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New York University School of Medicine

"BASIC STUDIES IN CLOTTING MECHANISMS AS PERTAIN TO TRAUMA AND MASSIVE TRANSFUSION THERAPY"

DA-49-193-MD-2375

ABSTRACT

1. Preparing Institution: New York University School of Medicine, New York City, N.Y.

2. Title of Study: "Basic Mechanisms in Blood Clotting as Pertain to Trauma and Massive Transfusion Therapy.

3. Principal Investigator: Harvey J. Weiss, M.D.

4. Number of Pages, Illustrations and Date: 3 pages, no illustrations, June 18, 1963

5. Contract Number: DA-49-193-MD-2375

6. Supported by: U.S. Army Medical Research and Development Command, Office of the Surgeon General, Washington 25, D.C.

The initial six months of the study have been confined to setting up a laboratory, standardizing assays and making basic purchases within the limited funds available prior to the anticipated full activation of the project on 1 July 1963.

The major objectives will be a study of factors effecting platelet function and the possible formation of AHG from a precursor.

Methods for studying platelet function have been established. These include assay of factor 3, as previously described by the investigator (Am. J. Med., 32:872, 1962), platelet agglutination, release of nucleotides by thrombin, agglutination by ADP and release of C^{14} serotonin. As a model for studying platelet damage, the effect of immune complexes, employing varying ratios of antigen and antibody will be used.

The possibility that AHG may be formed from a precursor is suggested by recent studies on von Willebrand's disease. Transfusion of hemophiliac plasma, fraction 1 or serum to patients with von Willebrand's disease produces an increase in AHG. To test the possibility that an AHG precursor (lacking in von Willebrand's disease) is activated by a cellular factor (lacking in hemophilia), serum will be incubated with various tissues and appropriate metabolic co-factors. A sensitive, reproducible method for measuring AHG has been developed, using a modification of the partial thromboplastin time with kaolin. Studies on this are now in progress.

REPORT

Because of fund limitations, the first six months of the project were spent in setting up a laboratory, making basic purchases with the available funds, standardizing assays and performing initial experiments prior to the anticipated full activation of the project on 1 July 1963.

The two major studies which will be conducted are concerned with factors which influence platelet function and the relationship between antihemophilic globulin and a possible precursor.

Platelet function is being studied by several methods. A sensitive technique for assaying platelet factor 3 has recently been described by the investigator. By means of this, twenty patients with mild bleeding disorders were found to be deficient in platelet factor 3. This test is being utilized to study various factors which may influence factor 3 activity. Preliminary studies on stored whole blood indicate that, in contrast to previous reports, factor 3 may become markedly decreased on storage. The extent of this decrease may depend on whether the platelets are stored in the presence or absence of red cells. As a model for studying mechanisms of platelet injury, the effect of immune complexes on platelet function will be studied. The complexes used will be albumin-anti-albumin and gamma-anti-gamma complexes, using varying ratios of antigen and antibody. In addition to studying factor 3, the effect of these complexes on other platelet functions will be studied. These include platelet agglutination, release of nucleotides by thrombin, agglutination by ADP and release of C^{14} serotonin.

A possible relationship between AHG and a precursor protein is suggested by recent studies on patients with von Willebrand's disease. The transfusion of hemophiliac plasma to patients with von Willebrand's disease produces a marked increase in AHG. Serum is similarly effective. This suggests that hemophiliac plasma contains a precursor, lacking in von Willebrand's disease, which may be converted to AHG by a cellular activator, lacking in hemophilia. To study this possibility, serum will be incubated with various tissue homogenates and appropriate co-factors and AHG activity assayed. A sensitive, reproducible method for measuring AHG has been developed, using a modification of the partial thromboplastin time with kaolin. Studies on this are now in progress.

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