Chapter (2)

Literature Review

Chapter [2]

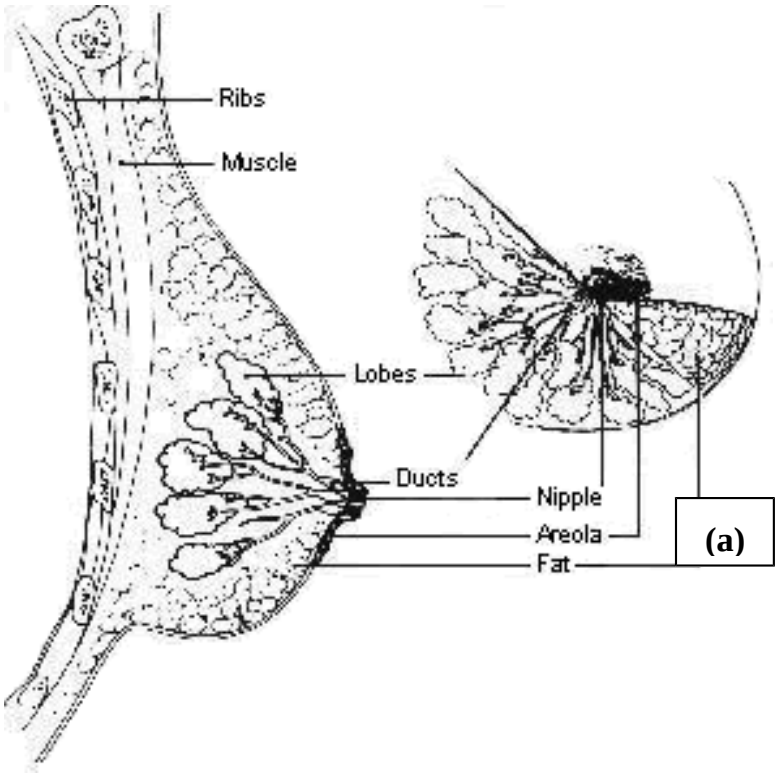
Section (1)

Theoretical background

2-1 Breast Anatomy and Physiology

2.1.1 Breast Composition

The breast is a mass of glandular, fatty, and fibrous tissues positioned over the pectoral muscles of the chest wall and attached to the chest wall by fibrous strands called Cooper's ligaments. A layer of fatty tissue surrounds the breast glands and extends throughout the breast. The fatty tissue gives the breast a soft consistency. The glandular tissues of the breast house the lobules (milk producing glands at the ends of the lobes) and the ducts (milk passages). Toward the nipple, each duct widens to form a sac (ampulla). During lactation, the bulbs on the ends of the lobules produce milk. Once milk is produced, it is transferred through the ducts to the nipple (Linda, 2006). The breast is composed of milk glands (lobules) that produce milk, ducts that transport milk from the milk glands (lobules) to the nipple, nipple, areola (pink or brown pigmented region surrounding the nipple), connective (fibrous) tissue that surrounds the lobules and ducts and fat.



