### ABSTRACTS

**Mario Baldini, M.D., Editor**

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**ERYTHROCYTES**


Experiments presented in this paper were performed on red cells isolated from children in the early stages of Duchenne-Erb myopathy. The activities of hexokinase, aldolase, and pyruvate kinase were significantly increased in the myodystrophic red cells. Long-term incubation (15 hr at 4°C) showed phosphofructokinase activation. With a shorter incubation (3 hr at pH 7.6 and 38°C) a similar behavior of glycolytic metabolites was observed in both normal and dystrophic red cells. Addition of ouabain to red cells incubated in a low-potassium buffer was followed by an increase of ATP in the normal and a decrease in the dystrophic red cells.

—M. C. V.


Pyruvate kinase activity was found to be 50% lower in RBC in a case with progressive muscular dystrophy. The abnormal pyruvate kinase was characterized by an increased Michaelis-Menten constant for the substrate phosphoenolpyruvate and an altered pH optimum. Although the life span of the erythrocytes was diminished, no clinical signs of hemolysis were present. The Mg²⁺-ATPase activity in the skeletal muscle was decreased. Measurements of phosphate transfer in the erythrocytes showed a twofold increase in ³²P efflux in the patient's, as compared to normal, RBC.

—M. C. V.

A 62-yr-old patient is described with siderochrestic anemia and glutathione reductase deficiency in the red cells. He also had liver cirrhosis, probably due to serum hepatitis. The anemia was hypochromic, and the activity of glutathione reductase was about 50% of normal. A possible connection between the three abnormalities is discussed.

—M. C. V.


The incorporation of intravenously administered glycine-2-14C and delta-ALA-3,5-3H into serum bilirubin and red cell hemin and globin in two patients with complete bone marrow aplasia was studied. The authors found a normal curve of early labeled bilirubin after the injection of delta-ALA-3,5-3H. The early 14C-labeled bilirubin curve showed a normal pattern characterized by two distinct peaks, the first of which had normal values while the second was significantly reduced. The 14C-hemin and 14C-globin curves were considerably flattened in comparison to values observed in normal subjects. These results are in support of the hypothesis that the first early 14C-labeled bilirubin peak has its origin primarily in nonhemoglobin heme, while the second early 14C-labeled bilirubin peak is of hemoglobin origin.

—G. L.


Renal erythropoietic factor (REF) was isolated from the nuclear fraction of rabbit kidney. An interaction between REF and plasma proteins was shown to be a prerequisite for the generation of active erythropoietin. The soluble cytoplasmatic fraction of renal cells was found to inhibit erythropoietin. The inhibitor could be identified with neuraminidase. The activity of REF was connected with the acid nuclear protein fraction (NPF). Histones isolated from rat an drabbit liver, as well as from chicken erythrocytes, inhibited completely the erythropoietic activity of NPF. Arginine-rich histone fraction produced the strongest inhibitory effect. The role of the kidney in the production and inactivation of erythropoietin is discussed. A tentative hypothesis concerning the mechanism of erythropoietin action is proposed.

—M. K.


Iron absorption was measured in 15 patients with chronic renal disease, who showed moderate to marked impairment of renal function (serum creatinin 1.4-7.85 mg/100 ml). Measurements were taken after an oral 59Fe dose by means of a whole body counter. Patients being hematologically normal were found to absorb iron normally, patients with clinical evidence of iron deficiency (serum iron, total iron-binding capacity, stainable marrow iron) showed higher resorption rates. The degree of renal failure per se had no demonstrable influence on the rate of iron absorption. Thus, for the group studied, the pattern of iron absorption was similar to that seen in patients without concomitant renai disease.

—H.-J. H.


The acid base status of a group of adults with sickle cell anemia, not in crisis, was studied by means of acid excretion, the effect of acute phosphate loading on urinary acidification, sulfate infusion, and bicarbonate reabsorption. It was considered that these subjects had a mild form of incomplete distal renal tubular acidosis.

—J. M. B.

