

The Use of the Psychogalvanic Reflex in the Evaluation of Drugs for Premedication. FREDERICK A. CARPENTER, M.D., JOHN E. STEINHAUS, M.D., and CLINTON C. McCORD, B.S., *Grady Memorial Hospital, Emory University School of Medicine, Atlanta, Georgia.* In an effort to minimize the subjective error inherent in the determination of the sedative effects of preanesthetic agents, we have utilized two methods during the past two years. The first method consisted of a series of rating scales employed by a single rater. The results of this double-blind study showed significant differences in the drugs investigated. Although these results were statistically valid, it would be necessary to use different raters to verify these findings, markedly increasing the complexity of the study. It was thought that a more accurate and concise method might be the use of the Psychogalvanic Reflex (PGR, GSR, or SGR) which is particularly sensitive to external stimulation, especially to the general arousal level. Consequently, it reveals anxieties otherwise hidden from simple questioning. Much research has been done with the PGR concerning emotional states under various stress conditions, and it is known that certain drugs depress the PGR response. These findings suggested that this technique might be adapted to a study of drugs which relieve anxiety. A 5×5 Latin Square experimental design was used to evaluate the effects of four drugs and a placebo on the PGR. Five volunteers (medical students) received standardized intramuscular injections on five separate days over a period of five weeks. The drugs were randomized and given on a weight basis by the double-blind technique. Continuous skin resistance was recorded for 75 minutes divided into five 15-minute intervals; the first 15-minute interval served as a control. Within each 15-minute cell, the subject was stimulated with three standardized flashes of light presented to the subject at random. Mean changes of the absolute resistance in each cell were calculated and analysis variance was performed. The analysis shows that hydroxyzine markedly depressed the change in skin resistance produced by the PGR and these differences were significant to the 1 per cent level of confidence when compared to the placebo effect. Promethazine resulted in

changes suggestive of a depressant effect on the PGR. Pentobarbital caused an increase in skin resistance apparently augmenting the PGR. The changes produced by meperidine showed some correlation to PGR depression but this was not statistically significant. Previous studies using rating scales and a large sample produced results similar to those of the PGR study in that the analysis showed statistical significance to the 1 per cent level of confidence for the two tranquilizers. Whereas pentobarbital showed no statistically significant difference from the placebo. The possibility of peripheral autonomic actions of these drugs must be considered. In addition, the relation of skin resistance changes and "anti-anxiety" effects must be further elaborated. With continued refinements there is promise that the PGR may be of value in screening the "anti-anxiety" type of agents and, in addition, demonstrate the onset and duration of action of these agents.

Spontaneous Readjustments in Acid-Base Balance at the Termination of Prolonged Hyperventilation. JAMES A. CUTTER, M.D., and BENTON D. KING, M.D., *University of Buffalo School of Medicine and the Edward J. Meyer Memorial Hospital, Buffalo, New York.* Respiratory alkalosis in an anesthetized man has been the subject of clinical and experimental investigation for many years, but until recently relatively few studies have been made on the effects of hyperventilation during anesthesia. Because hyperventilation appears to be a clinically useful adjunct to anesthesia, an extensive investigation of passive hyperventilation has been initiated. This report presents the methods used and preliminary observations made in one of the areas under study: the acid-base alterations which occur in anesthetized man during steady state of profound, passive hyperventilation and during the recovery periods. Throughout the initial phase of this study, ether was used as the sole agent following induction and intubation using thiopental and succinylcholine. A demand oxygen valve was used with an E.M.C. vaporizer to supply the three or four volumes per cent ether vapor employed. Respiratory rates between 30 and 40 per minute with tidal volumes between 500 and 700 cc. were pro-

