ABSTRACTS

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ERYTHROCYTES


The in vitro influence of 2,3-diphosphoglycerate on erythrocyte phospho-fructokinase activity was studied. In contrast with the results of Beutler, no inhibition was observed on the purified enzyme. In hemolysate, an apparent inhibition of 2,3-diphosphoglycerate was found. The authors suggest that this inhibition is due to the composition of the reaction mixture. When ADP was added no inhibition was found.

—K.P.


Hb-Gifu was discovered in a family in the Gifu prefecture by Matsutomo in 1967. Hb-Ichinomiya was encountered in Aichi prefecture in 1969. Chemical study of these abnormal hemoglobins revealed their identity. There was substitution of Lys for Asn (80, EF4) in both of these abnormal hemoglobins. In one of these families (Gifu) the carriers of the abnormal hemoglobin were slightly polycythemic, but the polycythemia could not be accounted for by a functional defect of the hemoglobin molecule, because its oxygen dissociation curve was normal.

—K.F.

A comparison was made between the absorption of $^{55}$Fe incorporated biosynthetically into food (intrinsic tag) and a tracer dose of inorganic $^{59}$Fe (extrinsic tag) administered with the same meal. The absorption of inorganic iron added to food closely approached the absorption of food iron. The authors suggest that a common pool of nonheme iron is formed and that the availability of this iron is determined by the composite effects of substances in the meal which either block or facilitate absorption.—R.O.W.


In mice, stepwise dilution after thawing of frozen hemopoietic cells greatly increased the reproducibility of an optimal stem cell recovery measured by the CFUc assay in vitro and the CFUs assay in vivo. Similarly, in monkeys, stepwise dilution after thawing of marrow frozen in DMSO and calf serum maximally preserved its proliferative capacity as measured by the thin layer agar technique. With the help of this in vitro assay, the dilution method was improved for handling stored monkey bone marrow. Frozen allogeneic bone marrow cells diluted stepwise after thawing were able to restore hemopoiesis of lethally irradiated Rhesus monkeys. Reproducible take were obtained by grafting limited cell numbers ($4 \times 10^8$ kg), which were the same amounts of fresh bone marrow cells necessary for hemopoietic repopulation. The results obtained indicate that in monkeys, bone marrow cells can be frozen and thawed without loss of proliferation capacity, when the cells are diluted gradually so that an osmotic shock is avoided.—G.M.


The most recent advances of our knowl-

edge on normal and abnormal hemoglobins are reported. A detailed analysis of the different abnormal hemoglobins is made according to the type of alteration: those with a structural defect and those characterized by an impairment in the synthesis of the different hemoglobin chains. Of the former, those with unstable hemoglobins are examined; among the latter, thalassemia and its numerous variants are described. One of the most important facts emphasized in this report is the connection between the spatial position of the mutation in the hemoglobin molecule and the severity of the corresponding disease. Consequently, a great value is given not only to the anomalies of the primary structure and the amino acid sequence, but also to the variations induced on the tridimensional structure of the hemoglobin molecule.—G.L.

LEUKOCYTES


A phase II, noncomparative clinical trial of chemotherapy of leukemia and solid tumors, was carried out during which the authors attempted the following: (a) To synchronize cells by first administering an antineoplastic agent which blocks them in mitotic phase M, and is verified by the mitotic index. Hence, they pass into the next phases of the cycle more or less at the same time, and this was verified by the tritiated thymidine test. (b) To destroy a larger number of cells by secondary administration of a cycle-dependent agent (cyclophosphamide) or phase-dependent agent, such as adriamycin or methotrexate. Remarkable results were obtained in inducing
remissions or apparently complete regressions in patients in whom previous trials had shown resistance to both of these agents administered singly. The cycles were administered intermittently with free intervals, the length of which depended on the time of restoration of the bone marrow and blood. The blood immunologic and visceral tolerance was, on the whole, excellent.


