ABSTRACTS

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LEUKOCYTES


Phytohemagglutinin-stimulated 48 hour lymphocyte cultures from patients treated with radium for cancer of the uterine cervix were studied. Unstable chromosome aberrations (dicentrics, tricentrics, ring forms) were seen in 38 per cent of cells 1 hour post irradiation. Within the next two years, there was an approximately exponential decrease in unstable aberrations with a half-time of about 0.8 year. Four and six years post irradiation, 3-4 per cent of cases had unstable karyotypes. Unstable aberrations were seen even 15 years after radiation. Based on quantitative considerations of the production of acentric fragments during formation of dicentric, tricentric and ring chromosomes and the distribution of acentric fragments between daughter cells in possible mitoses subsequent to the first mitosis post irradiation, it was concluded that practically all cells with the unstable chromosome aberrations were in their first division after irradiation. The plot of unstable aberrations against time post irradiation, therefore, should reflect the survival curve of (radiation damaged) lymphocytes.—S.-A. K.


Blood samples from men previously treated with x-rays for ankylosing spondylitis were cultured to detect chromosome abnormalities which may have been due to irradiation and thus to estimate lymphocyte life span. The percentage of circulating lymphocytes with unstable chromosome aber-
rations decreased with time after exposure, but such cells were still present in increased numbers nearly 10 years later. The mean life-span of the lymphocyte was estimated to be about 1600 days. Even if this estimate was inaccurate, some lymphocytes were considered to have a half-life in excess of three years.—A. L. B.


Five indices of radiation injury to lymphocytes of peripheral blood were studied in people exposed to ionizing radiation and were compared with a control group of unexposed people. The percentage of lymphocytes containing detached fragments of nuclear substance, the percentage of bisegmented forms, the ratio of large lymphocytes to small ones, the ratio of large lymphocytes and monocytes to small lymphocytes and the ratio of granular lymphocytes to agranular ones were assessed. The authors concluded that, although none of these indices was specific, they could be of some value in the detection of early radiation injury.—M. K.


The incidence of chronic inflammation due to bacteria, protozoa and allergic conditions was compared in two groups of patients: 115 with lymphatic leukemia or lymphoma and 115 with other diseases. Chronic recurrent inflammations were much more frequent in patients with lymphatic leukemia. The possible role of the antigenic stimulation of lymphocytes in the pathogenesis of lymphatic leukemia was discussed. —M. K.


Leukemia was the most important cause (acute and chronic myeloid, lymphatic) were studied. Proteinuria, leukocytes and/or other elements in the urine were observed in 50 per cent. Symptoms of renal failure were found in 25 per cent. Leukemic infiltration of the kidney was suggested. Excessive urate excretion was frequent, especially during treatment with cytotoxic drugs. The danger of kidney failure induced by this mechanism was discussed.—M. K.
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of morbidity and mortality from neoplastic disease in the age group 0–24. The percentage and age distribution of leukemia in children and adolescents in Poland did not differ from that observed in other countries. Acute myeloid leukemia was twice as common as acute lymphatic. An increase in the incidence of leukemia in the younger age group was noted in the last few years.—M. K.


The seasonal incidence was analyzed by months and quarters. Data covering several years and 1806 cases were grouped according to sex, age and type of leukemia. Analyses for each calendar year and for the Cracow region were made. Statistically significant differences were found only occasionally. The frequency of leukemia hospitalizations was neither characteristic nor uniform. The author did not agree with other investigators who claimed that there were seasonal differences.—S. R. H.


This leukemia developed in about 5 per cent of mice more than 11 months old, especially in females. Transplantation by subcutaneous or intraperitoneal injection of cell suspensions was possible only in animals of the same strain. Cells with aneuploid chromosome numbers (39–42) were observed. Intracytoplasmic virus particles, usually in the Golgi zone, were observed by electron microscopy. Two membranes were seen in the virus; the diameter of the outer was about 75 nm. The virus was similar to the A2 particles described by Dalton.—P. d. N.


