ABSTRACTS

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ANEMIA


Two hundred and sixty-two newborn Negro infants were tested for sickling trait by the cover-slip method on the first, third and fifth days of life. Positive reactions were obtained in nine, or 3.4 per cent, as compared to sixteen, or 7.6 per cent, in a group of 209 older children (one week to eleven years) similarly tested. Three of the newborns with sickling trait were examined at a subsequent date (seven to seventeen months) and the degree of sickling in each was found to be greater. No cases of sickle cell anemia were present in the group of newborns.

The factors which may contribute to the suppression of sickling trait in early infancy and to the lower incidence of active sickle cell disease in childhood are discussed. It is possible that further study using one of the more recently developed and sensitive tests or, as the authors suggest, by the alteration of the chemical composition of the blood of young infants, may furnish an answer to this latency phenomenon and perhaps even aid in determining which patients with the trait will develop anemia and why.

H.B.M.


The Ashby technic of differential agglutination was used to study the survival of transfused cells in relation to sickle cell disease. Normal red cells transfused to patients with sickle cell anemia showed a normal survival time. Red cells from patients with sickle cell anemia transfused to normal recipient subjects showed a shortened average time of survival. Red cells from healthy donors with the sickle cell trait transfused to normal recipient subjects and to a patient with sickle cell anemia showed a normal survival time. The findings indicate that the defect in sickle cell anemia is inherent in the red blood cell. There is evidence to suggest that sickling is not a function of age of the cell but that the cells in sickle cell anemia vary constitutionally in their liability to sickle. The authors suggest that the difference between the anemia and the trait is qualitative and not simply one of degree.

G.E.C.


A study of the blood of 181 persons in 47 families with Cooley’s anemia revealed that asymptomatic individuals with Cooley’s trait or the mild form of the disease were surprisingly common in New York City.

The diagnostic hematologic procedures employed and the characteristic blood changes are described in detail. The author stresses the importance of the hematocrit as a diagnostic procedure and of the findings of increased resistance of red cells to hemolysis in hypotonic solutions of sodium chloride, stippled red cells, and the presence of hypochromic macrocytes despite the tendency to microcytosis.
The hereditary aspects of this disease remain a subject of controversy, although perhaps the majority of investigators currently favor the hypothesis that the mild form results from heterozygosity of an inherited factor which, when homozygous, causes true Cooley's anemia. While the author's finding of characteristic hematologic abnormalities in healthy members of the families of affected children (both parents in every case of a severely anemic child) supports the view of a dominant hereditary factor, he does not consider this limited study conclusive evidence of such a genetic relationship. He does, however, stress the importance of the mild form of the disease and of the need for more widespread detection of these asymptomatic carriers who are a potential source of hereditary transmission of the overt form of the disease.

H. B. M.


Red blood cells from a patient with paroxysmal nocturnal hemoglobinuria were transfused (1) to an adult with rheumatoid arthritis, and (2) to an anemic premature infant who received at the same time some normal adult blood. Survival of both normal and abnormal erythrocytes was followed by the Ashby technic. The cells from nocturnal hemoglobinuria were destroyed more rapidly than normal, especially in the adult recipient. This fitted in well with the in vitro observation that the baby's serum showed less hemolytic activity than 10 adult and 6 other infant sera tested against the patient's red blood cells. Both the in vitro studies and the transfusion experiments suggest that the red cells in paroxysmal nocturnal hemoglobinuria vary in susceptibility to hemolysis. This variation does not appear to be related to age of the cells.

S. C.


This is a full report of a well investigated case of paroxysmal cold hemoglobinuria associated with chronic hemolytic anemia and Raynaud phenomenon. There was no evidence of syphilis and the Donath Landsteiner reaction was negative. A high titer cold agglutinin active over a wide thermal range was constantly present, and the mechanical fragility of the patient's red cells was increased. He died after four years' observation, of urinary infection. Necropsy findings are reported.

S. C.


The incidence of hemoglobinemia following transurethral resection in a series of 100 cases selected at random was 56 per cent. The criterion used for hemoglobinemia in this study was a concentration of more than 35 mg. of hemoglobin per 100 cc. of plasma. As is pointed out, this concentration is somewhat higher than that used by other investigators who have reported a higher incidence of hemoglobinemia in similar although smaller case studies.

Excessive bleeding, the weight of the tissue removed, and the difficulty of resection appeared to be the significant surgical factors in inducing hemolysis, presumably by allowing much larger amounts of irrigating fluid (sterile water in this series) to wash into the circulation through venous sinuses. An analysis of postoperative reactions showed that gastrointestinal symptoms occurred twice as frequently in patients who had high concentrations of plasma hemoglobin as in those with no significant hemolysis. It is of interest that none of the patients experienced a postoperative chill, that the incidence of fever was greater in the group without hemolysis, and that there were no instances of postoperative oliguria other than one patient without significant hemoglobinemia in whom the oliguria was attributed to cardiac failure. Only six patients in this series had more than 500 mg. of hemoglobin per 100 cc. of plasma (one patient had 1,000 mg.). While levels of plasma hemoglobin higher than this may induce renal insufficiency, this
study of a statistically significant number of patients indicates that the concentration of hemoglobinemia usually encountered during transurethral resection is not sufficient to be harmful.

H.B.M.


