ABSTRACTS

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ABSTRACTS

ABSTRACT OF SPECIAL INTEREST


Rats were placed in an atmosphere of 80 per cent nitrous oxide and 20 per cent oxygen for 6 days. After 6 days of exposure their peripheral white counts had fallen from the control level of 15,500 per cu. mm. to 1300 per cu. mm., and granulocytes had disappeared completely from the peripheral blood. In addition, the rats' bone marrows had become hypoplastic (though megakaryocytes seemed to be well-preserved) and consisted principally of plasma cells, stem cells, and degenerating forms. The mechanism of nitrous oxide toxicity for the bone marrow is not known. —T. E. B.


A patient with proved type III glycogen storage disease (characterized by deficiency of hepatic debranching enzyme) was found to have less than 5 per cent of normal debranching enzyme activity in her peripheral blood leukocytes. The patient's parents and one sibling, all of whom were clinically well, showed less than 50 per cent of normal leukocyte debranching enzyme activity suggesting that type III glycogen storage disease

LEUKOCYTES


By the use of DEAE cellulose column chromatography and also by the use of electrophoresis on starch gel or on cellulose acetate foils, the authors were able to demonstrate that normal human granulocytes contain five different proteins with LDH activity. Each LDH fraction behaved differently with regard to heat inactivation and reportedly also with regard to optimum substrate (pyruvate) concentration. The five protein fractions did not seem to be plasma proteins simply adsorbed on granulocytes, but they might conceivably have represented five different metabolic states of the same protein rather than five distinct proteins.—T. E. B.
has autosomal recessive type inheritance. Leukocyte debranching enzyme activity was found to be normal in four patients with glycogen storage disease of other types. Leukocytes can apparently be used for demonstrating the specific enzymatic defect in some kinds of glycogen storage disease. —T. E. B.

CONCENTRATION OF GALACTOSE BY LEUKOCYTES.

Leukocytes suspended in native plasma took up galactose and concentrated it to 3-6 times its plasma level. Conversion to galactose-1-phosphate, uridine diphosphogalactose, and other unidentified compounds occurred. The effects of insulin, iodoacetate, cyanide, and phloridzin on galactose uptake by leukocytes was studied.—T. E. B.


Incubation of normal human peripheral blood leukocytes with relatively high concentrations of $\beta$-mercaptopyruvate resulted in marked increases in leukocyte polyploidy, possibly because of inactivation of enzymes participating in the production of a functional spindle. $\beta$-mercaptopyruvate occurs physiologically in man, being a degradation product of cysteine. It is conceivable that under certain circumstances $\beta$-mercaptopyruvate might contribute to the development of polyploidy in vivo.—T. E. B.


The number, distribution, and the histologic and histochemical characteristics of macrophages in lymph nodes and spleens in germfree and conventional mice did not differ. Reaction centers and immunologically competent cells, however, were much less frequent in lymph nodes and spleens from germfree animals than in comparable tissues from conventional mice.—T. E. B.


A 15 year old girl taking propylthiouracil developed a chronic systemic illness compatible with a hypersensitivity response to the propylthiouracil. When blood smears from many subjects including the patient were exposed to the patient's serum and then to fluorescein-labeled antihuman globulin, intense fluorescent staining of the cytoplasm of the polymorphonuclear leukocytes resulted. The patient's serum had been obtained several weeks after propylthiouracil had been discontinued, and incubation of the patient's serum with propylthiouracil did not alter the intensity of fluorescent staining observed. The patient's serum was found to agglutinate normal leukocytes but not her own. It is suspected that antibodies against leukocytes have some relation to the patient's fever, arthritis, leukopenia, hyperglobulinemia, splenomegaly, and skin ulcerations. Over several months, after discontinuing propylthiouracil, she seemed to recover almost completely.—T. E. B.


