ABSTRACTS

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ERYTHROCYTES


Hemoglobin PA3, which is the minor component in hemolysates of erythrocytes of homozygous carriers of Porto Alegre hemoglobin, has an anodic mobility at pH 8.1 that is larger than the corresponding one (Hb A3) in normal hemolysates. This faster, minor hemoglobin component is characterized by the following properties: (1) The relative concentration in the aged hemolysate is 28±4.1%. (2) Two -SH groups per tetramer have been determined by p-hydroxymercuribenzoate titration, but after reduction by -mercaptoethanol, two additional free -SH groups per tetramer have been demonstrated, indicating that this minor Hb PA3 component derives from hemoglobin Porto Alegre where two extra free -SH groups per tetramer have been demonstrated. (3) After aging, it does not originate a product of polymerization of the tetramers as does the Porto Alegre hemoglobin from which it is formed. (4) The reaction with mercuric chloride does not determine the formation of a product of polymerization of the tetramers of the minor component as it does for the tetramers of the major band of the Porto Alegre hemoglobin. (5) Incubation with oxidized glutathione before and after the reaction with N-ethylmaleimide indicates that the extra thiol groups have formed a mixed disulfide with glutathione.


Ninety-five patients having Starr-Edwards ball and cage prosthesis were studied. Uri-
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nary hemosiderin test proved useful as a screening test for intravascular hemolysis that was common and marked, especially after aortic valve replacement. The degree of urinary hemosiderinuria correlated well with the activity of the hemolytic process. —J.M.B.


Saliva is known to be able to bind B12. Saliva from 48 normal individuals, 11 patients with chronic granulocytic leukemia, and 11 with pernicious anemia was tested for its ability to bind B12. No difference was found between the groups. Three patients with pernicious anemia bound B12 normally in their saliva, although they had intrinsic factor-blocking antibodies, and sera containing blocking antibodies did not prevent B12 binding by saliva when mixed with it. B12 bound to saliva was normally absorbed in a Schilling test. The clinical role and significance of the salivary B12 binder remains unknown.—F.W.G.


The full-term infants increased oxygen affinity decreases during the first 4-6 mo of life to normal adult values; this "shifting to the right" of the Ps0 correlates well with the "functioning DPG fraction" (DPG mmoles/ml RBC × Hb A %). Premature infants, with their higher levels of Hb F and lower levels of DPC, have greater oxygen affinity than do term infants and do not reach normal adult oxygen-hemoglobin equilibrium until about 6 mo of age. Infants with respiratory distress have lower DPG levels than healthy infants of similar gestational age. The resultant shift of the Ps0 to the left may be disadvantageous to the sick infant. In four infants who were exchange transfused, the increases in Hb A in DPG led to a marked increase (shift to the right) in the Ps0. Whether exchange transfusion with fresh blood is beneficial to small infants with respiratory distress syndrome (RDS) is not yet known.—J.B.S.


During a period of 3 yr, anemia was observed in 15 of 60 children with lambliasis. In 13 of these cases, anemia was hypochromic. In one case, anemia was associated with thrombocytopenia. In another one, pronounced hypoplasia of the erythropoietic, leukopoietic, and thrombopoietic systems was observed. Inhibition of the erythroblastic series, maturation arrest, and megaloblastosis are observed in the majority of cases with anemia. In 50% of patients, platelet counts were moderately diminished. Antiparasitic treatment induced normalization of the hematologic picture in all patients.—M.K.

Megaloblastic Anemia Due to Folic Acid Deficiency. M. Ochocka and A. Killander. Department of Pediatric Therapy, School of Medicine, Warsaw, Poland, and Institute of Medical Chemistry, University of Uppsala, Sweden. Pediat. Pol. 47:1-11, 1972.

