ABSTRACTS
Ernst R. Jaffé, M.D., Editor

LEUKOCYTES


Leukemia mortality has been rising steadily in New Zealand since statistics first became available in 1908, but the rise has been confined to the oldest age groups and has occurred in all types. This observation makes it unlikely that new leukemogens have been the cause. Surveys have produced some evidence of a genetic background in chronic leukemia and of excessive radiation exposure in a few cases of acute and chronic granulocytic leukemia. Case clusters have been found in several localities, and the overall geographic and temporal distribution of childhood leukemias differs significantly from a random one.—F. W. G.


Ninety-one samples of bone marrow and 19 samples of peripheral blood were obtained from 43 children with acute leukemia, mainly lymphatic in type. Twenty-seven similar samples were obtained from nonleukemic children. The samples were examined for the presence of mycoplasma by direct culture and by an indirect method in tissue culture. No mycoplasma were isolated from any of these samples or from three samples of cerebrospinal fluid obtained from children with leukemic involvement of the central nervous system. The author considered that his results cast considerable doubt on the theory that mycoplasma bear a causal relationship to acute leukemia in man.—A. L. B.


Material was obtained from the peripheral blood of 8 healthy individuals, 13 patients with chronic myelocytic, 6 with acute myelocytic, and 7 with acute lymphocytic leukemia. Observations using technics not previously available were reported. The appearance of the cells after glutaraldehyde fixation was recorded for the first time and several new features were reported with 42 excellent electron micrographs.—O. P. J.

Leukocyte and platelet groups are becoming better known and can be classified as follows: The antigens which seem to be specific for a cellular series and which can be likened to organ antigens. The antigens present in leukocytes of all series, in platelets and on all organs so far tested. These factors can be likened to histocompatibility tissue antigens. The hypothesis was advanced that most, if not all, of these antigens might be controlled by a chromosomal area forming a system which might be called HU-1 (Human Histocompatibility) since it has already been demonstrated that five of these antigens play an essential role in histocompatibility. Among them, I (Mac), 4a and 4b seemed to be most important. It has not become clear as yet whether there are one or two major histocompatibility systems. These systems appeared to be more complex than the Rh system, each of them consisting of a mosaic of antigenic determinants frequently associated in a given population.—G. M.


Leuko-agglutinins were searched for by Dausset's technic in blood from 1272 normal pregnancies, 369 abortion cases and 252 women with premature babies. Agglutinins were found in 13.7, 11.1 and 10.7 per cent, respectively. The conclusion was drawn that they do not play a significant role in the etiology of abnormal pregnancy. Normal women had agglutinins during their first (2.8 per cent), second (10.4), third (12.4) and fourth (19.3) pregnancies, the percentage rising to 21.3 in the fifth and subsequent pregnancies. The antibodies in several cases first appeared or increased in titer at delivery. In two instances, both the mother's and the cord blood contained leuko-agglutinins.—F. W. G.


Chronological observations were made on the "atypical plasma cell" appearing in the thoracic duct and the basophilic cell appearing in the lymph node after immunization of 79 rabbits. The "atypical plasma cell" was classified into three types. On Wright's stain, type I showed a relatively delicate nuclear structure; basophilia of the cytoplasm without azure granules was not so marked as that of types II and III. Very little endoplasmic reticulum was revealed by electron microscopy. Type II cells had a coarse nuclear structure and azure granules and small vacuoles were found in the cytoplasm with strong basophilia. Moderately developed tubular endoplasmic reticulum was noted. Many type III cells were irregularly round and the basophilia of the cytoplasm was stronger than that of type II. There were some type III cells with eccentric nuclei and perinuclear clear zones. Rarely, Russell body-like granules were seen. Type III cells had vacuolar endoplasmic reticulum throughout the cytoplasm. The "atypical plasma cell" showed maximal increase 4 days after immunization and rapidly decreased on and after the seventh day. This chronologic variation paralleled the appearance of the basophilic cell in the lymph node. The "atypical plasma cell" with a well-developed endoplasmic reticulum resembled the plasma cell, but differed from it as to the arrangement of the endoplasmic reticulum and the degree of development of the Golgi area. This cell was regarded as constituting an independent series in transit from the reticulum cell and definitely different from the lymphocyte or the plasma cell. The "atypical plasma cell" apparently was inhibited by 6 MP and prednisolone. From the fact that it was recognized in the early stage after immunization when 19S antibody made its appearance and that it had an ultrastructure resembling that of the cell of Waldenstrom's macroglobulinaemia, the inference was drawn that this cell produced 19S antibody.—K.F.