A mild case of serum sickness following an injection of equine tetanus antitoxin is reported. During the illness there was a plasmacytosis amounting to 30 per cent of the white cells in the peripheral blood. Three months after the illness, a skin test with equine serum produced an intense local reaction and the reappearance of plasmacytosis.—T. E. B.


Seven patients with myeloma were studied. The mean values of serum lipids were below normal in nine cases of $\gamma$-myeloma and in one case of $\beta$-myeloma. In two out of three cases of $\alpha$-2-myeloma, high levels of cholesterol, phospholipids and total esterified fatty acids were found. In another case of $\alpha$-2-myeloma, a decrease of serum cholesterol and total lipids was observed. No modifications of serum lipids were found in two cases of myeloma without dysproteinemia.—P. d. N.

Thirty cases were treated. In 18 cases the drug proved to be effective. Size of lymph nodes, spleen and liver, radiologic patterns, subjective manifestations, temperature, sedimentation rate, total proteins and electrophoretic patterns were taken into consideration. Marked reduction of lymph nodes and liver infiltrates was observed. In three of four cases with bone involvement, radiologic improvement was observed. Fever was sensitive to treatment, as were sedimentation rate and general condition. Leukopenia, thrombocytopenia and nervous complications are mentioned among side effects.—P. d. N.


In the German Democratic Republic, 3646 cases of leukemia were reported in the years 1953–1957. The morbidity rate has shown a continuous increase, attaining 911 in the year 1957. Among these, 40 per cent were cases of chronic lymphatic leukemia, 33 per cent acute lymphatic leukemia and 27 per cent chronic myeloid leukemia. Eighty-five per cent of all chronic lymphoid leukemias occurred in patients past 50 years of age. The incidence of acute cases showed a sharp increase until the age of 70 with a remarkable sex difference (males 69 per cent, females 31 per cent). Data concerning the uneven geographical distribution of the various forms of leukemia are presented. In the future, increased attention should be paid to the progressive increase of leukemia in cattle, its uneven geographical distribution and its correlation especially to chronic human lymphoid leukemia.—S. R. H.


After a survey of some theoretical questions concerning extramedullary hematopoiesis, a case of chronic myelosis treated for 3 years is presented. Blood and sternal marrow smears were characteristic of chronic myelosis, and an enlarged cervical lymph node showed distinct myeloblastic metaplasia. This finding supports the hypothesis of the extramedullary origin of pathologic myeloblasts. The importance of lymph node biopsy as a prognostic aid is emphasized.—S. R. H.


Chromosome analyses were performed on nine children with chronic granulocytic leukemia. The five older children with a clinical course similar to that seen in adults demonstrated the presence of the Ph1 chromosome. The four infants whose clinical course, laboratory findings, and response to therapy were more like acute than chronic leukemia did not show the abnormal chromosome. In two of the infants, as well as in one of the older children, a high degree of aneuploidy, primarily of 47 modal number was found, the extra chromosome in these patients being a minute element.—J. B. S.


During his 2nd week of life, a boy with mongolism was unaccountably found to have hepatosplenomegaly, 28 per cent myeloblasts on peripheral leukocyte differential, and 57 per cent myeloblasts in the bone marrow. It was reasonably concluded that he had acute congenital granulocytic leukemia. He was given busulfan 1–2 mg. daily for 2 weeks, but hepatosplenomegaly persisted, and myeloblasts remained present in the peripheral blood. He received no further specific anti-leukemia treatment at any time. Following a staphylococcal pneumonia at age 2 months, all abnormal findings gradually disappeared, so that by age 5 months there was no evidence of leukemia in the blood, and the bone marrow aspirate revealed a normal differential. Blood and marrow examinations at age 3 years were normal except for mild anemia. The patient died suddenly of an aspiration pneumonia at the age of 3 years and 9 months. At postmortem examination there was no evidence of leukemia. It is suggested that the patient never had acute leukemia, and that in mongolism there may be a defect in the regulation of white cell multiplication and maturation such that a picture resembling acute leukemia may appear in response to minor noxious stimuli.—T. E. B.

