safely depressed to $V = 1$ by infusion of base, since $V = 1$ suffices for normal oxygenation. In principle, the permissible rate of administration can be calculated. [Supported by Grant No. RG-9069 USPHS.]

**Cardiopulmonary Resuscitation: A Laboratory Evaluation.** LEROY C. HARRIS, JR., M.D., HERBERT G. KUNKEL, M.D., and PETER SAFAR, M.D., *University of Pittsburgh School of Medicine and Presbyterian-University Hospital, Pittsburgh, Pennsylvania.* *Method and Results:* Controversial points of cardiopulmonary resuscitation, *i.e.*, intermittent positive pressure ventilation (IPPV) plus external cardiac compression (ECC) were evaluated in 31 anesthetized dogs with ventricular fibrillation (produced by electric shock), utilizing standardized experimental protocols. Sternal pressures, 60 per minute, were kept regular and constant by the use of a Beck-Rand machine. All lung inflations were kept constant (15 ml./kg.; air), produced by compression of a Ruben bag or a piston respirator synchronized with the Beck-Rand machine. It has been shown that ECC alone can not be relied upon to ventilate the lungs adequately (Dis. Chest *41:* 1, 1962). *Coordination of IPPV and ECC:* (1) One lung inflation interposed after each two sternal compressions was compared with one lung inflation simultaneous with every second sternal compression. Carotid blood flows were higher with simultaneous than with interposed lung inflations in 7/15 observations, the same in 5/15, and lower in 3/15. Arterial oxygen saturations remained normal (85 to 97 per cent) with interposed inflations, but dropped to an average of 65 per cent with simultaneous inflations. The progressive drop in arterial *p*H during ECC was less during interposed inflations. (2) Oxygenation with IPPV/ECC ratios of 3/15 and 6/30: During 3/15 ratios, the arterial $O_2$ saturation was maintained at control levels. During 6/30 ratios, the arterial $O_2$ saturation dropped to an average of 74 per cent at the end of 30 seconds without ventilation. Arterial *p*H and $P_{CO_2}$ values remained closer to control levels with the 3/15 than with the 6/30 ratio. These data support our clinical recommendation to use the 3/15 ratio, at least in the nonintubated patient, where frequent interposing is difficult and brief interruptions of ECC for inflation allow recognition of airway patency. *Augmentation of Blood Flows during ECC by Pressure over the Abdomen:* Continuous pressure over the abdomen increased the artificial carotid blood flows during ECC by 25 to 50 per cent in 17/18 comparisons. This was not due to aortic compression, since both the carotid and femoral arterial pressures increased. (3) *Epinephrine and Norepinephrine during ECC:* Intravenous injections of epinephrine (0.25 mg., 0.5 mg.) given during ECC increased the artificial aortic pressures in all observations. Carotid flows did not increase in 9/14 observations and increased only minimally in 5/14. After defibrillation, intravenous epinephrine always significantly increased spontaneous aortic flows and pressures. Intravenous norepinephrine gave similar results. Subcutaneous injections of epinephrine 2 mg. given over the sternum never increased blood flows or pressures significantly in 20 minute observations. *Blood Volume Expanders during ECC:* Dextran, 25 per cent of estimated blood volume, given intravenously within five minutes to normovolemic dogs, increased the artificial carotid blood flows by 15 to 80 per cent in 7/10 and increased the arterial pressures slightly in 8/10 observations. Blood flows were more improved by intravenous dextran than by intravenous epinephrine.

**Measurement of Bronchomotor Tone in Man.** LAMAR P. JACKSON, M.D., and ARTHUR S. KEATS, M.D., *Division of Anesthesiology, Baylor University College of Medicine and Jefferson Davis Hospital, Houston, Texas.* Our knowledge of the action of many commonly-used anesthetic agents and adjuvants (such as narcotics and barbiturates) upon the bronchial musculature of man is tenuous. The literature revealed that many of our operational concepts regarding these actions are derived solely from *in vitro* or animal studies. These results may not represent the pharmacological actions *in vivo* and, more particularly, in man. The paucity of information seems to result from the lack of a quantitative, yet simple, method of measuring changes in bronchomotor tone in man. We have adapted a method used in dogs by Harasawa and Rodbard (J. Pharma-