The authors present an analysis of 35 cases of megaloblastic anemia due to folic acid deficiency (28 infants aged from 7 wk to 18 mo, and 5 children aged from 3 to 14 yr). These cases were selected from a group of 300 patients with anemia on the basis of determination of folic acid activity in the serum. In some patients, vitamin B12 level in serum and urinary excretion of FIGLU were also examined. Anemia was severe, particularly in infants. In 14 cases, the hemoglobin level was below 6 g/100 ml, and the highest level was 9.1 g/100 ml. The level of folic acid ranged from 0.5 to 2.2 ng/ml. In all patients, a megaloblastic transformation was observed in the bone marrow. The percentage of megaloblasts

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was from 7% to 50% of all nucleated cells of the erythrocytic series. The cause of megaloblastic anemia due to folic acid deficiency in infants was, most frequently, the poor quality of the food received and present or previous infections. In older children the causes included massive hemolysis, blood loss, and malabsorption. Five children died from the underlying disease. In the remaining cases, treatment with folic acid resulted in complete recovery. The strikingly good effect of folic acid on the psychomotor disturbances in these children is stressed. The particularly frequent occurrence of megaloblastic anemia in infancy shows that there is an evident predisposition for folic acid deficiency at this age.

—M.K.


The level of vitamin B₁₂ was determined in serum of 25 children with giardiasis and 12 children of the same age infested with Trichocephalus dispar. The results were compared with the values obtained for the control group. Significant reduction of vitamin B₁₂ level was found in giardiasis but not in cases of infestation with Trichocephalus.—M.K.

LEUKOCYTES


Forty-nine patients with Hodgkin’s disease were studied. Exploratory laparotomy including needle and wedge liver biopsies were performed for staging purposes, and the pathologic condition of the liver was compared with the preoperative liver scans. In this group of patients, focal filling defects on the liver scintigraph were always associated with hepatic Hodgkin’s disease, although this abnormality on the scintigraph occurred infrequently. A nonuniform uptake of radioactivity in the liver was the most common sign of liver disease, but this was not specific for Hodgkin’s disease and was often associated with liver granulomas. Hodgkin’s disease was never found in the liver biopsy specimens of the patients in this series in whom the liver scintigraph was normal. Laparotomy with liver biopsy remains the most specific means for staging abdominal Hodgkin’s disease.—J.E.U.


The data obtained in 42 patients with Hodgkin’s disease who underwent exploratory laparotomy with splenectomy were analyzed to assess the usefulness of the criteria leading to the interpretation of the preoperative splenic scintigraph. Focal defects and marked splenomegaly indicated Hodgkin’s disease in the spleen, although these findings were frequently not present. Other criteria were more sensitive but were less specific indicators of Hodgkin’s disease in the spleen. Clinical palpability was a poor method for determining splenic size or involvement with Hodgkin’s disease. Pathologic examination remains the most reliable means of detecting Hodgkin’s disease in the spleen.—J.E.U.


Three cases of Hodgkin’s disease of the lung with involvement of the bronchial mucosa are reported. In one of them, the initial diagnosis of Hodgkin’s disease was established by bronchial brush biopsy; in the two others the disease was known to
exist elsewhere, but this procedure made it possible to establish pulmonary involvement unequivocally. In contrast to epithelial tumors, cytologic examination was negative in all three cases, even though the diagnosis could be made without difficulty from examination of histologic sections. Involvement of the bronchial mucosa in pulmonary Hodgkin's disease occurs by direct extension of the disease from bronchial lymph nodes.

—J.E.U.


An abundance of foamy macrophages in tissues containing Hodgkin's disease is reported. Although this observation has been reported previously, in our series it was found only in nodular sclerosing Hodgkin's disease. The incidence of this histologic feature was 2% (six) of all 280 cases reviewed and 6% (six) of the 96 cases classified as nodular sclerosing Hodgkin's disease in this series. Necrosis was always evident in lymph nodes containing foamy macrophages. The abundance of these cells may give rise to an erroneous diagnosis of lipid storage disease. The histologic picture in the areas of abundant foam cells also resembles the recently reported and described new entity of massive sinus histiocytosis.—J.E.U.