A cytogenetic study of 13 cases of myelomonocytic leukemia in children showed, in two cases, clone abnormalities with 47 C+ chromosomes in one patient, and 47 Iq+C+ chromosomes in the other. These two patients both had altered blood groups. The relationship between altered blood groups and chromosome abnormalities is discussed.


Defects in erythroblastic and megakaryocytic maturation were found in a 13-yr-old patient in the preleukemic phase of acute leukemia (type not indicated). Polychromatophilic erythroblasts were found to accumulate in G1, and a decreased proportion were counted in S. In megakaryocytes, DNA values of 2C–8C, as compared to values of 4C–32C in normal subjects, were found. Abstractor’s comment: Megakaryocyte hypoploidy was previously described in other leukemic or preleukemic states. See Undritz and Nusselt-Bohaumilitzkv, in Platelet Kinetics, North Holland Publ. Cy, Amsterdam, p. 309, 1971; and Kinet-Denoel and Breton-Gorius, in preparation for the Nv. Rev. Franç. Hemat.—J.M.P.

Hydroxyurea Therapy in Chronic Myelogenous Leukemia. B. Kennedy. Department of Medicine, University of Minnesota.
Health Science Center, Minneapolis, Minn. Cancer 29:1052-1056, 1972.

Hydroxyurea was administered to 20 patients with chronic myelogenous leukemia. The white blood cell counts decreased to normal in all the patients, anemia improved, splenomegaly decreased or disappeared, thrombocytosis was corrected, and bone marrow improvement occurred in all the patients. Megaloblastosis was consistently noted. Hydroxyurea was effective in treating chronic myelogenous leukemia refractory to busulfan. Hydroxyurea did not prevent the development of the acute phase of chronic myelogenous leukemia, hemolysis, or myelofibrosis. The chief systemic reaction was reversible myelosuppression and an unusual dermatologic alteration. Hydroxyurea is as effective as busulfan and may be utilized as a primary therapy of chronic myelogenous leukemia.—J.E.U.


Based on studies of the chemotherapy of human leukemia and late stage animal neoplasms which may be kinetically analogous to disseminated reticulum cell sarcoma, a therapy program was devised using sequential cyclophosphamide–vincristine followed by weekly methotrexate–cytosine arabinoside. Each cycle of therapy consisted of cyclophosphamide 1.5 g/m² on day 0 and vincristine 1.4 mg/sq m on days 1, 8, and 15; subsequently, eight weekly doses of IV cytosine arabinoside 300 mg/sq m and oral methotrexate 120 mg/sq m over 24 hr were given followed by “Leucovorin rescue.” Fifteen patients received three such cycles with intervening 2-wk recovery periods. Nine patients achieved complete remission, and six had a partial response. Median remission duration was 10 mo. Median survival from onset of disease was 154 mo and from beginning of therapy was 141 mo. Five of seven patients who have relapsed are dead. Toxic manifestations included neutropenia below 1000/cu mm in 10 patients; of these, there were recurrent episodes of sepsis in one. Alopecia occurred in 10, and reversible neurotoxicity in eight patients.—J.E.U.


In this series of 38 patients with lymphosarcoma of the small intestine, 26 had no previously diagnosed lymphoma (Group A), and 12 had a histologically proven malignant lymphoma elsewhere in the body before diagnosis and resection of the bowel tumor (Group B). The clinical and pathologic features of these tumors are presented and correlations between the two are made. The overall 5, 10, and 15 yr survival rates in Group A were 48, 35, and 17%. Pathologic features which seemed to correlate with prognosis included gross type of tumor, size, microscopic type, lymph node involvement, presence of perforation, fistula formation, and multicentric lesions. The preferred treatment was a wide segmental resection of the lesion and adjacent bowel, as well as resection of the contiguous mesenteric lymph nodes. Radiotherapy is recommended if any of the following unfavorable features are present: lymph node involvement; tumor on the margins of resection; perforation; fistula, and multicentric tumors. Patients in Group B had similar clinical manifestations and pathologic findings. In contrast to Group A, however, all of these patients died.—J.E.U.


