HEMOSTASIS


Gastrointestinal symptoms were present in 67 percent of 35 patients. Abdominal pain, mucus or bloody diarrhea and vomiting were the usual symptoms. The radiologic picture of the small intestine was quite similar to that seen in certain malabsorption syndromes. Biopsies of three cases and autopsy of one did not show characteristic histologic features and studies of vitamin A absorption were normal.—E. S.


In 6 of 11 cases, retinal, nasal, gingival, cutaneous and uterine hemorrhages were present. Paraproteins are supposed to modify the protein environment around platelets, according to the authors' observations. Immunoelectrophoresis has shown that this environment is represented by pathologic macromolecules. This finding explains the false positive immunologic reactions in the thromboagglutination tests. Platelet functions are, therefore, altered in macroglobulinemia, thereby causing hemorrhagic manifestations.

—P. d. N.


Study of 35 patients with arteriosclerosis showed that r and r + k value shortening correlated well with the increase in serum cholesterol level. Correlation with serum total lipids and beta lipoprotein concentrations
was poorer. Lipemic turbidity did not correlate with thromboelastographic parameters. —M. K.


Injection of progesterone into castrated female rabbits induced shortening of r and k values in 69 percent of the animals, some prolongation in 11 and no changes in 20. Progesterone had no influence on fibrinolysis in the thromboelastographic picture. —M. K.


One of the cases also had consistently low fibrinogen, 120 mg./100 ml. —E. S.

Von Willebrand’s Disease with Hemorrhagic Manifestations in Rare Sites: Description of a Case with Gastointestinal Hemorrhages. C. P. Bassi, A. Antonelli and A. Guidugli. From the University, Siena, Italy. Sett. Med. 54:960–976, 1966.

In a 19 year old woman, Factor IX deficiency was present. Steroid treatment was effective. —P. d. N.


Factor XI was determined in 42 children, one to 75 days old, and in the umbilical and maternal blood of three children. A slight deficiency of Factor XI was found in the newborn with minimal values during the first 24 hours. Normal values were reached after the third week. —P. d. N.


In 47 children, one to 74 days old, and in the umbilical and maternal blood of three newborn children, Factor XIII was determined. The values were lower than in adults. Normal values were reached in the 7th to 8th year. —P. d. N.


Hyроверotoninemia in these subjects can be due either to an anomaly in tryptophane metabolism or to an anomaly in uptake by blood platelets. —J. C.

Determination of Glucose-6-Phosphate Dehydrogenase (G6PD) in Platelets of Children with Ictero-Hemoglobinuric Favism. W. Tangheroni, A. Cao, A. Falorni and M. Vespa. From the University, Cagliari, Italy. Pediatria (Napoli) 75:36–47, 1967.

Twenty-seven patients and normal controls were studied. In 16 homozygous males, marked reduction of G6PD activity in platelets was observed. In 11 probably heterozygous females, the reduction was less pronounced. —P. d. N.


Twenty-nine subjects from 7 families of Sardinia were studied. Transmission of the erythrocyte and of the platelet defect was similar with incomplete dominance in heterozygous women. —P. d. N.

ABSTRACTS

Description of a new method with plans of the apparatus used are given in the paper. Normal values vary within restricted limits. —P. d. N.


A potent procoagulant excreted with human urine converts prothrombin to thrombin in the presence of Pf3 and Factor V. The procoagulant is heat stable, its excretion rate is considerably lower in uremic patients and slow i.v. administration in rabbits and dogs produces a transient state of hypercoagulability.—E. S.

ERYTHROCYTES


The secretory acid, pepsin and intrinsic factor were studied in 9 children with true juvenile pernicious anemia, 3 with pernicious anemia associated with gastric atrophy, and 6 with specific intestinal malabsorption. Intrinsic factor secretion was reduced in subjects in the first two groups. Gastric biopsies and acid secretion were normal in subjects with either true juvenile pernicious anemia or specific malabsorption.—F. A. K.


A new case of anemia due to specific malabsorption of vitamin B12 with proteinuria was reported with a review of the pathogenesis, genetic and clinical findings in the two varieties of megaloblastic anemia in childhood due to primary vitamin B12 deficiency (Biermer's and Imerslund-Najman-Gräsbéck anemia) which were studied with radioactive vitamin B12.—J. C.


