Author's Summaries of Articles Accepted August, 1965

Rabinowitz, Y.: DNA polymerase and carbohydrate metabolizing enzyme content of normal and leukemic glass column separated leukocytes. Submitted May 27, 1965; accepted for publication August 6, 1965.

1. Enzymes of normal and leukemic glass column separated leukocytes were assayed with fluorometric (glucose-6-phosphate dehydrogenase, 6-phosphogluconate dehydrogenase, lactic dehydrogenase, glyceraldehyde-3-phosphate dehydrogenase and isocitric dehydrogenase) and radioisotope (DNA polymerase) micro-methods.

2. Most results were obtained by direct assay of the specific cell type. Some required simple calculation. It was demonstrated that the enzyme activity of mixed cell suspensions was the sum of the enzyme content of the component cells, at least for the enzymes studied.

3. Assays of mixed cell suspensions may give an erroneous picture. Changes in differential cell counts, as well as alterations in enzyme content of individual cells, must be taken into account for correct interpretation.

4. Changes in enzyme content of mixed cell suspensions after therapy were chiefly due to alterations in the differential cell count, rather than to changes in the enzyme content of individual cell types.

5. The patterns of assays of the carbohydrate metabolizing enzymes studied, except isocitric dehydrogenase, paralleled each other. Highest values were found in mature PMN leukocytes and lowest in blasts. With isocitric dehydrogenase absolute values were much lower, while the highest assays were found in myelocytes.

6. DNA polymerase content correlated well with the ability of a cell to divide. It was highest in blasts and lowest in mature PMN leukocytes.


The study of maturation of rabbit reticulocytes in vivo revealed an essential correlation between the degree of reticulocytosis, the RNA content of the circulating red blood cells and their ability to carry out amino acid incorporation into protein. Nevertheless, the frequent occurrence of considerable quantitative discrepancies between these parameters during the progress of maturation appears to be attributable to fluctuations in the reticulocyte population due to intrinsic difference in the life span of these cells and to release of young reticulocytes from the hyperplastic bone marrow into the circulation. The distortions in the pattern of maturation kinetics by the continued contribution of the bone marrow seem to be largely eliminated by blocking erythropoiesis at the height of reticulocytosis with the aid of Actinomycin D treatment.

Three hundred and ninety-nine patients with acute leukemia examined during the period of 1947–1964 were divided into three sequential series and their survival, from diagnosis to death, was compared.

A statistically significant increase in duration of survival for myeloblastic leukemia from a median of 2 to a median of 5 months occurred between series I and series III. This is the first convincing evidence that 6-mercaptopurine therapy influences survival in myeloblastic leukemia.

A steady increase in median survival of patients with lymphoblastic leukemia from 4 to 8 to 12 months was found in the three series. The results of analysis of these series are compared to other reported series. The hypothesis—suggesting that the longer survivals reported for patients treated in hematology clinics compared to that of patients selected from population areas reflects patient selection—was examined and appeared unlikely.


Protein starvation nearly arrested erythropoiesis in rats, and the red cell mass decreased during a period of 32 days from 4.0 to 2.5 ml. Protein-starved rats, injected daily with 1.8 units of rabbit erythropoietin, had reticulocyte counts within the normal range, and their cell mass increased during the same period to 4.26 ml., as compared to 4.52 ml. in normal controls. Red cell indexes, Price-Jones curve and osmotic fragility were normal on blood obtained from erythropoietin-treated groups. Differential counts on their erythroid marrow composition were not significantly different from those in normal rats. It is concluded therefore that daily injection of 1.8 units of rabbit erythropoietin induced over a period of 32 days a steady state erythropoiesis which, on basis of the parameters studied, could not be distinguished from that in normal rats. No evidence of a shortened life span of cells formed in response to erythropoietin was found after either random (Cr$^{51}$) or cohort (Fe$^{59}$) labeling. Random labeled (Cr$^{51}$) cells from untreated protein-starved rats had significantly shorter chromate survival times than cells from normal or erythropoietin-treated rats. The difference is attributed to the altered age distribution in their red cell population.


Malignant lymphoma was found in 4 of 20 NZB/B1 mice (of the 61st generation) selected for laboratory examinations and autopsy at 9–11 months of age. The malignant lymphomas were of two histologic types, reticulum cell sarcoma and pleomorphic malignant lymphoma, the latter term being used
to designate malignant neoplasms arising in lymphatic tissue, composed of mesenchymal cells of diverse appearance—mainly plasma cells of “blast, immature, mature and Russell-body types but also large primitive (stem) cells, reticulum cells, and lymphocytes of large and small size—and frequently associated with gammopathies. One of the reticulum cell sarcomas was transplantable to, and produced lethal disseminated growth in, other NZB/B1 mice.