A Comparison of Leukocyte Alkaline Phosphatase Determinations in 200 Patients

Patients with mongolism (trisomic for the No. 21 chromosome) were found to have an increased leukocyte alkaline phosphatase activity on stained blood films. Patients with chronic myelocytic leukemia regularly show decreased leukocyte alkaline phosphatase activity and an abnormally small No. 21 chromosome. It is suggested that one of the genetic loci controlling leukocyte alkaline phosphate activity may be present on the No. 21 chromosome.—T. E. B.


The authors studied the scattered total leukocyte counts obtained on the people of Hiroshima and Nagasaki during the first 9 weeks following the atomic bombing. It is noted that there was a good correlation between death and depression of the leukocyte count obtained during the 3rd to 5th week after radiation exposure. The total leukocyte count is probably a simple and effective means of estimating the biologic injury sustained by a person after a given radiation exposure. The chance of spontaneous survival seemed remote in individuals whose total white blood cell count was less than 1000 per mm.3 in the 3rd and 4th weeks after radiation exposure. Treatment with antimicrobials, fresh whole blood transfusions, and platelet transfusions can probably markedly reduce the mortality of persons with severe radiation injury. It is suggested that electronic methods of counting leukocytes should be made available to assist in casualty sorting and direction of therapy in case of atomic disaster.—T. E. B.


Normal leukocytes in vitro are able to transaminate and decarboxylate the three branched-chain amino acids (leucine, isoleucine, and valine). It has been suspected that the basic defect in maple syrup urine disease is a deficiency in oxidative decarboxylation of the ketoacids of the branched-chain amino acids. The authors incubated leukocytes from maple syrup urine disease patients with branched-chain amino acids tagged with radiocarbon. They showed that such leukocytes could transaminate the three amino acids, but oxidative decarboxylation was greatly reduced or absent. Investigation of the leukocytes may provide the earliest as well as the most specific approach to the diagnosis of maple syrup urine disease.—T. E. B.

ERYTHROCYTES


The nervous regulation of the blood cell system is a proved fact resting on definite morphologic bases. The means and ways of regulation are, however, mostly unknown. An important role is assigned to the diencephalon, the vegetative and spinal nerves, as well as to various neurohumoral and humoral factors. On a higher level the blood cell regulatory functions of these structures are integrated by the cerebral cortex. Interceptive stimuli starting from internal organs decisively influence the function of the blood cell system. On the other hand, afferent stimuli starting from the blood cell system exert a continuous influence in the diencephalon, on the cerebral cortex and through this on the functions of the entire organism. The greatest shortcoming of experimental and clinical research work carried out so far is that no attention has been paid to the fact that nervous regulation exerts its effect primarily through a modification of metabolic processes. It is wrong to limit the investigations to the final effects of nervous impulses, i.e., to the qualitative and quantitative changes of the blood cells. The connecting link—i.e., the cellular metabolic processes occurring on the effect of nervous stimuli and the consequential changes in blood cells—should be investigated simultaneously under both physiologic and pathologic conditions.—S. R. H.


Hemoglobin and packed cell volume measurements were carried out on several hundred pregnant females at various stages of pregnancy. The
median hemoglobin level was 12.0 Gm./100 ml.
early in pregnancy, 10.6 Gm./100 ml. at the 24th
week and 11.5 Gm./100 ml. near term. Approximately 22 per cent of these subjects had a hemoglobin level below 10 Gm./100 ml. and the MCHC was less than 30 per cent in about one-third of those with low hemoglobin values. The hematologic values found in the study did not appear to be influenced by the number of previous pregnancies or by the different ethnic origins of the subjects.—T. H. B.


The solvent partition method for separating the three major fractions of serum bilirubin was investigated in a large series of infants and children. The author found the method simple and reproducible. There was no evidence of significant monoglucuronide production in jaundiced infants. No difference in the proportions of the three fractions was evident regardless of the birth weight, presence of anoxia, or level of hyperbilirubinemia. Although the author states that the method is valuable, it is unclear from her results why this should be so.—J. B. S.


