
Arthus reactions were induced in the dorsal skin, and the subcutaneous connective tissues from the sensitized areas were examined at various stages. The subcutaneous connective tissue was used because of its simplicity of construction and because it could be studied conveniently by both supravital and fixed methods. This combination of tissue and technic allowed both an accurate classification of the various types of inflammatory cells and a close examination of their relationships to the blood vessels.

Cells transitional between adventitial cells and plasma cells were observed after antigenic stimulation. Their location on the walls of the venules and capillaries indicated that they were adventitial cells but their morphology was that of plasma cells. By supravital technic they exhibited a glassy and homogeneous cytoplasm, a circular formation of neutral red granules, and a diffuse distribution of janus green granules; and by fixed method they exhibited a chromatin pattern similar to that of plasma cells, an increased cytoplasmic basophilia, and a nucleolus was often present. Small plasma cells appeared simultaneously around the venules and capillaries. The local origin of plasma cells would appear to explain the absence of plasmacytosis during strong tissue plasma cell reactions.

Immunofluorescence was only found in plasma cells and in transitional adventitial cells, indicating a functional similarity between the 2 cells.


Copper deficiency was often found in severely malnourished infants rehabilitated on exclusive milk diets. Marked, persistent neutropenia was its earliest and most constant manifestation.


The cytotoxicity test has been shown to give reproducible information concerning specific isoantigens of human leukemic lymphocytes. The distribution frequency of these antigens is at least as great in chronic lymphocytic leukemic cells as in normal lymphocytes. There was no indication of deletion of normal antigens or of decreased cellular reactivity. The majority of patients were tested repeatedly and in most instances the cytotoxicity test remained constant regardless of drug therapy and disease status. Cells from 5 patients having acute granulocytic leukemia were typed in a similar fashion and contained antigens in common with normal lymphocytes.

Quantitative and qualitative studies of urinary iron excretion were performed in 12 patients with hemolytic disease and in one normal subject given an intravenous infusion of hemoglobin. In 9 patients with significant intravascular hemolysis, increased urinary excretion of nonhemoglobin iron was observed with amounts as high as 10.75 mg./24 hours. In 7 of 8 patients in whom fractions of the urinary iron were studied, the majority of the iron was in the sediment (hemosiderin). Ferritin was demonstrated in the urine by immunologic and electrophoretic technics and accounted for a significant percentage of iron excreted. In several patients, day-night variations in hemolysis were associated with parallel fluctuations in iron excretion.

The results were analyzed in relation to current concepts of glomerular clearance and renal tubular metabolism of hemoglobin. The significance to body iron balance of the massive "iron diuresis" occurring in some of these patients was discussed.

Tanaka, Y., Brecher, G., and Bull, B.: Ferritin deposition on the erythroblast cell membrane and rhexocytosis in hypersiderotic human bone marrow. First submitted Jan. 12, 1966; accepted for publication Apr. 4, 1966.

1. Preferential ferritin localization on specialized areas of the plasma membrane of erythroblasts with subsequent invagination into rhexocytotic vesicles, and the occurrence of rhexocytosis without ferritin being present in the vesicles, has been previously described.

2. In a study of bone marrows from patients with hypersiderosis we have confirmed the previous observations, but frequently found nonferritin rhexocytosis in erythroblasts adjacent to ferritin-laden reticulum cells. In addition, ferritin localization along the outer surface of erythroblasts was noted, particularly between continuous surfaces of 2 adjacent erythroblasts. Such intercellular accumulations of ferritin were not necessarily associated with a high ferritin content of adjacent cells.

3. These observations did not favor the hypothesis that ferritin iron was being transferred directly from reticulum cells to adjacent erythroblasts. It is suggested that the accumulation of ferritin along extended stretches of the erythroblast surface may signify that iron which is detached from siderophilin, but not immediately transported across the cell membrane, is incorporated into apoferritin produced on the cell membrane.


1. The effects of added 6-mercaptopurine (6-MP) on the in vitro incorporation of radioformate (C14) into the leukocyte nucleic acid purines and thymine of 6 cases of acute myeloblastic leukemia (AML) and 4 cases of acute lymphoblastic leukemia (ALL) have been compared with the patients’ clinical response to 6-MP.

2. In 7 cases subsequent therapy with 6-MP produced leukopenia. Of these, in vitro 6-MP diminished leukocyte C14 incorporation into the nucleic acid
purines in 3 cases of AML, had no effect in 2 cases of AML and 1 case of ALL, and enhanced C14 incorporation into the leukocyte purines of a second case of ALL. Thymine synthesis was slightly diminished by 6-MP in the AML leukocytes in which purine synthesis was inhibited, and in 1 drug-sensitive ALL leukocyte population in which purine synthesis was slightly increased by the analogue. Thus, no regular and consistent relationship between the antileukemic effect of the drug and suppression of purine or thymine synthesis by 6-MP in vitro could be demonstrated.

3. Studies of the leukocytes of 2 cases of drug-resistant ALL yielded results similar to those observed in presumably drug-sensitive ALL cells.

4. The leukocytes of 2 cases of AML with acquired drug-resistance showed an increased capacity for in vitro RNA purine synthesis; in the one case in which studies before and after the development of resistance were possible, this property was apparently acquired during therapy. This suggests that an increase in purine biosynthetic enzyme reserves may be a mechanism of 6-MP-resistance in some human leukemias.


1. In rats with acute turpentine-induced inflammation, there was a reduced reutilization of radioiron from transfused senescent erythrocytes but a normal utilization of transferrin-bound Fe20 after a 40-hour period. There was a pronounced retention of tracer from the nonviable red cells by the livers and spleens of the inflamed animals.