These Oliver-Sharpey lectures given at the Royal College of Physicians, London, in March 1948 give a general review of megalocytic anemias colored by the author's own views and experience. As they were delivered a year ago there is no mention of work resulting from the discovery of vitamin B\textsubscript{12}. There is an initial summary of what was then known of the stomach principal, extrinsic factor, the liver principal and folic acid, with emphasis on the work done by the author and his colleagues on the stomach factor. A discussion of the various types of megaloblastic anemia and the results of therapy follows. Finally, the prognosis and incidence of cancer and other complications in pernicious anemia is discussed in relation to Wilkinson's own carefully observed series of 1,600 patients.

Some of the views expressed here of the relative inefficacy of some types of liver preparations, particularly wartime and postwar British extracts, have been challenged and the suggestion made that a lowered protein intake in the diet is a more relevant factor in suboptimal responses. (G. E. Shaw, Lancet 1: 543-546, 1949.)

S.C.


One hundred and twenty-seven cases of severe, sometimes fatal and frequently refractory anemia were observed among sepoys serving in Assam and Eastern Bengal. Probable contributory factors were inadequate military hygiene, recent malarial infection and malnutrition, although evidence of these was not constantly present. Most of the blood examinations showed a macrocytic and either ortho- or hypochromic anemia. The bone marrow showed an increase in red cell precursors and an apparent shift to earlier forms but no megaloblastic change. The mortality was at least 38 per cent. Adequate diet, control of infection and transfusions were the most effective therapeutic measures but even with these recovery was slow. Eighteen of 56 patients given liver injections showed a response which was possibly attributable to the liver, but the general impression was that the anemia was not strikingly influenced by liver or yeast extracts.

Knowledge of the tropical macrocytic anemias is clearly far from complete. This group of cases does not seem to conform to the anemia described by Wills. The etiology is complex and the author suggests that long-standing nutritional defects and repeated malarial infections antedating military service were of prime etiologic importance.

S.C.


Liver extract was discontinued on 12 patients with pernicious anemia. Red count, hemoglobin and determinations of fecal urobilinogen were made. Relapse was defined as a fall in red count on two successive measurements to more than two standard deviations below the average red count of the patient's during treatment. Six of the 12 patients failed to show hematologic relapse over a period of twenty-six to twenty-nine months. Eight to eighteen months were required to produce relapse in these patients. Of interest was the increase in urobilinogen above 350 Ehrlich units in some cases when the red count fell to between 2.5 and 3.5 million.

C.A.F.

This survey of the incidence of the blood groups (O, A, A1, A2, B, AB, A1B, A2B, M, N, MN, Rh+, and Rh- negative) as well as the secretor and nonsecretor (gastric) attributes, was undertaken in the attempt to determine whether any relationship existed between them and pernicious anemia and stomach carcinoma. No relationship was found between pernicious anemia and the blood groups or Rh negativity. Patients with pernicious anemia secrete blood group specific substances in their saliva in the same proportion as normal individuals. The percentage of secretors and nonsecretors was approximately the same in pernicious anemia patients who showed gastric atrophy as it was in those who had a normal gastric mucosa. Patients with carcinoma of the stomach show an approximately normal distribution of blood groups and the secretor trait.

G.E.C.


Three patients with pernicious anemia and acute neurologic manifestations of posterolateral sclerosis were treated with vitamin B12. Typically, 15 micrograms of the material was given by injection every forty-eight hours for four injections. In all patients, there was a rapid subjective and objective improvement, beginning within two to five days after start of therapy.

S.E.


This clinical article reviews the effect of vitamin B12 in a group of patients with macrocytic anemia. Four patients had nutritional macrocytic anemia, one had nontropical sprue, 11 had tropical sprue, and 5 had pernicious anemia. In addition, 14 patients with known pernicious anemia who also had posterolateral sclerosis were studied. It was found that, in all cases, the administration of vitamin B12 (parenterally) was followed by rapid subjective and objective improvement. In the patients with anemia, there were increase in strength, return of appetite, elimination of paresthesiae of the tongue, and improvement in the character of the stools (in sprue). Reticulocytosis occurred and was followed by improvement in the levels of red cells, hemoglobin, and leukocytes. In the patients with neurologic lesions, there was alleviation of tingling, stiffness, and numbness, and remission of neurologic signs.

Details of dosage and management with B12 are noted to require individual management in each particular case.

S.E.


Pursuant to previous investigations (J. Lab. & Clin. Med., 32: 1455, 1947, Abst. 37), indicating the lack of response to folic acid of the microcytic anemia produced by the administration of radioactive strontium, the efficacy of this hemopoietic principle was tested in white rats receiving the approximate median lethal dose of total body x-irradiation, which is presumed to cause damage to viscera as well as to bone marrow. The results indicated that folic acid provided little or no stimulus to erythropoiesis following exposure to x-radiation. The authors conclude, therefore, that the resultant bone marrow damage was attributable to direct injury, and that irradiation damage to viscera involved in the elaboration of the anti-anemia principle must have played a relatively unimportant role in the production of anemia.

C.P.E.

DIETARY EFFECTS ON ANEMIA PLUS HYPOPROTEINEMIA IN DOGS. F. S. Rocheit-Robbins and G. H. Whipple. From the Department of Pathology, the University of Rochester, School of Medicine and Dentistry, Rochester, New York. J. Exper. Med. 89: 339-368, 1949.
ABSTRACTS

In order to study the production of hemoglobin and plasma protein by various specific food proteins, dogs were first depleted of hemoglobin and plasma proteins by frequent blood removal and a nonprotein diet containing all other dietary essentials.

