ABSTRACTS

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ERYTHROCYTES

Favism: Current Problems and Investigations. E. Bottini, National Research Council Center for Evolutionary Genetics, Department of Genetics, School of Science, University of Rome and Department of Pediatrics, School of Medicine, University of Rome, Rome Italy. J Med Genet 18:154-157, 1973.

In vitro studies of the action of extracts of Vicia faba with red cells from patients who had had episodes of hemolytic favism suggested that several active substances may act in a synergistic manner. Red cell acid phosphatase and thalassemia genes were important in determining the susceptibility of G6PD-deficient subjects to hemolysis. — J. M. B.


A deficiency of red cell glucose-6-phosphate dehydrogenase was found in an Iraqi Jewish family. All the children suffered from hemolytic jaundice as neonates. One child had died and two children had symptoms of kernicterus. Characterization of the abnormal glucose-6-phosphate dehydrogenase indicated a new variant which was termed Gd-Bagdad. — K. P.


The clinical and hematological abnormalities in hereditary dyserythropoietic anemia type II (HEMPAS) are discussed on the basis of the data obtained by examination of nine patients belonging to four families. The heredity in all probability is of the autosomal-recessive type.
Clearance of the Spleen in Malignant Lymphohemolytic Anemia or with an Increased Serum Bilirubin Level. New Cases of HEMPAS May Be Useful. Blood Splenectomy May Sometimes Be Indispensable. The prognosis is fairly favorable. Iron therapy is contraindicated. Splenectomy may sometimes be useful. Blood transfusions should be avoided as much as possible. New cases of HEMPAS may be detected by systematic examination of the bone marrow and the acidified-serum test of indirect bilirubin. In addition, systematic examination of families might lead to the detection of the heterozygous carrier of the anomaly.—K. P.


Clearance of the spleen for splenosensitive erythrocytes treated with BMHP was investigated in ten patients with malignant lymphohemolytic anemia. An absolute and relative decrease in clearance values was found in the examined patients. The greater the size the lower was the spleen clearance value for BMHP treated erythrocytes.—L.D.

Erythropoiesis in Hypothyroidism. R. M. Donati, J. W. Fletcher, M. A. Warnecke, and N. I. Gallagher. St. Louis Veterans Administration Hospital, Nuclear Medicine and Internal Medicine Services, and Department of Internal Medicine, Saint Louis University School of Medicine, St. Louis, Mo. Proc Soc Exp Biol Med 144:78, 1973.

Rats were thyroidectomized and given an ablative dose of sodium 131I iodide. Studies were done 8 wk thereafter. Hypothyroid rats demonstrated decreased red cell radioiron incorporation and a diminished GI iron absorption. Urinary erythropoietin was decreased. The administration of erythropoietin reversed erythropoiesis towards normal. D-triiodothyronine, L-triiodothyronine, or exposure to hypobaric hypoxia produced the same stimulating effect on erythropoiesis. However, erythropoietin did not correct the decreased GI radioiron absorption in spite of the fact that it completely corrected the erythropoietic depression in the hypothyroid rats. On the other hand, L-triiodothyronine restored both erythropoietic depression and GI radioiron absorption. These results suggest that in the hypothyroid rats there is a lack of erythropoietic stimulation by erythropoietin being the cause for the anemia. Erythropoietic compensation appears possible by the administration of nonspecific erythropoietic stimulants. However, the reduced gastrointestinal iron absorption can only be repaired by the administration of thyroid hormones.—M.G.B.


The site within the body from which desferrioxamine (DF) obtains its iron was investigated. A variety of selective radioiron probes were utilized to study the mode of action of DF in the rat. A quantitative radioautographic method for determining the cellular distribution of 59Fe in rat liver demonstrated that heat-damaged RBC and precipitated ferritin were selectively removed by the RE cells, while soluble ferritin and hemoglobin bound to haptoglobin labeled the parenchymal cells of the liver. Desferrioxamine induced a marked increase in the whole body excretion of parenchymal iron, whereas the increase in excretion in RE cell iron was no greater than could be accounted for by iron recirculation to the parenchyma after release to transferrin. Of the parenchymal iron labels, soluble ferritin 59Fe was chelated by DF to a greater extent than 59Fe from hemoglobin suggesting an interaction of the drug with parenchymal ferritin stores and not with iron released by heme catabolism.—M.S.

