ERYTHROCYTES


In various anemias with hemoglobin concentrations below 8 g per cent, mean erythrocyte DPG concentration was increased by 50 per cent and the mean ATP concentration by 100 per cent in comparison with control values. The difference was statistically significant for DPG (p = 0.05–0.1). There is no explanation for the increased DPG concentration, which may, however, be related to oxygenation of the tissues. The differences for ATP concentration were not statistically significant, possibly due to the large value of the standard deviation.—H.-J.H.

FLAVIN ADENINE DINUCLEOTIDE CONCENTRATION IN ERYTHROCYTES WITH NORMAL AND DEFICIENT GLUCOSE-6-PHOSPHATE DEHYDROGENASE. G. Flatz. Human Genetics Laboratory, Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. Klin. Wschr. 48:764, 1970.

FAD concentration in G-6-PD deficient red blood cells is on the average approximately 1.5 times higher than in normal cells. It seems likely that there is a causal relationship between the increased activity of glutathione reductase in G-6-PD deficient cells and the elevation of FAD concentration. The augmentation of glutathione reductase activity by increased binding of FAD may provide a useful compensatory mechanism for the defect in glutathione reduction in G-6-PD deficient erythrocytes. —M.C.V.

EFFECT OF RIBOFLAVIN SUPPLEMENTATION ON ERYTHROCYTE GLUTATHIONE STABILITY. G. Flatz. Human Genetics Laboratory, Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. Klin. Wschr. 48:764, 1970.
The author describes the effect of riboflavin supplementation on erythrocyte glutathione stability. In individuals with normal G-6-PD activity, the glutathione stability was not altered after administration of riboflavin for eight days in a dosage of 10 mg per day. In individuals with G-6-PD deficiency, GSH stability was significantly improved by riboflavin supplementation. It is suggested that the activity of glutathione reductase may be the limiting factor of GSH reduction in G-6-PD deficient cells.—M.C.V.

THE QUANTITATIVE ESTIMATION OF NON-HEME IRON IN HUMAN MARROW ASPIRATES. S. Trubowitz, W. L. Miller and J. C. Zamora. Hematology Research Laboratory, Veterans Administration Hospital, and Department of Medicine, New Jersey College of Medicine and Dentistry, East Orange, N.J. Amer. J. Clin. Path. 54:71-77, 1970.

A clinically feasible method for the estimation of non-heme iron in human marrow is described. Marrow aspirates, taken from patients with various disorders, were assayed for non-heme iron, and simultaneous evaluation of the marrow squashes for depot iron was done. The concentration of marrow iron was found to be 2.7 ± 1.9 μg per mg marrow protein. Despite broad agreement between the two methods, correlation is not good. The quantitative chemical assay may be of value in the diagnosis and investigations of the hypo- and hyperferremic states. It is interesting that some iron was found by the quantitative method, in patients who had no iron by histochemical technique.—J.B.S.


Serum folate was determined in 34 patients with iron deficiency. In 31 the serum folate level was low. It was raised by iron therapy. Of 25 bone marrow smears from patients with low serum folate levels only four showed megaloblastic changes, whereas 13 patients had nuclear-cytoplasmic asynchronism and other morphological disorders of granulopoiesis. The serum folate deficiency was attributed to a defect of folate metabolism and increased folic acid requirements due to iron deficiency.—H.-J.H.


One hundred seventy-two cases of acquired aplastic anemia have been investigated by a cooperative study in 15 hospitals of northeastern Switzerland. The aplastic anemia was drug-induced in 101 cases and idiopathic in 71. Forty-six patients had been exposed to chloramphenicol. In the light of this data, chloramphenicol must be regarded as the most dangerous and most common bone marrow poison, followed by phenylbutazone, hydantoïn, and gold. The prognosis of aplastic anemia is poor and mortality is highest in the type induced by chloramphenicol. The best prognostic criterion in aplastic anemia was found to be the reticulocyte count, the prognostic value of platelet and leucocyte count being somewhat lower.—H.-J.H.


