
Hodgkin’s disease, lymphosarcoma and acute leukemia have been studied after treatment with the *Vinca rosea* alkaloids (vinblastine and vincristine), in order to demonstrate and evaluate the mitosis-arresting effects of the two drugs on the malignant cells. Histologic sections, lymph node and bone marrow aspirations were performed immediately before and 24 hours after the intravenous administration of the drugs in 15 cases of Hodgkin’s disease, 12 of lymphoblastic lymphosarcoma, and 12 of acute leukemia, besides other miscellaneous cases.

In Hodgkin’s disease aspirates and sections showed a clear-cut metaphasic arrest in the post-VLB specimens, chiefly affecting the pre-Sternberg of Hodgkin’s cells. This effect, besides corroborating the fundamentally stathmokinetic mechanism of VLB in Hodgkin’s disease, was considered an additional factor in confirming the widely proposed conception that these cells represent the fundamentally proliferating and malignant tissue of this disease.

In the acute leukemias and lymphoblastosarcomata, cytomorphologic and quantitative studies demonstrated that the oncolytic effects correlated well with the magnitude of metaphasic blockade. It is postulated that only actively proliferating cells—the so-called “growth fraction”—are the target for these alkaloids.


Ribonuclease has been partially purified from human leukocytes and its properties investigated. The enzyme has a pH optimum between 6 and 6.5. It is equally active with RNA prepared from various sources, attacking phosphodiester bonds adjacent to pyrimidine bases. Activity in myeloblasts or lymphocytes is about one-tenth that of mature granulocytes.


Three cases of autoimmune hemolytic anemia in infants are described. This disease is rare in the first few months of life. The possibility of an etiologic relation with (perinatal?) cytomegalic inclusion body virus or mycoplasma infection is discussed. One case (No. 3) was complicated with a rare hemoglobinopathy which may have been coincidental. Corticosteroid treatment in large doses was partially and temporarily effective in controlling the disease. Immunosuppressive therapy (asathioprine-Imuran, 2–5 mg./Kg./day) produced a complete cure in case 1 and allowed a marked decrease in steroid
doses in the other two cases. Most probably a vicious circle of autoimmunity was broken by this drug. Failure to gain weight on steroids was more than compensated for by clear-cut “catch-up growth” in case 1, even though Imuran was being given. Indications regarding precautions and dosage of azathioprine are stated. The exact mode of action of these drugs is discussed in an attempt to explain the nature of immunosuppression.


1. Two patients with acute leukemia had considerable decreases in leukemic cells in the peripheral blood as well as reduction in size of spleen and leukemic masses after 10 injections of tritiated thymidine given over a 5-day period. Each injection was 0.25 μGm/body weight.

2. The pertinent aspects of cytotoxic effects of tritiated thymidine are reviewed.

3. The radiation doses delivered to the nucleus are estimated from autoradiographic data.

4. Evidence is presented for the observed effects being due to tritiated thymidine.


1. Whole blood histamine content was measured in 80 patients with myeloproliferative disease. Increased levels were found in 60 per cent of patients with uncontrolled polycythemia vera, in 7 per cent of patients with polycythemia vera being controlled by myelosuppressive therapy, and in 71 per cent of a group with “spent” polycythemia, myeloid metaplasia and myelofibrosis.

2. The excretion of histamine in the urine was measured in 60 patients, 30 with elevated blood histamine and 30 with normal blood histamine. The urine findings paralleled the blood findings in 90 per cent of the cases.

3. Measurements of cell-poor and cell-rich fractions of blood showed that the histamine is contained in the white cell fraction. Elevated basophil counts were present in 50 per cent of the patients and occurred with the greatest frequency in the groups with elevated blood and urine histamine. A rough correlation between the basophil count and the histamine content of blood and white cell fractions was observed in normal subjects and most cases with myeloproliferative disease. Data obtained in some cases of myeloproliferative disease suggest that the histamine content of the basophil may be abnormal and that other granulocytes may contribute to the total leukocyte histamine.

4. Myelosuppressive agents produced a reduction in histamine (expressed per 10⁶ myeloid cells) and a decrease in urine histamine as control of the myeloproliferative process was achieved. Treatment with phlebotomy alone produced no change in histamine levels.

5. The incidence of pruritus, upper gastrointestinal distress and urticarial manifestations were increased 7-fold, 4-fold and 12-fold, respectively, in pa-
patients with elevated histamine levels as compared with those who had normal histamine levels.

6. Cyproheptadine, a potent antihistaminic, successfully controlled pruritus, relieved pyrosis and suppressed urticarial eruptions in patients with elevated histamine levels. Suppression of the reaction to subcutaneously administered codeine (a histamine-releaser) afforded objective evidence that cyproheptadine blocked the effects of histamine release in vivo.

7. The metabolism of histamine and the role of elevated histamine levels in the clinical manifestations and pathophysiology of myeloproliferative disease are discussed.


All these findings and the contradictory data in the literature show that the different types of nuclear projections in neutrophils—excluding the genetically determined drumsticks and sessile nodules—are nonspecific pseudosegments of the leukocytes. Their appearance depends on the segmentation, aging and metabolism of the neutrophils. These features might be influenced by many factors, possibly including hormonal effects. Our observations have shown, for instance, that androgens might produce an increase in the number of nuclear appendages. Although the appearance of these figures may be associated with certain diseases, it should not be regarded as a specific sign for a single pathologic or physiologic condition.


