BLOOD COAGULATION


Normal plasma has been shown to contain, among other things, a globulin factor which affects the transformation of prothrombin to thrombin—a plasma 'accelerator substance' called 'Ac-globulin.' The present report concerns the stability of this substance and of prothrombin itself under various conditions. Under specific conditions, human venous blood was drawn into citrate or oxalate anticoagulant mixtures and then, after a variety of manipulations (centrifugation at various speeds; storage for various periods of time; use of various concentrations of oxalate or citrate), tested for the amounts of contained prothrombin and Ac-globulin.

For testing purposes, Ac-globulin was determined by a previously described method in which prothrombin, thromboplastin, and calcium are present in controlled amounts, so that the rate of thrombin formation measures the amount of Ac-globulin. The amount of prothrombin was determined (1) by a standard two-stage method, in which saline appears as a diluent; and (2) by a modified two-stage method, in which saline is replaced by bovine serum (containing, of course, Ac-globulin).

In both oxalated and citrated plasma, the prothrombin activity did not change for a period of several days. After this period, the original two-stage method detected a progressive fall in prothrombin. However, by the modified method—in which Ac-globulin was added—the amount of prothrombin was still unchanged for as long as fifty-six days. It seemed obvious, therefore, that the apparent fall in prothrombin was illusory, and that the fall was due to a loss of Ac-globulin and not prothrombin itself from the stored plasma. In addition, the apparent (illusory) prothrombin fall occurred earlier and was more marked in oxalated than in citrated plasmas; i.e., Ac-globulin was less stable in oxalated than citrated blood.

In a further experiment, a sample of oxalated plasma, which originally had a prothrombin content of 190 units/cc, was found, after 53 days of storage, to have an apparent prothrombin content, by the original two-stage method, of 15 units/cc. When this determination was modified by the addition of (a) bovine serum, or (b) pure Ac-globulin, or (c) an extract of bovine platelets; then the prothrombin content was found still to be 190 units/cc. It thus seems that not only serum, but also platelets, contain a prothrombin-accelerating substance. However, platelets were also found to contain a factor which decreased the stability of Ac-globulin; this factor was apparently operative after the platelet Ac-globulin supply had been dissipated (44 hours of storage).

These and further similar experiments will compel revision of the simple schemata of blood coagulation. It seems likely, however, that the plasma-, serum-, and platelet- Ac-globulin substances (which are similar) are the same as Quick's 'prothrombin A' and as Owren's 'factor V'; and that they play an important role during the initial stages of coagulation.

S.E.
CONCENTRATION OF PROTHROMBIN AND AC-GLOBULIN IN VARIOUS SPECIES. R. C. Murphy and W. H. Seegers.

From the Department of Physiology, Wayne University College of Medicine, Detroit, Michigan. Am. J. Physiol. 154: 134-139, 1948.

The authors determined the concentrations of prothrombin and Ac-globulin in the bloods of various animals, including man; and noted that there was a wide variation from species to species. For example, it was found that, although the plasma prothrombin content in dogs, man, and guinea pigs was the same (300 to 300 units/cc.), the plasma Ac-globulin of the dog measured 250 units/cc.; that of man, 12 units/cc.; and that of the guinea pig, 30 units/cc. Since the Quick one-stage method of prothrombin estimation measures, not the amount of prothrombin, but the amount of prothrombin plus the rapidity of its conversion to thrombin (this conversion depends to a large degree upon Ac-globulin), it can be seen that the differences in various species between the one stage and the two-stage methods of prothrombin determination may well be due to the marked variations in concentration of Ac-globulin in various species. Thus, dog, man, and guinea pig have identical prothrombin contents (two-stage method); but widely divergent prothrombin times (one-stage method), due probably to the different Ac-globulin concentrations found.

Man has a low plasma Ac-globulin activity, and therefore a relatively high ratio of prothrombin to Ac-globulin. Hence, the authors suggest, there may be a relatively narrow margin of safety, beyond which "hypoprothrombinemia" may occur.

PLATELET EXTRACTS, FIBRIN FORMATION AND INTERACTION OF PURIFIED PROTHROMBIN AND THROMBOPLASTIN. A. G. Ware, J. L. Fahey, and W. H. Seegers. From the Department of Physiology, Wayne University College of Medicine, Detroit, Michigan. Am. J. Physiol. 154: 140-147, 1948.

