# Chapter 2

# BREAST CANCER

Cancer is basically a disease, which occurs when cells behave abnormally and divide out of control. The clinical definition of cancer is a variety of diseases characterised by unregulated cell growth leading to the invasion of surrounding healthy tissues which may spread to other parts of the body (Roger, 1996). Eventually these cells form a visible mass or tumour. The term tumour simply means an abnormal growth.

There are two general types of tumours namely, benign (non-cancerous) and malignant (cancerous) tumours. A benign tumour is composed of cells that will not invade other unrelated tissues or organs of the body, although it may continue to grow in size abnormally. A malignant tumour is composed of cells that invade or spread to other parts of the body.

Different types of cancer behave very differently, grow at different rates and respond differently to treatments types. Cancer patients need specific treatments for their type of cancer to ensure recovery.

There are numerous types of cancer, which are commonly named after the parts of the body that are initially affected, although the tumour may have spread to other parts of the body. Some cancer examples are breast, lung (thorax), melanoma of the skin, colon and rectum (digestive), kidney (genitourinary), urinary bladder (genitourinary), nasopharyngeal carcinoma and others. Metastasis is a phenomena when cancer cells break away from the primary tumour and travel via the blood stream or lymphatic system, to different sites within the body.

Breast cancer is the most common of all cancers; it is second after lung cancer in causing fatality amongst women (Parker, 1997). Breast cancer is a malignant tumour that develops from the uncontrolled growth of cells in the breast.

## 2.1 Epidemiology

Epidemiology is the study of the distribution and factors involved in the development of diseases in human population. Prevalence is the estimated number of people with the disease in a specific location or all around the world, who are alive at any point of time or at some time during a definitive period (Bosch & Coleman, 1994). Estimated incidences of cancer seem to show a lower occurrence of breast cancer in Asian regions compared with several European nations (Mettlin, 1999).

Incidence quantifies the number of new cases of disease that has developed in a population, expressed as a fixed rate (number of cases per 100,000 people per year). In the year 2000, there were 1,050,346 cases of breast cancer reported with 372,969 deaths from breast cancer worldwide. The incidence ranged from an average of 95 per 100,000 in more developed countries to 20 per 100,000 in less developed countries. The mean age at diagnosis reported in most developing countries is around 50 years compared to 60 years in western countries.

In 2002, 4337 cases of female breast cancer were reported to the NCR (NCR, 2002). The incidence was estimated at 45.1 per 100,000 with 1 in 19 chance of getting breast cancer in a woman's lifetime. In UMMC, there were a total of 952 breast cancer patients over the years ranging from 1993 to 2000. The number of breast cancer patients seen in UMMC increased annually with the highest recorded in 2000, with three times the number of cancer patients recorded in 1993. The incidence of breast cancer amongst

the Chinese appears to be higher compared to Malays. The majority of breast cancer patients were within the 40-49 years age group when they were first diagnosed (Radiology, 2002).

Breast cancer awareness campaigns amongst women have been carried out in most parts of the world including Malaysia, making women attentive about the need to take care of their health more diligently. An increased cure rate is possible if the disease is diagnosed at an early stage and treatment is subscribed accordingly.

## 2.2 Risk Factors

The causes of breast cancer remain unknown, but numerous factors have been associated with it such as age, personal history of breast cancer and a family history of breast cancer (Harris et al., 1997). Increasing age is strongly associated with increased risk. The average woman has an 11% chance of developing breast cancer if she lives to an age of 85. However, 2% of the total risk occurs between birth and 50 years, 5% occurs between 50 and 70 years and 4% occurs from 70 to 85 years (Kelly, 1993). A woman who has had breast cancer is at risk for developing breast cancer again. The absolute lifetime risk of developing a second breast cancer is 30% (Henderson, 1993).

The risk to a woman with a first-degree relative (mother, sister, or daughter) who has breast cancer is further increased if her relative had breast cancer that occurred before menopause (Boyd, 1994). Other factors including hormones, diet and lifestyle; smoking and consuming alcohol seem to be important in breast cancer development.

## 2.3 Breast Anatomy

Inside women's breasts there are glands that produce and release milk in association with pregnancy. The anatomy of the breast is shown in figure 2.1. The normal breast has 6 to 9 overlapping sections called lobes and within each lobe there are several smaller lobules that contain the cells that produce milk. The lobes and lobules are linked by thin tubes called ducts, which lead to the nipple in the centre of the breast. The spaces around the lobules and ducts are filled with fat. Lymph vessels carry colourless fluid called lymph that contains important immune cells. The fluid is carried in lymph vessels that lead to small, pea-sized collections of tissue called lymph nodes. Clusters of lymph nodes are found in the axilla (under the arm), above the collarbone and in the chest.

