ABSTRACTS

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ABSTRACTS OF SPECIAL INTEREST


Trypan blue was injected into rats blinded 3 days after birth by enucleation of the eye, to provoke proliferation of the reticulohistiocytic system (RHS). In normal rats, proliferation was in the lymph nodes, the liver and the spleen; in the blinded animals, there was a non-coordinated reaction. In most of the nodes, the RHS reaction was slight. Only in the spleen were the intensity and character of changes the same as in the control group. From these experiments it appears that the hypothalamic vegetative centers are a component of the regulatory mechanism coordinating the RHS response to exogenous influence.—L. D.


Heretofore, an abnormally small chromosome, Ph1, has been observed only in cells after short-term cultures of leukocytes and bone marrow from patients with chronic granulocytic leukemia. It is, therefore, important to remove any possibility that the abnormality may be due to an artefact as a result of in vitro technic or any other treatment of the cells. In order to investigate this possibility, the author used blood and marrow from a patient with an unusually high white count, 510,000/mm.³, and a leuko-erythroblastic ratio of 22:1. A heparinized sample of blood was centrifuged at 80 g; the leukocytes were removed, washed in Hank’s saline, placed in hypotonic saline at 37 C. for 10 minutes and fixed. The sternal marrow specimen was aspirated into a warm hypotonic saline immediately. The cells were fixed in acetic alcohol, spread by air-drying, and stained with May-Grünwald-Giemsa. No attempt was made to culture the cells or to treat them with colchicine. The results of the chromosome counts showed a normal model number of 46 and a high frequency of the Ph1 chromosome in both leukocytes and marrow cells. This finding of the Ph1 chromosome in cells which were not cultured or treated with colchicine, from a patient who had received no therapy, can leave little doubt that the chromosome abnormality is present in vivo.—O. P. J.

THE TRANSFER OF SERUM PROTEINS FROM MOTHER TO YOUNG IN THE GUINEA FIG. I. PRENATAL RATES AND ROUTES. II. HISTOCHEMISTRY OF
Erythrocytes


The blood of an Australian aborigine previously described as lacking all antigens of the Rh system (Vos et al.: Lancet 1:14, 1961) has been further studied. This blood was totally ineffective in absorbing “anti-D like” reagents. Eluates failed to yield “D-like” material and immunization of guinea pigs failed to give an “anti-D like” response.—I. C.


An anterythrocyte antibody with a new specificity has been identified in a patient, Mrs. Au., who had received multiple transfusions, and whose serum also contained anti-E, anti-K, anti-Fy
antibodies, as well as antileukocyte and antiplatelet agglutinins. This new antibody, detectable by indirect Coombs’ test, shows an Au
antigen is transmitted by a gene capable of expressing itself in a single dose, with a frequency of 0.578, inherited independently of the ABO, MNs, P, Rh, Duffy and Kidd systems. No genetic association has been found between Au and the other blood systems. It is therefore likely that a new blood group system has been identified: the Auberger system.—H. F.


The content of glutathione was determined by three methods in erythrocytes, thrombocytes and leukocytes isolated from the blood of healthy human subjects. Erythrocytes and thrombocytes contained approximately 1.5 mM. of glutathione per Gm. of packed cells, and leukocytes had over five times more. After incubation of the blood cells, suspensions with cysteine, glutamic acid and (2-C
glycine, the labeled glutathione was found in erythrocytes, thrombocytes and leukocytes. The experimental data indicated that two reactions occurred: exchange of glycine and synthesis of glutathione de novo. The turnover of glutathione was particularly active in thrombocytes.—E. K.


Needle electrodes were implanted in the hypothalamic region of 28 adult rabbits, and the ani-
mals were stimulated for about 4 hours daily during 14 days. In eight rabbits a marked reticulo-cytosis and a significant increase in the red cell mass were observed. In ten animals the response was doubtful, and in ten rabbits there was no effect.—C. W.


The hypothalamic region of rabbits was electrically stimulated. The plasma of rabbits reacting with increased red cell mass and reticulo-cytosis was found to contain increased amounts of erythropoietin studied by means of intact as well as polycythemic mice.—C. W.


The serum haptoglobin level was studied by the method of Jayle. No haptoglobin was found in fetal or unbilical cord blood, nor in the majority of newborn, premature, and full-term infants. The haptoglobin levels tend to increase gradually during the first months of life, and after 8 months most infants show levels of more than 30 mg. per 100 ml. serum.—C. W.


