ABSTRACTS

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ERYTHROCYTES


The stoichiometric competition for albumin binding which exists between salicylate and bilirubin has been made the basis of a method of assessing the bilirubin saturation of serum albumin. The technic is described, as are the results of its application to evaluate the risk of encephalopathy in jaundiced neonates. A linear correlation appears to exist between the serum albumin-bilirubin saturation and the concentration ratio of serum bilirubin to total serum protein, when the jaundice is not due to hyperbilirubinemia. The observation that such linearity does not exist when hyperbilirubinemia is due to erythroblastosis, until after exchange transfusion, may limit the usefulness of the technic.—J. B. S.


A machine is described for making comparable blood films from standard volumes of blood. The films were processed by the Kleihauer technic and all the fetal cells counted. The size of the fetomaternal bleed was then quantitated by referring the count to a standard graph. It is claimed that the method eliminates many errors of other technics and should be capable of automation.—A. L. B.


Pregnant women undergoing therapeutic abortion by hysterotomy or being delivered of non-viable infants received intravenous injections of their own plasma labelled with 59Fe. Detection of the label in the placenta

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and fetus indicated that most placental iron transfer occurred very rapidly but that some was retained in the placenta and transferred more slowly or not at all. Calculation of the amount of iron transferred to the fetus each day suggested that the mother’s plasma rather than red cells is the main source of fetal iron. Iron released from the placenta into the fetal circulation was mainly taken up by the liver and not immediately used for hemoglobin synthesis. The level of transferrin saturation was higher in the fetal than maternal plasma throughout pregnancy but there was no qualitative difference in the binding of iron by maternal and fetal transferrins so that the latter should not compete for iron. It is suggested that there is a unidirectional pumping system for iron in the placenta.—A. L. B.

INHERITANCE OF AN INCREASED SODIUM PUMP IN HUMAN RED CELLS. J. S. Wiley. From Department of Medicine, University of Sydney, Sydney, Australia. Nature (London) 221:1222–1224, 1969.

In hereditary spherocytosis an increased number of cation pump molecules was indicated by measurements of ouabain sensitive ATPase and Na influx in normal and affected red cells. It is suggested that a mutation at a control gene locus may explain both the increased Na pump and greater Na leak in the red cells in this disorder. —A. L. B.


From titrations made on 45 patients with various neoplasms the authors have been able to conclude that the erythrocytic cholinesterase activity (acetyl-cholinesterase) is usually distinctly raised in the anemia of neoplasia. Neoplasms located in the kidney and in the liver appeared to be distinguished by an abnormal increase of the enzyme activity. Evidence is provided for the relationship between the severity of the anemia and the increase of the erythrocytic cholinesterase in the neoplastic anemia.—G. M.


The chronology of the mitotic cycle in thalassemic erythroblasts was studied by combining cytolologic analysis of bone marrow smears with measurement of the length of mitosis in its various stages directly on erythropoietic cells “in vitro” and studies by microcinematography in phase contrast. Compared with normal erythroblasts the thalassemia major erythroblasts showed more rapid mitoses, which indicates a much more rapid rate of renewal of the cells. At the level of the bone marrow, and quite apart from peripheral hemolysis, the mechanism of the anemia is not so much a defect in erythroblast production, but rather a reduction in the number of proliferating cells. —G. M.

LEUKOCYTES


The heretofore undescribed association between neonatal leukemia and multiple congenital anomalies suggesting Ellis-van Creveld Syndrome, is reported. This male infant who died of acute myelocytic leukemia at 18 days of age demonstrated scaphocephaly, low-set ears, hypoplastic upper lip, hepatosplenomegaly, bilateral cryptorchidism; absent breast areolae, short ribs and extremities, and a normal karyotype. There was a history of maternal exposure to rubella early in the second trimester, which had been preceded by a flu-like illness.—J. B. S.

PHAGOCYTOSIS IN THE NEWBORN INFANT: HUMORAL AND CELLULAR FACTORS. M. E. Miller. From the Children’s Hospital,
Phagocytic and opsonic activity against yeast particles was studied in infants 3 to 5 days old. The opsonic activity of infant plasma in a system using standardized PMN suspensions from adult donors was less than observed with adult plasma, particularly at a plasma concentration of 2½ per cent. Where infant and adult PMN’s were compared, the PMN’s from 17 neonates took up a significantly lower number of yeast particles than did those from adults. Again a plasma concentration of 2.5 per cent appeared critical.—J. B. S.