Surgical specimens, postmortem material, or both, from 22 patients with the syndrome designated as “Mediterranean abdominal lymphoma with malabsorption” were studied in detail. All patients exhibited a malabsorption syndrome. In most of those carefully followed from the onset of the disease, the syndrome seemed to have pre-
ceded the development of palpable abdominal masses. In 20 of the 22 patients, intestinal tissues were available for histologic study. In all specimens, diffuse severe plasma cell infiltrations were evident in the intestinal mucosa and submucosa. Malignant lymphomas in the form of single or multiple circumscribed intestinal tumors occurred in 14 of these 20 patients and malignant lymphomas of the mesenteric lymph nodes in two. In four patients, no malignant lymphomas were evident. These observations suggest that the diffuse plasma cell infiltrations, rather than the malignant lymphomas, were responsible for the malabsorption syndrome. There was no morphological evidence that the malignant lymphomas observed in 75% (16 of 20) of the patients were histogenetically related to the diffuse plasma cell infiltration. The possibility is suggested that this abnormal, though probably not neoplastic, proliferation of plasma cells is a morphological manifestation of an immune deficiency state which predisposes the patients to the development of malignant lymphoreticular neoplasms.—J.E.U.

Malignant Lymphoma, Histiocytic Type with Sclerosis (Sclerosing Reticulum Cell Sarcoma). A Rosas-Uribe and H. Rapaport. Department of Pathology, the Pritzker School of Medicine, University of Chicago, Chicago, Ill. Cancer 29:946-952, 1972.

A rare, previously undescribed malignant lymphoma of the histiocytic type with sclerosis or "sclerosing reticulum cell sarcoma" has a slower rate of growth and a lesser degree of aggressiveness than the corresponding nonsclerosing tumors.—J.E.U.


Two hundred and eighteen untreated patients with non-Hodgkin's lymphomas, classified according to the scheme of Rappaport et al., were investigated for bone marrow involvement. No pattern of pretreatment laboratory abnormalities predicted which patients would have a positive bone marrow for lymphoma. Open marrow biopsy demonstrated lymphoma after needle biopsy was negative, and both biopsy techniques were clearly superior to bone marrow aspiration in identifying marrow involvement. Bone marrow involvement correlated with advanced stage, cellular composition of the lymphoma, and, in the nodular lymphomas, splenomegaly and constitutional symptoms. Patients with histiocytic lymphomas uncommonly had initial marrow involvement whereas patients with mixed and lymphocytic types were frequently affected. Nodular or diffuse patterns did not influence the incidence of marrow involvement, but patients with nodular lymphomas and positive marrows survived significantly longer than those with diffuse lymphomas.—J.E.U.


Preliminary experience with irradiation as the primary modality of treatment for patients with generalized lymphosarcoma suggested a potential role for radiotherapy in at least selected stages of advanced disease. Specifically, cases with widespread lymph node involvement (with or without bone marrow infiltration) were frequently observed to have complete remissions which occasionally were sustained without maintenance therapy. More complete information
on the initial clinical responses for this presentation of the disease is described. Treatment consisted of total body irradiation (TBI), total nodal irradiation (TNI), or a combination of these approaches. The complete remission rate for 27 consecutive patients with previously untreated disease was 93% (25/27), and the median duration of unmaintained remission was 26 months. Following relapse, irradiation has continued to be effective in the subsequent treatment of most patients. The relatively prolonged symptom-free intervals and a 3-yr survival rate of 87% suggests that primary treatment with radiotherapy should be directed toward maximum control of disease rather than being limited to palliation of symptomatic areas, despite the anatomically extensive involvement at the time of diagnosis.—J.E.U.


