

**Comparative Respiratory Effects of Commonly Used Hypnotic and Analgesic Drugs in the Young and in the Aged.** YOSHIO KUROSU, M.D., AND ARTHUR S. KEATS, M.D. *Division of Anesthesiology, Baylor University College of Medicine and Jefferson Davis Hospital, Houston, Texas.* It is generally assumed that old people are more sensitive than young people to the respiratory effects of hypnotic and analgesic drugs. This study was undertaken to test the validity of this assumption, since little data can be mobilized in its support. The subjects in the aged group were 14 hospitalized patients between the ages of seventy and seventy-nine years who were free from cardiopulmonary disease by both physical and X-ray examinations, and who appeared to be their ages. For comparison, 5 healthy subjects between twenty and thirty years of age were studied. The respiratory response to 3 concentrations of carbon dioxide in oxygen were measured in all subjects before and at one and three hours following drug administration. Minute volume, respiratory rate, and alveolar carbon dioxide tension were recorded (Keats, A. S., Telford, J., and Kurosu, Y., *Anesthesiology*, 18: 690, 1957). The following drugs were studied: morphine 10 mg., meperidine 50 mg., pentobarbital 100 mg., and saline (placebo) 2 cc., all given intramuscularly per 70 kg. of body weight; chloral hydrate 1.0 Gm. and pentobarbital 100 mg. by mouth per subject. All 5 subjects received all 6 drugs. Each subject in the aged group received 2-3 drugs only. For each subject respiratory stimulus (alveolar carbon dioxide tension)-response (alveolar ventilation) curve was plotted. The displacement of this response curve from predrug control at alveolar ventilation of 8.5 l./minute was used as the quantitative index of degree of respiratory depression. The respiratory depression which followed pentobarbital both intramuscularly and by mouth in both groups was not significantly greater than that of the placebo; however, chloral hydrate depressed respiration to a significant degree in both groups. Morphine 10 mg. and meperidine 50 mg. were potent respiratory depressants in both groups, with morphine producing the greater depression. With all drugs studied, respiratory depression in the old people was greater than

in the young and drug effects persisted longer. However, the difference between the two groups was small and not statistically significant for any drug. Pentobarbital by both intramuscular and oral administration in the elderly patients produced the least respiratory depression among the drugs studied. No marked differences were noted between the young and old in the degree of sedation produced by these drugs in these doses.

**Cardio-circulatory Effects of Muscle Relaxants During Cyclopropane Anesthesia in Man.** T. H. LI, M.D., AND BENJAMIN ETSTEN, M.D. *Department of Anesthesiology, New England Center Hospital and Department of Surgery (Anesthesiology), Tufts University School of Medicine, Boston, Mass.* The purpose of this study was to compare the cardio-hemodynamic effects of *d*-tubocurarine and succinylcholine during cyclopropane anesthesia in man. Twelve patients without discernible cardio-pulmonary disease were divided into two equal groups and studied for the effects of: (A) *d*-tubocurarine and (B) succinylcholine. The patients were given premedication consisting of pentobarbital (1 mg./kg.) and scopolamine (0.006 mg./kg.) and anesthesia was induced with cyclopropane followed by tracheal intubation. Anesthesia was maintained at EEG level 3 with blood cyclopropane of 10-15 mg. per cent. Ventilation was automatically controlled by means of a displacement piston incorporated with the Etsten Ventilator to maintain the arterial pH,  $p\text{CO}_2$ , and  $\text{O}_2$  saturation within normal levels. In each experiment airway pressure, arterial blood pressure, EEG and ECG were simultaneously and continuously recorded on a Sanborn multi-channel model-150 oscillograph. Cardiac output was determined by the dye dilution method and stroke volume, mean circulation time and total peripheral resistance were calculated according to conventional formulas. Arterial pH (Cambridge Electron Ray pH meter-research model).  $\text{CO}_2$ ,  $\text{O}_2$  capacity and  $\text{O}_2$  content (Van Slyke manometric apparatus) were determined. Control observations were made after a steady state (pH 7.40 and arterial  $p\text{CO}_2$  from 36 to 44 mm. of mercury) was obtained during cyclopropane anesthesia. In group A observations were obtained at 15

