HEMATOPOIESIS

Hematopoiesis. G. E. Cartwright and M. M. Wintrobe. From the Department of Internal Medicine, University of Utah College of Medicine, Salt Lake City, Utah. Ann. Rev. Physiol. 11: 335-354, 1949.

This is a review of the literature appearing from July 1947 to June 1948 relative to porphyrin metabolism, vitamin B12, pteroylglutamic acid, macrocytic anemias, reticulocyte-ripening substances, iron metabolism, bone marrow, and possible hormonal factors in hematopoiesis. Granick's excellent work is quoted. The inadequacy of folic acid in the treatment of pernicious anemia is emphasized. The lack of correlation between plasma and red cell choline esterase activity and induced remissions in pernicious anemia patients on di-isopropyl fluorophosphate is cited as a logical objection to one suggested mode of action of pteroylglutamic acid. They divide the macrocytic megaloblastic anemias into two groups: those responding to purified liver extract and pteroylglutamic acid and those responding only to the latter. Although substantiation of the work on reticulocyte-ripening substances is needed, implications of their possible role in several anemias are made. The confusing state of knowledge about the relationship of the endocrine system to hematopoiesis is discussed briefly. The important work of Laurell is summarized. Several papers on bone marrow physiology and the microspectrographic technics of Thorell are quoted. Plum's concept of possible formation of erythrocytes by detachment of cytoplasmic pseudopodia of normoblasts is mentioned.

P.F.W.


Diabetogenic doses of alloxan given intraperitoneally in rats, provoke the following changes in the blood:

Anemia, with decreased reticulocytes, an increased osmotic fragility of the red cells, granulocytosis, and a decrease of the lymphocytes. A very striking atrophy of the spleen is observed. Lymph nodes, Peyer's patches, thymus, also show similar involution of the lymphoid tissue. These experiments demonstrate clearly that alloxan has a toxic effect not limited to the islets of Langerhans.

J.P.S.

Incidental Finding of Megaloblastic-like Cells in Bone Marrow of One of Two Swine with Macrocytic Anemia and Achlorhydria. F.D. Lawrason and E.P. Cronkite. From the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md. Yale J. Biol. & Med. 22: 57-66, 1949.

Hematologic observations are recorded in 2 swine followed for approximately seventeen months after exposure to atom bomb ionizing radiation at Bikini. In one animal who received only a relatively small amount of radiation, macrocytic anemia and achlorhydria were accompanied by a hyperplastic marrow
containing considerable numbers of megaloblastic-like cells. The second animal, which presumably received considerable more radiation than the first, developed macrocytic anemia and exhibited achlorhydria but no cells similar to megaloblasts were found in the marrow. The relative role of nutrition, radiation and disease could not be conclusively evaluated in these animals.

W.N.V.

INCREASED RADIORESISTANCE OF RED BONE MARROW AFTER ANOXIA. J. A. Schack and R. C. MacDuffie.


Jacobsen et al. have reported that the red bone marrow of rabbits, in which a regenerative anemia was produced by phenylhydrazine hemolysis or by repeated bleeding, showed less injury when treated with x-ray than the normal rabbit bone marrow.

The present work extends these observations to mice, using a decreased oxygen tension as a means of producing a stimulated bone marrow. Counts of the erythroid elements were made on the bone marrow in both groups of mice. Hyperplasia of the bone marrow produced by anoxia enhanced the resistance of the erythroid elements in the bone marrow of mice to a subsequent exposure to 500 r total-body irradiation by x-ray.

R.C.C.


From The Wilkie Surgical Research Laboratory and Department of Pathology, University of Edinburgh, Scotland. J. Path. & Bact. 63: 245-251, 1949.

