1.0 PROLOGUE

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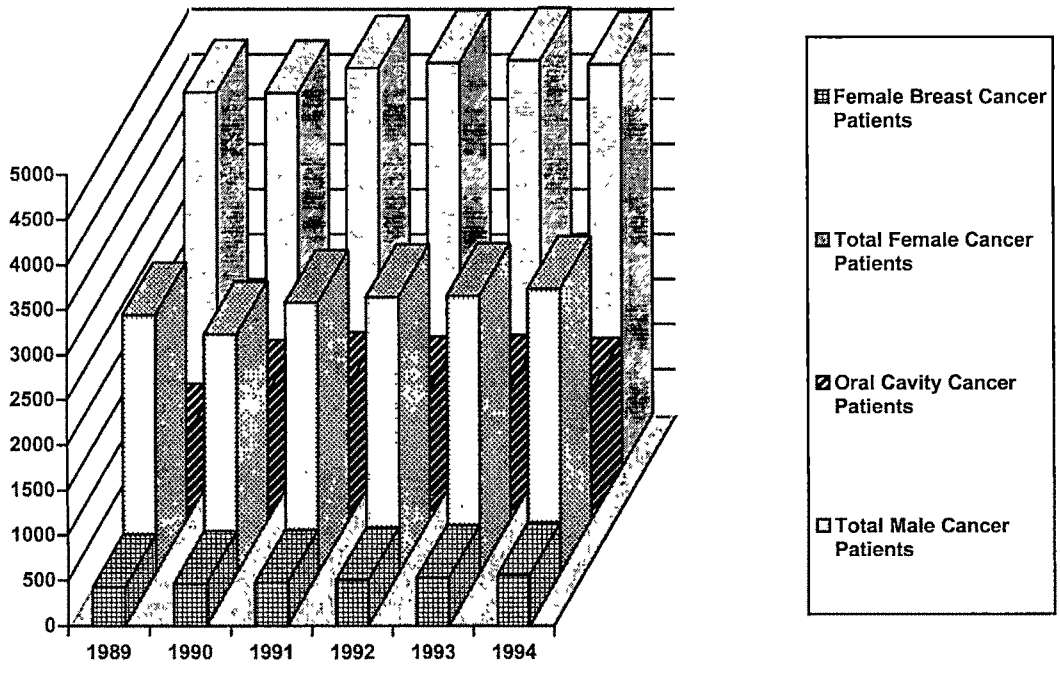
1.1 CANCER, A SERIOUS HEALTH HAZARD

Cancer is in second place in the list of fatal diseases. In essence, the concept of cancer is the seemingly autonomous and uncontrolled cell multiplication, which results in tissue in excess of requirement of the body. It is paradoxical that cancer arising from cell, the basic unit of life, is responsible for the death of one out of five people alive today. As the incidence and death rate due to cancer have shown a sharp acceleration since last two decades, more intense efforts are required to fight this life threatening disease.

Figure-1 : INCIDANCE OF BREAST CANCER AND ORAL CAVITY CANCER (at GCRI)



The data **(Figure - 1)** available from ***The Gujarat Cancer Research Institute (GCRI), Ahmedabad,*** a regional cancer centre recognised by the Government of India, indicate that in Gujarat, like other parts of the world, overall incidence of cancer is increasing year after year. The reports from the hospital registry show that cancer claims more than seven thousand lives per year only in

Gujarat. It is estimated that in Gujarat one out of 125 people may develop cancer over a lifetime (Cancer Registry Report 1994). Oral cavity is the leading site of cancer in males. The incidence of oral cavity cancer is around four times higher in males as compared to females. Among females, breast cancer is more frequent as represented in the hospital based cancer registry reports. It is documented that around 18% of all tumours arising in females are of breast. Because of unavailability of the markers which can help in early diagnosis of cancer and can predict treatment outcome, many lives are still lost every year due to certain cancers that could have been otherwise prevented or controlled. Thus, it is of prime importance to stamp early biochemical changes and to forecast treatment outcome for progress in cancer research.

