ERYTHROCYTES and ANEMIA


The literature on Cooley's anemia is reviewed briefly and an interesting report is made of 3 siblings in the fourth and fifth decades of life who showed advanced manifestations of this disease. The disease was inherited apparently through both parents. Unusual complications which were encountered included leg ulcers, pleuropericarditis which responded to cortisone, hyperuricemia resulting in renal calculi in one patient and in gouty arthritis in another.

Emphasis is laid on the varied clinical and pathologic manifestations of this disease. The fact that the "severe" homozygous form is not invariably lethal in infancy and childhood is brought out by this and other case reports in the literature. It is suggested that the broader term "Mediterranean hemopathic syndromes" of Chini and Valeri more aptly describes the disease than do the other commonly employed terminologies.—H. W. B.

PROLONGED TREATMENT OF PERNICIOUS ANEMIA WITH VITAMIN B₁₂. C. L. CONLEY, T. W. GREEN, R. C. HARTMANN AND J. R. KREVANS. From the Department of Medicine, the Johns Hopkins University and Hospital, Baltimore, Maryland. Am. J. Med. 13: 284-293, 1952.

Observations made on a large group of patients with pernicious anemia treated with vitamin B₁₂ for periods as long as forty months are reported. The experience with initial responses of previously untreated patients was essentially similar to that of other investigators. Comment is made on dosage requirements. While the authors believe it wise to continue to treat patients with neurologic involvement with amounts of the vitamin above that required for satisfactory hematologic effect, there was evidence that maximal neurologic improvement occurred with the dosages sufficient for maximal blood regeneration and was not accelerated by massive dose therapy.

Fifty-four patients were studied closely during maintenance therapy. Most of these had been treated previously with intramuscular injections of 45 units of refined liver extract every six weeks. With a few exceptions this group was given 45 µg. of vitamin B₁₂ intramuscularly every six weeks. This therapy proved as effective as liver extract in all respects. Of interest were the several patients receiving 150 µg. at four or five month intervals in whom the results were equally satisfactory.

Orally administered vitamin B₁₂ was effective when given in an amount about 100 times that required parenterally.

In view of recent reports to the contrary, it is noteworthy that macrocytosis was minimal and prothrombin times normal in these patients.

No evidence was obtained to show that patients with uncomplicated pernicious anemia need any therapy other than vitamin B₁₂. To be more conservative, however, further time
must elapse before one can state with any degree of certainty that the therapeutic effect of liver extract is due entirely to vitamin B\textsubscript{12}.—H.W.B.


A differential assay for the determination of folic acid and the citrovorum factor is described and other methods are criticized.

Assays of a number of natural products clearly indicate the presence of compounds that stimulate the growth of \textit{Leuc. citrovorum} and \textit{S. fecalis B} in the same manner as does folic acid and leucovorin. Chromatography of such natural products shows the presence of both free folic acid and free citrovorum factor. This suggests that the citrovorum factor may not mediate all of the reactions carried out by this group of compounds and that FA may have a distinct function in cellular metabolism.—C.E.R.


This article shows that a compensatory mechanism exists in healthy cows, sheep, goats and horses by which animals with a low erythrocyte count have corpuscles above average size. The existence of this correlation must be borne in mind when diagnosing macrocytic anemia in these species.—O.P.J.

LEUKOCYTIC DISEASE


The author has presented a careful analysis of 56 cases of infectious mononucleosis occurring in previously healthy West Point cadets. The academy environment provided a distinct advantage in the study and follow-up control of these patients.

This report is worthwhile reading not only for its content but also for its different and yet quite logical approach to the problem. Emphasis is laid not on the protean aspect but rather on the characteristic picture of this disease. The clinical, hematologic and serologic criteria for diagnosis are gone into in detail and doubt is cast on certain generally held conceptions. Among these are the observations, drawn from this and other studies, of the actual infrequency of central nervous system involvement, abdominal pain, rashes and a chronic form of the disease. Curiously, little attention is given to hepatic involvement in this report.

Considerable space is devoted to epidemiology. It is suggested that reported epidemics have been, more probably, instances of diseases related to, rather than identical with, infectious mononucleosis. The possibility of an incubation period of as long as five to eight weeks is discussed.