Rabbits, thymectomized at age 7 to 10 days and/or irradiated one week later, were tested for their immune response to a challenge of S. typhi, egg albumin and tubercle bacilli at 6 weeks of age. There was no difference in body weight curves between thymectomized irradiated and sham-operated irradiated rabbits. A reduction in number of circulating lymphocytes was observed in thymectomized rabbits; this reduction was much greater in the irradiated than in the non-irradiated group. Thymectomized rabbits showed
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In an attempt to elucidate the relation of the type of leukemia induced by the leukemogenic agent and the host factor, the role of Moloney virus and the effect of thymectomy in induction of myeloid leukemia by X-ray were studied in RF/Jax mice. The incidence of myeloid leukemia in unoperated irradiated mice was trebled (from 9.7 to 29.4 per cent) and the development of thymic lymphoma was prevented by thymectomy prior to irradiation. Thymectomy may have provided more chance for development of leukemia by preventing death from thymic lymphoma. The incidence of leukemia was further increased by Moloney virus infection (from 29.4 to 66.6 per cent) without affecting the incidence of lymphoma, suggesting the acceptance of the virus by the myelogenic cells during heightened proliferating activity after irradiation. Myeloid leukemias induced by X-ray plus Moloney virus were indistinguishable morphologically from those induced by X-ray alone and were transplantable in syngeneic adult mice.—K. F.


The erythroagglutinating, blast cell metamorphosis stimulating and mitogenic activities of partially purified extracts were measured in different dilutions. Adsorption of phytohemagglutinin with...
erythrocytes resulted in parallel loss of erythroagglutinating, metamorphosis stimulating and mitogenic activity. The authors suggested that the hemagglutinating and mitogenic activities were bound to the same chemical receptor group.—E. K.


The plasma membrane of guinea pig macrophages and polymorphonuclear leukocytes catalyzes the hydrolysis of ATP. The enzyme(s) is active in the presence of calcium or magnesium ions and is inhibited by sulfhydryl poisons and ADP. Enzymatic activity can be removed from cells by trypsin. The nucleotide phosphatase activity may have several functions. The fact that plasma membrane movement is a necessary part of phagocytosis and that the ATPases of certain other cells may act as mechanoenzymes, however, is consistent with the interpretation that the leucocyte enzyme(s) plays a part in phagocytosis.—O. P. J.


If lysosomes act as a store for the digestive enzymes in macrophages, there should be a shift of acid phosphatase activity from granules in the cytoplasm to the digestive vacuole. Light and electron microscopy were used to visualize the histochemical reaction product due to the activity of acid phosphatase in guinea pig mononuclear phagocytic cells. The reaction product was confined to granules distributed throughout the cytoplasm. The ingression of formalin-fixed red cells led to a disappearance of acid phosphatase granules from the cytoplasm and an accumulation of this enzyme around the ingested material. The results suggested that digestive enzymes were carried by cytoplasmic granules to the vacuoles containing ingested red cells.—O. P. J.


Human eosinophils were studied in a liver biopsy from a 41 year old icteric male and in peripheral blood from a 23 year old normal female, a 57 year old male with allergic eosinophilia and a 37 year old female with bronchial asthma. Bone marrow from the femurs of mice, rats and guinea pigs was removed under ether anesthesia. The eosinophil granules appeared in the electron microscope as elliptical or, more rarely, circular profiles, measured 0.3 to 1.2 μ in diameter, were limited by a well defined unit membrane about 95 Å thick and contained an amorphous or finely granular matrix. A dense core embedded in the matrix appeared as a band of varied width, usually disposed parallel to the long axis of the granule profile. The parallel bands or square lattice of the crystal showed a repeat of 30 Å in rodents and 40 Å in man with an additional 28 Å repeat encountered occasionally. The chemical composition of these crystals remained unknown. Of all the enzymes so far identified in eosinophil granules, the specific peroxidase appeared to be the most likely candidate for the protein of the crystalline core.—O. P. J.


