ABSTRACTS

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HEMOSTASIS

COAGULATION FACTORS IN CEREBROSPINAL FLUID IN NORMAL AND PATHOLOGIC CONDITIONS. P. Ottaviani, F. Mandelli and M. Saginario. From the Istituto di Clinica Medica Generale e Terapia Medica, and the Clinica delle Malattie Nervose e Mentali, University, Parma, Italy. Ateneo parmense 28:3-16, 1957.

The cerebrospinal fluid might exhibit an accelerating activity on the coagulation of plasma under normal and pathologic conditions. Such an activity seems to be due chiefly to tissue thromboplastin. In pathologic conditions other coagulation factors should be implicated. Prothrombin and fibrinogen are essential for the occurrence of the fibrin reticulum.—P. d. N.


In 39 subjects with cirrhotic and neoplastic ascites, the usual tests were not able to give a diagnostic differentiation of the fluid, including protein, fibrinogen, factor V and factor VII determinations. Prothrombin determinations gave, on the contrary, definite different results in the two groups of conditions, insofar as the cirrhotic fluid exhibited a marked decrease of the values, while slight diminutions were typically observed in neoplastic fluids.—P. d. N.


In 1944 De Sittő-Nagy extracted anticoagulant material from certain tissues which he considered to be related to sphingomyelin. The senior author of this publication has col-

The initials of abstracters not listed in the above masthead refer to those abstracters listed in the masthead of the December, 1958 issue of Blood, p. 1206.
lected evidence that sphingosine is a physiologic anticoagulant found in the circulating blood. This study concerns the action of synthetic sphingosine and that derived from pig brain, on the activation of purified prothrombin in the system of Johnson and Seegers. In extremely low concentrations sphingosine accelerated thrombin formation in mixtures containing calcium ion, platelet factor 3, and platelet co-factor I, and prothrombin. However, in larger concentrations sphingosine was inhibitory proportional to its amount. The inhibitory effect could be overcome with an excess of platelet factor 3 or co-factor I, but not by an excess of prothrombin and Ac globulin. Similar findings were obtained when prothrombin was activated with tissue thromboplastin except that the accelerating effect of dilute sphingosine was not encountered.

It is suggested that sphingosine may be the anticoagulant responsible for the coagulation defect of hemophilia.——T. H. S.

**EFFECT OF INTRAVENOUS SOY BEAN PHOSPHATIDES ON BLOOD COAGULATION IN RABBITS.**


This study concerns the use of intravenous Inosithin, a soy bean phosphatide preparation with platelet-like activity. Given to rabbits, small doses had little effect on clotting factors. Larger amounts produced depression of prothrombin, Ac globulin and AHF. In no case was there a significant change in the “serum factors,” PTC, Stuart Factor or factor X. Neither was fibrinogen depressed. The mechanism of action appeared to be dual: a degree of prothrombin to thrombin conversion, and a direct anticoagulant effect of the lipid both probably were involved.—T. H. S.


The preparation used is essentially similar to Folch fraction 3 (phosphatidyl serine?) obtained from hog brain. Stable solutions of the lipid are made with the aid of sodium desoxycholate as an emulsifier. Assay was accomplished by a method utilizing inhibition of tissue thromboplastin in the one-stage “prothrombin time.” Emulsions were injected intravenously into dogs. No toxic effects were observed and prolongation of the silicone-clotting time was achieved and persisted up to 48 hours. —T. H. S.


Two phospholipid materials active on blood coagulation were isolated from acetonedehydrated human brain tissue. One fraction was an accelerator, possibly phosphatidyl ethanolamine; the other fraction was an inhibitor, possibly phosphatidyl serine.—P. d. N.


Plasmas of patients with various coagulation disorders were clotted with thromboplastin of blood or tissue origin. Platelet-poor, hemophilic, PTC-deficient, PTA-deficient, and Hageman factor-deficient plasmas clotted normally with both these reagents. Proaccelerin-deficient and Stuart factor-deficient plasmas had prolonged clotting times with tissue thromboplastin, but normal clotting times with thromboplastin of blood origin. Plasmas from patients on dicumarol therapy, with vitamin K deficiency, with liver disease and blood anticoagulated with heparin all showed retarded clotting with either type of thromboplastin.—T. H. S.
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The present work from Owren's laboratory is a very accurate and detailed study of the properties of the intermediates in the "extrinsic" blood clotting system.