The present investigation was undertaken to test Sylvan's contention that reparative hyperplasia in the skin of the rat is initiated by a release into the tissues of a metachromatically staining substance derived from granules of histogenous mast cells. Samples of the tongue and skin from thirteen species, including man, were studied for (1) mast cells, (2) free chromotrope substances, and (3) alkaline phosphatase. A proportion of mast cells from the rat and mouse consistently showed the presence of the enzyme. Doubtful reactions were obtained in mast cells from the skin of the dog and guinea pig. The enzyme was absent from the numerous mast cells in a case of urticaria pigmentosa. When granules reacted weakly to the Gomori reagents they were still capable of staining metachromatically with toluidine blue. However, when granules reacted intensely to Gomori reagents they would not stain metachromatically. It was impossible to demonstrate the simultaneous presence of alkaline phosphatase and free chromotrope substance. In view of the fact that mast cells in the vicinity of small blood vessels contained alkaline phosphatase, it has been suggested that the presence of the enzyme there might be concerned with the maturation of the cell rather than its ultimate functional activity.

O.P.J.

ROENTGENOLOGIC FINDINGS IN OSTEOMYELITIS FOLLOWING BONE MARROW INFUSIONS IN INFANTS. E. C. Texter, W. A. Irwin and D. H. Kaump.


The clinical and roentgenologic findings in 2 cases of osteomyelitis secondary to intraosseous infusion are presented, and in addition 19 other such cases reported in the literature are summarized. The over-all risk of osteomyelitis in this procedure is low (0.41 per cent.) unless hypertonic solutions or continuous infusion is used, when the risk becomes much greater (6-13 per cent). Intraosseous infusions are contraindicated in the presence of severe infections. In none of the cases reported did the osteomyelitis prove fatal and in all, complete healing occurred.

P.F.W.

ERYTHROCYTES

INFLUENCE OF SNAKE VENOM ON MAMMALIAN ERYTHROCYTES IN VITRO. V. B. Philpot, Jr.

From the School of Medicine, Tulane University of Louisiana, New Orleans, La. Am. J. Physiol. 158: 77-83, 1949.

This work was performed because of the contrary results reported in the literature as to whether snake venom actually hemolyzes mammalian erythrocytes. The results obtained were that water mocassin and
copperhead venoms cause agglutination and hemolysis of washed human erythrocytes. The venom of the rattlesnake, C. adamanteus, gave similar results but to a lesser degree. Human serum inhibited the hemolytic activities of all three venoms mentioned above on human erythrocytes. Serum of the dog and sheep activate the hemolytic activity of the moccasin venom on their homologous erythrocytes. Serum of the rabbit and man inhibit. Dog cells are much more susceptible to rattlesnake venom than are human cells. Fresh dog serum, heated dog serum, and rabbit serum will activate rattlesnake venom hemolysis of dog cells. This work indicates that there is a great species variation in the susceptibility of erythrocytes to any snake venom.

R.C.C.


The authors present evidence to indicate that inhibition of the activity of the acetylcholine-cholinesterase system of the erythrocyte may affect changes in the permeability of that cell. Both methadon (2-dimethylamino-4,4-diphenylheptanone-5 hydrochloride) and physostigmine, which are inhibitors of cholinesterase activity, were found to produce alterations in erythrocyte permeability. The effect of these agents on permeability was influenced by the sodium and potassium content of the medium, by the pH and by the presence of acetylcholine.

W.N.V.

**ERYTHROCYTE AGE AND CHOLINESTERASE ACTIVITY. J. A. Pritchard. From the Department of Chemistry and Physics, Army Medical Department Research and Graduate School, Army Medical Center, Washington, D. C. Am. J. Physiol. 158: 72-76, 1949.**

Variations in cholinesterase activities of erythrocytes have been found in anemias. Red blood cells from patients suffering from blood destruction or blood loss have been found to show an elevated cholinesterase activity. This experiment was conducted in an attempt to determine the mechanisms responsible for this change. The author summarizes his work as follows: "Repeated hemorrhage in rats produces progressive increases in erythrocyte cholinesterase activity. Upon cessation of hemorrhage the ChE activity declines to normal levels. When centrifuged, rat erythrocytes distribute so that younger red cells are found in the upper part of the centrifugate. These red blood cells possess much higher ChE activities than the erythrocytes found in the lower regions of the packed cells. A possible mechanism explaining the variations of erythrocyte cholinesterase activity in anemias is offered."

