

except for one patient in each of the cyclopropane and ether series who showed low values on their seventh postoperative days (59.5 per cent and 53.9 per cent respectively). The level of alkaline phosphatase activity was also normal (1.5 to 5 Bodansky units), except for elevated values on the seventh postoperative day in one patient following Fluothane anesthesia (7.9 units), in one patient following anesthesia produced by cyclopropane (8.4 units), and in 3 patients after anesthesia produced by ether (5.1, 7.8, and 7.6 units, respectively). The values for total serum bilirubin concentration were normal (0.2 to 1.0 mg. per cent) in all instances except for borderline elevations on the second postoperative day in 2 patients who had received ether anesthesia (1.1 and 1.3 mg. per cent). The cephalin-cholesterol flocculation determinations were also normal in all instances following anesthesia produced by either Fluothane, or cyclopropane, but showed a 2+ determination after forty-eight hours on the second postoperative day in four patients and a 3+ determination after forty-eight hours on the seventh postoperative day in one patient following ether anesthesia.

The results are of interest in that they reveal less effect upon hepatic function than most previous investigations of liver function following anesthesia. This may have been due to the excellent health and nutritional status of the patients, the site and nature of surgery, the sensitivity of the liver function tests employed, or the determined efforts to prevent the occurrence of either hypoxia or excessive accumulation of carbon dioxide; all of these are factors which have been shown in the past to play an important role in the production of postoperative hepatic dysfunction.

**Respiratory Studies on Dogs with Arfonad Induced Hypotension and Constant Volume Ventilation.** ROBERT W. LOEHNING, M.D., Department of Anesthesiology, University of Utah, Salt Lake City, Utah, and WILLIAM K. HAMILTON, M.D., University Hospitals, Iowa City, Iowa.

THE increasing use of manual and mechanical ventilation and pump oxygenators during anesthesia makes it desirable to investigate changes occurring in respiratory gas tensions during abnormal states. One such state frequently encountered is hypotension. A decrease in oxygen uptake during hypotensive periods has been reported by many investigators. However, data on carbon dioxide output and changes in carbon dioxide tension are lacking.

Nine dogs were anesthetized with a single dose of pentobarbital, 20 mg./kg., a tracheotomy performed, and the animals placed on a fixed volume respirator breathing air through a nonrebreathing system. Gallamine triethiodide was given as needed for relaxation. A one to three hour period was used to establish a "control state." This state was defined as one having a constant rate of oxygen uptake and a  $pH$  and end expiratory  $pCO_2$  of minimum variation. After this period hypotension was maintained by Arfonad (trimethophan camphorsulfonate) drip for one-half to one hour.

End expiratory  $pCO_2$ , carbon dioxide output, and oxygen uptake fell at the onset of hypotension but during the course of the hypotension there was a gradual return towards "control state" values. The greater the initial fall in blood pressure the greater the reduction in oxygen uptake and output of carbon dioxide. All arterial and almost all venous plasma carbon dioxide content determinations were lower during hypotension but the post hypotensive carbon dioxide content determinations varied with the state of recovery of the animal.

**Laboratory Observations on the Cardiovascular and Respiratory Effects of Fluothane.** J. P. LONG, PH.D., AND C. B. PITTINGER, M.D., Department of Pharmacology and Division of Anesthesiology, Department of Surgery, College of Medicine, State University of Iowa, Iowa City, Iowa.

FLUOTHANE 1,1,1-trifluoro-2,2-bromoethane) is a volatile, potent, nonexplosive anesthetic agent. Favorable pharmacological and clinical reports in the literature prompted us to re-evaluate and extend the reported observations on this new anesthetic agent.

In dogs, Fluothane consistently lowers blood pressure. The degree of hypotension is closely related to depth of anesthesia. Blood pressure is very labile and will return to control levels within five minutes following cessation of administration of the agent. Simultaneous measurements of the force of left ventricular contractions using a Walton strain gauge suggest that myocardial depression contributes significantly toward the production of hypotension. The depression of the cardiac musculature is closely related to depth of anesthesia. Ether, tested under similar conditions, also demonstrated similar cardiac effects. Cardiac arrhythmias were observed only during induction. Except for inversion of the T wave there was no other alteration of the electrocardiographic pattern. If Fluothane administration is continued by artificial ventilation following apnea, increasing concentrations of the drug tend to cause a sudden cessation of cardiac contractions. On two occasions, animals were resuscitated by cardiac massage and ventilation with oxygen. Various anesthetic agents were bubbled through Tyrode solution perfusing isolated rabbit hearts, according to the classical method of Langendorf. Ether, cyclopropane, Fluothane, and chloroform produce myocardial depression when the concentrations of the agents in their gas-oxygen mixtures are similar to those required for anesthetization of rabbits. Fluothane and chloroform increase coronary flow, while ether and cyclopropane tend to decrease the rate.

In dogs, the electroencephalographic alterations with Fluothane are different from those caused by chloroform when severe hypotension has been produced. In contrast to the marked depression of electroencephalographic activity during deep chloroform anesthesia, Fluothane under similar conditions does not depress electrical activity of the brain to the same extent.

In dogs, increasing depth of anesthesia is also accompanied by respiratory depression as evaluated by minute volume measurements. Simultaneous measurements of the end-expired carbon dioxide concentrations demonstrate an accumulation that is proportional to the amount of respiratory depression. When respiratory arrest occurs spontaneously with Fluothane, there is approximately a 100 per cent increase in the carbon dioxide concentration of the end-expired air. Carbogen is capable of producing marked respiratory stimulation during very light Fluothane anesthesia, but this effect decreases with increasing depth. (This work was supported by grants from Imperial Chemical (Pharmaceuticals) Industries, England, and the State University of Iowa College of Medicine Trust Fund. The Fluothane was supplied by Ayrest Laboratories, Inc.)

**Biochemical Changes Induced by the Low Flow Pump Oxygenator During Cardiopulmonary By-pass in Man.** WALTER H. MANNHEIMER, M.D., YOSHIO KUROSU, M.D., AND ARTHUR S. KEATS, M.D., Department of Anesthesiology, Baylor University College of Medicine, Houston, Texas.

THE use of low flow perfusion (35–50 cc./kg./min.) in contrast to high flows (80–100 cc./kg./min.) during cardiopulmonary by-pass for intracardiac surgery offers two important advantages. These are decreased trauma to the blood by the pump and decreased bleeding into the heart when chemical asystole is not used or when collateral bronchial circulation is large. The hazards of subnormal perfusion rates are anoxic tissue damage, especially of the brain and kidneys, and metabolic acidosis from anaerobic cellular respiration. We have used low flow perfusion with a DeWall type bubble oxygenator in 170 intracardiac procedures in man without observing postoperative renal or brain damage attributable to the low perfusion rate. The present study was undertaken to determine the degree of metabolic acidosis produced under these circumstances.

Twenty-five patients who underwent surgical procedures requiring the use of a pump oxygenator were subjects of this study. The primary anesthetic agent was ether-oxygen with succinylcholine infusion. Respiratory alkalosis was produced by deliberate hyperventilation during anesthesia prior to by-pass. Oxygen without carbon dioxide or anesthetic agent was used as the aerating gas in the bubble oxygenator. All patients were perfused at 35–50 cc./kg./min. for 7–20 minutes with or without potassium arrest of the heart. Samples of arterial blood were collected from the femoral artery at the following