Leukokinetics in Peripheral Blood

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The leukokinetics in peripheral blood is recently becoming clear using radioisotope such as tritiated thymidine (^{3}H-TdR), diisopropylfluorophosphate ($DF^{32}P$), chromium 51 (^{51}Cr) and Sodium sulfate (^{35}S). At this meeting, the results of leukokinetics in normal subjects, chronic myelocytic leukemia (CML) and leukopenia were reported using $DF^{32}P$ in vitro or in vivo and ^{3}H-TdR in vivo methods.

In order to observe the uptake of DFP by peripheral leukocytes, the distribution of silver grains overlying neutrophils, eosinophils and lymphocytes of CML blood after the incubation with ^{3}H-DFP was examined. It was demonstrated that neutrophils were labeled by DFP, eosinophils and basophils slightly, but lymphocytes and myeloblasts were not labeled. Promyelocytes and myelocytes were more heavily labeled than metamyelocytes and polymorphonuclear neutrophils.

The methods for labeling blood in vitro or in vivo have been reported previously. Eight hematologically normal subjects were determined;

Granulocyte Disappearance Rate T½) 6.25 hours (3.3~9.3)
Total Blood Granulocyte Pool (TBGP) 35.8×10^{7} cells/Kg (14~92)
Circulating Granulocyte Pool (CGP) 18.4×10^{7} cells/Kg (8~30)
Marginal Granulocyte Pool (MGP) 17.7×10^{7} cells/Kg (0~80)
Granulocyte Turnover Rate (GTR) 98.3×10^{7} cells/Kg/day (14~198)

The disappearance curve of $DF^{32}P$-radioactivity by in vivo labeling method in four normal individuals could be divided into three phases. At first phase, there was rapid decrease (T½, 6~10 hours). Then, leukocyte radioactivity remained constant until the 8th or 10th day (second phase). At third phase, decrease of the activity in an exponential fashion was observed. Leukocyte radioactivity labeled by ^{3}H-TdR in vivo in a normal individual remained low in the peripheral blood until the fourth day, and after that it was shraply increased, reaching a peak level during a week. After two weeks, the curve reached to base line. From these data, it was suggested that granulocyte was reserved in bone marrow for about four days after their proliferation and maturation, then they appeared into the peripheral blood, where influx and eflux of them remained equilibrium.

In leukokinetics in CML, 13 studies were carried out on 10 patients. CML in relapse was characterized by prolonged GDR T½ (10 times than normal) and marked enlargement of TBGP. These GDR T½ and pool size index returned to normal with myleran therapy. In order to ascertain the reason for prolonged life span in CML, two kinds of isologous transfusions were performed. $DF^{32}P$ labeled leukocytes in CML were transfused into the hematologically normal and the leukopenic patient with malignant dsieases, in whom GDR T½ was slightly prolonged. On the other hand, when labeled leukocytes in normal man were transfused into CML patient, the life span was normal or slightly prolonged and the pool sizes were also increased. The prolonged life span in CML seems to be related to the presence of immature cells and the large size of the granulocyte pool, but these facts cannot explain the above reason completely.

GDR T½ of aplastic anemia was shortened in two cases of 4 studies. Pool sizes were smaller than normal in all cases. In cirrhosis of the liver with splenomegaly, GDR T½ was 2 hours and the pool sizes were small, but after splenectomy the pool sizes returned to normal and T½ became 3 hours.

In order to observe the leukocyte tissue pool, $DF^{32}P$ and ^{3}H-DFP labeled leukocytes were transfused into several rats and killed at predetermined intervals. Radioactivities in the lung and kidney were similar to GDR. In the spleen, the radioactivity was hihger at

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30 minutes than at 5 minutes. It was suggested that tissue granulocyte pool in the spleen was not synchronized with blood granulocyte pool.

Sequestration Function of the Spleen

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Circulatory dynamics of the spleen was studied and selective splenic sequestration was measured in relation to its unique ability to cull up such erythrocytes with minimal damage in the most sensitive and refined manner of the filtering organs.

Hemodynamics of the spleen. Hemoconcentration; In ferrokinetics studies relative splenic radioactivity to precordium was observed to be higher at the time when maximal level of radioiron incorporation into erythrocytes was reached, than that at zero time when all the radioiron existed in the plasma, indicating higher concentration of erythrocytes in the spleen than in general circulation.

After intravenous administration of ^{51}Cr labeled erythrocytes, mixing components, slow and rapid, were detected and assumed to be additional ones representing separate circulation of plasma and erythrocytes and also hemoconcentration phenomenon since mixing component was absent with lower level of relative splenic activity when RISA wsa used.

With sudden injection of ^{51}Cr erythrocytes or ^{131}I HSA through a catheter into the celiac artery, mean transit time through the spleen was calculated by analyzing respective radiosplenograms, and difference of the time between both radiotracers indicates hemoconcentration.

These findings were evident in hereditary spherocytosis, chronic congestive splenomegaly with portal hypertension and iron deficiency anemia, indicating concentration and stagnation of erythrocytes which suggest some cause and effect relationship to manifestation of "hypersplenic syndrome".

Exchangeable erythrocytes pool was detected by existence of slow mixing component in radiosplenogram with intravenously administered ^{51}Cr-erythrocytes. Results of isologous transfusion experiment using normal cells clarified the genesis of the pool primarily ascribed to abnormality of cells, as in hereditary spherocytosis, or to the histological alteration of the spleen, as in congestive splenomegaly.

By analyzing dilution curve of red cell activity this pool was quantitatively measured and transport coefficient into and out of the pool was calculated. Although half-survival of labeled cells was inversely correlated with fractional red cell mass in the pool in hereditary spherocytosis as well as congestive splenomegaly, it was proportionally correlated with the value of transport coefficient out of the pool in the former, while it was inversely correlated with that into the pool and the coefficient value out of the pool was disclosed to be correlated with the level of portal pressure in the latter.

Isolated erythrocytes pool was evidenced by noradrenalin-induced splenic contraction and transient change in red cell activity in the circulation. Repeated experiments disclosed gradual emigration of labeled cells into the pool, which was typically observed in cases with hereditary spherocytosis.

The clearance rate of heat-treated erythrocytes, which were so denaturated as to be selectively sequestered in the spleen, was measured in 10 normals and 95 cases with various hematological disorders. For deviation due to variable degree of damage, correction was made using close relationship between clearance rate and osmotic fragility of damaged cells observed in normals.

The clearance was noticed to be remarkably accelerated in portal congestive splenomegaly, moderately increased in hemolytic anemia,

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