ERYTHROCYTES AND ANEMIAS


The authors report observations on a patient with pernicious anemia who was sensitive to pork and beef liver extracts. While taking folic acid she developed severe neurologic manifestations of combined system disease. She was then treated with micrograms of Vitamin B12 for eight days without reaction. Reticulocytes began to rise on the fourth day and reached a peak on the sixth day. By the tenth day, neurologic regression was evident and the changes are tabulated by the authors. Discontinuance of B12 for seven days lead to some relapse which again responded to further treatment.

This report indicates that B12 in contrast to folic acid should prove effective against the neurologic as well as the hematologic manifestations of pernicious anemia and that B12 is not responsible for sensitivity reactions to liver extract.

C.A.F.


Injection of folic acid antagonists produced a diminution in the size and number of the blood islets of the yolk sac of the embryo and degenerative changes in the nuclei of the islet cells. Of the three antagonists used, 4-amino-pteroylglutamic acid produced the most marked histologic changes. Injection of folic acid prior to administration of the antagonist did prevent the changes in the hematopoietic tissue, but the preliminary injection of B12 did not have an effect in the amounts used.

R.S.E.


Hematologic studies are recorded on a group of 27 adults with nontropical sprue, 17 adults with tropical sprue and 19 children with celiac disease. In the majority of adults, macrocytic anemias were present and in those patients not under liver treatment, a megaloblastic marrow. Patients with celiac disease showed microcytic hypochromic erythrocytes. These studies are related to the morphology of the erythron and are somewhat difficult to interpret, since many patients were on therapy.

C.A.F.

THE ANEMIA OF INFECTION. VII. THE SIGNIFICANCE OF FREE ERYTHROCYTE PROTOPORPHYRIN, TOGETHER WITH SOME OBSERVATIONS ON THE MEANING OF THE "EASILY SPLIT-OFF" IRON. M. Grinstein, J. A. Silva
In pursuance of earlier studies demonstrating an increase in erythrocyte protoporphyrin and urine coproporphyrin associated with the anemia of infection, experiments were designed to establish the significance of free protoporphyrin in red cells (EP); also included in the present report are observations relative to the nonhemoglobin iron, or "easily split-off iron" (ESFe), of the erythrocytes. Data obtained in the course of reticulocytosis produced in animals by hemolytic agents (employing phenylhydrazine and immune erythrocyte antibodies), and by restoration of deficiency anemias (pyridoxine deficiency in pigs and pernicious anemia in a human subject), and studies of effluent blood from congested spleens in nembutal-treated animals indicated that the EP is greater, and the ESFe less, in immature than in mature red cells, and that the erythrocyte EP in splenic venous blood was increased following splenic stasis.

These findings are interpreted as indicating that: (a) an increase in EP usually signifies incomplete hemoglobin synthesis, as in reticulocytes, in red cells altered by iron deficiency and those damaged by toxins or other factors; or it may represent evidence of hemoglobin degradation; (b) the ESFe appears to be a degradation product of hemoglobin associated with the maturation, destruction, and perhaps senescence of red cells.

C.P.E.


In systems of washed cells of freshly drawn heparinized human blood to which various concentrations of resorcinol have been added, the loss of potassium increased with time. When potassium is made to re-enter cells which have previously lost it, the quantity of sodium which leaves the cell is approximately the same as the quantity of potassium which enters.

O.P.J.


Twenty-four male albino rats were hypophysectomized, the weight and blood cell counts were followed, and the bone marrow was examined. Histologic examinations using several technics were utilized, among them silver-impregnation of the reticulum and detection of iron.

Some of the results are mere confirmation of what was already known: namely, anemia, scarcity of the erythroblasts in the marrow smears, and splenic atrophy with increase of the lymphoid follicles.

Some points are of interest: the effect on the bone marrow concern not only the red cell series, but also the myeloid series.

The osmotic fragility of the red cells in saline solution is decreased in the hypophysectomised rats. The increase in the lymphoid follicles in the spleen is nothing but a reflection of a general hyperplasia of the lymphoid tissues (lymph nodes, "Peyer's patches").

The study, using iron staining, shows a striking hemosiderosis in the hypophysectomised animals. The authors believe that the bone marrow hyperplasia is linked to the thyroid atrophy which follows the hypophysectomy.

J.P.S.