LEUKOCYTES


These four drugs were given simultaneously in intensive 2-wk periods of each mo for a 6-mo period. Since the simultaneous utilization of combinations of drugs may result in antagonism as well as potentiating effect, a control group treated with the same drugs and with the same total dosage over a similar period of therapy, with the drugs used one at a time in a sequential manner, was necessary. Two hundred and forty-seven patients with disseminated Hodgkin’s disease were randomly treated with one of three intensive multiple-agent regimens. Partial or complete response rates of 90% were obtained with each one of these routines. The “MOPP” (mechlorethamine hydrochloride, vin-cristine sulfate, procarbazine hydrochloride, and prednisone) yielded the longest duration of response but had the highest toxicity. A second group of patients was treated by the ALB schedule. Therapy periods were defined at the first 2 wk of six successive 4 wk periods. Treatment in the first, third, and fifth periods consisted of vincristine sulfate and procarbazine hydrochloride. Treatment in the second, fourth and sixth periods consisted of vinblastine sulfate, chlorambucil, and prednisone. Another group of patients was treated by the sequential SEQ schedule. Drugs were given sequentially as single agents. The drugs were procarbazine hydrochloride taken orally each day for 28 days, followed by prednisone each day for 14 days, then vincristine sulfate i.v. weekly for 4 wk, then prednisone taken orally each day for 14 days, then chlorambucil taken orally daily for 28 days, then prednisone taken orally each day for 14 days, then vinblastine sulfate administered intravenously weekly for 4 wk, and finally prednisone orally each day for 14 days. The total amount of each drug given over the 6 mo period was the same as in the ALB schedule. There was no difference in survival rates among patients on the three routines. Major factors associated with good response were female sex and little or no prior therapy. Minor favorable factors were stage III disease, lack of systemic symptoms, former responsiveness to therapy, and age of less than 60 yr. The simultaneous dosage routine was superior in both response rate and lesserened toxicity, compared to sequential usage of the same drugs with the same total dosage.—M.G.B.


The history and success of combination chemotherapy of advanced Hodgkin’s disease is reported. Early results with combination of drugs for the treatment of acute childhood leukemia in 1963 prompted the first study with a similar philosophy of treatment in Hodgkin’s disease. The agents used at that time were vincaralkaloids, alkylating agents, prednisone and methotrexate. The results were encouraging enough to lead to an expanded program substituting procarbazine for methotrexate. This combined drug program was called MOPP. MOPP therapy has yielded results significantly different from those previously achieved with single agents and has proved that combination chemotherapy in Hodgkin’s disease is the treatment of choice because it produced a higher rate of induction of complete remissions in patients with advanced Hodgkin’s disease (80%) and prolongation of remission duration after all therapy is stopped (36 mo). In comparison to results previously obtained with treatment by the use of single agents, it is definite that there is a doubling or tripling of the complete remission rate and an eight to tenfold increase in remission duration with MOPP therapy. Data from the NCI showed that approximately 70% of the patients with stages III and IV disease who achieved remission with combination chemotherapy between 1964 and 1967, are alive at 5 and 6 yr.—M.G.B.

Prognosis and Survival of Patients With Chronic Lymphatic Leukemia. L. Donner, P. Klener, and Z. Roth. Department of Medicine, Charles University, Prague, Czechoslovakia. Cas Lek Cesk 112:710–714, 1973.

The prognosis and survival time of 208 patients with chronic lymphatic leukemia in the periods 1939–1953 and 1954–1968 were investigated. The survival time was established both from the time of appearance of the first symptoms of the disease and the time at which the diagnosis was made. The geometric means of survival time of patients aged 35–60 yr in the period 1954–1968 were significantly higher than in the period 1939–1953. There was no difference between the two groups in the survival time of patients aged 61–80 yr.—L.D.

Unusual Coincidence of Polycythemia Vera and Chronic Lymphadenosis. P. Klener and M. Bocanová. Department of Medicine, Charles University,
A case is reported of a patient with typical polycythemia vera treated with radioactive phosphorus and Myleran. In 14th yr of treatment, the number of lymphocytes began to rise in the peripheral blood, and, during the next year, a chronic lymphatic leukemia with a typical, clinical and laboratory picture developed. The patient died during a relapse phase of the lymphatic leukemia, because of sepsis due to underlying agranulocytosis. —L.D.