2. During inflammation, the plasma iron turnover fell by about 50 per cent, while the fraction of plasma iron removed per hour was increased. However, there was no marked change in the relative distribution of transferrin-bound Fe20 to the liver, spleen and bone marrow (after perfusion). Transferrin-bound Fe20 initially appeared at an increased rate in the circulating red cell mass.

3. Following administration of ferric ammonium citrate in order to raise the plasma iron level, there was a rise in the plasma iron turnover of the inflamed rats, in contrast to the control animals. Diversion of radioiron to the liver and spleen was not markedly increased under these conditions.

4. It is concluded that the immediate fall in plasma iron turnover and hypoferrernia during acute turpentine inflammation results mainly from an inhibition of the release of iron derived from senescent red cells into the plasma. An increased avidity of the liver, and of marrow red cell precursors and/or reticulocytes for plasma iron, may accentuate the fall in plasma iron levels. There appeared to be no inhibition of the bone marrow capacity to turn over larger amounts of plasma iron during inflammation. These results may help in the interpretation of disturbances of iron metabolism during the acute inflammatory state.


Three patterns of DNA replication in the interphase nuclei of short-term leukocyte cultures are described:
1. Light, homogenous labeling on the whole nucleus and no labeling over the nucleolus (nucleolus-negative phase).

2. Heavy labeling equally distributed over the whole nucleus and nucleoli (intermediate phase).

3. Heavy labeling over the nucleoli and moderate labeling at the periphery of the nucleus (nucleolus-positive phase).

These three patterns of labeling appear consecutively during the process of DNA synthesis. Thus, the nuclear and nucleolar associated chromatin replicates during the late stage of DNA synthesis.

The existence of nucleolar chromatin is discussed. Study of H³-thymidine incorporation in the nucleoli of leukemic and neoplastic cells may develop data regarding the possible metabolic disturbances of these cells.


Case reports of 4 patients, all Chinese, with Hb Q-H disease (also called Hb Q-α thalassemia) are presented. Three were siblings. Symptoms of chronic hemolytic anemia with jaundice and hepatosplenomegaly were present in all 4 subjects. The red blood cells were microcytic. Slight hypochromia was present in 3 of the cases. Poikilocytes and anisocytosis with target cells and small intracytoplasmic crystals were found in the blood. Starch-gel electrophoresis revealed the presence of a large amount of Hb Q, a small amount of Hb H, and a minor slow-moving hemoglobin component with a mobility as much behind Hb A₂ as Hb Q was behind Hb A. A small amount of Hb "Bart's" was probably also present. The minor slow moving component was thought to represent Hbα₂Q₂A₂ or Hb Q₂. Hb A and Hb A₂ were not seen except after recent blood transfusion. Study of hemoglobin polypeptide chains showed the presence of normal β chains and abnormal α²-chains, without demonstrable α²-chains in the first three patients. In Patient #4, normal α²-chains were demonstrable only after recent blood transfusion. The mother of the 3 siblings was heterozygous for Hb A; the father had α-thalassemia trait.


Serial immunologic measurements were used to study the metabolic behavior of the immune globulins (γ-globulins) in patients with agammaglobulinemia after plasmapheresis and plasma infusion and in newborn infants after exchange transfusion. These studies were supplemented by metabolic and distribution studies of I¹³¹-labeled γ-globulin (isolated from serum or breast milk) and I¹³¹-labeled γ-globulin in normal and agammaglobulinemic subjects. The therapeutic benefit of periodic plasma infusions in patients with agammaglobulinemia and the Aldrich syndrome was also assessed.

In the agammaglobulinemic patients, the mean half-lives of γ-globulin were 32, 9.6 and 5.9 days, respectively. In the transfused infants, the mean half-lives of γ-globulins were 7.4 and 4.3 days, respectively. Agreement existed between simultaneously determined immunologic and ra-
dioactive survival times, except when $^{131}$-labeled $\gamma\lambda$-globulin isolated from serum was used; this preparation had a shorter half-life than the $\gamma\lambda$-globulin of infused plasma, probably as a result of denaturation during the isolation procedure. Studies on 2 normal and 3 agammaglobulinemic subjects showed that 65 to 85 per cent of breast milk $^{131}$-labeled $\gamma\lambda$-globulin was distributed within the tissues. $^{131}$-labeled $\gamma\lambda$-globulin was not demonstrable in the breast milk of 2 lactating women or in the saliva of 2 normal subjects. No $\gamma\lambda$-globulin could be demonstrated in the saliva of an agammaglobulinemic patient after plasma infusion which raised the serum $\gamma\lambda$-globulin concentration to 50 mg./100 ml.

The use of plasma instead of commercial $\gamma$-globulin for the therapy of immunologic deficiency states has several advantages. Plasma contains all 3 immune globulins, provides greater quantities of $\gamma\omega$-globulin than can be given by intramuscular injections, and is more acceptable to the patient. Because of the risk of serum hepatitis, this mode of therapy in the routine management of agammaglobulinemia is endorsed only if special precautions are taken. A therapeutic trial of plasma infusions in 2 patients with the Aldrich syndrome gave promising results.


A byproduct of the preparation of platelet concentrates, by recently proposed methods, is fresh citrate-plasma at pH 6.5. Because this plasma might be a useful source of Factor VIII, the activity was investigated. Compared to unaltered citrate-plasma, the activity was found to be 54 per cent. However, after incubation with washed fresh erythrocytes the "acidified" plasma had the same Factor VIII activity as the control.

This suggests that after infusion, pH 6.5 plasma is probably as effective a source of Factor VIII as ordinary ACD plasma. This conclusion was supported by observations on Factor VIII concentrates prepared by cryoprecipitation. In such preparations additional ACD and pH are eliminated as factors in the assay system. Factor VIII concentration in the precipitates prepared from acidified plasma was found to be as high as in precipitates prepared from untreated plasma.