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Theodore H. Spaët, M.D., Editor

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ABSTRACT OF SPECIAL INTEREST


Amylo-1:6-glucosidase activity in red cells is reported here for the first time. The demonstration of the Debrancher enzyme in erythrocytes makes it certain that the breakdown of glycogen in these cells proceeds by the same twofold action of enzymes as in muscle and liver. The increased glycogen content of red cells in patients with Debrancher deficiency has been ascribed to reduced activity of the latter enzyme in red cells. The author demonstrated normal values of amylo-1:6-glucosidase in the red cells of 2 cases of increased glycogenosis due to deficiency of this enzyme, making this explanation of the cause of the increased glycogen content of the erythrocytes rather improbable. No other hypothesis has explained the increase of an abnormal glycogen in red cells in these cases, and no alternative hypothesis for those findings is presented.—B. R.

ERYTHROCYTES


Morphologic differences between old and young red cell membranes are described, as revealed by electron microscopy after preparation by gradual hemolysis. The membranes of young red cells have a “granular” surface structure and large concentric folds. The membranes of old cells are “smooth and thin,” larger in diameter, and generally show fine central folds. In normal human donors about 80 per cent of erythrocytes are morphologically young; only 50 per cent of the cell membranes are borderline, indicating a rapid transition (1 week) of the cell from ultrastructurally young to ultrastructurally old. Using the same method, the age-population distribution of erythrocytes of domestic animals of the same stock and living conditions was determined. The range of variation in the proportion of young erythrocytes was found to be smaller in domestic animals than in humans. The microelectrophoretic mobility of young erythrocytes was found to be 1.41 μ/sec./v/cm., and 1.08 μ/sec./v/cm. The whole population had a mean electrophoretic mobility of 1.34 μ/sec./v/cm., which indicates a majority of young cells. The question is still open if those electron microscopic changes are related to the age of the cell.—B. R.

Aging of Human Erythrocytes and Their Content of Cis-Vaccen-Acid. H. Baufeld and P. Luther. From the Medizinische Klinik der...

Human ACD erythrocytes aged in transfusion bottles showed an increase of cis-vaccen-acid (cis-Δ-11-octadecen-acid) concentration. This fatty acid is known to have hemolytic activity, which is accelerated by heamatin and porphyrins and inhibited by several plasma components (albumin, globulins, Ca++, cholesterol and lecithin). A method for spectrophotometric determination is given. —H. M.


The life span of saline-washed (up to 5 times) erythrocytes is as long as that of erythrocytes in ACD transfused without previous washing. —H. M.


Biochemical review, especially of hemoglobin A, the protein structure of which has been elaborated in the above institute. The α-chain consists of 141, the β-chain of 146 amino acids, the whole molecule of 574 amino acids. The present knowledges of the secondary, tertiary and quaternary structure of the hemoglobins is also presented. The abnormal hemoglobins are discussed briefly, particularly the different types of hemoglobin M. —H. M.


Newborns and infants are much more sensitive to drugs causing methemoglobin formation than are older children or adults. This is due a) to a higher oxidizability of the fetal hemoglobin (which depends on a lower content in free sulfhydryl groups), and b) to a diminished activity of those cellular enzymes which reduce the methemoglobin. The cause of the latter is to be seen in a reduction of diaphorase. In cases of congenital methemoglobinemia one has to distinguish two types. In cases lacking diaphorase, the disease is only manifest in homozygotes; in heterozygotes there are no symptoms. In cases due to a pathologic hemoglobin, the disease is a simple dominant. The frequency of hemoglobin M is low, but it is found over the whole world and it is well known that there exist different types of Hb-M. In the case of α-abnormal Hb-M the disease is evident at birth, whereas in cases of β-abnormal Hb-M the symptoms develop later because the fetal hemoglobin shows λ-chains instead of the β-chains of Hb-A. Heinz-body formation occurs in patients with a defect in glucose-6-phosphate-dehydrogenase (G-6-PDH) and in patients with the abnormal hemoglobin: HbZurich. Infants show a high incidence of Heinz-body formation, but they show elevated activity in G-6-PDH. The cause of this has been unknown. In the case of HbZurich it was shown that the isolated Heinz bodies consist mainly of the abnormal hemoglobin. —H. M.