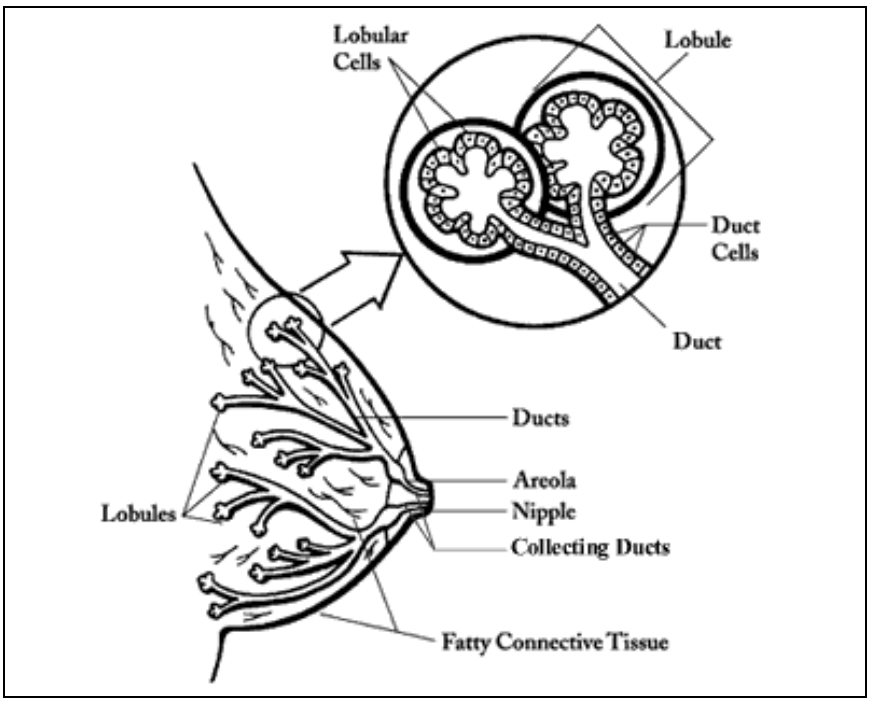


**Figure 2.1: Anatomy of the Breast**

The suspicion of breast cancer first arises when a lump is detected in the breast during breast examination or a suspicious area is identified during mammography screening. In order to diagnose the cause of the suspicious area or lump in the breast, a physician

needs to perform a biopsy. A brief description of mammography and biopsy can be found in the next section.

## 2.4 Diagnosis

Diagnosis is defined as a formal statement about the nature of a patient's disease. An accurate diagnosis can be made only after the clinician has obtained a full history, conducted a complete physical examination, and reviewed the results of relevant laboratory or radiological investigations. Breast cancer is most often detected because the patient herself notes a change in the breast like the appearance of a mass or thickening, development of skin dimpling, nipple retraction or nipple discharge.

A mammogram is performed on women with no evidence of lumps or other symptoms. This includes two x-ray views of each breast (top to bottom; side-to-side). A diagnostic mammogram includes additional x-ray views of areas of concern found on physical examination or on the screening mammogram to provide more information about the size and character of the abnormality.

Fine-needle biopsy is used to investigate breast lesions through the removal of a piece of tissue for examination under a microscope to see whether cancer cells are present. Various investigations will be carried out by the doctor to determine the extent of the disease. Other information obtained from the biopsy sample will play an important role in treatment decisions. If the biopsy indicates that cancer is present, additional surgery may be performed after the patient and doctor have selected a course of treatment.

## 2.5 Staging

Cancer staging describes how far cancer has spread anatomically and constitutes an important factor in planning and implementing the appropriate treatment. Staging is a process of describing the site of the disease during diagnosis and assists in answering prognostic questions. The most frequently used staging system for defining the extent of disease is the TNM classification (Appendix A) proposed by The American Joint Committee on Cancer (AJCC). A patient is treated depending on their particular TNM staging.

In the TNM staging, T refers to the extent of the primary tumour, and normally given as $T_0$ through $T_4$. $T_0$ represents a tumour that has not even started to invade the local tissues, also called "In Situ"; $T_4$ represents a large primary tumour that has probably invaded other organ by direct extension. N refers to the amount of regional lymph node involvement and only the lymph nodes draining the area of the primary tumour are considered in this classification. $N_0$ represents no lymph node involvement and $N_3$ represents extensive involvement. M refers to the presence or absence of metastasis with either $M_0$ if there are no metastases or $M_1$ if there are metastases. The combination of the T, N and M classification indicates the extent of the disease at the time of clinical evaluation.