The mother of a male infant with apparent CGD had normal leukocyte bactericidal function, normal leukocyte enzyme levels, normal myeloperoxidase, and normal NBT reduction. The authors speculate that these findings may be due to disproportionate inactivation of CGD-affected X-chromosomes. Because of the probability that different genetic mechanisms are operable among patients with CGD, speculation concerning the significance of the “silent carrier” must remain just that. —J.B.S.

Hematosis


In patients treated with Pelentan (Tromexan), a reduced serum antithrombin activity and a normal factor 4 in platelets were established. Release of the platelet factor 4 during irreversible aggregation after addition of collagen in Pelentan-treated patients did not reveal any difference, as compared with the control group. Also release of ADP and beta-glucuronidase from platelets by thrombin was not affected in these patients. Acetylsalicylic acid reduced ADP release but had no effect on the release of beta-glucuronidase. —L.D.


In 64 patients with myocardial infarction a set of coagulation tests (thrombelastogram, fibrinogen, fibrinolysis, fibrinogen degradation products and fibrin immunofluorescence in leukocytes) was studied during the first 5 wk of illness. A significant difference in the results obtained on the third and fourth day after the onset of infarction was found between patients dying within the first 35 days and those surviving this term. A decreased fibrinolysis, a higher amount of degradation products of fibrinogen and a higher fibrin immunofluorescence in leukocytes were found in patients with poor prognosis. —L.D.


Epsilon-amino-caproic acid, administered orally at the dosage level of 0.4 g/kg/day to dogs subjected to whole body irradiation, improved in part the postirradiation syndrome. In rats, rabbits and dogs subjected to whole irradiation, the ellagic acid administered intravenously markedly reduced the bleeding time and favorably influenced some blood coagulation tests. The dose in dogs was 10 ml/kg in a concentration of 2 x 10^{-4} M. —L.D.


In six patients with paroxysmal nocturnal hemoglobinuria, factor V, factor VII, factor VIII, thrombin time, prothrombin time, fibrin split products, fibrinolysis, platelet number, and platelet survival time were estimated. The results did not support the hypothesis that paroxysmal nocturnal hemoglobinuria may be due to intravascular coagulation. —L.D.


Levels of plasminogen activator were estimated in the endometrium in 40 women during the menstrual cycle, during functional metrorrhagia in 48 women, in the decidua and chorion of normal pregnancy during the first trimester in 32 women, and after spontaneous abortion in 17 women. Raised levels of activator were
found during menstruation, metrorrhagia, and spontaneous abortion. In 110 women menometrorrhagia was treated with the antifibrinolytic drug L-aminoacaproic acid and the inhibitor of pancreatic proteases antilysin. Hemostasis was obtained in 104 women, i.e., 94%. In 30 women, values of plasminogen activator were measured during antifibrinolytic therapy and after its termination. During therapy there was a significant decrease in activator levels. In ten women, serial sections of the endometrium showed fibrinolysis by the histochemical Todd’s method. In eight women, the activity was inhibited by antifibrinolytic therapy.—L.D.


Prostaglandins E2 and F2α are known to be formed and released by platelets in response to thrombin. This study investigates whether these prostaglandins are also released during collagen-, epinephrine-, and ADP-induced aggregation. All of these agents were found to induce formation of prostaglandins E2 and F2α in platelets. None however, equaled the level of prostaglandin formation observed in thrombin-aggregated platelets. The prostaglandins formed by the platelets were rapidly and completely released. With collagen, proportionality between its concentration in the aggregation system and the amount of prostaglandins released by the platelets was observed. In epinephrine-induced aggregation formation of prostaglandins was found associated with the second wave of aggregation, collagen, on the other hand, induced prostaglandin formation at the onset of aggregation. The authors suggest that formation and release of prostaglandins is associated with the secretion of endogenous ADP and serotonin from platelets.—M.S.


