were normovolemic with a hematocrit ranging between 37–43 per cent. Nine were hypovolemic with a deficit varying between 12–26 per cent from normal values, hematocrit values ranging between 30–45 per cent. Chromium-51 labeled red cells were injected to determine the control blood volume. Blood pressure was raised 30 per cent above resting level with norepinephrine (4 mg./1,000 ml. fluid) later followed by Angiotensin II, (2.5 mg./1,000 ml. fluid). Blood samples were analyzed for rate of radioactivity, hematocrit, and relative viscosity to normal saline solution. Venous pressure was monitored continuously using a water manometer attached to a cannula inserted in the median cephalic vein. *Results:* Norepinephrine caused an average loss of 11.2 per cent of circulating plasma volume, a rise in hematocrit of 2.3 points and an increase in viscosity 2.6 points, in the normovolemic group. The time for equilibration of labeled red cells was prolonged from 4.8 minutes to 5.9 minutes. In the hypovolemic group, the loss of plasma volume was 7.6 per cent, the hematocrit increased 3.2 points and viscosity increased 2.9 points. Equilibration time increased from an average of 4.5 minutes to 5.25 minutes. Protein and osmolality studies indicated a loss of intravascular fluid. In the normovolemic group, angiotensin II increased plasma volume by 3.1 per cent. The hematocrit dropped 1.5 points, and the viscosity dropped 2 points. The time for equilibration of labeled red cells decreased by 1.2 minutes, hematocrit decreased by 0.5 points, viscosity showed no apparent change. No apparent change in mixing time occurred. Protein and osmolality studies indicated an increase in intravascular fluid volume with dilution. The rise in blood pressure and venous pressure was equal in rate in both series; the only difference noted was the rate of return to normal levels after stopping the infusion. With norepinephrine, the fall was rapid with a rebound effect. With angiotensin II, it was slow and gradual, lasting three to four minutes with no rebound phenomenon. *Conclusions:* From these observations, one may infer that angiotensin II tends to increase plasma volume either by augmenting renal reabsorption or changes in dynamics of fluid transfer at the capillary level. It would, therefore, be the pressor agent of choice in hypovolemic states.

**Preanesthetic Drug Evaluation with the Galvanic Skin Response.** RAYMOND D. STONEBACK, Capt., MC, HAROLD RUDMAN, Capt., MC, WALTER L. LUMPKIN, Col., MC, *Brooke General Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas.* *Methods:* The Galvanic Skin Response (GSR) was utilized to evaluate the effect of premedication drugs in relieving apprehension and anxiety in preoperative patients. The GSR is mediated efferently by post ganglionic sympathetic cholinergic fibers which innervate the sweat glands. The responses elicited are attributed to electrolyte shifts across the semipermeable cell membrane of the sweat glands and may provide an evaluation of preoperative anxiety by measuring the sympathetic activity in surgical patients. The patients studied were seen and physically evaluated the day before operation. They were told that further evaluation would be done the following morning before going to the operating room. The purpose of the study was fully explained so the patient need not worry about the test itself. The GSR was measured on a Gilson EEG-ECG two-channel direct ink writer. Standard ECG electrodes were used for transmission of impulses. One electrode was placed over the thenar eminence, one on the posterior aspect of the hand and the third, a ground electrode, on the anterior forearm. At a paper speed of 2.5 mm. per second with standardization of one centimeter per millivolt, a vivid, biphasic GSR curve was obtained on the ECG paper. Stimulation of the GSR was accomplished by verbal stimuli from a tape recorder. The tape contains twenty words at fifteen-second intervals. Each word was repeated twice at random; thus each patient was exposed to forty stimuli. Ten of the words were so called "loaded" (pain, spinal, etc.) and ten were "benign" (blue, sky, etc.). The patient heard the words through an earphone to reduce external stimuli and reduce variables. The morning of operation the apparatus was set up and the patient rassured. He was reminded to relax, close his eyes and not to move since muscle movements produce artifacts on the GSR recording. The tape was played and the control GSR recorded. Upon