The author describes polymorphism of poultry hemoglobins. Hen, duck, goose, turkey, and pigeon were examined. The electrophoretic patterns in starch gel are presented as well as the results of double diffusion in agar gel using antiserum against hen Hb.—M.K.

ERYTHROPOIETIN IN PREGNANT WOMEN. F. Przala and M. Bielecki. Faculty of Animal Physiology, School of Agriculture, Olsztyn and Second Department of Obstetrics and Gynecology, School of Medicine, Białystok, Poland. Acta Physiol. Pol. 20:591-599, 1969.

Erythropoietic activity of plasma and deproteinized plasma filtrates was examined in the third trimester of pregnancy in both anemic and nonanemic pregnant women...
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and in nonpregnant controls. Erythropoietin content in plasma was examined by measuring its effect on incorporation of $^{55}$Fe into blood, bone marrow, liver, and spleen in normal BALB/C mice and in mice with moderate polycythemia induced by intraperitoneal injection of homologous erythrocyte suspensions. The level of erythropoietin was found to be significantly higher in pregnant women without anemia than in the control group. Still higher was the level of erythropoietin in pregnant anemic women. —M.K.


An abnormally high M.C.H.C. was found in six cases of IgG myeloma because the abnormal protein falsified the hemoglobin estimation.—J.C.

LEUKOCYTES


Granulocyte function was examined by the quantitative leukocyte mobilization test and by estimation of the phagocytic capacity of polymorphonuclear leukocytes in 10 patients with megaloblastic anemias. Untreated megaloblastic anemias showed a significant decrease in leukocyte mobilization from skin abrasions. The defective leukocyte mobilization in megaloblastic anemias is not associated with increased risk of infection. After therapy with vitamin $B_12$ or folic acid, definite improvement of leukocyte mobilization to subnormal levels was observed. The phagocytic capacity was found not to be significantly decreased in these anemias. —H.-J.H.


The role of benzene as an etiologic agent in causing leukemia or bone marrow aplasia is still controversial. From 1966 to 1969 the authors have investigated 401 patients with blood disorders after exposure to benzene and toluol by careful history and analysis of products used in the factory or at home. They compared the results with a control group of 124 patients not suffering from blood diseases. It appeared that susceptibility to benzene or toluol could have played a role in causing leukemia or aplasia in 46 of the 401 patients examined.—M.C.V.


In previous investigations the authors demonstrated that a proteolytic agent active in the presence of urea occurs in granulocytes, erythrocytes, and platelets. In the present work this proteolytic activity was examined in leukoblasts in various types of leukemia. High activity was found in granulocytes from patients with myeloid leukemia and in blast cells from patients with myeloblastic, promyelocytic and micromyeloblastic leukemia and with chloroma. Lympocytes, lymphoblasts, and blastic reticulum cells were found to be inactive.—M.K.

The Activity of Peptidase of Human Leukocytes in Inflammatory and Neo-
The enzyme activities of leucyl-amino-peptidase (LAP), gamma-glutamyl-transpeptidase (GGTP), glycyl-aminopeptidase (AG) and aspartylaminopeptidase (AA) were examined in homogenates of leukocytes from peripheral blood of patients with inflammatory and neoplastic diseases. As compared with healthy people, LAP, GGTP, and AG activities were significantly increased in both groups of patients while AA activity was diminished. It seems that a shift in differential blood cell counts was only partially responsible for the changes observed. —M.K.

THE LEUKOCYTIC REACTION IN EXPERIMENTAL CANDIDIASIS IN MICE. E. Kowal, A. Brylińska and A. Perzanowski. Faculty of Microbiology and First Department of Internal Medicine, School of Medicine, Białystok, Poland. Pat. Pol. 21:159-167, 1970.

Influence of intravenous injection of living Candida albicans cells on leukocytes of peripheral blood was examined. The fractions obtained by centrifugation from cells disintegrated by ultrasonication were also investigated. A common property of all examined preparations was the ability to induce marked granulocytosis and lymphopenia in peripheral blood and fairly pronounced RES stimulation in the spleen. —M.K.