The effects of collagen modification involving the protein and carbohydrate moieties of the molecule were examined. Purified rat skin (salt) soluble collagen was effective at 20 nM concentration in mediating platelet aggregation of human platelet-rich plasma. Both the α1(I) and α2 chains from rat skin soluble collagen produced platelet aggregation but only at concentrations of 13 μM and 55 μM, respectively. Collagen and isolated chains that were heat denatured failed to induce platelet aggregation and to inhibit platelet aggregation by native collagen. Modification of human skin insoluble collagen by digestion with collagenase and trypsin showed that the resulting glycopeptides were unable to induce platelet aggregation. Highly purified samples of hydroxylysyl glycosides, namely hydroxylysylgalactose (Hyl-Gal) and hydroxylysylgalactosyl-glucose (Hyl-Gal-Glc) were examined for their binding to platelet-rich plasma and for their ability to aggregate platelets. Hyl-Gal at concentrations greater than 50 nM was bound to platelets but Hyl-Gal-Glc in concentrations up to 250 nM did not bind. Neither of these glycosides was able to inhibit platelet aggregation by native collagen. The Gal-Glc-containing 36 residue rat skin soluble collagen α1(I)-cyanogen bromide No. 5 peptide had no platelet aggregating or inhibiting activity. A previous report by others provided evidence that this peptide isolated from chick skin collagen was able to induce platelet aggregation. Modification of at least 90% of the rat skin-soluble collagen carbohydrate by mild periodate oxidation had no effect on platelet aggregating activity. Similarly unaffected by this treatment was human skin insoluble collagen. Thus carbohydrate side chains of these collagens are not required for platelet interaction which produces a release reaction. The authors conclude that the collagen–platelet interaction appears to involve at least two distinct binding sites on the platelet surface—one being a protein binding site which apparently activates platelet aggregation and has high specificity for the collagen triple-helical fold or perhaps even for a particular amino acid sequence in the triple helix. The second site constitutes a carbohydrate binding site of lower affinity which may be a platelet glycosyltransferase. Although an extremely high concentration of glycopeptides may inhibit collagen-mediated platelet aggregation, under physiologic conditions where criteria for high specificity and affinity are met, the collagen carbohydrate appears not to be a determining factor in collagen binding to platelets. The latter is primarily a function of the protein moiety of collagen.—M.S.

Inhibition of Primary ADP-Induced Platelet Aggregation in Normal Subjects after Administration of Nitrofurantoin (Furadantin). E. C. Rossi and N. W. Levin. Department of Medicine, North-
The authors present evidence that nitrofurantoin is a potent inhibitor of primary ADP-induced platelet aggregation. The inhibitory effect of the drug was demonstrable already in concentrations of 10 μM. Nitrofurantoin displayed competitive kinetics with respect to ADP. Collagen-induced platelet aggregation was less sensitive to nitrofurantoin. The retention of platelets in glass bead columns was not affected by the drug unless extraordinarily large concentrations were used. Platelet rich plasma obtained from normal subjects administered nitrofurantoin in dosages of 180 mg i.v. or 200 mg orally demonstrated inhibition of ADP-induced platelet aggregation. The inhibitory effect correlated well with the log of the serum nitrofurantoin concentration. Collagen-induced platelet aggregation was also inhibited in a dose-related manner. The inhibitory effect of nitrofurantoin on collagen-induced platelet aggregation could be overcome in part by increasing the collagen concentration. Nitrofurantoin tested in combination with prostaglandin E1 or theophylline showed additive inhibition of platelet aggregation. These studies indicate that nitrofurantoin inhibits platelet function to a degree that is proportional to the serum concentration of this drug.—M.S.


Methylene blue (MB) can release 5-hydroxytryptamine (5-HT) from platelets. This release is not accompanied by aggregation of platelets. These studies delineate the biochemical characteristics of MB-induced serotonin release. The release studied by preloading platelets with 14C-5-HT was found to depend on the concentration of MB, the pH, and the temperature. At pH 8.4 MB in a concentration of 2 x 10^-4 M released 53% 5-HT during 5 min and 71% during 15 min incubation. MB did not induce degradation of 5-HT. Storage pool nucleotides were not released when MB triggered the release of serotonin from platelets. Neither did MB cause leakage of platelet cytoplasmic contents such as 3H-ADP and potassium. Stimulation of the hexose monophosphate shunt by MB did not seem to play a role in the release of 5-HT because a structurally related compound, phenazinemethosulfate, stimulated the hexose monophosphate shunt but did not release 5-HT. Thus methylene blue appears to selectively affect 5-HT storage sites.—M.S.

Effect of Epinephrine on Platelet Lipid Metabolism. D. Deykin and D. Snyder, Department of Medicine, Beth Israel Hospital and Harvard Medical School, Boston, Mass. J Lab Clin Med 82:554, 1973.