Fine structure was studied 5–15 days after inoculation of Shay's chloroleukemia i.p. in ultrathin sections from abdominal infiltrates in young CB rats. The tumor tissue consisted of a single cell type. The polygonal cells loosely joined each other and there were no cell-connecting structures. The varied pseudopodia in the intercellular regions and the pinocytotic vesiculae in the cytoplasm reflected the intense surface activity of these tumor cells. Submicroscopic structures of pigment granules and autophagic vacuoles were described. Intense acid phosphatase activity was demonstrated in both cytoplasmic inclusions.—S. R. H.


Homogenates of blast cells from the peripheral blood of patients with both acute myelocytic and acute lymphocytic leukemias were found to be able to incorporate radioiron into heme in the presence of protoporphyrin IX. These cells also could use delta-aminolevulinic acid as substrate for heme synthesis. Delta-aminolevulinic acid synthetase activity could not be demonstrated in immature leukemic cells, nor could these cells utilize glycine as substrate for heme synthesis. Leukocytes from healthy adults and from patients with chronic leukemia lacked the capacity to incorporate radioiron into heme, even when protoporphyrin IX was added. This work did not reveal whether the heme-synthesizing capacity of immature leukemic leukocytes was a function of their immaturity or of their malignant transformation.—T. E. B.


A patient with disseminated malignant melanoma had leukocyte counts up to 73,000 with 40 per cent of eosinophils. From the peripheral blood buffy coat, malignant melanoma and hematopoietic cells were cultured. The latter showed "leukovirus" similar to that seen in Burkitt's lymphoma.
The suggestion was made that, since severe leukocytosis is very common in malignant melanoma, maybe it, and other mechanisms weakening the defense mechanisms, predispose to a "leukovirus" effect.—C. R. M.


Leukocyte migration in patients with kala-azar, schistosoma mansoni infection, normal individuals and a control group (diseases not affecting white cells or host resistance to infection) was studied by the skin window technique. There was delayed and inhibited leukocyte migration in patients with kala-azar, but the number of mononuclear cells was greater than normal, increasing to 70 to 80 per cent in the seventh hour. In patients with the hepatosplenic form of schistosomiasis, leukocyte migration was also delayed and depressed, but less so than in kala-azar. This inhibition of the cellular reaction in the inflammatory exudate may be related, in part, to the intense leukopenia often observed. In the control group, the inflammatory reaction was somewhat inferior to that seen in normals. This deficient leukocyte migration in kala-azar and schistosomiasis may indicate an increased susceptibility of patients with these diseases to some infections.—M. J.


Some hydrolase activities of peritoneal mononuclear leukocytes from rats given three injections of killed Francicella tularensis vaccine increased: 37–69 per cent for ribonuclease, deoxyribonuclease and acid phosphatase activities in lysates of cells obtained from vaccinated animals. No deviation from normal was observed for β-glucuronidase, alkaline phosphatase, or cathepsin.—T. E. B.


The effect of separate and simultaneous administration of bacterial lipopolysaccharide (Piromen) and prednisolone on white blood cell count, differential count, alkaline phosphatase activity of granulocytes (GAP), and the osmotic resistance of white blood cells of human subjects was investigated. After intravenous administration of 10 μg. of Piromen, a significant leukocytosis and granulocytosis ensued with an increase in band cells. The GAP decreased in the first 4–8 hours. Five hours after administration, the osmotic resistance increased slightly. Following a single oral dose of 50 mg. of prednisolone, no leukocytosis was observed, although the differential count showed a cortisone type reaction. A slight increase in GAP was observed in the later phase of the experiment. The osmotic resistance increased one hour after prednisolone but it was much more significant after 5 hours. Leukocytosis was moderate in patients receiving Piromen + prednisolone simultaneously. Changes in the differential count, however, were roughly identical with that of the first group. GAP showed only a slight increase. The increase in osmotic resistance was most significant in this group. Donor white blood cells were incubated in plasma of heparinized blood obtained after both separate and simultaneous administration of Piromen and prednisolone. Plasma from patients having received Piromen increased the GAP content of the incubated granulocytes. Heparinized blood incubated with Piromen and prednisolone in different concentrations and with the mixture of the two caused no change in the GAP content. These results could be explained by discharge of young cells from the bone marrow and by the increase in the activity of the cells.—S. R. H.