Congenital methemoglobinemia may be due to an abnormal hemoglobin (Hb M) or to a deficiency of the erythrocyte reducing enzyme systems. In the latter case only homozygotes are symptomatic; heterozygotes appear to be unaffected. The enzyme defect in heterozygotes is demonstrable by measuring the discoloration of dichlorphenolindophenol in the presence of DPNH and hemolsate. The authors describe a direct measurement of methemoglobin reduction: 1.0 ml. erythrocyte suspension (5 Gm. per cent hemoglobin concentration) was incubated with 0.1 ml. 5 per cent Na-lactate under carbon monoxide for 3 hours at 37 C. CO-hemoglobin is measured after 15 and 180 minutes. The proband was a 14 year old girl with cyanosis from birth. In the above method, within 3 hours 14 per cent of methemoglobin was reduced, as compared to normal controls taken as 100%. In the siblings the corresponding values were: father 48 per cent, mother 45 per cent, brother 56 per cent; another brother and an aunt showed 96 per cent and 126 per cent respectively. —H. M.

Formation of Choleglobin from Adult and Fetal Hemoglobin. F. Vecchio, N. Rigillo and M. Miraglia del Giudice. From the University, Napoli, Italy. Pediatra 70:258–268, 1962.

The rate of choleglobin formation was studied in the blood of normal adult subjects and of newborns, as well as in subjects with Cooley's ane-
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ALKALI-RESISTANT HEMOGLOBIN IN INFANTS. F. Mollica. From the University, Palermo, Italy. Pediatr 70:231–244, 1962.

In 226 infants aged 1 month, without signs of blood diseases, and in 20 healthy children, aged more than 1 year, alkali-resistant hemoglobin was determined. The percentages were between 70 and 90 immediately after birth; these decreased during the first 6 months of life. In most children aged 6 to 12 months the percentages were similar to those of normal adult subjects. Higher values were observed in females than in males of the same age. Under the same conditions of sex and age, the values are lower in infants without blood diseases than in thalassemic subjects.—P. d. N.


In 350 samples of umbilical blood no Bart hemoglobin nor other pathologic hemoglobins were detected.—P. d. N.


In 12 patients aged 13 months to 12 years with thalassemia major, the following modifications were observed after blood transfusion, in the bone marrow: reduction of orthochromatic and polychromatophilic erythroblasts with positive Hoochis reaction, increase of lipids and peroxidase enzyme in the cytoplasm of granuloblasts.—P. d. N.


Case report of a 5 year old boy. The elliptocytic trait was inherited from the mother and the thalassemic trait from the father. In a brother only the thalassemic trait was present.—P. d. N.


The intestinal absorption of Co57-aquacobamid is equal to that of Co57-cyanocobamid, as evidenced by measurement of vitamin B12. Absorption is done by measuring the residual fecal vitamin B12. Measuring the urinary excretion gives false results because increased retention of the aquacobamid in the body—4–7 times decreased excretion in comparison to cyanocobamid. The same prolonged retention of aquacobamid is demonstrable after i.m. injection and is more pronounced with higher doses. The retention quotient H2O-B12/CN-B12 comes to 2.7 and 3.1 doses of 500 µg. and 1000 µg. respectively. The daily turnover is (CN-B12) 6.25 µg./day. Five hundred µg. of CN-B12 cover the requirements for 2 weeks; H2O-B12 in the same dose lasts 37 days. At a dose of 1000 µg. this is sufficient for 16 days with Cn-B12 and 49 days with H2O-B12.—H. M.


Serum vitamin B12 levels were determined microbiologically in patients with malignant diseases. Fifty per cent of cases with liver metastases demonstrated very high serum vitamin B12 levels (800–4100 µg./ml.)—B. R.