I. Some Proteins Further the Production of Hemoglobin and Others Plasma Protein Production. (pp. 339-358.)

Although there was a satisfactory production of total blood protein with the various egg fractions fresh and processed, fresh and processed meat, fresh beef heart and canned salmon muscle, certain quantitative and qualitative differences were noted. In general, a meat diet produced a greater amount of new blood protein than did the several egg products. Also, on a meat diet the hemoglobin production greatly exceeded the plasma protein production, whereas the egg protein diets favored the production of plasma proteins. More specifically, the hemoglobin production with fresh beef muscle was three or four times that of plasma protein, and the output of total blood protein, with fresh or processed beef muscle, twice that obtained with the egg diets. Beef heart and salmon muscle produced a pattern similar to beef muscle except that the total blood protein output was less. Processed egg albumin was the only egg product not well utilized.

II. The Findings with Milk Products, Wheat, and Peanut Flours as Compared with Liver. (pp. 359-368.)

Liver was used as a control in these experiments as it gives maximum amounts of newly formed blood protein with a hemoglobin production of approximately three times that of plasma protein. Casein was found to compare favorably with liver and meat. Lactalbumin was not as effective as casein but, like the egg proteins, it favored plasma protein production. Peanut flour gave a poor response. While the response to wheat gluten was better than that with peanut flour, its unpalatableness presented difficulties in experimental control.

These two papers are an extension of previously reported studies on body and blood proteins. Further work on this subject is being carried out with radioactive isotopes to determine more accurately the change which can take place between body and circulating proteins in protein-depleted dogs.

H.B.M.


Sulfonamides have been used successfully in reducing mortality rates following surgical procedures on Amblystoma embryos. Since some animals showed toxic effects, the present investigation was undertaken to study the effect of different concentrations of sulfadiazine and sulfanilamide on embryos at the blastula, gastrula and tail bud stage of development. The range of drug concentration in spring water was 0.12 to 1.0 per cent. Anemia was more frequent and more pronounced in sulfanilamide treated animals. Splenic development was markedly suppressed. Granulopoiesis in the subcapsular region of the liver was apparently unaffected. The anemia seemed to be a combination of aplastic and hemolytic types. Because of the hematologic response of these animals, they may be useful for testing the effects of other drugs.

O.P.J.


In order to determine the factors which may influence the blood picture in the newborn and which have mainly accounted for the present lack of standard blood values, the authors studied the effects of early and late clamping of the umbilical cord by heel punctures and blood volume determinations (see J. A. M. A. 116: 2568, 1941, and Am. J. Dis. Child. 69: 1123, 1945) and in the present report by observations on sinus blood.

The most important cause of variation in blood values is the time of clamping of the cord after delivery. When clamping is delayed until the placenta has separated, approximately 108 cc. of placental blood, otherwise lost by immediate cord clamping, is added to the infant's circulation; a rapid adjustment of plasma volume occurs; and the infant's blood volume is increased by the volume of these additional
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red cells. Significantly higher values for hemoglobin, red cell count and hematocrit were obtained when clamping was delayed. For example, the mean value of hemoglobin in sinus blood on the first day was 10.6 Gm. per cent compared to 16.4 Gm. per cent when the cord was clamped immediately on delivery.

Other variable factors were the source of blood (blood levels were higher with capillary than with sinus blood) and, of less significance, the time after birth at which the blood sample was taken.

That increased erythropoiesis is prolonged, probably as a compensatory mechanism, in the group deprived of the additional placental blood was indicated by a comparison of the reticulocyte counts made on the third day in the two groups.

H.B.M.

ERYTHROCYTE FRAGILITY


In order to avoid certain sources of error in the usual clinical fragility test with hypotonic salt solutions, as well as to shorten the time and reduce the number of solutions required for a test, an alternative procedure is suggested in which a continuous hemolysis curve is obtained, either with or without photographic recording, in a solution containing a penetrating solute such as thiourea or glycerol.

Using this method the hemolysis curves are similar to those obtained with hypotonic salt solutions, but small individual peculiarities are brought out.

G.E.C.


Utilizing a reproducible method, photographic records of the hemolysis of erythrocytes from 170 normal persons and 90 anemic individuals have been obtained. In white subjects, the osmotic resistance of the erythrocytes in the 0 to 10 year age group was found to be greater than that of normal adults. A comparable age difference was not found in a limited number of Negroes. The average osmotic resistance of the erythrocytes of the normal Negro was greater than that of the normal white in the corresponding age group. The erythrocytes of children with sickle cell anemia were more resistant than those of normal Negro children. The average for individuals with the sickle cell trait was between that for sickle cell anemia and that for the normal, but with considerable overlapping in both directions. In both Mediterranean anemia and its carrier state the blood was markedly more resistant than that of the normal controls, the carries showing a resistance as great as that of the anemic individual.

G.E.C.


It has been known that when red cells are suspended in solutions of different ionic composition but of the same depression of the freezing point, that there are discrepancies in the relation between tonicity and volume. Chlorides of monovalent cations obtained from two different sources were prepared in a 0.172 M solution in water. The salts used were LiCl, NaCl, KCl, RbCl and CsCl. Red cells were most fragile in LiCl and least fragile in NaCl. The K losses in LiCl were so small and slow that they could not account for the increased fragility. It has been pointed out that there are differences in the molarity of solutions which are isotonic with plasma.