Leukemic infiltration of one or both testes was seen in 4 boys with ALL, three of whom were young adolescents who had been on cyclic therapy for 2½ to 7 years. The fourth patient was a 5 year old in whom testicular involvement appeared 18 months after diagnosis. In all four, painless or almost painless non-tender testicular enlargement was noted. In the three patients who underwent contralateral biopsy, histologic evidence of leukemic infiltration was present. The appearance of testicular enlargement in these patients did not presage marrow relapse. The authors chose orchiectomy as the treatment in each patient. The one boy who developed enlargement of the remaining testis, received 1200 R over a 4 day period with an excellent response which persisted for 19 months, during which pubertal changes progressed normally. Abstractor’s comment: It is not clear, considering the response to irradiation, why the authors believe that orchietomy has a place in the therapy of this manifestation of acute leukemia.—J. B. S.


The new antitumor agent, a bisdiketopiperazine, caused considerable fall in circulating primitive cells when administered to patients with acute lymphatic leukemia and lymphosarcoma. In one patient there was bone marrow evidence of partial remission. Severe toxic effects—alopecia and gastroenteritis—were seen in only one patient. This drug is a member of a new class of antitumor compounds which may not show cross-resistance with other agents and merits further study.—A. L. B.


In two patients with acute leukemia (myelomonocytic and myeloblastic-promyelocytic), extracorporeal irradiation of blood (ECI) resulted in increased mitotic index in the marrow and increased incorporation of 3H-thymidine. The authors concluded that ECI caused increased proliferative activity of the leukemic cells suggesting in the first place that they are not end cells and secondly that a feedback mechanism may exist—destruction of peripheral leukemic cells leading to increased production by the marrow. It was suggested that ECI is of restricted therapeutic use per se but may be of value in stimulating marrow blast cells to move into a phase in which they are susceptible to intensive chemotherapy.—A. L. B.


A forty-one year old man had urticaria pigmentosa since 1954. Systemic mast cell disease became apparent in 1963 and progressed to involve bone, spleen and lymph nodes. There was roentgenographic evidence
of widespread involvement of the gastrointestinal tract and a large retroperitoneal mass thought to represent enlarged lymph nodes. Diffuse nodular interstitial infiltrates were apparent on chest roentgenograms and most likely represent pulmonary mastocytosis.—J. E. U.


A case is reported of a lymphoproliferative disorder with autoimmune hemolytic anemia and thrombocytopenia. Platelet agglutinins were demonstrated to be 19S gamma macroglobulins, a unique observation. The disease was initially manifested by lymphocyte and reticulum cell proliferation, and eventually by plasma cell proliferation with amyloid deposition. The patient's serum exhibited extreme diffuse hypergammaglobulinemia with an increase in both IgG and IgM components. The urine was remarkable for its high content of kappa and lambda light chains, Fd-like fragments and Fc-like fragments. The interrelationships between the pathologic findings and protein abnormalities are briefly discussed and compared with the lymphoma associated dysproteinemias reported in the literature. No other case reported in the literature has shown such a wide variety of pathologic, clinical and biochemical findings.—J. E. U.


The association between four factors—mother's irradiation before conception, in utero irradiation of the child, previous history of reproductive wastage, and early childhood virus diseases—was studied in children one to four years old. A simple rise in the number of factors did not consistently increase the risk for leukemia. Children with irradiation but without either of the pathologic conditions did not show a greater risk for leukemia, nor did those with the pathologic conditions but without irradiation. However, children exposed to two radiological factors who also had a history of one pathologic event had a significantly increased risk (2.69), as did those with a history of two pathologic factors who had also been exposed to one of the irradiation factors (3.36). The highest risk was 4.64 for children exposed to all four factors. Therefore, only when there was concordance of the two types of events, irradiation and pathologic, was the risk for leukemia significantly greater.—J. E. U.


