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ERNST R. JAFFÉ, M.D., Editor

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ERYTHROCYTES


A French Negro female child with mild hemolytic anemia (hematocrit 34; reticulocytes 13 per cent) was found to have red and white cells deficient in a glycolytic enzyme, triosephosphate isomerase. A brother and two cousins died with hemolytic anemia. Evidence was presented to support an autosomal recessive transmission of the disease with symptomless heterozygotes having an intermediate enzyme deficiency. Marked autohemolysis was corrected almost to normal by glucose, adenosine and ATP. Neurologic disease in this case and a presumably affected cousin may be a significant, but obscure, concomitant of this disease.—H. S. J.


A statistically significant increase in phosphohexokinase activity was found in the erythrocytes of 20 of 21 mongols. Activities of all other enzymes of carbohydrate intermediary metabolism measured were normal. Since the patient whose cells were normal was shown to be a normal-mongol mosaic with bone marrow cells predominantly of normal chromosome constitution, it was concluded that a gene on chromosome 21 directs the synthesis of phosphohexokinase.

—H. S. J.


A previous report by Dern et al. that different clinical manifestations in schizophrenic Negro patients could be correlated with the presence or absence of red cell G-6-PD deficiency was not confirmed.—H. S. J.


Incubation of heparinized blood with ace-
tycholine, physostigmine or atropine diminishes the firmness of the erythrocyte membrane. Mechanical resistance does not change, if the activity of acetylcholinesterase of washed cells has been suppressed by added physostigmine.—L. D.


Glucose consumption by fresh and stored washed red cells could be correlated directly with the cellular content of adenine nucleotides under a variety of conditions. Regeneration of depleted adenine nucleotides in stored red cells by exposure to adenine and inosine increased consumption of glucose. (Abstracter’s note: Incubation of depleted cells with adenine was performed in 50 mM phosphate buffer and the increase in cellular inorganic phosphate, as well as the increase in nucleotide content, might underlie the increased glycolytic rate.)—H. S. J.


Data from a Negro kindred in which several male and female members had red cells with ATP levels several standard deviations above normal were compatible with an autosomal dominant transmission of a gene which segregates independently of the genes for G-6-PD deficiency and sickle hemoglobin. The affected red cell may provide a useful tool in evaluating the role of ATP in red cell metabolism; such studies are in progress.—H. S. J.


Utilization of inosine was 3.6 μmoles/ml erythrocytes/hour, higher than utilization of glucose (2.4 μmoles) under the same experimental conditions. After incubation for 6 hours at 37 C. with inosine, a considerable increase in inosine-5-monophosphate was found (about 1/4 of total nucleotides), but no significant changes in ADP and ATP.—P. d. N.


In 100 normal subjects, reticulocytes were counted after staining with brilliant cresyl blue or with acridine orange and by means of fluorescence microscopy. Values of 3, 3.7 and 6.2 per cent respectively, were found. The reasons for these differences were discussed.—P. d. N.


The rate of incorporation of C14-glucosamine into glycoproteins of thalassemic reticulocyte stroma was greater than into those of reticulocytes from patients with mild favism or acute hemorrhage. The authors suggested that an abnormality in glycoprotein synthesis might underlie thalassemic oligocytopenia and microcytosis. (Abstracter’s note: Perhaps so, but the results were reported as radioactivity per ml. of reticulocytes. Due to the microcytosis, more reticulocytes per unit volume are present in this condition than in control cell suspensions, perhaps explaining these results.)—H. S. J.


To elucidate the nature of the spheroctytic hemolytic anemia which occurs in rabbits during pneumococcal infection, the authors studied the effects of broth cultures of type I pneumococci. Growing organisms released a potent, heat labile substance capable of increasing the osmotic fragility and ultimately causing lysis of rabbit and human red cells in vitro. Intravenous administration of the material resulted in spheroctytic hemolytic anemia with intravascular hemolysis in rabbits. (Abstracter’s note: Phospholipases probably would be released from degenerating organisms and leukocytes and the breakdown of phospholipids of the brain heart infusion broth to lysophosphatides might explain the spheroctytic activity observed.)—H. S. J.

THE METABOLISM OF THE INDIVIDUAL C14-LA-
ABNORMAL HUMAN HEMOGLOBINS.


