

variation, occurring more frequently after exposure during the day than during the night (8.0 per cent v. 1.9 per cent, $P < 0.001$). Incidences of vertebral and rib anomalies also show diurnal variation but at lower levels of significance, $P < 0.05$ for both. These findings are relevant to Matthews' work on periodicity analysis in mice (*Toxicity of Anesthetics*, ed. B. R. Fink, Williams and Wilkins, in press). The sex distribution in the halothane groups showed the normal preponderance of males, 54 per cent, while the starvation group showed a decrease in the proportion to 49 per cent. The significance of this difference is of low order ($P = 0.15$). It appears that halothane does have some teratogenic activity in rats. Comparison of these data with those from the study of nitrous oxide indicates that the abnormalities observed are strikingly similar both qualitatively and quantitatively, and suggests that the insult is inversely related to the duration of exposure during a susceptible period. It also raises the possibility that teratogenicity may be characteristic of anesthetic agents generally rather than being an isolated effect of a specific agent. Starvation and dehydration appear to contribute to the occurrence of malformations, but they do not account for the whole picture.

The Circle Semi-closed System Control of P_{aCO_2} by Inflow Rates of Anesthetic Gases and Hyperventilation. DONALD W. BENSON, M.D., Ph.D., THOMAS D. GRAFF, M.D., H. H. HURT, JR., M.D. and H. S. LIM, M.D., *The Johns Hopkins University School of Medicine, Baltimore, Md.* To investigate the semi-closed circle system incorporating mechanical ventilation and to ascertain the feasibility of eliminating carbon dioxide by means other than chemical absorption, the following studies were carried out with a conventional anesthesia apparatus. **Methods:** Utilizing directional valves in the chimney piece and a Ventilation/Ventimeter (Air-Shields) connected into the circuit at the rebreathing bag port, nitrous oxide, oxygen and halothane anesthesia was administered to a series of patients. The total capacity of this system excluding the patient was 8 liters and of this there was a total mixing space of 5.86 liters. The gas inflow

rates and minute ventilation were calculated in milliliters per pound body weight per minute. Ventilation was measured with a Wright Ventilometer. Respirations were controlled throughout. Ventilation and gas inflow rates were then varied at 20-40 minute intervals to secure a representative plot of P_{aCO_2} gas inflow rate and ventilation. At these same intervals arterial blood samples were obtained for measurement of P_{aCO_2} , pH, and standard bicarbonate. The flow rates were classified in four groups: I—no flow to 20 ml./lb. body weight per minute, II—20 to 40 ml./lb.; III—40 to 100 ml./lb.; IV—100 ml./lb. or more. The minute volumes were grouped in the same manner: I—30-50 ml./min. lb. body weight (average 6.5 l., 17 determinations); II—60-90 ml. (average 11.2 l., 35 determinations); III—90-120 ml. (average 16 l., 20 determinations); and IV—120-150 ml. (average 20 l., 22 determinations). **Results:** Equilibration of CO_2 production and loss from the system as indicated by a stable arterial P_{CO_2} occurred at approximately 40 minutes. It was apparent that both minute volume and gas inflow rates were important for CO_2 homeostasis. A P_{CO_2} of 40 mm. Hg or below could be maintained with a minute ventilation of 90 to 120 ml./lb./min. and an inflow rate of 40 ml./lb./min. If the ventilation were raised to 120-150 ml./lb./min. or an average of 20 l. per min. a P_{CO_2} of 40 or below could be obtained with only 33 ml./min./lb. of gas inflow. Conversely, with inflow rates of 20 to 40 ml./lb./min. any ventilation greater than 110 ml./lb./min. resulted in a P_{CO_2} below 40. An inflow rate of 50 ml./lb./min. and a minute volume of 100 ml./lb./min. uniformly resulted in a P_{CO_2} below 40. **Conclusion:** It is our impression at this stage of the study that satisfactory CO_2 elimination can be obtained consistently without chemical absorption by utilizing gas inflow rates totalling 50 ml./lb./min. and a ventilation of 100 ml./lb./min.