The effect of epinephrine was studied on the incorporation of tritiated glycerol into platelet-rich plasma. Aggregation of platelets by this biogenic amine altered their incorporation of tritiated glycerol into lipids. There was a transient reduction of lecithin and diglyceride synthesis and a persistent depression of triglyceride formation. The synthesis of phosphatidylinositol was stimulated approximately fivefold over that in the control. Aspirin which inhibits the platelet release reaction was shown to reduce the stimulation of phosphatidylinositol synthesis induced by epinephrine but did not completely suppress it.—M.S.

Inhibition of Activated Factor X-induced Platelet Aggregation: The Role of Heparin and the Plasma Inhibitor to Activated Factor X. E. T. Yin, L. C. Giudice, and S. Wessler, Department of Medicine, The Jewish Hospital of St. Louis and the Washington University of Medicine, St. Louis, Mo. J Lab Clin Med 82:390, 1973.

The authors confirmed the previously noted ability of Factor X to aggregate washed rabbit platelets in the presence of calcium ions. Supporting evidence for the absolute requirement of trace amounts of factors II and V in this type of aggregation was provided by the complete loss of aggregability of freshly-washed platelet preparations after aging at 4°C for 24 hr. Addition of fresh factor II and V completely corrected this aggregation defect. Factor X-induced platelet aggregation could be completely abolished by addition of plasma-activated factor X inhibitor. The effect was dosage dependent. While low concentrations of the plasma inhibitor were unable to prevent aggregation by activated factor X, addition of heparin in low doses resulted in inhibition of platelet aggregation. Alone, the amount of heparin added failed to inhibit platelet aggregation. This study provides additional convincing evidence for the use of low doses of heparin in preventing thromboembolic phenomena.—M.S.
ABSTRACTS

IMMUNOHEMATOLOGY


Intradermal response to 1:10,000 tuberculin was measured in 23 patients during the acute phase of infectious mononucleosis, and again 6 wk later. In eight patients, there was a negative reaction during the acute phase which became positive after recovery, indicating transient depression of cellular immunity. The mechanism of the depression and its possible relationships to malignancy are unestablished. — P.F.


The sequence of degranulation in rabbit granulocytes phagocytizing Staphylococcus aureus and Escherichia coli was, at the ultrastructural level, studied by cytochemical enzyme localization in phagosomes. Peroxidase was the marker enzyme for azurophilic granules, and alkaline phosphatase for specific granules. Alkaline phosphatase appeared first in the phagocytic vacuoles; later, vacuoles contained both enzymes. Results indicate that degranulation occurs sequentially, with specific granules fusing initially with the phagosome. This sequence of degranulation roughly parallels the decreasing pH of phagocytic vacuoles. The decreasing pH is associated temporally with optimal pH ranges for respective granule contents. — P.F.


Delayed hypersensitivity was assessed in 39 patients with SLE, and results were compared with 30 normal control subjects. Parameters were skin test responses to PPD, trichophyton, and nDNA, and in vitro lymphocyte transformation with PPD, and calf thymus nDNA. Patients with SLE, whether treated or untreated, showed diminished skin test responses to PPD and trichophyton, but two of the PPD-negative untreated SLE patients showed significant lymphocyte transformation in vitro with PPD. The skin test responses and in vitro responses of lymphocytes from SLE patients to nDNA did not differ significantly from those of controls. The majority of SLE patients had circulating antibodies to nDNA. The authors suggest that the use of standard PPD skin tests for tuberculosis screening in SLE may be misleading and that susceptibility to infections in SLE may relate to impaired delayed hypersensitivity. — P.F.


The proportions of T and B lymphocytes in peripheral blood of 46 patients with multiple myeloma and of 14 patients with "benign monoclonal gammopathy" were compared by immunofluorescent studies. IgA, IgG, and IgM surface receptor sites were assessed by direct immunofluorescence with fluorescein-conjugated rabbit antibody. T lymphocytes were estimated with absorbed rabbit antihuman fetal thymocyte antisera and with added fluoresceinated goat antirabbit α globulin in an indirect fluorescent system. In 50 normal subjects, normal mean for B cells was 22.9 ± 7.9; normal T was 75.3 ± 13.9. Anti-idiotypic antisera to isolated M-components were prepared in rabbits, and after adsorption with normal serum, were used to determine intrinsic cell surface localization of monoclonal protein. Mean B cell value in benign monoclonal gammopathy was near normal (21.4 ± 11.7), while in myeloma patients, it was 10.3 ± 6.9. Some myeloma patients in remission showed more normal proportions of B cells. Idiotype M-component markers were present in high proportions of blood lymphocytes in two myeloma patients, but not in cells from benign M-component patients. B cell values overlapped in some subjects of both categories, and with normal subjects. — P.F.