The use of several reducing substances to produce rapid reduction in oxygen tension so as to promote sickling of susceptible cells is the subject of this preliminary report. Of the substances used, a saturated solution of hydrogen sulfide was the most active in producing sickling. Solutions of BAL and cysteine were also effective. After exposure to these substances the sickling phenomenon was found to be still reversible when the suspension was exposed to air. The concentrations of each substance necessary to produce sickling were also sufficient to produce a positive nitroprusside reaction.

R.S.E.


The authors have used with equal success either a 0.1 per cent solution of methyl violet or crystal violet in 95 per cent ethyl alcohol. Freshly prepared, air-dried, moderately thick blood smears are covered with this solution for one-half minute. The surplus dye is removed in running tap water.

O.P.J.


It has been shown by the application of Brachet's ribonuclease test and Caspersson's ultra-violet absorption technic that young blood cells contain ribonucleic acid which diminishes progressively as the cells mature. The present study is an attempt to place some of these impressions on a quantitative basis. Marrow samples from 15 normal individuals and 22 suffering from various blood dyscrasias were prepared for studies of films, sections and chemical analysis. Quantitative determinations were made for total nucleic acid phosphorus, ribonucleic acid phosphorus and desoxyribonucleic acid phosphorus. The mean values of these for normal human marrow were 20.7, 14.1 and 6.9 mg. of P. per 100 Gm. of fresh tissue respectively. These values were increased in hyperplastic immature marrows. Nucleic acid levels decreased during reticulocytosis in pernicious anemia following specific therapy and eventually returned to normal. If a hyperplastic marrow contains many cells of medium maturity, then the desoxyribonucleic acid phosphorus value is elevated. The high ribonucleic-acid content of the cytoplasm and nucleoli of the younger marrow cells is apparently connected with the ability to pass through a series of mitotic divisions and to elaborate hemoglobin and specific granules. The nucleolus-associated chromatin which increases as the nucleolar ribonucleic acid diminishes appears to persist after the cell has lost its power to divide.

O.P.J.


A complete historical and bibliographical review on mustard gas is given. The results of the authors' observations in 40 cases of malignant blood diseases, 19 cases of Hodgkin's disease with nitrogen mustard are presented. The following conclusions were reached; Nitrogen mustard is often badly tolerated, and
therefore it should be reserved for cases which can not be treated by x-rays for practical reasons, and above all, for cases which become refractory to x-rays. The very widespread forms are also more easily treated by nitrogen mustard, but the results are usually of short duration. The importance of following hematologic changes is emphasized. Nitrogen mustard should not be given sooner than two months after radiotherapy. The results in the terminal cases of Hodgkins disease were disappointing.

The third part of this work is an experimental study of the methyl-bis-$\beta$-chloroethylamine, in regard to the skin-sensitivity, glucose and protein metabolisms, and antibody formation. In vitro, the bacterial activity of the drug was tested on several micro-organisms. The effect in vitro, on the osmotic fragility of red cells, on coagulation mechanism, and on different enzymes was also considered. Some derivatives, the ethyl instead of methyl and the brom-instead of chloride, were tried in different diseases with good results. Finally, the prophylactic effect of hexamethylen tetramine against the toxic manifestations of the drug appears effective in rabbits and mice, and confirms the previous in vitro studies.


Fifty consecutive cases of leukemia were studied from 1945 to 1947. A significant anemia was present in every case of acute leukemia, in 75 per cent of the cases of chronic lymphatic and 65 per cent of the chronic myelogenous leukemias. The anemia of chronic lymphatic leukemia tended to be more severe at the time of diagnosis and later toward the end. Nucleated red cells appeared in the blood commonly in chronic myelogenous and acute leukemias. The author emphasized that, in the absence of icterus or osseous metastases, erythroblastosis in an adult with only moderate anemia should bring myelogenous leukemia to mind. In both lymphatic and myelogenous leukemia blood loss and destruction may aggravate the anemia. But in addition, lymphatic leukemia has a hypoplasia of erythropoietic tissue through a crowding of the marrow by lymphocytes and myelogenous leukemia has a defective or disorderly erythropoiesis from a hyperplastic marrow. Some evidence has been presented to indicate that either pernicious anemia or a severe megaloblastic macrocytic anemia may precede the onset of acute leukemia.

BLOOD PIGMENTS


Methemalbumin consistently appeared in the serum of individuals receiving antimalarial therapy with both quinine and pamaquine, but did not complicate treatment with either drug when supplied alone, or develop in patients receiving pamaquine and quinacrine concurrently.

