and duration of action were obtained by the preliminary alkalinization of the tongue prior to application of the drug than when using the alkaline suspension. Vasoconstrictors allegedly retard absorption of the local anesthetic drug and prolong its effect. This is true intrathecally and perineurally but not topically. Neither norepinephrine, epinephrine, or ephedrine exerted any significant effect on the duration of the block. Angiotensin (Hypertensin) and vasopressin exert their effects by direct action on the smooth muscle and not on the adrenergic receptors. These were also studied in view of these differences in behavior. They exerted no significant prolonging effect on the block when mixed with cocaine and tetracaine. Hyaluronidase and demulcents caused no change.

The addition of various cations to solutions of local anesthetics allegedly prolongs the block. Calcium, potassium, sodium, magnesium and ammonium ions did not prolong the block of either tetracaine or cocaine when used in concentrations up to 5 per cent. No significant prolongation of action occurred when two local anesthetics at their optimal concentrations were mixed. A mixture of 15 per cent cocaine and 1 per cent tetracaine produced no greater duration of the block or period of latency than either of these drugs used alone.

Halothane and Cardiac Work. MILTON H. ALPER, M.D., and WERNER FLACKE, M.D., *Division of Anesthesia, Peter Bent Brigham Hospital, and Department of Pharmacology, Harvard Medical School, Boston, Massachusetts.* The administration of halothane in concentrations of 0.5 per cent or higher in the inspired gas significantly depresses myocardial contractility in the heart-lung preparation of the dog (Flacke, W., and Alper, M. H., ANESTHESIOLOGY 23: 793, 1962). The depression is manifested by a rise in right and left atrial pressures and a fall in systemic cardiac output at a constant height of the venous reservoir. *Method:* In the present experiments, this observation was extended to study the influence, if any, of the type of load imposed upon the heart. In the heart-lung preparation, systemic cardiac output and arterial resistance can be altered independently. Cardiac output was increased by raising the venous reservoir in measured steps. Arterial pressure was varied by adjusting the setting of the Starling resistance. Halothane was administered from a Fluotec vaporizer. Determination of halothane concentrations in blood by gas chromatography showed that, at constant inspired concentration, about 90 per cent of the steady-state concentration was reached within ten minutes. It was found that, under halothane, an increased cardiac output was accompanied by a much smaller rise in left atrial pressure than with increased arterial pressure. In order to study this difference quantitatively, cardiac work was calculated as the product of systemic output and arterial pressure under conditions of increased output ("volume work") or increased pressure ("pressure work"). Ventricular function curves (Sarnoff, S. J., and Berglund, E.: Circulation 9: 706, 1954) were constructed by plotting left ventricular work against filling pressure, either measured directly by intraventricular catheter or approximated from left atrial pressure. *Results:* In control experiments, the ventricular function curves for "volume work" and for "pressure work" were not significantly different. After administration of 0.5 per cent halothane for at least 15 minutes, the curve resulting from increase in output was displaced in the direction of increased filling pressure, but the slope of the curve paralleled that of the control curve. The same maximal work could be obtained although at greater filling pressure. In contrast, the function curve resulting from increase in arterial pressure was not only displaced farther in the direction of increased filling pressure but also its slope was strikingly reduced. The maximum work obtainable at any filling pressure was greatly lowered. Recovery from the effect of halothane, measured 15 to 20 minutes after discontinuation of the anesthetic, was more complete with regard to "volume work" than with regard to "pressure work." Finally, infusion of *l*-norepinephrine at a rate of 1 to 3 μg/minute enables the heart, under halothane, to increase its output with normal filling pressures; it did not restore completely the ability of the heart to work against a high resistance. *Conclusion:* It can be concluded that the depression of contractility by halothane com-

promises the performance of the isolated heart more severely in the presence of elevated arterial pressure. The heart is still able to increase its volume output albeit at increased filling pressures. If the observed phenomenon applies also to the heart *in situ*, the fall in arterial pressure clinically observed during halothane anesthesia may be beneficial in that it may enable the heart to maintain an adequate output.

Rapid Blood Ether Determinations Using Gas Chromatography. JOHN M. BAKER, M.D., and BENTON D. KING, M.D., *Department of Anesthesiology, School of Medicine, State University of New York at Buffalo.* Renewed interest in the uptake and distribution of anesthetics by the body has pointed up the need for analytical methods capable of rapidly and accurately estimating the anesthetic concentration of multiple serial blood samples. Previously described procedures for the measurement of diethyl ether in blood have suffered from inaccuracy or prolonged and complicated manipulations. For this reason, a method for the measurement of blood ether was developed using gas chromatography that is simple, rapid, and accurate.

To minimize inaccuracy, solvent extraction was chosen in preference to manometric extraction or direct injection of the blood into the chromatograph. Because of its availability and solubility characteristics, carbon tetrachloride was used in a one-to-one ratio with blood, which was drawn and handled anaerobically until extraction with the solvent. For this purpose, 1 ml. of carbon tetrachloride was placed in a 3 or 5 ml., stoppered vial or Vacutainer. An equal amount of blood was withdrawn from the patient into a 2-ml. syringe provided with a Chaney adapter. The blood was transferred directly into the vial by attaching a needle to the syringe and puncturing the stopper. The vial was shaken gently for several minutes and then centrifuged stopper end downwards at high speed. The solvent layer next to the stopper was removed anaerobically using a microliter syringe and needle assembly. A 10 microliter sample was injected into the chromatograph for analysis. A Beckman model GC-2 gas chromatograph with a Carbowax 400 column material was used to achieve separation of the ether from the carbon tetrachloride. This instrument employs a thermal conductivity detector whose output is fed to a potentiometric strip chart recorder. The areas under the signal peaks as written by the recorder in response to ether flowing through the detector are a linear function of the amount of ether by weight in each sample; and when compared with the areas obtained with injection of known amounts of ether, the concentration of ether in the sample can be estimated within 1 per cent. When blood was extracted with carbon tetrachloride, a 95 per cent extraction of the ether was usual, with a standard deviation of 1.5 per cent. Thus, the overall accuracy was 3.9 per cent at the 99 per cent confidence limit. Because the extraction ratio tended to increase slowly with time, to 96 or 97 per cent if the samples were left in contact with the solvent overnight, separate reference standards were made for each sample and extracted in the same manner as the unknown samples. Overall accuracy was enhanced in this manner, since extraction time for both samples and standards was the same.

Increased Physiologic Shunting During Anesthesia and Surgery. H. H. BENDIXEN, M.D., J. HEDLEY-WHYTE, M.D., and M. B. LAVER, M.D., *Anesthesia Laboratory, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts.* This study proposed to determine whether falls in arterial oxygen tension occur during clinical anesthesia, simultaneously with falls in pulmonary compliance; and to determine also if such falls in oxygen tension are reversible by sustained hyperinflation of the lungs. In the absence of periodic deep breaths, pulmonary compliance is known to decrease progressively (Mead, J.: Physiol. Rev. *41:* 281, 1961), caused, at least in part, by collapse of air spaces (atelectasis). The fall in compliance is reversible by sustained hyperinflation. If the perfusion of collapsed air spaces should continue, venous admixture to arterial blood, or increased physiologic shunting, would lead to a fall in arterial oxygen tension. If such a fall in oxygen tension is caused by collapse of air spaces, it should be reversible by sustained hyperinflation of the lung. *Method:* Fourteen surgical