A clinical trial of Alkeran was performed in 63 patients with multiple myeloma. In 43 per cent of the evaluated cases objective regression of symptoms was noted. 60 per cent showed subjective improvement. At the end of the study, median survival times were estimated for various groups of patients. It was concluded that the prognosis of multiple myeloma is affected by the following factors: class of myeloma protein, type and degree of symptoms, and number of symptoms.—H.-J.II.


Fourteen of these patients were affected by acute lymphoblastic leukemia and five by acute myeloblastic leukemia. Meningitis occurred during relapse of the disease, half of the time discovered during routine examination of the CSF; sometimes it occurred with cranial hypertension. Treatment consisted in immediate intrathecal amethopterin associated with local radiotherapy in cases with blast cells in the spinal fluid. The prognosis was severe due to the frequency of relapses within a short period of time which were no more sensitive to treatment.—J.C.


In a study of neutrophil leukocytosis involving electron microscopic, genetic and histochemical observations, the author suggests that the left shift is a protective mechanism in the inflammatory process whereby the blood is provided with functionally more active cells—the immature granulocytes.—J.V.


In patients suffering from chronic (low dose) irradiation, carbon bisulphide intoxica-
tion and silica tuberculosis, peripheral blood lymphocytes were studied for alpha-glycerophosphate dehydrogenase and succinic dehydrogenase activity. The average number of granules per cell was noted and statistical indices computed, these being used to analyze the results. Considerable variations from normal in enzyme activity was observed in all groups and a distinct rise observed in patients with silica tuberculosis; the rise appears to correlate with relative immaturity of the lymphocyte. Assessment of the basic significance of such changes must await further data from normal subjects.—J.V.


A group of 53 patients between 27 and 80 years old, with initial diagnoses including hypoplastic anemia, anemia of unknown etiology, leukopenia of various kinds, and chronic lymphocytic leukemia were, on study, regarded as cases of chronic leukoreticulosis, among which subacute and chronic groups could be recognized. The peripheral blood, sternal marrow aspirate, and iliac crest bone trephine were studied but, despite variations, leukemic changes could be observed in all; these included systemic hyperplasia of the hematopoietic tissue, aleukemic peripheral blood picture with monocytosis, and the presence of reticulum cells. Reticulum cells and monocytes were increased in the sternal aspirate, while the bone trephine demonstrated foci of reticulum cell proliferation, these changes being more distinct in the subacute cases. The authors attach particular diagnostic value to the demonstration of reticulin fibers in the bone marrow trephine by silver impregnation.—J.V.


The presence of protein in the urine was examined in a group of patients suffering from chronic lympholeukosis and lymphoreticulosis as well as in a group of patients suffering from other varieties of hemoblastoses, including also multiple myeloma. Besides the routine qualitative and quantitative tests for the identification of the urinary protein, tests were also conducted to measure the solubility of the protein by subjecting it to boiling together with sulfosalicylic acid. Tests for the identification of its electrophoretic properties were also done after concentration of the urine. In 25 percent of patients suffering from chronic leukosis and lymphoreticulosis a urinary protein was found and was either a γ or a β globulin. In cases of other disorders (with the exception of multiple myeloma) a urinary protein was found only in a few cases. Origin and significance of this variety of urinary protein are being studied, the type being possibly analogous to the Bence Jones protein variety.—J.K.

HEMOSTASIS


The authors studied 26 children with the hemolytic-uremic syndrome and found a variety of abnormalities in hemostasis. Thrombocytopenia was a constant finding. Factors VIII, IX, and XI were usually either normal or high; very low values were rarely found. Fibrinogen was normal or increased. Fibrinogen split products were found occasionally in the serum of seven of the 26 patients studied. The findings were clearly not that of acute disseminated intravascular coagulation (DIC) in most cases. The authors suggest a slow, progressive process of intravascular coagulation and hypercoagulability. Abstractor's comment: Despite the difficulties involved in diagnosing DIC or in defining the hypercoagulable state, several reports have indicated that these children may benefit from heparin therapy.—H.J.W.