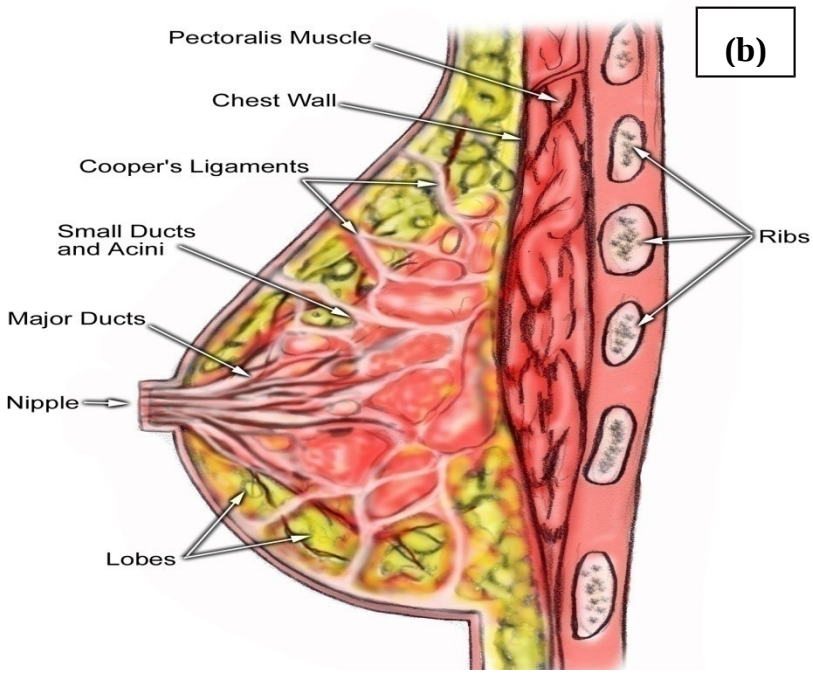
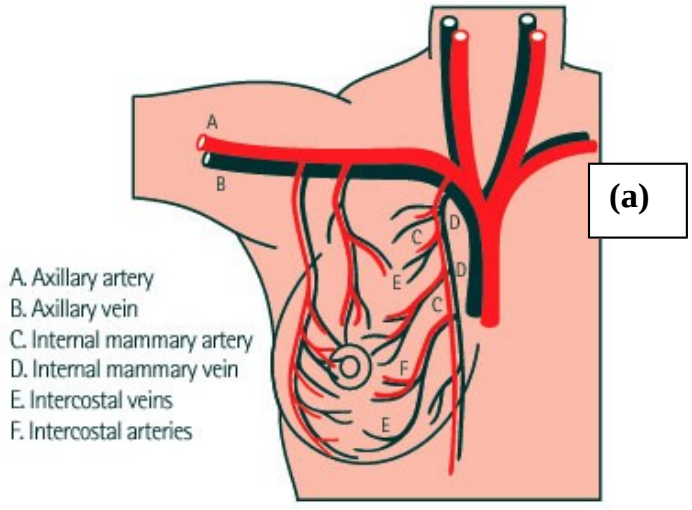


Figure (2- 1) a. & b. Shows the Anatomy of the Breast (Linda, 2006).

The blood of the breast skin depends on the subdermal plexus, which is in communication with underlying deeper vessels supplying the breast parenchyma. The blood supply is derived from: perforating branches of the internal mammary artery, the lateral thoracic artery the thoracodorsal artery, intercostal artery perforators and the thoracoacromial artery

This rich blood supply allows for a variety of reduction techniques, ensuring the viability of the skin flaps after surgery (Allen, 1994). Sensory innervations of the breast is dermatomal in nature. It is mainly derived from the anterolateral and anteromedial branches of thoracic intercostal nerves T3-T5. Supraclavicular nerves from the lower fibers of the cervical plexus also provide innervation to the upper and lateral portions of the breast. Researchers believe sensation to the nipple derives from the lateral cutaneous branch of T4 (Linda, 2006). An area of breast tissue, under the skin, leads into the armpit (axilla). The armpits have many lymph glands, also known as lymph nodes. The diagram above shows the network of lymph glands around the breast. They are part of the body's lymphatic system. There is also a chain of lymph nodes that runs up the centre of your chest, by your breast bone. This is called the internal mammary chain. The lymphatic system is made up of a network of lymph glands, connected throughout the body by tiny tubes (vessels) called lymph vessels. Lymph glands are part of the natural drainage system of the body. Lymph is a yellow fluid that flows through the lymphatic system and eventually drains into veins. This system helps to get rid of waste products from the body. Tissue fluid bathes the body's cells, drains into the lymphatic system and is re circulated. Lymph glands are important in cancer care because any cancer cells that have broken away from a tumor can be carried by this tissue fluid to the nearest lymph glands (Cancer Research UK, 2009).



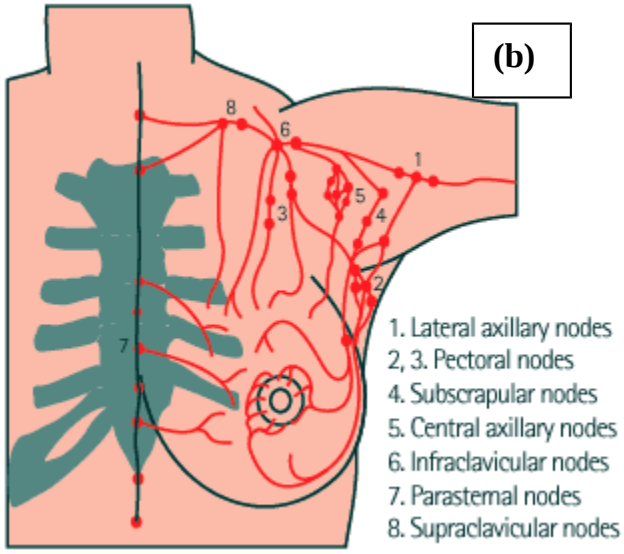


Figure (2- 2) a. & b. Shows blood and lymphatic system of the breast (Mathes, 1997)

