ABSTRACTS

Ernst R. Jaffé, M.D., Editor

ABSTRACTERS

Klaus Betke, M.D., Tübingen, Germany
Arthur Bloom, M.D., Cardiff, Wales
T. H. Bothwell, M.D., Johannesburg, South Africa
T. E. Brittingham, M.D., Nashville, Tenn.
Jacque Caen, M.D., Paris, France
J. B. Chatterjea, M.D., Calcutta, India
F. J. Cleton, M.D., Leiden, The Netherlands
Pietro deNicola, M.D., Pavia, Italy
Ludvik Donner, M.D., Prague, Czechoslovakia
A. J. Erslev, M.D., Philadelphia
H. Hugh Fudenberg, M.D., San Francisco
Katsuhito Fukutake, M.D., Tokyo, Japan
Robert Goldstein, M.D., New York City
Ira Green, M.D., New York City
F. W. Gunz, M.D., Christchurch, New Zealand
Susanna R. Hollan, M.D., Budapest, Hungary

LEUKOCYTES


Among 180 patients undergoing by-pass open heart surgery, 30 developed a postoperative syndrome with circulating atypical mononuclear cells and often fever and splenomegaly, but rarely lymphadenopathy, 5 to 60 days after operation. The more severe manifestations had an onset 3 weeks or more post-operatively. Two patients who did not have by-pass operations but were given large transfusions of fresh blood had a similar syndrome. The post-transfusion mononucleosis thus was significantly associated with the giving of large quantities of fresh blood, rather than with the use of a by-pass. Since the atypical cells resembled lymphocytes transformed after PHA stimulation, the suggestion was made that the syndrome was an immunologic phenomenon, possibly a graft rejection directed against viable transfused foreign lymphocytes.—F. W. G.


Four children beginning therapy for acute leukemia developed anorexia, nausea, persistent vomiting, lethargy and extreme weakness; 2 convulsed, 3 became comatose, and all died. Serum uric acid levels ranged between 20 and 55 mg. per 100 ml. The authors believed that the symptomatology was related to the hyperuricemia, inasmuch as a similar clinical picture had been described in patients infused with 20 mg. of uric acid per kg. In two postmortem examinations of the brain, edema was the only prominent abnormality.—J. B. S.


In a man of 37 affected with acute leukemia of the Naegeli type, the onset was marked by cutaneous lesions. A large pericardial effusion (2.3L.) with a massive multinodular attack of myocarditis was noted at autopsy. The latent character of cardiac localization of acute leukemia and the rarity of the "tumor" type were stressed.—J. C.
ABSTRACTS


An 8 month old infant developed the typical physical and laboratory findings of CML. Fetal hemoglobin values were normal and the Philadelphia chromosome was found in peripheral blood and bone marrow preparations. The infant’s course at first was typical of CML, but 6 months after onset “blastic” transformation of the marrow occurred. The picture of the “adult” type of CML occurring at this age was a rarity.—J. B. S.


Hydroxyurea therapy led to many remissions in 26 patients with chronic myeloid leukemia in various stages. The characteristic features of this therapy were: 1) low toxicity, 2) extreme rapidity in obtaining remission, 3) possible effectiveness in cases resistant to other therapy and in acute transformations, and 4) short duration of remissions if long-term therapy was not instituted.—J. C.


The author analyzed the foundations of visual “quantitative” photometry of cytological objects and the causes for possible errors. Simple mathematical analysis was carried out as an error in visual photometry without consideration of the volume of the object. For an example of diploid nuclei, the author presented an estimate of the minimal number of measured nuclei required to obtain the mean DNA value which approached the true value. It was impossible to differentiate nuclei into diploid and tetraploid types with visual photometry. The change in DNA content in acute leukemia caused by frequent aneuploidia proved to be undetectable by visual photometry.—J. K.


In a study of 653 cases, the authors confirmed the diagnostic value of lymphography. Lymphography was indispensable in malignant lymphohemopathy before any treatment, for it showed precisely the degree of spread, its variation in relation to the clinical stage and the localization of supra- or sub-diaphragmatic adenopathy. The authors noted the limitations of lymphography and its “evolutionary value” because node opacification lasted several months.—J. C.