Analysis of extracts of bovine platelets led to a revision of the relatively naive concept that platelets initiate blood coagulation by the liberation of initial amounts of thromboplastin. Actually, a small amount of thromboplastin was found in platelets, but it was only a very small amount. In addition, two other substances were present: (1) an Ac-globulin type of substance, and (2) a new factor called "platelet factor 2." 1. Platelet extract was found to contain something which accelerated the conversion of prothrombin to thrombin in the presence of thromboplastin and calcium. This substance acted similarly to serum Ac-globulin, and was quantitatively identical with serum Ac-globulin in its ability to convert prothrombin into thrombin. In addition, platelet Ac-globulin and serum Ac-globulin were both similarly precipitated by half-saturated ammonium sulfate; and were both destroyed by heating to 53 C. On the other hand, there was a difference between the two substances in their length of stability at 53 C.; and, more dramatic, only platelet Ac-globulin could be sedimented in the ultracentrifuge. Hence, it was concluded that platelet Ac-globulin and serum Ac-globulin are probably two different proteins with similar prothrombin-activating activities. The authors estimated that some 5 per cent of the total accelerator activity comes from the platelets.

2. Platelet extracts were found to contain a previously undescribed action or substance which hastened the action of thrombin on fibrinogen. The factor was inferred from the following types of data: thrombin + fibrinogen = clot in 16 seconds
platelet extract + thrombin + fibrinogen = clot in 11 seconds
platelet extract + fibrinogen = no clot in 10 minutes

This substance was rapidly diluted out. It is still under investigation.

It is pointed out that neither serum Ac-globulin nor platelet Ac-globulin is absolutely necessary for the production of thrombin: these substances apparently act merely as catalysts. A detailed schema is presented in which the roles of these accelerator substances in the initial stages of coagulation is incorporated. The schema, of course, is still speculative.

ABSTRACTS

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 43 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 2 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 K2, 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.


To evaluate the significance of the reported increased susceptibility of thrombocytopenic blood to heparin (Ann. Int. Med. 27: 381, 1947), these investigators studied the clotting times of platelet-free and platelet-rich plasmas prepared in silicone coated apparatus, which were mixed in different proportions and contained graded concentrations of added heparin. The data presented justifies the conclusion that the magnitude of the clot inhibitory effect of heparin is inversely proportional to the number of platelets present, and that the increased susceptibility of thrombocytopenic purpura blood to the action of heparin is attributable to the reduced platelet concentration rather than to a supplemental anticoagulant effect introduced by the presence of hypothetic heparin-like substance. The results further suggest that the concentration of active heparin normally present in plasma is minute, i.e., 0.0005 mg./ml. or less.

C.P.E.

CONCERNING THE RELATION BETWEEN PITUITARY ADRENOCORticOTROPIN AND THE CIRCULATING BLOOD PLATELETS. M. A. Greer and B. R. Brown. From the Joseph H. Pratt Diagnostic Hospital and the Depart-

Since an increase in platelet concentration is usually found in the peripheral blood attending infection, trauma, hemorrhage, and asphyxia, conditions which stimulate a release of pituitary adrenocorticotropic (ACTH), the possible effect of the latter was tested in rats injected either with hog pituitary tissue or purified ACTH. A preparation of the latter was also given by repeated intramuscular injection to five human subjects, including three normal individuals, one male and two female, a young woman with hypopituitarism and another with thrombocytopenic purpura following an unsuccessful splenectomy. No change in platelet count was detected following these procedures. Moreover, although pituitary ACTH is capable of causing a dissolution of lymphoid tissue with peripheral lymphopenia (Endocrinology 35: 1, 1944), no reduction of circulating lymphocytes occurred in these experiments, the only hematologic effect noted being a transient polymorphonuclear leukocytosis.

C.P.E.


For many years it has been generally accepted that ionized calcium is essential for coagulation. The use of amberlite which quantitatively removes calcium from the blood and other new technics have been utilized by the authors to reinvestigate some of these problems. Sodium oxalate and citrate act in different manners. The oxalate not only precipitates ionized calcium, but it also removes it from a compound which is essential for coagulation. Citrate combines with prothrombin and renders it inactive. The addition of magnesium or strontium restores the prothrombin to its original state. Studies of prothrombin activity under various types of condition have suggested the presence of a labile factor which is indispensable for coagulation and unstable in decalcified plasma.