Five infants are described in whom there occurred a syndrome characterized by acute hemolysis, thrombopenia, nephropathy and frequent hepatosplenomegaly. In each case the illness was preceded by a mild diarrhea, the hematologic and renal abnormalities appearing after a symptom-free interval of 1 to 10 days. Azotemia and oliguria were moderately severe and accompanied by hypertension which was thought to have been the cause of convulsions in 2 patients. Despite the moderate thrombopenia, petechiae were not seen, and only 2 patients had notable evidence of bruising. The infants were treated with parenteral fluids, transfusions, and steroids. All recovered completely; however, in an addendum, the authors allude to 4 cases seen subsequently. Two of these infants died, and necropsy in 1
case demonstrated lesions limited to the kidneys and consisting of bilateral cortical necrosis. The authors believe that the disease is initiated by a viral infection, which stimulates an immunologic response affecting erythrocytes and platelets, as well as renal tissue. The extent of the renal damage appears to be the decisive factor in determining the prognosis. — J. B. S.


Three infants are described in whom evidence of gastroenteritis was accompanied by a syndrome of hemolytic anemia, nephropathy and hepatosplenomegaly. Two of the patients also had moderate thrombopenia. All 3 infants developed oliguria with progressive azotemia and hypertension, and each died approximately 3 weeks after onset of illness. Autopsy revealed pulmonary alveolar hemorrhage, cardiomegaly with left ventricular hypertrophy, and siderosis of hepatic and splenic RES. The kidneys were enlarged in each patient, and the microscopic pathology consisted of glomerular swelling with endothelial proliferation accompanied by thickening of the capillary basement membrane, and by hyalinization. Cortical necrosis was minimal. None of these patients was treated with steroids; however, there is no substantial evidence to suggest that the difference in outcome between these infants and those described in the preceding paper was related to steroid administration.—J. B. S.


The cardiac lesions present at autopsy in 40 infants who died of erythroblastosis are described. Dilatation of the heart was a frequent finding, and a number of the hearts were of greater-than-expected weight. Epicardial hemopoietic foci were common, as were epicardial petechiae. The myocardial nuclei were often enlarged. The endocardium demonstrated varying degrees of fibroelastosis, and intravascular nucleated erythrocytes were present except in those infants treated with exchange transfusions. These findings can be explained by the presence of prolonged anemic anoxia.—J. B. S.


A brother and sister with Fanconi’s anemia were followed for 2 years. Blood levels rose and were maintained without the need for blood transfusion as long as adequate doses of testosterone and prednisone were given. Interruption of therapy on 2 occasions was followed by relapse in each patient.—T. H. B.


No statistically significant differences in Hp1 gene distribution among Ashkenazi, Iraqi, North African, Persian, or Kurdish Jews or Arabs from Tirah were found. The Hp1 gene frequency in the Eastern Mediterranean basin was found to be 0.30. This figure fits the suggested hypothesis of a gradient from North Europe to the south, the Hp1 gene frequency in Israel being intermediate between that of Europe and of Asia.—B. R.


Description of a method for quantitative estimation of porphyrins in urine, erythrocytes, and tissues using high voltage electrophoresis on paper and spectrophotometry of the eluates. Normal urine contains 25–100 mg. coproporphyrin/24 hours and 5–20 mg. uroporphyrin/24 hours. No protoporphyrin was found in normal urine. Normal erythrocytes contain 20–35 mg. protoporphyrin and traces to 4 mg. copro-, and only traces of uroporphyrin/100 ml. Porphyrins with 4, 5, 6, 7 and 8 carboxyl groups were found in pathologic urines and were quantitatively measured.—H. M.
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In experiments with mice, rats and rabbits, it was shown that tetanus toxin could be detoxified by incubation with hemosiderin, ferrous sulfate, ferric chloride, ferritin, and reducing substances such as ascorbic acid and cystein. Since iron accumulates in areas of inflammation and in the cells of the RES in the form of hemosiderin and ferritin, it seems highly probable that toxins and "breakdown products of the organism" are detoxified by iron ions. An organism rich in iron shows better resistance than an iron deficient organism.—H. M.


Ferritin in normal subjects and in patients with hemochromatosis has been compared by several techinics: gel and starch electrophoresis, ultracentrifugation and chromatography electrophoresis (fingerprinting) after tryptic hydrolysis. No differences were shown by these methods.—G. M.


A series of studies were done to find out whether the transferrin in subjects with idiopathic hemochromatosis was different from normal. The electrophoretic mobility, solubility in ammonium sulfate and capacity to compete for iron with a strong chelate were all normal. In addition, the in vivo clearance rate of radioiron bound to hemochromatosis plasma was identical with that of radioiron bound to normal plasma in a normal subject and in a patient with the disease.—T. H. B.