Combination chemotherapy (MOPP) employing four drugs—nitrogen mustard, vincristine, procarbazine, and prednisolone, all with different modes of action at cell level—was used in the management of 55 patients suffering from advanced progressive Hodgkin's disease. The drugs were administered under a strict protocol over a 10-day period each month for 6 mo, with subsequent maintenance therapy being administered at longer intervals. Each period of drug administration was followed by a period during which no drug was given. Forty-four patients had stage IV disease, and 11 had stage III disease. All but six of the patients had received previous therapy with irradiation and/or chemical drugs. Twenty-seven had received previous irradiation and chemotherapy, and 22 had received irradiation alone. Forty-six out of 55 patients (83.6%) had complete remission (total regression of all lesions) to the four-drug combination, and three patients had partial remission. The median length of remission has been estimated at 28 mo. Those patients treated previously with both radiotherapy and chemotherapy have not responded as well as those who received irradiation alone. Those patients whose tissue biopsy showed greater than 50% atypical histiocytes tended to have a shorter remission time. Drug toxicity has not proved to be a major problem in the protocol employed. The first 27-mo progress in this group of 55 patients is discussed. This study emphasizes usefulness of MOPP and results to be expected in patients previously treated by radiotherapy, chemotherapy, or both.—J.E.U.


Chromosome studies were carried out by a direct method in 28 subjects with malignant lymphomas. Lymph node cells were analyzed in 24, ascitic fluid sediments in three, and bone marrow cells in one. Chromosome abnormalities, both numerical and structural, were found in 12 of 14 cases of well-differentiated and poorly differentiated lymphocytic lymphomas and reticulum cell sarcomas, and in eight of 14 cases with Hodgkin’s disease. The karyotypes were different from case to case, and there was no correlation with the histology. In individual cases, the abnormalities followed a clonal pattern indicating a common precursor for the abnormal cells. The modal number of chromosomes was near diploid in the lymphocytic lymphomas and reticulum cell sarcomas. Hodgkin's disease showed two main features: a predominant popula-
tion of cells with normal karyotype accompanied by a small number of cells of an abnormal clone with a predominantly hypertriploid number of chromosomes. It is suggested that the first population represents mitoses in the "surrounding" lymphocytes. Its cytogenetic normality is an argument against its neoplastic origin, and they could be components of an inflammatory reaction, the true neoplastic cells being the abnormal reticulum cells.—M.J.


Two patients (female, aged 45 and male, aged 68) developed profound neutropenia with septicemia some 6 wk following treatment with procainamide. Both recovered from the septicemic episode, and the agranulocytosis resolved. However, the female subsequently developed positive antinuclear antibody and died from hemorrhagic pancreatitis and anuria.—J.M.B.


The incidence, clinical manifestations, course, and treatment of central nervous system (CNS) involvement are described in 60 children with acute leukemia, diagnosed and treated at the Chaim Sheba Medical Center, Tel-Hashomer between 1965 and 1970. The median survival time in the 60 patients was 19 mo, 31 mo for patients with acute lymphoblastic leukemia and 9 mo for patients with other forms of the disease. CNS involvement was diagnosed in 30% of the cases, in 36% of those with lymphoblastic leukemia and in 17% of those with myeloblastic or undifferentiated leukemia. The median survival of patients with lymphoblastic leukemia and CNS involvement was 20-27 mo. The median survival of the patients without CNS disease could not be calculated. It was, however, longer than 31 mo. The deleterious effect of CNS infiltration on the survival of children with leukemia clearly indicates the need for more aggressive therapeutic and prophylactic measures in such cases. Treatment with methotrexate intrathecally was effective in alleviating the clinical symptoms but not in eradicating CNS infiltration.—B.R.

Thromboplastic Activity of Lymphocytes from Patients with Chronic Lymphatic Leukemia (CLL). B. Maikiewicz, B. Bierułacka, and J. Lisiewicz. Department of Clinical Chemistry and Department of Hematology, School of Medicine, Kraków, Poland. Przegl. Lek. 28:625-629, 1971.

Lymphocytes were separated from the blood of patients with CLL, were homogenized in Owren's buffer, and were centrifuged for 30 min at 105,000 g. The slightly active sediment was discarded, and the supernatant was subjected to column chromatography on Sephadex G-200. The high molecular fraction isolated by chromatography and showing a pronounced thromboplastic activity was partially characterized. Heating for 2-8 min at 20°C and 37°C had no effect, but temperatures of 65°C or 100°C induced a marked fall in activity. The pH optimum was found to be approximately 8.0. The activity could be transferred into chloroform-methanol by extraction of aqueous solutions.—M.K.