O.P.J.


Experiments are reported which fail to confirm published reports ascribing to aminophyllin (theophyllin-ethylenediamine) a thromboplastic action with an accelerating effect on blood clotting which might predispose to intravascular thrombosis. Following the administration of aminophyllin orally or by vein, no statistically significant changes were detectable in the clotting time or prothrombin activity of hospital patients with normal hepatic function and hematological findings.

C.P.E.


In search for a form of heparin which might have a more prolonged action in the body than those currently available, the authors devised a concentrated form of heparin (200 to 300 mg. per cc. of aqueous solution) emulsified in a mixture of cholesterol derivatives, peanut oil, and beeswax. The use in this form of about 2 milligrams of heparin per pound of body weight resulted in satisfactory prolongation of the coagulation time for seventeen to twenty-four hours after a single injection. There were no toxic effects and no hemorrhagic phenomena with high coagulation times. According to the authors, "pain was negligible." Compared with this method, the use of concentrated aqueous heparin increased the coagulation time for only six hours; and the use of heparin dissolved in Pitkin's menstruum was associated with severe pain at the site of injection.

Although the authors list expensiveness as a disadvantage in the use of other forms of heparin, they do not mention the relative cost of the current preparation.

S.E.
ABSTRACTS


This is a well documented article (57 references) in which the literature on hemorrhagic hereditary telangiectasia is reviewed. A family with the disease is described and particular reference made to the pulmonary arteriovenous fistula which occurred in two cases. Clinical, pathologic, physiologic and roentgenologic aspects of this complication are discussed.

C.A.F.


This monograph includes, among other topics, the following discussions on hemorrhagic disorders: mechanism of coagulation, heparin, vitamin K and other vitamins, pseudohemophilia, hypoprothrombinemia, and the metabolic alterations following hemorrhage.

S.E.

ERYTHROCYTE MORPHOLOGY AND PHYSIOLOGY


By means of phase microscopy, according to the author, it is possible to demonstrate the presence of intracellular granules and rods, exhibiting Brownian movement, in unstained wet preparations of mouse blood diluted with hypotonic oxalate solutions. Similar findings were obtained on examining dried unfixed smears mounted in 10 per cent formalin or 1.1 per cent ammonium oxalate. The number of cells presenting these characteristics corresponded with the number of reticulocytes counted by routine methods. Moreover, their identification as reticulocytes was confirmed by the device of adding brilliant cresyl blue or new methylene blue to the oxalate diluent, these rods and granules being incorporated into stainable reticulum. Similar observations have been made in preliminary studies of human blood.

C.P.E.


Fifty normal full-term infants and 7 premature infants were examined daily for the first 8 days of life. Parallel observations were made using the aa' dipyridyl staining technic and the prussian blue method. Reticulocytes were also counted. The percentage of granule containing cells (siderocytes) was very similar with both methods. The number in the blood of normal new-born infants gradually decreased during the first 8 days to approximate the value reported for normal adults. There was a rise of siderocytes from the second to fourth days in infants exhibiting physiologic jaundice. Premature infants had an even higher siderocyte percentage with the maximum occurring on the fourth day.

O.P.J.


The increase in blood viscosity attending the sickling of red cells previously demonstrated in cases of sickle cell disease (J. Clin. Investigation 19: 788, 1940) has been utilized by these authors as the basis for a viscometric method adaptable for the study of this trait. Employing an Ostwald viscometer and testing preparations of red cells washed and suspended in Tyrode's solution, an increased viscosity was observed following equilibration of the samples with nitrogen or carbon dioxide, an effect which was prevented by preliminary equilibration with carbon monoxide but not effected by alterations of pH, by
repeated washing of the erythrocytes with saline solution, or by the addition of heparin, oxalate, or cyanide.

C.P.E.


Red cell fragility may be quantitated by counting the number of erythrocytes which survive treatment in a given solution or by measuring the hemoglobin liberated. For precise work the hemoglobinometric method using a photo-electric absorpiometer is essential. That concentration of salt which produces 50 per cent lysis is designated the mean corpuscular fragility or M.C.F. When plotted on arithmetic probability paper the points for normal subjects fall on or close to a straight line. Fragility curves from patients with classical acholuric jaundice vary considerably in form and suggest two or three groups of cells differing in M.C.F. and its standard deviation. The affected members of one family suffering from acholuric jaundice yielded straight line curves. It is suggested that this family has a genetically distinct form of the disease.