Liver biopsy was performed in 6 descendants of patients with hemochromatosis. All 6 were clinically well but had a persistent high serum iron concentration. In 5 of the patients, the liver contained excess iron pigment, confirming that the abnormality of iron metabolism is hereditary.—G. M.


Evidence is presented to suggest that among infants with iron deficiency, there is a group in which the anemia is not due primarily to a deficient iron supply. In this group of infants, early exposure to whole cow's milk leads to milk sensitization. Gastrointestinal dysfunction resulting from this hypersensitivity culminates in a loss of red cells and plasma proteins into the G.I. tract. Data are presented indicating that precipitins to cow's milk are present in the serum of many infants with iron deficiency anemia. These patients demonstrate a significant increase in both serum albumin and y-globulin in the fasting gastric juice, and their stools are frequently guaiac-positive.—J. B. S.

HEMOSTASIS


Under normal conditions, factor V is completely utilized within 1 hour after blood coagulation. In factor VIII deficiency, factor V is incompletely utilized, in direct proportion to the degree of the defect. In severe factor IX deficiency, incomplete utilization of factor V takes place, whereas the cases of mild deficiency are characterized by a normal factor V utilization. Defective and delayed utilization of factor V takes place in thrombocytopenias, and a direct proportion was observed between factor V utilization and platelet count. Normal factor V utilization is observed in patients under treatment with phenylindandione. According to the authors, factor V participates in the formation of thromboplastin at a later stage than other factors.—P. d. N.

In the Shwartzman-Sanarelli-phenomenon (SSP) there is an increase in anti-blood thromboplastin and a decrease of the activity of antithrombin III; this goes parallel with the prolongation of clotting time and with the decreased factors of the prothrombin complex. It is concluded that the changes in blood coagulation after SSP are due to consumption of clotting factors resulting from intravascular thrombin formation.—H. M.


In 14 patients with polycythemia vera, the following coagulation tests were carried out: clotting time, recalcification time, factor V, factor VII, fibrinogen, lysis time, antithrombin activity, heparin tolerance, platelet count and functions (adhesiveness, platelet factor 3), clot retraction, bleeding time, tourniquet test. Significant modifications were detected after treatment with P³² in platelet count [decrease from 422,000 (mean values) to 186,200] and heparin tolerance (decrease of tolerance in connection with the improvement of the thrombotic tendency).—P. d. N.

**CIRCULATING ANTICOAGULANTS IN LIVER DISEASES.**


Case report in a 13 year old girl with hypertrophic, splenomegaly cirrhosis, thrombocytopenia, and factor V and factor VII deficiency. The inhibitor was detected in the globulin fractions after precipitation by the Sia method.—P. d. N.

**DIAGNOSTIC SIGNIFICANCE OF SOME COAGULATION TESTS IN LIVER DISEASES OF CHILDHOOD.** G. Digilio. From the University, Roma, Italy. Arch. ital. pediat. puercolt. 21:323-350, 1962.

Coagulation studies were performed in 16 children with various liver diseases (4 cases of acute hepatitis, 7 of liver cirrhosis, 5 of congenital atresia of the biliary tract). A decrease of prothrombin and factor VII and an increase of antithrombin II were observed in acute hepatitis. In the other patients there was also a decrease of factors IX and X, of antithrombin II and III, and of fibrinogen.—P. d. N.


In 23 cases, blood coagulation was studied in cord blood from normal newborn. Recalcification time was shortened, heparin tolerance was increased, and a reduction of antithrombin II and III was detected.—P. d. N.


Case report in a 1 year old boy. Splenectomy was performed successfully, as far as the thrombocytopenia was concerned.—P. d. N.

**THROMBOTIC THROMBOCYTOPENIC PURPURA, REPORT OF AN UNUSUAL CASE AND CHROMIUM RED CELL SURVIVAL STUDIES.** K. Swaiman, M. Schaffhausen and W. Kriv. From the University of Minnesota Medical School, Minneapolis, Minn. J. Pediat. 60:823-829, 1962.