A father and daughter exhibiting hemoglobin M disease are described. Spectroscopic analysis of the hemolysates did not reveal any abnormalities. An abnormal spectrum was demonstrated after conversion of the hemoglobin to met-Hb. The typical normal met-Hb peak at 630 was absent. On starch block and agar gel electrophoresis, the hemolysates separated into two fractions. The abnormal pigment comprised 30 per cent of the total. Spectral analysis of the normal and M fractions demonstrated definite differences between them. On starch gel electrophoresis the A2 fraction also contained brown pigmentation, which implies that the mutation is in the α-chain. There was a partial clinical response to ascorbic acid. —B. R.


The amino-acid composition and the products of tryptic digestion of a sample of fetal hemoglobin isolated from a Negro with the persistent fetal hemoglobin syndrome proved to be the same as fetal hemoglobin obtained from cord blood. It is concluded that the results do not favor the hypothesis of a “persistent F gene” but rather a failure to produce functional β-chains.—I. C.


A high incidence of the thalassemia gene was found in a survey of two coastal areas in Papuan New Guinea. Five women from one of these areas had thalassemia minor or intermedia and presented with megaloblastic anaemia of pregnancy, as did another patient with hemoglobin H-thalassemia from another district. The author considers the thalassemia a possible factor predisposing to the onset of megaloblastic anaemia of pregnancy in the absence of primary folic acid deficiency, of which there was no evidence.—F. W. G.


Cyanocobalamin in small quantities (1 μg. or less) can be converted to hydroxycobalamin by exposure to direct sunshine for 4 hours or to dull daylight for 8 hours. Ordinary glass tubes were used as containers. An acid pH is recommended. —I. C.


In a series of 73 patients with primary hypothyroidism, achlorhydria was found in 24, low serum vitamin B12 levels in 16 and a megaloblastic anaemia in 9. The low B12 level was shown to be due to loss of intrinsic factor. The authors suggest a common factor tending to produce destruction of both the thyroid gland and gastric mucosa.—I. C.

Following oral doses of 20 Gm. of histidine, abnormal amounts of formiminoglutamic acid appeared in the urine in 11 of 18 patients with vitamin B₁₂ deficiency. Three patients were still excreting abnormal amounts after 9, 16 and 24 weeks of B₁₂ therapy although they had had good hematologic responses. Folic acid alone was found to be ineffective in abolishing abnormal formiminoglutamic acid excretion in B₁₂ deficiency. The authors conclude that the enzyme formimino transferase is impaired in vitamin B₁₂ deficiency and that tetrahydrofolic acid as such is not required for hemopoesis.—I. C.


The urine passed in the 6 hours following an oral dose of 20 Gm. of histidine was tested for the presence of formiminoglutamic acid, using an electrophoretic method. The result was abnormal in almost all patients with idiopathic steatorrhea but was often normal in patients with post-gastrectomy steatorrhea and Crohn’s disease. —I. C.


The pteridine ring forms part of the folic acid molecule as well as taking part in phenylalanine-tyrosine conversions. A substance which was tentatively identified as a pteridine was isolated from the urine of a child who died within 6 days of the onset of an illness of uncertain nature.—I. C.


Clinical assessment of blood loss was unreliable. The most reliable index was an interference with normal activity due to difficulty in containing the loss. Blood loss in patients described as normal varied from 21 ml. to 495 ml.—I. C.

SERUM IRON AND COPPER IN ANEMIAS. H. Dabski. From the Medical School, Lublin, Poland. Polski tygodnik lęk. 17:8, 1962.

Serum iron and copper were studied in 200 cases of various anemias. Attention is drawn to the decreased serum iron and increased copper level in patients with neoplastic disease. In patients with hypochromic anemia, serum copper is normal and iron is decreased. Simultaneous determination of both those metals may be helpful in differential diagnosis of anemia caused by bleeding stomach cancer or ulcer.—E. K.


Transferrin levels after oral administration of iron was studied in 40 cases of anemia. Control levels were estimated twice at 3-hour intervals when fasting to eliminate spontaneous fluctuations, then in the same patients when fasting and 3 hours after oral administration of 1 Gm. of glucose. Finally, transferrin was estimated when fasting and 3 hours after oral administration of 4 tablets of ferrous sulphate. It was suggested that iron administration mobilized transferrin stored in the liver. This is consistent with the Muirhead thesis, that transferrin is present in two forms, circulating and stored, the latter available when needed. —E. K.


