Cardiovascular Research Institute, University of California Medical Center, San Francisco, California. Loeschcke and associates have described a superficial *p*H sensitive area in the fourth ventricle which can influence respiration (*Loeschcke, H. H., and others: Pflug. Arch. 266: 569, 1958*). In 18 dogs, we performed a suboccipital craniotomy under chloralose anesthesia and perfused the fourth ventrical with a mock spinal fluid of known P_{CO_2} and *p*H at 38 C. Changing the HCO_3^- in the perfusate from 45 mEq./l. to 15 mEq./l. increased minute ventilation an average of 350 per cent. P_{CO_2} was kept constant in both solutions at 51 mm. Hg and isotonicity was maintained by altering Cl^-. In a number of animals, the perfusion response was diminished or absent after accidental trauma of the obex of the medulla oblongata. There is in this region a superficial glomus-like structure, the area postrema, which has many of the histological characteristics of a chemoreceptor. In 9 out of 12 dogs, where a normal perfusion response had previously been demonstrated, destruction of the area postrema abolished this response. In a series of 8 dogs and 1 cat, the ventilatory response to topical application of nicotine, acetylcholine and norepinephrine at the area postrema was studied. Nicotine produced an inhibition of ventilation in all animals, acetylcholine gave a similar effect in 3 animals and norepinephrine stimulated ventilation in one. Histamine, serotonin, phenyldiguanidine and strychnine did not produce any effect. In conclusion, it can be said that there is definite evidence for the existence of a chemoreceptor in the fourth ventricle sensitive to *p*H of spinal fluid. The function of this receptor is impaired by lesions in the region of the area postrema. The area postrema is a pharmacological trigger zone sensitive to nicotine and probably to acetylcholine. So far topical application of mock spinal fluid with varying *p*H values to the isolated area postrema has failed to give ventilation responses. Therefore, the pharmacological trigger zone is not necessarily identical with the *p*H sensitive receptor. [Supported in part by USPHS Graduate Training Grant 2G-63.]

Changes in Central Venous Pressure During Controlled Blood Loss and Transfusion During Operation. CAPT. THOMAS P. MATHEWS, MC, AND LT. COL. JOHN A. JENICEK, MC., *Anesthesia and Operative Service, Brooke General Hospital, Fort Sam Houston, Texas.* This study of central venous pressure changes was carried out on two groups of patients. The first group of 10 patients was subjected to a controlled phlebotomy of 500 cc. of whole blood and then retransfused with 500 cc. of blood and preservative solution after a ten-minute wait. The second or control group had no phlebotomy and were subjected to 100 cc. or less of surgical blood loss. The patients were all males, Class I surgical and anesthetic risks, ages 18 to 48 years, and all were subjected to inguinal herniorrhapy under nitrous oxide oxygen ether anesthesia. Results of this limited number of cases indicated that venipuncture of the median basilic vein with subsequent passage of a plastic catheter into the superior vena cava, just proximal to the right atrium is safe, and even under local anesthesia subjects the patients to only mild discomfort. Post-catheterization morbidity did not occur in any of the patients. Venous pressure fell during phlebotomy, leveled off during a "rest period" and rose during the retransfusion. Results indicated that this is not a reliable parameter for the purpose of measuring the fluid loss or the amount of blood transfusion given because it is affected by such factors as anesthetic agent, anesthetic technique, depth of anesthesia, positive pressure breathing (assisted or controlled), airway management and the unpredictable occurrence of airway obstruction, coughing, straining or wheezing. However, when the anesthesiologist controls those factors named, the venous pressure may be used as a fairly sensitive indicator of parenteral fluid loss and may be also used to indicate when to terminate fluid, especially blood, replacement. In the control series of patients, a rise of venous pressure occurred with induction, it remained at an elevated "plateau" during anesthesia, and then fell toward normal levels at the end of anesthesia. This phenomenon has not been studied to provide a satisfactory explanation at this time.