A nomogram has been constructed from which the per cent exchange can be predicted when the recipient’s blood volume and the amount of donor blood administered are known. The nomogram is designed primarily for use in evaluating exchange transfusions being performed on patients undergoing treatment for some form of intoxication.—T. H. B.


“Autoantibody” against gastric intrinsic factor, characterized by its ability to reduce the power of normal human gastric juice to facilitate absorption of vitamin B₁₂, reduces the vitamin B₁₂ binding capacity (B₁₂ BC) of normal human gastric juice. Using the reduction of B₁₂ BC as an assay for “autoantibody,” it was found in 33 of 100 sera from patients with pernicious anemia and none of 55 control sera. The authors confirm the y-globulin nature of the “autoantibody,” indicated in other studies such as those of Jeffries and Sleisenger (J. Clin. Invest. 42:442, 1963). In a later study, the authors report use of the “autoantibody” to assay human intrinsic factor (Biochim. et biophys. acta 71:227, 1963).—V. H.


Serial measurements of the serum vitamin B₁₂ level were made in a group of patients with megaloblastic anemia, before and after therapy with folic acid. In 17 subjects, gastric hydrochloric acid was present and vitamin A absorption was normal. Sixteen showed a rise in the vitamin B₁₂ level of more than 100 μg./ml. on folic acid treatment. This rise usually started between 1 and 10 days after therapy. In contrast the level rose only slightly or not at all in eight patients with achlorhydria. The difference between the two groups could not be explained on the initial B₁₂ levels, since these were all 100 μg./ml. or less, nor did it correlate with the presence or absence of intrinsic factor. In further studies no rise in the serum B₁₂ level was observed in two patients with fat malabsorption, but a significant rise occurred in three of six patients with iron deficiency anemia. It is suggested that these various results indicate that folic acid therapy either increased the absorption of B₁₂ from the gut or facilitated its release from tissues in a proportion of the subjects studied.—T. H. B.


There should be an interval of 120 minutes between the ingestion of an iron compound and the next meal. If the interval is 180 minutes, the absorption of iron reaches its maximum, and iron resorption from food is substantially higher than otherwise. The absorption of an iron compound taken during or after meals is practically negligible.—S. R. H.

Clinical Data on the Mechanism of the Development of Transfusion Hemosiderosis.

Idiopathic hemochromatosis and transfusion hemosiderosis are characterized by identical signs and symptoms. One or another of the symptoms may often be absent, but the histologic pattern is essentially similar. Animal experiments indicate that hepatic damage may play a decisive role in the development of hemochromatosis. The authors present a case of severe aplastic anemia originating from lymphadenitis tuberculosis disseminata. The patient was treated with whole blood transfusions for 18 months, when she contracted a homologous serum hepatitis. Further series of transfusions elicited hemochromatosis with bronze diabetes.—S. R. H.


Plasma iron turnover and incorporation of iron into erythrocytes by means of Fe59 were studied. In two cases iron turnover was normal (one acute and one chronic case); in another case (chronic) it was increased. The incorporation of Fe59 into erythrocytes was very low in all cases.—F. d. N.


The authors present the results of plasma Fe59 turnover and Cr51 red cell survival in one patient with chronic hemolytic anemia, autoimmune type. There was a functional deficiency of the bone marrow, with a blockage of iron incorporation into the erythroblastic cells. This defect was corrected by administration of corticosteroids.—M. J.