Death rate by age of sickle cell trait patients derived from a large autopsy population failed to demonstrate a significant decrease in the number of sicklers with increasing age. There was no evidence from this study that sickle cell trait causes increased mortality. (Abstractor’s note: Notwithstanding, a growing number of reports of sudden, lethal thrombosis in patients with sickle cell trait in the absence of obvious hypoxia, have been published recently: E. A. Schenk. Ann. Int. Med., 60:465, 1964 and W. B. Ober et al., New England J. Med., 263:947, 1960.)—H. S. J.


When centrifuged, thalassemic and normal erythrocytes sedimented in direct relation to their MCH. The bottom layers of centrifuged thalassemic red cells contained significantly greater quantities of hemoglobin F than their less dense counterparts in the upper layers. No differences in hemoglobin A or A2 concentrations were noted. The overall increase in MCH in bottom cells correlated well with an increase in their mean corpuscular fetal hemoglobin content. The authors concluded that the quantitatively heterogeneous content of hemoglobin in thalassemic cells depends significantly on their compensatory capacity to synthesize gamma chains. This compensatory capacity may be important in determining survival of cells in the circulation. —H. S. J.


Storage iron concentrations were measured in 738 specimens of liver obtained at necropsy in Durban and Johannesburg. In males, median values (in μg./Gm. wet weight) were 264 in Whites, 851 in Bantu and 182 in Indians, while the corresponding values in females were 192 in Whites, 270 in Bantu and 118 in Indians. These figures reflected the incidence of iron overload and of iron deficiency anemia in the different groups, as previously described by other workers.—T. H. B.

The Effect of Age on Iron Absorption in Rats. S. D. J. Yeh, W. Soltz and B. F. Chow.
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A possible explanation for mild anemia among the aged is a decrease in absorption of iron. Iron absorption decreased with advancing age in male and female rats, as evidenced by fecal excretion, radioactive iron uptake by different organs and radioactivity in blood. There was no evidence of impairment of erythropoiesis; young and old rats were equally capable of blood formation when exposed to reduced atmospheric pressure to stimulate erythropoiesis or when iron was injected prior to a test dose of radioactive iron.—O. P. J.


Treatment for 4 months resulted in return of acid and intrinsic factor secretion, normal vitamin B₁₂ absorption and regeneration of gastric mucosal glands containing abundant chief and parietal cells. There was also a decrease in the titer of intrinsic factor antibody in the patient’s serum, but no change in the titer of parietal cell antibodies. This steroid effect was considered to be consistent with the hypothesis that gastric mucosal atrophy is due to an autoimmune destruction of gastric glands.—F. A. K.


Sera from 86 patients with pernicious anemia and 16 with biopsy-proven chronic atrophic gastritis were tested for antibodies to gastric parietal cytoplasm, gastric mucosa, intrinsic factor, thyroglobulin and thyroid acinar-cell cytoplasm. Of the group with pernicious anemia, 84.5 per cent had parietal cell antibodies by immunofluorescent technics, 53 per cent had gastric mucosa antibodies by complement-fixation tests, and 56 per cent had antibodies to intrinsic factor. Of the group with chronic gastritis, 62.5 per cent had parietal cell and 38.5 per cent gastric mucosa antibodies, but antibody to intrinsic factor could not be demonstrated. Both groups showed a significant incidence of antibodies to thyroglobulin (25.5 per cent in pernicious anemia and 50 per cent in gastritis). Common etiologic factors and autoimmune phenomena may occur in both diseases and the specific lesion in many cases of pernicious anemia may be due to the formation of antibodies to intrinsic factor.—F. A. K.

SURVIVAL OF ERYTHROCYTES LABELED WITH Cr⁵¹ IN PERNICIOUS ANEMIA WITH A POSITIVE DIRECT COOMBS TEST. D. Radiocoak, A. Smid and J. Štanda. From the First Medical Department, Hradec Králové, Czechoslovakia. Lék. 9:37-40, 1965.

Investigations confirmed the shortened survival of erythrocytes in decompensated cases. After treatment with vitamin B₁₂, the survival was normal in all. In two, a positive Coombs test became negative after treatment. There was no difference in the survival of erythrocytes in patients with a positive Coombs test when compared with the other patients.—L. D.