A new and convenient procedure is described for the photometric determination of methemalbumin concentrations in serum, utilizing an absorption band at 405 m$\mu$. This method is applicable in the absence of hemoglobinemia and entails only the determination of the serum bilirubin concentration to obtain a factor for correction of the serum blank.


The normal red cell mechanism for reducing methemoglobin and the ways in which this can be influenced are discussed. Methods of identifying methemoglobin and sulphhemoglobin, clinical pictures associated with these pigments, etiologic agents in their production, and treatment are reviewed.
LEUKOCYTIC DISEASE


The serum of a patient with agranulocytosis was found to exert an inhibitory effect on the phagocytic activity of normal neutrophils. Normal leukocytes suspended in the patient's serum failed to ingest bacteria at the same rate as the control. Bacterial growth also took place readily in the same suspension. The inhibitory activity of the serum on leukocytes appeared to increase with the passage of hours. With varying percentages of the patient's serum in the suspension it was observed that the inhibitory effect seemed to be present in high dilution and high concentration, a paradoxical finding which is not explained. The inhibitory effect of the patient's serum could be due either to something toxic for the leukocytes or to the lack of something necessary for normal activity of leukocytes. These significant observations will bear repetition with blood from any patient with neutropenia, particularly the 'primary splenic' variety.

R.S.E.

**Primary Splenic Neutropenia with Arthritis (So-called Felty's Syndrome): Its Treatment by Splenectomy.** S. Smith, and E. S. McCabe. From the Department of Medicine, University of Maryland, Baltimore, Maryland. Ann. Int. Med. 29: 445-455, 1948.

The cases showing chronic neutropenia, splenomegaly, and advanced arthritis were carefully studied, before and after splenectomy. In the first patient the sternal marrow was hyperplastic, in the second hyperplastic. In both instances splenectomy resulted in a normal leukocyte picture. No evidence of white cell phagocytosis was found in either spleen, but supravital stains were not made.

Cases of this type, carefully studied, are important in clarifying our present ideas of spleen-bone marrow relationships.

C.A.F.

**Blood Coagulation and Hemorrhagic Diatheses**


The etiology and pathogenesis of Schönlein-Henoch purpura is discussed in considerable detail in this paper. Twelve cases of the disease are reported, 7 of whom had skin biopsies. Each biopsy showed an acute inflammatory exudate around the small vessels of the corium. There were changes in the collagen of the area involved, but fibrinoid degeneration of the collagen was not present. Eosinophils were prominent in some cases, but the main cells of the infiltrate were polymorphs and histiocytes. The rash may be present with the above changes in the skin without advancing to the stage of purpura. Hematologic examinations, including bleeding, coagulation and capillary fragility tests are normal. The relation of the syndrome to anaphylaxis, allergy and preceding infections, particularly the frequency of hemolytic streptococcal disease is discussed. The authors conclude that the type of lesion encountered in the small vessels brings the syndrome into close relationship with glomerulonephritis, rheumatic fever and polyarteritis nodosa.

R.S.E.


The study of capillary fragility by a suction test during pregnancy and labor shows that the fragility increases at the end of the pregnancy and that during labor it becomes very great. Escluside (40 to 100 mg.) appears to be effective in preventing this 'labor fragility.'

Seven nonpregnant women were given 15 mg. of estradiol, to ascertain if this hormone would reduce capillary resistance. In all but one case, the resistance fell from 30 or 35 centimeters of mercury (normal value to 15 or 7). In one case, progesterone was found to have the opposite effect.
ABSTRACTS

Twenty new-born infants were found to have a high capillary resistance, about 50 centimeters of mercury. Among 16 premature infants, only 5 had a similar increased resistance, while 11 had a lower resistance, and 2 of the latter group (twins of 920 and 900 grams birth weight) had only 5 and 10 centimeters of mercury. The esculoside given to the mother during the labor seemed not to be effective on the capillary resistance of the child.

In conclusion, the authors believe that estrogen plays a great part in the capillary fragility of pregnancy and believe that the administration of folliculin to premature infants is not without danger.

J.P.S.

THREE-STAGE ANALYSIS OF BLOOD COAGULATION. J. H. Milstone. From Department of Pathology, Yale University School of Medicine, New Haven, Conn. J. Gen. Physiol. 35: 301-324, 1948.

