ERYTHROCYTES


Microangiopathic hemolytic anemia (MHA) was diagnosed in patients with malignant hypertension by the presence of anemia with burr cells and fragmented red cells, and of reticulocytosis. A relationship to intravascular coagulation was suggested by the presence of thrombocytopenia, circulating fibrin breakdown products, increased fibrinolytic inhibitor, increased levels of Factor VIII and by the histological demonstration of fibrin-like material in renal vasculature. Morphological evidence of MHA was found in the blood films of 66 per cent of patients with malignant-phase hypertension, but were absent in other hypertensive patients. The association between malignant hypertension and MHA is explained by postulating that raised arterial pressure or primary vascular disease increases the permeability of small blood vessels to fibrinogen. Fibrin is laid down in the wall and the lumen, and its abnormal persistence results in fragmentation of red cells, further fibrin deposits and possibly a vicious circle. The authors suggest that the localized coagulation disorder is a necessary step in the development of the malignant phase of hypertension and not merely a complication of the disease.—A. L. B.

**RED CELL SHAPE IN HYPOTHYROIDISM.** C. Wardrop and H. E. Hutchison.


Irregularly contracted red cells were found in 15 of 23 proven cases of hypothyroidism. The appearance of the red cells...
was similar to that seen in microangiopathic hemolytic anemia, but the authors do not suggest or comment on an association between these disorders. Abstractor’s comment: This type of red cell abnormality has not been observed previously in hypothyroidism and deserves further study.—A. L. B.


An interlaboratory quality control scheme has been established in Britain by the British Committee for Standards in Hematology. In the first trial stabilized glutaraldehyde-fixed donkey red cell suspension, hemolysate and standard cyanmethemoglobin solution were circulated to hospital laboratories throughout Britain. It was found that red cell counts were more variable between laboratories when counted with electronic counters than with visual methods. The results suggested that some counters were incorrectly calibrated for cell suspensions containing small cells (donkey red cell MCV = 45 cu.μ). A wide scatter of results was also found in the estimations of PCV and of the hemoglobin content of the hemolysate and cyanmethemoglobin solution. The errors in the latter estimation were not in general due to the use of uncontrolled standards. In a second trial, participants were asked to calibrate the settings of electronic counters with stabilized red cell suspension and were supplied with two test samples of blood in Alsever solution and an ICSH cyanmethemoglobin reference standard of stated value. Red cell counts were now much more precise, but PCV determinations and colorimetric measurements of hemoglobin still showed wide scatter. The role of pipette and PCV scale reader errors is discussed. The results illustrate the desirability of using both fresh blood and appropriate reference preparations for quality control, with periodic interlaboratory trials, as well as regular intralaboratory procedures to ensure adequate accuracy as well as precision.—A. L. B.

RELATIONSHIPS BETWEEN IRON–DEXTRAN AND VITAMIN E IN IRON DEFICIENCY


The red cell membrane in children with vitamin E deficiency is excessively fragile when exposed to hydrogen peroxide in vitro; clinically these children display a hemolytic anemia. Vitamin E is thought to act as a potent antioxidant at the cellular level to protect the lipid component of the red cell membrane. In this study, iron-deficient cells also were found to be excessively fragile even though vitamin E levels were normal when exposed to hydrogen peroxide; fragility was enhanced even more when these patients were treated with iron-dextran. Priming doses of vitamin E during administration of iron prevented the rise in fragility to peroxide, but also delayed reticulocyte and hemoglobin response. Possible explanations for the excessive fragility to peroxide of iron deficient cells are: 1) associated hypercromia, 2) effect of iron deficiency on lipid synthesis, 3) effect of iron deficiency on enzyme system responsible for the protection of red cells, 4) iron may increase the fragility by enhancing red cell lipid peroxidation. The delay in reticulocytosis may simply be a function of vitamin E excess.—R. O. W.


Case report of a baby girl aged two years-eight months, of Sicilian extraction, with only mild signs of HbS disease. Normal amounts of HbA₂ increased amounts of HbF (16.6 per cent of the total Hb), elevated HbS (up to 82.1 per cent of the total Hb) and complete absence of HbA₁ were found. The parents had normal hematologic findings with a hemoglobin pattern similar to that of heterozygous carriers of HbS. In both parents as well as the patient, the sickling of erythrocytes was absent. Only the chemical investigation and characterization of hemoglobins by means of fingerprinting and the Itano’s test made the diagnosis possible. The finding seems to be rare.—F. d. N.