Of 323 cases autopsied between 1960 and 1964, 203 had pathologic changes in the gastrointestinal tract. The cases were divided into reticulum cell sarcoma, lymphosarcoma, and Hodgkin's disease on the basis of the final histologic diagnosis. Upper gastrointestinal bleeding was most often of non-tumor origin particularly when there was no evidence of tumor in the stomach. Perforation was found to be more commonly due to the tumor itself rather than to therapy. Obstructions were found only in patients with reticulum cell sarcoma, and 60 per cent of these were in the jejenum or ileum. Ileocecal intussusception was found in 5 children or young adults. Obstructive jaundice was a complication in 14 cases, a slightly higher incidence than in previous series.—J. E. U.


Contrary to earlier reports, placentas from
humans, rats and guinea pigs failed to contain detectable L-asparaginase activity. — G. M.


Twenty-one healthy children and 10 children with Down's syndrome were examined. Cytochemical examinations of alkaline and acid phosphatase, nonspecific esterase and naphthol-ASD-chloralacetate esterase were carried out in peripheral leukocytes of all of them. The activity of alkaline and acid phosphatase was markedly decreased in neutrophilic granulocytes of the children suffering from Down's syndrome. Activities of the nonspecific esterase and naphthol-ASD-chloralacetate esterase of the leukocytes did not show any abnormality. — L. D.


Two females with clinical evidence of coagulation disorder had normal coagulation studies except for Factor VIII levels below 10 per cent. One had a hemophilic father and an apparently non-carrier mother; the other had a normal father, a hemophilic brother and a mother whose AHG level was 20 per cent. Since each patient seemed to be heterozygous for the abnormal X chromosome and since each had a normal karyotype, the genetic explanation for the presence of hemophilia is unknown. The possible mechanisms are discussed. — J. B. S.


Unconjugated bilirubin, in concentrations greater than 15 mg. per 100 ml., causes morphologic and functional changes in human platelets which are directly related to the bilirubin level. At increasing concentrations of bilirubin the platelets swell, develop filametous projections, aggregate, take on a yellow color, and finally lyse. Platelets exposed, in vitro or in vivo, to high concentrations of bilirubin frequently are relatively inactive in the TGT, and, although no change in platelet ATP content was noted, ADP-induced PF 3 activation appeared to be inhibited by high bilirubin concentrations. Clot retraction is also progressively inhibited by increasing concentrations of bilirubin. The authors suggest that these abnormalities are related to an inhibitory effect of bilirubin on ATP-ADP dependent systems. — J. B. S.


Aggregation of sheep platelets by 5-hydroxytryptamine (5-HT) was reduced by low concentrations of lysergic acid diethylamide and dibenzyline which are substances which block the D-receptors of intestinal smooth muscle. Platelet aggregation by ADP was not affected. Substances which block smooth muscle M-receptors were much less active. The results suggest the presence of D-receptors for 5-HT on platelets and that 5-HT does not necessarily aggregate platelets by releasing ADP. — A. L. B.


A study was made in the U.S.A., U.K. and Sweden of the blood types of young women who developed venous thromboembolism while taking oral contraceptives, during pregnancy or the puerperium, or at other times. There was a deficit of patients with blood type 0 in all groups studied but particularly when thromboembolism was associated with the use of oral contraceptives or with pregnancy. — A. L. B.

FIBRINOLYSIS PRODUCED BY CONTACT WITH A CATERPILLAR. C. L. Arocha-Pilango and M. Layrisse. From the Department of Physiopathology, Venezuelan Institute
Patients who had come into contact with Venezuelan caterpillars of the family Saturniidae developed a long-lasting fibrinolytic state. Caterpillar products digested human and bovine fibrin but activated only human plasminogen. Activity was completely inhibited by aprotinin (Trasylol) and partially by EACA. **Abstractor's comment:** This paper is important in suggesting a source of fibrinolytic activity developed which could be partly corrected by the addition of native fibrinogen. The inhibitor of plasma could be removed by heat defibrination, but it was not adsorbed to barium sulphate. Quantitative evaluation of fibrinogen showed a great decrease (16.4—53 per cent). There was also a decrease of thrombin adsorption to the ultrasound exposed fibrinogen during the first minute of incubation. Antithrombin, fibrinolytic activity or the urea solubility of the coagulum was not influenced under the conditions of ultrasound exposure mentioned above. The electrophoretic mobility of fibrinogen in the exposed plasma was changed so that it moved to the zones of β- and γ-globulins.—L. D.