In a typical case of sideroblastic anemia, large amounts of hemosiderin were found in the liver as well as in the bone marrow. The patient had mild diabetes, and it is concluded that there probably was generalized hemosiderosis in this case. After a histidine load, the excretion of formiminoglutamic acid was well above normal, but was reduced to normal levels after treatment with folic acid. The serum B₁₂ was normal. —C. W.

THE RELATION OF PORPHYRIA CUTANEA TARDA TO NEOPLASM FORMATION. J. Berman and A. Braun. From the University, Prague, Czechoslovakia. Vnitř. lék. 8:152-154, 1962.

Autopsy findings in 26 cases of porphyria cutanea tarda were compared to those in 20,000 unselected autopsies. It was found that liver
STUDIES ON THE ANEMIA OF CANCER. D. Lockner.

Twenty-seven patients with cervical cancer were compared to 14 controls. The hemoglobin concentration was only slightly decreased in the cancer patients, but their plasma iron clearance was accelerated by 40 per cent, plasma volume increased by 15 per cent, and apparent Cr51-erythrocyte half-life decreased by 20 per cent. Plasma iron clearance and plasma volume were more abnormal in cases with cancer in situ than in patients with epithelial metastasis only. Plasma iron clearance was slower at night than in the morning. A decrease after 20 days in the specific activity of hemoglobin labeled by the injection of Cr51-lysine suggests a short-lived erythrocyte population in one cancer patient. Studies of rats with cancer agree with the human studies, but also suggest an increased uptake of iron by the RE system in enlarged spleen and liver.—P. G. R.

STUDIES ON AVIAN ERYTHROLEUKEMIA. J. Pontén.

In 12 experiments on about 200 chicks inoculated with different doses of chicken erythroleukosis virus, the morphology of the leukemia cells and the course of the disease were studied. After low virus doses, survival was longer, erythroblasts of all degrees of maturity were encountered, the clinical picture varied, and some animals recovered. After high doses, rapid death, only immature cells, and a uniform clinical picture without recoveries were seen.—P. G. R.

LEUKOCYTES


Although the ultrastructure of lymphocytes and monocytes from the peripheral blood has been described, the lymph nodes themselves have received little attention. Many problems remain which merit continued study. With respect to reticular cells, these include determination of the different types of cells, their developmental interrelationships, their relationship to fibers and their structural participation in phagocytic activity. In regard to lymphocytes, the ultrastructural modifications occurring during development of mature forms are not fully known. The origin of plasma cells remains under debate and their fate has not been fully revealed. In order to answer some of these questions, the author used female Sprague-Dawley rats of about 200 Gm. body weight. Electron microscope studies emphasized the cellular interrelationship. Reticular cells were divided into three types. The development of lymphoblasts from nondifferentiated reticular cells was characterized by augmentation of cytoplasmic volume, expansion of endoplasmic reticulum, increase in the number of ribosomes, and development in the structure of mitochondria and of the Golgi apparatus. In the development of lymphoblasts to mature lymphocytes, all of these trends were reversed except for changes in the nucleus.—O. P. J.


Current information about the life span of the lymphocyte has led to a hypothesis that there are two populations of lymphocytes, one long-lived and the other short-lived. The diffusion chamber technic allows the investigator to grow cells of one animal species in the peritoneal cavity of another animal species. The peritoneal fluid of the host enters the chamber through fluid-permeable, but cell-impermeable, cellulose membrane filters and provides the metabolites needed for the growth or survival of cells contained in the chambers. In the experiments reported here, rabbit cells from thoracic duct lymph were grown in diffusion chambers placed in the peritoneal cavity of CAF, female mice by laparotomy. Of the 15 chambers that were put into mice, only two were allowed to stay in the animal for 200 days. One of the chambers opened at 200 days had an initial inoculum of 0.5 x 10⁶ cells. Only one small lymphocyte was seen in the fluid of the chamber, and no cells were attached to the center Millipore filter. In the second chamber (initial inoculum, 3.6 x 10⁶ cells) there was a small, loose, fibrous clot, part of which was examined by phase micro-
scopv. Many living lymphocytes were seen associated with the clot and many were observed floating free in the fluid. It was estimated that the cell number was in the order of 5 to 10 thousand. Since mitoses were not observed after 14 days, the presence of a long-lived component in this lymphocyte population was indicated.

—O. P. J.

PROLIFERATION OF THE RETICULO-HISTIOCYTIC SYSTEM IN RATS, PRODUCED BY TRYPAN BLUE. V. Bilek. From the University, Brno Czechoslovakia. Scripta med. 34:169-182, 1962.