Of 26 children with septic shock studied for coagulation defects, 24 received heparin in addition to standard therapy. Disseminated intravascular coagulation was diagnosed in 96 per cent. Of the heparin-treated patients 58 per cent died in shock; laboratory evidence of improvement in the coagulation defects occurred in all who survived and in three who died in shock. Thus, heparin does not appear to improve survival in patients with septicemia and associated hypotension but may improve the coagulation defects. Improvement in the hypotension probably has a major role in abolishing disseminated intravascular coagulation.—H.J.W.


Since 1959, one knows that heparin is able to prevent intravascular coagulation (reduced factor V and thrombocytopenia) which seems to be responsible for bleeding into the adrenals. Heparin may thus prevent the state of irreversible secondary shock and permit antibiotics and other restorative measures in acute meningococcal septicemia (A.M.S.). Three cases of A.M.S. were cured in children aged 1, 2, and 9 years.—J.C.


The authors compared four assays for both fibrinogen and fibrin degradation products (FDP). This included the staphylococcal clumping test (SCT), tanned red-cell hemagglutination inhibition immunodiffusion (TRCHII), latex agglutination (Fi test) and immunodiffusion. FDP titers were markedly elevated in patients with disseminated intravascular coagulation and, except for immunodiffusion, there was a good correlation between the results obtained by the various methods. In lymphoproliferative and renal diseases, however, increased values were only obtained with the TRCHII method. By contrast, in cirrhosis, higher values for FDP were obtained with the SCT and Fi test than with the TRCHII method. In patients with cancer, the Fi test and TRCHII gave higher values for FDP than did the SCT. The authors concluded that different types of FDP may be produced in various diseases and that the several tests used to measure them may vary in their sensitivities to the different FDP.—H.J.W.


The authors studied the procoagulant and fibrinolytic properties of the venom of the southern copperhead snake (Ancistrodon contortrix). A procoagulant fraction, separated by chromatography and gel filtration, clotted fibrinogen directly and possessed proteolytic, esterolytic, and amidase activities. In its action upon fibrinogen, the fraction released fibrinopeptide B at a much faster rate than fibrinopeptide A, the reverse of the effect of thrombin. Despite the rapid release of fibrinopeptide B, visible clotting did not take place until appreciable fibrinopeptide A was also removed. These experiments support the view that visible clotting depends upon the removal of fibrinopeptide A from the fibrinogen molecule, permitting aggregation of monomeric units.—H.J.W.

Simultaneous Determination of Radioactive Fibrinogen, Haptoglobin and Orosomucoid from Small Plasma Samples. W. Dobrzeszyczka, R. Zienek, J. E. Pollitt and J. C. Kukral. Department of Biochemistry, Faculty of Pharmacy, School of Medicine, Wrocław, Poland, and Hektoen Institute for Medical Research of Cook County Hospital, Chicago, Ill. Arch. Immun. Ther. Exp. 18:201–207, 1970.
A new method for simultaneous determination of fibrinogen, haptoglobin and orosomucoid from the same 0.5-2.0 ml sample of plasma is described and compared with previously used procedures requiring 5-8 ml of plasma. The principle of the method is as follows: Fibrinogen is clotted with thrombin, and the clot is removed, washed, and dissolved in concentrated ammonium hydroxide. The supernatant remaining after fibrin removal is applied to a DEAE-cellulose column and pure haptoglobin is isolated as a Hb-haptoglobin complex. After separation of haptoglobin, acidic proteins eluted from the DEAE-cellulose are applied to a CM-cellulose column. A fraction containing pure orosomucoid is obtained from this column. Specific activities of the three examined proteins labeled with $^{14}$C-glucosamine were determined by the new method and by the previous ones. The procedure described was found to be quantitative, specific, and applicable to small volumes of blood.—M.K.


A decrease of PF$_4$ was found in some thrombocytopenias characterized by an empty releasable pool. Collagen acts on platelets by a different pathway than adrenaline or ADP and, for instance, releases normally nucleotides from thrombasthenic platelets. PF$_4$ release can be diminished when the plasmatic environment is abnormal as it is in chronic myeloid leukemia before treatment. **Abstractor’s comment:** This effect of collagen should be compared with polyelectrolytes’ behavior on platelets (Jenkins et al., Blood, this issue).—J.C.