2-1-2 Musculature Related to the Breast

The breast lies over the musculature that encases the chest wall. The muscles involved include the pectoralis major, serratus anterior, external oblique, and rectus abdominus fascia. The blood supply that provides circulation to these muscles then perforates through to the breast parenchyma, thus also supplying blood to the breast. By maintaining continuity with the underlying musculature, the breast tissue remains

richly per fused, thus preventing complications arising from aesthetic or reconstructive surgery requiring the placement of a breast implant (LaTrenta, 1994). **Pectoralis major** is a broad muscle that extends from its origin on the medial clavicle and lateral sternum to its insertion on the humerus. The thoracoacromial artery provides its major blood supply while the intercostal perforators arising from the internal mammary artery provide a segmental blood supply. The medial and lateral anterior thoracic nerves provide innervation for the muscle, entering posteriorly and laterally. The action of the pectoralis major is to flex, adduct, and rotate the arm medially. The pectoralis major is extremely important in both aesthetic and reconstructive breast surgery, since it provides muscle coverage from the breast implant. In reconstructive surgery, the pectoralis major muscle covers the implant, providing a decreased risk of extrusion of the implant since the skin and underlying subcutaneous tissues are often diminished greatly following mastectomy. The muscle provides additional tissue between the implant and the skin, thus decreasing the palpability of the implant. Often, placement of the implant beneath the muscle causes it to be noticeable when the pectoralis is contracted. In these instances, it may be helpful to release the pectoralis muscle from its inferior and medial attachments to decrease the incidence of noticeable contractions. In addition, with inferior release of the pectoralis muscle, lower positioning of the implant can be achieved, resulting in a more aesthetic appearance (LaTrenta, 1994).

Serratus anterior is a broad muscle that runs along the anterolateral chest wall. Its origin is the outer surface of the upper borders of the first through eighth ribs and its insertion is on the deep surface of the scapula. Its vascular supply is derived equally from the lateral thoracic artery and branches from the thoracodorsal artery. The long thoracic nerve serves to innervate the serratus anterior, which acts to rotate the scapula, raising the point of the shoulder and drawing the scapula forward toward the body (LaTrenta, 1994).

Rectus abdominus muscle provides the inferior border to the breast. It is an elongated muscle that runs from its origin at the crest of the pubis and interpubic ligament to its insertion at the xiphoid process and cartilages of the fifth through seventh ribs. It acts to compress the abdomen and flex the spine. The 7th through 12th intercostal nerves

provide sensation to overlying skin and innervate the muscle. Vascularity of the muscle is maintained through a network between the superior and inferior deep epigastric arteries (David, 1995).

External oblique muscle is a broad muscle that runs along the anterolateral abdomen and chest wall. Its origin is from the lower 8 ribs, and its insertion is along the anterior half of the iliac crest and the aponeurosis of the linea alba from the xiphoid to the pubis. It acts to compress the abdomen, flex and laterally rotate the spine, and depress the ribs. The 7th through 12th intercostal nerves serve to innervate the external oblique. A segmental blood supply is maintained through the inferior 8 posterior intercostal arteries (David, 1995).

2-1-3 Initial Breast Development

Human breast tissue begins to develop in the sixth week of fetal life. Breast tissue initially develops along the lines of the armpits and extends to the groin (this is called the milk ridge). By the ninth week of fetal life, it regresses (goes back) to the chest area, leaving two breast buds on the upper half of the chest. In females, columns of cells grow inward from each breast bud, becoming separate sweat glands with ducts leading to the nipple. Both male and female infants have very small breasts and actually experience some nipple discharge during the first few days after birth. Female breasts do not begin growing until puberty (the period in life when the body undergoes a variety of changes to prepare for reproduction). Puberty usually begins for women around age 10 or 11. After pubic hair begins to grow, the breasts will begin responding to hormonal changes in the body. Specifically, the production of two hormones, estrogen and progesterone, signal the development of the glandular breast tissue. This initial growth of the breast may be somewhat painful for some girls. During this time, fat and fibrous breast tissue becomes more elastic. The breast ducts begin to grow and this growth continues until menstruation begins (typically one to two years after breast development has begun). Menstruation prepares the breasts and ovaries for potential pregnancy (Olivia, 2009).