Mathematic analysis of the effect of 1-methyl-2-mercaptoimidazole treatment on the leukocyte count in 100 unselected patients with thyrotoxicosis is presented. The total doses of Metizol applied ranged from 2 to 15 g. No significant changes were found in the total leukocyte count and percentage of granulocytes. In seven patients only a decrease of the order of 9% of the initial values per 0.5 g of Metizol was observed.—M.K.

HEMOSTASIS


Blood platelets have the ability to incorporate labeled uridine into a high molecular weight fraction sensitive to RNase but not to proteolytic enzymes. Together with the demonstration by Seitz (Adv. Cancer Res. 9:303, 1965) of a rapid turnover rate of RNA phosphorus in platelets, this finding leads the author to suggest that protein synthesis in these cells, although directed by a stable mRNA, depends on the availability of tRNA. Mitochondria may be involved in the synthesis of this class of RNA. —J.M.P.

Inhibitory Effect of Acetylsalicylic Acid on Platelet Metabolism. W. Schneider and C. Doenecke. Medical University Clinic, Homburg, Saar, Germany. Abstracts of IIth Int. Symp. on Metabolism and Membrane Permeability of Erythrocytes, Thrombocytes and Leukocytes, Vienna Academy of Medicine, Vienna, Austria, p. 61, 1972.

Aspirin caused an inhibition of hexokinase activity both in platelet homogenates and platelet-rich plasma. No other enzyme of glucose metabolism in platelets was found to be affected.—J.M.P.


The adhesion of platelets to collagen appears to be mediated by glucosyl- and galactosyl-transferases present on the platelet membranes, interacting with incomplete heterosaccharide chains present in collagen. Arguments in favor of this thesis are: (1) the parallel inhibitory effects of various reagents on both adhesion and the enzymatic reaction; (2) the inhibitory role of collagen-derived glycopeptides; (3) the loss of aggregating activity when collagen is treated with galactose oxidase and its reappearance on subsequent reduction to galactose.—J.M.P.

Oat-cell Carcinoma Associated with Multiple Endocrinal Hypersecretions and Consumption Coagulopathy. J. Verschraetan, M. Kraytman, G. Destailleur, H. Brauman, B. Futeral and J. Corvilain. Clinique Médicale, Hopital Brugmann and Service de Biologie Clinique, Fondation
ABSTRACTS


The author analyzed degrees and causes of bleeding in 1308 patients subjected to various operations on the lungs. In 228 selected cases laboratory tests were performed. In 72% of the patients in this group pronounced disturbances of hemostasis were observed during surgery, most frequently a significant fall of the fibrinogen level, prolongation of the thrombin time, and activation of fibrinolysis. DIC with concomitant activation of fibrinolysis is considered to be the most common cause of the observed laboratory changes and of excessive bleeding. Good results were obtained by treatment with inhibitors of fibrinolysis applied together with heparin.—M.K.


In 32 workers of Plant Protection Stations and Spraying Brigades, examination of clotting system and fibrinolysis were performed. The examined workers were chronically exposed to different pesticides for 2–20 yr. The real exposure time was 4–16 mo. In all subjects decreased numbers of thrombocytes were found; in five persons disturbance in prothrombin consumption was observed, and in some cases different levels of factors V and VII + X were noted. Results of fibrinolysis were normal.—M.K.


Thromboelastographic investigations were carried out in 20 young subjects immediately before an intravenous infusion of 500 ml of dextran 40 000, and 90 min and 24 hr after completion of the infusion. A statistically significant prolongation of the “r” and “k” segments was found together with a decrease in the maximum elasticity of the clot (“ma”). The value of dextran 40 000 as an agent capable of decreasing mildly and for long time periods coagulability of the blood is stressed.—M.K.

IMMUNOHEMATOLOGY

ABSTRACTS


Mortality attributable to graft-versus-host reaction, induced by grafting parental lymphoid cells into irradiated F1 recipients, has been delayed and reduced by treating the donors with high or low doses of soluble recipient H-2 antigens. GVH reaction seems a good model to study "high and low dose tolerance" with histo-compatibility antigens. Possible implications in leukemia treatment by specific adoptive immunotherapy are suggested.—G.M.