Effects of Anesthesia and Operation upon Respiratory Flow-Volume Loops. KALMAN J. BERENYI, M.D., STANLEY W. WEITZNER, M.D., I-PING TANG, M.D. and MEREL H. HARMEL, M.D., *State University of New York-Downstate Medical Center, Brooklyn, N. Y.*

Hyatt and Fry (Hyatt, R. E., Schilder, D. P., and Fry, D. L.: *J. Appl. Physiol.* 13: 331, 1958; Fry, D. L., and Hyatt, R. E.: *Amer. J. Med.* 29: 672, 1960) described the characteristics of flow-volume loops, plotting flow and volume data against each other. Dery and Hendler (Dery, D. W., and Hendler, E.: *Engineering in Medicine and Biology. Proceedings of the 18th Annual Conference, Philadelphia, 1965*) used a Wedge spirometer, which generates separate electrical signals for flow and volume as the patient breathes, to produce respiratory flow-volume loops. Flow and volume signals are plotted on an XY recorder (EAI model 1100E Variplotter). Volume data are presented along the X axis, flow data along the Y axis. The portion of the loop below the zero flow line represents inspiration, the upper portion expiration. The flow-volume loop is recorded clockwise. After recording a tidal exchange loop the patient produces a maximal inspiration and exhales the air with maximal force. Analysis reveals that the expiratory portion of a flow-volume loop corresponding to the first $\frac{2}{3}$ of forced vital capacity depends on the breathing effort of the patient. The final part of the expiratory loop depends upon mechanical properties of the airway.

Our preliminary investigations (Weitzner, S. W., Berenyi, K. J., Harmel, M. H.: Unpublished data) with eighteen volunteers, using this method, prompted the present study. It is concerned with the applicability of flow-volume loops to the evaluation of changes in respiratory mechanics following light general anesthesia and minor surgery. *Method:* Ten female patients (mean age 37.6 years) and five male patients (mean age 28.2 years) without cardiopulmonary abnormalities were studied. The women underwent minor gynecological operations. The men had minor urological procedures. Premedication consisted of pentobarbital 100 mg., atropine sulfate 0.4 mg. intramuscularly one hour preoperatively. Anesthesia was induced with sodium thiopental (4 mg./kg. body weight). Halothane-nitrous oxide (4.0 l./min.) oxygen (2.0 l./min.) anesthesia was administered in a semi-closed system. Flow-volume loops were recorded as follows: control measurements were taken on the day before operation or be-

fore premedication. Loops were recorded immediately before induction of anesthesia, in the postoperative period as soon as the patient could cooperate, then at intervals of 30 minutes and 60 minutes. The flow-volume loops thus obtained yielded data about 1. tidal volume (V_t), 2. forced vital capacity (FVC), 3. maximal expiratory flow rate (MEFR), 4. maximal inspiratory flow rate (MIFR). *Results:* In the men the premedication caused lowering of V_t and MEFR (14.3 per cent and 11.7 per cent of control respectively), with no change in FVC and MIFR. In the women MEFR and MIFR decreased (10.5 per cent and 10.9 per cent of control, respectively), and FVC and V_t were unchanged after premedication. The first postoperative loops showed decreases of all parameters in women and of FVC, MIFR in men, with only insignificant changes in V_t and MEFR in men. Loops 30 and 60 minutes after operation showed gradual increases in all values toward control. However, V_t and MIFR in men, V_t , MEFR and MIFR in women did not return to control values completely. The portion of the loop significantly affected by this anesthesia sequence was that which is dependent upon respiratory effort. The change appeared commensurate with the level of anesthetic depression. The mechanical property-dependent portion of the loop was not influenced, which may be recorded. In order to study changes in airway caliber. Since the present technique for the production of flow-volume loops requires the subject's cooperation, only those effects of anesthesia upon respiratory mechanics which are present after consciousness returns indicate indirectly absence of significant change which may occur in respiratory mechanics in the unconscious patient under the influence of anesthetic drugs or procedures the technique must be altered so as to simulate a maximal voluntary inspiratory-expiratory effort. The next phase of our study will concern itself with this problem.

Effects of Different Respiratory Waveforms on Distribution of Inspired Gas During Artificial Ventilation. NORMAN A. BENGMAN, M.D., *Division of Anesthesiology, University of Utah College of Medicine and*