Two general types of antibody activity to intrinsic factor were found in sera obtained from a group of 79 subjects with pernicious anemia. Type I antibody was found to block the binding of Co60B12 to intrinsic factor when added to intrinsic factor before the vitamin. Type II antibody was shown to react with the intrinsic factor-B12 complex and to prevent the absorption of vitamin B12 from intrinsic factor in subjects with pernicious anemia.—F. A. K.


Vitamin B12Co58 binding capacity of blood serum was studied in 86 cases of blood dyscrasias. The greatest increase was observed in iron deficiency anemia, thought to be dependent on the presence of unsaturated siderophyllin. Marked elevations were also found in chronic myeloid and lymphoid leukemia, polycythemia and Hodgkin's disease. There was no correlation between binding capacity and vitamin B12 serum levels.—M. K.


Serum muramidase activity was found to be increased in patients with untreated megaloblastic anemia and to return to normal coincident with an increase in granulocyte count following treatment with the appropriate vitamin. Since the major portion of measurable serum muramidase activity normally is derived from degraded granulocytes, the authors proposed that leukopenia in megaloblastic anemia results primarily from increased turnover of granulocytes.—F. A. K.

EXAMINATION OF FOLIC ACID METABOLISM IN PREGNANT WOMEN. M. Jakschitz, M. Langfelder, P. Letkea and E. Soós. From

Folic acid metabolism, serum iron concentrations and latent iron-binding capacities were examined with the determination of FIGLU in the urine. In the 104 pregnant women chosen at random, folic acid deficiency occurred more frequently than did iron deficiency.—S. R. H.


A group of 102 subjects with neoplastic disease were studied. Both serum and red cell folate concentrations were found to be normal in patients with localized disease, whereas serum, but not red cell, folate concentration was subnormal in 85 percent of subjects with disseminated disease.—F. A. K.


Serum folate levels in patients in a geriatric unit were lower than those of healthy young controls and of elderly subjects living at home. In contrast with the findings reported in other regions of the United Kingdom, there was little evidence of folate deficiency in the aged.—A. L. B.


Many patients admitted to a geriatric unit for various reasons showed evidence of deficiency of iron and low levels of serum folate, vitamin B₁₂, and blood ascorbic acid. Megaloblastic changes were not seen. Low serum folate levels occurred most often in patients with organic brain disease and may have been due to inadequate intake.—A. L. B.


Bone marrow aspiration in 26 male alcoholic patients showed abnormal vacuoles in erythroid precursors in 10 of 18 subjects with normoblastic erythropoiesis, in 2 of 5 subjects with megaloblastic erythropoiesis, and in 2 of 3 subjects with megaloblastoid erythropoiesis. The occurrence of these vacuoles did not correlate with diet, serum folate concentration, type of alcoholic beverage, liver histopathology, or with the type or degree of anemia. Vacuolization disappeared rapidly following alcoholic abstinence.—F. A. K.


Studies in 23 hypothyroids showed reduced values of red cell mass with normal hematocrits in 85 percent. Red cell survival with Cr⁵¹, turnover of plasma iron and the T½ of Fe⁵⁹ were normal. Treatment with triiodothyronine caused normalization of the red cell mass.—E. S.


Iron absorption in 16 subjects measured by a simple inexpensive whole-body counting technic correlated well with absorption measured by a double isotope method. Absorption measured by fecal recovery correlated poorly with the other two methods, probably because of incomplete stool collection. Technical details were given.—A. L. B.


Studies of the capacity for serum iron transport in chickens, hens, sheep and bulls
were performed. In mammals, when the unsaturated iron binding capacity of transferrin was surpassed, the values for free iron were those predicted. In birds, serum always contained more iron than the corresponding transferrin. This additional iron transport probably was performed by conalbumin.—E. S.


C and CB types of transferrin were found in the population of southern Poland. The gene frequencies approximated those reported for other European populations.—M. K.


Denervation of the spleen caused a lasting and marked anemia of splenic and neurogenic origin which was accompanied by an increase in serum iron level in the first three weeks, followed by an increase in the level of alpha-globulin, bilirubin and hemosiderosis of the liver and spleen. In the first month, the anemia was hemolytic. Erythropoietic activity in the blood of the animals was greatly increased.—S. R. H.