The iron content of scalp hair was determined by absorption spectrophotometry in 22 normal children, 60 with proven iron deficiency and 9 with a positive iron balance. The ages were 6 mo-3 yr. There were no significant differences in the iron content of the hair, or between different segments of the hair, among these groups. The authors conclude that only small amounts of iron are necessary for normal hair growth in children and that these are available irrespective of the over-all body iron balance.

—F. W. G.


Iron lack, due to blood loss into the dialyzer and to repeated blood sampling, is a frequent contributory cause to the anemia of patients on maintenance hemodialysis. Nine patients were given iron supplements for a period of 7 mo. The blood Hg level, serum Fe concentration, and percentage saturation of Fe-binding capacity all rose but not to normal levels. Iron administration saves blood transfusions in patients on maintenance hemodialysis.

—F. W. G.

LEUKOCYTES


The ability of rabbit polymorphs to kill staphylococci under a variety of experimental conditions was studied. The predominant bactericidal system was the liberation of cationic proteins from the lysosomes, both into the phagocytic vacuoles and into the surrounding medium. The efficiency of the polymorphs in killing staphylococci was inhibited by Fe++ and hematin but not by hemoglobin.

—J. M. B.


Intact nuclear preparations (bald lymphocyte nuclei) from healthy donor lymphocytes were added to cultures with leukemic cells and with isologous lymphocytes stimulated by phytohemagglutinin. The effects on DNA and RNA synthesis of the intact cells were measured. There was a reduction in DNA and RNA synthesis both in the stimulated isologous cells and in the allogenic leukemic cells.

—J. M. B.


The karyotype of peripheral blood lymph-
ABSTRACTS

ocytes was studied in 12 persons (11 females, one male, 31-61 yr of age) in whom chronic benzene poisoning with considerable leukopenia had been diagnosed 8-10 yr previously. The subjects were removed from further exposure to benzene at that time. The lymphocytes were cultured by means of a 51-hr whole blood micmocultume, and the karyotype was studied in metaphase plates. In 1911 cells of previously benzene-exposed persons, 12.8% of aneuploidy was found (0.57% with 47 centromeres). Corresponding data in 1534 cells of 16 control subjects were 6.0% aneuploidy and none with 47 centromeres. According to the U test, both the hyperploidy and total aneuploidy were significantly more frequent \( (p < 0.01) \) in subjects with chronic benzene poisoning in their history. Of all chromosomal and chromatic aberrations in euploid cells, only the frequency of acentric fragments in previously intoxicated persons (0.031/cell) was significantly elevated above that in the controls (0.014/cell, \( p < 0.01 \)).

—M. K.


The effect of heparin, administered intravenously to rats, on the distribution of 51Cr-labeled transplanted lymphocytes in organs and tissues was studied. It was found that increase of heparin level in blood causes of prolongation of the average retention time of transplanted lymphocytes in the lungs.

—M. K.


Skin-delayed hypersensitivity to tuberculin (T.T.) was examined repeatedly in the course of Hodgkin’s disease in 45 patients. A negative correlation was observed between the activity of Hodgkin’s disease and the anergy to tuberculin. Moreover, remissions during treatment were achieved much more frequently in patients with a positive T.T. This test was found to be negative in the majority of patients who died during the first year after diagnosis. According to author’s opinion, T.T. may be useful not only as a diagnostic element in Hodgkin’s disease but also for its prognostic value.

—M. K.


The authors investigated the presence of a correlation between the activity of alkaline phosphatase in polymorphonuclear leukocytes (LAP) and the number of segments in granulocyte nuclei. The granulocytes were divided into four main groups depending on the number of all narrowings in the nucleus, and these groups were subdivided into subgroups according to the number of threadlike narrowings. Using a score method, the LAP activity was calculated for each granulocyte subgroup. In the subgroups, a tendency was found toward an increased activity of LAP with increasing number of threadlike narrowings. On the other hand, no significant differences were observed among the mean LAP activity values of main granulocyte groups.

—M. K.