Before puberty	Early puberty	Late puberty

the breast is flat except for the nipple that sticks out from the chest	the areola becomes a prominent bud; breasts begin to fill out	glandular tissue and fat increase in the breast, and areola becomes flat

2.1.4 **Breast Size, Appearance, and Changes over Time**

The size and shape of women's breasts varies considerably. Some women have a large amount of breast tissue, and therefore, have large breasts. Other women have a smaller amount of tissue with little breast fat. Factors that may influence a woman's breast size include: volume of breast tissue, family history, age, weight loss or gain, history of pregnancies and lactation, thickness and elasticity of the breast skin, degree of hormonal influences on the breast (particularly estrogen and progesterone) and menopause.

A woman's breasts are rarely balanced (symmetrical). Usually, one breast is slightly larger or smaller, higher or lower, or shaped differently than the other. The size and characteristics of the nipple also vary greater from one woman to another. In some women, the nipples are constantly erect. In others, they will only become erect when stimulated by cold or touch. Some women also have inverted (turned in) nipples. Inverted nipples are not a cause for concern unless the condition is a new change. Since there are hair follicles around the nipple, hair on the breast is not uncommon. The nipple can be flat, round, or cylindrical in shape. The color of the nipple is determined by the thinness and pigmentation of its skin. The nipple and areola (pigmented region surrounding the nipple) contain specialized muscle fibers that respond to stimulation to make the nipple erect. The areola also houses the Montgomery's gland that may appear as tiny, raised bumps on the surface of the areola. The Montgomery's gland helps lubricate the areola. When the nipple is stimulated, the muscle fibers will contract, the areola will pucker, and the nipples become hard (Olivia, 2009).

Breast shape and appearance undergo a number of changes as a woman ages. In young women, the breast skin stretches and expands as the breasts grow, creating a rounded appearance. Young women tend to have denser breasts (more glandular tissue) than

older women. On mammogram films, breast masses, including both non-cancerous and cancerous lesions, appear as white regions. Fat appears as black regions on the films. All other components of the breast (glands, connective tissue, tumors, calcium deposits, etc.) appear as shades of white on a mammogram. In general, the younger the woman, the denser her breasts. As a woman ages, her breasts become less dense and the space is filled with fatty tissue shown as dark areas on mammography x-rays. It is usually easier for radiologists to detect breast cancer in older women because abnormal areas are easier to spot. During each menstrual cycle, breast tissue tends to swell from changes in the body's levels of estrogen and progesterone. The milk glands and ducts enlarge, and in turn, the breasts retain water. During menstruation, breasts may temporarily feel swollen, painful, tender, or lumpy. Physicians recommend that women practice monthly breast self-exams the week following menstruation when the breasts are least tender (Olivia, 2009).

2-1-5 Breast Changes during Pregnancy

Women should continue monthly breast self-exams during pregnancy. It is especially important that a clinical breast exam be performed by the physician or nurse during the first doctor's appointment of the pregnancy, before the breasts go through significant physiologic changes. Clinical breast exams should then continue on a monthly basis during pregnancy. Screening mammograms in asymptomatic women (women who have no symptoms of breast cancer) are not performed during pregnancy or lactation and may be performed at a later time. During pregnancy, a variety of breast changes occur. Typically, breasts become tender and the nipples become sore a few weeks after conception. The breasts also increase in size very quickly. It is not uncommon for a woman's breasts to increase by one or two cup sizes during and after pregnancy. The most rapid period of breast growth is during the first eight weeks of pregnancy. The Montgomery's gland surrounding the areola becomes darker and more prominent, and the areola itself darkens. The nipples also become larger and more erect as they prepare for milk production. The blood vessels within the breast enlarge as surges of estrogen stimulate the growth of the ducts and surges of progesterone cause the glandular tissue to expand (Olivia, 2009).

