CHAPTER II

PLAN OF WORK
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In leukaemia the inevitable complication anaemia has been studied for long period29,55,109,173. The knowledge regarding the exact pathogenesis of anaemia still remains obscure. Various theories have been advanced so far to elucidate the cause of anaemia include erythropoietic inhibition, haemolysis due to an intraerythrocytic defect9,60,65,129, "haemopathic" environment in leukaemic circulation49,56,164 demonstrated by the rapid elimination of the radio-isotope tagged normal red cells injected in the leukaemic patient142,150, autoimmune mechanism139,146,164, disturbance of haemoglobin synthesis including enhanced production of foetal haemoglobin18,148 and unstable haemoglobin172, red cell destruction by erythrophagocytosis101,102 and autoimmune mechanism66.

The factors controlling the bone marrow depression and haemolysis remain to be identified with the recognition and characterisation of the various haemolytic states conditioned by the deficiency of certain essential intraerythrocytic enzyme, it has been felt necessary to investigate the role of the relevant enzymes, if any, in the causation of early lysis of the red cells of leukaemic patient resulting anaemia.
Reduced glutathione is known to play an important role in the maintenance of the structural integrity of the red cells by protecting it against oxidative damage. The deficiency of erythrocytic reduced glutathione (GSH) leads to a chronic haemolytic state. Existing knowledge regarding the nature and activity of glutathione in leukemic red cells, however, is sketchy and fragmentary and inconclusive. In the Embden-Meyerhof pathway of glycolysis, the pyruvate kinase (PK) deficiency was the first abnormality to be identified as associated with hereditary haemolytic anaemia. There are reports regarding the PK value in various types of leukemia. The PK value appeared to be low in some leukemic patients, especially in acute leukemia where the red cell life-span was shortened. This also requires further work to conclude anything about the cause or effect of the disease leading to anaemia by early lysis of the red cells. In this present communication, it has been tried to fill up the lacunae.

In this present thesis, attempts have been made to investigate the status of the red cell enzymes in various types of leukemia in respect of their quantitative change, if any, which may cause early hemolysis. Particular attention has been given to investigate the status of enzymes - GSH, G-6-PD, GR and PK, as deficiency of these
enzymes may produce early lysis of the red cells. Serial study during different phase of the disease with a view to correlate the findings with various phases of the illness was done.

The subjects studied in the present thesis include the patients investigated and treated in the Haematology Department of Calcutta School of Tropical Medicine. These patients attended the Out-patients' Department of Haematology and some of them were subsequently admitted in the Carmichael Hospital for Tropical Diseases under the care of Late Prof. J. B. Chatterjea and Dr. A. K. Basu. The clinical findings were evaluated in the light of blood and bone marrow picture. The final diagnosis was done from the nature of the cells, predominating in the bone marrow. The other methods adopted for investigations are given in their respective chapters. Normal subjects in respect of clinical and haematological status were taken for control study. Members of the staffs and students also kindly allowed themselves for examination for the control study. The subject matter of the work is presented in the following three parts.

Part I.

Haemopoiesis includes the records of haemoglobin, reticulocyte count, red cell morphology, electrophoresis of
haemoglobin, alkali resistant haemoglobin, WBC count and thrombocytes in their qualitative and quantitative change, in various phases of the disease. Studies of the bone marrow in different stages are included here.

**Part II.**

In this part studies on haemolysis in different types of leukaemia in their different phases are included. This comprises of osmotic fragility, incubation fragility, mechanical fragility, auto-haemolysis, acid serum haemolysis, sucrose lysis test, estimation of plasma bilirubin and plasma haemoglobin, Coombs' test, auto and iso-agglutination in blood and estimation of faecal urobilinogen content. Detection of Heinz bodies in red cells is also included in this part.

**Part III.**

This part includes study of enzymes in the red cells. In the pentose phosphate pathway the enzymes G-6-PD, GSH, GR and in the Embden-Meyerhof pathway, the activity of the enzyme PK are discussed.