Persistent nucleoli were studied in Chinese hamster and human long-term cultures, human peripheral blood short-term cultures and in direct bone marrow preparations. No colchicine or hypotonic treatments were applied and the cells were differentially stained with the Feulgen method and light green. Persistent nucleoli were not included in daughter nuclei. They either degenerated in the cytoplasm or were eliminated from the cell. The three systems used may represent different intensities of metabolism, reflected in the amount of nucleolar material formed and the amount that persists.—O. P. J.

**HEMOSTASIS**

The rise in Factor VIII induced by adrenaline in human subjects was prevented by intravenous infusion of the β-blockers, pronethalol and propranolol, but not by infusion of the α-blocker, phentolamine. The effect of adrenaline on Factor VIII may be mediated by β-receptors.—A. L. B.

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The reaction kinetics of thrombin were investigated in citrated plasma. The thrombin effect, resulting in fibrinogen-fibrin transformation, and the thrombin decreasing effect of antithrombin were considered. From the two-phase process (thrombin effect in euglobulin system and antithrombin effect in fibrinogen-free environment), the simultaneous processes were described mathematically and agreed well with the experimental data. In citrated plasma, there was a thrombin minimum which was able to perform coagulation. This thrombin threshold was determined by the amount of antithrombin.—S. R. H.

**EFFECT OF EXTRACTS OF NORMAL LEUKOCYTES ON THROMBIN GENERATION IN PLASMA.** I. Lisieciwicz. From the School of Medicine, Krakow, Poland. Haemat. Hung. 6: 69, 1966.

A factor with thromboplastin activity was found in saline extracts of normal leukocytes. Thrombin generation time in platelet poor plasma was normalized by leucocyte extracts to a lesser extent than by extracts of brain or platelets. Preliminary data indicated that this factor seemed to be very similar to platelet factor 3.—E. K.


Sera from 312 pregnant women, 97 women not pregnant for 1-10 years, and 43 women without history of pregnancies were tested. Platelet iso-antibodies were demonstrated in the sera of 7 pregnant women (2.24 per cent). Demonstration of platelet iso-antibodies may be useful in the diagnosis of neonatal thrombocytopenic purpura.—E. K.


Sera from 485 patients with various blood disorders, transfused or not, were tested for antibodies by agglutination and complement fixation. It was stated that the complement-fixation test was more sensitive and more convenient than the agglutination test. It was impossible to detect platelet antibodies in the blood of thrombocytopenic patients not treated with transfusions with either test.—E. K.


Severe hemorrhages occurred after intramuscular injections and other minor injuries in patients with chronic myeloid leukemia. Thrombocytopenia was not detected. The hemorrhagic disorder was induced by pathologic fibrinolysis. Serial thromboelastographic studies were performed in various stages of the leukemia in 20 patients and significantly increased fibrinolysis was observed in all stages.—S. R. H.

**ERYTHROCYTES**


In an attempt to devise practical methods of assessing the iron stores in many members of different populations, the W.H.O. initiated a collaborative study in which the iron content of postmortem specimens of liver from patients dying traumatic deaths was analyzed. Preliminary results in South Africa showed a lower iron content in females than males, iron overloading in Bantu males and some Bantu females, and less iron in Indian males and females than in whites. Among males, 5.4 per cent of whites, 0.6 per cent of Bantu and 9.2 per cent of Indians showed abnormally low iron concentrations; in females, 6.7 per cent of whites, 4.5 per cent of Bantu and 17.8 per cent of Indians. An international comparison showed the South African figures to be the highest in the world with the lowest among Indians living in New Delhi. Subjects living in the U.S.A., Venezuela, Nigeria, Sweden and England showed
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Iron absorption was measured by whole body counting after intragastric administration of radioactive iron. Administration of pancreatin with the test dose slightly reduced iron absorption in normal rats. Markedly increased iron absorption was demonstrated in rats treated with D,L-ethionine to damage the pancreas. In these animals, absorption was reduced to normal by pancreatin. All animals treated with D,L-ethionine showed severe pancreatic damage, but there was no relationship between iron absorption and the degree of damage to the liver—A. L. B.