Wistar rats and a local strain twice weekly were given a 0.33 per cent solution of trypan blue intraperitoneally. About 84 total mg. of dye were injected in 28 doses. Some of these animals were killed immediately after the injections; the remainder were allowed a period of 100 days without treatment. In all injected animals there were proliferative changes in certain organs, suggesting reactive reticulosis. Early changes were irreversible and were progressive even in the absence of further drug administration.—L. D.


In a series of 75 splenectomies, pneumococcal or meningococcal septicemia was found in four patients, and was fatal in two of these. One of these cases had hereditary spherocytosis and the other three had idiopathic thrombocytopenic purpura. The authors suggest that the risk of infection is greatest if splenectomy is performed within the first 2 years of life.—I. C.


The relationship between the nucleus and cytoplasm offers the cytologist one of his most exciting problems. It is now generally agreed that cytoplasmic inheritance plays a much more important role than was thought probable 20 years ago. During the course of studying nucleolar fusion in the newt heart interphase cells, the author noted the occasional presence of eosinophilic granular leukocytes. The first few cells selected for microbeam irradiation of the cytoplasm showed such dramatic results that further experimentation was prompted. For this purpose, tissue cultures rich in granular leukocytes were made from the newt peritoneal capsule. Ultraviolet microbeam irradiation of the granular cytoplasm of newt eosinophils resulted in nuclear pyknosis; the reasons for such a dramatic effect upon the nucleus are not clearly understood. Ultraviolet microbeam irradiation probably converted some normal constituent of the granular cytoplasm into a toxic intracellular substance analogous to the "spindle-poison" postulated by Zirkle. Granules in the irradiated area were presumably disrupted because they eventually were not seen with phase microscopy. The breakdown products from these granules may have produced the nuclear changes.—O. P. J.

LEUKERY IN ALLERGIC REACTIONS TO DRUGS. A. Kasperlik. From the Bielany Hospital, Poland. Polski tygodnik lek. 17:45, 1962.

Allergic reactions to various drugs given by mouth or parenterally, were subjected to leukocyte studies, and leukergy was observed in the first few hours after the allergic signs had appeared. It persisted for 3-5 days. The agglutination involved 15-50 per cent of all white cells. Leukergy was observed for longer periods in diabetic patients who were given insulin at the same time.—E. K.


The pedigrees of two unrelated families are presented. Pelger nuclei were found in one family in three, in the other in four generations. In the latter, the apparent deviation from Mendelian law as to the ratio of Pelger and non-Pelger nuclei, is explained by the death of five family members in early childhood. Attention is drawn to the coexistence of the Pelger-Huet phenomenon and the typhoid fever hemogram.—E. K.


131I-labeled human serum albumin is taken up by Ehrlich ascites tumor cells in vitro, but not in vivo. Membrane activity confined to dying cells is believed to be the explanation.—P. G. R.

SELECTIVE UPTAKE OF SPECIFICALLY BOUND COBALT58 VITAMIN B12 BY HUMAN AND MOUSE
ABSTRACTS


Ehrlich ascites tumor- and HeLa cells took up 20 times more of the CO$^{15}$ B$_{12}$ that was bound to mouse ascites fluid or mouse or human serum, than of free or intrinsic factor-bound B$_{12}$. (Abstractor's note: Perhaps the membrane activity present in dying cells described in the previous abstract explains not only the present findings, but also the enhancement of B$_{12}$-uptake by liver slices or homogenate or perfused liver found after incubation with different B$_{12}$ binders?)—P. G. R.


The influence of azauridine, aminopterin and phosphorylamine in vivo on the nucleic acid content in the thymic cells of leukemic AK mice has been described. Both nucleic acids were determined by biochemical methods, DNA was also determined microspectrophotometrically in arbitrary units. It has been established that the amount of nucleic acids contained in one "average" cell does not change after the antimetabolites and phosphorylamine. The analogs produce statistically significant lowering of DNA values in the individual nuclei of various categories in the thymus of leukemic mice. Phosphoramide, in contrast, increases the concentration indices of DNA in the nuclei of different categories in the thymus of normal mice, whereas in leukemic mice, it acts in the opposite direction. The differential counts of the thymic nuclei of experimental groups have shown that phosphorylamine increases the relative number of large lymphocytes in normal thymus by 100 per cent.—L. D.