Parenteral doses of 1000 μg. Co⁵⁷-hydroxycobalamin resulted in significantly less urinary excretion of radioactivity than did similar doses of Co⁵⁷-cyanocobalamin in normal subjects, in anemic subjects with and without B₁₂ deficiency and in subjects with corrected B₁₂ deficiency. These results imply greater tissue retention of injected hydroxycobalamin and suggest that chronic anemia, per se, is a significant factor in the amount of urinary radioactivity excreted after parenteral Co⁵⁷-hydroxycobalamin.—F. A. K.


A second plasma protein, a beta globulin designated transcobalamin II, has been isolated and is able to bind parenterally or orally administered vitamin B₁₂. Studies conducted following re-injection of this protein fraction labeled with Co⁵⁷ suggest that its major function is the transport of recently ingested B₁₂, whereas the previously recognized transport protein, an alpha globulin designated transcobalamin I, transports
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principally endogenous B₁₂. Transcobalamin II appears to have some intrinsic factor activity. —F. A. K.


A new method is described in which allowance is made for the presence of other radioactive substances in commercial Co⁵⁷-labeled "vitamin B₁₂." The method is rapid, accurate and needs no special equipment beyond a scintillation counter.—T. H. B.


Patients with chronic bronchitis and pulmonary emphysema were carefully investigated from the clinical and laboratory point of view. Anemia was never found, but if present a complication may be the underlying cause. In emphysema of medium severity, hemoglobin levels over 17 Gm. per cent were the exception. In severe cases with oxygen saturation below 80 per cent and CO₂ tension over 55 mmHg, higher hemoglobin levels were found in more than half. Macrocytosis was present in 80 per cent of severe cases, even with normal red cell counts. A hemolytic component was not found. In some cases, the red cell count may really be higher, but was masked by an enlarged circulating plasma volume.—L. D.


Bone marrow cells injected into x-ray irradiated mice produced 3 types of clones in the spleens: erythroid, myeloid and mixed. In transfusion-induced polycythemic mice, erythroid clones were markedly inhibited, while the number of myeloid clones was enhanced.—B. R.


Of 329 patients with active rheumatic fever, 80 per cent had mild to moderate anemia. More detailed examinations, including red cell survival and ferrokinetic studies in a few patients, indicated that the anemia resulted from multiple disturbances: increased red cell destruction, increased plasma volume and possibly bone marrow depression. Marked improvement followed treatment with steroid.—B. R.


The authors present a case (another has been seen since publication) with anomalies in size and shape of erythrocytes, negative Coombs test and vascular thrombi. They compare this form with gastric cancer and hemolytic anemia without red cell anomalies and with a normal thrombocyte count.—J. C.


Serum haptoglobins were determined in horses, mules, asses, bulls, sheep, goats and pigs. No haptoglobins were identified in sheep, goats and bulls. In the other species, a band equivalent to the Hp I-I type was identified.—E. S.


Microhematocrit capillary tubes were used for separating different sizes of red cells. Using reticulocyte counts and estimations of acetylcholinesterase activity, the top and bottom layers obtained showed good separation. The only limitation was the small number of cells recovered from each tube.—C. R. M.

LEUKOCYTES

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A new technic for the absolute basophil count is based on neutral red staining, saponin hemolysis, and formaldehyde fixation. A basophil count of more than 50 per cu. mm. is often a sign of allergic sensitization, whereas a count below 20 regularly accompanies allergic reactions. Increased basophil counts are found in association with erythroderma, myxedema, ulcerative colitis, polycythemia vera and myelocytic leukemia, as well as in the sensitized individual.—T. E. B.


Normal newborns (325) were examined repeatedly during the first day of life; in 30, examinations were carried out for 3 days every 6 hours. Premature children (984) and 474 newborns suffering from disease were also examined. The leucocyte count was not influenced by sex, presence and intensity of physiologic jaundice, loss of weight after birth, food or application of normal medicaments to mothers during delivery. Premature children reacted to pathologic stimuli in the same way as normal newborns.—L. D.


Over 400 cases were studied and 152 patients were selected for treatment with over 300 cycles. In chronic myeloid leukemia, C 69 (N-allylalanilidethylenediamine phosphate) proved to be effective. Trenimon (2,3,5-tris-ethylenimino-benzoquinone) seemed to be a good substitute for TEM, as it was less toxic and more appropriate for long-term treatment. Chronic leukemias, one fourth of the cases with Hodgkin’s disease, Waldenström’s disease and hemorrhagic thrombocytopenia responded to Trenimon. It was also effective in polycythemia.—P. d. N.