1.2 CELL SURFACE CHANGES AND CANCER

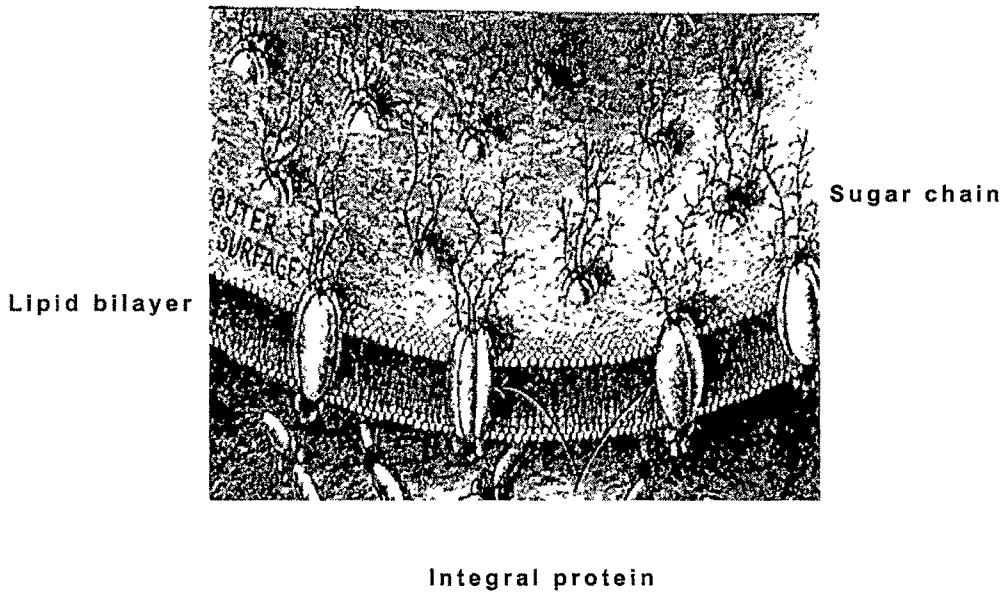
In 1838, Johnannes Muller provided a break through by the demonstration that malignant tumour consists of cells. Since this observation that cancer is a cellular disease, the cell has remained the basis of cancer research. Cancer is called a disease of the cell rather than a disease of an individual. It is usually considered as irreversible changes in a cell that takes it from normal to malignant. One can not determine which particular cell will become malignant. The exact mechanism "How a cell becomes malignant?" is also not yet understood.

Malignant neoplasia can be regarded as a caricature of certain normal biological processes. However, the changes associated with the development of malignant behaviour of a cell are poorly known. Hence, to understand neoplasia, it is necessary to clearly identify the distinguished characteristics of tumour cell. Therefore, to study biochemical alterations of a tumour cell is the ultimate object of cancer biology.

The quest to define the differences between normal and cancer cell has driven the research to focus on progressive deeper level of organisation, from

organ to tissue to cell and from cell to subcellular organelles. Many properties of living cells are expressed or mediated through cell surface. Among various organelles, the plasma membrane is of paramount interest, as it presents a barrier between extracellular and intracellular molecules, holds the cell together and also believed to play important role in cell growth and differentiation **(Figure 2).**

Figure-2
A DIAGRAM SHOWING STRUCTURE OF CELL SURFACE



It is unequivocally clear from the data in the literature that malignant transformed cells have different profile and structure of cell surface. Majority of the functions of cell surface is attributed to the embedded glycoproteins. Therefore, the important approach for understanding altered cell surface phenomenon has been mainly to analyse its glycoprotein constituents and to characterise their chemical properties.

Over the past several decades' experience gained from the study of tumour has led to the recognition of the significant role of glycoproteins in malignant transformation. As majorities of presently known tumour markers are glycoproteins in nature, these constituents of the cell membrane have drawn

considerable attention. Efforts have been made to study the role of glycoproteins in neoplasia, although several areas need more thorough elucidation. The putative relationship between glycoproteins and cancer, which has emerged from several research studies, may yet be recognised as the nadir of biological achievement in the study of this disease. Understanding the intricate nature of this interaction can reveal insight into the mechanisms of tumorigenesis.

1.3 SCOPE OF THE PRESENT STUDY

Tumour, like the tissues of the body needs nutrients, which are derived from blood. As blood flows through and connects all tissues, and also mediates the metabolic interactions among them, is obviously bound to reflect disease status. This connective path is the major route for spread of the disease. It is valuable to detect blood-based biochemical changes not only as a step towards diagnosis but also to establish the disease status of patients receiving anticancer treatment. The idea of screening and following patients with malignancy by serum tests is appealing from several points of view, including its ease, economic advantage and possibility of repeated sampling and non-invasiveness. Evaluation of more sensitive and specific biochemical changes may help to detect the disease at an early stage and these advances may prove to be significantly advantageous in the direction of predictive medicine. The early and continuing research in neoplasia has yielded many tumour markers but none fulfils all the criteria. In some instances association of the changes with cancer are only seen at the time of diagnosis. In such cases, the efficiency of the study would be greatly enhanced if they were to be concentrated on population with precancerous conditions as well as patients during and after anticancer therapy. Hence, the attainment of the better blood based biochemical alterations for cancer has continued to be of paramount interest for the foreseeable future.

In an effort to contribute to the reduction of both incidence and the morbidity as well as mortality due to malignancy, aiming of identifying blood-based

biochemical changes, the present study was focused on the alterations of glycoproteins and their constituents in blood as well as tumour tissues. The goal of the present study was to determine if glycoprotein changes in the circulation correlate with the risk of cancer and with disease status before and after initiation of anticancer therapy. The glycoprotein changes are studied in healthy individuals, patients with benign breast diseases (BBD), patients with oral precancerous conditions (OPC), as well as breast cancer patients and oral cavity cancer patients at the time of diagnosis and after initiation of anticancer treatment. The work was undertaken with the emphasis on following major **Aspects**:

- Determination of serum levels of glycoprotein constituents including different forms of sialic acid, fucose and seromucoid fraction.
- Study of serum glycoprotein electrophoretic pattern by polyacrylamide gel electrophoresis.
- Evaluation of sialoprotein and fucoprotein levels in sera using specific lectins.
- Analysis of serum levels of glycoprotein metabolism enzymes including fucosidase, sialyl transferase and fucosyl transferase.
- Confirmatory analysis of the parameters in tumour tissues.