Eight of 20 patients given cephalothin (Keflin) developed positive direct Coomb’s tests. All eight were azotemic, on extremely large intravenous doses (8-14 Gm. per day) and anemic, although evaluation of the latter was impossible because of intercurrent infection, azotemia, recent blood loss and the like. Eluates from Coomb’s positive cells were inactive and 85 percent of normal sera caused normal red cells, coated in vitro with the drug, to become Coomb’s positive. Eluates from Coomb’s positive cells coated normal red cells, in vitro, in antibody produced by administration of dopa or cephalothin. The evidence did support the concept that the Coomb’s positive reactions associated with cephalothin were related to non-specific binding of a drug-globulin complex, manifest when very high serum levels of the drug existed. No evidence for hemolytic disease was noted.—H. S. J.


Premature infants of low birth weight (ca. 1200 Gm.) develop hemorrhagic anemia at 6-11 weeks of age, characterized by abnormally low hemoglobin, reticuloctosis, pyknocytosis and shortened red cell survival (Cr<sup>1/2</sup> 11-15 days). Serum tocopherol levels were low and peroxide hemolysis in vitro was increased. Hemolytic disease was ameliorated after administration of vitamin E. In a prospective study, infants supplemented from birth with vitamin E maintained significantly higher hemoglobin concentrations and lower reticulocyte counts than did those not treated. (Abstracter’s note: This contribution has obvious significance in preventive medicine. Drugs which might potentially form peroxides, such as vitamin K, sulfonamides, etc., might heighten the hemolytic state in unsupplemented premature infants.)—H. S. J.


Treatment of 19 children with kwashiorkor with oral vitamin E for 5 days was associated with a reticulocyte response and a rise in hemoglobin concentration. In contrast, 41 children receiving only protein supplementation became progressively more anemic. These results were similar to those reported previously from the Middle East (Amer. J. Clin. Nutr. 12:374, 1963 and 18: 362, 1966).—F. A. K.

PEROXIDATIVE HEMOLYSIS OF RED BLOOD CELLS FROM PATIENTS WITH ABETALIPO-
ABSTRACTS


Acanthocytic human red cells, previously shown to be vitamin E deficient, and E-deficient rat red cells underwent sequential alterations in their membrane lipids when exposed to H₂O₂ which ultimately resulted in hemolysis. Lipid peroxidation, as measured by the appearance of 2-thiobarbituric acid chromogens, loss of polyunsaturated membrane fatty acids, decrease in ethanolamine and serine phosphatides preceded hemolysis. The whole sequence was prevented by administration of vitamin E in vivo or in vitro. It was suggested that patients with this rare disorder not be given peroxide-generating drugs, such as 8-aminoquinoline antimalarials and sulfonamides. (Abstracter's comment: Data from another laboratory confirm this work and indicate that peroxidation of membrane sulfhydryl groups may also be of importance in H₂O₂ hemolysis of E-deficient red cells. Jacob and Lux. Clin. Res. 15:280, 1967)—H. S. J.


Free water reabsorption was studied using mannitol and saline diuresis in patients with sickle cell anemia and in normal subjects. The authors concluded that their data suggested that the defect in renal concentrating ability was due to limitation in the ability of the kidneys to maintain a high concentration of solute in the medullary interstitium. The data did not pinpoint the source of this defect, but the authors speculated that the limitation in the rate of free water reabsorption from the collecting tubules was related to the tortuosity of the renal microcirculation in the sickle cell syndromes.—T. F. N.


A "new" human hemoglobin variant was found in a newborn infant with multiple congenital anomalies and complex autosomal chromosomal mosaicism (normal/trisomy 16/short arm 17–18 deletion). This hemoglobin was unique in that it consisted of two dissimilar pairs of polypeptide chains, neither of which were similar to the usual α-chain. The authors proposed the structural formula: X₂γ₂ where the γ-chains appeared to be identical to those in normal Hb F. The non-γ-chain might be a new type, but the authors suggested that it might be identical with the Σ-chain. Hemoglobin Portland-I may represent an embryonic hemoglobin which persisted in this newborn with multiple congenital anomalies; it was not demonstrable in either parent.—T. F. N.