Another staging system called Overall Stage Groupings is grouped into four stages, Stage 0 through Stage IV. Stage 0 is a very early breast cancer that has not spread within or outside the breast. Stage I cancers are small localized cancers that usually curable, Stage II and III cancers are usually locally advanced and/or with involvement of local lymph nodes, while stage IV represent inoperable or metastatic cancer.

## 2.6 Treatment

Treatments in breast cancer can be separated into Local Therapy and Systemic Therapy. Local therapy refers to treatment of the breast and surrounding lymph nodes usually in a combination of surgery and radiation therapy. Systemic therapy on the other hand refers to chemotherapy or hormone therapy to control cancer cells that may spread to other parts of the body.

### 2.6.1 Local Therapy

Surgery is the most common method used for localized breast cancer. The more often used procedures include lumpectomy with axillary node dissection and modified mastectomy. Lumpectomy with axillary node dissection entails excision of the tumor mass, including a clear margin of normal breast cancer around the tumor, along with lymph nodes under the arm. Modified radical mastectomy entails complete removal of the breast, the chest wall muscles under the breast, and some of the axillary nodes (Harris et al., 1997). Radiation therapy is used to destroy cancer cells left behind in the breast, chest wall, or lymph nodes after surgery. Surgery and radiotherapy are very effective in removing or destroying malignant tissue if exact location of cancer cells is known and adjacent normal organs and tissues can be preserved without injury.

### 2.6.2 Systemic Therapy

Systemic therapy refers to chemotherapy or hormone therapy to control cancer cells that may spread beyond the breast and nearby tissues. Chemotherapy is the use of drugs to kill cancer cells by damaging the cancer cells that are dividing. The drugs travel in the bloodstream and move throughout the entire body. Hormonal therapy is an approach to suppress the growth of hormone that promotes the growth of cancer. Estrogen, a

hormone produced by the ovaries and the adrenal glands, causes some breast cancers to grow. In order to block the effect of estrogen and slow or stop the growth of cancer cells an anti-estrogen such as Tamoxifen is most commonly used.

### 2.6.3 Adjuvant Therapy

Adjuvant therapy is a treatment that is added to increase the effectiveness of a primary treatment. It usually refers to hormonal therapy, chemotherapy, or radiation added after surgery to kill any cancer cells still remaining and which may increase the chances of curing the disease.

## 2.7 Prognosis

The medical definition of prognosis is the prediction of the future course and the outcome of disease process, which may either concern their natural course of their outcome after treatment (Abu Hanna & Lucas, 2001). Prognosis is the principal factor in determining the treatment that will immediately follow the diagnosis of the disease. Prognosis is important because the type and intensity of the medications are based on it. However, prognosis is only a prediction and like all predictions, it is not hundred percent accurate.

Data in the form of cancer stage, aggressiveness, individual age and treatment effectiveness could result in a clear indicator, which would assist in coming up with a workable prognosis. In breast cancer patients, stage of disease and tumour size are primary predictors of disease-free and overall survival. Other significant prognosis indicators include age, lymph node involvement, estrogen receptors (negative or

positive), grade, the type of therapy used and many others. Genetic factors are beginning to be examined as indicators of survival (Cheryl et al., 2000).

At the time of diagnosis, patients with Stage I-III cancers had a 93 to 100 percent probability of surviving the first year, while Stage IV patients had a 64 percent probability of surviving the first year (Henson et al., 1995). A report on a treatment for 508 patients with stage I and II cancer indicates that patients with $T_2$ tumours had a shorter survival rate than those with $T_1$ tumours (probability (p)<0.001) (Slotman et al., 1994). Increasing age is also strongly associated with increased risk and had been discussed in section 2.2. In our study the prognosis indicators include age, race, stage, TNM classification, lymph node involvement, estrogen receptors, grade and treatment options. The descriptions of the variables are given in chapter 4.

## 2.8 Summary

Breast cancer is a malignant tumour that develops from uncontrolled growth of cells in the breast. The incidence of breast cancer in Asian regions is lower as compared to several European nations. Cancer staging is an important factor in planning the appropriate treatment by determining the extent of spread or stage of the cancer. In defining the extent of breast cancer, the TNM classification proposed by the AJCC is the most frequently used staging system. Effective means of treating breast cancer are widely available and may be used alone or in combination, depending on individual's circumstances. Breast cancer can be treated using surgery, chemotherapy, radiation therapy, tamoxifen or a combination of these. The prognosis of an individual with breast cancer can be affected by many factors, such as breast cancer stage, age, tumour size, lymph node involvement etc. Prognosis is crucial in recognizing and assigning the treatment that will be used with respect to the diagnosis of a particular cancer type.