O.P.J.

It has been thought that heating red cells for short periods between 49.6°C and 50.6°C had small effect on the swelling which occurs in hypotonic media of different tonicity. Suspensions of washed red cells in NaCl were heated for two minutes at 48°C and 52°C, and then allowed to cool to 25°C. After an hour at this temperature, samples were obtained for the determination of cell volume and the extent of hemolysis. At 48°C, heated and unheated cells behave equally well as osmometers, but those heated at 52°C have an impaired ability to swell in hypotonic solutions. Heated cells lyse in higher tonicities than unheated ones. Some of these findings may be accounted for by the large K losses and K-Na exchange.

O.P.J.

IMMUNOHematology and transfusion


The third child of a family, with an Rh negative mother and Rh positive father was affected by a hemolytic anemia which did not appear until the seventh week after birth. Antibodies were found at the examination 23 days after delivery (1/1 in saline, 1/8 in albumin medium). The Coombs test was positive.

The second child had had a similar anemia when he was 6 weeks old, probably of the same nature. Between the first and the second pregnancy the mother received a transfusion with Rh positive blood, which may have increased her iso-immunization.

The child was fed with cow milk, and thus the maternal antibodies could not have been given by any other route than the transplacental. It is difficult to decide whether the maternal antibodies fixed themselves on the infant red cells a long time after birth, or whether they were fixed early and destroyed the cells only after a long interval.

The very severe anemia of this third child was treated with Rh positive transfusions, which was believed to be preferable to Rh negative blood, since there were no more maternal antibodies in the infant's circulation at this time.

J.P.S.


Sixteen patients with negative serologic tests for syphilis were studied after receiving injections of plasma from blood donors with positive STS. The period of storage before separation of plasma from the luetic donor bloods varied from one to ten days, and the intervals between freezing and thawing of the plasma ranged from two weeks to two months. In all instances a positive STS was acquired by the recipient, the initial titer of which represented the dilution in the recipient's blood volume of the reagin contained in the injected plasma. Reversion of the tests to negative occurred in all instances within a period of four days. It is concluded that the blood of donors with syphilis should be acceptable for use in any blood bank with a plasma program, inasmuch as infectivity of the material is abolished by freezing or by storage for a minimum of four days in the refrigerator.

C.P.E.

The Very Rare Rh Genotype R,r (Cde/cde) in a Case of Erythroblastosis Fetalis. C. van den Bosch. From the Department of Pathology, University of Louvain, Belgium. Nature, London 162: 781, 1948.

In a case of erythroblastosis fetalis, the mother's blood group was OMNP and the cells were agglutinated by anti-C, anti-E but not by anti-D. Her serum contained complete and incomplete anti-D. She thus belonged to the very rare allelic combination Cde (Wiener's r, r?) predicted by Fisher in 1944.
Detailed study of the family made it possible to identify CdE as an inherited combination on one chromosome. This discovery brings additional support to Fisher's already very well founded theory.

S.T.C.

A Hemolysin Associated with the Mumps Virus. H. R. Morgan, J. F. Enders, and P. F. Wagley. From the Research Division of Infectious Diseases of the Children's Hospital, Children's Medical Center, and the Thorndike Memorial Laboratory, Second and Fourth Medical Services (Harvard), Boston City Hospital, Harvard Medical School, Boston, Massachusetts. J. Exper. Med. 86: 503-514, 1948.

The observations made on an hemolysin found in the amniotic and allantoic fluids of chick embryos infected with the virus of mumps are presented. Chicken, sheep and human erythrocytes were all susceptible to hemolysis although those of man were less affected.

It appears evident from the following observations that this hemolytic activity is due to a specific product of the mumps virus: (1) a similar hemolysin could not be demonstrated in normal egg fluids or in those infected with two strains of influenza virus; and (2) the hemolysin could be inhibited by mumps convalescent sera from man and monkey but only slightly by normal monkey serum taken during the early stage of the disease in man.

The authors have inferred from their study of the effect of heat, temperature and time of incubation, and of pH on the hemolysin that this hemolytic activity is not identical with the hemagglutinative property of the infected fluid. That some as yet undefined relationship exists between these two factors, however, is indicated by the similarity of their behavior in respect to adsorption on and elution from chicken red blood cells, and their inhibition by specific immune serum. Attention is also drawn to the enzyme-like behavior of the hemolysin.

H.B.M.


This note records the phenotypes and genotypes of four families, three of whom show transmission of the gene R' and one of the extremely rare r'.

S.T.C.

Hemolytic Anemia Associated with Atypical Hemagglutinins. W. J. Kuhns and P. F. Wagley. From the Department of Medicine, School of Medicine, Johns Hopkins University, and Baltimore Rh Typing Laboratory, Baltimore, Md. Ann. Int. Med. 30: 408-423, 1949.

A very interesting case is reported showing intravascular thrombosis and atypical hemagglutinins in high titer. In addition to cold hemagglutination, a warm hemagglutinin was demonstrated which reacted at 37 degrees with the patient's cells and with 63 per cent of bloods compatible for A1, A2, O, M, N, Rh, and Hr. The nature of these agglutinins and their possible role in hemolytic anemia and intravascular thromboses are discussed in competent and interesting fashion.

C.A.F.


