Chicago, Pritzker School of Medicine, Chicago, Ill.* The rates of uptake of methoxyflurane at constant inspired and alveolar concentrations have been reported by Eger (ANESTHESIOLOGY 25: 94, 1964). In the present investigation, the rates of whole-body methoxyflurane uptake at constant arterial concentration (12 mg/100 ml or 2 ml vapor/100 ml blood) were calculated in twelve unselected patients from the individual organ volumes, blood flows, and anesthetic solubilities. *Methods:* Following induction with thiopental and intubation, liquid methoxyflurane was injected into the closed system by means of a Harvard infusion pump. The uptake curve for a 100-kg patient was plotted on a potentiometer curve follower (Data-Trak) and connected to the infusion pump by means of a rheostat which permitted reduction of the infusion rate in proportion to reduction in the weight of the patient. *Results:* At the programmed rates, the blood methoxyflurane concentrations gradually fell from maximum values (12–15 mg/100 ml) observed 15–20 minutes after induction to 9–12 mg/100 ml during the remaining 90–120 minutes of anesthesia. Since fat is the only tissue compartment with a sufficiently long time constant to contribute significantly to uptake after two hours of anesthesia, it was concluded that the blood flow to fat was 200 to 300 ml greater than that used in the model compartment system. *Summary:* In all cases, the program was satisfactory for surgical anesthesia. Blood methoxyflurane concentrations in the recovery room were all less than 3.5 mg/100 ml.

Effects of Volatile Anesthetics on Nonexcitable Tissue. T. N. MACKRELL, M.D., and M. SCHWARTZ, PH.D., *Departments of Anesthesiology and Engineering Physics, University of Louisville, Louisville, Ky.* To determine the fundamental effects of volatile anesthetics on nonexcitable living tissue, the gastric mucosa of the frog, *Rana pipiens,* was studied. *Methods:* An *in vitro* technique in which the frog gastric mucosa was mounted between cylindrical chambers was used. The secretory and nutrient solutions were aerated with a gas mixture containing a concentration of anesthetic, 5 per cent CO_2, and the remainder O_2. The effects of methoxyflurane, halothane, fluroxene, chloroform, and trichloroethylene upon the H^+ secretory rate were determined. *Results:* All agents of sufficient potency showed a marked increase in resistance as the H^+ rate decreased to zero. A striking effect was the correlation of the H^+ rate decrease with the relative potencies of the anesthetics. The mean concentrations of the firsty three agents necessary to produce a 40 per cent decrease in H^+ rate (methoxyflurane 0.54 per cent, halothane 2.4 per cent, fluroxene 3.4 per cent) were each approximately three times the mean alveolar concentration (MAC) (ANESTHESIOLOGY 28: 994, 1967). From this study we predict the MAC for chloroform to be about 0.6 per cent. Preliminary estimates suggest that the MAC for trichloroethylene is about the same as that for chloroform.

Pulmonary Venous Admixture before, during and after Halothane–Oxygen Anesthesia with Spontaneous Respiration. B. E. MARSHALL, M.D., P. J. COHEN, M.D., S. AUKBERG, M.D., and C. H. KLINGENMAIER, M.D., *Department of Anesthesia, University of Pennsylvania, Philadelphia, Penna. Methods:* Pulmonary venous admixture (Q_s/Q_t) was measured in ten patients premedicated with morphine and atropine before, during and after halothane–oxygen anesthesia with spontaneous respiration. *Results:* The preanesthetic Q_s/Q_t (mean 4.4 ± 0.6 per cent) was positively correlated with age. After 40 minutes of anesthesia the Q_s/Q_t had increased threefold (mean 12.1 ± 2.1 per cent) but only a minor further increase (mean 14.8 ± 2.8 per cent) occurred after three hours. When anesthesia was discontinued, Q_s/Q_t returned to normal (mean 5.2 ± 0.9 per cent) after three hours and to intermediate values at 40 minutes (6.5