Methionine deficient diets were given to rats to determine if the effect on iron absorption simulated the effect of administering ethionine, a metabolic antagonist of methionine. The methionine deficient diet resulted in a decrease in total body iron, due to a decrease either of absorption or retention of iron. There was inhibition of growth, development of anemia and shift of body iron to the liver. There was no extensive pancreatic or liver damage. The findings were different from the reported effects of ethionine which cannot, therefore, be altogether due to methionine deficiency.—A. L. B.


Following vitamin B₁₂ therapy in 4 cases of untreated pernicious anemia, these sequential changes were observed: a decline in plasma folate and plasma iron and a rise in red cell folate coincident with the onset of reticulocytosis. The authors proposed that vitamin B₁₂ facilitated the formation of methyl folate and its incorporation into red cells during the nucleated stages of erythropoiesis.—F. A. K.


Follow-up studies on 3 unrelated males who had presented during infancy with megaloblastic anemia due to vitamin B₁₂ deficiency were described. All 3 had absent intrinsic factor but otherwise normal gastric secretions and mucosal histology which remained unchanged after 5, 11 and 29 years, respectively, of therapy with vitamin B₁₂. There was no increase in the incidence of parietal cell antibodies among 43 relatives studied.—F. A. K.


The method proved to give reproducible results and was quicker and simpler than using starch gel. The new method clearly distinguished the secretion of intrinsic factor in the gastric juice, obtained after histamine stimulation, of subjects with pernicious anemia from those with normal acid output—A. L. B.


Therapy with oral tetracycline was associated with a prompt return of serum folate concentrations to within normal limits in 3 of 4 patients with tropical sprue who had presented with a megaloblastic anemia secondary to combined deficiency of folate and vitamin B₁₂. Folate repletion was associated with a hematologic remission. Serum vitamin B₁₂ levels remained subnormal throughout the study. The factors responsible for folate repletion during such therapy remain unknown.—F. A. K.

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Bacteria, principally coliform organisms or enteroetri, were isolated from the proximal small intestine of 21 residents of rural Haiti who had malabsorption. These bacteria were found to be capable of synthesizing monoglutamate forms of folate, as well as 5-methyltetrahydrofolic acid or pteroylmonoglutamate or both. The authors suggested that folate synthesized by intestinal bacteria may protect these Haitian subjects from folate deficiency and that this may account for the infrequent occurrence of folate deficiency in patients with tropical sprue in that country.—F. A. K.


Whole blood folate activity was markedly decreased in the cord blood of severely anemic, folate-deficient mothers. On the other hand, reduced forms of folate (active for P. cerevisiae) in the same blood samples were within the normal range. An efficient mechanism appeared to operate to supply the fetus with the required concentrations of active folate in the final stages of pregnancy, regardless of the state of maternal folate stores.—B. R.


The prevalence of anemia was studied in 890 women in the 2nd and 3rd trimester in Kiryat Shemona. Special attention was paid to the country of origin, parity and socioeconomic status. Over 22 per cent were found to have a hemoglobin level below 10 Gm./100 ml. Quantitative determinations revealed that the anemia was due to combined deficiencies, mainly of iron and folic acid. Inadequate food intake and increased requirements by the developing fetus were considered to be the main factors responsible, especially in multiparous women.—B. R.


Changes in the incidence of anemia over the past 20 years and its variation among different groups of pregnant women in Jerusalem were reviewed in relation to demographic and nutritional trends and to the influence of health services. There was a considerable difference in the anemia rates among various groups. The data from a particular program in one area of the city suggested the favorable influence which a health service could have.—B. R.


