HEMOSTASIS


Vascular fragility and bleeding times were studied in x-irradiated mice and guinea pigs, at the period of maximal thrombocytopenia. The increased vascular fragility and prolonged bleeding times encountered in these animals were transiently improved by doses of serotonin sufficient to produce pulmonary toxic manifestations.—T. H. S.


This is a retrospective survey of a heterogeneous series of patients with ITP, treated with corticotrophin, cortisol, or prednisolone in various dosages, and/or by splenectomy, at various stages of the disease. The authors arbitrarily divide their cases into two groups according to whether the onset was more or less than 100 days before treatment started. They conclude from the results of treatment in the reported cases that patients with a short history of purpura should be treated with cortisol or prednisolone for three weeks, with the likelihood that any remission will be maintained, and then by splenectomy if there is no improvement, with the prospect of a good result in 75 per cent of cases; those with a long history should also receive steroids for three weeks, but as none of the remissions produced by steroids in this group lasted longer than 60 days, it is recommended that splenectomy should be carried out either during a steroid-induced remission or as soon as it is apparent that no such remission can be obtained. Remissions were maintained for one year after splenectomy in 19 of 29 reported cases in this group, and in seven of 14 cases followed up for eight years.—R. M. H.

This is a clinical and histopathologic documentation of a relatively rare localization of senile purpura (Bateman) in the tongue. The most significant patterns on histologic examination were degenerative processes, particularly evident in the perivascular collagen tissue, a slight increase of the fundamental amorphous substance, and reduction and degeneration of the elastic fibers, as well as marked sclerosis and hyalinization of the veins, which were thin and dilated. Hemorrhagic alterations were visible around the vessels.

—P. d. N.


A patient with a two year history of ecchymoses and epistaxis was seen at the age of 2½ years. She presented with a severe hemorrhagic anemia and a platelet count between 162,000 and 700,000 (96 per cent nonagglutinated). The skin bleeding time varied between 4 and 40 minutes, the Rumpel Leede test was positive, and clot retraction was deficient to absent. The bone marrow was rich in megakaryocytes, many of which were immature. The symptoms were not affected by administration of ACTH or platelet-rich plasma. A sister had a history of purpura and died of hemorrhage at the age of six years. The patients are cousins, both of whom present platelets variable in size with decreased agglutinability.—J. G.


Blood collected in one-ninth volume of of 1 per cent (0.027 M) disodium ethylenediaminetetra-acetate (EDTA) contains spherical, spiny platelets which do not adhere to each other or to glass. Thrombin does not produce clot retraction. Thrombin clotting times increase and concentration of Ac-globulin (factor V) decreases precipitously in several hours at 37 C. Addition of magnesium, barium, strontium or calcium corrects the thrombin clotting time and diminishes Ac-globulin destruction. Magnesium also changes the platelets to discs and increases platelet adhesiveness and agglutinability. The concentration of divalent ions required to correct the defects of EDTA blood is much less than the concentration of calcium required to produce even trace fibrin formation. Blood collected with barium or magnesium EDTA as anticoagulant, or with half the usual concentration of disodium EDTA, does not clot and does not show these defects.—M. B. Z.


One hundred and ninety-five patients with various forms of congenital coagulation disorders have been studied and classified with a variety of laboratory tests. In the group, derived from Pittsburgh and from North Carolina, 73 per cent were found to have hemophilia A (AHF), 21 per cent hemophilia B (PTC), 1 per cent hemophilia C (PTA), 0.5 per cent Hageman factor deficiency, 2 per cent hypoprothrombinemia, 2 per cent hypoproaccelerinemia, 2 per cent Stuart factor deficiency, and 0.5 per cent fibrinogenemia. No cases of factor VII deficiency were encountered. The occurrence of “mild” deficiencies requiring sensitive laboratory methods for detection is stressed.—I. S.


As in most other studies of hemophilia carriers, the majority of such persons are found to have normal coagulation tests and appear to be free of hemorrhagic symptoms. However,
in the present series about 20 per cent of the carriers had AHF or PTC assays below the normal range. The defect corresponded to that of the involved males. Abnormalities could not be detected by glass clotting times, were suggested by silicone clotting times or prothrombin consumption technics, and were best established by the thromboplastin generation test or specific assay procedures. When defects in carriers were found they appeared to be consistent over a prolonged period of time.—T. H. S.