The level of HbF was higher in bronchial asthma than in normal controls, but no correlation between HbF content and changes in respiratory capacity or erythrocyte count was observed.—M. K.


The average hematocrit of G6PD-deficient Negro patients with various acute infections was significantly lower than in non-deficient infected patients (27 compared to 35). No particular drug therapy could be implicated, although pneumonia was the commonest infection noted in the anemic group. Significant anemia with an acute infection in Negro patients should be taken as evidence for possible G6PD deficiency. Documentation of the suspicion was considered important with regard to the subsequent choice of therapeutic agents.—H. S. J.

THE ROLE OF MEMBRANE PHOSPHOGLYCERATE KINASE IN THE CONTROL OF GLYCOLYTIC RATE BY ACTIVE CATION TRANSPORT IN HUMAN RED BLOOD CELLS. J. C. Parker and J. F. Hoffman. From National
ABSTRACTS


Active K+ influx and lactate production increased and became more sensitive to ouabain in human red cells in which internal Na+ had been experimentally increased. Hemolysates enriched with Na+ converted glycolytic intermediates above the triose phosphate dehydrogenase (TPD) step to lactate at a rate slowed by ouabain, whereas ouabain had no affect on ghost-free hemolysates. Since intermediates below the phosphoglycerate kinase (PGK) step were not accumulated, it was implied that ghosts contain the dual enzyme system TPD and PGK. This thesis was confirmed and the system was stimulated by ADP. By blocking ATP degradation to ADP, ouabain inhibited this sequence. It was concluded that membrane PGK was the point at which the Na+–K+ transport system influenced the metabolic rate of red cells.—H. S. J.


As with some species of sheep, two types of Australian possums exist with either high (HK) or low potassium (LK) erythrocytes. Another marsupial, the quokka, has red cells in which Na+ and K+ are approximately equal in concentration. Erythrocyte membrane preparations from these animals showed basal ATPase activities, unaffected by Na+ plus K+ or by ouabain. LK membranes, however, contained no (Na+ + K+)-activated (pump) ATPase, whereas membranes of quokka erythrocytes had pump ATPase levels intermediate between LK and HK. Low erythrocyte potassium concentrations in LK possums may be due to absence of (Na+ + K+)-activated ATPase and, therefore, absent cation pump activity in their cell membranes.—H. S. J.


A membrane-bound ATPase system has been conclusively demonstrated to be involved in active cation pumping in a variety of biological tissues. The enzyme, activated by Na+, K+ and Mg++ together, was inhibited by cardiac glycosides, such as ouabain. The involvement of phospholipid has also been suggested by numerous previous studies. A soluble enzyme system, isolated from brain and renal cortex, had all the characteristics of "pump" ATPase and required the presence of phospholipid. Of the purified phosphatides added (lecithin, P-inositol, and P-serine), only phosphatidyl serine was effective in activating enzymatic activity. (Abstractor's note: These results are of interest in the light of recent similar observations in red cell preparations by Ohnishi et al., J. Biochem. 56:377, 1964, and the more recent demonstration that the metabolism of P-serine is greatly increased in hereditary spherocytes in which cation pumping and ATPase activities are concomitantly accelerated, Jacob and Karnovsky, J. Clin. Invest. 46:173, 1967.)—H. S. J.


In this 18 year old patient, hematologic study failed to demonstrate any difference between this polycythemia and that observed in Vaquez disease. The diagnosis of Budd-Chiari syndrome was particularly difficult to establish because of the enormous hypertrophy of the caudate lobe. The relation between polycythemia and hepatic vein thrombosis remains uncertain. The occurrence in a young person, in contrast to the average age of patients with polycythemia vera, must be pointed out.—J. C.


Glutathione influences both the shape and the position of the dissociation curve of oxyhemoglobin. A higher concentration of GSH causes a shift of the dissociation curve to
the right (Hill’s constant is decreased). Both the shape and the position of the curve may be influenced in vitro either by addition of GSH or by blockade of sulphydryl groups, e.g., by mercury compounds. Shift of the dissociation curve to the right improves the conditions for supplying oxygen to the tissues since, under otherwise identical conditions, a given amount of blood liberates a greater amount of oxygen at a decreased partial pressure of oxygen. Addition of GSH to preserved blood or to plasma expanders, protein or non-protein in character, increases the percentage survival in animals subjected to a standard hemorrhagic shock.—S. R. H.