By the aid of incubation and centrifugation experiments it is shown that tissue thromboplastin, proconvertin and calcium react quantitatively in a time-consuming reaction and form convertin. Convertin is quantitatively sedimented by high-speed centrifugation, and it maintains its high activity through several washings. No reaction takes place in the absence of calcium, and by decalcification convertin is broken down again, leaving the original thromboplastin and proconvertin activities. The components do not change in these reactions. By the addition of calcium they once more form convertin, which is thought to be a complex of the three components.

Convertin is inactivated in a time-consuming, reversible reaction by an anticonvertin present in serum. It is shown that the inactivation probably is due to the formation of a reversible complex of convertin and anticonvertin in the presence of calcium.

The activation of proaccelerin to accelerin by several proteolytic enzymes has been carefully studied, thrombin being the main activator.

In a mixture of convertin and accelerin some activation takes place rapidly, suggesting the formation of a final prothrombin conversion principle, prothrombinase. The author believes that prothrombinase is a complex of the two components. It can be sedimented by high-speed centrifugation, but some of its activity disappears by repeated washings. Prothrombinase clots human plasma in 3 to 4 seconds.

An initial lag period observed in different thrombin generation curves was eliminated by a preliminary formation of accelerin. Thrombin thus catalyzes its own formation by a co-autocatalytic mechanism, through the activation of proaccelerin to accelerin.

The present monograph with its accuracy and simplicity gives an important contribution to our present knowledge about this stage of blood coagulation. It should be owned and studied by all who are working with blood clotting problems.—M. S.


This paper discusses the importance of standardization in the preparation of thromboplastin extracts. Turbidimetry can be used to standardize saline extracts of an individual batch of brain powder only. It cannot be applied to a new batch; here resort must be made to biologic standardization.—T. H. B.


The basis for this study is 43 families harboring hemophilia or PTC deficiency. Among the families residing permanently in metropolitan Cleveland, 29 out of 31 had hemophilia, whereas 7 out of 12 who came for study from other areas had PTC deficiency. The authors indulge in some speculation as to the possible cause of this astonishing distribution.—T. H. S.


The authors review 32 infants and children with a diagnosis of "hemophilia" in their clinic. Each of the patients was reevaluated employing the thromboplastin generation test, prothrombin consumption of mixtures of various blood derivatives, clotting time and serum
prothrombin time. Of the 32 patients, 9 were found to have PTC deficiency and 23 were found to have AHG deficiency. The thromboplastin generation test gave much better results than the "differential mixture" test. The importance of selecting severely deficient serum for use in mixtures and pitfalls in the use of BASO₄ absorption are emphasized. Normal coagulation times were found in 9 of the 32 patients and 3 had normal prothrombin consumption. Prolonged bleeding time was found in almost half of the AHG deficient subjects and in one-fourth of the PTC deficiency group. In only one patient did a diagnosis of a combined vascular and humoral defect seem justified. Three of 23 patients with AHG deficiency were found to have anticoagulant activity.—N. I. S.


In a series of 13 patients suffering from "Hemophilia Syndrome" the relative incidence of AHG, PTC and PTA was 9 : 3 : 1, respectively.—J. B. C.


In a series of 65 patients suffering from hemophilia (AGH deficiency), 19 (29%) were found to have normal whole-blood coagulation time. These patients suffered from a mild form of the disease as assessed clinically and on the results of laboratory tests. Ages ranged from 9 to 67 years. Seventeen families were involved; in eight of these other members were affected. Hemorrhagic episodes were mostly related to periods when the hemostatic mechanism was placed under stress, as after tooth extraction or surgical procedures. Spontaneous hemorrhages and hemarthroses were uncommon.—G. C. de G.


Using an assay method based on mixing studies in the thromboplastin generation test, the author finds that in hepatocellular liver disease there is depression of plasma thromboplastin component (PTC) and plasma thromboplastin antecedent (PTA). The degree of depression corresponds roughly to changes in other tests of liver function. Similar reduction of these factors was encountered as a result of intestinal malabsorption (vitamin K deficiency) and restoration was induced with vitamin K administration. In addition to previously noted effects of Dicumarol, this drug was found to cause lowering of PTA in human subjects. It is concluded that the vitamin K-dependent coagulation factors may share common metabolic pathways.—T. H. S.


A nonspecific correction of the coagulation defect in hemophilia A following the addition of serum to hemophilic plasma was discussed on the basis of coagulation and thromboelastographic experiments. Barium sulfate adsorption or acetone treatment does not abolish such an effect. Heating at 56° C. for 30 minutes destroys this effect, as well as a 15-day storage of serum at room temperature. Sera from thrombocytopenic patients do not exhibit the correcting activity. Platelets do not present such an activity. The nonspecific action of serum was ascribed to the platelet-like activity of serum according to O'Brien and referred to an intermediate product.—P. d. N.