*col:* Normal dogs: seven mongrel dogs were each studied two times during halothane-oxygen anesthesia, breathing spontaneously. The initial study consisted of bleeding the dog serially into sterile ACD blood transfusion packs, with a 12-minute interval between bleedings. A constant infusion of balanced electrolyte solution was run as rapidly as necessary to maintain arterial blood pressure at adequate levels. One hour after the final blood was withdrawn, the first unit of blood withdrawn was reinfused. The rest of the red blood cells were then reinfused after separation from the plasma. The dog was restudied after at least one week. Cyanotic dogs: six dogs were bled and hemodiluted as above. The dogs were given ambient air to breathe at maximum dilution, and then sacrificed. *Results:* A. Normal dogs. All dogs had satisfactory blood pressures, heart rates, and arterial oxygen and carbon dioxide tensions at all times. The average lowest hematocrits were 5.8 per cent and 4.7 per cent for the two series, respectively. The average amounts of blood withdrawn in the two series were 182 cc./kg. and 192 cc./kg., while saline solution replacement amounted to 522 cc./kg. and 575 cc./kg. The dogs weighed 136 per cent and 135 per cent of their control weights after the studies, and survivors were back to their original weights 48 hours later. The dogs had a mean base deficit of 9 mEq./l. at minimum hematocrit; 11 mEq./l. after reinfusion. Blood volumes (RISA) were not significantly different from control levels at maximum dilution, while six of seven dogs had small increases over control values after reinfusion. Cardiac output rose from 2.3 l./min. to 5.4 l./min. at maximum dilution, and returned to 2.6 l./min. after reinfusion. B. Cyanotic dogs. The response to dilution was the same as in normal dogs, except that the base deficit was slightly greater (13 mEq./l. vs. 9 mEq/l.); the mean blood pressure lower (64 mm. Hg vs. 97 mm. Hg); and the $Pa_{O_2}$ rose progressively with hemodilution, from 60 mm. Hg at 40 per cent hematocrit to 262 mm. Hg. at 4.6 per cent hematocrit while breathing 100 per cent $O_2$. *Conclusions:* Blood volume and circulatory integrity may be maintained by replacement of whole blood loss by balanced saline solution (hemodilution) in normal and cyanotic dogs under these conditions, if the volume and rate of infusion is adequate. The fluid cannot be administered by a pre-determined formula. In the normal dogs, the amount of blood withdrawn was about twice the measured blood volume, and replacement about six times the blood volume, yet all dogs survived. No buffers were necessary to maintain circulatory integrity in spite of a moderate acidosis. (Supported by USPHS Grant GM-14738-01.)

**The Effect of Alpha-methyldopa on the Alveolar Concentration of Halothane Required for Anesthesia.** RONALD D. MILLER, M.D., and WALTER L. WAY, M.D., *University of California Medical School, San Francisco, Calif.* Alpha-methyldopa (Aldomet®), an antihypertensive agent, probably produces its effect by formation of a false transmitter displacing norepinephrine from its binding sites (Day, M. D., and Rand, M. J.: J. Pharm. and Pharmacol. *15:* 221, 1963). We have observed that patients receiving alpha-methyldopa appear to require lower halothane concentrations to maintain a given plane of anesthesia. We proposed to quantify the decrease in halothane requirement produced by the prior administration of alpha-methyldopa. We used the minimum alveolar concentraton (MAC) of halothane required to eliminate movement in response to a painful stimulus as our standard of potency (Eger, E. I., Saidman, L. J., and Brandstater, B.: ANESTHESIOLOGY *26:* 756, 1965). *Method:* MAC was determined for five unpremedicated mongrel dogs with halothane once a week for six weeks. The first, third and sixth weeks served as controls. The dogs were given alpha-methyldopa, 200 mg./kg./day, for three days prior to the second week's MAC determination; 50 mg./kg./day for three days prior to the fourth week's MAC determination; and 100 mg./kg./day for three days prior to the fifth week's MAC determination. After determination of a control MAC, the effect of chronically administered alpha-methyldopa was determined by administering 200 mg./kg./day for ten days to three dogs. On the tenth day of treatment, MAC was redetermined. Alpha-methyldopa reduces the cardiovascular responses to indirect acting vasopressors (Stone,