Utilizing their technic of measuring porphyrin synthesis by cultured chick embryo liver cells, the authors provided evidence that numerous steroids and their metabolic degradation products stimulate porphyrin synthesis. Etiocholanolone and other products of testosterone degradation were especially active. These results suggested mechanisms for the increased red cell production in Cushing’s syndrome or induced by androgen therapy and for the worsening of hepatic porphyria in women receiving contraceptive steroid mixtures.—H. S. J.


Studies of the ability of hemolysates, obtained from 10 patients with acquired sideroblastic anemia, to synthesize heme and porphyrin revealed apparently normal synthesis of δ-aminolevulinic acid from glycine and succinyl CoA and failed to demonstrate any deficiency in activity in the steps of heme synthesis between δ-aminolevulinic acid and heme. Coproporphyrin synthesis was found to be excessive in one patient.—F. A. K.


A cell-free system, prepared from rabbit reticulocytes, synthesized a labeled protein from labeled amino acids characterized as a globin dimer, probably the alpha-beta form. The dimer was unstable, probably dissociating into monomeric alpha or beta chains, but could be converted by exogenous hemin, in part, to a stable molecule characteristic of hemoglobin (Hb). The dimer may be an intermediate in the synthesis of Hb, an interpretation in agreement with the proposals of Winterhalter and Huehns (J. Biol. Chem. 239:3699, 1964) and of Colombo and Baglioni (J. Mol. Biol. 16:51, 1966) derived with other technics.—H. S. J.


The presence of CO in expired air has been well documented to arise directly from the alpha-methene bridge carbon of heme during its catabolism. A technic is presented by which expired C14O can be measured after administration of C14-glycine (the precursor of methene carbons of heme) to small mammals. The method which utilizes absorption of contaminating C14O2 and oxidation of remaining C14O seems an inexpensive and easy tool with which to document further the physiology of heme catabolism. "Early" and "late" phases of heme catabolism are readily apparent and are predictably and appropriately perturbed by various experimental maneuvers. (Abstracter’s note: The abstracter is indebted to Dr. Rudi Schimid for making this important contribution available).—H. S. J.

LEUKOCYTES


A herpes-like virus, probably not Herpes virus hominis, was isolated from cultures of...
ABSTRACTS

Burkitt lymphoma superinfected with Maloney sarcoma virus.—A. L. B.


In 70 percent of patients with Hodgkin's disease, low serum iron and high serum copper levels were found. During the first year of disease, lymphography showed typical retroperitoneal changes in 50 percent.—E. S.


The following results were noted: Confirmation of the diagnosis in 16 cases, on the basis of already established criteria, i.e., positive PAS, negative MPO and negative esterase reactions. A negative PAS reaction in 3 cases with certain lymphoblasts demonstrating a positive esterase reaction. The level of peroxidase activity in peripheral blood polymorphonuclear leukocytes was less than in normal subjects, but higher than in patients with myeloid leukemia.—J. C.


A negative daily balance was found in 15 cases of anemia with chronic lymphatic leukemia. Ineffective erythropoiesis and increased hemolysis were suggested as the main cause for anemia.—M. K.


This work was based on three observations of plasmocytic leukemia illustrating the essential aspects. A man of 66 presented distinct signs of acute leukemia with increased leukocytes, but without bone changes. A woman of 60 developed the picture of a subleukemia with diffuse decalcification of the skeleton. The third observation was characterized by coexistence of plasmocytic leukemia and classic manifestations of Kahler's disease, notably the existence of bony lacunae. The study of these three patients, compared with the description of similar cases in the literature, brought forward important arguments in favor of a unified interpretation of malignant plasmocytosis. Between typical Kahler's disease with primarily medulary myelomatous foci and the leukemic picture, there exists a series of intermediate states with varying degrees or combinations of bone lesions and blood changes. —J. C.