Seven cases were treated for 3–5 days with huge doses of prednisone (500–1000 mg. daily). Histologic studies were performed on the same lymph nodes before and during therapy. A significant reduction in the size of the tumors, a diminished number of cells and a tendency to form normal follicular patterns were observed. Imprints showed chromatin condensation and cytoplasmic shedding or budding in lymphocytes, reticulum cells and undifferentiated lymphomatous cells. Reticulum cells were observed with phagocytized nuclear rests. I. v. administration of 16 mg. of dexamethasone or 200 mg. of hydrocortisone resulted in cytoplasmic shedding or budding in small and medium sized lymphocytes 30–60 minutes after injection. A fall in the number of peripheral lymphocytes to ½–1½ of the original number was also reported.—E. S.


Malabsorption as the presenting clinical feature of malignant lymphoma of the small bowel was observed in Arabs and non-Ashkenazi Jews and preceded the diagnosis of the disease by 1 to 4 years. X-ray findings were confined mostly to the duodenum and proximal jejunum; terminal ileum was less frequently involved. Prognosis, therapy and post mortem findings were discussed.—B. R.


Tiselius electrophoresis showed an M-component in 90 per cent of cases, but immuno-electrophoresis demonstrated paraproteinemia in all. Twenty-five per cent were of the \( \gamma_A \) variety. Hypercalcemia and impaired renal function were more frequent in this group than in \( \gamma_{\text{M}} \) and \( \gamma_{\text{NS}} \) myeloma and prognosis was poorer. Seven patients had shown anticomplementary serum activity for up to 8 years before diagnosis. Para-amyloidosis was not found in any of 37 autopsied cases.—S.-A. K.


Coon’s immuno-fluorescent technic reveals some cells in spleen and lymph nodes with granules that have a very bright autofluorescence which
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During specific phases of the luteal stage and during early pregnancy after progesterational administration, there is a marked mobilization of lymphoblast-like cells in the connective tissue of the plica. Estrogenic treatment induces a marked modification of these cells with morphological reorganization and destruction in oviductal tissues. The morphological reorganization is noted in eosinophilic granulation of the cytoplasm, followed by fragmentation of nuclear chromatin. The products of these cells may be involved with the increased bactericidal activity noted in the genital tract during estrous.—O. P. J.


Thymocytes of young rats were studied with the electron microscope. There were no protoplasmic bridges between thymocytes and epithelial cells and there was no clear evidence of epithelial-thymocyte transformations. Cytoplasmic fragments appeared to be separating from thymocytes by a process similar to the separation of platelets from megakaryocytes.—O. P. J.


Polymorphonuclear leukocyte lysomes were extracted and a basic protein was obtained which when applied to small mesenteric blood vessels produced sticking and emigration of leukocytes, stasis of blood flow and finally tiny hemorrhages. This basic protein also produced platelet aggregation in vitro and was essentially devoid of other active materials commonly found in lysomes. The authors conclude that the release of this material may play an important role in inflammation.—I. G.


Bradykinin markedly increases phagocytosis of leukocytes in vitro. This can be demonstrated in a 1:10,000,000 dilution and the effect is 25 to 30 times greater than that of histamine. This phenomenon is seen with cells from blood and from sterile inflammations of the abdominal cavity.—S. R. H.


These metabolic activities were found to be considerably lower in leukemic leukocytes than in normal leukocytes.—P. d. N.
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The authors measured the respiration of platelets completely freed of plasma with the Gilson oxygraph.—J. C.


Platelet aggregation, rather than fibrin formation, is thought to be the initial event in thrombus formation in vivo. Evidence is presented that platelet aggregation in the Chandler’s tube is significantly delayed in patients receiving full therapeutic doses of warfarin and dindevan, and is also delayed in the presence of small amounts of heparin.—P. B.


Thrombi, produced in a Chandler’s tube, closely resembled pathological thrombi in structure and studies with them may have more relevance to the in vivo response to thrombolytic agents than in vitro experiments with blood clots. After perfusion with streptokinase, the fibrin component of the clot was largely dissolved, but platelet fragments were released into the circulation. Blood from 4 patients with hyperlipidemia yielded thrombi which were resistant to lysis by streptokinase. Epsilonaminocaproic acid inhibited thrombolysis.—P. B.