Two hormones are responsible for milk production: prolactin and oxytocin. Prolactin is

sometimes referred to as the "mothering hormone" because some people believe it also causes a tranquilizing effect that makes women feel more maternal. The body begins producing prolactin approximately eight weeks after conception. As the pregnancy progresses, the levels of prolactin steadily increase, peaking when the woman gives birth. As the body produces more and more prolactin, high levels of estrogen and progesterone block some of the prolactin receptors and inhibit milk production until after the baby is born. After birth, estrogen and progesterone levels decrease and the production of prolactin declines. The breasts will usually begin to produce milk three to five days after a woman has given birth. During these few days before milk is produced, the body produces colostrums, a liquid substance that contains antibodies to help protect the infant against infections. Some physicians believe that colostrums also decreases an infant's chances of developing asthma and other allergies. Within a few days, the infant's own immune system will develop and he or she will not need colostrums. The other hormone responsible for milk production, oxytocin, delivers the milk that prolactin has produced. When an infant suckles at the mother’s breast, it brings milk out of the nipples. This suction signals the body to make more milk (using prolactin) and deliver more milk (using oxytocin). The body also produces a variety of other hormones (insulin, thyroid, cortisol) that provide the infant with nutrition when he or she takes the mother’s milk. A woman’s body will continue to produce milk until she stops breast-feeding, and even then, it may take several months for milk production to completely stop. The breasts will usually return to their previous size (or slightly smaller) after breast-feeding is completed (Olivia, 2009).

2-1-6 Breast Changes after Menopause .

When a woman reaches menopause (typically in her late 40s or early 50s), her body stops producing estrogen and progesterone. The loss of these hormones causes a variety of symptoms in many women including hot flashes, night sweats, mood changes, vaginal dryness and difficulty sleeping. During this time, the breasts also undergo change. For some women, the breasts become more tender and lumpy,

sometimes forming cysts (accumulated packets of fluid).The breasts' glandular tissue, which has been kept firm so that the glands could produce milk, shrinks after menopause and is replaced with fatty tissue. The breasts also tend to increase in size and sag because the fibrous (connective) tissue loses its strength. Because the breasts become less dense after menopause, it is often easier for radiologists to detect breast cancer on an older woman's mammogram films, since abnormalities are not hidden by breast density. Since a woman's risk of breast cancer increases with age, all women should begin receiving annual screening mammograms at age 40, and continue monthly breast self-exams and physician-performed clinical breast exams every year (Olivia, 2009).

2.2 Breast Pathology

2-2-1 Benign Changes

Benign breast changes refer to a heterogeneous group of lesions which can be divided into two major types: inflammatory (including infectious, traumatic, etc.) and benign epithelial lesions (also known as fibrocystic changes). Both hormones and genetics are believed to play causal roles in benign breast changes. Some lesions are palpable while

others are detectable only with breast imaging or biopsy. Many appear similar to breast cancer, yet the vast majority of lumps, inflammations, nipple discharges and other breast changes are neither cancerous nor rare. In fact, benign changes of the breast are very common. According to the American Cancer Society, if breast tissue is examined under a microscope, benign breast changes can be found in as many as 9 out of 10 women (American Cancer Society, 2006). The most common types are those described as fibrocystic changes. The exact cause of fibrocystic changes is not completely understood but is known to be associated with hormonal activity. These types of changes may vary during the menstrual cycle and usually subside with menopause. Symptoms of fibrocystic changes include lumps, lumpiness, areas of thickening, and tenderness. Fibrocystic changes are often grouped into three descriptive subtypes, based upon the appearance of tissue cells under a microscope. Each of the following subtypes confers differing relative risks for developing into subsequent breast cancer: Nonproliferative changes include histologic findings as various as cysts, nonsclerosing adenosis, ductal ectasia, lactational adenoma, simple fibroadenoma, and mild hyperplasia, among others. In women with nonproliferative breast changes, the risk of subsequent breast cancer is about the same as that of the general population. Over the next 15 years, 6% of cases diagnosed as nonproliferative breast lesions will develop into breast cancer compared to 5% of the general population (Mayo Clinic, 2006). Proliferative changes without atypia are characterized by excessive cell growth, especially of the duct linings, but with no cells appearing abnormal. Cells show few genetic changes. Examples include intraductal papilloma, radial scar, sclerosing adenosis, complex fibroadenoma, and moderate or florid hyperplasia. Proliferative breast changes without atypia is associated with a slightly elevated risk of developing breast cancer - approximately 1.5 to 2.0 times that of the general population. Over the next 15 years, 10% of these cases will develop into breast cancer (Mayo Clinic, 2006). Proliferative changes with atypia are characterized by excessive cell growth with some cells appearing abnormal. Cells show genetic changes that could make them potentially invasive. Both atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH) may be difficult to differentiate from carcinoma - either ductal