O.P.J.


In view of the demonstration (Fed. Proc. 5: 126, 1946; J. Biol. Chem. 165: 723, 1946; Cancer Res. 6: 497, 1946) that the toxic properties of cobalt are related to its effect on —SH groups, the action of BAL, a protector of —SH groups in arsenical poisoning was studied with reference to the possible presentation of cobalt-induced polycythemia in rats. No such inhibitory influence of BAL on the development of polycythemia was demonstrable when the drug was supplied three times weekly in a dose of 0.2 mm/Kg concomitantly with cobaltus chloride.

C.P.E.


The authors performed gasometric measurements of the oxygen content and capacity of blood samples obtained from the sternal marrow cavity of 23 patients with polycythemia vera, 6 with secondary polycythemia, 11 with chronic anemia, and 11 with leukemia and myeloid metaplasia. Control studies were conducted on 34 individuals whose hematologic status was essentially normal. The range of percentile oxygen saturation was similar in all groups studied with the exception of patients with secondary polycythemia, in whom there was a reduction of marrow oxygen saturation corresponding to the relative unsaturation of the peripheral arterial blood. Although data were obtained in some cases suggesting an increased oxygen utilization relative to the blood flow the technic of sampling used by the authors precluded, in their opinion, a satisfactory demonstration of local hypoxia, to which increased red cell production in anemic states has been attributed, and which may be responsible for chronic erythropoietic stimulation in patients with polycythemia vera.

C.P.E.


This excellent monograph comprises six articles on the architecture, production, and destruction of the red cell. There are four comprehensive but concise reports on the fundamental aspects of red cell cytochemistry, endocrines and erythropoiesis, experimental hemorrhage, and iron-porphyrin metabolites, and two more clinical articles on the macrocytic anemias, and the hemolytic mechanisms.

S.E.

These data should provide a useful baseline for those investigators studying hematologic changes in the dog. The authors demonstrate a similar differential cell distribution in different areas of marrow, although the degree of cellularity was variable.

C.A.F.

THERAPY OF ANEMIA

Observations on the Etiologic Relationship of Acrhyia Gastrica to Pernicious Anemia X. Activity of Vitamin B12 as Food (Extrinsic) Factor. L. Berk, W. B. Castle, A. D. Welch, R. W. Heinle, R. Anker and M. Epstein. From the Thorndike Memorial Laboratory and Harvard Medical School, Boston, Massachusetts and from the Departments of Medicine and Pharmacology, Western Reserve School of Medicine, Cleveland, Ohio. New England J. Med. 239: 911-913, 1948.

The Boston investigators had previously demonstrated a heat stable food substance, so-called extrinsic factor, which in combination with a heat labile factor of normal gastric juice produces a hematopoietic response in patients with pernicious anemia. They report the potentiation of crude and concentrated liver extracts by gastric juice as well. This article is concerned with the action of normal gastric juice on four patents given 5 gamma of vitamin B12 daily by mouth. In each a greater reticulocyte rise occurred with the simultaneous administration of gastric juice and B12. It is suggested that the extrinsic factor may be identical with or closely related to the antipernicious anemia factor of liver which itself is presumably identical with B12. Since patients with pernicious anemia have normal amounts of B12 in their feces, it appears that the function of normal gastric juice is to facilitate its absorption.

C.A.F.


This review of folic acid knowledge delves into extensive historical data on vitamin M, vitamin B12, xanthopterin, norite eluate factor, and Streptococcus lactis R. factor; and then discusses the analysis, synthesis, and properties of pteroylglutamic acid. The role of the material in the nutrition of various animals (mice, dogs, guinea pigs, pigs, mink, insects) is covered; and the interrelationships of conjugated forms. There is a closing section the clinical uses of the drug.

S.E.


This monograph details information on the history, chemistry and pharmacology of folic acid, and presents a few notes on its clinical effects in pernicious anemia and nutritional macrocytic anemia. The data cover the knowledge of the substance up to November, 1948.

S.E.