The usefulness of differential absorption tests in diagnosis is stressed and rightly so. A possible criticism, however, is that the author has tended to discard certain reported observations on the sole basis that absorption tests were not done.—H.W.B.


A case is presented of a 21 year old female with symptoms and signs suggestive of infectious mononucleosis but in whom the diagnosis could not be established until the seventh week of illness when, for the first time, the serologic and hematologic picture became characteristic. While this is a distinctly unusual situation, the case illustrates the practical importance of persisting with these laboratory tests in similar patients in order to exclude other diagnoses of more serious import.—H.W.B.
ABSTRACTS


Well documented evidence is presented to stress the importance of differential absorption tests in the serologic diagnosis of infectious mononucleosis. Although it is widely recognized that the specificity of the sheep cell agglutination is greatly enhanced by absorption tests, this fact evidently needs re-emphasis.

Since normal Forssman antibodies may be present in elevated titers in conditions other than infectious mononucleosis and because the heterophile antibodies in infectious mononucleosis show a characteristic pattern on absorption even at low titers, it is recommended that absorption technics be employed routinely in all cases where the antibody titer is 1:896 or lower. The practical advantages of confirmation by absorption in certain instances of much higher titers are outlined and illustrated.

It is quite apparent that our clinical conception of infectious mononucleosis would become more clearly defined if future reports on this disease included differential absorption data on all patients.—H. W. B.


The authors report 4 cases of a relatively rare type of neutropenia which they call chronic hypoplastic neutropenia or "primary hypoplastic neutropenia." This syndrome, in which the neutropenia is persistent and severe, is characterized clinically by repeated and slowly healing infections, most frequently involving the skin and oral cavity. Splenomegaly of slight to moderate degree is the rule but the condition is considered to be nonsplenic in origin because of the marked granulocytic hypoplasia of the marrow and the lack of hematologic response to splenectomy.

The etiology of this syndrome is completely obscure. The defect appears to lie in the inability of the bone marrow to produce granulocytic precursors and may be possibly a variant of aplastic anemia. Prognosis depends upon the effectiveness of antibiotic therapy in controlling the numerous infectious episodes.—H. W. B.


Current research into adrenocortical function has revived general interest in the eosinophil and prompted the present study of the response of the eosinophil in acute infectious disease. In tracing the accumulated and somewhat controversial literature, it became apparent that there had been underemphasis of the nonspecificity of the behavior of the eosinophil and of the significance of eosinopenia in acute infectious disease.

Serial blood eosinophil counts were made on 26 patients with acute infectious disease. The eosinopenia, which occurred quite regularly during the acute phase of the illness, correlated best with the general clinical condition of the patient and rather inconsistently with fever per se, neutrophilic leukocytosis and sedimentation rate.

It was concluded that the eosinopenia of acute infectious disease is a manifestation of the "alarm reaction", the degree of reduction in eosinophils varying directly with the severity of the stress. This concept while logical is based mainly on published observations of the effect of adrenocortical hormones on infectious disease.—H. W. B.

BLOOD COAGULATION and HEMORRHAGIC DISEASE

A HEMORRHAGIC STATE DURING PREGNANCY. WITH THE PRESENCE OF MATERNAL Rh ANTIBODIES, DEATH OF THE FETUS AND HYPOFIBRINOGENEMIA. O. D. Rutnoff, C. F. Lauster, J. G. Sholl and M. O. Schilling. From the Departments of Medicine and Obstetrics and
ABSTRACTS

Gynecology, and the Ultracentrifuge Laboratory, the Western Reserve University School of Medicine, and The Mount Sinai and University Hospitals, Cleveland, Ohio. 

A patient is described who exhibited various hemorrhagic phenomena associated with hypofibrinogenemia during the eighth month of pregnancy. The patient was Rh negative, her blood contained Rh antibodies and she was carrying a fetus which had died during the sixth month. Unlike 3 somewhat similar patients reported previously, this patient did not go into labor spontaneously and the hypofibrinogenemia persisted for at least a month. An interesting and unexplained feature was the immediate correction of the hypofibrinogenemia and hemorrhagic state when the pregnancy was terminated by a subtotal hysterectomy performed during an intravenous infusion of fibrinogen. (Previously, injected fibrinogen had disappeared from the plasma at an excessive rate.)