C. A., and Porter, C. C.: Pharmacol. Rev. *18:* 569, 1966). To test this effect at MAC, ephedrine (0.5 mg./kg.), a primarily indirect-acting vasopressor, was given in each experiment. All drugs were intravenous. *Results:* The control mean MAC's (in per cent halothane) at the first, third, and sixth weeks were $0.98 \pm 0.08$, $1.00 \pm 0.12$, and $1.05 \pm 0.08$, respectively. Mean MAC was decreased to $0.73 \pm 0.08$ with 200 mg./kg./day of alpha-methyldopa ($P < 0.01$); $0.79 \pm 0.08$ with 100 mg./kg./day ($P < 0.05$); and $0.85 \pm 0.11$ with 50 mg./kg./day. The correlation between dose of alpha-methyldopa and decrease in MAC was significant ($r = 0.91$, $P < 0.05$). In the chronic studies, control mean MAC was $0.93 \pm 0.07$, and after ten days of alpha-methyldopa administration, mean MAC was $0.66 \pm 0.09$. The mean peak increase in systolic blood pressure (in mm. Hg) was $86 \pm 22$ in control dogs; $30 \pm 10$ in dogs receiving 50 mg./kg. of alpha-methyldopa ($P < 0.01$); $23 \pm 7$ in dogs receiving 100 mg./kg. ($P < 0.01$); and $14 \pm 6$ in dogs receiving 200 mg./kg. ($P < 0.01$). *Conclusions:* The results of this study support the clinical observation that halothane require is significantly decreased by prior administration of alpha-methyldopa. There is an inverse relationship between the dose of alpha-methyldopa and MAC for halothane. The administration of alpha-methyldopa for a ten-day period did not decrease MAC below that level obtained at three days. This suggests that alpha-methyldopa exerts maximum depressant effect at three days and that tolerance does not develop with chronic administration. (Supported by USPHS Grant 2 TO1 GM00063.)

**Physiologic Alterations Induced by Blood-warming during Light Ether Anesthesia.** R. H. Morris, M.D., and H. A. Trachtenberg, M.D., *Department of Anesthesia, Massachusetts General Hospital Harvard Medical School, Boston, Mass.* Eleven patients undergoing major surgery were studied to ascertain whether warming infused ACD blood causes hemodynamic and/or metabolic changes during ether anesthesia. *Method:* After premedication with pentobarbital and atropine induction and intubation were accomplished with intravenous thiamylal and succinylcholine. Anesthesia was maintained with ether-oxygen via a semiclosed-circle system, with gallamine for relaxation. Ventilation was controlled. The following parameters were measured or calculated: esophageal temperature; venous pressure; systolic, diastolic and mean intra-arterial pressures; heart rate; cardiac output by dye-dilution and planimetry; peripheral resistance (mean arterial pressure minus venous pressure divided by cardiac output); minute ventilation; arterial $P_{CO_2}$, $P_{O_2}$, *p*H and hemoglobin; base deficit (using the alignment of Siggaard-Andersen). Control measurements were made 80–120 minutes after induction before transfusion was required. Subsequent measurements were evaluated as changes from control values. Six patients received cold blood (Group I), and five received blood warmed during infusion (Group II). *Results:* Group I patients received an average of 2.4 l. of cold blood and Group II patients an average of 3.5 l. of warm blood intraoperatively. Mean control esophageal temperature for Group I patients was 35.4° C; this decreased only 0.4° C. (1.0 per cent) with transfusion. Group II patients had a mean esophageal temperature of 35.5° C. and an increase of 0.3° C. (0.8 per cent). Temperature changes were small, but the difference between the groups was statistically significant ($P < 0.01$). No significant difference between the groups was found for mean blood pressure, venous pressure, or heart rate. Control cardiac output for Group I was 5.7 l./minute and remained essentially unchanged (−0.02 l./min.). In Group II control cardiac output was 4.6 l./min. and this increased by 2.5 l./min. (54.3 per cent). The difference between the groups in per cent cardiac output changes was significant ($P < 0.01$). Mean peripheral resistance for Group I started at 15.2 units and increased 0.65 P.R.U. (4.3 per cent). Mean resistance for Group II was initially 23.7 P.R.U.; this decreased by 6.8 P.R.U. (28.6 per cent). The difference in per cent peripheral resistance changes was significant ($P < 0.01$). Control $P_{CO_2}$ was 34 mm. Hg for both groups. In Group I it decreased 1.7 mm. Hg (4.8 per cent), whereas Group II patients had an increase of 3.0 mm. Hg (11.3 per cent); this difference was also significant ($P < 0.02$). No significant difference between the groups