

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<sub>2</sub> 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. KIKAWA, 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 biosyn-

thesis 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 ( $\pm$  SD) lidocaine seizure dosage was  $13.8 \pm 3.0$  mg/kg. Arterial plasma lidocaine concentration at the onset of seizure activity was  $24.5 \pm 4.5$   $\mu$ g/ml. Animals that ventilated spontaneously developed a significant ( $P < 0.01$ ) metabolic acidosis ( $15.9 \pm 6.8$  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 (PaCO<sub>2</sub> 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

described in cats and rabbits during lidocaine infusion (ANESTHESIOLOGY 28: 155, 1967) were not observed. Although no seizure focus was evident, spike and slow-wave complexes were recorded in cortical and depth leads and were quite evident in the amygdala and caudate nuclei. (Supported in part by USPHS Grants NB-07844 and FR00169.)

**The Effects of Acidosis on Glycolysis and Pentose Shunt in Skeletal Muscle.** G. G. NAHAS, M.D., J. KYPSON, M.D., L. TRINER, M.D., and Y. VULLIEMOZ, M.S., *Department of Anesthesiology, College of Physicians and Surgeons, Columbia University, New York, N. Y.* Acidosis *in vivo* produces marked metabolic and functional alterations. The purpose of the present study was to investigate *in vitro* the effect of acidosis on carbohydrate metabolism. *Methods and Results:* Rat diaphragm was incubated in Krebs-Ringer phosphate buffer for one hour at pH 7.4 or 6.8. At pH 6.8 there were significant decreases in lactate (-36 per cent) and pyruvate (-22 per cent) production in the medium. Concurrently, glycogen content was significantly increased (+25 per cent). In a second series, the site of action of acid pH of muscle on glycolysis was investigated by comparing the concentrations of intermediates of the glycolytic pathway in diaphragm incubated at pH 7.4 or 6.8. At pH 6.8 glucose-6-phosphate was increased significantly (+22 per cent); fructose-6-phosphate was consistently, but not significantly, higher. Fructose-1,6-diphosphate was decreased significantly (-30 per cent), indicating a decrease in phosphofructokinase activity. Similar changes in intermediates also occurred when muscle was incubated with ouabain  $10^{-4}$  M in medium at pH 7.4 or pH 6.8. There was no significant change in citrate concentration or  $O_2$  uptake, which might indicate that the Krebs cycle was not affected by pH or by ouabain. Glucose-6-phosphate dehydrogenase activity was increased by 100 per cent at pH 6.8 (with or without ouabain), indicating an increase in activity of the pentose shunt. Ouabain at pH 7.4 did not change the activity of this enzyme. Decrease in phosphofructokinase activity at low pH could account for the decrease in lactate production. Maintenance

of the Krebs cycle could account, in part, for decrease in pyruvate. Marked increase in the pentose shunt by acid pH, with resulting increase in TPNH, might be a compensatory mechanism in the presence of decreased glycolysis. *Summary:* Acid pH produces marked alteration in some of the key enzymes which regulate carbohydrate metabolism.

**The Effects of Halothane on Mitosis.** F. NUNN, PH.D., F.F.A.R.C.S., K. L. DIXON, and J. D. LOVIS, B.Sc., PH.D., *Departments of Anesthesia and Botany, University of Leeds, Leeds, Yorkshire, England.* In cultures of the ciliate *Tetrahymena pyriformis*, halothane rapidly causes inhibition of growth, the 50 per cent effective dose being about 1.25 per cent of normal atmospheric pressure at room temperature. The rapidity of action suggested interference with mitosis, although inhibition of DNA synthesis cannot be excluded. *Methods:* Studies of mitosis were carried out on root-tips of *Vicia faba* (the broad bean) exposed for periods of two to 24 hours to concentrations of halothane (prepared by volumetric dilution of saturated vapor) ranging from 0.5 to 2.0 per cent. Germinating beans were exposed to halothane when lateral roots had attained length of more than one cm. Experimental treatments were carried out in a desiccator which was continuously swept with vapor at a flow rate of about 250 ml/min. The roots were completely exposed to the vapor, their tips not being immersed in water. Controls remained exposed to room air or to air in contact with water containing crystals of thymol, some of which floated. At certain intervals after the commencement of treatment lateral roots were removed and fixed in acetic alcohol. The chromosomes were stained by treatment of the root-tips with the Feulgen reagent following controlled acid hydrolysis. Permanent squash preparations were then made and examined by light microscopy. *Results:* Four hours' exposure to 2 per cent halothane resulted in a very marked reduction in the proportion of the later mitotic stages, anaphase and telophase. Prophases were normal in appearance, but the great majority of mid-division figures showed abnormalities entirely comparable to those associated with exposure to