Rather exhaustive investigative studies indicated that the hypofibrinogenemia was due to increased destruction or utilization rather than decreased rate of synthesis of fibrinogen. There was no evidence of excessive plasma proteolytic activity in this patient. The possibility of intravascular clotting and the role of an antigen-antibody reaction between fetal tissues and maternal serum in the pathogenesis of the hypofibrinogenemia remain to be investigated.—H.W.B.

HYPERCOAGULABILITY OF THE BLOOD OF PATIENTS WITH HEPATIC CIRRHOSIS FOLLOWING ADMINISTRATION OF ACTH. W. J. Eisenmenger, R. J. Slater and A. M. Bongiovanni. From the Hospital of The Rockefeller Institute for Medical Research, New York, N. Y. 

Fourteen patients with hepatic cirrhosis were treated with ACTH. Hypercoagulability of the blood was observed in certain of these treated patients despite persistent deficiencies in plasma prothrombin, fibrinogen and platelets. Three patients showed evidence of portal thrombosis during ACTH therapy and in 3 instances the coagulation time was reduced to subnormal levels. Plasma antithrombin activity was found to be subnormal in 6 of 7 patients with advanced cirrhosis but no change in antithrombin activity was detected during therapy. As has been the case in other reported studies, investigation of the major coagulation components failed to disclose the mechanism of this increased clotting tendency in patients under treatment with ACTH.—H.W.B.


In the course of studies on clotting changes in myocardial infarction and its thromboembolic complications, diabetic patients were investigated and observations resulted which suggested a relationship between carbohydrate metabolism and the coagulation mechanism.

Clotting time and protamine titration of heparin-like substance in the blood were studied in patients during an intravenous glucose tolerance test.

The fifteen minute maximal hyperglycemia is accompanied by a maximal use in protamine titration. The clotting times were also prolonged at this time. The only test which did not create these effects was in a patient who received 50 mg. of cortisone parenterally. Similar findings result from oral glucose administration. If a slow intravenous drip of a dilute glucose solution is given, only protamine titer depression is observed.

The insulin tolerance test produces a drop of the protamine titer below normal. This is also caused by epinephrine injected subcutaneously, but the latter also causes a drop in clotting time.

A single intramuscular injection of ACTH produces a transient rise of protamine titration and clotting time.

The mechanisms of these reactions are discussed, but cannot be established as yet.—T.R.T., Jr.
HEMORRHAGIC DIATHESIS ASSOCIATED WITH FIBRINOPENIA AND FIBRINOLYSIS. T. Bennike and S. Mülertz. From the Epidemic Hospital, Copenhagen, Denmark. Acta haemat. 8: 147-154, 1952.

Two fatal cases of fibrinopenia are reported. The first patient had a carcinoma of the stomach with metastases. In the second case, no definite diagnosis could be established. A marked extramedullary hemopoiesis and an aplastic blood picture were conspicuous features. In contrast to previous cases described, the authors could not find any liver involvement. In Case 1 an affection of the reticulo-endothelial system with a blocking of the formation of fibrinogen is suggested. In Case 2 a high fibrinolytic activity in the blood is proposed as the main cause.—C.M.


Study of the optical density of the clot obtained after coagulation of human plasma by thrombin was made. The clot opacity is a function of pH, ionic strength, calcium, coagulation rate, fibrinoplastic and antifibrinoplastic substances. Clot opacity is lower at higher pH. Its values as a function of ionic strength are represented by a curve possessing a minimum. Calcium raises clot opacity, especially in the higher pH range; such is also the case with dextran and polyvinylpyrrolidone. Delayed coagulation also raises the final opacity. Clot opacity is lower after addition of urea, glycerol, KMnO₄, and higher after addition of moranz and heparin.—J.P.S.


This is a description of a case of a 33 year old female patient with thrombopenia and enlarged spleen. After splenectomy the patient recovered, the thrombocytes rose from 4000 to 1.4 millions. Histologically, the diagnosis of sarcoidosis was made.—C.M.

OBSERVATIONS ON TWO CASES OF SPORADIC THROMBOPATHIA. F. Koch and H. E. Schulze. From the Pediatric Clinic, Justus Liebig University, Giessen, Germany. Schweiz. med. Wchnsr. 82: 924-927, 1952.

