

3636872 SCPA/D : MAJOR : PATHOBIOLOGY ; Ph.D. (PATHOBIOLOGY)
 KEY WORD : THALASSEMIA / RETICULOCYTE / ERYTHROID
 PRECURSOR / PHOSPHATIDYLSERINE / PATHOL-
 OGY / FLOW CYTOMETRY / CELL CULTURE /
 ELECTRON MICROSCOPY

ARCHROB KHUHAPINANT : BIOLOGY AND PATHOLOGICAL
 CHANGES OF THALASSEMIC ERYTHROID PRECURSORS. THESIS
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Thalassemia is a heterogeneous group of hereditary hematological disorders generally characterized by accumulation of either unmatched α - or β -globin chain in β - or α -thalassemia, respectively. By using the fluorescent flow cytometric technique, thalassemic peripheral blood reticulocytes have been investigated for their number, maturation state, *in vitro* maturation, volume, hemoglobin concentration and content. All symptomatic thalassemic patients show increased reticulocytes in both percentage and absolute number. These cells are also younger ones compared to those from normal persons as shown by their decrease in Low Fluorescence Ratio. These abnormalities are strikingly obvious in α -thalassemia with hemoglobin Constant Spring (CS), i.e. hemoglobin H with CS (H/CS) and homozygous CS (CS/CS). The splenectomized β -thalassemia/ hemoglobin E (β E-S) patients have much increased reticulocyte number and cells with high DNA content, probably nucleated red cells, designated as the upper particle count parameter. However, there is no difference for the degree of reticulocyte maturation in non-splenectomized (β E-NS) and splenectomized cases. Simultaneous measurement of reticulocytes and mature erythrocytes by flow cytometry revealed that discrepancy in erythrocytic hydration state of H/CS and CS/CS occurred as early as their reticulocyte state. The reticulocyte MCV/ mature erythrocyte MCV ratio in H/CS is significantly lower than that of H and such ratio in CS/CS reduces significantly compared to the normal one.

In vitro culture of β E erythroid precursors using the method of Two Phase Liquid Culture revealed increased proliferation of cells in β E-S more than β E-NS and normal control. Using the flow cytometric analysis of surface glycoprotein A (GA) and transferrin receptor (CD71), it was observed that the number of GA⁺ cells, CD71⁺ cells and both GA⁺, CD71⁺ cells was more in β E-S than that in β E-NS or normal ones in almost every week. Scanning electron microscopy of thalassemic erythroid precursors showed the dyserythropoietic features of proliferating erythroblasts in all types of thalassemia, rather striking in β E, H/CS and CS/CS. The increased loss of membrane lipid asymmetry by detection of phosphatidylserine exposure on external membrane leaflet using annexin V was found in erythroid precursors from all types of thalassemia ranging from the primitive stages to reticulocyte. Such abnormalities would partly explain the ineffective erythropoiesis in thalassemia.