**Changes in the Myelogram in Panencephalitis Nodoso (Subacute Sclerosing Leucoencephalitis). A. Peter, E. Szatmári, J. Romhányi and K. Letenyei. From University Medical School, Budapest, Hungary. Haematologica 1:79–84, 1967.**

The cytology of the bone marrow was studied in 18 cases of subacute sclerosing
leukoencephalitis (SSL). In 61 per cent, lymphoid reticular cells were increased, in 50 per cent eosinophilic cells and in 33 per cent plasma cells. Four patients had eosinophilia. In one case of cerebral cysticercosis, the myelogram showed a similar increase of reticulum and eosinophilic cells, and in one patient with polymyositis the plasma and lymphoid reticular cells were increased. The pathologic changes in the myelogram of patients with SSL confirmed the view that the immunologic processes were different in multiple sclerosis and in SSL. In SSL, allergic components may play a significant role, beside the immune processes. The relation between the humoral and cellular defensive activities of the RES was rather peculiar: humoral antibodies increased in the cerebrospinal fluid, while the cellular reaction was manifest in the nervous tissue and bone marrow.—S. R. H.


A case of Franklin’s disease, a variant of plasmocytoma characterized by the presence of an abnormal protein with a sedimentation constant lower than that of classical plasmocytoma paraproteins, was described. Immuno-electrophoretic study and the sedimentation constant (S\textsubscript{20} 4.27) were consistent with “heavy chain disease.”—M. K.

HEMOSTASIS


In five children with cyanotic congenital heart disease, hemostatic defects, including thrombocytopenia, prolonged thrombin clotting time and prothrombin time, reduced levels of Factor V and VIII and fibrinogen breakdown products in serum, were detected, although all defects were not present in each patient. The abnormalities were improved by treatment with heparin for 3 days to 2 weeks. The authors concluded that the defects were due to utilization of clotting factors and that heparin treatment in such cases reduces the hazards of surgery.—A. L. B.


After heparin infusion, phospholipase activity acting in vitro on the phosphatidylcholine of circulating lipoproteins was demonstrated.—J. C.


Characteristic lesions were observed in paraffin sections of aspirated bone-marrow obtained from two patients, one of whom was an infant with the hemolytic-uremic syndrome.—A. L. B.


Confirmation was obtained that ellagic acid reduces traumatic bleeding without causing thrombosis. A few thrombi, however, were found following ellagic acid administration where circulatory flow was abnormal. ADP alone caused formation of platelet thrombi, but when ellagic acid was added platelet-fibrin thrombi were found. This effect was reduced, but not prevented, by administration of heparin immediately after ADP.—C. R. M.


The effectiveness of 24 procedures in 526 patients, 320 of whom showed abnormalities of one or more tests, was analyzed. It is really not possible to summarize the material presented in a reasonable space—the
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Coagulation studies were performed on more than 30 patients with the nephrotic syndrome. Factor IX deficiency was found in four who had particularly low levels of serum albumin. The low Factor IX levels were corrected when the nephrotic syndrome responded to steroid therapy.—A. L. B.


Prolongation of the clotting time of recalcified plasma was observed in lead acetate-intoxicated rabbits. Prothrombin time and prothrombin consumption did not change significantly. Platelet counts increased markedly. Prophylactic injections of CaNa₂EDTA did not prevent prolongation of plasma clotting but induced a decrease in plasma fibrinogen. Disturbances of liver parenchymal function were suspected in animals receiving both lead acetate and CaNa₂EDTA.—M. K.


Diminution in capillary resistance was noted in 34 of 42 patients with spontaneous retinal hemorrhages in the absence of hypertension or diabetes. This capillary fragility was always found alone; the other tests of coagulation were normal, except for an abnormal prothrombin consumption test in 10 cases. The finding was as frequent in either sex and at all ages and appeared to justify prophylactic or curative treatment.—J. C.