A previously reported patient with PTA deficiency developed “transfusion resistance” during the period of observation. No anticoagulant was detected by the recalcified clotting time method when 50:50 dilutions of the patient’s with normal plasma were tested. However, on incubation, one-tenth volume of the patient’s plasma reagent caused loss of potency of normal plasma reagent in the thromboplastin generation test. The anticoagulant, precipitable by 25 to 33 per cent ammonium sulfate saturation, did not appear to inhibit either AHF or PTC.—T. H. S.


Cohn’s fraction I of human plasma was purified by treating it with a glycine solution containing ethanol and citrate. The fibrinogen yield of the fraction obtained was 95 per cent, and the antihemophilic activity of it was 10 to 40 times that of plasma. It was freeze-dried and stored at −20 C. until used. Twelve patients with hemophilia A were successfully treated during bleeding episodes or before surgery. No resistance developed on repeated treatments, and no antibody against AHG could be demonstrated.—C. W.


The ability of the plasma or serum of patients on routine treatment with phenindione to correct the defect of Christmas disease plasma or serum was measured. Technic included recalcification times, prothrombin consumption, thromboplastin generation and thrombin-thromboplastin generation of undiluted plasma mixtures. All these methods showed a progressive impairment of correction of the Christmas defect during the first 72 hours of phenindione treatment, with return to normal during a similar period after stopping therapy. The mean results of prothrombin consumption tests carried out on the whole blood of 13 subjects treated with phenindione (period of treatment not stated) did not differ markedly from those of 13 normal controls.—R. M. H.


Thrombelastographic determinations and the evaluation of prothrombin, factor V, factor VII, recalcification time and platelet count were carried out in 115 cases of malignancy. A tendency toward hypercoagulability was observed, particularly in the malignancies of the digestive system and in lung carcinomas, whereas hypocoagulability was observed in a number of malignancies of the female genital apparatus.—P. d. N.

THE HEMORRHAHIG: MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS. DESCRIPTION OF A CLINICAL CASE INITIATED BY A CONSPICUOUS MENORRHAGIA, AND CRITICAL REVIEW
ABSTRACTS


This is a case report of an 18 year old woman. The most significant features were: marked thrombocytopenia, antiplatelet antibodies (in vivo test), positive Coombs test, pronounced septic state, which did not respond to antibiotics but to ACTH in 48 hours, and marked menorrhagia. The pathogenetic importance of the spleen is stressed.—P. d. N.


The patient was a 50 year old man with a long-standing coagulation defect, asymptomatic for the most part. The anticoagulant had an inhibitory effect on tissue thromboplastin, both human and rabbit, on Russell viper venom, and on blood thromboplastin. A thromboplastin generation test in the patient gave a normal curve with the use of normal substrate. The result of the prothrombin consumption test was unusual, since there were repeated normal values by two different methods. In its effects and characteristics this anticoagulant was very similar to that described in systemic lupus erythematosus.—L. D.


Four deaths have been reported resulting from acute nonspecific pericarditis; and the patient reported is the second in which anticoagulant therapy had been given. The patient was an elderly woman who was treated with dicumarol because symptoms suggested a myocardial infarct. Two weeks after the initiation of anticoagulant therapy she died suddenly, and autopsy confirmed the diagnosis stated in the title.—T. H. S.


Because the Shwartzman reaction is accompanied by widespread fibrin deposition, coagulation studies were performed on rabbits given intravenous injections of Shear’s polysaccharide. Two injections were given at 24 hour intervals. The first was characterized by mild, the second by more severe changes. At autopsy there were numerous thrombi confined to the lungs, liver, spleen and kidneys. Each injection was followed by a fall in blood leukocytes and platelets, and shortening of the silicone clotting time. Prothrombin and thrombin times were unchanged, and no increased fibrinolytic activity was detected. After the first injection there was an inconsistent and slow increase of plasma fibrinogen; but this fell sharply following the second injection, corresponding to the increased thrombus formation. The authors consider the “defibrination” in the Shwartzman reaction to be basically different from that encountered with intravenous thromboplastin.


Shear’s polysaccharide produced in vitro shortening of the whole blood silicone clotting time, but failed to affect the clotting time of recalcified plasma plasma in glass. Similar findings were obtained with hemophilic blood. Its action did not appear to be via platelets, nor was fibrinogen directly clotted. Its in vivo mechanism of action is therefore not clear.—T. H. S.
ABSTRACTS


Rabbits rendered severely hypocoagulable by warfarin injections failed to develop the generalized Schwartzman reaction when injected with Shear’s polysaccharide.—T. H. S.