carcinoma in situ (DSIS) or lobular carcinoma in situ (LCIS). Atypical hyperplasia carries an approximate 4.0 to 5.0 times increase in the relative risk of developing breast cancer. For every 100 cases of atypia, 19 are expected to develop into breast cancer over the next 15 years (Mayo Clinic, 2006).
Benign lesions are usually confirmed by imaging tests or biopsy. Thus, every irregularity should be brought to the attention of a healthcare provider for conclusive diagnosis. Whether or not treatment is required depends upon a number of factors including the exact nature of the diagnosis, a woman's discomfort, and the potential of the lesion for developing into breast cancer (Mayo Clinic, 2006)

2-2-2 Breast Cancer

Cancer is a process in which normal cells go through stages that eventually change them to abnormal cells that multiply out of control. Many breast cancers arise from a sequence that begins with an increase in the number of breast cells (hyperplasia) to the emergence of atypical breast cells (atypical hyperplasia) followed by carcinoma in situ (noninvasive cancer) and finally, invasive cancer. Not all breast cancers necessarily follow this progressive pattern. It also appears that some cancers may never progress beyond in situ disease (Mayo Clinic, 2006).

Causes of breast cancer and risk factors

Definite causes still unknown but certain risk factor has been linked to it.
A risk factor is anything that affects your chance of getting a disease, such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx (voice box), bladder, kidney, and several other organs.

But risk factors don't tell us everything. Having a risk factor, or even several, does not mean that you will get the disease. Most women who have one or more breast cancer risk factors never develop the disease, while many women with breast cancer have no apparent risk factors (other than being a woman and growing older). Even when a woman with risk factors develops breast cancer, it is hard to know just how much these factors may have contributed to her cancer.

There are different kinds of risk factors. Some factors, like a person's age or race, can't

be changed. Others are linked to cancer-causing factors in the environment. Still others are related personal behaviors, such as smoking, drinking, and diet. Some factors influence risk more than others, and your risk for breast cancer can change over time, due to factors such as aging or lifestyle

Risk factors you cannot change

Gender

Simply being a woman is the main risk factor for developing breast cancer. Although women have many more breast cells than men, the main reason they develop more breast cancer is because their breast cells are constantly exposed to the growth-promoting effects of the female hormones estrogen and progesterone. Men can develop breast cancer, but this disease is about 100 times more common among women than men (Jemal, 2010).

Aging

Your risk of developing breast cancer increases as you get older. About 1 out of 8 invasive breast cancers are found in women younger than 45, while about 2 out of 3 invasive breast cancers are found in women age 55 or older (Jemal, 2010).

Genetic risk factors

About 5% to 10% of breast cancer cases are thought to be hereditary, resulting directly from gene defects (called mutations) inherited from a parent.

BRCA1 and BRCA2: The most common cause of hereditary breast cancer is an inherited mutation in the BRCA1 and BRCA2 genes. In normal cells, these genes help prevent cancer by making proteins that help keep the cells from growing abnormally. If you have inherited a mutated copy of either gene from a parent, you have a high risk of developing breast cancer during your lifetime. The risk may be as high as 80% for members of some families with BRCA mutations. These cancers tend to occur in younger women and more often affect both breasts than cancers in women who are not born with one of these gene mutations. Women with these inherited mutations also have an increased risk for developing other cancers, particularly ovarian cancer.

Changes in other genes: Other gene mutations can also lead to inherited breast cancers. These gene mutations are much rarer and often do not increase the risk of breast cancer as much as the BRCA genes. They are not frequent causes of inherited

breast cancer (Jemal, 2010).

Genetic testing: Genetic tests can be done to look for mutations in the BRCA1 and BRCA2 genes (or less commonly in other genes such as PTEN or p53). Although testing may be helpful in some situations, the pros and cons need to be considered carefully.

Family history of breast cancer:

Breast cancer risk is higher among women whose close blood relatives have this disease. Having one first-degree relative (mother, sister, or daughter) with breast cancer approximately doubles a woman's risk. Having 2 first-degree relatives increases her risk about 3-fold.