A seven year old girl is described who developed thrombotic thrombocytopenic purpura (TTP) while convalescing from measles. The initial episode of hemolysis and thrombopenia was controlled by steroid therapy. After a 6-month remission, purpura and anemia reappeared accompanied by neuropsychiatric symptoms. When therapy with prednisone and nitrogen mustard was unsuccessful, splenectomy was performed. One week later she developed multiple cerebral thromboses and expired. The autopsy findings were typical of TTP. Shortly before splenectomy, chromium⁵¹ red cell survival studies were performed. Normal cells when transfused into the patient had a Cr⁵¹ T½ of 3 days, and the patient's RBC had a Cr⁵¹ T½ survival of 15 days.
LEUKOCYTES


Sera from patients with infectious mononucleosis show lower titers when, instead of native erythrocytes, sheep erythrocytes pretreated with papain are used. Normal sera show a contrary behavior. This is due to the inactivation of the mononucleosis antigen on the sheep cells by papainization. In mononucleosis there are present the normal sheep cell antibodies and the mononucleosis sheep cell antibodies. In the new test, papain-pretreated sheep erythrocytes are used for absorption of the normal sheep cell antibodies and in the second step the remaining mononucleosis antibodies are titrated with native sheep erythrocytes, papain-pretreated erythrocytes serving as the control. With this test there were 83 positive results out of 106 sera from patients with mononucleosis. The sensitivity was better than in the Paul-Bunnel reaction (70 per cent positive results). Many false positive reactions in the Paul-Bunnel test were negative with this test. —H. M.


Ten per cent of multiparous pregnant women show antibodies against the white blood cells of the fetus. The antibodies develop in cases of antigenic incompatibility between the maternal and the fetal leukocytes only when the leukocytes of the mother lack a certain antigen which is present in the child's leukocytes. The number of antigens in the white blood cells is large; some are widely distributed whereas other antigens are rarely found. —B. R.


Eleven Yemenite Jewish families exhibiting a benign familial neutropenia are described. The mode of inheritance appears to be dominant and is not sex-linked. The reviewer has observed 7 similar families. —B. R.


The low frequency of mitosis in bone-marrow smears of acute leukemia is at variance with the concept that in this disease cell division is rapid. The mitotic indices were within the normal range, and there was no reason to suspect proliferation by amitotic division. It is concluded that the life span of "paraleukoblasts" is longer than that of normal granulocytes, so their proliferation acts to increase the number of the immature cells. Thus, a positive balance develops with increased leukocyte count and infiltration of organs. —H. M.


The uptake of 1-C^14-glycine into proteins and nucleic acids of isolated human leukocytes is dependent upon age, being much higher in infants and children than in adults. In comparison to normal cells, synthesis is higher in pathologic leukocytes, and highest in the leukocytes from patients with acute leukemia. A nitrogen atmosphere inhibited uptake, anti-leukemic drugs were only partially inhibitory, and there was poor correlation with therapeutic effect. —H. M.


From 1954 to 1960 there were 10 deaths from leukemia in Stuttgart among persons with pulmonary tuberculosis of longer than 14 years duration. This represents 91,550 patient years. Only 2 patients were younger than 50 years. Although a frequency of only 5.86 deaths was expected, the difference is not significant. There was no evidence that x-ray diagnosis leads to the development of leukemia. —H. M.

Leukemic Transformation in Lymphosarcoma of Childhood. M. P. Sullivan. From the Texas

Leukemic transformation occurred in 42 per cent of 29 children with lymphosarcoma. The leukemia appeared between 10 and 60 weeks after the diagnosis of LSA was established, the mean duration of disease being 27 weeks. The likelihood of leukemic transformation was not related to age, sex, or site of primary involvement. If splenomegaly or hepatomegaly was present at the time of diagnosis, leukemia developed frequently. A time relationship between therapeutic radiation and onset of leukemia was suggested in 9 instances. The most effective therapy once leukemia appeared was ACTH or the adrenocorticosteroids; however, the response was often of short duration, and more than half of the patients died within 6 months.—J. B. S.