**Inhibition of Blood Coagulation by Ultrasound.** B. Bilková. From the Department of Medical Physics, University of Brno, Czechoslovakia. Vnitřní Lék. 15:216–222, 1969.

Blood plasma was exposed to the ultrasound waves of a frequency of 0.8 Hz and of an intensity of 3.5 W/cm² for 10–60 minutes. By this exposure increased anti-thrombin activity developed which could be partly corrected by the addition of native fibrinogen. The inhibitor of plasma could be removed by heat defibrination, but it was not adsorbed to barium sulphate. Quantitative evaluation of fibrinogen showed a great decrease (16.4—53 per cent). There was also a decrease of thrombin adsorption to the ultrasound exposed fibrinogen during the first minute of incubation. Antithrombin, fibrinolytic activity or the urea solubility of the coagulum was not influenced under the conditions of ultrasound exposure mentioned above. The electrophoretic mobility of fibrinogen in the exposed plasma was changed so that it moved to the zones of β- and γ-globulins.—L. D.


The authors present a case of deficiency of fibrin stabilizing factor (factor XIII). It is the first case described in Brasil. A family was examined and one member (propositus) presented a hemorrhagic con-
dition. Marriage among relatives was present. The disease is hereditary and it is probably due to recessive autosomic gene transmission. Tests for fibrin instability, to point out absence or decrease of FSF, were abnormal in solutions of 5M urea or 2 per cent acetic acid. The patient was a female child, 16 months of age. Hemorrhagic symptoms were present as intracranial hemorrhage and hemorrhages through the umbilical cord. Treatment was symptomatic. Hemostasis was observed after transfusions of fresh plasma or whole fresh blood.—M. J.

IMMUNOHEMATOLOGY

NATURAL ISOHEMAGGLUTININ PRODUCTION BY THE FETUS. T. Thomaidis, A. Agathopoulos and N. Matsianiotis. From the University of Athens, St. Sophie's Children's Hospital, Athens, Greece. J. Pediat. 74:39-45, 1969.

Anti-A and/or anti-B isohemagglutinins were found in 57 per cent of 137 randomly selected cord bloods. More than half of the positive specimens contained IgM agglutinins, and a small number of infants had both IgG and IgM antibodies. Antibodies of IgA specificity were found in 2 specimens. The IgG isohemagglutinins, present in 23 specimens, were usually of low titer (below 1:4) which the authors interpret as suggesting they may have been of fetal origin, as were the IgA and IgM isoagglutinins.—J. B. S.


Immature rabbit marrow erythroblasts were less susceptible to immune lysis than mature erythroblasts possibly because antigenic sites on the external membrane increase during maturation. The process normally coincided with transition of cytoplasmic basophilia to acidophilia but experimental evidence was presented suggesting that the association of resistance to immune lysis with basophilia was coincidental.—A. L. B.


Administration of the drug combination to rabbits for several weeks reduced the production of precipitating antibodies to bovine serum albumin without altering total or differential white cell counts. Either drug alone was ineffective. Epinephrine may potentiate the effect of propiomazine on cell and subcellular membranes but the effect of the drugs on resistance to infection or other leucocyte functions is not yet known. This combination of drugs would be worth investigating as possible immunosuppressive agents.—A. L. B.


Lymphocytes of presumably extrathymic origin were obtained from an immunologically deficient child in whom there was complete failure of development of the thymus. They were poorly responsive to phytohemagglutinin and to antigens, and responsiveness was not induced by incubation with thymic or transfer factors.—J. E. U.


The incidence of antinuclear antibodies was determined to be 39 per cent in a group of 26 patients with Coombs positive acquired hemolytic anemia who lacked evidence of collagen disease or primary disturbances of the lymphoreticular system. There was no correlation between antinuclear antibodies and such factors as anemia, reticulocytosis, hypogammaglobulinemia and whether the Coombs reaction was related to pure IgG or to serum complement on the red cells. It has become increasingly apparent from the accumulating information on serum antibodies in patients with autoimmune diseases that multiple auto-antibodies against different tissue constituents are characteristic of this group of diseases. The significance of the antinuclear antibodies and their relationship