This survey of the field of blood derivatives summarizes the advances of therapeutic knowledge of these substances especially during the past ten years. In brief, the following points are covered:

1. Blood Cells. White cells and platelets can as yet not be satisfactorily separated and preserved; red cells can. Red cells resuspended in saline to a hematocrit of 65 per cent constitute an ideal treatment for certain patients with anemia, for (a) it is possible thus to supply more hemoglobin with less loading of the circulation; and (b) the removed plasma may be reserved for use for other patients. Hemoglobin itself has been prepared from red cell fractions for possible use in traumatic shock: experimentally, its high oxygen-carrying capacity combined with its high osmotic activity make it theoretically excellent for shock treatment; but actually injection of pure hemoglobin is often followed by depression of renal function, so that its clinical use has had to be cautious to the extreme. Globin itself may be used as a substitute for plasma proteins.

2. Plasma. Whole plasma is, of course, used widely in the treatment of shock. The occurrence of "homologous serum hepatitis" after the administration of plasma, however, has been a drawback. Statistics are presented as to the incidence of this disorder under various conditions: single transfusion of blood
or serum (hepatitis rare); use of fraction I from pooled plasma (hepatitis in 10 per cent of subjects); use of pooled plasma or serum (hepatitis in 4 to 7 per cent of recipients). Methods of preventing this hepatitis are mentioned: of these, only sterilization of the plasma seems potentially practicable. The author suggests the use of pooled plasma only if neither blood nor serum albumin are available.

3. Plasma Fractions. Discussed are factors important in coagulation (fibrin, thrombin, fibrinogen, antihemophilic globulin), blood-grouping globulins, disease antibodies (gamma globulin for measles, hepatitis, mumps), and albumin. All these substances have already found widespread clinical use for their particular qualities.

The article is not meant to be all-inclusive, but covers the salient material in a brief, salient manner.

S.E.

IRON METABOLISM

CHEMICAL, CLINICAL, AND IMMUNOLOGICAL STUDIES ON THE PRODUCTS OF HUMAN PLASMA FRACTIONATION.

XXXIX. THE ANEMIA OF INFECTION. STUDIES ON THE IRON-BINDING CAPACITY OF SERUM. G. E. Cartwright and M. M. Wintrobe. From the Department of Medicine, University of Utah, School of Medicine, Salt Lake City, Utah. J. Clin. Investigation 28: 86-98, 1949.

From determinations of the serum iron concentrations and unsaturated iron-binding capacity of serum, from which the total iron-binding capacity and per cent of iron saturation of serum were calculated, the authors conclude that the hypoferremia accompanying infections is not the result of a reduction in the iron-binding capacity of serum but must depend upon some other factor. The total iron-binding capacity of serum in 30 normal individuals averaged approximately 360 gamma per cent, the iron-binding protein being approximately 35 (±6) per cent saturated with iron. In 13 patients with chronic infection, in 3 dogs with sterile abscesses and another with an acute infection, the total iron-binding capacity was significantly reduced but the reduction in serum iron was proportionately greater, with the result that the per cent saturation was lowered.

Measurements of serum iron concentration following intravenous iron injections indicated that the concentration peaks were limited by the capacity of the serum to bind iron, and when the total iron-binding capacity of the serum was exceeded, the unbound iron rapidly left the blood stream, with the concomitant development of toxic symptoms. The administration of metal-combining globulin (fraction IV-7) to 3 patients with chronic infection resulted in a temporary increase to normal in the total serum iron-binding capacity. Subsequent intravenous injections of iron resulted in a greater initial five minute rise in the serum iron concentration than had previously been noted but the rate of iron disappearance from the serum was not significantly affected. Moreover, the temporary artificial increase in iron-binding capacity was not followed by a detectable mobilization of iron in the blood.

C.P.E.

CHEMICAL, CLINICAL AND IMMUNOLOGICAL STUDIES ON THE PRODUCTS OF HUMAN PLASMA FRACTIONATION.


A protein constituent of plasma, a beta-1 globulin with the capacity to bind metal ions, particularly iron, copper and zinc (Science 104: 340, 1946) has been measured in normal and pathologic sera by these authors, who performed concomitant measurements of the serum iron concentration and computed the unsaturated iron-binding capacity as well as total iron binding capacity of these sera. In a group of 30 normal subjects the serum iron concentration averaged 100 gamma, iron-binding capacity 200 gamma, and total capacity 300 gamma per 100 cc. of serum; the circulating iron-binding protein was, on the average, 34 per cent saturated with iron.

In cases of iron deficiency, whereas the serum iron concentration was lowered, both the unsaturated iron-binding capacity and the total iron carrying capacity of the serum were elevated. In the presence of infection not only the serum iron but also the iron-binding capacity and total capacity were reduced. In a variety of debilitating conditions with associated hypoproteinemia, there was a reduction in the iron-binding capacity of the serum and no elevation of the latter was observed even when iron deficiency was present as an additional complication. No deviation from the normal was found in pregnant women. Elevated values for serum iron and percentage saturation of the iron-binding protein were found in refractory anemia, pernicious anemia, hemochromatosis, transfusion hemosiderosis, and liver disease.
ABSTRACTS

Human plasma fraction IV-7, binding iron in the proportion of 1 ml. per ml. of protein, was injected intravenously into 22 individuals in amounts of 2.5-5.0 grams, the injection times ranging from 15 to 30 minutes. The injections, which were without incident, were followed by a rise in serum iron which reached a peak 12 to 24 hours after injection and subsided over a period of 2 to 6 days, excepting in cases of hemosiderosis and hemochromatosis in whom a more sustained elevation occurred.