The authors studied bone marrow transplantation in benzene induced aplastic anemia in rabbits which closely resembles aplastic anemia in man. Conditioning of the recipients was performed with horse anti-rabbit ALS. In a strain combination known to result in fatal graft-versus-host reaction (GvH) if total body irradiation is used for conditioning, a high percentage of takes was achieved and no GvH was seen. The absence of GvH could be explained by the fact that only the B-equivalent of the immunologic system became donor in origin, but the T-system remained recipient.—G.M.


Lymphocyte replicating ability is a quantitative test of lymphocyte function following radiation exposure. Its use was extended to patients undergoing cancer chemotherapy. The procedure was simplified for clinical practice and a quick filtration processing method was adopted. Lymphocytes stored in DMSO at —196°C, stored reference lymphocytes (S.R.L.), were employed as an absolute standard to allow comparison of results over a prolonged period of time. —G.M.


Between Hodgkin’s disease and control subjects no difference was found in HL-A 5 frequency, both being 12%. This was in contrast with findings of Zervas et al., who found a higher HL-A 5 frequency in Hodgkin’s disease than in control subjects, using the same anti-HL-A 5 serum in the lymphocytotoxicity test. In accordance with the findings of Kissmeyer-Nielsen, however, a higher HL-A 5 frequency was found in Hodgkin’s disease and other lymphomas, than in control subjects. —K.P.


Blastic transformation of lymphocytes in in vitro culture was examined in 38 patients with various proliferative diseases of the leukopoietic and lymphatic system, and in 11 healthy people. Impaired blastic transformation (evaluated by 14C-thymidine incorporation) after stimulation with PHA was observed in multiple myeloma, Hodgkin’s disease, lymphatic leukemia, and granulocytic leukemia. Spontaneous (without PHA) blastic transformation was demonstrated in cultures of lymphocytes from patients with myeloma. The sera of these patients were found to possess the ability to stimulate blastic transformation in lymphocytes from healthy people and from patients with proliferative disorder.—M.K.

Quantitative Analysis of IgG, IgA and IgM Immunoglobulins in Acute and Chronic...

The results of quantitative determinations of IgG, IgA, and IgM and the electrophoretic pattern of serum proteins are presented in 22 patients with AGL, 12 with CGL, 8 with PV, 6 with OM, and 25 healthy blood donors. In AGL, normal mean values of Ig and IgA and elevated values of IgM were observed. In CGL the levels of all these immunoglobulins did not differ significantly from the controls. In PV, significant increases of the IgA and IgM concentrations were found, while in OM the level of all immunoglobulins examined was increased.—M.K.


The authors investigated the synthesis of gamma globulins by bone marrow cells and lymphocytes of blood in some patients with multiple myeloma and Waldenström's macroglobulinemia. They demonstrated that bone marrow cells of these patients can synthesize in vitro a homogeneous protein component which electrophoretically and antigenically appears similar to that present in blood, and also other homogeneous components not present in the serum. Antibody deficiencies in multiple myeloma are thought to be due to deficit in the production of the nonmyelomatous gamma globulin fractions.—G.L.


This paper is based on a review of the literature as well as on the authors' personal experience and describes the clinical, pathological, and immunological characteristics of heavy-chain disease. Despite clinical and histopathological heterogeneity, the common hallmark is an immunological abnormality with accumulation in the blood (occasionally also in other biological fluids) of an immunoglobulin which is devoid of light chains and corresponds to the Fc fragment of heavy chains from one or another immunoglobulin class. Gamma-, alfa-, and mu-chain disease have so far been described. Lambda-chain and epsilon-chain disease (corresponding to IgD and IgE), although postulated, are yet to be described. Structural studies of these anomalous proteins seems to indicate that an internal deletion is the underlying abnormality, which accounts for the lack of synthesis of the Fd fragment.—G.L.