Freshly dispersed cells from four Burkitt’s lymphoma biopsies, and three ‘lymphoblast’ cell lines derived from the tumour were tested for capacity to synthesize immunoglobulins in vitro. Using labelled amino acid incorporation, electrophoretic, radio-immunoelectrophoretic and ultracentrifugation technics, it was possible to demonstrate the release of labelled proteins with antigenic characteristics of immunoglobulins by all four biopsy samples, and the two cell lines tested by these technics. One cell line produced IgG and type-k light chains, while another cell line produced IgA. Immunoglobulin synthesis was not detected in a third cell line. Cells from each biopsy specimen or cell line produced not more than one type of immunoglobulin, although there was a wide variation in the sedimentation coefficient of the protein molecules synthesized.—J. E. U.


Experiments were carried out on superlethally irradiated dogs with transplantation of allogeneic bone marrow. As shown, administration of methotrexate inhibited, but did not prevent lymphoid transformation in the transplants. Methotrexate produced an equal cytostatic effect on the hemopoietic stem cells (of mice), proliferating in the autologous, syngeneic and allogeneic organism. It is supposed that the mechanism of action of methotrexate consisted in nonspecific depression of proliferation of hemopoietic stem cells, not in a selective blocking effect on differentiation of hemopoietic cells in the lymphoid direction.—J. K.


Bone marrow obtained from 5 to 8 unrelated donor dogs was injected to irradiated dogs (a dose of 1,000 r.). In 8 of 9 such experiments there occurred only lymphoid differentiation of transplanted elements as when administration of bone marrow was from only one donor. Normal hemopoiesis was observed in one of the transplants. Consequently, the presence of an acute immune reaction of the “graft-versus-host type” did not prevent normal histogenesis of hemopoietic tissue from the recipient. Only one of 56 donor-recipient combinations proved to be adequate. Possibilities of clinical use of bone marrow mixture from many donors are discussed.—J. K.


On the basis of data in the literature and personal experimental results the author analyzes the main routes of histogenesis of the hemopoietic tissue under conditions of transplantation. The direction of differentiation of the parent hemopoietic cells depends on the induction effects from the recipient. In case of autotransplantation, the latter provide a priority to hemopoietic direction of histogenesis, whereas under conditions of allotransplantation, in the presence of marked differences in transplantation antigens, priority is acquired by the lymphoid direction of histogenesis, thus causing acute secondary disease. The necessity of a thymic factor for lymphoid differentiation of transplanted hemopoietic cells was proved. The possible significance of the phenomenon of allogeneic inhibition in reduction of the rate of proliferation of an allogeneic hemopoietic transplant is discussed.—J. K.

APPEARANCE OF ANTINUCLEAR ANTIBODY AFTER NEONATAL THYMECTOMY IN SWISS CF1 AND BALB/C MICE. I. ANIMALS UNDER STANDARD CONDITIONS. J. Thivolet and J. C. Monier, Laboratoire d’Hygiène,
ABSTRACTS


The authors have previously demonstrated that thymectomy in newborn Swiss mice is followed, a few months later, by the development of antinuclear antibodies in many of these animals. This study has been extended to CF1 and BALB/C mice of pure origin. These new experiments have shown that after thymectomy at birth, antinuclear antibodies are present in 81 per cent of Swiss mice at the thirtieth week, with a maximal titer of 2048 units; in 71.3 per cent of CF1 at the thirty-second week with a maximal titer of 512 units, and 66.6 per cent of BALB/C at the twenty-eighth week with a maximal titer of 64 units. Afterwards there was diminution of the number of positive animals and reduction of the antibody titer in these. In many other animals that remained positive, auto-antibodies were found first at the twelfth week in the Swiss, at the eighth in CF1 and at the sixteenth in BALB/C mice. Five of the thymectomised CF1 mice were anemic with an hematocrit between 9 to 20 per cent. There was no correlation between the presence of auto-antibodies and wasting disease in CF1 and Swiss mice. In these, thymectomy at birth was frequently followed by wasting disease. The mechanisms by which suppression of the thymus at birth may be responsible for the appearance of antinuclear antibodies, and the reasons why these diminish with time are discussed.—G. M.


Lymphocyte regeneration was studied after administration of Myleran in higher than lethal dosage and after bone marrow grafting in thymectomised rats. The lymphocyte regeneration appeared to be thymus-dependent as has already been shown after irradiation.—G. M.