A girl with hemolytic anemia, intraerythrocytic Heinz bodies, and slow-moving hemoglobin is described. Her clinical and hematologic findings resemble closely those of the inclusion body anemia reported by Scott et al. Chemical studies by the use of electrophoresis, chromatography, hybridization test, fingerprinting, and p-chloromercuribenzoic acid titration of SH group reveal that this abnormal hemoglobin is a hemoglobin of β chain anomaly with blocked Cys (β 93) SH group. The hemoglobin is therefore expressed by the formula a2β 93(SX), and it is adequately labile to form large Heinz bodies in erythrocytes. The authors presume that some unknown congenital enzymatic defect in erythrocytes will be responsible for the production of this abnormal hemoglobin.—K. F.


The propositus had hemolytic anemia with increased fetal hemoglobin. One brother had hemoglobin D and in another there was combined Th-D. This last patient had chronic anemia and a malabsorption syndrome due to regional ileitis.—M. J.


Four cases are described (two unrelated couples of brothers from the area of Naples). Three patients were splenectomized, and exhibited after operation a marked erythroblastosis. Differential diagnosis from Cooley’s disease and thalassemia minor is outlined. The possible genetic interrelations between the microcythemic trait and the high Hb F level is discussed.—P. d. N.


113I-Triiodothyronine incorporation by erythrocytes of patients with polycythemia is increased. According to studies made by the authors this is due to an increased erythrocyte mass and not to functional disorders of the erythrocytes. The relation between the evaluation of the test and the hemocrit value is discussed in detail. The 113I-triiodothyronine incorporation into the erythrocytes of a patient with hemolytic anemia and glucose-6-phosphate dehydrogenase deficiency is increased.—S. R. H.
HEMOSTASIS


In previous investigations authors have found that Chinosol has an inhibitory effect on the thrombin inactivating system producing increased thrombin stability. Quinine also has the same effect. Both Chinosol and quinine increase the quantity of thrombin produced in the course of coagulation. In normal blood, this effect will result in an overproduction of thrombin; in hemophilic blood it will increase the quantity of thrombin produced, but it will not entirely normalize the rate of production. Tachostyptan speeds up the production of thrombin, without, however, essentially increasing the quantity of thrombin produced. A combined application of the two drugs—Chinosol and Tachostyptan—increases both the quantity and the rate of thrombin production. This effect is similar to that of antihemophilic globulin. The in vitro effect of Chinosol and Tachostyptan was confirmed by rabbit experiments.—S. R. H.


Partial thromboplastin time (PTT) determinations were used because of their simplicity, specificity and their suitability for quantitative estimation. The basic requirement for this purpose is the separation of the most adequate partial thromboplastin. Therefore, eight substances known and assumed to have such properties were used in the investigations. Comparing their characteristics, chloroformic cephalin extract and RBC hemolysate were satisfactory partial thromboplastins whereas the lyophilized hemolysate gave best results.—S. R. H.


Case report of a 31 year old patient: No modifications of factors V and VII were detected; no effect of vitamin K₁ (100 mg.); hemorrhagic symptoms since the age of 18 months, with joint involvement; prothrombin deficiency in other members of the family was of lesser degree.—P. d. N.


In cases of polycythemia vera, the hypocirculatory state, sequential to increased blood volume and viscosity, plays a decisive role in the development of coagulation disturbances. Another cause of the coagulation disturbance is a relative lack of fibrinogen. Increased fibrinolysis, as well as other unknown factors, may also play a role. In reactive polyglobulia there is a relative lack of fibrinogen. This ceases as soon as the normal blood volume is restored as a result of P₃₂ treatment.—S. R. H.


In 35 newborn infants, fibrinolytic activity was determined in cord blood and within 4 days after birth according to the method of Sgouris et al. Free fibrinolytic activity was below 0.10 casein units, as in the mother and in older subjects. Available fibrinolytic activity was decreased as compared with mother and older subjects (0.30 ± 0.14 in cord blood and 0.23 ± 0.10 in venous blood). Total fibrinolytic activity was also decreased (0.96 ± 0.29 and 1.13 ± 0.26). The values for the mother and for older subjects were as follows: 0.84 ± 0.44 and 0.60 ± 0.22 for the available fibrinolytic activity, and 3.02 ± 0.62 and 2.30 ± 0.62 for total fibrinolytic activity. —P. d. N.


