

and most lasted from six to seven hours, though several were over eight hours. Ages ranged from 30 to 80 with most in the 40 to 70 group. Patients were not eliminated from the use of this method because of hypertension or other cardiovascular disease. We have demonstrated, then, that when compensatory cardiovascular reflexes are prevented, blood volume changes are accurately reflected in the blood pressure.

**Renal Function Studies During Extra-Corporeal Circulation.** DONOTIY Y. MA., Chief, Anesthesiology Section, U. S. Veterans Administration Hospital, Instructor in Section on Anesthesiology, Department of Surgery, University of Louisville School of Medicine, Louisville, Kentucky. Hypotension is a problem which confronts anesthesiologists from time to time. With open-heart surgery and the use of extra-corporeal circulation, hypotension becomes a real threat. The dangers of profound hypotension and the damage caused to vital organs have been well defined. However, whether the renal function is influenced by the change of systemic circulation as discussed by Borst (*Borst, J. G. C.: The Kidney, Ciba Foundation Symposium, 1954, p. 255*) is still an open question. This study was to find out the adequacy of renal circulation during cardiopulmonary bypass with Kay Cross rotating disc-oxygenator. Dogs were used in our experiments. The dog was anesthetized with thiopental sodium and maintained with nitrous oxide-oxygen by endotracheal closed circle CO<sub>2</sub> absorption. Ventilation was maintained by a mechanical respirator. Small amounts of ether were added when necessary. EEG and ECG electrodes were connected to a Cambridge four-channel recorder equipped with a 16-inch oscilloscope. Left femoral artery and vein were cannulated for pressure recordings. Ureters were catheterized individually through the ureteral orifices for urine collection. Para-aminohippuric acid (PAH) and creatinine (10 per cent solution) 100 mg./kg. each were injected subcutaneously. Urine specimens were collected every 20 minutes. At the mid-point of each collection, 5 ml. of arterial blood was taken for estimation of plasma concentrations of PAH and creatinine (*Knoefel, P. K., and others: Amer. J. Physiol.*

*196: 1224, 1959*). Three control experiments were made. Glomerular filtration rate measured by creatinine clearance was found to be approximately 19-23 ml./minute, which was quite constant and similar from both kidneys. Renal plasma flow measured by PAH clearance was found between 50-70 ml./minute. There was no significant difference between the right and left kidneys. The plasma concentration of PAH was approximately 4 mg. per cent. The experiment using cardiopulmonary bypass with Kay Cross oxygenator was set up exactly like the control experiment. After obtaining 2-3 control samples, the dog was prepared to go on the pump. The pump set up was similar to that reported by Cross (*Gross, R. E., and others: Ann. Surg. 151: 285, 1960*). Continuous observation of the arterial pressure was made on the oscilloscope with frequent intermittent recording of EEG, ECG, arterial and venous pressures on the four channel paper. Regular sampling of urine and blood specimens at 10 minute intervals was made throughout the whole experiment, during partial bypass and complete bypass as well as during a period of recovery after the dog was taken off the pump. Four experiments have been done. Glomerular filtration rate measured by creatinine clearance was the same as the control during the whole 140 minutes, except during cardiac manipulation when it decreased slightly. Renal plasma flow measured by PAH showed greater variation. Renal plasma flow decreased during cardiac manipulation to 45-52 ml./minute. Once the pump started, the renal plasma flow recovered rapidly to 90-98 ml./minute, which was approximately 30 per cent greater than the control value. During complete bypass, glomerular filtration rate remained constant, renal plasma flow gradually diminished, but still remained above the control level. In conclusion, our experiments on dogs indicated that during cardiopulmonary bypass there were no deleterious effects on the kidney as indicated by changes in the glomerular filtration rate or renal plasma flow.

**Respiratory Chemosensitivity of the Area Postrema in the Fourth Ventricle.** WALTER H. MASSION, M.D., ROBERT A. MITCHELL, M.D., AND JOHN W. SEVERINGHAUS, M.D.,

*Cardiovascular Research Institute, University of California Medical Center, San Francisco, California.* Loeschcke and associates have described a superficial pH 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 ventricle with a mock spinal fluid of known  $P_{CO_2}$  and pH 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<sup>-</sup>. 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, phenylidguanidine 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 pH 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 pH values to the isolated area postrema has failed to give ventilation responses. Therefore, the pharmacological trigger zone is not necessarily identical with the pH sensitive receptor. [Supported in part by USPHS Graduate Training Grant 2C-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 herniorrhaphy under nitrous oxide oxygen ether anesthesia. Results of the 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