Cold urticaria was found to be the solitary symptom in a patient with chronic lymphocytic leukemia and an associated cryoglobulinemia. Following therapy there was a concurrent remission in both the cold urticaria and cryoglobulinemia. It was then possible to produce local sensitization to cold in the patient's skin by injecting serum collected during the pretreatment phase. The injection of post-treatment serum was without effect. Cold urticaria could be induced not only by injection of the cryoprecipitate, an IgG immunoglobulin, in concentrations as low as 25 mg./100 ml. but also by the supernate after removal of the cryoglobulin. Addition of streptomycin to the serum prevented both cryoprecipitation in vitro and cold sensitization in vivo. Attempts to demonstrate an immunologic mechanism for the production of cold urticaria were unsuccessful.—J. E. U.


The red blood cells of an 11 year old boy suffering from acute lymphatic leukemia demonstrated after routine blood typing absence of antigen A and very weak properties of antigen B. His saliva contained A and B substances and in his serum anti-A and anti-B antibodies were absent. With more refined technic it was revealed that red cell antigens were of Am and B3 type. Although modification of A and B antigens has been encountered occasionally during the course of myeloblastic leukemia, this is the first case in which change of serologic properties was demonstrated in a patient with acute lymphatic leukemia.—Z. R.

Serum paraproteins of the patients with multiple myeloma often display sudanophilic “wax phenomenon” on the lipidogram following paper electrophoresis. Same phenomenon has been demonstrated in the urine of such patients. Molecular weight of such urinary paraproteins was found to be lower than albumin. The results of the thin-layer chromatography on silica-gel suggested that lipid constituent represents mostly neutral lipids. Beta and alpha lipoproteins were not detected by immunoelectrophoresis. Therefore authors assume that urinary paraproteins represent a complex of immunoglobulin subunits and lipids.

Abstractor's comment: To interpret the presented data one could also consider Hartmann's et al. conclusion that normal IgM as well as IgM paraproteins contain a certain quantity of lipids (Ann. Biol. Clin. 26:891-893, 1968).

Z. R.

MISCELLANEOUS


A boy with recurrent episodes of apparent iron-deficiency anemia is described. Despite negative GI workup, he had previously undergone surgery for a peptic ulcer, not demonstrable in the surgical specimen. Aside from pallor, and growth retardation the only unusual physical finding was a scattering of petechiae, one of which was biopsied, revealing hemosiderin deposition. Further workup revealed a few hemosiderin-containing macrophages in the gastric juice, and many in a needle biopsy and aspirate of the lung. At no time were roentgenograms of the chest abnormal, nor were there signs of pulmonary disease.—J. B. S.


In Greece, where exchange transfusion is usually performed because of neonatal jaundice resulting from causes other than Rh-erythroblastosis fetalis, mortality from the procedure is less than 1 per cent. The authors use a four-way valve which permits blood administration by gravity drip, rather than by “push,” which they believe decreases the hazards of the procedure.—J. B. S.


The PSP dye-binding capacity (D.B.C.) of infant sera was studied, along with serum albumin and bilirubin concentrations. The D.B.C. and albumin concentration were significantly greater in full-term than in premature infants. The observation that the amount of PSP bound per gram of total serum albumin was lower in premature infants may relate to previous observation that 1.5 Gm. per cent of the serum albumin is not available for PSP binding. In addition, the dye-binding ratio was lower in the presence of a hemolytic state, perhaps due to competition by heme pigments for binding sites. In vitro studies failed to reveal an effect of pH on the D.B.C. In general D.B.C. fell as serum bilirubin levels rose. In two jaundiced premature infants, administration of 2 Gm. albumin raised the D.B.C., with only a transient elevation of serum bilirubin. The authors describe the technic for measuring D.B.C. as too time-consuming to be of much clinical usefulness.—J. B. S.


After a study of the theoretical aspects of the zeta potential of particles in suspension, the authors studied the physiologic zeta potential of blood cells and platelets using venous blood and two electrophoretic apparatuses (zetameter and cytophosphometer). The results show that the latter is influenced by the suspending medium but that it reflects the physico-chemical equilibrium at the interface between the particles and the suspending medium.—G. M.