Sickle cell (HbS) trait was discovered in eight of 15 members of a family located in the village of Konculja (Serbia-Yugoslavia). Abnormal hemoglobin was identified by starch gel electrophoresis using tris-EDTA borate buffer of pH 9.0 and by producing the sickling phenomenon with two per cent sodium metabisulfate. The trait was distributed among the male and female members of the family and was followed in three generations. In spite of the rather high concentration of abnormal hemoglobin Hb-S was between 43-50 per cent in affected persons anemia and other clinical manifestations were absent. Abstractor's comment: This is the first family observed in Yugoslavia with Hb-S.-Z. R.

DILUTION ANEMIA IN PATIENTS WITH SPLENOMEGALY. V. Dolgova-Korubin. From the Institute of Pathophysiology, Faculty of Medicine, University of Skopje, Yugoslavia. Serbian Arch. Med. 97:45-51, 1968.

Simultaneous red cell and plasma volume were determined using the double radioisotopic (51Cr and RISA-125I) method in 14 patients with splenomegaly. The splenic enlargement was of the congestive type in eight patients and was secondary to other diseases (myeloid metaplasia, lymphosarcoma and acquired hemolytic anemia in six patients). A normochromic or hypochromic anemia was present in 12 patients. A normal red cell volume was found in all but one patient under study. Simultaneously, the plasma volume was increased above the normal value. It is concluded that expansion of the plasma volume is a contributing factor to the anemia in the presence of splenic enlargement.—Z. R.


The method consists in the dilution of blood with its own plasma and its vertical agitation in test tubes containing steel spheres. The resistance of the erythrocytes is assayed by means of the microhematocrit value. In normal conditions the values range within narrow limits, and for this reason the method seems to be dependable.—F. d. N.

LEUKOCYTES


Based on statistics of the causes of death in cities and counties of selected prefectures (Shiga, Nagano), the possibility of temporal clustering of various causes of death including leukemia was tested by the Edler's method. No clustering was observed for diabetes, appendicitis, liver cirrhosis, hernia, hypertensive diseases, meningitis, tetanus, cancer of the lung, uterus and breast. However, significant "one year clustering" were detected for leukemia as well as for Japanese B encephalitis, scarlet fever, bacillary dysentery and influenza. It should be noted that similar results were obtained in the two prefectures. Stimulated by the fact that the pattern of temporal clustering of leukemia was similar to that of communicable diseases, the tendency to "two years clustering" was also tested in four prefectures (Shiga, Nagano, Ehime, Kanagawa). Although a striking "one year temporal clustering" was observed in all these prefectures, no tendency for a "two year clustering" was found, except in one prefecture (Nagano). A spot map of leukemia cases was made in Okayama City (1962-66) and also in Shizuoka City (1954-65). Pinkel method was applied to detect time-space clustering in small areas in both cities. It was observed that the time interval between pairs occurring within short distance (600-1250m.) was significantly shorter than for the distant pairs. The annual trend of leukemia death by age groups was studied in different districts in Japan. A striking fluctuation with a magnitude resembling that of measles was observed in the annual death
rate from leukemia in patients two to four years of age. The tendency to oscillation in Tokyo coincided with that in neighboring prefectures (Kanagawa, Chiba, Saitama) \( (R = +0.7697) \). The age distribution of childhood leukemia could be considered as a synthetic curve composed of two components with different modes of age: one with mode at zero–one year and the other with mode at two–four years of age. The former may be influenced strongly by prenatal exposure and the latter by postnatal exposure. Cohort analysis of leukemia deaths in different prefectures also showed the validity of this hypothetic model for age distribution. It was found that the shape of the actual distribution of childhood leukemia by age in different years in Tokyo, in all Japan, in U. S. whites and U. S. non-whites, could be well explained by such age distribution model. In summary, the existing epidemiological data on human leukemia, such as time–space clustering, yearly fluctuation by age group, complex shape of age distribution, etc., could be considered as being compatible with the horizontal viral transmission theory, although the possibility of coexistence of vertical transmission appeared to be quite high.—K. F.