The authors reviewed 107 cases of apparently localized forms of lymphosarcoma and reticulosarcoma of the cervico-facial area treated and observed at the Gustave-Roussy Institute from 1951 to 1964. They studied the distribution by sex, age and histology, the clinical and biological characteristics, the results of treatment and the eventual evolution. Attention was drawn to several points: the particular characteristics of the facial mass, the necessity for systematic lymphography which permitted the diagnosis of the localized form to be made more precisely and the differences, more apparent than real, between cervico-facial tumor and disease located elsewhere.—J. C.


Murine leukemia virus (Rich) was inoculated into one of the 2 thymuses of infant mice which were sacrificed 2 months later. The incidence of lymphoma evolving in the inoculated thymus was compared with the incidence in the uninoculated thymus. In 90 per cent of cases in 30 animals suitable for analysis, the tumor arose in the inoculated thymus, supporting the view that the mechanism of viral leukemogenesis was direct.—H. H. F.

A cytopathogenic agent was isolated in cultures of human embryos and on chorio-allantoic membranes of chick embryos from organs of a mouse suffering from spontaneous leukemia. This agent could be passed on cellular cultures and chick embryos.—J. K.


Congenital alymphocytosis in a male infant was diagnosed on the first examination at age 15 days because of a family history. On the 28th day, a graft of thymus was taken from a 6 month old girl, but it was a complete failure. Autopsy revealed the lesions of the syndrome, but the lymphocytic load in the spleen was normal. The patient’s lymphocytes were cultured in the presence of phytagglutinin. The authors analyzed the present status of early diagnosis and reviewed the published cases in regard to thymic grafting.—J. C.


The synthesis of RNA and replication of DNA in normal human lymphocytes was studied in an in vitro culture system containing phytohemagglutinin. Addition of prednisolone-21-phosphate to the system effected inhibition of RNA synthesis and DNA replication which was logarithmically dose related. The decline in number of blood lymphocytes after treatment with corticosteroids may have resulted, in part, from a decrease in the replication of lymphocytes. When serum has been added to media used for the investigation of the response of lymphocytes to phytohemagglutinin, the potential effects of any corticosteroid in the serum must be considered.—A. L. B.

THE FINE STRUCTURE OF LYMPHATIC TISSUE GERMINAL CENTERS’ RETICULAR REMNANT AF-

Pig thymus tissue was cultured with organ culture techniques in the presence and absence of phytohemagglutinin (PHA). Morphologic and autoradiographic observations indicated that, in the pig, lymphocytes capable of responding to PHA were located predominantly in the medulla of the thymus. Of interest was the peculiar association of PHA-responsive lymphocytes with reticular-epithelial cells in the medulla. Perhaps thymic cortical lymphocytes and, possibly, immigrant cells from the circulation (bone marrow derived?) must reach the medulla before they mature into immuno-competent cells in the special micro-environment of the reticular-epithelial cells.


The aim of this study was to determine if thymic grafts placed within millipore diffusion chambers in neonatally thymectomized rats could influence the level of circulating lymphocytes or stimulate lymphopoiesis in the spleen and other lymphoid tissues. In spite of the obvious role of the thymus in lymphopoiesis, the possible release of a potent factor affecting lymphoid tissues or the circulation was not borne out by this study.—O. P. J.


Until recently, it was accepted that sterile damaged and disintegrating tissues did not attract polymorphs chemotactically. Experiments with an in vitro test system practically identical to that used by Harris (1953) provided results indicating that certain types of damaged tissue regularly were chemotactic to polymorphs. For example, human polymorphs were attracted towards severely damaged tissue from burned rat skin, but not towards tissue from areas of less severe heat injury. Fragments of rat cardiac muscle or liver became chemotactic after incubation in fresh rat serum, but not after a similar period of incubation in saline. Perhaps damaged tissue may interact with serum to produce a factor that is chemotactic to polymorphs.—O. P. J.


The ability of neutrophil leukocytes to extravasate into the peritoneal cavity in response to an intraperitoneal injection of bacterial endotoxin was studied in mice. The normal response of a marked accumulation of intraperitoneal neutrophils was completely abolished by halothane anesthesia. No other reports of this effect of anesthetics have been found. The phenomenon appeared to be caused either by a change in vascular permeability or by a change in the ability of the leukocytes to escape the vascular confines. The effect of the commonly used, volatile general anesthetics on the microcirculation has not been defined, so the former possibility should be seriously considered. Perhaps, however, the effect was on the neutrophil, rendering it less deformable and less able to undergo trans-vascular diapedesis.—O. P. J.