A 56-year-old woman had chronic thrombocytopenic purpura resistant for 4 years to corticosteroids and immunosuppressive agents and showed clinical and laboratory signs of hyperthyroidism. Radical treatment with I-131 was followed by two phenomena: (1) The chronic thrombocytopenia and the hyperthyroidism regressed together permanently; (2) later, myxedema appeared localized to the pretibial area with exophthalmia, koilonychia, and very-high-serum long-acting thyroid stimulator activity. The authors discuss this case in the light of other similar published cases and recent knowledge of the physiopathology of Graves’ disease.—J.C.


The authors used Honour and Mitchell procedure (1963) by pinching rabbit cortical arteries in order to obtain reproducible formation of white bodies in cerebral arteries. As a therapeutic approach, they administered dipyridamole, methysergide, BC 105 Sandoz, and hydergine with inconsistent effects depending on the drug used, the type of infusion, and the dosage. **Abstractor’s comment:** It does not seem that the method presented here is the most useful for reproducing thrombosis in cortical arteries and one does not know whether the different drugs used in this experiment acted on vessel walls or on platelets.—J.C.


Shortening of plasma thrombin time and reduction of "t" and "k" values in thrombelastograms were demonstrated in rabbits in which atheromatosis was induced by oral administration of cholesterol during 90 days, as compared with an untreated control group. In a previous study the authors were able to show that caffeine treatment lowers
the cholesterol level and exerts some protecting effect against experimental atherosclerosis in rabbits. For this reason the influence of simultaneous treatment with cholesterol and caffeine on blood clotting in rabbits was also examined. The results in this group, however, did not differ from those obtained in the animals fed with cholesterol alone.—M.K.


The influence of EACA on lipids and lipoproteins in blood serum was investigated in 14 patients with nephrotic syndrome and in 14 healthy individuals. EACA was administered during three consecutive days (first day 0.2 g/kg, second and third 0.1 g/kg of body weight). EACA was found to reduce significantly the concentration of total lipids, lecithins, cephalins, triglycerides, free cholesterol, and β-lipoproteins in sera of nephrotic patients and to induce a marked increase in free fatty acid level. In healthy individuals, the only significant changes were an increase of free fatty acids and a lowering of the free cholesterol level.—M.K.

IMMUNOHEMATOLOGY


Seventeen attempts of allogenic bone marrow grafts in patients with total bone marrow aplasia, after conditioning with antilymphocytic serum (ALS) alone, administered before the transfusion of allogenic bone marrow cells, are analyzed. The graft of allogenic bone marrow was established in eight cases. Five involved acute leukemia, of which three were acute myeloblastic leukemias, two of which in the visible phase of the disease and two acute lymphoblastic leukemias in the visible phase of the disease. The three others were bone marrow aplasias, one secondary to chloramphenicol, the other to virus hepatitis, and the third with an unknown cause; their clinical state was transformed by the bone marrow graft. There were no early or serious signs of secondary disease in any case, whether the bone marrow donor was or was not conditioned beforehand by ALS. These observations establish the strong immunosuppressive effect of antilymphocytic serum (ICI-Choay antilymphocyte globulins) given alone in man. They show that bone marrow graft after conditioning of recipient alone by ALS is a nondangerous therapy that can be effective in bone marrow aplasia, the prognosis of which has always been severe.—J.C.


The authors describe morphological and biochemical symptoms in guinea pigs treated with hydrazinphthalazine (Apresoline A) in doses of 25 mg/kg/day during 3 months. Decrease in blood erythrocyte count, diuresis, and urinary excretion of hyaluronidase was observed. Histological examination revealed the thickening of basement membrane of kidney glomeruli, small focal lymphohistiocytic infiltrates in the skin, homogenization, and edema of collagen fibers in connective tissue. In some animals LE cells were found. Tryptophane metabolism was found to be distinctly disturbed.—M.K.