The treatment of acute vascular obstruction must raise for discussion the use of streptokinase in parallel with other therapy: surgery, heparin, macromolecular solutions. Indications were: acute arterial ischemia not amenable to surgery, obstruction located distally in a region that contraindicated surgery and old thromboses with an uncertain distal vascular bed. Streptokinase also had contraindications: risk of hemorrhage, history of recent cerebral vascular accident or an acute obstruction seen after the third day. Under strict medical and biological supervision, such treatment was able to produce restoration of the artery by lysing the clot.—J. C.

ERYTHROCYTES


A comprehensive review of the functionally abnormal hemoglobins and of the relationship of an abnormality in structure to changes in function.—T. F. N.


Three members of a German family showed evidence of excessive hemolysis without anemia or splenomegaly. The propositus had a long history of recurrent jaundice, and other relatives not available for study had similar histories. There were very few spherocytes in the blood, but Heinz body formation was marked and there was some decrease in GSH stability. Cellulose acetate electrophoresis revealed an atypical hemoglobin moving between A and A₂ and constituting 30 per cent of the total hemoglobin. Preliminary study suggested that this was a new type of hemoglobinopathy and that it was inherited as an autosomal dominant characteristic.—F. W. G.

A BOSTON-TYPE HAEMOGLOBIN M IN HUNGARY: HAEMOGLOBIN M KISKUNHALAS. S.

An a-chain hemoglobin M was described previously as Hb M Kiskunhalas. This anomaly was identified by fingerprint analysis as Hb M Boston. The relative amounts of Hb M showed definite fluctuations and there was a change in the Hb M percentage after a stay under lowered atmospheric pressure.—S. R. H.


A 41 year old male of Sicilian ancestry was found to have a relatively severe form of thalassemia: “thalassemia intermedia.” He underwent splenectomy at age 7 and had received 6 units of blood in the intervening years. During childhood and adolescence, he received oral iron medication and deliberately ate iron-rich foods. At 41, he was found to be severely iron-loaded with signs of hemochromatosis, including skin pigmentation, liver dysfunction, cardiac failure, diabetes mellitus and hypopituitarism. Of interest also were the presence of porphyrins and dipyroles in the urine, ascribed by the authors to the marked ineffective erythropoiesis, and the demonstration of megaloblastic erythropoiesis and decreased serum folate levels with a hematologic response to oral folic acid. His severe iron loading, associated with clinical and biochemical evidence of hemochromatosis, was presumably primarily due to increased gastrointestinal absorption of iron.—T. F. N.


Seventeen patients heterozygous for beta-thalassemia, 4 heterozygous for alpha-thalassemia and 9 normal subjects were studied. Erythrocytes were divided into two groups on the basis of different specific weights. In heterozygous beta-thalassemia, the younger circulating erythrocytes had a higher Hb A2 content, a lower Hb F content, a relatively reduced osmotic resistance and a reduced survival. The older group had a lower Hb A2 content, a higher Hb F content and increased osmotic resistance. In heterozygous alpha-thalassemia, there was a group of erythrocytes with reduced survival and a high content of Hb H and Hb Bart's.—P. d. N.

P. d. N.


In a four year old girl with measles, hemoglobinuria developed one day before the rash and lasted 11 days. The Donath-Landsteiner antibody was no longer detected after 37 days. The antibody was an IgG globulin with anti-P1 and P2 specificity, but a positive direct antiglobulin test was due to absorption by the red cells of complement.—A. L. B.


AChE activity was studied by histochemical methods. In 2 patients, one group of erythrocytes was completely devoid of AChE activity, was sensitive to the lytic action of normal fresh acidified serum and had a reduced survival. The percentage of these cells was considerably higher among reticulocytes than in the remaining erythrocytes. The other group of cells had properties identical with the erythrocytes of normal subjects. The absence of AChE was demonstrable in erythroblasts. The marrow probably produced such altered cells which were rapidly destroyed. According to the authors, there should be a genetic alteration in the marrow causing the production of these erythrocytes and the onset of the disease. In some cases, FNH may be due to other causes acting directly on circulating erythrocytes.—P. d. N.

In 50 cases of hemolytic disease due to anti Rh and ABO isoimmunization, 20 per cent presented with metaphyseal radiotransparent striate not observed in normal newborns.—F. d. N.