Thirty-two cases of acute leukemia of various types, including 18 cases of childhood leukemia, were treated with L-aspara-
The presence of M component in the serum preceded the onset of symptoms of multiple myeloma in three patients by 15, 16, and 24 yr, respectively. During these periods the patients were asymptomatic, the M component, but none of the other stigmata of multiple myeloma, was present. Following onset of symptoms, all patients died within 12 mo.

—M. K.


Results of treatment of acute (lymphoblastic or myeloblastic) leukemias with L-asparaginase are reported. The drug was used in association with Daunorubicin in acute myeloblastic leukemias, and with Vincristin-Daunorubicin in acute lymphoblastic leukemias. The therapeutic effect of L-asparaginase alone in acute myeloblastic leukemias is discussed. The most important side effects of this cytostatic treatment were on liver function, with a more or less striking impairment, and on clotting factors.

—G. L.


The histologic appearances of tissue from spleen, liver, and abdominal lymph nodes in 50 patients with Hodgkin’s disease, having laparotomy for diagnostic purposes, are presented. No correlation was found between the appearances of the lymph node originally biopsied and involvement of the spleen. However, a higher percentage of patients with the histologic types considered to have a better prognosis, i.e., lymphocytic predominance and nodular sclerosis, had invasion of the spleen, as compared with the mixed cellularity type. It was not possible to assess whether removal of spleens with only small foci of involvement is therapeutically important. A high percentage of patients with lymphocytic predominant disease in the original lymph node biopsy had infiltrated livers.

—J. M. B.


A rate of 28.6% of complete remissions in 21 adults with acute myeloid leukemia is reported under intravenous therapy with cytosine arabinoside. Remission duration ranged from 2.0 to more than 13 mo. Toxic effects were not marked.

—F. W. G.


The presence of M component in the serum preceded the onset of symptoms of multiple myeloma in three patients by 15, 16, and 24 yr, respectively. During these periods the patients were asymptomatic, the M component, but none of the other stigmata of multiple myeloma, was present. Following onset of symptoms, all patients died within 12 mo.

—J. M. B.

HEMOSTASIS


Hemarthrosis is a frequent and disabling manifestation of severe hemophilia A and B. Knee, elbow, and tibiotarsal joints are commonly affected. The authors performed synovectomy as a therapeutic and preven-
A case of mild hemorrhagic diathesis is described in a 39-yr-old man with a congenital deficiency of factor XII and with prolonged bleeding time, probably due to an associated platelet defect.


The amount of both functional antihemophilic factor (AHF) activity and AHF-like antigen was determined in known female carriers of hemophilia. Whereas AHF activity alone only detected 12 of 25 carriers, the ratio of AHF activity to AHF antigen was decreased in all but two carriers. Further data suggested that the proportion of antigen to AHF activity in carriers is determined by random activation or inactivation of the X chromosome.

—H. J. W.


Using cryoprecipitate as starting material, the authors obtained factor VIII preparations that were 10,000 times purified. The protein was largely homogeneous by electrophoretic, ultracentrifugal, and immunological examination and contained about 76% amino acids, 10% carbohydrates, and 11% lipid.

—H. J. W.


A case of mild hemorrhagic diathesis is described in a 39-yr-old man with a congenital deficiency of factor XII and with prolonged bleeding time, probably due to an associated platelet defect.

—M. K.


A case of a 10-yr-old patient presenting simultaneously a moderately severe hemophilia A and a hemolytic microspherocytic anemia is described. The postoperative course under coverage with antihemophilic cryoprecipitate was uneventful. The hemorrhagic manifestations did not become more intensive after splenectomy, while increased hemolysis was abolished. The level of factor VIII did not change after the operation, which supports the view that the spleen is of no significant importance in factor VIII formation.

—L. D.

The authors studied 16 infants with the hemolytic-uremic syndrome (HUS). There was no evidence to suggest disseminated intravascular coagulation or increased fibrinolysis. However, an increase in fibrinogen degradation products was demonstrated. The authors suggest that in the HUS an antigen-antibody mediated reaction occurs with the kidney as the "target organ."