The authors describe 2 new sporadic cases of the disease, the hereditary form of which was first seen by Willebrandt and Jürgens in 1933. A girl was followed from birth to the age of 16. The second case concerns a boy two years old. In both cases, the coagulation time and the clot retraction were normal. The bleeding time was definitely lengthened. Thrombocyte count normal; the girl had premenstrually slightly reduced platelets. The coagulation time of the bone marrow megakaryocytes was lengthened. Plasma electrophoresis normal. Prothrombin consumption test strikingly shortened. In one case, Ac-globulin was reduced and the recalcification time lengthened. Treatment consisted in blood transfusions. Local hemorrhages responded very well to thrombin application.—C.M.

THE EFFECT OF CORTICOTROPIN (ACTH) AND CORTISONE ON IDIOPATHIC THROMBOCYTOPENIC PURPURA. S. J. Wilson and G. Eisemann. From the Department of Medicine, University of Kansas School of Medicine, Kansas City, Kansas. Am. J. Med. 13: 21-26, 1952.

Complete remissions of variable duration were observed in 5 of 12 patients with idiopathic thrombocytopenic purpura treated with ACTH or cortisone. Six of the patients who did not respond to the hormones subsequently underwent splenectomy and an excellent response was obtained in 5 of them.

Evaluation of therapy was based apparently on clinical condition and platelet counts. Mention is not made of capillary fragility tests. In the light of other studies it is perhaps significant, therefore, that only 1 of the 7 patients, who did not have a platelet rise, failed to show clinical improvement in purpuric manifestations.—H.W.B.
ABSTRACTS

HEMOGLOBIN


Most vertebrate hemoglobins have a molecular weight in the neighborhood of 67,000 and contain 4 protohemes. Oxygen equilibrium studies of the erythrocruorin of invertebrate marine worms indicate interactions between at least 6, and presumably more of the large number of hemes (180) in the molecule.

In the second paper, the oxygen equilibrium of duck hemoglobin is very similar to that of other vertebrate hemoglobins.—O.P.J.

IMMUNOHEMATOLOGY


During the early development of vertebrate embryos there appears a generation of primitive erythroblasts which are soon replaced by a generation of smaller definitive erythroblasts. The rapid decline of the large primitive blood cells is followed by a serologic change indicating that appreciable amounts of proteins of alpha-beta-antigenicity have been released. Serogenesis by cellular disintegration is a normal process in early development, but it may not be the only source of serum proteins.—O.P.J.

RADIATION EFFECTS


In an area affected by an A-bomb radiation, some organisms, including man, will die within a matter of hours due to high roentgen exposure. Towards the perimeter of the area there will be organisms which will die days or weeks following A-bomb radiation. In order to better understand the problem of x-radiation death, the hamster was selected because it might be expected to react in much the same way as the guinea pig and it has not been used extensively in radiobiologic investigations. Two dosage levels were used, 1500 r for 2 min., 44 sec. and 110,000 r for 3 hrs., 15 min. The tissues were fixed in Bouin’s fluid and studied with at least 4 different stains.

In the hamsters killed under the high voltage x-ray beam, there was immediate hemorrhage and edema of the red pulp of the spleen with enlargement of the organ. The spleen in those slowly killed showed no hemorrhage, but rather a definite cytopenia due to cessation of myelopoiesis. In lymph nodes from hamsters killed under the x-ray beam, germinal centers contained pyknotic lymphocyte nuclei, diffusely scattered nuclear fragments and enlarged sub-capsular lymph sinuses. The capsule was thickened in lymph nodes from the other group and the peripheral sinus filled with erythrocytes, edema fluid, fibroblasts and ameboid cells. The thymus, before death under the x-ray beam loses the distinction between cortex and medulla. In animals dying one week after exposure, there was a 50 per cent reduction in the original volume, and lymphocytes were in the medullary rather than cortical portions. The reticulum and Hassall’s corpuscles appeared to be increased. Bone marrow from hamsters after intensive irradiation showed a 60 per cent reduction in leukopoietic elements. Marrow cells from the slow death series were reduced to 10 to 20 per cent of the original number. Only a few normal erythrocytes, many ghost erythrocytes, some lymphocytes, reticular cells and fibroblasts remained.

The order of decreasing sensitivity of the cell types appears to be lymphocytic > myelopoietic > erythropoietic.—O.P.J.
ABSTRACTS