duced by a Jefferson Ventilator equipped with a modified nonrebreathing head which permitted the high gas flows required. Respiratory volumes of three to six times normal resting values were produced. Brachial artery blood samples were analyzed for P_{CO_2} and pH within two minutes after being drawn in order to avoid the unpredictable errors introduced by preservatives, refrigeration, etc. This speed was made possible by the use of a Severinghaus P_{CO_2} electrode and an anaerobic glass pH electrode system contained in a thermostated water bath. A method employing an electrometer tube amplifier was devised for rapid, direct readings of the P_{CO_2} from a meter calibrated in mm. Hg and the pH from a meter calibrated in appropriate units. In the group of 10 patients included in this preliminary report, preanesthesia arterial P_{CO_2} values ranging from 38 to 44 mm. Hg were reduced to levels between 10 and 20 mm. Hg for periods of 2 to 7 hours of hyperventilation. pH values ranging from 7.42 to 7.46 in the control period were elevated as high as 7.83. Rapid falls of P_{CO_2} and rises of pH were typically seen in the first 15 to 30 minutes of hyperventilation, following which plateau values were maintained with relatively little change during the remainder of hyperventilation. Spontaneous respirations were found to return rapidly upon discontinuing controlled respirations, usually within the first minute. In contrast with classic physiologic concepts, arterial carbon dioxide tensions taken at the time of resumption of breathing showed values of less than 30 mm. Hg. Two distinct phases were usually observed following the termination of hyperventilation. P_{CO_2} values showed a rise during the first 15 minutes to values approaching controls, followed by slight falls and gradual returns to normal. pH values during the first 15 minutes of spontaneous respiration showed marked falls to acidotic levels far below control values, followed by gradual returns to normal over periods of several hours. [This study was supported in part by the U. S. Public Health Service, N.I.H. Grant RG-5882.]

Effects of Halothane on Liver in Protein-Deficient Mice. HAMILTON S. DAVIS, M.D., DONALD D. LEONARD, M.D., AND VINCENT E. QUITMEYER, M.D., *Department of Anesthesi-*

ology, University Hospitals of Cleveland, Western Reserve University Medical School, Cleveland, Ohio. This preliminary study was undertaken to determine the effect of halothane on the livers of mice on normal and low protein diets. There have been reports indicating a benign effect of halothane on the liver of man (Johnstone, M.: *Brit. J. Anaesth.* 28: 392, 1956; Brindle, G. F., and others: *Canad. Anaesth. Soc. J.* 4: 265, 1957; Stephen, C. R., and others: *Anesthesiology* 19: 197, 1958; Virtue, R. W., and others: *Anesthesiology* 19: 478, 1958; Little, D. M., Jr., and others: *Surg. Gynec. & Obstet.*: 107: 712, 1958; Visser, E. R., and Tarrow, A. B.: *Anesth. & Analg.* 38: 301, 1959; and New and Non-Official Drugs, J. A. M. A., 170: 1811, 1959) and experimental animals (Virtue, R. W., and others: *Anesthesiology* 19: 478, 1958; Raventos, J.: *Brit. J. Pharmacol.* 11: 394, 1956; Krantz, J. C., Jr., and others: *Anesthesiology* 19: 38, 1958; and Gibson, J. A.: *Canad. Anaesth. Soc. J.*, 6: 148, 1959), while other reports in animals have indicated pathological changes in the form of massive fatty infiltration (Jones, W. M., and others: *Anesthesiology* 19: 715, 1958) and centrolobular fatty alteration and scattered necrosis (Stephen, C. R., and others: *Anesthesiology* 19: 770, 1958). At least one presumptive case of severe halothane liver damage has been reported in man (Virtue, R. W., and Payne, K. W.: *Anesthesiology* 19: 562, 1958). Two hundred thirty-five white male Swiss mice, 20-25 grams weight, in good condition and acclimatized at least one week, were studied. Three groups were included: Group A. Ninety mice on regular diet; 10 served as controls, 40 were anesthetized with halothane 1 per cent in air for 45 minutes, and 40 with halothane 1 per cent in oxygen for 45 minutes. Test animals were sacrificed on the second, fifth and tenth postanesthetic days. Group B. Fifteen mice on regular diet; 5 served as controls and 10 were anesthetized with halothane 1 per cent in oxygen for 45 minutes every other day for 5 exposures, then sacrificed two days post-anesthesia. Group C. One hundred thirty mice on low (8%) protein diet. There were three subgroups. Subgroup 1: Fifty animals, 10 serving as controls, were on diet alone. Batches of 10 were sacrificed weekly for five weeks. Subgroup 2: Forty-five