taken during surgery indicated that there was a definite correlation between the time of peak blood pressure and the time of lowest hematocrit, further suggesting that hypervolemia was the cause of the observed elevation of blood pressure. Studies were carried out in thirty-five 10–12 kg. mongrel dogs. All animals were anesthetized using pentothal-nitrous oxide by endotracheal technique to a depth similar to that used in the majority of neurosurgical patients. Continuous recordings of arterial and venous blood pressure, ECG and EEG were made during the experiment using a Gilson 4-channel polygraph. Animals receiving urea were administered 1.5 Gm. per kilogram body weight as a 30 per cent solution in 10 per cent invert sugar. The solution was injected at a uniform rate over a 30 minute period. Blood was removed via venapuncture at predetermined periods relating to the time of urea administration to simulate bleeding. It was found necessary to remove 30–35 per cent of the total blood volume to produce the desired level of shock. The animals were divided into 5 groups as follows: (I) urea alone, (II) bleeding alone, (III) bleeding simultaneous with urea infusion, (IV) bleeding followed by urea infusion, and (V) bleeding simultaneous with urea infusion followed by transfusion. Heart rate together with pulse pressure is generally considered to be a good index of cardiac output. In these experiments, changes in heart rate were more subtle than the changes in pulse pressure, but generally in the same direction. We have, therefore, presented our data in terms of per cent change in the stabilized pulse pressure to simplify illustration. As one would predict, group (I) animals experienced an increased pulse pressure and a decreased hematocrit as in human subjects. Animals in group (II) showed the expected decrease in pulse pressure followed by a period of partial compensation after the bleeding had been stopped. Group (III) received urea simultaneously with bleeding and showed no significant tendency to compensate while the pulse pressure was being dropped to nearly the level of group (II) after compensation. It is felt that these animals were not bled as much as the animals in group (II) since the fluid being withdrawn and measured contained urea solution, fluid from the interstitial spaces and blood. The animals in group (IV) were bled and then given urea. It is interesting to note that while there was an increase in pulse pressure when urea was given, the amount of compensation achieved was essentially the same as when no urea was administered. It is felt that this illustrates the fact that the fluid removed by hypertonic solutions of urea comes mostly from the interstitial spaces and not from the intracellular spaces. Further evidence of this is the fact that no significant shift in blood electrolytes was observed in human subjects and animals. The animals in group (V) were treated in a similar manner to those in group (III) except that a transfusion was given after a period of stabilization. In these dogs the pulse pressure returned to normal. Whereas, the elevation of blood pressure after urea is slight it should be pointed out that during craniotomy, should excessive blood loss occur, the impending fall in blood pressure may be masked temporarily during the initial period. In other words, urea may temporarily maintain the arterial blood pressure in the face of significant blood loss. Following this initial period diuresis usually occurs. The hypervolemia is succeeded by comparative hypovolemia. At this time previous blood loss may become a significant factor. Further blood loss may be much more serious in that even adequate and rapid blood replacement may not return the blood pressure to satisfactory levels. Clinically speaking, this indicates a need for awareness as to the time and amount of blood loss during those craniotomies where excessive blood loss is encountered within a short period of time. In these cases, blood replacement should be adequate and simultaneous with urea. [*Supported in part by the Wisconsin Alumni Research Foundation.*]

Prophylaxis and Treatment of Hypotension During Anesthesia and Surgery in Man. DONALD P. TODD, M.D., JOHN P. BUNKER, M.D., MARIE-LOUISE LEVY, M.D., JOHN C. DALTON, M.D., AND ALLEN L. FRIEDLICH, M.D. *Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital, Boston, Massachusetts.* Cardio-vascular failure remains the most common serious complication during anesthesia and surgery (*Beecher, H. K., and Todd, D. P.: Ann. Surg.*

140: 2, 1954). Elderly patients have been shown (*Briggs, B. D., and others: J. A. M. A. 160: 1439, 1960*) to be the most susceptible group. Beyond surgical causes direct depressant effects of general anesthetics are most frequent. In this pilot study of a very large problem our attention has been directed toward: (1) Is hypotension during actual operating conditions due primarily to peripheral vasodilatation or depression of cardiac output? (2) In the absence of the usual medical indications for digitalis, does prophylactic digitalization in the elderly protect against hypotension during anesthesia, and if so, by what mechanism? (3) In treatment of hypotension by sympathomimetic amines, are those having primarily vasoconstrictor or primarily positive inotropic action more effective? Patients over 60 having intra-abdominal operations were digitalized or not at random, anesthetized with thiopental, nitrous oxide-ether and followed with constant intra-arterial pressures, ECG, EEG and repeated cardiac output determinations. If hypotension occurred, it was treated by different vasopressors, also selected at random, hemodynamics being followed the while. In this preliminary study of 10 patients a moderate to marked fall in cardiac output occurred in 7, accompanied by a simultaneous rise in calculated total peripheral resistance—the blood pressure being relatively well maintained. During the course of surgery this pattern tended to reverse although blood levels of anesthetic (ether) remained high. The initial fall in output may reflect direct depressant effect of anesthetic on the myocardium or, secondarily, an elevation in peripheral resistance due to norepinephrine elevations, demonstrated by Price (*Anesthesiology 20: 563, 1959*) to accompany ether anesthesia in man. Hypotension requiring vasopressor treatment occurred in four patients. Response to vasopressor drugs was variable and numbers too few to draw conclusions. There was no apparent difference in cardio-vascular response between the four digitalized and six non-digitalized patients, but again the numbers are too few for valid comparisons.

The Response of Radiated Animals to Anesthetics. HOWARD L. ZAUDER, M.D., PH.D., AND LOUIS R. ORKIN, M.D. *Department of Anesthesiology, Albert Einstein College of Medicine, New York 61, New York.* White mice (Webster) weighing 20–25 Gm. were irradiated with a 250 kv. radiotherapy unit. Physical factors were such that the dose rate was 52 roentgens per minute. A dose response curve relating dose of radiation to thirty day mortality was constructed. Thirty day LD_5, LD_{25}, and LD_{95} doses were selected. These represent total body irradiation of 350*r*, 450*r*, and 750*r* respectively. At intervals of 1, 2, 4, 7, 14, 21, and 28 days following cardiation, the animals were placed in a specially designed chamber (*Zauder, H. L., and Orkin, L. R.: Anesthesiology 20: 707, 1959*) and anesthetized with 6 per cent diethyl ether, 7 per cent divinyl ether, 2.5 per cent trichloroethylene, and 1.5 per cent halothane. Mortality was determined 30 days post anesthesia except for the animals subjected to 750*r* where 7 day mortalities were used. Statistical significance of the results was determined by the chi square test. At the 350*r* level mortality was not significantly increased if the animals were anesthetized with diethyl ether or halothane within 14 days following exposure. After this period mortality was greatly increased in the anesthetized groups. Ether was somewhat safer than halothane at this time. Divinyl ether was associated with high mortality. During anesthesia with this agent, mortality was high in the experimental group whereas there were no deaths in the control animals. Trichloroethylene occupied an intermediate position. At 450*r* divinyl ether and trichloroethylene anesthesia were associated with a high death rate. At this level of radiation, however, mortality following diethyl ether was high when anesthesia was administered within the first two weeks; death associated with halothane was highest during the latter half of the experimental period. When the mice were exposed to 750*r* mortality with all agents was 100 per cent at the end of seven days. Vaporization of the anesthetic agents in an oxygen enriched atmosphere did not affect the results at any level. [*Supported by Research and Development Division, Office of the Surgeon General Department of the Army. Contract No. DA-49-007-MD-962.*]