In each example of malignant lymphoma, warm hemagglutinins (to papain-treated mouse red cells) were demonstrable in serum. Autoimmune hemolytic disease and chronic membranous glomerulonephritis, both of common occurrence in NZB/B1 mice of comparable age, were also present. In one instance of pleomorphic malignant lymphoma, hypergammaglobulinemia of unusual quantity and quality drew attention to the possibility of lymphomatous disease.

Some evidence was brought forth indicating that, in the majority of instances, the autoimmune diseases preceded the malignant lymphomas. While the coexistence of autoimmunity and lymphoid neoplasia conceivably reflects nothing more than chance occurrence, other interpretations were considered: The proliferative advantage engendered in immunologically competent cells in autoimmune disease may be a step in the direction of lymphoid neoplasia; or, in some instances autoantibodies may be produced by, or in response to, the neoplastic lymphoid cells.


The metabolism of adenosine-8-C14, at relatively high and low concentrations, was studied in human erythrocytes freshly obtained and after 6 and 9 weeks of storage in ACD. At high adenosine concentration (3.6 umoles/ml. cells), considerable conversion to ATP was found in fresh and stored cells, suggesting that direct phosphorylation of adenosine occurred, a reaction that is minimal at low (0.36 μM/ml. cells) adenosine concentration because of extensive rapid deamination. Incorporation of the label via hypoxanthine or adenine is unlikely, since at high adenosine concentration no dilution of ATP labeling in the presence of unlabeled inosine (hypoxanthine) was found, nor was free labeled adenine detected in erythrocyte extracts.

A study of the metabolism of adenine-8-C14 in fresh and stored erythrocytes suggests that the presence of a suitable nucleoside (e.g., inosine) is required for efficient utilization of adenine-8-C14 for ATP formation in the erythrocytes of blood stored for prolonged periods.

Erslev, A. J.: The erythropoietic effect of hematocrit variations in normovolemic rabbits. Submitted June 14, 1965; accepted for publication August 20, 1965.

Measurements of erythropoietin titer and serum iron turnover were carried out in rabbits 48 hours after the induction of normovolemic anemias
and polycythemias. Although viscosity studies of blood at various hematocrits indicate that the oxygen flow to the tissues is impaired both in anemia and polycythemia, only anemias were found to be associated with production of erythropoietin and with accelerated serum iron turnover. It was concluded that if polycythemia with its associated high viscosity leads to tissue hypoxia, this tissue hypoxia will not cause production of erythropoietin.


Through the kindness of Dr. J. H. Milstone we were able to perform clotting studies with purified bovine thrombokinase. Phenylmethyl sulfonylfluoride was found to inactivate bovine thrombin. Bovine thrombokinase, freed of traces of contaminating thrombin by treatment with phenylmethyl sulfonylfluoride, behaved in a manner similar to activated Stuart factor. Kinetic studies with this purified clotting factor and partially purified bovine proaccelerin supported the hypothesis that bovine proaccelerin is changed by the enzymatic action of thrombokinase to an agent which converts prothrombin to thrombin. The reaction between thrombokinase and bovine proaccelerin requires phospholipid and calcium and is blocked by soybean trypsin inhibitor. The similarities between human activated Stuart factor and bovine thrombokinase are apparent.


Our observations of 135 patients indicate that 37 per cent of those suffering from Hodgkin’s disease exhibit abnormal cells in the leukocyte concentrates of the peripheral blood during the course of their illness. Typical Sternberg-Reed cells were found in 18.5 per cent of patients and were present only in the advanced stages of generalized Hodgkin’s disease.

The presence of Sternberg-Reed cells in the peripheral blood indicates an advanced stage of the disease but does not necessarily predict an immediately fatal outcome.

Comparative studies, searching for Sternberg-Reed cells in the splenic circulation, showed no Sternberg-Reed cells to be present in the splenic arteries of patients with Hodgkin’s disease; but numerous Sternberg-Reed cells were present in the splenic vein, particularly after mechanical squeezing of the spleen.

A possible hypothesis is given to support the evidence for the circulation of Sternberg-Reed cells and an explanation for their lower incidence in the peripheral blood.

Our observations support the hematogenous metastasis of Hodgkin’s disease.
McCurdy, P. R., and Donohoe, R. F.: Pyridoxine-responsive anemia conditioned by isonicotinic acid hydrazine. Submitted April 8, 1965; accepted for publication August 2, 1965.

Three patients are described who had a pyridoxine-responsive anemia while under treatment for pulmonary tuberculosis with INH and PAS. The red cells were hypochromic, and target cells common. Two cases also had microcytosis and one had ringed sideroblasts in the bone marrow. None became hematologically normal with therapy. A somnolent reaction occurred in two of the patients following the parenteral administration of large amounts of pyridoxine, and seemed related to it. The concentration of erythrocyte glutamic oxaloacetic transaminase was less than 25 per cent of the normal mean in two of the patients at the time of relapse.