In this series of papers, Hallberg and co-workers continued their efforts to bring a rational basis to oral iron therapy. In the first paper, three series comprising a total of 1496 blood donors were studied. A daily dose of 180 or 222 mg. of elemental iron was given as sulfate, fumarate, gluconate or glycine sulfate. Side effects to placebo was given as sulfate, fumarate, gluconate and Fe59 were given on alternate days; every other day was statistically significant. There was no significant difference. Absorption studies of various combinations of iron and succinic acid, using the double radioiron method, were done in 106 subjects. Succinic acid caused increased iron absorption of 28–30 per cent. Since succinic acid had no side effects and increased iron absorption significantly, it was concluded to be of clinical value.—S.-A. K.


Iron-binding capacity of gastric juice was measured by a previously described technic and was found to be reduced in persons with iron-deficiency anemia due to blood-loss. The iron-binding capacity reverted to normal when anemia was corrected. The authors considered that the gastric juice contains an iron-binding protein (gastroferrin) which regulates iron absorption and that reduced levels in iron-deficiency states permit increased iron absorption.—A. L. B.


A whole body counter of high efficiency enabled measurements of the absorption of oral Fe59 and the distribution of oral and intravenous Fe59 when administered in very small doses to control subjects and patients with iron-loading. After both routes, equilibrium of whole body counts and distribution were attained within 14 days, but the absorption of iron was greater in patients than in controls. A higher proportion of radioactivity occurred over the liver during
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the first few days in patients compared with controls and this difference was more marked after oral than intravenous administration. In contrast to normal subjects, the route of administration thus affected the distribution of iron in patients with iron-loading. This fact may affect the validity of iron absorption studies by the double isotope method in such patients.—A. L. B.


Sideroachrestic anemias with megaloblastic hemopoiesis sometimes are differentiated from pernicious anemia with difficulty. Two cases of this group are reported. The role of enzyme defects in the synthesis of heme and the significance of drug-induced disorders are emphasized.—S. R. H.


Patients with vitamin B12 deficiency have increased urinary excretion of methylmalonic acid (MMA) because vitamin B12 is necessary for the conversion of methylmalonyl coenzyme A to succinyl coenzyme A. Administration of valine and isobucine increases urinary excretion of MMA in vitamin B12 deficient patients, but not in healthy controls. Urinary excretion of MMA after administration of valine may form the basis of a loading test for vitamin B12 deficiency.—A. L. B.


Antibodies against gastric mucosa were studied with a complement fixation test. Antibodies were found in 71 per cent of patients with pernicious anemia and 44 per cent of diabetics. The test was negative in healthy people and in patients with hypochronic anemia.—M. K.


After treatment with ammonium sulphate, DEAE Sephadex A-50 chromatography and filtration on Sephadex G100 in 0.1 N acetic acid, components completely depleted of blood group substance were recovered. A component was obtained which was able to transport Vitamin B12 and which had the characteristic antigenicity of swine intrinsic factor. The molecular weight was 4395 ± 215.—J. C.


The therapeutic effect was studied in 11 patients. Total remission was observed in respect to hematologic and clinical features, as well as in the objective state. Remission was observed even in cases refractory to other therapeutic measures. No harmful side-effects were observed. Mean period for obtaining remission was 40 days and the average total dose was 9 Gm (250 mg daily). The mean duration of remission was 13.7 months, although this was not a final figure because most of the patients were still in remission without drugs. Further administration of Myelobromol in maintenance doses was not necessary.—S. R. H.


The minor but definite, differences in ribosomal proteins of rabbit and guinea pig reticulocytes contrasted with the identity of the ribosomal proteins of rat heart and rabbit reticulocytes.—J. C.


A rapid, accurate quantitative method for measuring adenylate kinase activity (ATP + AMP → 2 ADP) in the soluble fraction of erythrocytes is described. The reaction, coupled to the oxidation of DPNH, may be
followed spectrophotometrically. The conditions and requirements of the reaction, including substrate-velocity relationship and pH optimum, are described. Normal values and preliminary data bearing on activity in disease states are recorded.—S. R. H.


