of denitrogenation with 4 l./min. flow of oxygen. The expiratory side of the system included a Wright anemometer for measurement of respiratory tidal or minute volumes. The lead-2 electrocardiogram was recorded continuously and bilateral femoral veins were cannulated for infusions. A femoral artery was also cannulated for continuous measurement of arterial pressure and for intermittent arterial blood sampling. Arterial plasma potassium and sodium concentrations were measured with an internal standard flame photometer. *p*H, P_{CO_2}, P_{O_2}, and buffer base levels of arterial blood were measured by the Astrup technique. Three concentrations of epinephrine solution (4, 8 and 16 microgram/ml.) were prepared with 5 per cent dextrose in water just before use, and a chosen concentration of the solution was infused by intravenous drip with a constant rate throughout the study to produce cardiac arrhythmias. 0.3 M. THAM Solution TRIS (Abbott, *p*H: 8.6) or 0.15 M. sodium bicarbonate 5 per cent solution (Abbott) was used by intravenous drip with a constant rate for buffering. Lidocaine solution, 1.0 per cent, was injected intravenously in a single dose on the basis of 1–3 mg./kg. body weight. Forty mEq./l. of potassium chloride solution was also prepared in 5 per cent dextrose in water. Following measurements of arrhythmic threshold to epinephrine at a stable anesthetic concentration, these measurements were repeated in the same dog at regular sinus rhythm threshold to epinephrine during intravenous infusions of THAM, sodium bicarbonate, lidocaine, and potassium chloride solution. The types of cardiac rhythm observed were classified according to conventional methods. *Results:* Epinephrine-induced cardiac arrhythmias were always associated with lowered arterial *p*H and increased P_{CO_2}. In acidotic conditions, these arrhythmias invariably were reversed by correcting the arterial *p*H, using THAM or $NaHCO_3$ solution, in spite of significant increases in P_{CO_2}. No relationship was established between arrhythmias and arterial blood pressure or potassium concentrations. In severe alkalosis associated with extreme decreases in arterial potassium concentrations, arrhythmias were not abolished by THAM, $NaHCO_3$, or lidocaine infusion, but were abolished by KCl administration. In epinephrine-induced arrhythmias with acidosis, THAM or $NaHCO_3$ was more effective, with longer duration, than lidocaine infusion, in therapeutic doses. *Summary and Conclusions:* 1. Epinephrine-induced cardiac arrhythmias with acidosis invariably were reversed by correcting *p*H with THAM or $NaHCO_3$, in spite of significant increases in P_{CO_2}. Lidocaine in therapeutic doses was less effective. 2. In severe akalosis associated with lowered arterial potassium concentrations, potassium chloride infusion was most effective for correction of the epinephrine-induced arrhythmias. The data indicate that maintenance of normal arterial *p*H may be of utmost importance in reducing the incidence of cardiac arrhythmias during cyclopropane anesthesia.

Coagulation of Heparinized Blood During Open-Heart Surgery. JAN D. HASBROUCK, M.D., *University of Kentucky Medical Center, Lexington, Ky.* The formation of clots in heparinized blood during the course of cardiopulmonary bypass is a potentially fatal complication. This is a report on an *ex-vivo* study of the effects of glucose, lidocaine, mannitol and lactated Ringer's solution on coagulation of blood obtained from patients undergoing open-heart surgery. *Method:* Studies were conducted on 47 adult patients who underwent open-heart repair of intracardiac lesions on cardiopulmonary bypass. Prior to heparinization, 40 ml. of blood were withdrawn from a central venous catheter and centrifuged at 200 *g* at 2° for five minutes. Two ml. of the resultant plasma was added to each of six siliconized tubes. Tube 1 was used as a control to indicate clotting time. Tube 2 contained 1 ml. of a 2 μgm./ml. solution of lidocaine; tube 3, 1 ml. of 5 per cent dextrose; tube 4, 1 ml. of 0.5 per cent mannitol; tube 5, 1 ml. of lactated Ringer's solution; tube 6, 1 ml. of physiologic saline solution. Five minutes after heparinization was accomplished at a dose of 2 mg. (200 units)/kg. of body weight, a second set of identical samples was drawn. All tubes were incubated at 37°, *p*H maintained between 7.45–7.90, and were observed for a maximum of 300 minutes. For