Lymphocytes were activated with phytohemagglutinin in vitro. By means of cytokinetic, cytochemical, ultrastructural, metabolic and cytogenetic studies, it was shown that blastic transformation of lymphocytes was not inhibited by Busulfan, while the frequency of chromosome aberrations was significantly increased mostly with chromatid (rarely isochromatid) breaks. The synthesis of DNA was also depressed. **Abstractor’s comment:** These investigations are very extensively documented by means of many illustrations and tables. According to the authors, the data on DNA synthesis should need confirmation.—P. d. N.


Antilymphnode serum antibodies were detected in 11 of 12 patients with Hodgkin’s disease. In the two patients whose lymphnodes were available for testing, antilymphnode antibodies proved to be autoactive. One of these two patients with advanced and untreated disease was submitted to more extensive immunologic studies.—P. d. N.


Three patients with blood dycrasias following the use of chloramphenicol are reported. One patient developed a transitory granulocytopenia during the treatment with a rather high dose (25 Gm. in total) of the drug. Discontinuation led within a week to the normalization of granulocyte count. A fatal bone marrow aplasia with pancytopenia occurred in two other patients after treatment with small doses (four and 12 Gm. respectively, in total) of the drug. The history of previous exposure to chloramphenicol was noted in one of the patients. The onset of clinical manifestations in both patients lagged two weeks after the drug was discontinued. One of those patients died after three weeks with sepsis and without signs of bone marrow regeneration. The second patient died after three months. Death was due to cerebral hemorrhage. In this patient, serial bone marrow examinations revealed signs of recovery in the granulocytic and, to a lesser degree, in the erythrocytic series, but not in the precursors of the thrombocytic cell line.—Z. R.

**ACUTE LEUKEMIA IMITATING BURKITT TUMOR.** P. Kemény, G. Köteles, L. Nagy and J. Hődösi. From Departments of Internal Medicine, Roentgenology and Pathology, Madaraș street Municipal Children’s
ABSTRACTS


In two leukemic patients, a clinical and cytologic picture deceptively similar to Burkit tumor was observed. The question, already propounded by several authors, is raised of whether the African lymphoma is only a special manifestation of a lymphoproliferative disease.—S. R. H.


Trials were made in five children aged between two years, seven months and eight years, five months. Two of them had not been treated previously. L-Asparaginase from E. coli was given at the daily dose of 300 I.U./kg. for 15–23 days. The results obtained suggested to the authors that L-Asparaginase acts via a cytotoxic effect, by causing depletion of the nutritional requirements indispensable for the growth of leukemic cells and not for the growth of normal cells. It does not act by an antimitic mechanism. L-Asparaginase attacks, therefore, the leukemic cells, while there is a normal growth of normal erythroblasts, leu-koblasts and megakaryocytes in the bone marrow, with increase of platelets in peripheral blood. Among the untoward reactions the authors have observed anorexia, nausea, vomiting, weight loss, reduction of serum proteins and, in some cases, increase of blood transaminases. They feel that it is not yet proven that this drug can be definitely introduced in common practice. Abstractor’s comment: The paper is of interest also for the comprehensive and critical review of the literature on therapy of acute leukemia in childhood.—P. d. N.


The results of the treatment with Dibromdulcit of 18 patients suffering from chronic myelosis are presented. The new Hungarian cytostatic drug was administered orally (150–750 mg./day) and after having achieved remission, a maintenance treatment (with 50–200 mg./day) was given in each case. In 14 of the 18 cases, a state of remission lasting 3–19 months was obtained, while the treatment of four patients in the advanced stage of the disease was unsuccessful. The advantages of the new drug are that it can easily be administered, it has no considerable side effects and has no effect on erythropoiesis or thrombopoiesis in therapeutic doses. It seems to be especially suitable in chronic, maintenance treatment.—S. R. H.