completion of the tape, intravenous premedication was given, through a previously started glucose and water infusion, according to patient's weight and according to the drugs being studied. Ten minutes later the same tape was played and the experimental GSR recorded. Pre- and postmedication responses were measured from the tracing. A positive response is empirically one greater than 0.15 millivolts (1.5 MM). After medication some or all of the previously positive responses would be negative; less than 0.15 millivolts (1.5 MM). Each patient's responses were then subjected to a chi squared analysis as well as a chi squared analysis of each group in a specific drug study. *Results:* In our preliminary studies of 40 patients, 20 given morphine and 20 meperidine, there was a statistical significant difference between the two groups' responses. Morphine produced depression of the GSR from 215 positive responses before medication to 86 responses after, while with meperidine there were 144 positive responses after medication compared to the 188 before medication. Thus meperidine did not depress the GSR to the same extent as morphine did.

**The Effect of Adrenergic Blocking Agents on the Hepatic Toxicity of Halothane in Mice.** ROBERT B. SWEET, M.D., and GERALD L. BRODY, M.D., *The University of Michigan Medical School, Ann Arbor, Michigan.* Hepatotoxic agents would appear to have two primary mechanisms for the production of liver damage: (1) the direct, in which the drug itself attacks the hepatic cell producing physical changes which in turn interrupt the vital functions of the cell, and (2) the indirect, where the drug produces a disturbance of cellular function through interruption of the normal blood supply or source of oxygen to the cell. Calvert and Brody: (Amer. J. Physiol. *198:* 669, 190) proposed an hypothesis which suggested that the liver cellular changes seen after carbon tetrachloride administration were the result of anoxia produced by the stimulation of the sympathetic nerves causing constriction of the blood vessels of the liver. Jones, Margolis and Stephen: (ANESTHESIOLOGY *19:* 715, 1958) using the hand feeding of mice technique of Morris and Thompson were able to develop a laboratory screening method for the evaluation of the relative hepatotoxicity of several anesthetic agents. Using this method of esophageal installation of a mixture of 50 per cent halothane and 50 per cent peanut oil, we were able to produce a fairly consistent pathological change in the liver of mice. *Method:* White mice weighing approximately 20 g., sexes mixed, were utilized. Ten mice were fed 0.2 ml. of peanut oil; 20 mice were fed 0.2 ml. of a mixture of 50 per cent peanut oil and 50 per cent halothane; 36 mice were fed 0.2 ml. of a mixture of 50 per cent peanut oil and 50 per cent halothane shortly after an intramuscular dose of 5 mg./kg. of phenoxybenzamine (Dibenzyline); 16 mice were fed 0.2 ml. of a mixture of 50 per cent peanut oil and 50 per cent halothane after an intramuscular dose of 4.4 mg./kg. of diphenhydramine (Benadryl). Seventy-two hours after esophageal installation of the drugs, the mice were sacrificed and the livers were placed in Formalin, sent to the pathologist for staining and examination without his knowledge as to the specific pretreatment of the mice involved. *Results:* The 10 mice fed 0.2 ml. of peanut oil showed no pathological hepatic changes. All of the mice fed 0.2 ml. of the mixture of 50 per cent halothane and 50 per cent peanut oil showed hepatic fatty changes varying from mild diffuse lipidic deposits to very severe, almost panlobular lipidic degeneration without evidence of cellular necrosis. The 16 mice given intramuscular diphenhydramine prior to the halothane-peanut oil mixture were found in 72 hours to have no hepatic fatty infiltration. Of the 36 mice receiving intramuscular phenoxybenzamine prior to the esophageal installation of the 50 per cent halothane—50 per cent peanut oil, were found to have positive hepatic changes and 14 were found to have normal livers. *Conclusion:* This would suggest that diphenhydramine and the ganglionic blocking agent, phenoxybenamine, provided a protective influence over the livers of the mice against the fatty infiltration seen following intragastric halothane, and tends to support the theory of Calvert and Brody that the blocking agents may prevent epinephrine and norepinephrine from constricting the hepatic vessels and the resulting anoxia.