Cerebral arteries in the rabbit were damaged by mechanical and electrical stimuli, and the formation of platelet thrombi was studied by electron microscopic techniques. There were differences in the reactions to anodal and cathodal stimuli. There are many excellent photographs to illustrate the changes found.


The authors used a modified system to evaluate quantitatively the antieheparin activity of serum and of isolated platelets in individuals treated with Tromexan (Pelentan). It was found that 1 ml of normal serum could inactivate 0.7 U heparin. Similar activity was found in normal platelets after disintegration by repeated freezing and thawing (concentration of about 5.5 × 10⁹/ml). In individuals treated with Tromexan (Pelentan) there was a fall in serum antieheparin activity, and a significant correlation was found between this fall and the decrease in prothrombin time. Freezing and thawing of the platelets from these subjects released antieheparin activity equal to that found in the control platelets. It is suggested that the release of antieheparin activity from the platelets into the serum is impaired during Tromexan (Pelentan) therapy.


In 31 patients with chronic idiopathic thrombocytopenic purpura and in 34 patients with symptomatic thrombocytopenia, antiplatelet antibodies in the serum were sought using various methods. The methods of complement fixation and agglutination in 0.15 M NaCl yielded isoantibodies only in the group of patients who had received previous blood transfusions. Using the indirect antiglobulin consumption test and the agglutination reaction in dextran, positive results were obtained in most cases exposed to isoimmunization. Autoantibodies were demonstrated in four patients with chronic idiopathic thrombocytopenia, using the direct antiglobulin consumption test. It was possible to examine this reaction only in patients during remission, when the platelet count exceeded 80,000/cu mm. The obtained results suggest that there is as yet no satisfactory method for in vitro diagnosis of autoantibodies to platelets in idiopathic thrombocytopenic purpura.


A hemorrhagic disorder due to defective platelet adhesion to collagen is a rare oc-
ABSTRACTS

Investigations on the Activity of Certain Platelet Aggregation. It is characterized by normal platelet aggregation with ADP and no aggregation with collagen. Since the symptoms are usually not severe and complete examination of platelet function is usually required to discover the disease, its diagnosis is not easily made. The author reports the results of investigations performed on the members of a family with this platelet disorder. The patients also showed a significant deficiency in platelet factor 3.

—G. L.


The authors report the results of their investigations on purification of a thromboplastic substance from eosinophils isolated from the blood of a patient with eosinophilic leukemia. Purification was done by chromatography on Sephadex G-200 and DEAE and with deoxycholate. The best purification was obtained using deoxycholate with Sephadex G-200 chromatography. With this method, accumulation of the whole thromboplastic activity was obtained within a fraction corresponding to one protein peak. Characteristics of thromboplastic substance from eosinophils and those of tissue thromboplastin were found to be similar.

—M. K.


Urinary specimens of 20 patients with renal transplants were examined systematically for presence of fibrinogen breakdown products. Immunodiffusion methods were used. Split products were found regularly, immediately after surgery for a period of approximately 3 wk. Thereafter, split products disappeared in patients with properly functioning kidneys. They reappeared however in connection with rejection crises. Presence of split products beyond 3 wk after operation may indicate early rejection, and patients with persisting breakdown products in their urine deserve close clinical control.

—H.-J. H.

IMMUNOHEMATOLOGY


The authors describe a modified charcoal method that does not interfere with the serum IF titer and avoids false positive results. Modifications include presaturation of test sera with unlabeled B12 and use of buffers and of freshly prepared, washed albumin-coated charcoal. The technique is relatively simple and inexpensive.

—F. W. G.

Titers of natural antibodies against somatic antigen of Salmonella typhi, Staphylococcus aureus, and antigens of blood groups A and B were examined in blood plasma of normal donors stored for up to 36 days in glass or siliconized containers at 4°C. For comparison the same antibodies were investigated in blood sera stored in standard glass bottles. It was found that rather low initial titers of natural antibacterial antibodies decreased significantly during the 36 days of storage of plasma, while the titers of alpha and beta isoagglutinins did not change. No significant differences between the results obtained with plasma stored in glass and siliconized containers were found.