Investigations on serum macroglobulins are reviewed, including personal experiences of the author. It is emphasized that abnormal macroglobulins can be found in various pathological states as a result of various enzymatic or chemical alterations of normal macroglobulins. The results of experiments on isolation of a 7S IgG fraction

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inactivating completely rheumatoid factor are presented.—M.K.


This typical case was treated for 10 months with antibiotics (Sigmamycine, Tapen, and Mycostatin), and a complete clinical, histological, and biological remission was obtained. Since spontaneous remissions can sometimes be seen, the authors are cautious in interpreting the effect of these drugs. However, they recommend this association in preference to chemotherapy and corticosteroids in treatment of this disease. —J.C.

MISCELLANEOUS


Bone marrow from dogs and rabbits was lyophilized and stored between 4°C and 6°C for 2 months to 2 years. After resuspension in physiological solutions, these were injected intramuscularly into four groups of animals, including normal dogs and rabbits, irradiated dogs, and rabbits with phenylhydrazine-induced anemia. Hematopoiesis was stimulated in all groups, particularly erythroid and granulocytic elements, and survival times and mortality rates of irradiated animals were improved compared to controls; anemic rabbits showed earlier restoration of indices compared to controls. —J.V.


Smears of spleens removed from 20 patients with hypoplastic anemia and from 10 normal subjects (for trauma) were studied. Statistically valid variations from normal were noted in the anemic spleens. Elevated were RNA, mucopolysaccharide, and alkaline phosphatase (granulocytic), and decreased were DNA, glycogen, and acid phosphatase. No changes in lipid content or in activity of succinic dehydrogenase, cytochrome oxidase, or lipase were noted. RNA levels failed to correlate with the presence or absence of antibodies. —J.V.


In September 1969, the German Society for Hematology organized a symposium on the spleen. The Editors and the publishing firm of this monograph are to be complimented because the lectures given in this symposium were already published after six months. The book is well edited and illustrated. Two chapters deal with the results of spleen puncture and with spleen scanning. Then, physiology and pathology of the red and the white pulp are discussed. There are several articles on the role of the spleen in immunology and articles on "hypersplenism." Finally, sequelae of splenectomy are described. —M.C.V.


A survey is reported of hematological values in 1000 healthy children aged 6-36 months attending baby health centers in Sydney. Iron deficiency (Hb less than 10.0 mg/ml with hypochromia) was found in only 3 per cent, compared to 20 per cent of children attending hospitals. Mean Hb values were 12.2 ± 0.05 g per cent for children aged 6-12 months, 12.3 ± 0.06 for 12-24 months, and 12.6 ± 0.11 for 26-36 months. Iron deficiency, when found, did not correlate with family income, social status, prematurity, anemia in mothers during pregnancy, increased maternal age or numbers of children in the family. The common denominator, regular attendance at
a baby clinic with adequate dietary supervision, probably accounted for the favorable hematologic status of the great majority of these children.—F.W.G.

Serum Iron and Copper in Adults with Active Rheumatic Fever. J. Kedracka and E. Kot. Third Department of Internal Medicine, School of Medicine, Lublin, Poland. Pol. Tyg. Lek. 24:1800-1802, 1969.

Serum iron and copper levels were determined in 35 adult patients in acute phase of rheumatic fever and in 30 healthy people. Iron level was found to be significantly decreased and copper level increased. After 6 weeks of treatment, normalization of iron level was observed in 60 per cent of patients and Cu level in 87 per cent. The number of previous attacks of rheumatic fever was found to be without influence on Fe and Cu changes in serum. The ratio of Fe and Cu levels may be considered, according to the authors' opinion, as an index of activity of rheumatic disease.—M.K.


Twenty cases of polycythemia vera were examined. Mycosis was detected by positive culture of sputum, blood, and urine in 14 cases. Candida albicans was much more often detected than Candida tropicalis and pseudotropicalis. Clinical symptoms of mycosis were observed in only four cases. Abstractor's comment: The percentage of positive cultures in controls is not given.—M.K.