Anemia is responsible for 20 to 40 per cent of maternal deaths in Indian hospitals; 80 per cent of women are anemic at the beginning of pregnancy, due to malnutrition and infections. The different types of anemia have been analyzed and the routine use of iron and folic acid is recommended.—B. R.


Two successful cases with severe anemia were described. Interpretations of spectrophotometric analyses of amniotic fluid obtained by amniocentesis were surveyed. The authors concluded that intraperitoneal blood transfusion was to be preferred to the more hazardous intra-uterine exchange transfusion.—F. J. C.


Loss of 4 ml. of blood and administration of hemolysates significantly stimulated erythropoiesis in normal laboratory rats. The combination of blood loss and administration of hemolysates produced an earlier onset of repair of damage from a...
single radiation dose of 600 r, if given within the first 3 days after irradiation.—L. D.

IRRADIATION DISORDERS OF ERYTHROPOIESIS INFLUENCED BY HYPOXIA OR HYPOXIA ACCOMPANIED BY BLOOD LOSS.


The influence of daily hypoxia (6000 M. for 8 hours) and its combination with a 4 ml. blood loss upon the erythropoiesis of normal rats and of rats receiving a single whole body dose of 600 r was studied. Hypoxia exerted a stimulating effect on erythropoiesis in rats exposed to irradiation until the 7th day following irradiation when compared to rats exposed to irradiation alone. Hypoxia with blood loss was an unfavorable combination. Rats subjected to irradiation alone exhibited higher red cell counts 2 weeks after irradiation than did those subjected to irradiation, hypoxia and blood loss.—L. D.


A comprehensive review of the racial constitution of South and Central America and the Caribbean islands and of present day knowledge concerning the incidence of these disorders in this large area was presented. In spite of many lacunae, the general picture, because of the admixture of African, Mongoloid and European races, showed an astonishing variety of abnormal genes, including those for hemoglobin A, C, D, and assorted slow-moving hemoglobins.

The thalassemias seem to have existed for many hundreds of years to judge from radiologic studies of ancient Inca and Mayan skulls. G-6-PD deficiency existed in those with African blood, but probably not in pure Indians.—F. W. G.


The rate of synthesis of a chains relative to that of B chains in erythrocytes of patients with B thalassemia was determined by column chro-
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The incidence and significance of acanthocytes seen in the blood of two patients with steatorrhea, one of them with neurologic abnormalities and retinitis pigmentosa and regarded during life as an adult example of Refsum's syndrome, were discussed. Connections between the Bassen-Kornzweig and Refsum's syndromes have been suggested previously. Heterozygotes for both conditions may be relatively common and the demonstration of acanthocytosis may be one of the means by which they can be discovered. A survey of the New Zealand population was proposed to discover the true incidence of these genetic abnormalities.—F. W. G.


Hemolysate, without preliminary separation or purification of the abnormal hemoglobin, was treated with p-chloromercuribenzoic acid in acid and was subjected to starch gel electrophoresis at pH 8.65. As control, hemolysate without PCMB treatment and PCMB-treated normal hemolysate were applied to the same gel. Three main stripes appeared in PCMB-treated normal hemolysate: "anodal," β chain, "intermediate," undissociated Hb A, and "cathodal," α chain. In PCMB-treated hemolysate of a hemoglobinopathy, another group of stripes, namely the "new," appeared in addition. The chain anomaly of the abnormal hemoglobin was presumed from the electrophoretic migration of the "new" in comparison with the "anodal" and the "cathodal" bands.—K. F.


The activity of crude and purified δ-aminolevulinate dehydratase of human erythrocytes was shown to be inhibited competitively by heme acting at a site on the enzyme other than the SH-groups. Hemoglobin, but not the hemoproteins cytochrome c and catalase, also inhibited δ-aminolevulinate dehydratase. This inhibition was about 1/10 as effective as that of heme itself. Feedback inhibition by heme of porphyrin synthesis at the level of erythrocyte δ-aminolevulinate dehydratase was suggested.—A. L. B.