Leukocyte resistance tests, before and after injection of adrenalin, were studied in normal and splenectomized subjects. The early leukocytosis (after 20 min.) was due to "emptying-out" of cellular elements from storage organs. Delayed leukocytosis (after 3 hours) was due exclusively to hemodynamic variations in the peripheral circulation. The adrenalin test was not useful for obtaining information about bone marrow function.—S. R. H.


Generalized lymphadenopathy with a clinical course resembling Hodgkin's disease occurred in a patient receiving hydantoin. Full remission was accomplished following withdrawal of the drug.—E. S.


Three cases were described. The protracted clinical course and the histological pattern characterized by small epithelioid areas, sinusoidal histiocytosis and follicular hyperplasia were stressed. The disease was considered to be a form of toxoplasmosis.—E. S.

MISCELLANEOUS


One of the chief mechanisms proposed for the immunogenicity of penicillin is the degradation of penicillin into reactive intermediates, such as benzylpenicillenic acid. These reactive intermediates could then form covalent linkages with body proteins to form immunogenic materials. Benzylpenicillenic acid could thus act as a hapten. These two articles, however, indicate that another important aspect of allergy to penicillins is the trace contamination of penicillin with a high molecular weight proteinaceous material. These authors have shown that some forms of allergy to penicillin are due to these latter materials, since some patients considered allergic to ordinary penicillins did not demonstrate any reactivity toward specially purified preparations of penicillin which did not contain any of these high molecular weight proteinaceous materials. (Abstracter's comment: Considering the time and magnitude of the use of penicillin and the concomitant serious problems of sensitization entailed, it is hard to understand why these facts took so long to reach the reading public.)—I. G.


A combination of immuno-electrophoresis and autoradiographic localization of incorporated radioactive C14 amino acids can be employed to determine which tissues or cells are capable of synthesizing components of the complement system. The site of production of human and monkey C1 q 11S component was studied. Liver, spleen, bone marrow and lung were found to be active. Purified peritoneal and lung macrophages also could synthesize this component. The authors concluded that it was most likely that macrophages of these organs were chiefly responsible for the synthesis of complement components.—I. G.


The structure of the combining sites of immunoglobulins are determined by the amino acid sequence of the polypeptide chains of which they are composed and this in turn is determined by the DNA of the corresponding structural genes. The author presents evidence and discusses in detail the two possible mechanisms for the enormous variability of antibody specificities which are
ABSTRACTS

observed. The first mechanism is simply that the animal carries in its genome a gene for any type of peptide it may need. The second involves some type of somatic mutation and/or chromosomal rearrangement. The author favors the second mechanism.—I. G.


A new genetic system, ISf, related to γG was described. This system was independent of Gm and inv and probably controls the formation of the heavy chains of γG of the type 2b(We). In Caucasians, phenotypic expression of the gene varies as a function of age: ISf(i) was found in 25 percent of infants, 40 percent of adults and 60 percent of subjects over 70.—J. C.


The possibility of isoimmunization in the ABO and Rh system was examined in 150 artificial abortions. The following tests were carried out: 1) Determination of the titer of complete saline agglutinin, 2) Demonstration of complete immune agglutinins in the macromolecular milieu with enzyme-modified cells, indirect Coombs test and partial neutralization technique of Witebsky. Interpretation of results was based on the comparison of the isoserologic findings in blood samples taken before and after artificial abortion.—S. R. H.


The titers of these antibodies in defibrinated plasma obtained by prolonged plasmapheresis did not differ from those in control sera. Plasmapheresis can be exploited for the production of diagnostic sera.—M. K.


Human erythrocytes, washed free of plasma and stabilized by 5 percent formaldehyde in isotonic Na acetate, were stored in 0.5 percent formaldehyde. The particle count was set at 5 million/cu. mm. to agree with the procedures used with whole blood. The effects of acid, alkali, heat, freezing and thawing, dessication and shaking were studied; the cells did not hemolyze and their stability during storage was satisfactory. The cells maintained their original character, only slightly changed in shape, size, optical and electrical properties. They were found to be suitable for calibration of Bürker chambers and electronic particle counters and for the control of cell diameter and hematocrit determinations. By using this standard blood cell suspension, every phase of the counting method, from the pipetting through the dilutions and counting, can be standardized.—S. R. H.