R.C.C.

**FREEZING OF WHOLE BLOOD. M. M. Strumia. From the John S. Sharpe Research Laboratory and the Laboratory of the Bryn Mawr Hospital, Bryn Mawr, Penn. Science 112: 398-400, 1949.**

It is a generally accepted hypothesis that freezing and thawing of red cells causes hemolysis. In the present work, 100 blood samples were frozen and subsequently thawed with less than a 1 per cent hemolysis of the red cells. Best results were obtained with the quick freezing methods. The best way to thaw the blood, no matter what method of freezing was used, is rapid thawing at +37 degrees C. in a water bath with agitation. Further studies are in progress.

R.C.C.

**RED CELL FRAGILITY, ENDOGENOUS URIC ACID AND RED CELL SURVIVAL IN POLYCYTHEMIA VERA. C. Merskey. From the Department of Medicine, University of Cape Town, Cape Town, South Africa. South African J. M. Sc. 14: 1-6, 1949.**

In cases of polycythemia vera the osmotic red cell fragility was found practically normal. The endogenous uric acid metabolism was not considered consistently abnormal (as judged by uric acid content of twenty-four-hour urine specimens collected with patient on a "purine poor" diet). The red cell survival times of polycythemia cells in normal recipients and of normal cells in a polycythemic recipient were found to be normal.

P.F.W.
ABSTRACTS

Effects of a High Protein Diet on the Anemia Induced by Hypophysectomy in Adult Female Rats, Including Further Details on Post-hypophysectomy Anemia. R. C. Crafts. From the Department of Anatomy, Boston University School of Medicine, Boston, Mass. Endocrinology 41: 159-169, 1949.

Hypophysectomy induced an anemia in adult rats which had the following characteristics: (1) a 30 per cent decrease in erythrocyte count, (2) a 33 per cent decrease in hematocrit, (3) a 31 per cent decrease in hemoglobin, (4) a slight decrease in mean corpuscular volume, (5) a slight decrease in mean corpuscular hemoglobin, (6) a normal mean corpuscular hemoglobin concentration, and (7) a hypoplasia of the bone marrow with a decrease in percentage of erythroid elements.

Previous work showed that thyroxine or androgen therapy prevented all manifestations of this anemia except for the fall in hemoglobin. This present work was undertaken to determine whether this lack of hemoglobin formation was due to a lack of available protein. Fifty-seven hypophysectomized rats were divided into five groups: (1) no treatment, (2) fed a high protein diet, (3) a high protein diet plus thyroxine, (4) a high protein diet plus androgen, and (5) a high protein diet plus thyroxine and androgen.

Best results were obtained in the last group with the high protein diet plus 0.005 mg. of thyroxine per day plus 1.0 mg. testosterone propionate per day. This therapy maintained the hematocrit and hemoglobin at normal levels while elevating the erythrocyte count. The author concludes that the anemia which is induced by hypophysectomy can be prevented by a high protein diet plus therapy to enhance the utilization of such a diet.

R. C. C.


Three cases with predominantly abdominal manifestations of sickle cell crisis are discussed. Two were laparotomized with death in one and recovery after a stormy postoperative course in the other. The causes of abdominal pain in sickle cell crisis are reviewed. The authors consider it due to multiple factors including mesenteric and retroperitoneal lymphadenitis and lymphadenopathy which were observed in their two surgically explored patients. Other factors considered were splenic and hepatic thrombosis, hepatitis and hepatosis, and possibly neurogenic factors resulting from rarefaction of vertebral bodies with pressure on the nerve roots.

