COAGULATION


Two types of cases are presented to illustrate the way in which fibrinolysis is capable of producing the serious hemorrhagic diathesis encountered occasionally in surgical patients.

The first group of four patients, studied during profound surgical shock, exhibited a marked but varying degree of plasma proteolytic activity. The occurrence and the severity of a hemorrhagic state appeared related to the magnitude of the increase in fibrinolytic enzyme and its subsequent lysis of hemostatic fibrin clots and reduction of plasma fibrinogen content.

Two patients with cancer demonstrated how a prolonged although less severe increase in plasma proteolytic activity, associated with neoplastic disease, may so lower the plasma fibrinogen that adequate hemostatic fibrin clots at operation cannot be formed and a hemorrhagic state ensues.

The administration of adequate amounts of fibrinogen intravenously as an immediate although temporary control measure in patients with this type of severe hemorrhage is recommended.—H.W.B.


The concept that prothrombin exists in human adult blood in both a free and an inactive form (prothrombinogen) suggested a new approach to the problem of the prothrombin in the newborn. Determinations of free and total prothrombin and of labile factor were made on maternal, cord, and infant’s blood in cases where vitamin K was given and where it was not administered prepartum. When the vitamin was omitted, a moderate prolongation of prothrombin time of cord and infant’s blood, and frequently a slight prolongation in maternal blood was found. Normal prothrombin times were demonstrated, however, in all three bloods when vitamin K was given.

The most significant finding was the observation that the prothrombin time and the total prothrombin time in the newborn were equal, thereby indicating that all of the prothrombin here was in the active stage. A failure of vitamin K to increase total prothrombin suggested the inability of the newborn to form prothrombinogen. The significance of this lack in early life is as yet unknown. Adult values for total prothrombin are gradually obtained during the first year of life.
ABSTRACTS

It is stated that the one stage test measures only active prothrombin and the two stage procedure measures essentially total prothrombin. The concept of a lack of prothrombinogen in the newborn could explain the low prothrombin found with the two stage method and the apparent discrepancy in reported results by these two procedures in newborns and slightly older infants.—H.W.B.

ON THE ACTION OF THE PLATELET HYALOMERE ON THE BLOOD CLOT RETRACTION. A. Fonio.
Theodor-Kocher-Institute, University Bern, Switzerland. Acta haemat. 8: 363-367, 1952.

The action of ultra-sonic agents on platelets permits the differentiation of the structural elements; i.e. hyalomere and granulomere. The author proves experimentally that only the hyalomere can initiate clot retraction.—C.M.


Based upon personal experiments, the opinion is expressed that the blood clot retraction is merely a function of the thrombocytes. The retraction may be prolonged by a quantitative fall, or by a qualitative, acquired, or hereditary defect of the blood platelets.—C.M.


Other workers have adapted the photoelectric method to prothrombin time determinations, and on a preliminary basis for whole blood.

The apparatus described permits a continuous recording from which can be measured the beginning, rate, and completion of fibrin formation in whole blood. The author states that the apparatus has the advantages that it gives a well defined end-point; it measures the entire process of coagulation; agitation of the blood due to tilting of the tube is eliminated; and progressive formation of fibrin may be graphically recorded.—T.R.T.


The authors point out that a number of workers in the field of blood coagulation have sought to explain the conversion of fibrinogen to fibrin in terms of a proteolytic change. Furthermore, papain and some snake venoms can bring about clotting.

In this study comparisons were made of the free amino groups of both bovine fibrinogen and bovine fibrin. It was concluded that fibrinogen contains N-terminal groups of glutamic acid and tyrosine, while fibrin has N-terminal groups of glycine and tyrosine. It was further concluded that during the fibrinogen-fibrin transformation two α-amino groups of glycine are liberated. Such a change is a strong argument in favor of the proteolytic nature of the clotting mechanism. The authors do not suggest that these findings with bovine fibrinogen are necessarily applicable to human fibrinogen.—T.R.T.


The clotting activity of thrombin is accompanied by the liberation of nonprotein nitrogen. A peptide appears in the fibrinogen-thrombin system: it is suggested that this hitherto unknown substance should be called fibrino-peptide, since it is believed to be derived by the splitting off of part of the fibrinogen molecule.—R.H.G.
ERYTHROCYTE DISEASES


On the assumption that symptomatic polycythemia and erythremia are due to over-activity of the pituitary gland and that p-hydroxypropiophenone depresses this gland, the drug was used in the treatment of symptomatic polycythemia and in erythremia. Therapeutic results are claimed in both types of polycythemia.—R.H.G.

FAMILIAL MEDITERRANEAN (COOLEY’S) ANEMIA COMPLICATED BY CHRONIC HEPATITIS.