Changes in the medium after short-term culture of white blood cells from leukemic patients were examined by polyacrylamide gel electrophoresis. In cases of lymphatic leukemia, a significant fall in gamma globulins, while in cases of myeloid leukemia a rise of α2-globulins, was observed. Degradation of immunoglobulins present in the medium is considered as a probable cause for the changes observed.—M.K.

Activity of Leukocyte Alkaline Phosphatase
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During Treatment with Typhoid Vaccine. H. Hanczyc, B. Maj-Sampiowska, and P. Hanczyc. Department of Gastroenterology and Department of Ophthalmology, School of Medicine, Wroclaw, Poland. Pol. Tyg. Lek. 27:48-50, 1972.

Activity of leukocyte alkaline phosphatase (LAP) was examined by the histochemical method of Kaplow in 14 people before intravenous injection of 0.05 ml of typhoid vaccine, as well as 24 and 48 hr thereafter. Significant increase of LAP scores was observed 24 hr after vaccine injection.


The influence of aflatoxin B₁ on normal lymphocytes cultured for 72 hr in the presence of PHA was examined. Cytolytic effects, complete inhibition of mitoses, and pronounced inhibition of PHA-induced blastic transformation were observed in cultures containing 0.05 μg/ml of aflatoxin B₁. The significance of the toxic effects on lymphocytes of aflatoxin B₁ is discussed with reference to its oncogenic activity.


Ten patients with malignant lymphoma (Hodgkin's disease, lymphosarcoma, giant follicular reticulosarcoma, and lymphoreticulosarcoma) were treated by intralymphatic administration of 131I Lipiodol Ultra-Fluid. Follow-up x-ray examinations demonstrated a systematic reduction in the size of the lymph nodes. Disappearance of systemic manifestations was also observed. Duration of the remission ranged from 1 mo to 3 yr. Undesirable side effects were not observed.


The activity of alkaline phosphatase of neutrophils (GAP) was determined in 16 girls on the first, seventh, 14th, and 21st day of the menstrual cycle. Significant fluctuations were observed. GAP activity was found to be lowest on the first day of the cycle (first day of menstruation) and the highest on the 21st day. These fluctuations may be connected with changes in estrogen concentration during the cycle.


Diurnal variations of serum muramidase activity and of percentage of neutrophils were demonstrated in the peripheral blood of healthy rabbits. Simultaneously with the increase in the percentage of neutrophils, a slight increase in the number of young forms was also observed. A fixed time for blood withdrawal is emphasized as an essential factor for the standardization of the methods for determination of muramidase activity in the serum.

The Effect of Indospicine on Bone Marrow Cells in Liquid Culture. F. G. de Munk, G. S. Christie, and M. P. Hegarty. Department of Pathology, University of Melbourne, Parkville, Victoria, Australia. Pathology 4:130, 1972.

Indospicine (L-2-amino-6-amidino hexanoic acid) is a naturally occurring arginine antagonist extracted from the seed of a tropical legume, Indigofera spicata. When added to liquid cultures of mouse marrow cells, concentrations of Indospicine ten times those of the arginine in the culture medium almost completely inhibited 3H-thymidine
incorporation after a culture period of 96 hr. Inhibition was competitive and reversible. Cells were insensitive during the first 4 hr of culture and became progressively more sensitive up to 4 days when maximal inhibition occurred.—F.W.G.

HEMOSTASIS


The circulatory changes observed in the retina during diabetes are similar to those found in macroglobulinemia, hemoglobinopathies, Eales' disease, and retinal thrombosis. Although the physiopathology of retinal vascular changes is known in most of these diseases, the cause of diabetic retinopathy is still unknown. The author suggests that the retinal capillary thrombosis noted in diabetes is due to increased platelet adhesiveness, for it occurs before any sign of retinopathy. The ultrastructural evidence of spontaneous platelet aggregation suggests a possible pathogenetic theory for diabetic retinopathy.—J.C.


The authors measured factor VIII levels by one- and two-stage methods in 16 women using oral contraceptives (OC) and 16 control subjects. In women on OC, factor VIII, measured by one-stage assay, was increased, while no increase was obtained by the two-stage assay. Studies on fibrinogen turnover were normal in most women on OC. These results suggested that the elevated one-stage factor VIII levels were not the result of intravascular coagulation (IVC) although occult IVC may be present in an occasional woman taking OC.—H.J.W.