The evidence indicated that the body iron is completely protein-bound, which perhaps explains the lack of a physiologic mechanism for iron excretion. Excepting in terminal hemochromatotic patients, in whom some of the excessive serum iron is apparently bound to other proteins, the serum iron is found exclusively in combination with the beta-1 globulin designated as the iron-binding protein (J. Clin. Investigation 28: 73, 1949). The elevations in iron-binding protein observed in cases of iron deficiency may be responsible for the enhanced iron absorption in this condition, but the relation of iron-binding capacity to the facility and rate of iron absorption remains to be established. The finding of increased iron saturation implying the co-existence of bone marrow block, iron excess and severe liver disease proved of great value in the differential diagnosis of hemochromatosis and simple cirrhosis.

C.P.E.


Combined histochemical, radioautographic and tracer methods were used to study the absorption and distribution of single test meals of radioiron in guinea pigs, rats and one dog. The iron demonstrated histochemically in the duodenal mucosa the mesenteric and cervical lymph nodes, liver and spleen was derived largely from sources other than the single test meal. This visible iron did not undergo well defined cyclic changes after a single test meal. It accumulated over a period of days or weeks of continued intake of a diet containing considerable iron. It behaved more like storage iron than iron in transport. The visible granular iron in the duodenal epithelium exerted no demonstrable effect on the amount of iron absorbed, and it did not appear to be a morphologic expression of mucosal block. Most of the radio iron of the test meal traversed the duodenal epithelium rapidly. In one dog it was transported from the intestine via the portal vein, only insignificant amounts being found in the thoracic duct lymph. There was no evidence to indicate that the reticulo-endothelial system participated directly in the absorption of iron from the intestine or transport of the absorbed iron from the intestine to the liver, blood, and other organs and tissues.

G.E.C.

POLYCYTHEMIA VERA


Determinations of the arterial blood oxygen saturation were made in 74 individuals of whom 48 were cases of polycythemia vera. The data presented indicated that the degree of arterial oxygen saturation was within the limits of normal in resting polycythemic subjects, normal values being found in patients with hematocrits as high as 81 per cent. The authors suggest that low oxygen saturation figures reported in the literature may have been attributable to technical errors inherent in gasometric measurements, or may have resulted from failure to conduct tests promptly after the blood samples were obtained. Thus, erroneously low oxygen saturation values may depend on the fact that “inactive hemoglobin” (J. Biol. Chem. 138: 563, 1941), as well as carboxyhemoglobin, are converted in vitro to normal reactive hemoglobin, with resultant increase in the apparent oxygen capacity.

C.P.E.

LEUKOCYTES

PRIMARY SPLENIC NEUTROPENIA. M. S. Sacks and T. N. Carey. From the Department of Medicine, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore. South. M. J. 41: 922-925, 1948.
This is a case presentation of a 56 year old woman who, at the age of 55, developed fatigue followed by otitis followed by furunculosis. Examination revealed hepatosplenomegaly. There was a slight anemia, but the striking finding in the blood was a leukopenia (1,100) with granulocytopenia (19 per cent neutrophils). The bone marrow was "somewhat hypocellular" and was considered to show "decreased number of granulocytes with a shift to the left." Ultimately, splenectomy was undertaken. The spleen weighed 2,100 grams and showed congestion. Following operation, the white count rose to normal levels (e.g., 10,700) with normal granulocyte counts (e.g., 69 per cent). The blood count remained normal during the following two years, when the patient died of pulmonary atelectasis and apparent hepatic disease. The liver at autopsy showed congestion.

Unfortunately, meager data are presented, and the exact mechanisms of neutropenia cannot easily be interpreted. It seems likely, however, that the case is one of the generic "hypersplenic neutropenia" group, relieved by splenectomy.

S.E.


A patient with a marked leukopenia (1,500 per cu. mm.), marked splenomegaly without anemia or thrombocytopenia was splenectomized with complete alleviation of the leukopenia. This patient was followed 56 days postoperatively. No specific pathology was found in the spleen. The bone marrow as determined by sternal puncture was cellular. The author concludes that this was a case of primary splenic neutropenia and that the disease results from splenic dysfunction as a result of selective destructive action of the reticulo-endothelial cells of the spleen. It is to be regretted that this patient was followed for such a short period of time.

G.E.C.


This note discusses the occurrence, over a period of twenty years, of periodic ulceration of the mucous membranes in association with leukopenia and neutropenia. The patient, a woman, developed recurrent ulcers of the tongue, mucosa of the cheek and skin of the angles of the mouth, approximately every four weeks from the age of 12 on. During pregnancy at the age of 30, additional lesions at the vulva occurred. At the age of 31, ulcers developed also at the lower leg, and resisted healing.

Physical examination, except for the ulcerations and their scars, was regularly negative. Spleen, liver, and lymph nodes were not palpable. The red cell count, hemoglobin, and sternal marrow punctures were normal. The persistent abnormality was leukopenia, which was due to neutropenia. Typical counts ranged from a total white count of 1,300 to 4,800, with granulocytes from 500 to 3,000 per cu. mm. (normally, granulocytes range 3,000 to 6,000 per cu. mm.). Treatment with liver, hog's stomach, nicotinic acid, pyridoxin, pentnucleotide, nucleic acid, yellow bone marrow extract, and iron had no effects either on the blood count or the lesions.