An interesting case is reported of an adult Italian female with Mediterranean anemia who also presented chronic hepatitis and cirrhosis. The evidence which established these conditions as separate clinical entities and the possible influence of each on the other is well discussed. Treatment with ACTH produced only temporary improvement in the patient’s clinical condition and anemia, and failed to affect the liver function tests, hemolytic index, red cell morphology, and hepatosplenomegaly.—H.W.B.


Three patients with pernicious anemia were treated by inhalational administration of vitamin B12. Two received 15 µg. per day in saline administered by nebulizer. One patient was given the vitamin in lactose powder in the form of “dust” inhalations.

All three patients obtained a satisfactory hematologic remission.—T.R.T., Jr.


Observations were made upon fifteen patients with pernicious anemia under controlled dietary conditions. No consistent evidence was obtained for potentiation of the hematopoietic effect of vitamin B12 by simultaneous daily intravenous injection with intrinsic factor. A reciprocal rather than a stoichiometric relation exists between Vitamin B12 and intrinsic factor with respect to the potentiation of Vitamin B12 by intrinsic factor upon simultaneous daily oral administration.

The hematopoietic effect of the daily oral administration of 1 µg. of vitamin B12 may be detectably increased by as little as 10 ml. of normal human gastric juice. However, the hematopoietic effect of 1 µg. of vitamin B12 and 50 ml. of gastric juice does not equal that of the daily injection of 1 µg. of vitamin B12 alone. When separated by an interval of three or four hours the hematopoietic effect of the serial administration of vitamin B12 and of intrinsic factor is greater when the intrinsic factor precedes the vitamin B12. These and other recent clinical observations suggest that the essential physiologic function of intrinsic factor is merely to increase somewhat the assimilation of vitamin B12.

They indicate the possibility that the primary effect of intrinsic factor is upon the intestinal wall rather than upon the vitamin B12.—T.R.T., Jr.

MAINTENANCE THERAPY OF PERNICIOUS ANEMIA WITH VITAMIN B12. G. C. Meacham and R. W. Heine. From the Department of Medicine, Western Reserve University School of Medicine, Cleveland, Ohio. J. Lab. & Clin. Med. 41: 65-77, 1953.
Forty-three patients with Addisonian pernicious anemia are included in this study. Twenty-one patients received 3 μg. daily of a concentrate (Normocytin); nine were given 1 μg. daily of crystalline vitamin B₂ (Betalin); thirteen were given either one or the other of these as initial treatment. This program was followed for eleven to sixteen months before this report was made.

Responses to both of the compounds were satisfactory. Slight macrocytosis persisted in the average patient, which did not change, following intramuscular purified liver extract or daily administration of folic acid.—T.R.T., Jr.


Because of previous reports of hematopoietic responses to oral cobaltous chloride in patients with anemia associated with infection and a variety of other diseases, a program was initiated with the oral use of this compound in the anemia of chronic renal disease.

Each patient was given 50 to 150 mg. daily by mouth. Seventeen patients were followed for four or more weeks. Each patient had complete blood counts including reticulocyte counts, and in nine patients the plasma and total blood volumes were measured by means of Evans blue before and during therapy.

The majority of patients had minimal reticulocytosis of from 1 to 4 per cent prior to therapy, and there was no consistent or significant increase during treatment. All of the patients had a significant increase in hemoglobin, red cell count, and hematocrit. In some patients the drug was stopped and these values returned to previous levels.

There were numerous evidences of toxicity due to the compound: nausea and vomiting at doses greater than 100 mg.; tinnitus in four patients, of whom one had deafness lasting ten weeks after cessation of therapy, and in whom the same symptoms recurred with repeated therapy.

No explanation of these effects, either beneficial or toxic, is attempted.—T.R.T., Jr.


The hemoglobin levels of one hundred seventy-seven men, aged 66 to 85 years, and two hundred forty-six women, aged 61 to 87 years, were determined. Over a certain age range there was a significant decrease in the hemoglobin level with increasing age in both sexes. For males the mean level was 14.4 Gm./100 ml. and for females 13.8 Gm./100 ml. There was no significant social class difference.

Eight men and thirteen women had iron deficiency anemia while one man and three women had macrocytic anemia. The main factors causing anemia appeared to be poor diet and rheumatoid arthritis.—R.H.G.


A survey of eighteen thousand eight hundred forty-eight prescriptions issued under the National Health Service in Scotland during October 1951 was carried out. This was an approximately 1 per cent sample of all the forms issued in Scotland during the month. The number of prescriptions for vitamin preparations was unnecessarily high, exceeding the number of prescriptions for iron and constituting about 5 per cent of all prescriptions. Liver extract was also ordered unduly frequently (one hundred twenty-five times in the sample). Folic acid was prescribed thirty-two times in the sample and the authors point out that three thousand prescriptions per month for folic acid in Scotland is excessive as it is only of value in tropical sprue and some rare cases of megaloblastic anemia. The population of Scotland is approximately five million.—R.H.G.