The oral, intramuscular and intravenous administration of 50 to 100 mg. of vitamin E daily caused in most cases a shortening of the whole blood coagulation time, of the recalcification time, a decrease of the residual prothrombin and an evident increase of antithrombin. The author suggests that the hypercoagulant activity is predominant as compared with the inhibition due to the increased antithrombin activity.—P. d. N.


By controlling the amount of contact surface and the platelet content, the clotting time of recalcified plasma can be made much more sensitive to small changes in the concentration of plasma coagulation factors. A method for the diagnosis of coagulation defects based on this principle is described, and examples of its reproducibility, sensitivity and routine use are given. The method consists of measuring the clotting time of platelet-poor plasma in the presence of a suspension of kaolin and lysed platelets, and determining the type of defect by assessing the corrective effect of various derivatives of normal blood.—R. M. H.


Brain thromboplastin was prepared by ultracentrifugal sedimentation of the usual saline extract of acetone-dried rabbit brain. It is lethal upon intravenous injection into mice, very active in the Quick prothrombin time test, effective in converting purified prothrombin to thrombin in the presence of calcium and accelerator globulin (factor V) and even more effective when factor VII was added in addition. The saline extract of acetone-dried brain, called brain extract thromboplastin; saline extract of lung, called lung extract thromboplastin; and the sedimentable portion of the latter, called lung thromboplastin, behave like brain thromboplastin and contain protein as well as lipids. In contrast, brain thromboplastin does not contain protein although it behaves like a “complete thromboplastin.” Some sphingosine is probably present. After hydrolysis, glutamic acid, serine, ethanolamine and perhaps arginine are found. Activity is only slightly diminished by boiling for 30 minutes or by refluxing 90 minutes in ether but the material behaves like lipid activator after refluxing for 90 minutes in boiling alcohol. Lipid extracts of brain and platelets, called lipid activator, were not lethal to mice, were ineffective in conversion of prothrombin to thrombin, had only weak activity in the prothrombin time test, and were effective platelet substitutes in the thromboplastin generation test. Platelet factor 3 alone, although a lipoprotein, behaved similarly.—M. B. Z.


The activation of fibrinolyisin was examined in bovine blood globulin preparations: (1) rich in antifibrinolyisin or purified, (2) containing a full thrombinogenic system or
adsorbed, i.e. obtained from plasma devoid of prothrombin, and (3) containing fibrinogen or obtained from plasma defibrinated by heating. The spontaneous activation of fibrinolysin in oxalated globulins was compared with the fibrinolysin activation in globulins after the generation of thrombin. In the globulins containing antifibrinolysin the generation of thrombin was found to accelerate the spontaneous activation of the fibrinolysin; it does not affect the spontaneous activation of fibrinolysin in globulins purified from anti-fibrinolysin. The generation of thrombin exerts no effect on plasminogen activation according to Mullertz's method in purified globulins, i.e., in globulins purified from antifibrinolysin, whereas it accelerates this activation in globulins containing anti-fibrinolysin. The adsorption of prothrombin on BaCO₃ suppresses none of the factors required for the spontaneous activation of fibrinolysin; it removes, however, a part of antifibrinolysin. The generation of thrombin stimulates the fibrinolysin activation in defibrinated but not purified globulins, the yield of the activation being invariably lower than in nondefibrinated samples.—E. K.


The authors review current methods for determining blood fibrinolytic activity, and conclude that for clinical purposes the “euglobulin technic” is most satisfactory because of its speed and sensitivity. In this technic the “euglobulins” are precipitated from plasma by reduction of ionic strength and acidification with CO₂. The precipitate is dissolved in buffered saline and clotted with thrombin, following which the lysis time is determined. Lysis times of one hour have been observed when the whole blood clot lysis time was about 24 hours, and similar orders of difference were noted with greater blood lytic activity.—T. H. S.


When studied at the time of delivery, mothers had elevated levels of plasma fibrinogen while levels in the newborn infants fell into a low normal range, with prematures having slightly lower levels than term infants. Free and total fibrinolysins and inhibitors of the fibrinolytic system were also significantly higher in the mothers than in the infants. The levels of total fibrinolysis tend to increase with birthweight. A possible relationship between the low proteolytic enzyme activity with plasma and the occurrence of hyaline membrane disease in the premature infant is suggested.—I. S.