In summary we have demonstrated that hemopoietic stem cells of man contain all five isoenzymes, and not a single pure type. Our data and the results of others obtained from fetal tissue also indicate that embryonic LDH of man exists as multiple forms. We have demonstrated that differentiation, with respect to LDH isoenzymes, of stem cells along erythrocytic, granulocytic, and lymphocytic lines, occurs in different sequences. It appears that LDH-1 synthesis is necessary in mitotic granulocytic cells, but ceases at the metamyelocyte level where LDH-5 synthesis begins. LDH-5 synthesis occurs in early erythroid cells and probably ceases at the reticulocyte level. This is not accompanied by stimulation of LDH-1 synthesis. The maturation of lymphocytes is characterized by a stimulation of LDH-5 synthesis, which is not diminished in the normal circulating cell. Lymphocytes obtained from normal individuals and cultured in vitro in the presence of phytohemagglutinin demonstrate reversion of LDH patterns to those seen in acute leukemias. Our data further indicate that the isoenzyme pattern obtained from hemopoietic cells are indicative of the degree of cellular differentiation, and substantiate the concept of a defective differentiation and maturation process in acute leukemic cells.

Studies of certain aspects of lymphocyte kinetics were performed in nine patients with malignancies but who were hematologically normal.

Following the administration of tritiated thymidine, well-labeled large lymphocytes appeared very promptly in thoracic duct lymph along with some lightly labeled small lymphocytes. Specific activity was higher in the thoracic duct lymph lymphocytes as compared to the peripheral blood leukocytes for at least the first 50 hours.

When male patients were transfused with thoracic duct lymphocytes obtained from female donors, lymphocytes with a female karyotype were observed as early as 10 hours in the thoracic duct lymph and as early as 1 hour in the peripheral blood.

The evidence presented in these studies confirms data previously obtained only in animal experiments and indicates that homologous lymphocytes may circulate as long as 9 days in appropriate recipients.


Circulating lymphocytes were isolated from normal individuals and from patients with IM. IM lymphocytes synthesized RNA at 10 times the rate of normal lymphocytes. A 1-hour exposure to PHA did not result in the stimulation of 4-30S RNA synthesis which occurs in a similarly treated normal lymphocyte. RNA synthesis in IM lymphocytes actually appeared to be depressed by this short exposure to PHA.


The in vitro proliferative activity of human thymocytes significantly differs from either lymph node or peripheral blood lymphocytes. Thymocytes, in culture, show an autonomous proliferative activity not observed in lymphocyte cultures. Furthermore, thymocytes do not appear to replicate in response to PHA stimulation, a potent stimulus for in vitro lymphopoiesis. The technic employed, the 1-hour pulse labeling with H3T, shows that thymocytes maximally incorporate the radioactive label in the first hour of culture. After 3 days there is a significant decline in H3T incorporation in both the PHA-stimulated and control cultures. The degree of isotope incorporation does not appear to be influenced by PHA stimulation, indicating that these cells do not replicate in response to this stimulation. The in vitro proliferative activity corresponds to the activity observed in the intact thymus in animal studies.


Lymphocytes from a patient with lymphocytic leukemia were found to contain cytoplasmic globules. The globules varied in size, the largest appearing identical to Russell bodies. Histochemical staining was used to demonstrate the glycoprotein composition of these bodies. Electron microscopy revealed this material to be within dilated cisternae of rough endoplasmic reticulum. It is proposed that these globules are abnormal accumulations of glycoprotein which represent stages in the evolution of Russell bodies. The generic description of these cytoplasmic globules would seem to be preferable to the continued use of eponyms.


Heterozygotes for the Mediterranean type of severe G-6-PD deficiency were investigated by a variety of tests. The methemoglobin reduction test was most successful in detecting heterozygotes (about 80 per cent). Enumeration of methemoglobin-containing cells on blood films (Kleihauer-Betke technic) did not improve these results. Quantitation of enzyme level was less successful (65 per cent) and determination of decolorization time by the BCB technic least sensitive in heterozygote detection.

Methemoglobin reduction technics reflect a more indirect effect of the mutant gene than enzyme assay. The superiority of these technics in heterozygote detection is probably caused by the genetically determined presence of both normal and enzyme deficient cells in G-6-PD heterozygotes. Since methemoglobin reduction is carried out by individual cells, the population of enzyme-deficient cells does not reduce methemoglobin, and therefore even a minority of deficient cells leads to abnormal test results. In contrast, enzyme assay is less successful for heterozygote detection, since measurement of enzyme level is carried out on hemolyzed red cells, where cellular mosaicism no longer exists.

An additional source of variation of enzyme levels in heterozygotes is caused by the existence of genetically determined control of normal enzyme level. Possession of a high-capacity allele for G-6-PD activity may place a heterozygote in the normal range of enzyme activity.

The various tests were also applied to subjects with the mild Greek type of G-6-PD deficiency. Males with this mutation had enzyme levels varying between 10–50 per cent of the mean of normal males. Methemoglobin reduction test results were considerably less abnormal in hemizygotes with the mild type of Mediterranean deficiency than in heterozygotes with the severe deficiency. Fewer heterozygotes with the mild deficiency were detected.

Treatment of serum with folic acid conjugase, obtained from fresh chicken pancreas, indicated the presence therein of polyglutamyl derivatives of pteroi acid. The polyglutamyl derivatives appeared to belong to a group higher than the triglutamate.

Two groups of subjects, one with normal level and the other with low level of unconjugated folate were studied. In the normal group, folate varied between 3.2 and 18.0 ng./ml., while that of total folate (unconjugated plus conjugated) varied between 14.0 and 47.0 ng./ml. In the other group, the level of unconjugated folate varied from 2.0 to 2.6 ng./ml., while that of total folate varied from 14.5 to 31.0 ng./ml. No significant difference either in the individual values or in their means was noticed in the two group of subjects.