Cancer of the uterine cervix is the leading malignancy affecting women in developing countries and is the commonest malignancy among Indian women. Enzyme levels were determined in fresh hemolysate from cervical cancer patient and normal women. All such samples showed increased activity of enzymes (HK, PFK, Ald, PK and LDH). The profile of glycolytic-enzyme increases except PGI shown in Table 2-7 (chapter 1) in these cervical tumors gives some insight into the possible rate limiting steps in glycolysis. In terms of the enzyme catalysed reactions with the least activity it would seem that HK, Ald and PFK were rate limiting in normal cervix. The activity of LDH isozyme 3 and 5 are more pronounced in cervical cancer. Glucose-6-phosphate dehydrogenase and transketolase activity (Table 8,9 and10) in HMP Shunt pathway (chapter 2) was observed to decrease in cervical cancer. Thus, supply of NADPH is reduced and it alters antioxidant status of the pathologic erythrocytes. It can be inferred that GSH regeneration either directly by glutathione reductase or indirectly by glucose 6-phosphate dehydrogenase are not sufficient to regenerate GSH to meet up the cell's requirement. Thus lower level of reduced glutathione reveals the erythrocyte to be in a pro-oxidant conditions and may be a partial cause of increased hemolysis and shortened RBC survival observed in cervical cancer RBC. Thus changes occur during malignant transformation to the levels of both 'regulatory' enzymes and enzymes catalyzing reversible reactions, in a consistent and orderly manner, which justifies the conclusion that the general metabolism of tumors is convergent.

Cancer development includes three major steps, initiation, promotion and progression, in which oxidative stress is involved. Oxidative stress is defined as an imbalance between the levels of prooxidants and antioxidants in favour of the former and resulting in irreversible cell damage. Membrane lipid hydroperoxides has been also determined. However, both reduction in antioxidants and elevation of lipid peroxidation has been observed in general. In addition, lipid hydroperoxide levels were negatively correlated with superoxide dismutase, glutathione peroxidase activities and catalase activity. Catalytic activities of superoxide dismutase and glutathione peroxidase in cervical cancer RBC may affect in scavenging superoxide radical \( O_2^- \). Catalase is responsible to counteract hydrogen peroxide and protect the cell from peroxidative damage. But significant decrease in catalase activity was observed, which reveals the fact that complete removal of hydrogen peroxide in cervical cancer red blood cells is not possible at all. The obtained results (chapter 3 and chapter 4) also show that perturbation of the antioxidant status is more...
pronounced in blood of patients with malignant (cervical carcinoma) lesions compared to normal.

Osmotic fragility studies also showed that the cervical cancer red blood cells are less osmotic-resistant compared to normal erythrocytes (figure 15). The peripheral red blood cells of cervical cancer patients show different kind of cell morphologic abnormality (Figure 21 in chap 4). This study has revealed that peroxidation of membrane lipids reflect strongly on the lipid packing density and microviscosity of lipid bilayer and the in vitro oxidative damage of human red blood cells (Figure 14). Membrane fluidity is very important for membrane elasticity, permeability, aggregation, diffusional movements and biological transport of the protein and lipid and also membrane bound enzyme activities.

Proteins are also easily attacked by ROS directly or indirectly through lipid peroxidation. Protein radicals can be rapidly transferred to other sites within the protein infrastructure. This can result in further modification of enzyme activity, stimulation or inhibition. This study indicates that antioxidant defense mechanisms are impaired in human uterine diseases, and it also points to elevated levels of lipid peroxidation products, as markers of oxidative stress, in the plasma of such patients. Protein oxidative damage can result in modifications in the structure, enzyme activity, and signaling pathways.

The membrane lipid fluidity and membrane protein organization of cervical cancer erythrocyte membrane has been presented in chapter 4. From steady state fluorescence polarization studies, it was found that cervical cancer RBC membranes are more fluid at 25°C than normal erythrocyte membrane (Figure 19). With increase in temperature the fluidity of the membrane also increases but in contrast, cervical cancer erythrocyte membranes remained in less fluid states during the experimental temperature range (Figure 18). The decrease in membrane fluidity in cervical cancer erythrocytes, obviously resulted due to some defect in membrane organization, which has been manifested as increased rigidity and decreased deformability. These modifications are definitely responsible for declined ability of cervical cancer erythrocytes to deform and accelerate the disturbance in microcirculations. The decreased deformability of cervical cancer erythrocytes could impair the passage of RBCs through the sinusoidal walls of reticulo-endothelial organs and consequently trigger the removal of these cells from the circulation, which ultimately causes anemia.
This study demonstrates structural and functional abnormalities in the erythrocytes of cervical cancer patients by measuring *in vitro* lipid peroxidation, enzymatic antioxidant status, and the osmotic fragility of erythrocytes. These results indicate the potential for oxidative injury to erythrocytes and erythrocyte membranes in cervical cancer.