HEMOSTASIS


Synoviectomy was carried out in 16 patients (19 joints) in order to obtain functional recovery and to avoid relapses of intraarticular bleeding. Such procedure was suggested because of presence of inflammatory lesions in the synovia already after two or three bleeding episodes and because of remissions after local introduction of corticosteroids, as is observed also in cases of relapsing hydarnarthrosis. In 17 operations synoviectomy was carried out in the knee, in one case the tibio-tarsic joint was opened upon, and in another case the elbow. In the first two cases only frozen plasma was used for 35 days (20 mL/kg.) to prevent bleeding. In the remaining, the amount of plasma was reduced to 8–10 mL/kg. daily for 10 days, and antifibrinolytic agents were added (200–400 units of trasylol and epsilon-aminocaproic acid between 0.3 and 0.9–1.0 Gm./kg. daily for three to four weeks). The joint was mobilized for 12–15 days after the operation. Antibiotics were given for 10–15 days. No hemorrhagic relapses were observed in the operated joints.

During normal pregnancy the plasma fibrinogen and plasminogen levels rose. Similar levels were maintained during labor and the puerperium, but by the sixth week they had returned to those observed in the nonpregnant state. Euglobulin lysis times increased steeply after the first trimester and were interpreted as indicating decreased levels of plasminogen activator. Prolonged euglobulin lysis times persisted throughout the first and second stages of labor, but fibrinolytic activity increased to normal or slightly above during the puerperium. There was no alteration in the sensitivity of plasma clots to lysis by urokinase suggesting that levels of inhibitor of plasminogen activation

ABSTRACTS


This is a case report of a 27-year-old woman after delivery, with a circulating anticoagulant which inhibited thromboplastin formation. The authors describe a test called “anticoagulant exhaustion test,” for the detection of the exact nature of the inhibitor. The test is based on the incubation of various mixtures with the patient's plasma. Corticosteroids did not consistently improve the syndrome. Treatment with 6-mercaptopurine caused a complete recovery within two months. Abstractor's comment: This description is of interest because of the therapeutic success and the diagnostic procedure.—P. d. N.
ABSTRACTS

did not change. The authors suggest that the presence of high fibrinogen and decreased fibrinolytic activator may enhance hemostatic mechanisms during separation of the placenta, but at the same time set the stage for possible intravascular coagulation. —A. L. B.


The assay of fibrin-stabilizing factor (Factor XIII) could be carried out in the euglobulin precipitate, after inhibition of fibrinolytic activity with epsilon-aminocaproic acid. The values were slightly lower than in whole plasma. According to the authors, the addition of epsilon-aminocaproic acid is indispensable for an exact evaluation of Factor XIII in the plasma and in the euglobulin precipitate.—P. d. N.


In 31 patients with acute rheumatic fever, aged 20-22, the mean fibrinogen level was found to be 564.5 mg. per cent. In untreated patients the mean value was 684.6 mg. per cent. In treated patients it was 418.6 mg. per cent. The difference was statistically significant (p < 0.01). The mean euglobulin lysis time was 43 hours, 15 minutes (normal values between 12 and 30 hours). No significant correlation was found between fibrinogen level, ASO titer, erythrocyte sedimentation rate and leukocyte count. In untreated patients there was a correlation between fibrinogen and erythrocyte sedimentation rate (p < 0.01). Abstractor’s comment: The main interest of this paper consists in the finding of a low fibrinolytic activity, which was clearly proved also by statistical evaluation.—P. d. N.


The authors investigated the effect of streptokinase on the behavior of human platelets in vitro. Streptokinase in vitro caused marked aggregation of human platelets. Streptokinase-aggregated platelets had no tendency to spontaneous disaggregation. By the slow onset, the aggregation effect of streptokinase resembled the aggregation effect of collagen. Streptokinase potentiated the aggregation effect of ADP and prevented the spontaneous disaggregation of platelets aggregated by ADP.—L. D.


Pure phospholipase A derived from Crotaulus Terrificus Borhinger had a thrombin-mimetic action which was quite different from that due to thrombin itself, as it did not stabilize Factor XIII and had only antithrombin III antagonism.—J. C. DIGESTIVE TRACT HEMORRHAGE FOLLOWING INGESTION OF ANTI-INFLAMMATORY DRUGS. F. Bodin and M. Conte. From
During the course of one year, the authors observed 118 cases of gastrointestinal hemorrhage after drugs, of which 29 (25 per cent) occurred after aspirin administration. The ulcerogenic effect of these drugs seemed to be linked to their antiinflammatory effect. No doubt also that they could affect the platelets themselves.—J. C.