Meningeal involvement, the most common cause of neurologic symptoms in childhood leukemia, was present in 11 per cent of a group of 232 children with acute leukemia. Symptoms not infrequently appear in patients who are in partial or complete hematologic remission. The early signs include headache, nuchal rigidity, vomiting, listlessness, anorexia, and irritability. Papilledema is a frequent finding and in most cases skull x-rays reveal separation of the cranial sutures. Cranial nerve involvement and convulsions are infrequent. Spinal fluid changes are variable. The CSF pressure is increased, and there is usually a mild to moderate degree of pleocytosis. CSF protein levels may be elevated, and the sugar content is frequently in the low or low-normal range. Radiation therapy is usually effective, but neither is temporary alopecia. Intrathecal Methotrexate was equally effective, but neither therapy was of much value when meningeal leukemia appeared during hematologic relapse. Massive intracranial hemorrhage, the second most common neurologic complication of childhood leukemia, occurred in 7 per cent of the cases. All of the children who had advanced disease along with evidence of thrombocytopenic bleeding. The hemorrhage was heralded by a convulsion and followed by terminal coma. Neurologic signs due to infiltrative compression of the spinal cord and nerve roots was occasionally seen, as was viral meningoencephalitis.—J. B. S.


Vincaleucoblastin, dimeric alkaloid of periwinkle (Vinca rosea), an antimitotic that acts on the spindle and has an antmitoblastic effect, shows promise in the treatment of Hodgkin’s disease. Twenty-four courses of therapy were followed by 7 apparently complete remissions and 9 incomplete. There were 4 partial and 4 total failures. Remissions appear rapidly. They occur in patients who have reached an advanced stage of the disease with resistance to radiotherapy and alkylating agents, and also in new patients previously untreated. Incomplete remissions were obtained in patients with reticulosarcomas, histioblastosarcomas and mycosis fungoides. However, the number of patients of this category is too low for proper evaluation.—G. M.


Study of 22 cases: in 19 cases abnormal γ-globulins were detected, in 1 case no characteristic alterations were found, and in 2 cases normal findings were observed.—P. d. N.

MISCELLANEOUS


Neonatal rabbits injected simultaneously with human serum albumin and bovine fibrinogen developed immunologic tolerance to the former and an active immune reaction to the latter. The results are discussed according to different theories. Using the clonal theory the above may be interpreted as indicating that different clones achieve maturity at different times.—B. R.

CURRENT TRENDS IN HOMOTRANSPLANTATION RESEARCH IN RELATION TO PEDIATRICS. R. Fowler, Jr. From the Royal Children’s Hospital, Melbourne, Australia. J. Pediat. 60:917–946, 1962.

The author presents a review of the current concepts of homotransplantation, its terminology,
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and its relationship to immunologic responses. Included are discussions of homograft rejections, immunologic tolerance, and graft-versus-host reactions. Finally there is a discussion of maternal-fetal immunologic relationships, and of the potential applications of tolerance in man, with particular respect to red cell antigens and erythroblastosis fetalis.—J. B. S.


Three families were examined in which more than 1 member suffered from systemic lupus erythematosus (SLE). In the first family 2 sisters had the disease: 1, with hemorrhagic phenomena, showed antibodies against red cells, white cells and platelets, and also a circulating anticoagulant. The other sister presented mainly anemia and hemorrhage respectively attributed to hemolysis and thrombocytopenia. In the second family, two sisters were observed, the picture being an arthropathic one, without hematologic deviations. In the third family, father and daughter were afflicted, the father with a cutaneous form and the girl with a severe form of SLE with arthropathic disorders, fever and systemic manifestations. The patients revealed definite hypergammaglobulinemia, while the others members studied in the 3 families presented only slight deviations of γ-globulin. The so-called familial constitution would be a special type of response from the reticuloendothelial system to many antigenic agents which, in some subjects, produces the autoimmunization of lupus erythematosus. In these cases antierythrocyte, antileukocyte and antithrombocyte antibodies and even anticoagulant substances (heparinoid type) would be present, as in the first patient described by the authors.—M. J.


Direct lymphography using a specific oleagenous substance renders possible the opacification of the ilio-lumbo-aortico thoracic lymph node chain. Systematic application of this technic in malignant hemopathies, for detection of lymph node invasion by cancer, as well as in certain edemas, provides precious information. The innocuousness of the method should make it one of routine investigation in the type of patient mentioned herein.—G. M.