The etiology for this type of abnormality has never been explained. The ulcerations are considered the result of "lowered resistance" due to granulocytopenia. Treatment is universally ineffective. (See H. A. Reimann, J. A. M. A. 136: 238-144, 1948.)

S.E.


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G.E.C.

This case report concerns chronic neutropenia associated with splenomegaly in a 17 year old girl. These abnormalities were first discovered at the age of 15 during the course of investigation of an acute gastroenteritis. In the following six months she required hospitalizations for persistent and recurrent fever, pallor, and infections, including a severe bout of pneumonia. The positive physical findings included a just-palpable liver, and an easily palpable spleen; there was no lymphadenopathy. Anemia was present (R.B.C. 1,54 million; hemoglobin 25 per cent); platelets were normal; and the white count was low (e.g., 3,200 with 11 per cent granulocytes). A bone marrow puncture was normal.

After blood transfusion and recovery from pneumonia, the patient remained in good health and developed normally. The spleen, however, continued to increase steadily in size; and the white count and granulocyte count were regularly low. The question of splenectomy was tabled because of a negative adrenalin test.

This case, of course, is different from the cyclic neutropenia without anemia and without splenomegaly.
ABSTRACTS

described by Barling (Proc. Roy. Soc. Med. 41: 653-4, 1948, see preceding abstract) and others, and perhaps corresponds better to splenic neutropenia or splenic neutropenia with anemia (Doan and Wiseman; Dameshek), in which splenectomy may be expected to give beneficial results.

S.E.


Exudative material withdrawn from the pleural cavities of dogs injected with turpentine are usually alkaline and they contain an extractable leukocytosis-promoting substance. When this material is allowed to age for several months some of its properties change by becoming insoluble in isotonic saline. The leukocytosis-promoting substance is in the supernatant while a leukopenic component is in the insoluble residue. This leukopenic component differs from the one found in acid exudates by being inactivated by incomplete hydrolysis with tenth-normal hydrochloric acid. However, it appears that both of these factors exist in combination in fresh exudates and therefore help to explain the mechanism of leukopenia with inflammation.

V. Menkin.

Destined Granulocytes Transfused. (Fate of Transfused Granulocytes.) Bernard Dreyfus. Sang 19: 570-574, 1948.

A transfusion of 600 cc. of myeloid leukemic blood containing 250,000 granulocytes by cubic millimeter was done in each of two recipients affected with subacute hemocytoblastic and lymphoblastic leukemias.

In both, the increase was very short and the survival of the white cells was under 30 minutes. The blood examination shows in this initial period many forms of destruction. Thus, the cell's destruction seems to be intravascular, and not intracellular, as has been said. The lysed cells also disappear very quickly from the blood stream, and this explains the difficulty encountered in observing the phenomenon.

The total white cell count was lower 2 hours and 24 hours after the transfusion that it was before (31,500 against 50,000 in the first case; 41,400 against 51,000 in the second case). This suggests that some of the white cells of the recipient are destroyed in the first hours following transfusion.

These results are to be compared with those of Minot and Isacs (1935) who found a similar reduction of the injected white cells, injecting lymphoid leukemic cells to a patient with lymphosarcoma, but injecting only 450 cc. of blood containing 89,000 white cells per cubic millimeter. They found a very slight modification in the white count and they did not find any lysed cells.

Dreyfus's conclusions are that no substitutive effect is to be found for white cells in blood transfusion, and that all increase in white cell count found after blood transfusion expresses only the regeneration capacity of the recipient.

O.P.J.


When embryonic chick spleen fragments were implanted, it was observed that in some instances cultures containing 25 per cent normal rabbit serum would produce great numbers of phagocytic cells which ingested myelocyte debris. Experiments were undertaken to determine the occurrence and nature of this macrophage promoting factor (MPF). Control hanging drop preparations were grown in a medium of 50 per cent fowl plasma, 25 per cent embryonic juice and 25 per cent Tyrode's solution. In the test preparations, heterologous sera or resuspended fractions of sera were substituted for the Tyrode component. In cultures containing MPF, the area of outwandering cells was markedly reduced, myelocytes were not at the periphery, and many macrophages were at the peripheral zone. This factor was not present in all animals and it even varied within a given animal over a period of months. Oddly enough, MPF was present only in the species known to have the Forssman antigen. Properties of the MPF are: it is thermolabile and resists freezing-drying, it is insoluble in absolute alcohol or acetone but soluble in Tyrode after precipitation in 1/3 saturated ammonium sulfate. It does not seem to be identical with any of the factors in inflammatory exudates as reported by Menkin.
ABSTRACTS

BLOOD COAGULATION


Data obtained from experiments on dicumarolized dogs suggests that the hemorrhagic diathesis produced by dicumarol is attributable not alone to a disappearance of prothrombin but also to the loss of a factor, the function of which is to facilitate the conversion of prothrombin to thrombin. Variations in the concentration of this conversion factor present in plasma, serum, or serum pseudo-globulin may explain the familiar discrepancies in the results of one and two-stage methods of estimating prothrombin activity. It may also account for the therapeutic efficacy of serum in the treatment of cattle with sweet clover disease, a phenomenon otherwise difficult to explain.