Factor VIII and IX were measured by one-stage technics and normal pooled plasma was the standard. In 30 normal females, Factor VIII activity was 65–220 per cent (mean: 112 per cent) and Factor IX was 78–180 per cent (mean: 108 per cent). The 95 per cent probability intervals in 28 definite carriers of hemophilia A and 11 definite carriers of Christmas disease were 16–60 and 20–47 per cent, means being 34 and 32, respectively. Confidence limits for genetic prognosis in case of potential carriership were given.

—E. A. L.


Carbohydrates, galactose, mannose, hexosamines, sialic acid and fucose contents were determined in 16 patients and a significant increase of these components was found in all.—P. d. N.


A 20 months old female developed typical skin lesions (excellent photographs) and signs of defibrination about 3 weeks after a febrile sore throat. A fibrinogenemia disappeared after 2.5 Gm. fibrinogen and 200 ml. fresh citrated blood. Penicillin, streptomycin and prednisone were given, but heparin was not used. Recovery took 2 months.—E. A. L.

“THROMBOTEST” AND PROTHROMBIN TIME: A CONTROLLED CLINICAL TRIAL. M. C. Rozenberg, H. Kronenberg and B. G Firkin. From Royal
One-stage prothrombin-continue estimation. To reach for the control of long-term anticoagulant therapy required less intensive therapy than when the range was determined with the Quick test. Thrombotest was found sensitive to Factor IX depression only below 10 per cent Thrombotest activity. Significantly fewer reinfarctions occurred in the “Quick” group, but the “Thrombotest” group had fewer hemorrhagic complications. It was concluded that no entirely satisfactory test for the control of long-term anticoagulant therapy is yet available.

F. W. G.


Two comparable groups of patients, mostly survivors after myocardial infarctions, were followed for 5½ to 8 years. Overall mortality and 5-year survival rate were not significantly changed by prophylaxis, but mortality through years 2 to 5 was reduced in poor risk patients on dicumarol and the incidence of thromboembolic complications was significantly lower in this group. The incidence of hemorrhagic complications was significantly lower in this group. In good risk patients, the two series (dicumarol and placebo) had equally low mortality and incidence of thromboembolism. The authors concluded that long-term anticoagulant prophylaxis should be reserved for patients with a permanently increased risk of thromboembolism.

H. H. F.


Ten subjects, exposed to CS₂, but without clinical signs of intoxication, and 10 patients with chronic vasculopathy due to CS₂, but no longer exposed, were studied. Slight, inconstant modifications in lipoprotein metabolism were observed. Blood coagulation was profoundly affected in most subjects of the first group and in all of the second group. Signs of hypercoagulability were detected (thromboelastographic studies and heparin and dextran tolerance tests).

P. d. N.

Miscellaneous


Injections of infectious polyoma DNA produced local and, occasionally, distant tumors in newborn hamsters, raising the question of transport of biologically active DNA in blood and lymph. DNA, prepared from pneumococci, polyoma virus and L₁₂₁₀ leukemia cells, was injected I.P. and I.V. into Swiss mice. P₃₂-DNA infected I.P. appeared rapidly in blood and 2 to 3 times more DNA was found in cellular elements than in plasma. Incubation with plasma caused marked inactivation of transforming ability of pneumococcal DNA, but produced a 2–3 fold increase in plaque-forming activity (a measure of tumor producing capacity) of polyoma DNA. In vivo, after 10 minutes, pneumococcal DNA was completely inactive, but polyoma DNA retained from 2–8 per cent of its plaque-forming activity, an amount sufficient to produce tumors. Infectious DNA could be released from tumors in an active form and might be one mechanism for the spread of tumors. Antibodies against nucleic acids might be used as a method to prevent this type of spread.

I. G.


Transplantable Sarcoma 37 was inoculated in 809 CF₁ mice with 99 per cent takes. The number of cells inoculated influenced tumor growth, spontaneous cure and survival time. In cured mice, retransplantation of Sarcoma 37 was followed by complete resistance, even on the fifth attempt. Four hundred r to the entire body accelerated tumor growth and extension, shortened survival time and diminished the percentage of spontaneous cures. Sera from resistant animals did not influence the evolution and growth of Sarcoma 37, but the percentage of takes diminished from 99 to 92.

M. J.