**ABSTRACTS**

**IMMUNOHEMATOLOGY**


Serum IgM levels were highest in women with an additional X-chromosome (XXX), intermediate in normal women and lowest in normal men. Mean IgM levels in seven XXY and three XXXY individuals were similar to those of normal women and XXX women, respectively. It is suggested that IgM levels are related to the number of X-chromosomes. The factors influencing the levels may be set before activation of the X-chromosome during embryonic development.—A. L. B.


Immunoglobulin levels were measured in patients with warm autoimmune hemolytic anemia. The patients included those with autoimmune disease and lymphoma, a group on methyldopa therapy, an idiopathic group and four miscellaneous cases. Half the patients, excluding those on methyldopa, had low serum levels of one or more immunoglobulins, and IgA was most frequently affected. Immunoglobulin levels in patients with methyldopa-induced hemolytic anemia were normal. The roles of genetic or inherited factors, increased utilization, suppression of production and autoimmunoglobulin antibodies in the pathogenesis of the reduced levels of immunoglobulins are discussed.—A. L. B.


Human peripheral lymphocytes were stimulated with phytohemagglutinin and incubated with labeled amino acids. The proteins in the medium were analyzed by means of radioimmunoelectrophoresis. IgG was isolated by chromatography on DEAE cellulose and its specific activity was evaluated by liquid scintillation counting. Radioactive lines due to alpha-2-macroglobulin, haptoglobin, transferrin, alpha-1-antitripsin, IgG and IgM were identified. The two immunoglobulin lines were very weak, but liquid scintillation counting of the isolated IgG showed that a definite amount of radioactivity has been incorporated into this protein.—F. d. N.


Observations are reported in 19 cases of plasmocytoma, four cases of macroglobulinemia and one case of chronic idiopathic cryoglobulinemia. Bone marrow and lymph-node preparations were used. Except for two cases of IgG plasmocytoma, the reactions were always intense and typical with diffuse and homogeneous fluorescence of the plasma cell cytoplasm. In two cases of IgA plasmocytoma, an elevated concentration of pathologic immunoglobulin was found in the peripheral hyaline-flaming zones of the cells, with the tendency toward clasmatisis. In four cases of macroglobulinemia, an intense fluorescence of the cytoplasmic ring in the most voluminous lymphatic cells was obtained. In the bone marrow lymphocytes of
a case of chronic cryoglobulinemia, fluorescence was obtained using anti-IgM and anti-K sera. Abstractor's comment: The paper deserves to be read in the original because of the very rich photographic documentation and of the detailed introduction.

-P. d. N.


By the thrombocyte-immuno-adhesion test a serum factor reacting with homologous aortic antigen was detected in the sera of 60 per cent with arteriosclerosis. A hepatic nuclear fraction was used as control antigen. There was no interrelationship between the result of the serologic reaction and the blood lipid parameters investigated by the authors.

-S. R. H.


One of the cases was a very rare form of Waldenström macroglobulinemia showing a high degree IgM macroglobulinemia accompanied by IgG and Bence Jones paraproteinemia. Histological and pathological findings supported the diagnosis of Waldenström macroglobulinemia. In the other case the clinical symptoms and serum protein investigations indicated Waldenström macroglobulinemia. Histology, however, showed generalized lymphosarcomatosis. The results of paper electrophoresis, cellulose acetate membrane electrophoresis, agar gel and immunoelectrophoresis and of ultracentrifugation are presented. Immunoelectrophoresis and examination of sediment and supernatant separated by preparative ultracentrifugation are described. It is emphasized that the diagnosis of Waldenström macroglobulinemia is to be based on morphological findings, clinical symptoms and also on protein chemistry investigations. —S. R. H.

THREE CASES OF BENCE JONES' (IgU) PLASMOCYTOMA IN HUNGARY. A. Patakfalvi, R. Backhausz, J. Lajos and A. Somos. From First Department of Medicine, University Medical School, Pécs, Hungary. Orv. Hetil. 110:882-885, 1969.

Three cases of plasmocytoma of the Bence Jones (IgU) type are presented. The characteristics of this rare type of plasmocytoma, differentiating it from macromolecular plasmocytoma are discussed. IgU-paraproteinemia was accompanied by symptoms of antibody deficiency developing gradually. —S. R. H.


Pruritus is described for the first time as a presenting symptom of paraproteinemia. Three such patients, diagnosed as having benign monoclonal gammopathy, are reported. One later showed progression to Waldenström's macroglobulinemia. The relationship between the findings, laboratory and clinical, is discussed. —B. R.