and 45-minute intervals after the intravenous injection of 0.6 mg./kg. of *d*-tubocurarine. The average fall in mean arterial blood pressure at the 15- and 45-minute intervals was 11 and 13 per cent respectively. However, immediately after the injection of *d*-tubocurarine, mean arterial blood pressure fell to an average of 16 per cent (range - 8 to - 28). The duration of this change varied from 10 to 90 minutes. In all instances blood pressure returned to control levels. The average cardiac output and stroke volume fell 15 per cent during the 15- and 45-minute intervals, but there were no significant changes in heart rate and total peripheral resistance. In group B during the continuous intravenous infusion of 0.2 per cent solution of succinylcholine (8 mg. per minute), the determinations were repeated at similar time intervals. Mean arterial blood pressure fell 12 per cent (range: 3 to 16 per cent) within one to 6 minutes. Immediately following this transient fall, mean arterial blood pressure gradually increased to an average of 14 per cent above the control level (range: + 9 to + 35 per cent). The duration of this increase varied from 4 to 20 minutes. Cardiac output was unchanged at the 15-minute interval and was decreased 14 per cent at the 45-minute interval (range: + 7 to - 42 per cent). The reduction of the stroke volume paralleled the decrease of cardiac output while heart rate and mean circulation time remained unchanged. Total peripheral resistance was increased 18 per cent at the 15-minute interval and 28 per cent at the 45-minute interval. The results indicate that the reduction of cardiac output following the administration of *d*-tubocurarine is primarily due to reduction of stroke volume. The fall of blood pressure can be related to diminished cardiac output since there was no significant change in the total peripheral resistance. The cause for the transient drop of mean arterial blood pressure during succinylcholine infusion is obscure. Although cardiac output was reduced, there was a subsequent rise in mean arterial blood pressure which can be attributed to the increase in total peripheral resistance. It is of interest to note that reduction of stroke volume appears to be the primary cause for the decrease in cardiac output with both drugs. Further study on the mecha-

nisms of these changes is in progress. (*Supported by a grant from the U. S. Public Health Service No. H-1711 C5.*)

**Measurement of Electrical and Mechanical Events of the Cardiac Cycle During Cyclopropane Anesthesia.** DAVID M. LITTLE, JR., M.D., AND JAMES B. GIVEN, M.D. *Department of Anesthesiology, Hartford Hospital, Hartford, Conn.* Most previous observations of the effect of cyclopropane anesthesia on cardiac activity have been concerned primarily with two aspects of cardiac activity, output and rhythm. The present study was designed to investigate some of the other effects of cyclopropane anesthesia upon the heart by measuring the relationship between certain of the electrical and mechanical events of the cardiac cycle. Simultaneous records of the electrocardiogram and the phonocardiogram, and of the electrocardiogram and the carotid pulse tracing, were obtained on a Sanborn Twin-beam photographic recorder. The following time intervals were then measured from the recordings: (1) Q wave to first tone (electrical ventricular systole); (2) first tone to second tone (mechanical ventricular systole); (3) first tone to carotid pulse rise (approximate isometric contraction period); (4) Q wave to carotid pulse rise (indirect isometric contraction period); and (5) R to R' interval (heart rate). Control records were taken on 10 normal, healthy female patients following premedication for pelvic surgery, and repeat records were taken towards the end of operation under cyclopropane anesthesia. Cyclopropane was administered by the closed circle, carbon dioxide absorption technique with controlled and/or assisted respiration, and anesthesia was monitored electroencephalographically to maintain pattern four as described by Possati and coworkers. Arterial blood samples were drawn at the time that the cardiac cycle records were taken during cyclopropane anesthesia, and were analyzed for pH,  $p\text{CO}_2$ ,  $\text{O}_2$  content and hematocrit. The mean arithmetic average of the Q wave to first tone interval during the control period was 0.062 seconds, while the average for this same interval during cyclopropane anesthesia was 0.069 seconds. The difference between these two figures is not statistically significant. The total duration of