W. N. V.


Of 132 babies receiving blood by exchange transfusion from male donors, 17 died (mortality of 19.7 per cent) but of 55 babies receiving blood from female donors only, none died. The beneficial component of the female donor blood is not known. Exchange transfusion, using blood from a female donor, is the treatment of choice in babies with erythroblastosis fetalis according to the authors.

P. F. W.


The authors have classified a series of 409 apparently normal infants into four groups according to the maternal-infant blood group relationship. In Group I, the ABO and Rh factors of mother and child were compatible; in Group II, there were incompatibilities in the ABO system; in Group III, incompatibilities in the Rh factors and in Group IV, incompatibilities in both groups of factors. Minor statistical differences in the mean hemoglobin levels and in color indices were encountered, these being somewhat lower in groups where some incompatibility was present. No similar differences were observed in comparing erythrocyte levels in the various groups. The possible interpretations of these findings are discussed with emphasis on the possible inhibition on the normal utilization of iron in instances of maternal-fetal incompatibilities of the types described.

W. N. V.
ABSTRACTS

SOME OBSERVATIONS ON ANTI-O AGGLUTININS. R. Jakubowicz and L. M. Bryce. From the Red Cross Blood Transfusion Service (Victorian Division) and the Queen Victoria Hospital, Melbourne, Australia. M. J. Australia 2: 373-376, 1949.

Theories concerning the nature of O substance and the corresponding agglutinins are reviewed by the authors. Two sera are described, both of which react strongly on adult red cells of group O and A2 and weakly on cells of group A1 and on the donors' own cells. In one instance, the agglutinins were thought to have resulted from maternal isoimmunization by the fetus. The agglutinins present were active at room temperature but inactive at 37°C, were active in all the usual suspending diluents, and had disappeared fifteen months after delivery of an infant of blood group AO. The agglutinins of the second serum were active at room temperature and at 37°C, required an absence of ionized calcium and the presence of an excess of sodium and, unlike those of the first serum, could be absorbed by A and B substances, and by O substance derived from human ovarian cysts. The agglutinins of the second serum are thought by the authors possibly to be synonymous with the anti-H agglutinin as described by Morgan (Brit. J. Exp. Path., vol. 29, page 159) and those of the first serum to represent true anti-O agglutinins.

W.N.V.

LEUKOCYTES


This is a critical and excellent review of the literature on the lymphatic system appearing since 1946. The factors (nutritional, age, hormonal, radiant energy, chemical and physical agents) affecting the structure and size of lymphoid tissue are discussed. The experimental work and theories bearing on the site and mechanism of antibody production are discussed in a stimulating manner. Again it is apparent that relatively little thought or work has been devoted to the study of degradation of antibodies.

P.F.W.


The following procedure is used to obtain a small amount of unaltered leukocytes from the blood: 10 to 30 cc. of blood are taken in heparin, and kept at 37°C in a flask at a 45 degree angle. One part of polyvinylpyrrolidone (1 per cent concentration) is added to four parts of blood to accelerate the sedimentation rate. At the end of forty-five minutes the plasma is removed with a pipet and centrifuged for two minutes at low speed.

The centrifugate is treated by 5 cc. of saline (0.9 per cent NaCl). After thirty minutes of sedimentation, the saline is decanted, the aggregates are twice washed with saline, and a suspension of leukocytes is ready for cytologic and physiologic studies. The vitality (mobility and phagocytosis of starch granules) is unaltered.

J.P.S.


Previous work indicated strong stimulation of the adrenal cortex during and after convulsions induced electrically in the treatment of mental disease. As the steroid hormones are known to have several functions, it was decided to gain insight into which of the functions had beneficial effects to the patient electrically stimulated. The eosinophilic elements of the blood stream were counted in patients so stimulated in an attempt to understand the above effects.

