The work presented in the thesis has been described in three parts. The studies include (i) the role of ascorbic acid in hemopoiesis and in the metabolism of iron; (ii) transport iron and non-hemoglobin iron in different mammalian species; and (iii) the transport iron in patients suffering from infectious diseases like cholera, tetanus and meningitis.

Anemia in scurvy: its relation with iron metabolism.

Scurvy is associated with anemia but the role of ascorbic acid in hemopoiesis is far from clear. The work presented in the thesis was, therefore, undertaken to understand and to explore the part played by ascorbic acid in the metabolism of iron. Monkeys and guinea pigs, like human beings, need an extraneous source of ascorbic acid. These animals were, therefore, selected for the studies. Scurvy was produced in monkeys and guinea pigs by feeding them a scorbutogenic diet which contained all the dietary essentials with the exception of ascorbic acid. During the progress of development of scurvy some animals were fed extra doses of iron. A few animals were allowed to recover from scurvy by treatment with ascorbic acid. Effect of inanition was also considered. Hematological and biochemical studies were undertaken in the animals under different treatments.
Scorbutic monkeys and guinea pigs suffered from anemia of variable degrees. Anemia was usually normocytic and normochromic in character, despite the presence of a few microcytic-hypochromic and macrocytic red blood corpuscles. There was an increase in the percentage of reticulocytes. The rate of sedimentation of erythrocytes was enhanced. There was leukopenia with reduction in the percentage of neutrophils and lymphocytes. Bone marrow contained increased number of normoblasts, diminished number of granulocytes with preponderance of immature forms of erythrocytes and leukocytic series of cells. Megaloblastosis could not be seen in a single scorbutic monkey or guinea pig. The changes observed in scorbutic animals were indicative of maturation defects of erythrocytes and leukocytes. The total blood volume and cell volume diminished considerably in scorbutic monkeys while the plasma volume remained unaltered. Hemolysis or external blood loss were not observed in the scorbutic animals. Transition associated with scurvy was not responsible for the blood changes.

Supplementation of iron to guinea pigs during the progress of scurvy did not improve or alter the type of anemia, but aggravated the condition. This has been suggested to be due to the increased depletion of ascorbic acid content of
tissues as a result of the administration of iron.

In the scorbutic animals plasma iron, total iron-binding capacity, liver ferritin and sideroblast percentage diminished. Free erythrocytic protoporphyrin and hemosiderin of liver increased. There was increased deposition of iron in tissues and bone marrow. Inanition was not responsible for these changes. Treatment with iron during the progress of scurvy did not increase the soluble iron-fraction but increased the insoluble iron-fraction of the liver, could not correct the hypoferremia and increased the deposition of hemosiderin in tissues including the bone marrow. Iron uptake by the liver of scorbutic guinea pigs was less than the liver of normal animals. Administration of ascorbic acid in vitro, however, had no effect on iron uptake by liver of guinea pigs under different treatments. Most of the above changes could be reversed when the scorbutic animals recovered from the condition after supplementation with ascorbic acid. Ascorbic acid deficiency does not interfere with the intestinal absorption of iron, indicating that the role of ascorbic acid in increasing iron absorption is not through any change in cellular behaviour. Ascorbic acid is concerned in the transference of iron into normoblasts. It may be responsible for both the formation and splitting of ferritin. It seems to take part in the utilisation of iron for hemoglobin synthesis.
Blood iron in different species of animals.

Plasma iron, total iron-binding capacity of plasma and non-hemoglobin iron of erythrocytes were determined in different species of animals, e.g. camel, cow, goat, sheep and monkey. The values of plasma iron and total iron-binding capacity were lowest in the cow, highest in the goat, with intermediate values in the other species of animals. A high percentage of non-hemoglobin iron was present in the erythrocytes of the cow although the plasma iron value was lowest in the animals.

Transport iron in infectious diseases.

Serum iron and total iron-binding capacity of serum were studied in patients suffering from cholera, tetanus and meningitis. In cholera and tetanus both serum iron and total iron-binding capacity diminished markedly within 24 hours of the onset of illness. In cholera, serum iron and the serum total iron-binding capacity dropped respectively to 24% and 55% of the normal figures within the short period of infection. Per cent saturation was found to be significantly reduced. No relation between the serum iron or serum total iron-binding capacity and the different fraction of serum proteins including albumin could be observed.