The authors describe a serial dilution protamine sulfate (SDPS) test for detecting fibrin monomers and fibrin degradation products (FDP). The test is sensitive to 2–5 mg/100 fibrin monomer and 5–10 mg/100 ml early FDP. The test was approximately 20 times as sensitive in detecting FDP as the ethanol gelation test. The SDPS was negative in normal plasma and primary fibrinolytic states, and was positive in diffuse intravascular coagulation and when fibrin digestion was induced by thrombolytic drugs.—H.J.W.


A Puerto Rican boy whose only evidence of bleeding disorder was frequent, severe epistaxis was found to have factor VII levels below 7%. His parents and two of his four siblings had factor VII levels of 40%–50%. Two other siblings had levels of 95%–100%. The mother (factor VII 45%) had a history of menorrhagia and excessive bleeding following tonsillectomy. Several maternal relatives had a history of epistaxis.—J.B.S.


Pregnant sheep and their attached fetuses were studied after thromboplastin infusion into one member of the pair, with or without prior heparinization, and after infusion of fibrin split products (FSP). Following infusion of thromboplastin into the ewe, there was a rapid fall in platelets and a marked increase in PTT, PT, and TT, with appearance of FSP in serum and urine. Within 25 min fetal thrombocytopenia appeared, followed by prolongation of PTT, PT, and TT, but without the appearance of FSP. When the fetus was infused with thromboplastin, changes in the fetus were the same as when the mother received the thromboplastin. Changes in the mother
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A case of Waldenström macroglobulinemia with leukemic changes in the peripheral blood and complex disturbances in hemostasis is reported. Defective structure of the clot, due to inclusion of large amounts of carbohydrate-rich macroglobulin in the fibrin net and to severely impaired platelet function only partially due to coating of thrombocytes by macroglobulin, were the main laboratory findings explaining the observed hemorrhagic tendency.—M.K.

IMMUNOHEMATOLOGY


A case of Waldenström macroglobulinemia were less marked. Her platelets fell moderately, fibrinogen levels decreased slightly, and FSP were found in her serum and urine. Even at 7 wk of age, lambs infused with sufficient thromboplastin to produce intravascular coagulation did not demonstrate FSP production. When heparinization preceded thromboplastin infusion into either ewe or lamb, all coagulation levels and factor assays remained normal. Following administration of FSP to the mother, coagulation tests and factor assays remained unchanged in both animals. When FSP, at a higher per kilogram dosage, was infused into the fetus, there was a marked fall in platelets and minimal changes in coagulation tests. The coagulation status of the mother remained normal. That some factor or factors capable of inducing intravascular coagulation cross the placenta in either direction seems clear. The study demonstrates that neither thromboplastin nor FSP can be implicated. This study, in contrast to others, suggests that young animals have a poorly developed fibrinolytic mechanism.—J.B.S.


Fibrin-stabilizing factor (FSF) activity was examined in 92 patients with various hematologic disorders and in 31 blood donors. Decreased FSF activity was demonstrated in two cases with liver cirrhosis and in eight hematologic cases mainly with malignant proliferative diseases of the hematopoietic system. Addition of cysteine induced a pronounced increase of FSF activity particularly in plasma from cases with abnormally low activity of FSF.—M.K.

The Mechanism of Rosette Formation between Rh (D) Positive Erythrocytes and Peripheral Blood Lymphocytes from Rh Isoimmunized Individuals. The Role of Surface Micro Projections. C. J. Elson, J. Bradley, and R. E. Howells. Immunopathology Division, Nuffield Unit of Medical Genetics, Department of Medicine and Department of Parasitology, Liverpool School of Tropical Medicine, University of Liverpool, Liverpool, England. Immunology 22(6):1075, 1972.

When A Rh (D) positive erythrocytes were added to peripheral blood leukocytes from Group A Rh (D) negative male volunteers injected with A Rh positive erythrocytes, rosettes were formed. Differences in the number and pattern of the rosettes were noted at 4°C and 37°C. Electron microscopic studies of the rosettes showed the erythrocytes to be often attached to microprojections from the surface of the central rosette-forming cell. Further studies suggested that the contractile activity of the surface of the rosette-forming cell is important in rosette formation.—J.M.B.