Maintained from the time of weaning on a pteroylglutamic acid (PGA) deficient diet and a PGA antagonist, later supplemented with succinylsulfathiazole, mice developed granulopenia, lymphopenia, and anemia in 30-60 days. Histologic examinations of the spleen at this stage indicated practically complete cessation of normal hematopoietic activity and excessive hemosiderin deposits in that organ. Simultaneous bone marrow changes are described, indicating marked hyperplasia of immature elements identified as primitive blastic cells, and a depletion of more adult forms, interpreted as evidence of maturation arrest. Following the parenteral administration of PGA, the regimen being otherwise unaltered, the characteristics of the peripheral blood, spleen and marrow promptly reverted to normal. Thus, whereas
the vitamin may not be required in mice for the formation of the most immature blood elements the maturation of these cells apparently depends on the presence of PGA.

C.P.E.

FAILURE OF XANTHOPTERIN TO INFLUENCE HEMATOPOIESIS AND GROWTH IN RATS. J. A. Pritchard. From the Department of Pharmacology, School of Medicine, Western Reserve University, Cleveland, Ohio. Proc. Soc. Exper. Biol. & Med. 66: 221-225, 1948.

The effects of pteroylglutamic acid (PGA) and of xanthopterin were studied in weanling female albino rats maintained on a purified folic acid-deficient diet supplemented in one series by sulfathiazole and, in another, by succinylsulfathiazole, a portion of the latter group being subjected to repeated bleedings in order to produce anemia. The majority of sulfathiazole treated rats developed anemia regarded as hemolytic in origin, accompanied by evidences of reticulocytosis, leukocytosis and increased excretion of bile pigments, not completely correctible by PGA or xanthopterin. Those receiving succinylsulfathiazole, and in which blood-loss anemia was artificially imposed, exhibited erythrocytic, leukocytic and growth responses when PGA was supplied, xanthopterin proving completely inert.

C.P.E.

A METHOD FOR STUDYING THE EFFECT OF VARIOUS SUBSTANCES UPON RED CELL MATURATION IN-VITRO. E. E. Hays. From the Department of Biochemistry, University of Vermont College of Medicine, Burlington, Vermont. Am. J. M. Sc. 216: 518-533, 1948.

The author describes in more detail his method of assaying hematopoietic factors in vitro. The bone marrow cells of rats are used and the number of reticulocytes counted after a period of incubation with various substances. His studies would indicate that normal rats serum, human serum, liver extracts potent in treatment of pernicious anemia, B12, Tyrosine, glutathione and Bacto-yeast extract appear to have a red cell maturing effect, i.e., a high reticulocyte count in the incubated marrow. Folic acid was not active.

In vitro methods of studying hematopoiesis are needed. This method, while perhaps a rough index of alteration in the marrow cells, has the advantage of being simple and has been shown by the author in other studies to be a worth-while assay method for potency of liver factors.

C.A.F.


This is a general review article which emphasizes that the necessary and sufficient therapy in pernicious anemia is refined parenteral liver extract, and that all other drugs (pteroylglutamic acid, iron, hydrochloric acid, vitamins, oral preparations of liver) are useless and unnecessary. There is no discussion of vitamin B12.

S.E.

LEUKOCYTES, LEUKEMIA AND LYMPHOMA


The blood of most crustacea contains two main classes of cells when examined in the living condition, viz., those with refractile granules or globules and those without. Careful examination with higher magnification reveals that only a few have a truly hyaline cytoplasm. In general four types of blood cells are recognizable. Lymphoid cells which are few in number, small, and globular or spindle shaped. The second type are thigmotactic amoebocytes, which are semi-hyaline and sometimes finely granular. These cells are the most active phagocytes of the blood and they can ingest India ink when injected into the animal. A third type consists of those cells with coarse, refractile and acidophilic granules. The fourth type of cell contains refractile granules which are intermediate in size between the fine granules usually seen in semi-hyaline thigmocytes and the cells with coarse refractile granules. Type I is comparable to the mammalian lymphoblast or hemocytoblast and type II to the monocyte or free macrophage. Hematogenesis occurs in the blood channels. The clotting mechanism is powerful in some crustacea; weak in others.

O.P.J.