The blood-clotting mechanism has been analyzed by a procedure which devotes a separate experimental step to each of the three primary reactions. The activation of prothrombin by thrombokinase followed the course of a unimolecular reaction. The activation of prothrombokinase involved an autocatalytic reaction.

O.P. J.


A series of in vitro experiments are reported, designed to characterize more completely an accessory clot promoting factor variously designated as "labile factor" (Quick), "factor V" (Owren), and "accelerator globulin" (Ware, Guest and Seegers). This factor, present in fresh plasma, apparently potentiates, by some mechanism unrelated to the plasma protease system, the conversion of prothrombin to thrombin in the presence of active thromboplastin and the calcium ion. Tests conducted with a purified fraction of bovine plasma containing the factor demonstrated a loss of potency with aging, its deterioration under these conditions occurring independently of prothrombin inactivation. Applied in the fresh state, however, or after storage in the frozen state, this factor effectively restored the original activity of aged prothrombin preparations.

The factor is possessed of no antihemophilic properties, its action being unrelated to that of thromboplastin, or any of its precursors or activators. A naturally occurring deficiency of this plasma factor is believed to be the basis of a specific bleeding disorder, "Owren's disease," (Lancet 252: 446, 1947) to be distinguished from hemophilia, idiopathic hypothyrombinemia and other hemorrhagic syndromes.

C.P.E.


The first reaction involved in the mechanism of blood clotting, according to the authors, is the enzymatic conversion of the thromboplastic precursor "thromboplastinogen," a normal plasma constituent, to active thromboplastin through the agency of a platelet factor. In hemophilia the clotting defect is related primarily to a deficiency of thromboplastinogen, the platelets in this disorder exhibiting normal clot promoting activity when added to deplateletized normal plasma. Evidence is cited (J. Clin. Investigation 25: 814, 1946, and Science 106: 473, 1947) indicating that the situation in hemophilia is occasionally complicated by the appearance of an inhibitory factor in the blood, which imparts to the latter anticoagulant properties.

A case is described in which a hemophilia-like disorder developed following pemphigus. The prothrombin activity assayed with serial dilutions of thromboplastin was normal, thus excluding the presence of an antithromboplastin. The clotting time of this patient's blood was markedly prolonged; moreover, it was essentially unaltered by the addition of normal blood; hence, the abnormality was presumably not attributable to a deficiency either of thromboplastinogen (as in true hemophilia) or of the platelet factor. Since the clotting time of normal blood was delayed when mixed with the patient's blood, it is assumed that a clot inhibitor was operative. Finally, since measurements of prothrombin
activity in the hemophiliac-like blood, and in combinations of the latter with normal blood, demonstrated only a slight consumption of prothrombin in the course of the clotting process, it is concluded that the effect of this inhibitory agent was to impede the conversion of thromboplastinogen to thromboplastin. An explanation is thus afforded for the failure of certain patients with hemophilia and hemophiliac-like disorders to respond satisfactorily to transfusion therapy or the administration of antihemophiliac globulin.

C.P.E.


The role played by complement in the conversion of prothrombin to thrombin was studied by means of one and two-stage assays of thrombin production, after recalcification and addition of thromboplastin, in plasma freed of complement activity by aging, by treatment with zymun and with ammonia. It was concluded that inactivation of complement by these methods prevents thrombin formation without significantly impairing the activity of prothrombin.

C.P.E.


The influence of anticoagulant therapy on the suspension stability of red cells was studied in 10 subjects receiving heparin, 10 receiving dicumarol, and in 5 recipients of both drugs concurrently. It was determined that, in therapeutic dosages, heparin and dicumarol do not significantly alter the erythrocyte sedimentation rate and that the results of this test are therefore not invalidated by interference from the effects of these drugs.

C.P.E.

BLOOD PRESERVATION AND FRACTIONATION


This article with its bibliography of 381 references serves as an excellent review of the large amount of work undertaken during the war years on blood preservation and the uses of its various products.

Some of the general topics dealt with are blood preservation, reactions to blood products (especially serum hepatitis), procurement and fractionation of plasma, therapeutic uses of albumin and other plasma components.

C.A.F.

BOOK REVIEWS


This is a beautifully printed and illustrated work in which the pathologic disturbances associated with various nutritional deficiencies are described. The book is divided into six sections dealing with dietary deficiencies in general, the essential elements, the essential amino acids, the fat and water soluble vitamins, the essential fatty acids, and the pathologic anatomy of specific tissues.

There are 791 references and 71 superb illustrations, both of gross and histologic material. There has