A variant of blood group B is described. It occurred in a father and son of an Austrian family three generations of which could be investigated. It was similar to, but not totally identical with, the weak variant of the blood group B known from the literature as Bw. —S. R. H.

STUDY OF THE ALTERATIONS OF ERYTHROCYTE ANTIGENS I, I, H, A AND B IN VARIOUS PATHOLOGIC CONDITIONS. V. Boccardi

One hundred and fifty-two patients with leukemia, congenital and acquired hemolytic anemia, aplastic anemia, cirrhosis of the liver and other nonhematologic disorders were studied. In 29 patients the i antigen was detected; i positive subjects were found particularly in acute leukemia, hemolytic and aplastic anemia and liver cirrhosis. In some cases also I, H, A and B antigens were altered.—P. d. N.

SEROLOGIC SPECIFICITY OF PLATELETS. F. Milgrom, W. A. Campbell, and E. Witebsky. From Dept. of Microbiology, State Univ. of New York School of Medicine, Buffalo, N. Y. Vox Sang. 15:418-426, 1968.

Potent rabbit sera immune to human platelet extracts were utilized for the study of platelet antigens by the double diffusion gel precipitation and tanned cell hemagglutination tests. By these methods, a human platelet specific antigen was defined with an electrophoretic mobility in the range of serum a-globulins.—M. B.

MISCELLANEOUS


In two patients treated with vincristine or vinblastine, a thrombocytosis occurred which did not seem to be related to regression of the underlying malignancy. Vincristine administered to rats caused a thrombocytosis much greater than that observed in control animals. The authors suggest that vinca alkaloids may increase marrow production of platelets. *Abstractor’s comment:* G. D. Soppitt and J. R. A. Mitchell, Lancet 2:539, 1969, made the interesting suggestion that vinca alkaloids may alter platelet structure and function leading to loss of reactivity and prolongation of their lifespan. If these effects can be shown to occur in vivo they may have important implications with reference to antithrombotic agents.—A. L. B.


The author studied clinical cases with more than 200-ml. blood loss during operation and devised a formula by which it can be predicted how much blood loss a patient can tolerate without risk during an operation and the postoperative period. The author studied control of the postoperative hypovolemia, safety limits of hemodilution, and recovery from it, and came to the following conclusions: 1) In the early stage after operation, approximately 10 per cent decrease of the total blood volume was found; 2) When a plasma expander was given in more than 1.2 times the volume of the total blood lost and also fluid in the amount of 5 ml./kg./hr., the decrease of the total blood volume was eight per cent on the average, regardless of age and of speed of bleeding during operation; 3) It was established that blood constituents could be lowered to 30 per cent without complications in both operative and postoperative course; 4) For a few days after the operation, data suggesting low red cell production and accelerated red cell destruction were obtained; 5) At the beginning of the second postoperative week, production of red cells became remarkably active and the greater the dilution the faster was the production rate; 6) From the above data, the author devised the formula: \[ Y = V[1-(b/z)] \] where \( Y \) = allowable quantity of blood loss, \( V \) = total blood volume, \( z \) = preoperative hematocrit, \( b \) = theoretical hematocrit after dilution.—K. F.

BLOOD AND BLOOD-FORMING ORGANS IN HYPERTHYROIDISM. A REVIEW. J. Bogusz and J. Lisiewicz. From First Department of Surgery and Third Department of Internal Diseases, Medical Academy, Cracow, Poland. Haematologia 2:393-400, 1968.

The paper presents a review of recent data concerning blood and blood-forming organs in hyperthyroidism. The peripheral blood, bone marrow, lymphnodes and spleen changes occurring in hyperthyroid patients, as well as the hematological findings after surgical and pharmacological
treatment of hyperthyroidism, are discussed. The results of the authors’ own investigations are also mentioned.—S. R. H.


The cytochemical reactions of cells from punctates were investigated with respect to whether: 1) there exists a difference between the reaction of leukocytes deriving from peripheral blood and serous fluids; and 2) whether the reaction of leukocytes, endothelial and tumor cells in the same pathological states is the same. Diagnostic conclusions that may be drawn from the results are discussed.—S. R. H.