Twenty-one patients with various mental conditions were studied. Range of age was from 12 to 65 years. Fourteen were female. Blood was removed before convulsions and four, eight, and frequently twenty-four hours after treatment. In addition, one patient was studied who had been treated with adrenocorticotropic hormone.
All patients exhibited a decrease in eosinophils regardless of diagnosis, duration of disease, or clinical response to the shock therapy. The patient treated with ACTH showed a more marked loss of eosinophils than those with the shock treatment but showed no clinical improvement. It is therefore concluded that the beneficial effects of shock therapy are not due to the decrease in eosinophils.

R.C.C.


This paper presents results similar to those noted in several others, namely, that the number of circulating eosinophils in mice decreases under conditions of stress, with injections of adrenal cortical extracts, or with adrenocorticotropic hormone. The main contribution of the paper is a very detailed account of the method for counting eosinophils and for obtaining the blood samples, for showing that this decrease in eosinophils does not occur in adrenalectomized mice, and that the spleen is not involved.

R.C.C.


The author suggests that the response of circulating leukocytes to brief stress is consistent with known mechanisms of adrenal function. It is felt that the initial lymphocytosis may represent an initial epinephrine-like action and the subsequent lymphopenia and neutrophilic leukocytosis an expression of adrenal cortical activity.

W.N.V.


Intravenous injections of Ascaris suum, hydatid cyst fluid, solutions of acacia, glycogen, dextran, and other substances were given to rabbits. Observations of the leukocytes were made through transparent chambers inserted into the ears. As a result of the injections, the leukocytes adhered to the endothelial walls of the capillaries. During the time when the leukocytes were adhesive, there was a leukopenia which lasted about ninety minutes. The leukopenia is attributed to the fact that the leukocytes are temporarily out of circulation.

R.C.C.


Using intact rat lymphocytes, it has been shown that KCN and anaerobic conditions produce a reduction of supravitally stained mitochondria. The effect of KCN was reversed by washing the cells in Lock's solution and the subsequent addition of lactic acid produced a reduction of the dyes. It has been concluded that cytochrome oxidase and lactic acid dehydrogenase are located on the mitochondria of the undisrupted cell.

P.F.W.


Aminopterin and a-methoprin used in the treatment of patients having acute leukemia have produced complete remissions lasting up to four months in 5 of 21 children and 3 of 33 adults. No remissions were maintained.

P.F.W.
ABSTRACTS


Removal of the adrenal glands of rats minimized the changes induced in the spleen, thymus gland, peripheral blood and bone marrow on the administration of amino-teropterin (and aminopterin). Toxic amounts of these two folic acid antagonists greatly enlarged the adrenal glands.

P.F.W.

A CASE OF DIFFUSE PLASMACYTOMA WITH DEPOSITION OF PROTEIN CRYSTALS IN THE KIDNEYS. H. Sikl. From the First Department of Pathology, University of Prague, Czechoslovakia. J. Path. & Bact. 61: 149-163, 1949.

MULTIPLE PLASMA-CELL MYELOMA WITH CRYSTALLINE DEPOSITS IN THE TUMOR CELLS AND IN THE KIDNEYS. V. Neumann. From the Pathological Department, University of Brno, Czechoslovakia. J. Path. & Bact. 61: 165-169, 1949.

These two cases of multiple myeloma are of interest for several reasons. In the first one no plasma cells were found in the blood but they constituted 2 per cent of the cells in the second case. A diffuse plasmacytoma involving the bone marrow, liver, spleen, kidneys and lymph nodes was found in the first case, whereas a discrete plasmacytoma of the right 7th rib was regarded as the primary lesion in the second case. The presence of crystalline formations—presumably of a protein nature—were found in both cases. In Sikl's case, these crystals were found in many of the tubules and most of the epithelial cells of the proximal convoluted tubules. In Neumann's case, crystals were present in Bowman's capsule and all segments of the nephron from the glomerulus to the ducts of Bellini. In addition to this, small rhomboid and larger prismatic forms were also found in some of the tumor cells. These crystals gave a positive reaction with Weigert's fibrin stain and showed some affinity for congo red.