Bone marrow plasma cell counts were obtained from aspirates of normal infants and children, and from ill children. Values of 1/1000 or less were generally found in infants below the age of 6 months. Thereafter, mean values progressively increased, reaching adult values after 5 years. Increased numbers of plasma cells were present in children with sickle cell anemia and decreased numbers in patients with hypogammaglobulinemia. Normal values were present in iron deficiency and accompanying the Wiskott-Aldrich syndrome. Because of the low values in healthy infants and young children, it was not possible to diagnose immunoglobulin deficiency by counting bone marrow plasma cells in patients younger than 5 years.—J. B. S.


In a γ-A myeloma with hyperlipidemia, the serologic antilipoprotein (anti-Pg) activity was associated with an abnormal γ-A globulin. The whole abnormal globulin was isolated in a complex of γ-lipoprotein with Pg antigen.—J. C.
HEMOSTASIS


The clinical course of ITP in 152 children was reviewed. Although boys and girls were equally affected, the tendency to chronicity, demonstrated in about 8 per cent, was twice as frequent in girls. More than 80 per cent had an acute febrile illness during the 3 weeks prior to onset. The absence of a history of antecedent infection was also associated with a tendency to chronicity. The incidence in Negroes was less than expected, and eosinophilia was universal. The patients were classified as mild, average, or severe. The latter term was reserved for children with massive cutaneous purpura, profuse epistaxis, and/or retinal hemorrhages and only in this group was steroid therapy routinely administered. In 117 of the mild or average cases, therapy consisted of restriction of activity and occasional transfusions. Twenty-four of the mild and average cases and all 11 of the severe cases were treated with corticosteroids, usually prednisone, 2 to 3 mg. per kg. per day. Except for one child admitted moribund and in deep coma, no instance of bleeding into the central nervous system was observed. Steroid therapy was not accompanied by more rapid return of platelet counts to normal, even among the mild cases, and chronicity was not significantly different in treated and untreated groups. Nine of 12 patients who developed chronic ITP underwent splenectomy. The only failures occurred in 2 youngsters in whom there had been no response to steroids.—J. B. S.


Studies of platelet adhesiveness were performed on 45 healthy young adults before and after a 50 mile walk. Platelet adhesiveness, measured in the presence of ADP or celite, was significantly reduced after the exercise in a majority of the subjects. There was no definite pattern of change in platelet counts after the exercise, but white cell counts increased to twice the normal value. The fall in platelet adhesiveness was considered to be due to a change in environment, rather than to an alteration in the platelets themselves.—A.L.B.
ABSTRACTS

abnormal response. The authors concluded that in thrombasthenia there is a defect in the binding of ADP to the platelet surface.—A. L. B.

PLATELET BEHAVIOR IN HEMORRHAGIC DISORDERS.

A study of platelet function in the course of congenital or acquired hemorrhagic diseases permitted the authors to confirm the fact that plasma fibrinogen contributes to platelet aggregation, while anti-hemophiliac factors are deprived of any role. Divergent results were found for Hageman factor. Thrombocyte anomalies have been noted rarely in von Willebrand’s disease and frequently in cases of isolated prolonged bleeding time. Thrombathenic platelets were but moderately aggregated by bovine fibrinogen; preincubation with ADP inhibited this effect. In some cases of paraproteinemia, a plasma factor inhibited platelet deaggregation. This activity appeared diminished in the plasma of subjects with chronic myeloid leukemia.—J. C.


In a series of patients with obstetric hypofibrinogenemia, those with abrupto placenta responded well to fibrinogen therapy without relapse and with no evidence of an anticoagulant in the thrombin-fibrinogen reaction. In these cases, fibrinogen depletion was attributed to intrauterine fibrinogen utilization with serum absorption, rather than to fibrinolysis or intravascular coagulation. In patients with proved or possible amniotic fluid embolus, there was evidence of increased clot lysis, an inhibitor of the thrombin-fibrinogen reaction or incomplete response to fibrinogen therapy. Erythropoiesis was thought to be a major factor causing the hemostatic defect in this group. Continuing intravascular coagulation was thought to be the cause of fibrinogen deficiency in one case of retained dead fetus. The clinical diagnosis may give a strong lead to the type of hematologic abnormality. This substantial paper contained a detailed discussion of the pathogenesis and diagnosis of obstetric hypofibrinogenemia.—A. L. B.

