

**Cryoproteinemia and Hyperheparin States—Possible Role in Bleeding During and After Hypothermic Operations.** VIVENTE B. SANTELICES, M.D., ROBERT N. HEDGES, JR., M.D., PAUL W. SEARLES, M.D., *Presbyterian-St. Luke's Hospital, Chicago, Illinois.* A cold-precipitable plasma fraction which dissolves at 37° C. has been implicated as a possible cause of bleeding in various clinical disorders such as cryoglobulinemia (Lerner and others: *Amer. J. Med. Sci.* 214: 410, 1957), cryofibrinogenemia (Heinrick, R. A., and others: Tenth Annual Symposium on Blood, Wayne State Univ.: 21, Jan. 1962), multiple myeloma, various collagen diseases and other diseases. Heparin is considered necessary to precipitate these plasma proteins (Kalbfleish, J. M. and others: *New Engl. J. Med.* 263: 881, 1960). During cooling in hypothermia blood coagulability and sludging of formed elements are increased. On rewarming considerable heparin is released and can cause marked increase in the clotting time (Spohn, K., and others: *Thoraxchirurgie* 8: 288, 1960). Cryoglobulin is not a normal constituent of the blood. Unlike normal globulin it has a very low solubility, thus its easy precipitability. Its formation and adsorption of fibrinogen and other clotting factors indicates its significance in hypothermia and heparinization. The occurrence of a cold-precipitable plasma fraction in heparinized plasma of patients admitted for elective operation has been confirmed by several workers. Their evidence has shown that these precipitates are manifestations of incomplete coagulation. They have suggested that these precipitates may be dangerous in patients undergoing operation with hypothermia. *Present Study:* The bleeding problems in eleven patients undergoing hypothermia were studied. Hypothermia was induced by blood cooling in ten and surface cooling in one. There were five bleeders in this series. Three showed a cold-precipitable plasma fraction in the form of a beta-fibrinogen-gamma-globulin complex in one or more of three plasma samples obtained before hypothermia, during hypothermia, and after hypothermia. Bleeding was attributed to increased fibrinolytic activity in another bleeder and increased heparin activity in the fifth bleeder.

**Influence of Various Drugs and Anesthetic Agents on Cardiac Excitability in Man.** JAMES HENRY SPROUSE, M.D., ANIBAL H. GALINDO, M.D., and ANDREW G. MORROW, M.D., *Department of Anesthesia, Clinical Center, Section on Neuroanesthesiology, National Institute of Neurological Diseases and Blindness, and the Clinic of Surgery, National Heart Institute, National Institutes of Health, Bethesda, Maryland.* Cardiac excitability may be characterized by determining the response of the ventricle to threshold electrical stimuli presented at various times in the cardiac cycle. If the amplitude of current necessary for threshold stimulation is plotted as the ordinate of a graph and the time interval after the R wave as the abscissa, the curve obtained is the strength-interval curve. This delineates the absolute, relative and total refractory periods of the cycle; and also, the diastolic period when complete repolarization has occurred and the heart is most susceptible to stimulation. Such curves, and some of the factors modifying them, have been determined in experimental animals, but recently for the first time have been described for the human heart. *Methods:* The studies were carried out in patients undergoing elective cardiac operations. The electrocardiogram, from one of the standard limb leads, was amplified and recorded. A signal from this amplifier was fed to a trigger circuit, which, after a switch was opened, generated a pulse coincident with the next R wave. This pulse was used to trigger a Grass stimulator, which generated a 2 millisecond rectangular pulse of adjustable amplitude and with adjustable time delay from the trigger pulse. The stimulating pulse was coupled through an isolation unit to a bipolar electrode placed in the outflow tract of the right ventricle. The amplitude of this pulse was increased until threshold values were determined at 10 millisecond intervals of delay. *Results:* Control values were similar in all patients, the absolute refractory, relative refractory, and diastolic periods comprising 35, 15, and 50 per cent of the cycle, respectively. The diastolic threshold was 1 milliamperes  $\pm$  10 per cent. Epinephrine infusion reduced the duration of absolute refractoriness to 15 per cent of the cycle and lowered the diastolic threshold strikingly. Intravenous lidocaine (Xylocaine) consistently