O.P.J.

THE PHYSICAL PROPERTIES OF A CRYOGLOBULIN OBTAINED FROM LYMPH NODES AND SERUM OF A CASE OF LYMPHOSARCOMA. A. Abrams, P. P. Cohen, and O. O. Meyer. From the Laboratory of Physiological Chemistry and the Department of Medicine, University of Wisconsin, Madison, Wis. J. Biol. Chem. 181: 237-245, 1949.

The sedimentation constant, diffusion constant, ultraviolet absorption spectrum and electrophoretic mobility of a cryoglobulin isolated from the lymph nodes and serum of a case of lymphosarcoma have been determined. The protein did not completely correspond in its properties to any cryoglobulin previously described. It seems likely, in the opinion of the authors, that the pathologic cells were directly involved in the formation of the cryoglobulin.

P.F.W.

METHODOLOGY


As the title indicates, this paper presents a method for determining the amount of heparin in the blood. The blood is citrated and the heparin precipitated from the plasma with N-octylamine. The heparin is reprecipitated with brucine. Recoveries of from 80 to 90 per cent of the heparin are obtained from whole blood, and complete recoveries of heparin from plasma.

R.C.C.


During their important studies on trace elements in blood, the authors have presented a method for
zinc analysis by TCA precipitation accurate for samples of leukocytes, erythrocytes and plasma containing as little as 1 microgram of zinc.

P.F.W.


A method of partial purification of plasminogen is described and the suggestion is made that human serum contains only one proteolytic enzyme that is activated by streptokinase.

P.F.W.

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**BOOK REVIEWS**


This is a valuable contribution to the obscure subject of the agglutinogen O of the ABO blood groups. The author shows that immunization of chickens with smooth Shiga bacilli results in the production of agglutinins acting most strongly on human cells containing the antigen O. This observation is based on the work of Eisler (1930) who produced such anti-O sera by injecting Shiga bacilli into goats. These antisera and also selected normal eel sera, as suggested by Jonsson (1944), were used in the present study. Furuhata and Sugishita, in 1935, has shown that certain Japanese eel sera agglutinated all group O cells and some A, B, and AB cells strongly, due to a factor which they designated as E. It seems almost certain, however, that factors E and O are identical. In analyzing the differences in content of agglutinogen O in the various ABO blood groups and subgroups, Grubb used a quantitative (titration) technic. He failed to point out, however, that differences of one or even two or three tubes in titrations are not necessarily significant, due to the crudeness of the technic. Despite this, his findings support the theory proposed by the reviewer (1944) that anti-O sera react with a property shared by the agglutinogens O and A and determined by genes $I^1$ and $I^2$ respectively. This is lacking from the products of genes $I^3$ and $I^4$. Grubb refers to the observations of Morgan on his so-called H substance. The present reviewer has never been able to understand the essential differences, if any, between the H and O substances. Anti-O sera, like anti-Rh and other antisera, contain antibodies which may be either univalent or bivalent. Differences between the behavior of univalent and bivalent anti-O sera may have been mistaken by Morgan and perhaps by Grubb for differences in specificity.

Despite Dr. Grubb's excellent study, the subject of the agglutinogen O remains as obscure as ever. The main difficulty to the present time has been the inability to obtain anti-O sera of high titer and specificity. Unless a consistent method is evolved for obtaining such potent and highly specific anti-O sera, the chances for resolving the problem satisfactorily are slim.

A. S. Wiener


*Haematologische Tafeln, Sandoz.* Basel, Switzerland, A. G. Sandoz, 1949. 218 illustrations, 38 plates in color. (In German or French text.)

Before me are three recent atlases dealing with the blood and bone-marrow. Others have been reviewed in previous issues and still others occupy more or less prominent places on my bookshelves. I must confess an attachment to the most famous of all hematologic atlases, that of Doctor Karl Schleip. It was beauti-