ERTHROCYTES

The effect of the source of donor tissue on erythropoiesis in regenerating spleens was studied by the injection of spleen or bone marrow cells into irradiated mice. Erythropoiesis was quantitated by measuring the splenic uptake of iron per unit weight of spleen. In 8–10 week old and 4–6 month old mice, spleens containing colonies derived from bone marrow tissue were found to be more active than those containing colonies derived from splenic tissue. In young mice, the erythropoietic activity of regenerating spleens containing either splenic or bone marrow tissue was greater than that of normal spleen. In older mice, only regenerating spleen containing bone marrow tissue had greater erythropoietic activity than that of normal spleen. The source of the donor hemopoietic tissue, therefore, influenced its subsequent initial activity in the irradiated host.—A. L. B.


In a 16 month old boy with the Imerslund syndrome, gastric juice contained IF and serum contained no IF antibodies. Schilling test without and with IF showed no B₁₂-absorption. Intestinal juice from the duodenum and jejunum (80 cm. distal to the pylorus) obtained during gall bladder operation did not induce absorption of radioactive vitamin B₁₂, but intestinal juice from about 1–1.5 M down the jejunum from two normal persons induced B₁₂-absorption. In this case, the cause of the specific B₁₂-malabsorption was probably lack of “releasing factor”.—S. A. K.


Two B₁₂-binding components were separated from hog intrinsic factor concentrate by recycling gel filtration and their molecular size was estimated. The larger component was antigenically similar to a B₁₂-binder in hog bile, while the smaller component resembled human intrinsic factor and reacted with sera from patients treated with hog IF. Only this smaller component had IF-activity, as determined by Schilling tests.—S.A.K.


The saliva of 4 healthy controls and 3 patients with pernicious anaemia was examined for antibody to intrinsic factor with ammonium sulfate precipitation and a complex of radioactive vitamin B₁₂ and intrinsic factor. Precipitable antibody, found in the saliva of one patient with pernicious anaemia, was shown to be IgA. Salivary antibody may neutralize intrinsic factor and thus accelerate the development of overt B₁₂ deficiency.—A.L.B.


Antibodies against B₁₂-binding components in human and hog IF preparations were studied by employing a precipitin reaction combined with autoradiography after diffusion in agar gel. Sera from 78 patients with pernicious anaemia (p.a.), 71 patients with other diseases and 116 healthy persons were studied. Antibodies against B₁₂-binders in human gastric juice were found in 9 p.a. sera, but not in other sera. Antibodies against B₁₂-binders in hog IF were found in 19 of 31 p.a. patients treated with hog IF orally, but only in one of 47 patients treated otherwise. Antibodies to hog IF were also found in non-p.a. patients, notably those who had been treated with hog IF, and in 7 of the healthy persons. It was concluded that the antibodies demonstrated were IF antibodies and that hog IF antibodies were to a great extent the result of immunization due to oral hog IF therapy, whereas antibodies against human IF were thought to be autoantibodies.—S. A. K.


Of 24 patients with megaloblastic anaemia of pregnancy, 6 had medical disorders predisposing to development of folate or vitamin B₁₂ deficiency and 6 had excessive bleeding associated with thrombocytopenia at the time of parturition. Serum folate concentrations were subnormal in 83 per cent of patients with megaloblastic anaemia, as well as in 26 per cent of a group of 50 non-anemic pregnant women. Microbiologic estimates of serum vitamin B₁₂ activity were subnormal in 71 per cent of patients with megaloblastic anaemia.
and in 46 per cent of non-anemic women. The finding that the binding capacity of serum proteins for B₁₂ was increased and that added ∆cob₃B₁₂ was bound by beta and not alpha-1 globulin in these subjects indicated that actual deficiency of vitamin B₁₂ was rare in pregnancy.—F. A. K.


Following an oral test dose of tritiated folic acid, plasma levels of radioactivity were below normal in a group of 10 alcoholics with recent exposure to alcohol, but were normal in 13 alcoholics who had abstained from alcohol for a week. The 24 hour urinary excretion of radioactivity was within the normal range in both groups. In 4 of 5 normal subjects, the acute ingestion of alcohol did not alter H₃PGA absorption. The authors considered that the saturating dose of 30 mg. folic acid given parenterally one-half hour before the absorption study was sufficient to preclude inadequate folate saturation as a cause for the subnormal results in the actively imbibing group and proposed that sustained alcohol ingestion resulted in malabsorption of crystalline folic acid.—F. A. K.