The pathogenesis of spontaneous and transplanted lymphatic leukemia of inbred AK mice has been described from the hematologic and histologic point of view, and the transplantability of this type of leukemia within the isologous strain has been defined; simultaneously, the generation time of leukemic cells has been determined by means of a series of stepwise diluted cell inocula. A comparison of the generation time in lymphatic and blast leukemias with that in Ehrlich ascitic carcinoma shows that the mitotic index of tumor cells need not be an absolute measure of their proliferative activity.—L. D.


SLD activity was determined by the colorimetric method in 100 patients with various blood diseases and in 32 healthy subjects. The normal values of SLD activity are 9.5, 1.9 M./ml./H. The greatest increase of SLD activity was found in acute and chronic myelogenous leukemia and in bone marrow fibrosis. During remission the enzyme activity returned to normal values. In pernicious anemia, anemia of cancer and infection, congenital hemolytic jaundice and infectious mononucleosis, activity of the enzyme was less marked. Only a slight increase in enzymatic activity was found in Hodgkin's disease and lymphatic leukemia.—E. K.


In 26 patients with chronic leukemia (13 myeloid and 13 lymphatic), 10 showed defective excretion of 17-ketosteroids after ACTH stimulation and 8 had a paradoxical Thorn test. Serum sodium and potassium and their excretion with urine did not reveal any significant deviations from the normal condition. Control subjects were 8 normals and 2 patients with iron deficiency.—E. K.


This report concerns clinical experience with Mitomycin-C followed by homologous bone marrow transplantation in 32 patients with advanced cancer during the past 2 years. Thirteen patients are still alive. The results showed the possibility that relatively large doses of Mitomycin-C were able to be given safely and effectively by improved methods of administration. Singly administered large doses of drug (over 50 mg.)
ABSTRACTS

were uniformly fatal, but intermittent administration of small doses (10 mg.) or single administration of intermediate doses (20 mg.) with clamping of superior mesenteric and splenic arteries seemed practical. The interruption of blood supply was used in the expectation that occurrence of "secondary disease" might be prevented by sparing intestinal mucosa and lymphatic tissues from drug damage. Although cancer-chemotherapy using bone marrow graft is precluded by the relatively few cases of drug-sensitive human cancers, a reaction of immunity against the host by the grafted myeloid and lymphoid tissue originating from the homologous donor might result with the elimination of the residual cancer cells.—K. F.


Previous experiments by Jacobson and Lorenz demonstrated increased survival of irradiated mice obtaining isologous spleen or marrow tissue about 30 minutes after irradiation. The optimal time for administering bone marrow was studied here, using inbred CBA mice irradiated with 1092 r, and receiving suspensions of 20 x 10⁶ bone marrow cells intraperitoneally between 4 hours and 8 days after irradiation. Ninety percent of the animals getting marrow within one day after irradiation survived for 30 days, as compared to 26 percent of the controls. Fewer animals survived in the groups receiving bone-marrow later. Control-animals were given Tyrode's solution, which also increased significantly the number of animals surviving, although only slightly.—P. G. R.

INDUCTION OF TOLERANCE TO A CANINE RENAL HOMOTRANSPLANT WITH 6-MERCAPTOPURINE. J. C. Pierce and R. L. Varco. From the University of Minnesota Medical School, Minneapolis, Minn. Lancet 1:781–782, 1962.

A renal homotransplant has continued to function for 18 months in a dog. Treatment with 6-mercaptopurine was continued for the first 8 months of this period.—I. C.

HEMOSTASIS


The author reviews his concept of blood coagulation mechanisms and new experiments are described in support of the concept that tissue thromboplastin and thromboplastic cell component (TCC) of blood cells are lipoproteins in their native states; that TCC, unlike thromboplastin, requires thromboplastic plasma component (Factor VIII) for its prothrombin kinase activity; and that the liberation of these lipoproteins from cells and tissues is of considerable significance in physiologic and pathologic blood coagulation mechanisms. The finding of TCC in plasma obtained from patients with sickle cell disease probably represents the first report of lipoprotein release from cells as an intravascular phenomenon. The prothrombin levels were normal in all four cases; TPC elevated in three; Factor V elevated in two; and fibrinogen slightly above normal in two. Individuals who were clinically well and about to be discharged were also investigated. One of these, Case No. 3294, had a history of admissions in crises usually following exposure to cold. Therefore, with his full knowledge of the purpose, he voluntarily immersed one hand in ice to six inches above his wrist for 5–6 minutes. Hemoglobin appeared in plasma 5 hours later, at which time the plasma TCC was 2.1 units per ml. in contrast to 0.0 units per ml. found before cold exposure. Evidence of hemolysis persisted for 48 hours.—K. F.
ABSTRACTS