Tissue mast cells have been the objects of many researches, but it took the work of Holmgren and Wilander (1937) to focus our attention on their probable physiologic role with respect to heparin production. This has stimulated investigators to apply various physical and histochemical technics in order to ascertain the nature of the metachromatic granules in these cells. Wislocki and Dempsey (Anat. Rec. 96: 249, 1946) studied mast cells in the human and rat, and found a species difference with respect to the presence of lipoidal material. The basophilic granules were not digested by ribonuclease or hyaluronidase. Noback and Montagna (Anat. Rec. 96: 279, 1946) showed that alkaline phosphatase was localized in the majority of mast cell granules. The cytochrome C-cytochrome oxidase system was also present. Wislocki, Bunting and Dempsey (Am. J. Anat. 71: 1, 1947) showed that the metachromatic reaction was unaltered by hyaluronidase and that the granules did not give the Bauer reaction after digestion with saliva. Montagna and Noback (Anat. Rec. 56: 355, 1948) have extended our knowledge by demonstrating mast cell granules contain phospholipin, peroxidase and lipase. Janes and McDonald have studied the distribution of these cells in a wide variety of human tissues and have concluded that their presence in synovial membranes may explain why the hemarthrosis is often fluid in closed injuries of joints. There is a definite increase of mast cells in the synovial membrane in tuberculosis and other chronic infections. When a solution of protamine was added to fluid blood aspirated from a knee, it formed a definite coagulum. This suggests that heparin may in part be responsible for the prevention of clotting in hemarthrosis.

O.P.J.


Polynuclear leukemia is a type of myeloid leukemia described by P. E. Weil in 1937 (Sang 5: 539, 1937) with the following characteristics: moderate increase of the leukocytes (average 30,000 to 50,000), 80 to 99 per cent of these leukocytes being adult polynuclears, myelocytes very scarce (1 to 3 per cent or absent), very few metamyelocytes. Bone marrow, liver, spleen show the usual features of myeloid leukemia, with more than the usual ratio of adult cells (for instance, 30 per cent myelocytes, 30 per cent metamyelocytes, 30 per cent polynuclears). The evolution of the disease usually is very slow (ten years).

Since the original description, Weil has seen 15 cases of such polynuclear leukemia. The red cells are usually slightly modified, and some nucleated red cells can be found in the peripheral blood. In the 12 cases reported in the present communication, a polycythemia between 6 and 8 millions was observed. The authors discuss the relation between myeloid leukemia, myeloid metaplasia of the liver and spleen, and polycythemias. Numerous forms of transitions are possible between these syndromes, with an initial onset of polycythemia or of myeloid hyperplasia, and with a more or less malignant character of this hyperplasia.

J.P.S.


The case described shows, as an outstanding symptom, a platelet count up to 3,3 millions without anemia or leukosis. In the bone marrow, enormous increase of megakaryocytes with normal differential count and morphology. Clinically good general condition, no lymphomata and only slight enlargement of spleen. Treatment with urethane, arsenic and nitrogen mustard caused a decrease of thrombocythemia and splenomegaly.

The case shows a selective increase of megakaryocytopoiesis, without participation of hematopoiesis or leukopoiesis.

C.M.


This article encompasses in its discussion therapeutic agents of theoretic and practical value in leukemia. The current literature is briefly and critically summarized (89 references).

C.A.F.
BOOK REVIEWS


The authors present convincing evidence that folic acid orally or parenterally did not influence the leukopenia produced in cats by exposure to 2000 whole body irradiation. C.A.F.


What is known of the natural history of lymphosarcoma is discussed. The various advantages of surgical, radiation, mustard, and other miscellaneous agents in the management are reviewed. C.A.F.

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BOOK REVIEW


This short booklet by three eminent British authorities summarizes present knowledge of the Rh-Hr factor and presents this information in an understandable manner. The subject is roughly divided into three main headings, and each is discussed by the investigator most intimately concerned with that phase of the topic. Dr. Race describes the present concept of the genetic inheritance of the various Rh genes, their distribution in the population and the roles which the various factors of the Rh-Hr complex (C, D, E, c, d, e, ) play in incompatibility matings. Dr. Mollison takes up the clinical considerations of this subject. He discusses in detail the ways in which iso-immunization to the Rh factor occurs, the role of sensitization in hemolytic transfusion reactions and in the causation of hemolytic disease of the newborn. The topics of diagnosis, pathologic anatomy and therapy of this affection of the fetus are well handled and most of the disputed points and unsolved problems are clearly discussed. Dr. Mourant describes the actual mechanics of the various tests and manipulations now in use in the routine typing procedures in the diagnosis of sensitization and the establishing of the presence of hemolytic disease in the newborn.

This booklet expounds concisely and quite clearly our present state of knowledge concerning this important subject.

Jacob Neber