In the serum of twenty-four patients with anemia due to ankylostomiasis this amount of zinc was found reduced. In seven patients the zinc level in the erythrocytes was increased. In one patient the changes of the zinc content in the serum and in the cells were followed during treatment. The observations agree with the theory that in anemia there is an increase of carbonic anhydrase in the red cells. The necessary zinc needed is drawn from the blood serum.—C.M.

ERYTHROPHAGOCYTOSIS: STANDARDIZATION OF A QUANTITATIVE TISSUE CULTURE TEST AND ITS APPLICATION TO HEMOLYTIC, MALIGNANT, AND INFECTIOUS DISEASES. C-S. Wright, M. C. Todd, N. G. Brandt, S. M. Elliott, and J. A. Bass. From the Departments of Medicine and Bacteriology, Ohio State University, Columbus, Ohio. J. Lab. & Clin. Med. 41: 169-178, 1953.

This is an extremely interesting report of well conceived and nicely executed work. It is the outgrowth of a search for some in vitro method for studying the factors which influence red cell destruction which would have some counterpart to the in vivo processes. Tissue cultures were prepared of rabbit splenic macrophages. The susceptibility to phagocytosis of erythrocytes by such a culture is termed the phagocytic index (PI). Three hundred fifty-two individuals in health and disease were studied by this method; fifty-nine were normal. The patients included acquired hemolytic anemia, the leukemias, lymphoma, carcinoma with and without known metastasis, tuberculosis, polycythemia and thrombocytopenic purpura.

The normals all fell within a narrow range. All of the diseases listed contained a major number of that group's individuals outside this normal range.

Further studies to elucidate these findings are in progress.—T.R.T., Jr.

IRON METABOLISM


In the African Bantu, the iron intake is often high, as much as 200 mg. per day. In an investigation of various groups of Bantus, many were found to have a high serum iron and total iron-binding capacity.—R.H.G.


The author describes a further case of idiopathic pulmonary hemosiderosis in a 4 year old child which was completely cured by splenectomy.—C.M.


A man aged 69 was given 100 mg. of saccharated iron oxide intravenously. He became hot and flushed, then cold and drowsy, and died thirty minutes after the injection. At autopsy the only evidence of disease was in the coronary arteries, both of which were calcified; the right artery was completely occluded. The report does not state whether this was a fresh occlusion.—R.H.G.

PORPHYRIN METABOLISM

This case report is of value in that the authors briefly review the various therapeutic procedures which have been carried out unsuccessfully in the treatment of acute porphyria. In this particular instance, ACTH did not seem to alter the clinical course or the urinary excretion of porphyrins. With the intravenous administration of procaine hydrochloride a remission followed but as the authors point out, this may have been a coincidental relationship.—P.F.W.


Large amounts of coproporphyrin, mainly of type III, are usually found in the urine of mammals to which salts of lead have been administered, whereas this increase does not occur in the feces. In addition, that which is present in the feces is predominantly type I. Recent studies in Watson's laboratory have shown that at least a portion of the urinary coproporphyrin is excreted in the form of a precursor which is easily changed to coproporphyrin during extraction. They did not exclude the possibility that all of the urinary coproporphyrin is excreted as the precursor with conversion either in the bladder or during storage after collection. If all of the urinary coproporphyrin is excreted as a precursor, an explanation is provided for the discrepancy between the normal biliary excretion of injected coproporphyrin and for the appearance of coproporphyrin in the urine in lead poisoning. The abnormal metabolite in animals exposed to lead would then be the precursor and not coproporphyrin per se.

The authors attempted to test this hypothesis by studying the precursor in the urine of rabbits treated with lead and by the intravenous administration of coproporphyrin III to normal and lead-treated rabbits and the amounts found in urine and bile determined.

It was found that there is ample evidence that over half of the urinary coproporphyrin is excreted as a precursor, and it is entirely possible that it is all excreted this way. When bile is extracted it does not appear likely that a significant portion of the coproporphyrin is present as the precursor.

When coproporphyrin III was administered intravenously to rabbits no additional urinary excretion was found, but the biliary excretion rose so that 35 to 75 per cent of the dose was accounted for in four hours. There was no difference between the lead-treated and normal rabbits in this regard.

"It is suggested that the coproporphyrin found in the urine of lead-treated rabbits is excreted entirely as a precursor, and that the metabolic disorder produced by lead is an overproduction or failure of utilization of a precursor of coproporphyrin and not of coproporphyrin itself."—T.R.T.