these apparently related to the anesthetic used. A more critical comparison of methoxyflurane and halothane was therefore initiated to evaluate their possible roles in the ventilatory response to severe hemorrhage. *Method:* 20 unpremedicated dogs of comparable weights were anesthetized lightly with thiopental, 2 per cent, sufficient to allow for endotracheal intubation and cannulation of femoral vessels (skin infiltrated with lidocaine, 1 per cent). After the dogs had wakened completely, while breathing room air, blood volume (T-1824), arterial *p*H, P_{O_2}, P_{CO_2}, respiratory rate and minute ventilation were measured. Anesthesia was then instituted with either halothane or methoxyflurane to equipotent levels, based on the principle of minimum alveolar anesthetic concentration (MAC), adding only oxygen as diluent flow. Once MAC was reached, arterial blood samples, as above, were taken, ventilatory response to CO_2 was measured by removing the soda lime from the breathing circuit and adding minute measured amounts of CO_2, and a response curve was constructed. The animals were then bled 50 per cent of their measured blood volume in graded fashion over a 30-minute period, and all measurements were repeated. *Results:* In the *halothane* experiment, mean values before bleeding were: $P_{O_2} = 477$ mm. Hg, $P_{CO_2} = 39.1$ mm. Hg, $pH = 7.31$, base deficit $= -6.1$ mEq./l., respiratory rate $= 20$/min. and minute ventilation $= 3.9$ l. Mean values after bleeding were: $P_{O_2} = 431$ mm. Hg, $P_{CO_2} = 34.5$ mm. Hg, $pH = 7.26$, base deficit $= -10.5$ mEq./l., respiratory rate $= 32$/min., minute ventilation $= 7.1$ l. In the methoxyflurane experiments, mean values before bleeding were: $P_{O_2} = 470$ mm. Hg, $P_{CO_2} = 32.3$ mm. Hg, $pH = 7.33$, base deficit $= -8.1$ mEq./l., respiratory rate $= 18$/min., minute ventilation $= 3.8$ l. Mean values after bleeding were: $P_{O_2} = 453$ mm. Hg, $P_{CO_2} = 40.0$ mm. Hg, $pH = 7.23$, base deficit $= -10.9$ mEq./l., respiratory rate $= 24$/min., minute ventilation $= 3.8$ l. *CO_2 response* curves after hemorrhage during halothane anesthesia showed a fairly marked shift to the left and a slope indicating increased sensitivity of the respiratory center. During methoxyflurane, little if any significant changes were noted after hemorrhage. *Conclusions:* The preliminary findings in this study suggest that although halothane depresses respiration more than methoxyflurane in the normal animal breathing spontaneously, in the hemorrhagic shock state, the relative respiratory depressant effects of these agents are reversed.

Effect of Hyperthyroidism and Hypothyroidism on Halothane and Oxygen Requirements in Dogs. ARTHUR A. BABAD, M.D., *University of California Medical Center, San Francisco, Calif.* Hyperthyroid and hypothyroid patients have been thought to require more and less anesthetic, respectively, than normal patients. *Method:* To test the effect of these altered metabolic states upon halothane requirement, six euthyroid mongrel dogs were studied (q.v. below); these same six dogs were made hyperthyroid with dessicated thyroid, thyroxine and/or triiodothyronine and the studies were repeated; four of the six dogs were made hypothyroid with radioiodine and the studies were again repeated. At each metabolic level, the minimum alveolar concentration of halothane was determined (MAC, Eger *et al.*, ANESTHESIOLOGY *26:* 756, 1965); and oxygen uptake was measured at 3 multiples of MAC—approximately 2.0, 1.5 and 1.1 times MAC. Oxygen consumption at 1.5 MAC was chosen as the most reasonable reference point for comparing differences in metabolic activity in the various studies; anesthesia at 1.5 MAC was not so deep as to produce profound cardiovascular or respiratory depression, nor was it so light as to permit shivering and erratic ventilation. Body temperature was controlled during the MAC and oxygen consumption measurements. Mean body temperatures for all MAC and oxygen consumption studies were between 36.9 and 37.1 degrees C. Except for one (euthyroid) study in which one-third of the MAC measurement was carried out at 36.3 to 36.4 degrees C., all body temperatures were between 36.5 and 37.5 degrees C. *Results:* (1) Mean oxygen consumption at 1.5 MAC was 111.6 ± 13.1 ml./min./sq. m. in the euthyroid state; 140.7 ± 18.2 ml./min./sq. m. in the maximally hyperthyroid state; 72.8 ± 8.2 ml./min./sq. m. in the hypothyroid state. Mean euthyroid MAC closely approximated previously re-

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