Respiratory, Circulatory and Hepatic Effects of Methoxyflurane in Dogs. WILLIAM

C. NORTH, M.D., PH.D., PAUL R. KNOX, M.D., V. VARTANIAN, M.D., AND C. R. STEPHEN, M.D., *Division of Anesthesia, Duke University Medical Center, Durham, North Carolina.* Methoxyflurane (1,1-dichloro-2,2-difluoro-3-methoxyethane) is a liquid that has been reported to be a potent inhalation anesthetic (*Artusio, J. F., Jr., Van Poznak, A., Hunt, R. E., Tiers, F. M., and Alexander, M.: Anesthesiology 21: 512, 1960*). This study is concerned with the effects of the agent in dogs. Mongrel dogs were intubated awake following intravenous succinylcholine or after being lightly anesthetized with open-drop methoxyflurane or an intravenous thiobarbiturate. The anesthetic was vaporized in a wick-type ether vaporizer in a circle system or in a copper kettle with a nonrebreathing technique. Anesthetic vapor concentrations were measured with a gas chromatograph. In concentrations of 1.5 vol. per cent, or less, the vapor was not irritating to the awake dog, and induction proceeded smoothly, requiring 5 to 10 minutes. Initial concentrations of 3 per cent (the maximum obtainable) were mildly irritating at first. No evidence of respiratory stimulation was seen. Respiratory rate and volume were depressed to a degree proportional to the depth of anesthesia. Inhalation of 1 per cent methoxyflurane for 30 minutes reduced the tidal volume by about 40 per cent and reduced the rate to about 10 per minute. Greater concentrations led to a more rapid decline in respiratory function. An acidemia and hypercarbia resulted from this respiratory depression, but it did not develop when the dogs were artificially respired, even after three hours. Heart rate and rhythm were not altered appreciably except at very deep anesthetic levels when the rate became very slow. No spontaneous irregularities have been noted at any concentration of drug. ECG changes were minimal except for a reduction in voltage at high anesthetic concentrations. The blood pressure consistently fell to an extent dependent upon the depth of anesthesia. In six dogs after spontaneous inhalation of 1 per cent methoxyflurane the average blood pressure was 120/80. (Initial average blood pressure = 165/110.) In 10 dogs artificially respired with the same mixture the average blood pressure was 95/60 after one hour and 75/45 after three hours. Inhalation of higher concentrations reduced the blood pressure to similar levels in a shorter period. Using artificial respiration it was possible to reduce the blood pressure to 20/10 without cessation of regular cardiac action. This depression was reversible if ventilation without the drug was instituted. Intravenous injection of epinephrine, rapidly or slowly, in doses of 0.002 to 2.0 mg./kg. failed to cause ventricular fibrillation at all levels of anesthesia. These doses caused a hypertension and tachycardia in all instances except when the blood pressure was below 15 mm. Nodal and ventricular rhythms were noted when marked hypertension occurred, but these could be abolished by oxyphenonium (Antrenyl). Isoproterenol produced a more dramatic circulatory response than epinephrine at hypotensive levels. Methoxamine and phenylephrine produced little or no response when the blood pressure was below 60 mm. It seems that methoxyflurane in high concentrations is a potent direct cardiac depressant. Eleven dogs were exposed to 1 per cent methoxyflurane for three hours on five different occasions. Six breathed spontaneously; five were on controlled respiration. Two dogs (spontaneous) showed an increase in BSP retention 48 hours after the last exposure. Microscopic changes in the livers of these dogs were variable. There was little or no cellular damage and little to marked fatty infiltration in the centrolobular areas. These findings were comparable to those seen with halothane under similar circumstances.

The Effect of Specific Adrenal Medullary Blockade on the Blood Pressure Response to Ephedrine. RYLAND P. ROESCH, M.D., ROBERT W. GARDIER, PH.D., AND V. K. STOELTING, M.D., *Department of Anesthesiology, Indiana University School of Medicine, Indianapolis, Indiana.* Data obtained on reserpine treated animals indicate that the pressor response to ephedrine results from a release of catechol amines (*Burn, J. H., and Rand, M. J.: J. Physiol. 144: 314, 1958*). Since reserpine evidently depletes catechol amine stores in the adrenal medulla (*Callingham, B. A., and Mann, M.: Nature 181: 423, 1958*) and the peripheral blood vessels (*Burn, J. H., and Rand, M. J.: Brit. Med. J. 1: 903, 1958*),