The exact risk is not known, but women with a family history of breast cancer in a father or brother also have an increased risk of breast cancer. Altogether, less than 15% of women with breast cancer have a family member with this disease. This means that most (over 85%) women who get breast cancer do not have a family history of this disease (Jemal, 2010).

Personal history of breast cancer

A woman with cancer in one breast has a 3- to 4-fold increased risk of developing a new cancer in the other breast or in another part of the same breast. This is different from a recurrence (return) of the first cancer.

Race and ethnicity

White women are slightly more likely to develop breast cancer than are African-American women. African-American women are more likely to die of this cancer. At least part of this seems to be because African-American women tend to have more aggressive tumors, although why this is the case is not known. Asian, Hispanic, and Native-American women have a lower risk of developing and dying from breast cancer.

Dense breast tissue

Women with denser breast tissue (as seen on a mammogram) have more glandular tissue and less fatty tissue, and have a higher risk of breast cancer. Unfortunately, dense breast tissue can also make it harder for doctors to spot problems on mammograms.

Certain benign breast conditions

Women diagnosed with certain benign breast conditions may have an increased risk of breast cancer. Some of these conditions are more closely linked to breast cancer risk than others.

Lobular carcinoma in situ

Women with lobular carcinoma in situ (LCIS) have a 7- to 11-fold increased risk of developing cancer in either breast.

Menstrual periods

Women who have had more menstrual cycles because they started menstruating at an early age (before age 12) and/or went through menopause at a later age (after age 55) have a slightly higher risk of breast cancer. This may be related to a higher lifetime exposure to the hormones estrogen and progesterone.

Previous chest radiation

Women who, as children or young adults, had radiation therapy to the chest area as treatment for another cancer (such as Hodgkin disease or non-Hodgkin lymphoma) are at significantly increased risk for breast cancer. This varies with the patient's age when they had radiation. If chemotherapy was also given, it may have stopped ovarian hormone production for some time, lowering the risk. The risk of developing breast cancer from chest radiation is highest if the radiation was given during adolescence, when the breasts were still developing. Radiation treatment after age 40 does not seem to increase breast cancer risk.

Diethylstilbestrol exposure

From the 1940s through the 1960s some pregnant women were given the drug diethylstilbestrol (DES) because it was thought to lower their chances of miscarriage (losing the baby). These women have a slightly increased risk of developing breast cancer. Women whose mothers took DES during pregnancy may also have a slightly higher risk of breast cancer

Lifestyle-related factors and breast cancer risk

Having children

Women who have had no children or who had their first child after age 30 have a slightly higher breast cancer risk. Having many pregnancies and becoming pregnant at

a young age reduce breast cancer risk. Pregnancy reduces a woman's total number of lifetime menstrual cycles, which may be the reason for this effect.

Recent oral contraceptive use

Studies have found that women using oral contraceptives (birth control pills) have a slightly greater risk of breast cancer than women who have never used them. This risk seems to decline back to normal over time once the pills are stopped. Women who stopped using oral contraceptives more than 10 years ago do not appear to have any increased breast cancer risk. When thinking about using oral contraceptives, women should discuss their other risk factors for breast cancer with their health care team.

Hormone therapy after menopause

Hormone therapy with estrogen (sometimes with progesterone) has been used for many years to help relieve symptoms of menopause and to help prevent osteoporosis. Earlier studies suggested it might have other health benefits as well, but these benefits have not been found in more recent, better designed studies. This treatment goes by many names, such as post-menopausal hormone therapy (PHT), hormone replacement therapy (HRT), and menopausal hormone therapy (MHT).

There are 2 main types of hormone therapy. For women who still have a uterus (womb), doctors generally prescribe both estrogen and progesterone (known as combined hormone therapy or HT). Because estrogen alone can increase the risk of cancer of the uterus, progesterone is added to help prevent this. For women who no longer have a uterus (those who've had a hysterectomy), estrogen alone can be prescribed. This is commonly known as estrogen replacement therapy (ERT) or just estrogen therapy (ET). .

Combined hormone therapy: Using combined hormone therapy after menopause increases the risk of getting breast cancer. It may also increase the chances of dying from breast cancer. This increase in risk can be seen with as little as 2 years of use. Combined HT also increases the likelihood that the cancer may be found at a more advanced stage, possibly because it reduces the effectiveness of mammograms by increasing breast density.

The increased risk from combined hormone therapy appears to apply only to current

and recent users. A woman's breast cancer risk seems to return to that of the general population within 5 years of stopping combined treatment.