Phytohemagglutinin-stimulated cultures of lymphocytes from 26 patients with myelomatosis showed binucleated blast cells in 17, whereas of 16 cultures from normal individuals these cells were noted in only...
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Differential leukocyte counts in the blood and bone marrow and the reaction of peripheral blood leukocytes to a single intravenous injection of hydrocortisone were examined in a large group of patients with severe and advanced rheumatoid arthritis (RA). Hyperplasia of the granulopoietic system in the bone marrow with a shift to young forms and an absolute increase of peripheral granulocytes were demonstrated in the majority of the cases of RA as compared with control, healthy subjects. The increase of granulocyte counts after hydrocortisone injection was smaller, and the fall of lymphocyte counts greater in patients with RA than in the controls. Nine per cent of RA patients showed persistent leukopenia. Leukopenia occurred more frequently in the cases of RA with the presence of antinuclear factors in the blood or with splenomegaly than in patients without these symptoms. In a group of RA patients with positive LE test, the frequency of leukopenia was the same in cases with and without splenomegaly. In 9.6% of patients, reactions of the hematopoietic system were strikingly different from the characteristic ones. These atypical reactions consisted of: (1) hypoplastic granulopoiesis with concomitant proliferation of lymphoid cells in the bone marrow and with chronic leukopenia; (2) lymphocyte proliferation in the bone marrow, lymph nodes, and spleen and high lymphocytosis in the peripheral blood; (3) pronounced proliferation of plasmacytes in the bone marrow; and (4) hyperplasia of eosinophilic granulocytes in the bone marrow and high percentage of eosinophils in the peripheral blood. Differentiation of these proliferative reactions from lymphatic leukemia, plasmacytoma, and eosinophilic leukemia was at times difficult. In the second part of this paper, the cell-mediated immunologic reactions were described. It was found that stimulation by PHA of lymphocytes in cultures was impaired in a high proportion of cases. RA patients also showed a much higher percentage of negative skin reactions to tuberculin and to 1-chloro-2,4-dinitrobenzene. Both stimulation of lymphocytes in vitro and skin-delayed hypersensitivity were mostly impaired in patients with a very high erythrocyte sedimentation rate, with generalized involvement of multiple joints, or with lung interstitial fibrosis, lesions of the heart, and liver and kidney involvement. Tests of

Separation of Antibodies from Subcellular Components of Lymphocytes. E. Merler and M. Silberschmidt. Immunology Division, Department of Medicine, Children's Hospital Medical Center and Departments of Bacteriology and Immunology and Pediatrics, Harvard Medical School, Boston, Mass. Immunology 22(5):813, 1972.

Three populations of antibody molecules were obtained from supernatant fluids derived from disrupted human lymphocytes. One of these was a fragment of IgG globulin and the other two, the one associated with residues of RNA and the other with residues of DNA, were IgG globulins, indistinguishable immunologically from serum IgG globulins.—J.M.B.


Australia antigen and antibody were examined in the sera of 24 children with Down's syndrome using the technique of Ouchterlony, double diffusion, and complement fixation. Australia antigen was detected in three of nine children living in special-care institutions but in none living with their parents. In sera of a control group of seven children living in the same special-care houses, because of other types of mental retardation, Australia antigen was not detected. Australia antibodies were absent in all cases examined. The results obtained confirm earlier observations of other authors indicating a high frequency of carriers of Australia antigen among the children with Down's syndrome living in institutions but not in family life conditions. —M.K.