—M. K.


Anti-D immunoglobulin was separated from small samples of anti-Rh serum from Rh-sensitized women with a history of obstetrical complications, late abortions, stillbirths, or newborns with hemolytic disease. The results of anti-D immunoglobulin administration as a prophylactic means against Rh-sensitization demonstrated in 120 cases the high effectiveness of the preparation. Passive immunization of women was performed under control of fetal erythrocyte clearance from maternal blood. For identification of fetal erythrocytes in maternal blood, smears prepared by the Kleihauer’s and Jones’ methods were used.

—M. K.


In 51 cases of Addison-Biermer’s disease, intrinsic factor antibodies type I (so-called blocking antibodies) were found in 45% of patients, while type II antibodies (so-called binding antibodies) were found in 13.7% of cases. The observations reported show that there were virtually no differences in the clinical course, disturbances in the metabolism of vitamin B₁₂ (assessed by determinations of serum vitamin B₁₂ level, unsaturated binding capacity of serum for vitamin B₁₂, and vitamin B₁₂ clearance), and in the levels of immunoglobulins (IgA, IgG, IgM) between the group of patients with antibodies to intrinsic factor in the serum and the group without these antibodies.

—M. K.


The coexistence of two autoimmune diseases in a 50-yr-old woman is reported: Hashimoto’s thyroiditis with hypothyroidism and hemolytic anemia. The presence of Hashimoto’s thyroiditis was confirmed by positive tests for antithyroglobulins and tests of immunofluorescence, while the immune character of the anemia was diagnosed on the basis of presence of warm and cold antibodies (auto- and isoantibodies of the Rh system). Hemolytic anemia that developed in the patient immunized with Rh antigen was complicated by the reaction known as the Ogata-Matuasi phenomenon. This reaction includes additional development of anti-I antibodies in patients immunized by transfusion of isoantigens. The present case differs from other reported cases in the fact that immunization occurred during pregnancy and not during blood transfusions. Treatment with adrenocortical hormones, azathioprine, and desiccated thyroid gave a striking improvement.

—M. K.
ABSTRACTS


Six patients with autoimmune hemolytic anemia were examined. In all cases, the serum IgM content was increased; in four, high titers of cold hemagglutinins were present. After isolation of the IgM fraction, the monoclonal character of the macroglobulin containing K chains could only be established in four cases and was polyclonal in two. In none of the examined sera was the M component visible in the electrophoretic and immunoelectrophoretic patterns.


Glucose metabolism was studied in blood cells of 35 schizophrenics and 24 control subjects. A statistically significant reduction in the oxygen consumption rate by leukocytes and erythrocytes of schizophrenics could be established. The results of this study suggest an impaired glucose metabolism, probably due to decreased hexokinase activity and decreased phosphoglucomutase. Degradation of fructose-1, 6-diphosphate in schizophrenia blood cells in the course of treatment showed no statistically significant differences when compared with the control group. Chlorpromazine administered in therapeutic doses accelerated the oxygen consumption rate in blood cells; it inhibited glycolysis and the citric acid cycle but activated the G-6-P oxidation system. In vitro, chlorpromazine in low concentrations caused an augmentation in oxygen consumption of erythrocytes similar to that of NAD but considerably less than that seen with methylene blue.

ABSTRACTS

As expected, leukopenia, lymphopenia, and anemia occurred in mice given 0.2–1.6 \( \mu \text{Ci} \) \(^{90}\text{Sr} \)/g body weight. The marrow became hypoplastic or, sometimes, necrotic, and more regeneration was seen in central than in peripheral bones. Extramedullary hemopoiesis with thrombopoiesis was also seen. During regeneration, granulocytosis with proliferation of myeloid elements resembling a leukemoid reaction was sometimes seen.

—P. G. R.