ported results—0.90 ± 0.04 per cent halothane, as compared with 0.87 per cent halothane reported by Eger *et al.* When the dogs were maximally hyperthyroid, MAC was 0.96 ± 0.10 per cent halothane; when they were hypothyroid, MAC was 0.84 ± 0.06 per cent halothane. (2) A tendency toward decreased oxygen consumption was noted as anesthesia was deepened from 1.1 MAC to 2.0 MAC. This tendency was most pronounced in the hyperthyroid animals. Per cent mean oxygen consumptions at 2.0 MAC as compared with those measured at 1.1 MAC were as follows: euthyroid, 93 ± 7 per cent; hypothyroid, 94 ± 4 per cent; and hyperthyroid, 85 ± 6 per cent. Of these comparisons, only the hyperthyroid metabolism was significantly ($0.05 > P > 0.01$) lowered by increasing depth. However, when all the studies were considered jointly, the decrease in mean oxygen consumption from 123.2 ± 27.5 ml./min./sq. m. at 1.1 MAC to 110.9 ± 22.4 ml./min./sq. m. at 2.0 MAC was highly significant ($P < 0.01$). *Conclusions:* (1) Although mean MAC values increase in proportion to metabolic rate, there is no significant difference between these means ($P > 0.05$). Moreover, even if a large series of animals did prove these differences significant, the change in MAC values is slight for so wide a range of metabolic activity. Thus, in dogs, there appears to be little or no correlation between metabolic state and halothane requirement. (2) This study reaffirms the concept that deepening of anesthesia decreases oxygen requirement, and suggests that such a decrease in oxygen requirement is most pronounced in hypermetabolic animals. (Supported by USPHS Grant 5 RO1 HE07946.)

Teratogenicity of Halothane in Rats. ALICE B. BASFORD, M.D., and B. RAYMOND FINK, M.D., *University of Washington School of Medicine, Seattle, Wash.* Recent work by Fink, Shepard, and Blandau (Nature *214:* 146, 1967) indicated that exposure of pregnant rats to nitrous oxide produced a significant incidence of abnormalities in the fetuses and prompted this study to determine whether halothane has similar potential. *Method:* Pregnant Sprague-Dawley rats were placed for 12 hours in boxes through which gases were run. Groups were exposed on day 6, 6½, 7, 7½, 8, 8½, 9, 9½, or 10 of their expected 21-day gestation. Experimental groups received 0.8 per cent halothane-25 per cent oxygen-74.2 per cent nitrogen, and were allowed food and water. Control groups received air but were deprived of food and water. (Experimental animals ate and drank little during the test period and continued to lose some weight for 24 hours thereafter.) Rats were sacrificed on day 20, the fetuses examined grossly, and resorptions noted. Fetuses were then prepared by the KOH-alizarin-glycerine technique for examination of the skeleton. About 90 fetuses were examined for each set of conditions. *Results and Conclusions:* The skeletal abnormalities observed were mostly of two types: separation of the normally fused ossification centers of lower thoracic and upper lumbar vertebral bodies, and the appearance of lumbar ribs or rib rudiments. Vertebral anomalies were seen more frequently following halothane than following starvation in all time periods from day 7 through 9½. The peak incidence, 54 per cent of fetuses, occurred at day 9. Significant differences between halothane and controls were seen at day 8 (48 per cent v. 29 per cent, $P < 0.05$), day 9½ (52 per cent v. 21 per cent, $P < 0.001$), and in the totals, all fetuses exposed to halothane on any day compared to all fetuses in starvation groups (42 per cent v. 34 per cent, $P < 0.05$). The peak incidence of lumbar ribs occurred at day 9½ with 70 per cent of fetuses affected. The incidence after halothane was greater than after starvation from day 8 through 10, the difference being significant on day 8 (29 per cent v. 6 per cent, $P < 0.001$), day 9½ (70 per cent v. 32 per cent, $P < 0.001$), day 10 (50 per cent v. 17 per cent, $P < 0.001$), and in totals (31 per cent. v. 20 per cent, $P < 0.001$). In gross appearance and weight, halothane-treated fetuses did not differ significantly from controls. Starvation on day 6 produced more resorptions than halothane (14 per cent v. 2 per cent, $P < 0.05$), while halothane produced more on day 9 (9 per cent v. 0 per cent, $P < 0.05$). The incidence of resorptions following halothane showed distinct diurnal

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 Pa_{CO_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 Pa_{CO_2} gas inflow rate and ventilation. At these same intervals arterial blood samples were obtained for measurement of Pa_{CO_2}, *p*H, 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.*