MISCELLANEOUS


Splenectomies were carried out in 46 patients of whom 33 had preoperative studies with G²¹ labeled red cells or platelets. The best results were obtained in congenital spherocytosis and "idiopathic" acquired hemolytic anemia. In all cases where red cell survival and splenic uptake studies had been made, the operative results were correctly predicted. Results of splenectomy were less certain in I.T.P. and were less certainly predicted from studies with labeled platelets. A mixed group, including leukemias, lymphomas and myelofibrosis, gave variable results.—F. W. G.


Isotopic tests were carried out in 13 patients before and after splenectomy. In hemolytic anemias, red cell life span can be correlated with the results of external counting over liver and spleen. In only two cases, life span approached normal values after splenectomy and in these patients the hemolysis was solely splenic. In six patients where external counting over liver and spleen were abnormal, red cell life span increased, but never attained normal values. External counting after splenectomy showed persistent hepatic hemolysis. One patient with Marchiava-Micheli disease was studied with glycine-2-C¹⁴ before and after splenectomy. The hemolytic component of the anemia disappeared, but shortening of red cell life span persisted. In two cases with myeloid metaplasia, ineffective erythropoiesis existed before splenectomy, characterized by an enormous uptake of iron and poor cellular incorporation. Ineffective erythropoiesis was considerably reduced following
splenectomy. Radio-iron tests demonstrated an overall improvement in erythropoiesis. In two patients with malignant lymphoma in remission, splenectomy resulted in increased efficiency of erythropoiesis.—G. M.


From a comparison of papers presented at American and European hematologic meetings, it appears that the nature of the topics discussed is similar, but in Europe there is a special interest in basic work on cell renewal systems and coagulation problems. The era of classifying hematologic abnormalities according to clinical and morphologic criteria is past. Most work goes into exploration of the reasons for functional disturbances of cell renewal systems, i.e., “Adaptation Hematology”—a problem of human ecology: why do cell-renewal systems in certain conditions fail to adapt to changing internal or external environments? Many disciplines are involved and only the great development of basic and applied sciences has made it possible to make co-operative efforts to solve some of these fundamental questions.—F. W. C.

ABO AND RH BLOOD GROUPS AND DISEASES.

Comparisons of ABO and Rh blood groups were made in 3657 consecutive patients. This material was compared with four normal distribution patterns in a normal population. Diseases of the digestive tract and gallbladder occurred less frequently in patients of group Rh than in the normal population. Rheumatic fever was more frequent in patients of group AB. Patients of group B generally were less prone to diseases than others.—E. K.

GAUCHER’S DISEASE WITHOUT SPLENOMEGALY.

A 17 year old girl of Jewish descent was found to have Gaucher’s disease. The only signs were mild anemia and typical cells in the bone marrow. Splenomegaly was absent. Pregnancy was well tolerated. Only five cases of Gaucher’s disease without splenomegaly have been reported. In this case, there was no thrombocytopenia, pingeucueal, malar flush or pigmentation. Rosette formation of lymphocytes surrounding a typical Gaucher cell was observed in the marrow. The possible immunologic implications of this finding were discussed.—F. J. C.

FACTOR IN SERUM INHIBITING BONE MARROW MITOTICES AFTER X-IRRADIATION OF THE SPLEEN.

Blood was obtained from rabbits after local irradiation of the spleen. Intramuscular injection of serum depressed the reticulocyte count of recipient rabbits. It was concluded that local irradiation of the spleen released an antimitotic substance into the circulating blood.—A. L. B.


An interpretation of human evolution on the basis of blood group distribution among primates and humans was attempted. Some groups, especially ABO, MN and P, were present even among lower primates and must have evolved long before “hominization” began. The Rh system was of more recent origin, while such groups as Diego and Sutter did not evolve until after racial subdivisions had occurred. The overall geographic distribution of blood groups has resulted from basic genetic components which were diversified by the influence of a varying environment.—F. W. C.