In a 27-yr-old phenotypically normal male, a diagnosis of chronic myelocytic leukemia was established on the basis of blood count, granulocytic hyperplasia, and low alkaline phosphatase score. Six months after diagnosis and Myleran treatment, blastic crisis occurred. In the chronic stage, two cell lines were identified in bone marrow: 45, X0, Ph' and 46, XY, Ph; peripheral blood lymphocytes in remission showed 46 XY. After blastic transformation, 46 XY Ph' cells showed gradual increase and there was development of three modal lines with 46, 60, and 85 chromosomes. It was considered that the bone marrow mosaicism was acquired. The constant presence of the Y chromosome after blastic transformation was considered to provide evidence of origination of the acute transformation from a single clone.—P.F.


Skin manifestations are common in patients with immunodeficiency states. Among the most common are pyoderma (staph. or strep.), candidal infections, eczema, progressive vaccinia after vaccination, herpetic infections, warts, and oral ulcerations.—P.F.


In normal children and adults, modal class size of peripheral blood lymphocytes is 9.5-10.4 μ, with the curve skewed slightly to the right. Acute infections result in irregular alterations in the size distribution curve. Abnormal size distribution curves were found in immunodeficiency states. In combined immunodeficiency, two peaks were found, at 13 μ and 15 μ. In one patient with Wiskott-Aldrich syndrome, normalization of the curve occurred following successful bone marrow transplantation.—P.F.


The authors report findings in the thymus of three patients with systemic sclerosis (scleroderma). At necropsy, changes of scleroderma were evident in viscera and skin. Thymus tissue was studied histologically and compared with normal age involution. Two of the three showed some degree of atrophy greater than age would account for, and all three showed relative cortical atrophy. Plasma cells were also present. Possible explanations include superimposed "stress involution," or the possibility of hyperplasia followed by involution as part of a national history of autoimmune disease (analogous to Hashimoto's disease).—P.F.


Thrombopenia in sarcoidosis may result either from hypersplenism or immunologic destruction. Only in the latter case is there likely to be evidence of significant bleeding. In some patients whose sarcoidosis is not accompanied by portal hypertension, relatively asymptomatic thrombopenia may be seen; in others, acute fulminating hemorrhage necessitating steroid and/or surgical therapy is necessary.—J.B.S.


Although pericarditis is common in SLE, massive pericardial effusion as the presenting sign is not. A 15-yr-old girl admitted with complaints of fever, shortness of breath, and nonpleuritic left chest pain had such. Diagnosis of SLE was made on the basis of a positive LE prep, and on an ANA titer of 1024. Steroid therapy led to a prompt remission.—J.B.S.


Twenty-one per cent of the patients with Hodgkin's disease and other lymphomas, vaccinated with a vaccine containing Influenza A Singapore virus did not respond with a fourfold rise in titer. In the control group, every-
one showed an adequate antibody response. No correlation was found between antibody response in the patients and treatment, during the immunization period, with prednisone, cytostatics, or a combination of the two. The incapacity of antibody formation, however, was associated with radiotherapy. A significant difference in HL-A 12 frequency was found between patients with adequate antibody response to influenza vaccination (HL-A 12 frequency 13%), and those without antibody formation (HL-A 12 frequency 62%). — K. P.

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The Sézary Syndrome is characterized by pruritic and pigmented erythroderma, lymphadenopathy, and the presence of abnormal leucocytes in the skin infiltrates and in the peripheral blood. Ultrastructural studies of the Sézary cells have demonstrated that their main feature is a cerebriform and serpentine aspect of the nucleus. Abnormal karyotypes with polyplody and heteroploidy and with marked chromosomes were documented by cytogenetic studies. Whether Sézary cells belong to the lymphocytic or the monocytic series has been much disputed in the past. The results of recent studies are strongly in favor of the lymphoid nature of these cells. In the present study, in four of six patients with this syndrome, the abnormal cells were smaller than the classic large Sézary cells. The membrane properties of the abnormal cells were studied by various techniques including electron microscopy, cytogenetic analysis, immunofluorescence, and rosette formation. The results demonstrated that these cells have similar ultrastructural and chromosomal characteristics as the typical large Sézary cells. The abnormal cells were devoid of membrane-bound immunoglobulin detectable by immunofluorescence, did not bind aggregated human IgG, were able to form spontaneous rosettes with sheep erythrocytes, and, in three patients studied, were killed by specific rabbit antihuman T cell antiserum. These findings all indicate that these cells are related to thymus-derived lymphocytes. — M. G. B.