A method for determining the cobalt-binding capacity of serum with the aid of gel filtration on Sephadex D-50 resin was described. Cobalt-binding capacity was normal in iron-deficiency anemia and was reduced in infectious-toxic anemias, especially in anemias associated with neoplasms.—J. K.


A potpourri of data was presented to indicate that among females with sickle cell anemia, onset of menarche was delayed, dysmenorrhea was more frequent, fertility was decreased, first pregnancies were delayed, and fetal wastage and premature delivery were greater when compared to non-sicklemic negroes. In addition, low mean values for weight, height, span and ratio of upper to lower body segments were obtained among sicklemic youngsters. Occasional children with this disorder demonstrated hypogonadism or delay in development of secondary sex characteristics. Chemical determinations revealed a tendency to low serum alkaline phosphatase levels, low borderline urinary excretion of 17-ketosteroids and low serum folic acid levels in many of the undersized patients, none of whom demonstrated any hematologic evidence of folate deficiency.—J.B.S.


Observations on over 221 patients with sickle-cell anemia and its variants (SC, SD and S-thalassemia) included the multiple clinical manifestations, the results of laboratory examinations and roentgenotherapy, and the differential diagnosis. Peculiarities in the course of these diseases in patients of different age were described, as well as differences in the clinical picture of sickle-cell anemia according to the date of its description in various countries.—J. K.


Toads have no diaphragm or ribs and depend upon valves in the throat for lung inflation and deflation. The position of toads in the evolutionary scale makes them interesting forms for study of respiratory processes. The effects of three physicochemical factors (temperature, hydrogen ion concentration, partial pressure of oxygen) on the respiratory functions of blood have been studied. These functions conform to the pattern of respiratory mechanisms available for gas exchange between the environment and tissues.—O. P. J.

Serum haptoglobin content was determined in the blood of 31 children, aged 6 months to 14 years, with various forms of hemolytic anemia. The determination of haptoglobin was a sensitive test in the detection of hemolysis of any origin and the efficiency of therapy could be judged by the change in concentration.—J. K.


The incidence of G-6-PD deficiency, HgbS and HgbC was determined in the red cells of 100 Nigerian children suffering from severe falciparum malaria with parasite counts of 100,000 per mm.² or greater and in 200 control children. A significantly lower proportion of children with malaria had G-6-PD deficiency or HgbS, but the proportion of children with HgbC was similar in both groups. The results supported the hypothesis that inheritance of G-6-PD deficiency or HgbS protected against falciparum malaria, but HgbC offered no such advantage.—A. L. B.


A screening test for G-6-PD deficiency was carried out over a two year period on all severely jaundiced infants in whom there was no serologic evidence of blood group incompatibility. Twenty-two were found to have a deficiency which was confirmed by a number of more quantitative tests. Eight of the infants weighed less than 2,500 Gm. at birth or when first brought to medical attention. Fourteen were Colored, 4 were White, 2 were Asiatic and 1 was a Bantu. Blood smears in a number of instances showed reticulocytosis, while polychromatric red cells and normoblasts were also present. The level of unconjugated bilirubin, however, was raised in only 1 instance.—T. H. B.


The effect of ammonium chloride on cellular Na⁺, K⁺ and water were examined in human and horse (high K), cow (medium K) and cat (low K) red cells. The mechanism for movement of water and Na⁺ in high K cells remained unsolved, but the response of low K cells to ammonium chloride was similar to that of a cation exchange resin.—O. P. J.

MISCELLANEOUS


Complete or partial remission was obtained in 13 of 14 patients with generalized Hodgkin’s disease treated with Natulan. Four patients previously were untreated. Remissions lasted from one to more than 12 months. Cross-resistance with other cytostatic drugs was not noted. Results in reticulosarcomatosis and lymphosarcomatosis were much less encouraging. Generalized solid tumors responded poorly.—S. A. K.


A γ-globulin isolated from human plasma and containing 96.6 per cent 7 S component had no anticomplementary activity: 32 mg. of this protein had no effect on 50 units of hemolyzing guinea pig complement. The γ-globulin differed from γ-globulin in respect to the effect of 63 C heat; its behavior towards complement was not changed and it did not show the phenomenon of molecular aggregation.—J. C.
ABSTRACTS