± 1.2 per cent). Oxygen consumption and cardiac output changed proportionately at each phase of measurement and, therefore, arteriovenous oxygen content remained in the normal range (3.5–5.5 ml/100 ml). This was confirmed by direct measurement of arterial and mixed venous oxygen contents. *Summary:* The rapid onset, offset and lack of progression of the increased venous admixture observed in this study suggested a pharmacologic action of the anesthetic agents on the pulmonary circulation rather than progressive atelectasis. Furthermore, the increased Q_s/Q_t found during the early postoperative period was sufficient to account for much of the postoperative hypoxemia that has been demonstrated in similar patients breathing air after extremity surgery. (Supported in part by USPHS Grants 5-T01-GM-215-10, 1-P01-GM-15430-01 and 5-P01-GM-09070-06.)

Cardiovascular Effects of Halothane and Halothane–Nitrous Oxide Anesthesia during Controlled Ventilation. W. E. MARTIN, M.D., F. G. FREUND, M.D., T. F. HORNBEIN, M.D., and J. J. BONICA, M.D., *Department of Anesthesiology, University of Washington School of Medicine, Seattle, Wash.* *Methods:* Eight healthy unmedicated male volunteers 21 and 28 years old were studied. Arterial and venous catheters were placed under local anesthesia, the subjects rested for 30 minutes and control measurements obtained. Anesthesia was induced with halothane and nitrous oxide, the trachea intubated under topical anesthesia, and respiration controlled in a constant pattern thereafter. Following one hour of constant 1 per cent end-tidal halothane anesthesia, the level was shifted in a random sequence to 0.3 per cent halothane in 70 per cent nitrous oxide, 0.8 per cent halothane in 100 per cent oxygen, and 0.8 per cent halothane in 70 per cent nitrous oxide; and measurements were made at Pa_{CO_2} values of approximately 20, 40, and 60 torr. *Results:* Three primary observations emerge. First, as the CO_2 rises from 20 to 40 to 60 torr, cardiac performance improves, since minute work, stroke work, mean arterial pressure, cardiac output, stroke volume, central venous pressure, and the first derivative of arterial pressure all increase; heart rate is relatively stable, and total peripheral resistance decreases. Second, cardiac output is not dependent on the anesthetic level, since at any given Pa_{CO_2} cardiac output is the same with all three anesthetic levels. Third, the data support but do not prove the concept that nitrous oxide has a sympathetic stimulating effect, since the addition of 70 per cent nitrous oxide to 0.8 per cent halothane results in an increase in total peripheral resistance and venous pressure and a greater rate of rise of the first derivative of arterial pressure as Pa_{CO_2} increases. *Summary:* The increased cardiac output resulting from a higher Pa_{CO_2} coupled with a lower total peripheral resistance and a higher mean arterial pressure suggests that a modest increase in Pa_{CO_2} (up to 60 torr) might be a desirable clinical goal during halothane or halothane–nitrous oxide anesthesia.

Myocardial Metabolism and Hemodynamics in the Halothane-depressed Canine Heart. R. C. MERIN, M.D., *University of Rochester School of Medicine and Dentistry, Rochester, N. Y.* Limited information concerning the mechanism and significance of the myocardial depression produced by inhalation anesthetics is available. This study has looked at one phase of energy kinetics in the heart by assessing the effect of halothane on the manner in which the dog heart handles its fuels and oxygen. *Methods:* Fasting, nonmedicated dogs were intubated and artificially ventilated with halothane and oxygen. With fluoroscopic guidance catheters were placed in the femoral artery, left ventricle, right atrium and coronary sinus. Temperature, arterial blood gases and blood volume were maintained constant. A very low halothane concentration was used as the control (0.6 per cent mixed expired) and 1.6 per cent served as the test, each animal being his own control. At each concentration, heart and arterial pressures, left ventricular dp/dt, ECG, cardiac output, myocardial blood flow (MBF) (by a radioisotope technique) and arterial and coronary venous levels of O_2, glucose, nonesterified fatty acids (NEFA), lactate and pyruvate were determined. Myocardial uptake was calculated from MBF and coronary A-V differences. *Results:* Significant myocardial depression was