C.P.E.


In the first series of experiments using 16 rabbits, the authors found that phenyl-indane-dione (P.I.D.) had a very marked effect on prothrombin level. Doses of 10 to 20 milligrams per kilo produced a decrease of prothrombin to a level of 30 to 40 per cent, this effect being reached before the eighteenth hour. There was no modification of platelets, clot retraction, or fibrinogen level. Higher dosage did not produce greater hypoprothrombinemia and the authors did not find any hemorrhages, even with a dosage ten times the standard dosage. The lethal dose was well over 600 mg./kilo, which gave a very high safety margin. Histologic examinations of the rabbits given very high doses of P.I.D. (under 400 mg./kilo) did not show histologic injuries.

The P.I.D. was used in the prevention of thrombosis in 45 women after pregnancy. In all these cases, doses of 10 to 20 mg./kilo yielded a very constant decrease of prothrombin level. The decrease began earlier than with dicumarol, about the twelfth hour and the full effect was obtained between the twenty-fourth and the forty-eighth hour, which is a 30 to 40 per cent level. Return to a normal level was quite constant and 100 per cent prothrombin was reached by about the ninety-sixth hour.

This constancy in the chronology is very different from that observed with dicumarol. Individual susceptibility to the drug seems also to be less important than in the case of dicumarol.

In 1 cases, the P.I.D. was given to patients with known thrombophlebitis (every 3 days 10 mg./kilo). This dose was effective in controlling the prothrombin level around 30 per cent. The patients’ state was, in both cases, favorably affected. In the 41 cases where the drug was given prophylactically, no phlebitis was observed.

In contrast with these advantages, the complete inactivity of vitamin K, even in huge doses, and even when given prior to the administration of the P.I.D., must be emphasized. But this fact is perhaps of minor importance, since in no case, was hemorrhage or hypoprothrombinemia of less than 10 per cent observed.

J.P.S.

LEUKOCYTES, LEUKEMIA AND LYMPHOMA


Myelocytosis, eosinophilia, megakaryocytosis, are common bone marrow reactions in case of carcinoma bone metastasis. Erythroblastosis is most significant, but plasmacytosis is, according to the authors, the prominent feature. Rohr and Heglin, Nordenson, and above all Stüger discussed this relation. Marchal and Mallet found between 3 and 6 per cent of plasmacytes, in more than half the cases of carcinoma bone metastasis, and often this moderate plasmacytosis was useful to detect micrometastasis lost in the bone marrow, and even in some cases permitted discovery of a latent carcinoma of the lung, breast, stomach or prostate. The morphology of these plasmacytes is indistinguishable from that of the plasma cells in multiple myeloma. The more or less deep basophilia of the cytoplasm, the presence or absence of vacuoles or nuclei, are the same; multinucleated cells may be found.
When there are only 4 to 6 per cent plasma cells in the bone marrow, the histologic differentiation from myeloma is easy. But it is possible to find more than 10 per cent of plasma cells in metastatic cancer, and in 3 cases of prostatic carcinoma, between 25 and 50 per cent of the cells were plasma cells. In such cases, differentiation from myeloma is very difficult if aggregates of neoplastic cells are not present in the smear. Moreover, hyperproteinemia may be present (13.3 grams per cent in one of the cited cases). In such cases, the possibility arises that a true myeloma may exist, complicating the metastatic carcinoma.

In addition to involvement of the bone marrow, a plasmacytic reaction may be found in the liver, and was observed by the authors in a case of metastatic carcinoma of the stomach.

J.P.S.


It is now well known that atrophic cirrhosis of the liver may follow infectious hepatitis, and that hepatitis is a common feature of infectious mononucleosis, but we had not found any description of atrophic cirrhosis following infectious mononucleosis, so this observation seemed interesting to us.

A 38 year old male was affected, in February 1946, with typical infectious mononucleosis (with adenopathy, enlarged spleen, mononucleosis and a Pau and Bunnel reaction positive at a dilution of 1:16). Recovery was very slow, and in June jaundice appeared which lasted ten days and which reappeared in September. The liver was now enlarged, and ascites appeared. Different hepatic tests were strongly pathologic. After aspiration of the ascitic fluid, the liver was no longer palpable.

After treatment with transfusions, plasma, methionine, vitamin B and Patek diet, the patient improved slowly, and following seven months of this treatment was in good health.

This patient had never consumed any alcoholic beverage, and the authors believe that the succession of mononucleosis and cirrhosis in this case was not a mere coincidence.

J.P.S.


The authors studied the histology of 1,300 lymphoid tissues submitted to the Army Institute of Pathology during the past war. Of these, 700 cases were Hodgkin’s disease. They employed the Jackson-Parker classification and distribution was 14.3 per cent paragranuloma, 71.1 per cent granuloma and 14.6 per cent sarcoma. The authors presented illustrations of alterations in histologic composition of lesions and discussed their nature and frequency. A virtually complete alteration in histologic pattern of tumors was noted in 39 per cent of 138 autopsied cases in which biopsies were available. In 384 of 700 cases there were a variety of histologic pictures in different areas.

While classification of lymphoid tumors was useful chiefly from the standpoint of prognosis, with the increased therapeutic armamentarium it is of particular importance to correlate the histologic picture with therapeutic response. It may be that the variable nature of the lesion is in part responsible for the inconsistencies in response of this group of neoplasms.

C.A.F.