± 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. G. 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

evidenced by decreased mean arterial pressure (from 120 to 64 torr) left ventricular dp/dt (from 16 to 7), cardiac output (from 2.63 to 1.71 l/min) and left ventricular stroke work (from 37.33 to 10.02 gm meters) with increased right atrial (from 2.6 to 6.7 torr) and left ventricular end-diastolic (from 4 to 11.4 torr) pressures with no change in heart rate or peripheral vascular resistance. While MBF (from 42 to 23 ml/100 gm/min) and myocardial O_2 consumption (from 5.5 to 3.1 ml/100 gm/min) decreased, myocardial excess lactate also decreased. NEFA and pyruvate uptake decreased, lactate uptake did not change, and an elevated threshold for glucose uptake was seen. *Summary:* The results indicate that there was no myocardial hypoxia in the halothane-depressed heart and that the depression may be related to an interference in glucose transport.

The Effects of Inhalation Anesthetics on Pulmonary Surfactant. E. K. MOTOYAMA, M.D., L. GLUCK, M.D., Y. KIKKAWA, M.D., M. V. KULOVICH, M.D., and Y. O. SUZUKI, M.D., *Section of Anesthesiology and Department of Pediatrics, Yale School of Medicine, New Haven, Conn., and Department of Pathology, Albert Einstein College of Medicine, New York, N. Y.* The effects of halothane and cyclopropane anesthesia on pulmonary surfactant were investigated in 25 rabbits. *Methods:* Animals were anesthetized and artificially ventilated for four to seven hours and their lungs were compared with those of control animals sedated with pentobarbital and ventilated for equivalent lengths of time. *Results:* Successive measurements for eight to 24 hours of the minimum surface tension values of lung–saline extracts showed that animals anesthetized with halothane had significantly higher surface tension values than control animals. These results indicate that halothane in some way decreases the surface activity of the lung. This effect was not observed with cyclopropane anesthesia. Biochemical analysis showed that halothane anesthesia was associated with a significant decrease in the alveolar lining of the surface-active lecithin fraction containing myristic acid on the beta carbon. This finding indicates: 1) depression of the lecithin biosynthesis by the transmethylation of phosphatidyl ethanolamine, a major lecithin synthetic pathway which takes place within the alveolar lining (Pediat. Res. 1: 247, 1967); or 2) reduced transport of these lecithin molecules from the intracellular store onto the alveolar surface. This reduction of the lecithin containing myristic acid was not significant with cyclopropane anesthesia. Lung tissues were studied with electron microscopy, but no apparent abnormalities of the Type II alveolar cells with osmiophilic inclusions or of the alveolar-lining layer were found. (Supported by grants: USPHS HD-00989, HD-01299, HD-02459, and Josiah Macy, Jr., Foundation.)

Acid–Base Changes during Lidocaine-induced Seizures in *M. Mulatta*. E. S. MUNSON, M.D., and I. H. WAGMAN, PH.D., *Departments of Anesthesiology and Physiology, School of Medicine and the National Center for Primate Biology, University of California, Davis, Calif.* Lidocaine-induced seizure threshold, acid-base, equilibrium and behavioral and electrical changes were studied during intravenous infusion of lidocaine into unanesthetized rhesus monkeys at a constant rate (4 mg/kg/min). *Method:* Sixty-six experiments were performed on 19 male *M. mulatta* (4–7 kg). Nine animals were prepared with chronically-implanted electrodes in various depth locations. Arterial plasma lidocaine concentration was measured using the methyl orange method. *Results:* Mean (± SD) lidocaine seizure dosage was 13.8 ± 3.0 mg/kg. Arterial plasma lidocaine concentration at the onset of seizure activity was 24.5 ± 4.5 μg/ml. Animals that ventilated spontaneously developed a significant ($P < 0.01$) metabolic acidosis (15.9 ± 6.8 Meq/l base deficit). Duration of seizures in these animals was longer than that in artificially-ventilated (paralyzed) animals. No correlation between plasma lidocaine levels at the onset of seizures and base deficit of arterial blood was observed. Mild hypercarbia (Pa_{CO_2} 68 mm/Hg) also did not influence lidocaine seizure threshold. Alterations in behavior were similar to those observed in other animals. In addition to tonic–clonic seizure activity nystagmus and drowsiness were always present. The characteristic electrical responses previously