col. Exp. Ther. *133:* 246, 1961) which is accurate and simple. *Method:* Unpremedicated, healthy adults requiring anesthesia were the subjects, prior to surgical intervention. After nitrogen washout with oxygen at high flow rates for five minutes, anesthesia was induced with 100 per cent $N_2O$. Endotracheal intubation was accomplished immediately after induction of anesthesia and the administration of 40 mg. of succinylcholine intravenously. Anesthesia was maintained with 50 per cent $N_2O$ in $O_2$ with a continuous 0.2 per cent succinylcholine infusion to produce complete muscle paralysis. Respiration was controlled with a calibrated pressure-cycled Takaoka respirator. After five minutes of automatic ventilation to provide a steady state of anesthesia and paralysis, the cycling rate of the respirator was measured as the control value. The intratracheal pressures at which cycling occurred varied between 2.5 and 5.0 cm. of water. The cycling pressure was adjusted in the control period to that which would produce an end-expiratory $P_{CO_2}$ of approximately 40 mm. of mercury, since alterations in $P_{CO_2}$ itself can produce changes in bronchomotor tone. The drug to be studied was injected intravenously and 30 seconds allowed for circulation and distribution. The respirator-cycling rate was continuously measured until a stable level was achieved (within ten minutes). Cycling rate per minute was calculated and peak change from control value (expressed in percentage) was considered the quantitative expression of change in bronchomotor tone through alteration in tracheobronchial resistance. *Results:* Measurements were made on 26 patients using histamine sulphate (0.002 mg. kg. to 0.016 mg./kg.) given intravenously. From these data, a standard dose-response curve for histamine was constructed and expressed by the equation: $Y = 422 \log X - 292$ where $X$ is mg./kg. $\times 10^{-3}$ of histamine and $Y$ is peak percentage increase in cycling rate. The histamine curve represented the standard against which the bronchomotor effect of other drugs was to be compared. Twenty-one healthy adults (ages 18–54 years) were then given morphine intravenously in doses of 2.5 to 40 mg. under similar conditions. The change in cycling rate following morphine ranged from no change at 2.5 mg. to 22 per cent increase in peak rate at 40 mg. dose. The dose response curve for morphine had a smaller slope and was displaced to the right compared to the histamine curve. The bronchoconstrictor action of morphine can be considered mild. (Studies are in progress with meperidine. To date each of five patients has received 75 mg. of meperidine. The peak increase in cycling rate averaged 7.8 per cent.)

**Atrial Activity During Halothane Anesthesia in Man.** MYRON B. LAVER, M.D., and HERMAN TURNDORF, M.D., *Anesthesia Laboratory, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts.* The importance of sequential atrioventricular contraction for proper ventricular performance, and adequate atrioventricular valve closure, has never been demonstrated satisfactorily in normal man. Recently, we were able to alter the sequence of atrioventricular activity during operation in patients anesthetized with halothane. The following combination of conditions was found effective in producing this change: (1) halothane-oxygen anesthesia utilizing an average inspired concentration of 0.5 per cent halothane; (2) controlled ventilation following muscle paralysis with *d*-tubocurarine; and (3) an exogenous stimulus, most conveniently supplied by the onset of surgery. The onset of atrioventricular dissociation is characterized by a rapid diminution in the P-R interval with the P-wave moving into the QRS complex. Fusion of the two complexes is associated with an immediate fall in arterial blood pressure and a rise in central venous pressure, while the heart rate shows no significant changes. The hemodynamic significance of this alteration was demonstrated in ten patients, ages 40 to 63, undergoing operation with halothane-oxygen anesthesia and whole-body hypothermia by surface cooling. The following parameters were monitored: intra-arterial blood pressure, central venous pressure (superior vena cava or right atrium) esophageal and standard limb lead 2 of the electrocardiogram, airway pressure and blood gases with modified Clark and Severinghaus electrodes. Transition from sinus to nodal rhythm was associated with the following changes: fall in systolic pressure averaging $17.1 \pm 4.75$ per cent ($22.6 \pm 9.25$ mm. of mercury), rise