Leukocytes from one of 696 specimens of umbilical cord blood were observed to transform into rapidly and persistently multiplying lymphoid cells. This finding was interpreted as a manifestation of in utero infection by the Epstein-Barr virus. The neonate whose blood contained leukocytes that transformed has been under observation for 24 mo and he has so far had no significant abnormalities. The study was performed because of the possibility that in any immunologically deficient host, such as a fetus, a lymphostimulatory process caused by a virus may result in acute leukemia. This is a provocative hypothesis and the observation of the interesting newborn will continue. — M. G. B.


Idiopathic pulmonary hemosiderosis is a life threatening disease the cause of which is unknown. An immunologic basis has been suggested by various investigators. For this reason, immunosuppressive therapy has been utilized in a small number of cases and was believed to have been responsible for the subsequent remission (Lancet, 1:140, 1965. Acta Med Iugosl, 24:61, 1970). In this report, a 22-yr-old man with life threatening idiopathic pulmonary hemosiderosis of three yr duration experienced prompt and lasting remission of his disease with the institution of immunosuppressive therapy with azathioprine. Response of this patient is encouraging and suggests further trials with immunosuppressive therapy in this life-threatening disease. — M. G. B.

**MISCELLANEOUS**


The authors were able to determine the blood volume (BV) of 16 normal full-term newborns during the first day of life without perinatal pathology. The method used was to dilute the human serum albumin labeled with technetium-99m (HSA-99mTc). The results showed a mean
When the first edition of this classical book appeared exactly 20 years ago under the title Human Blood Coagulation and Its Disorders, the entire text was written by Biggs and MacFarlane. In that era the clinical and research aspects of blood coagulation seemed less complicated than they do today. Thus the 20th anniversary of this text reflects the passage of time in a marked increase in overall size, multiple authorship, and an appropriate change of title. Although MacFarlane has since retired, it is gratifying to see that he has written both the initial and concluding chapters of this edition, in which his lucid and objective approach to the theory of blood coagulation and the hemostatic mechanism is reflected. Forty years of personal research experience are combined with a survey of pertinent contributions from the world literature. As a matter of fact, it is suggested that these two chapters be read by way of introduction to the remaining contributions, as they offer a perspective which renders other parts of the book even more intelligible.

The opening chapter discusses the thrombin-fibrinogen reaction as well as fibrin stabilization. An overview of the extrinsic system for prothrombin activation is given by Esnouf, covering in some detail recent contributions from both his own laboratory and that of Nemerson. The section on the intrinsic prothrombin activation written by Biggs has been a mainstay of all previous editions and concludes with a chart whose summary of three possible alternative theories of the blood coagulation mechanism is especially helpful for teaching purposes.

One of the highlights of this edition is a meticulous consideration of the contact system by Hymie Nossel. The chapter is almost a monograph and includes an extensive reference list. The biochemical properties of Hageman factor, PTA factor, and the information contained in the text make this section especially useful for those unfamiliar with the contact mechanism. The final chapter by Biggs and MacFarlane provides a comprehensive review of the hemostatic mechanism, emphasizing the role of platelets and the clotting factors in maintaining normal hemostasis.


Hematology: Principles and Practice being issued in temporal proximity to Williams' Textbook of Hematology will bear comparison to the latter by a prospective purchaser. The two texts, however, serve different purposes. Williams' textbook is encyclopedic. Mengel's text appears designed to survey concisely each area in the field of hematology. Background material is succinctly but usually adequately presented with ample references listed for more detailed investigation by the reader. Indeed, some chapters are delightful distillations of complex areas, for example, Gurney on erythropoiesis, Mengel and Rosse on hemolytic anemias, Frei on chemotherapeutic principles, and Marcus on the platelet. The discussions of therapy are also succinct, usually reflecting the consensus and not the individual author's preferences. An aficionado might find fault with discussions of particular treatment regimens, for example, therapy of hematologic malignancies, but the audience for whom the text is apparently designed, namely medical students, house officers, and general internists, should relish the emphasis on pathophysiology and the clinical aspects of hematologic states, for these are the areas that will engage them in the workaday world—Jonathan Glass, M.D.


When the first edition of this classical book appeared exactly 20 years ago under the title...