Differential leukocyte counts in the blood and bone marrow and the reaction of peripheral blood leukocytes to a single intravenous injection of hydrocortisone were examined in a large group of patients with severe and advanced rheumatoid arthritis (RA). Hyperplasia of the granulopoietic system in the bone marrow with a shift to young forms and an absolute increase of peripheral granulocytes were demonstrated in the majority of the cases of RA as compared with control, healthy subjects. The increase of granulocyte counts after hydrocortisone injection was smaller, and the fall of lymphocyte counts greater in patients with RA than in the controls. Nine per cent of RA patients showed persistent leukopenia. Leukopenia occurred more frequently in the cases of RA with the presence of antinuclear factors in the blood or with splenomegaly than in patients without these symptoms. In a group of RA patients with positive LE test, the frequency of leukopenia was the same in cases with and without splenomegaly. In 9.6% of patients, reactions of the hematopoietic system were strikingly different from the characteristic ones. These atypical reactions consisted of: (1) hypoplastic granulopoiesis with concomitant proliferation of lymphoid cells in the bone marrow and with chronic leukopenia; (2) lymphocyte proliferation in the bone marrow, lymph nodes, and spleen and high lymphocytosis in the peripheral blood; (3) pronounced proliferation of plasmacytes in the bone marrow; and (4) hyperplasia of eosinophilic granulocytes in the bone marrow and high percentage of eosinophils in the peripheral blood. Differentiation of these proliferative reactions from lymphatic leukemia, plasmacytoma, and eosinophilic leukemia was at times difficult. In the second part of this paper, the cell-mediated immunologic reactions were described. It was found that stimulation by PHA of lymphocytes in cultures was impaired in a high proportion of cases. RA patients also showed a much higher percentage of negative skin reactions to tuberculin and to 1-chloro-2,4-dinitrobenzene. Both stimulation of lymphocytes in vitro and skin-delayed hypersensitivity were mostly impaired in patients with a very high erythrocyte sedimentation rate, with generalized involvement of multiple joints, or with lung interstitial fibrosis, lesions of the heart, and liver and kidney involvement. Tests of
humoral immunity did not show abnormalities. The significance of the deficiency of cell-mediated immunity is illustrated by the description of an outbreak of *Herpes zoster* and of varicella in RA patients showing these abnormalities. The deleterious as well as the probably beneficial effects of immunologic deficiency on tissue damage in RA are discussed, particularly with respect to immunosuppressive therapy of this disease.—M.K.

**MISCELLANEOUS**


In 1846, academician I. V. Buyalski, an eminent surgeon, published a paper "On Blood Transfusion" (Military Medical Journal, St. Petersburg, Vol. 1, part 18, 7–23, 1846) that significantly spread the concept of human blood transfusion. This operation, he wrote, is of great practical benefit and in extreme situations, a valuable last resort. He established indications for transfusion foremost of which was acute hemorrhage, although in each case many individual features had to be considered; he discussed dangerous factors and the decision to transfuse. Thus, a loss of 5–8 lb of blood, even if only a rough estimate, was a sure indication. He thought that indications were perhaps expanding and, in particular, he admitted the advisability of transfusion for hemorrhage from external wounds. Like tracheostomy in croup, blood transfusion was a lifesaving measure. He was the first to recommend transfusion in military medicine, a contribution of indisputable priority and noted in numerous monographs and textbooks on transfusiology. Blood donors, he stated, should be healthy persons, preferably relatives of the patient; a husband's blood could be used for the wife. In actual transfusion, he insisted on the meticulous observation of several rules, most important of which were to keep the blood warm and to avoid introduction of air into the vein. His technique varied little from that suggested by Dr. Volfo, a St. Petersburg obstetrician who, in 1832, performed the first human blood transfusion in Russia. Buyalski also issued warnings. A recently delivered woman surviving severe hemorrhage but remaining weak for 48 hr may be helped by transfusion but could also be harmed. This opinion, he admitted, was based on evidence inadequate for publication but was derived from personal experience and several communications. Interestingly, Buyalski himself did not perform a single human blood transfusion. A man of national prestige, he did not hesitate to administer a severe rebuke when required, yet at all times he retained his position in the van of medical opinion even though many of his colleagues subscribed to the authority of physicians in other countries. In discussing obstacles to the progress of transfusion, he mentioned the ignorance of some physicians who while conceding that transfusion might benefit a patient felt that it might somehow alter his individuality. To further the concept of transfusion he published the facts not only in a medical journal but also in a newspaper, the St. Petersburg Gazette. Hoping to see wide implementation of blood transfusion, he felt that he would be happy for his paper to become a focus from which the use of this new treatment would spread. Soviet hematologists and transfusiologists who, by the wide application of blood transfusion on a scientific basis, have developed a blood service in the USSR can remember with pride this outstanding scientist and his contributions to the development of transfusion—I. V. Buyalski, one of the first leaders in blood transfusion.—J.V.