Using phytohemagglutinin (PHA-M) stimulation, the blastic transformation of peripheral blood lymphocytes was studied in 15 Indians in a state of hyperimmunity. They were from the Parque Nacional do Xingú, with holoendemic malaria infection. While the rates of blastic transformation in ten normal (non-Indian) donors ranged from 44% to 55%, in the Indians they ranged from 11% to 55% and showed depression of blastogenesis in six subjects. Lymphocytes of non-Indian normal donors were incubated with autologous serum, with serum from Indians showing normal blastic transformation, and with serum from Indians showing depression of blastic transformation. In the two first groups, the rate of blastogenesis was normal and was depressed in the latter group. These results led the authors to postulate an inhibiting factor in the serum of the affected Indians. Such factor might be a toxic substance due to malaria infection. However, new incubations were set up 3 mo later using new serum from 12 of the 15 Indians previously studied. Data of the two measurements showed a fluctuation in the levels reached by each subject in both measurements, and led to the conclusion that the possible toxic factor is a transitory one.—M.J.

During the past two years two new techniques for studying chromosomes have been proposed: fluorescent technique after staining with quinacrine derivates, "denaturation" and enzymatic breakdown. Karyotype analysis is now more precise than before and new approaches to the problem of cytogenetics are possible: study of normal variants, study of constitutional and acquired anomalies, gene localization on autosomes, evolution of species, and chromosomal structure.—G.M.


Seven patients, treated with bone marrow transplantation, were kept in reverse isolation to prevent exogenous colonization, i.e., contamination followed by colonization after admission. Such colonization often leads to infection in these patients, as they suffer from a severe impairment of their immunologic defense capacities. Two different types of isolation systems were used, i.e., ultra-clean rooms (U.C.R.) and laminar flow isolators (L.F.I.). Description and microbiological testing of both types showed that they differ in several aspects. In U.C.R. personnel entered after taking standard precautions; food and beverages were pasteurized. In L.F.I. personnel did not enter; food and beverages were sterilized. In this study, U.C.R. were partial reverse isolation systems, reducing but not eliminating exogenous contamination, whereas L.F.I. were used for strict reverse isolation. For that reason two patients in whom antibiotic decontamination of the digestive tract was performed, were treated in L.F.I.—G.M.

Reduced Viscosity of Human Blood Sera at Various Temperatures and in Various Age Groups. T. Turczynski. Faculty and Department of Physics, Silesian School of Medicine, Zabrze, Poland. Acta Physiol. Pol. 23:113–124, 1972.

The viscosity of human blood sera has been examined at various temperatures in two groups of men. One group included persons around the age of 20 yr, the second of age 70–80 yr. Viscosity calculated as a ratio of specific viscosity to the concentration of serum proteins constituted the basis for comparison. Viscosity was measured at the temperatures of 20, 50, and 59°C. Serum protein fractions and the level of cholesterol were also examined. It was confirmed that reduced viscosity is significantly higher at all temperatures, in old age than in the young age group. A negative correlation between reduced viscosity and the ratio of serum albumin to globulin was found and the increase of viscosity with age could be partially connected with the decrease of this ratio. The sera of young people responded with greater decreases of viscosity to increase in temperature than the sera of aged persons.—M.K.


Twenty patients with bronchial asthma and six healthy persons were treated for seven days with vitamin A given in a dose of 72,000 U per day. Muramidase activity in blood serum and saliva, seromucoid level, and fibrinogen concentration in plasma were determined before and after treatment. In healthy people, vitamin A remained without any effect on the examined parameters while in patients with bronchial asthma significant increase of seromucoid and fibrinogen levels was demonstrated. The muramidase activity of blood serum was higher in bronchial asthma than in controls but did not change after vitamin A treatment.—M.K.
ABSTRACTS

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