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presence of an invertible clot. For heparinized plasma, the end point was the unheparinized plasma, clots were wound on glass rods, washed, dried and weighed. The yield of clots in the heparinized samples was expressed as a percentage of the total clot available as determined by adding protamine to the control tube. *Results:* The results are divided into two parts: 1. unheparinized clotting time, and 2. clot yield in heparinized plasma. The unheparinized plasma clotting time averaged a near-normal value of 35.8 minutes (Hardaway, Robert M.: Syndromes of Disseminated Intravascular Coagulation. Charles C Thomas, Springfield, Illinois, 1966, p. 116). This was accelerated nearly 45 per cent in the presence of lidocaine at a concentration of 2 μgm./ml. Dextrose mannitol lactated Ringer's solution and physiologic saline solution had no appreciable effect on clotting time. The clot yield in heparinized plasma was 60–72 per cent with lidocaine, 75–95 per cent with dextrose, 50–75 per cent with mannitol and less than 25 per cent with lactated Ringer's solution and normal saline solution. *Discussion:* Classically, heparin is described as an anti-thrombin agent. That it is also an anti-thromboplastin, an anti-PTA, an anti-Christmas factor, and inhibits platelet agglutination is poorly appreciated (Davis, E. W., and Ratnoff, O. D.: Science *145:* 1310, 1964). It has also been demonstrated that full heparin activity requires the presence of a cofactor, anti-thrombin II (Fantl, P.: Aust. J. Exp. Biol. Med. Sci. *43:* 45, 1965). It is postulated that dextrose and mannitol interfere with the activity of anti-thrombin II, allowing sufficient prothrombin to be converted to thrombin to allow some clotting to take place (*ibid*). The point at which lidocaine acts can only be inferred. Injected locally into tissue, lidocaine liberates large quantities of thromboplastin which would tend to reduce the relative effectiveness of heparin. As an intravenous agent it is associated with a positive charge which would cause platelet aggregation and also PTA activitation. *Conclusions:* Though these experiments were *ex vivo* and limited in scope, sufficient observations have been made that disseminated intravascular coagulation does occur unexpectedly in heparinized blood. Therefore, when lidocaine is used as the local anesthetic agent for the "awake cannulation" technique of Danielson, or when glucose is part of a pump-priming solution, or when mannitol is to be rapidly infused, it is recommended that the heparin dosage be at least 3 mg. (300 units)/kg. In some cases 4 mg (400 units)/kg. may be required.

The Effect of Age on Lung Mechanics and Ventilation-perfusion Relations in Respiratory Failure. J. HEDLEY-WHYTE, M.D., J. MORRIS, M.D., H. K. DARRAH, M.D., P. BERRY, M.D., N. R. FRANK, M.D., and S. W. WOO, *Respiratory Units and Departments of Anesthesia, Beth Israel and Massachusetts General Hospitals, Harvard Medical School, Boston, Mass. Method:* Six young (16–42 years) and four elderly (54–68 years) patients, all with diffuse interstitial pneumonitis and alveolar-arterial oxygen tension gradients sufficiently severe to require long-term controlled ventilation, have been studied in the sitting position. Ventilation with an Emerson postoperative ventilator via a tracheostomy was at tidal ventilations of, consecutively, 20 ml./kg. body weight at a respiratory rate of 12/min., 10 ml./kg., at 24/min., 20 ml./kg. at 24/min., and 10 ml./kg. at 12/min. Inspiratory time always equalled expiratory time. Each pattern of ventilation lasted five minutes. Physiologic deadspace was measured using the Enghoff modification of the Bohr equation. Inspiratory, expiratory and average pulmonary flow resistances were measured with an esophageal balloon, Fleisch pneumotachograph and Sanborn respiratory panel and integrator. Functional residual capacity was measured, using a modification of the closed-circuit helium technique. *Results:* Deadspace to tidal volume ratios in young patients (mean 0.63, range 0.40 to 0.82) were not significantly different from those in older patients (mean 0.73, range 0.57 to 0.86); however, lung volumes (range 1.9 to 5.2 liters) at corresponding transpulmonary pressures from −5 to −20 cm. H_2O were significantly higher ($P < 0.01$) in older patients. Increase in tidal volume at each respiratory frequency always decreased $V_D/V_T (r_w = -0.60,\ r_t = -0.84)$. Dynamic

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