Tagged thrombi were produced in dog veins by injection of ¹¹³I-labeled fibrinogen into isolated segments, followed by introduction of thrombin. The progress of these thrombi was followed by histologic and radioactive counting technics. Following the intravenous injection of plasmin there was complete lysis of clots under two days old; but older clots were unaffected. The resistance of the clots to lysis appeared to be correlated with histologic evidence of an endothelial lining over the thrombi. In some of the clots that had shown complete lysis, there was replacement by a new and nontagged clot. Side effects of the plasmin injections included a fall in plasma fibrinogen, leukopenia and transient hypotension.—T. H. S.

ABSTRACTS

Patients were given tablets of streptokinase prepared for buccal administration. The dosage schedule was one 20,000 unit tablet every 4 hours continued for 1 to 14 days. Although most of the patients had antibody titers against the enzyme or developed them subsequently, there was usually a rise in antithrombin titers. Blood fibrinolytic activity was not measured! The clinical responses claimed included rapid reduction of inflammatory edema and hematomas, and significant improvement in cutaneous ulcerations and thrombophlebitis. The study is innocent of control data.—T. H. S.


The present study is based on an earlier finding that restoration of "prothrombin" in chloroform-intoxicated animals was better with a combination of vitamin K and methionine than with either reagent alone. Normal dogs given this combination developed increased "accelerator" activity of the blood without alteration in prothrombin itself. Further studies were performed on dogs with bile-renal fistulas. Such animals presumably developed vitamin K deficiency because of the bile diversion, and within about 3 months prothrombin and accelerator levels fell to about 50 per cent of normal. At this point the institution of a protein-free diet produced a striking drop of accelerator activity without much change in prothrombin. The addition of DL-methionine to the diet raised the accelerator activity above control levels. Similar results were obtained with a methionine-free diet followed by the use of methionine supplement. This latter experiment repeated on normal dogs again gave similar results with a higher starting accelerator level. When bile fistula dogs were given vitamin K, prothrombin promptly returned to normal, but accelerator was only moderately affected. Methionine alone produced some elevation in accelerator, but little change in prothrombin. The combination caused rapid and complete restoration of both prothrombin and accelerator. It was concluded that methionine and vitamin K worked synergistically. On the basis of these considerations, a sulfhydryl-substituted methylnaphtoquinone (vitamin K-S[II]) was prepared. In the bile fistula dogs this compound caused prompt restoration of accelerator but partial improvement of prothrombin. In rats partial hepatectomy was followed by a marked fall in prothrombin and accelerator. Within a week both recovered spontaneously; but the addition of either methionine or K-S(II) to the diet appeared to hasten accelerator recovery. Vitamin K was without effect; and no treatment affected prothrombin recovery. In normal animals K-S(II) produced no evident toxicity. Two patients are reported. The first of these was a 57 year old man with a hemorrhagic disorder and reduced levels of fibrinogen, prothrombin, accelerator, and platelets (hepatic origin?). Elevation of accelerator alone and relief of hemorrhagic manifestations was produced only by a combination of vitamin K and methionine or by K-S(II). The second patient was a 22 year old pregnant woman with a coagulation disorder mainly involving accelerator activity. (Because of poor prothrombin consumption and low "factor VII" this may well be a case of Stuart factor deficiency.) The administration of K-S(II) was followed by prompt remission. This is a most exciting study, and has wide theoretical as well as practical implications. If certain of the clotting factors are indeed prothrombin derivatives (i.e., factor VII, PTC, Stuart factor), it may be that methionine will provide the clue to their synthesis from the prothrombin base.—T. H. S.

ALTERATIONS IN THE PROTHROMBIN TIME OF THE BLOOD OF RABBITS' FETUSES AT DIFFERENT STAGES OF INTRAUTERINE DEVELOPMENT AND IN ASPHYXIA. A. A. Orekhova.


Prothrombin times on the blood obtained by cardiac puncture from rabbits' fetuses at different periods of gestation were estimated by Kozantzeva's modification of Quick's method. It was shown that the nearer to term the shorter were the prothrombin times, ranging from 70 sec. on the 26th day of gestation to 15 sec. at term. It is postulated that the fetal prothrombin time is the function of intrauterine development of liver. In asphyxia, the prothrombin time was markedly prolonged.—T. J. B.