A synthesized, purified methemalbumin was studied in detail. The most important observation was that it was not resistant to the effects of cyanide. Electrophoretically-separated methemalbumin from PNH serum behaved in the same way as the synthetic product. Another, cyanide-resistant heme pigment(s), however, was found in the serum of all five PNH patients examined.—C. R. M.


A method for performing osmotic fragility determinations on the Autoanalyzer with apparently only minor adaptations of the machine was described. The results, recorded graphically, can be placed in the patient's chart. Repeating the determination after 24 hours of incubation at 37 C was recommended because some samples showed abnormalities only after incubation. For anybody who wishes to perform significant numbers of fragility studies, this procedure would seem well worth investigating.—C. R. M.


Red cells from patients with active multiple sclerosis were more fragile than those from patients in a quiescent phase and those from normal individuals. The possibility that ADP released from abnormally fragile red cells might account for the increased platelet adhesiveness seen in multiple sclerosis was discussed.—A. L. B.

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MISCELLANEOUS


This monograph includes an extensive review of the literature on antinuclear antibodies (AA), the results obtained by the authors and a study of the so-called anti-perinuclear factor (APF). The authors used two substrates: cryostat guinea pig liver sections and human leukocyte smears. Both total and specific antihuman globulin FITC-conjugated rabbit and goat antisera were used. In the study of the L. E. phenomenon, the homogeneous appearance of the engulfed nuclei was identical to the equally homogeneous appearance of the cryostat sections, indicating the nucleolytic activity of the anti-DNAP antibody. Of 28 cases of SLE (7 treated), 85.6 per cent had a strongly positive homogeneous reaction and had LE cells. After treatment, 60 per cent were LE-negative, 28.5 were ANF-negative. 57.3 were borderline positive and 14.2 had shifted to weak speckled fluorescence. Of 100 cases of RA, 62 were ANF-positive, 54 of the speckled type and 8 homogeneous of whom 5 had LE or LE-like cells and were the most severe. APF may be present alone or in combination with ANF in cases of RA with SLE features. APF was present in 51 of 100 unselected cases of RA. APF-positive tests were associated with stronger RF reactions and were more frequent in the more severe cases.—P. d. N.


Using fluorescein labeled antibody and normal human leukocytes, the incidence of antinuclear factors (ANF) in children was studied and the presence of rheumatoid factor was investigated by use of the latex fixation test. ANF was present in 15 of 16 youngsters with S.L.E and in almost 1/4 of the
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children with rheumatoid arthritis, ulcerative colitis or "suspected collagen disease." Positive tests for ANF among children with rheumatoid arthritis were seen almost exclusively in girls, and there was a positive correlation between the presence of ANF and latex fixation.—J. B. S.


ATP, AMP and NAD increased during the second month of treatment with atherogenic diets and then decreased. The total amount of free nucleotides did not change, indicating that there was not an abnormality in nucleotide synthesis. The increase in CTP appeared to be related to an alteration in lipid metabolism.—J. C.


The extent of improvement in certain cases was such as to permit surgical intervention for what constituted inoperable carcinomas. In a large number of cases, improvement was substantial. While these results did not permit any definite conclusion, they were sufficiently encouraging to justify further studies with a control series to provide a more specific basis on which the findings could be judged.—J. C.


Liver biopsies were studied with light and electron microscopy. In Crigler-Najjar, an almost normal liver was found. The Rotor type showed definite pathology, especially in the mitochondria. No abnormal pigments were found in either kind of constitutional hyperbilirubinemia.—M. J.


Blood, bone marrow and spleen were studied in experimental portal hypertension in dogs and rabbits. Lymphopenia, thrombocytopenia and anaemia were accompanied by biphasic changes in the marrow. In the early phase, transient hyperplasia of the erythropoietic and leukopoietic systems was observed. After 3–4 weeks, marrow cellularity decreased. Spleens were enlarged and showed functional and histologic patterns of reticuloendothelial hyperplasia. Similar changes were induced in intact animals by injections of extracts of normal spleens. The therapeutic value of splenectomy in early portal hypertension was discussed.—M. K.