In 40 premature newborns, fibrinolytic activity was determined in cord blood and after 24 hours and 3 and 10 days respectively according to the method of Sgouris et al. Thirty-five full-term newborns were taken as controls. Free fibrinolytic activity was below 0.10 casein units, as in full-term newborns. The same is true for the available fibrinolytic activity (0.30 ± 0.13 casein units). Total fibrinolytic activity was decreased (1.13 ± 0.26). These results suggested diminution of plasminogen in premature newborns.—P. d. N.

THROMBOPHILIA AND ALIMENTARY LIPIDS. PHYSIOLOGIC PATHOLOGIC AND THERAPEUTIC STUDY. P. Introzzi and P. de Nicola. From the Clinica Medica,
the University, Pavia, Italy. Clin. terap. 22:197–
223, 1962.

A review of the literature and discussion of personal experiments. The following points were particularly outlined: (1) increase of blood coagulability, decrease of fibrinolytic activity and increase of erythrocytic aggregation in circulating blood following fat intake; (2) more marked intensity of these findings in arteriosclerotic subjects; (3) differences between vegetable and animal fats and between unsaturated and saturated fats; (4) effectiveness of preventive measures, as administration of essential fatty acids associated to phosphorylcholine.—P. d. N.

SOME BIOCHEMICAL AND BLOOD COAGULATION DATA IN A CASE OF GLANZMANN-NAEGELI THROMBOPATHY. M. Berni Canani, M. Miraglia and M. Scala. From the Clinica Pediatrica, the University, Naples, Italy. Pediatria 70:1095–1104, 1962.

In a 3-year-old girl with Glanzmann-Naegeli thrombopathy, no modifications of platelet factors 3 and 4 were detected, but a marked deficiency of AlP and ATP-ase (Ca++-dependent) was observed.—P. d. N.

CASE OF ACUTE, SECONDARY THROMBOCYTOPENIC PURPURA DUE TO SULPHAMETOXYPYRAZINE. F. De Rosa. From the University, Naples, Italy. Riforma med. 76:1407–1410. 1963.

A case report in a 28 year old man.—P. d. N.

MISCELLANEOUS


In about one-fifth of all mothers, rapid cessation of lactation gives rise to the formation of passively hemagglutinating and complement-binding autoantibodies against the antigens in human milk.—H. H. F.


The authors have found leukocyte and thrombocyte antibodies in 23 and 14 per cent of polytransfused patients respectively. Antibody formation showed significant correlations with the number of transfusions, but it was found to be influenced also by sex and the underlying disease.—S. R. H.


Two subjects with malignant blood diseases were studied by means of the direct incubation technic with colchicine. Multiple chromosomal abnormalities in ascitic cells of a subject with reticuloendotheliosis in the final stage and a number of polyploid mitoses containing the “Philadelphia chromosome” in the pleural effusion of a patient with chronic myeloid leukemia were found.—P. d. N.


The author developed a method of evaluation of electrophoretograms without any dyeing, thus eliminating the errors originating from the use of various dyes; the proteins can be evaluated directly on the basis of their ultraviolet absorption. Another advantage of this method is that the spectra of the proteins can be directly made on the paper strip without any isolation. This method can be used to determine not only proteins but also any other serum components on the same running strip.—S. R. H.

CONFERENCE ON AUTOIMMUNITY

A conference on Autoimmunity under the auspices of the New York Academy of Sciences and the Chairmanship of Drs. William Dameshek and Ernest Witebsky will be held in New York on February 3 to February 5, 1964. The three-day, eight-session program is a comprehensive one and will present papers and discussions by world-wide leaders in the field. Those wishing to participate should write to Dr. Felix Milgrom, State University of New York at Buffalo, Sherman Hall, The Circle, Buffalo 14, New York.