Breast-feeding

Some studies suggest that breast-feeding may slightly lower breast cancer risk, especially if breast-feeding is continued for 1½ to 2 years. But this has been a difficult area to study, especially in countries such as the United States, where breast-feeding for this long is uncommon. The explanation for this possible effect may be that breast-feeding reduces a woman's total number of lifetime menstrual cycles (similar to starting menstrual periods at a later age or going through early menopause).

Alcohol

The use of alcohol is clearly linked to an increased risk of developing breast cancer. The risk increases with the amount of alcohol consumed. Compared with non-drinkers, women who consume 1 alcoholic drink a day have a very small increase in risk. Those who have 2 to 5 drinks daily have about 1½ times the risk of women who drink no alcohol. Excessive alcohol use is also known to increase the risk of developing cancers of the mouth, throat, esophagus, and liver. The American Cancer Society recommends that women limit their consumption of alcohol to no more than one drink a day.

Being overweight or obese

Being overweight or obese has been found to increase breast cancer risk, especially for women after menopause. Before menopause your ovaries produce most of your estrogen, and fat tissue produces a small amount of estrogen. After menopause (when the ovaries stop making estrogen), most of a woman's estrogen comes from fat tissue. Having more fat tissue after menopause can increase your chance of getting breast cancer by raising estrogen levels. Also, women who are overweight tend to have higher blood insulin levels. Higher insulin levels have also been linked to some cancers, including breast cancer (Jemal, 2010).

Physical activity

Evidence is growing that physical activity in the form of exercise reduces breast cancer risk. The main question is how much exercise is needed. In one study from the Women's Health Initiative (WHI) as little as 1.25 to 2.5 hours per week of brisk walking reduced a woman's risk by 18%. Walking 10 hours a week reduced the risk a

little more.

To reduce your risk of breast cancer, the American Cancer Society recommends 45 to 60 minutes of intentional physical activity 5 or more days a week (Jemal, 2010).

Symptoms of breast cancer

In its early stages, breast cancer usually has no symptoms. As a tumor develops, you may note the following signs: A lump in the breast or underarm that persists after your menstrual cycle; often the first apparent symptom of breast cancer, breast lumps are painless, although some may cause a prickly sensation. Lumps are usually visible on a mammogram long before they can be seen or felt, swelling in the armpit, although lumps are usually painless, pain or tenderness in the breast can be a sign of breast cancer, other symptoms; a noticeable flattening or indentation on the breast, which may indicate a tumor that cannot be seen or felt, any change in the size, contour, texture, or temperature of the breast; a reddish, pitted surface like the skin of an orange could be a sign of advanced breast cancer, a change in the nipple, such as an indrawn or dimpled look, itching or burning sensation, or ulceration; scaling of the nipple is symptomatic of Paget's disease, a localized cancer, unusual discharge from the nipple that may be clear, bloody, or another color. It's usually caused by benign conditions but could be due to cancer in some cases, a marble-like area under the skin and an area that is distinctly different from any other area on either breast (Fred, 2005).

2-2-3 Types of Breast Cancer

Noninvasive Breast Cancer

Ductal carcinoma in situ (DCIS**)** is the most common type of noninvasive breast cancer, accounting for about 15% of all new breast cancer cases in the United States [18]. The term in situ means in place, so ductal carcinoma in situ refers to an uncontrolled growth of cells that are confined to the breast duct. As such, some experts

believe DCIS to be a precancerous condition. Others, however, classify any cellular changes beyond atypical hyperplasia as cancer. Frequently a single lesion, DCIS is classified into several histological subtypes associated with varying prognostic implications. Invasive cancer usually occurs within the same breast, but women with DCIS are also at higher risk of developing cancer in the opposite breast. Very few cases of DCIS present as a palpable mass; most are diagnosed by mammography, usually as clustered microcalcifications. DCIS may also present as pathologic nipple discharge, with or without a mass. The frequency of diagnosis of DCIS has greatly increased with greater use of mammography. With early detection and treatment, the five-year survival rate for DCIS is nearly 100%, providing that the cancer has not spread past the milk ducts (Imaginis, 2006).

Lobular carcinoma in situ (LCIS) is characterized by abnormal changes in the cells that line the milk-producing lobules, or lobes, of the breast. LCIS is much less common (accounting for only about 4,200 cases annually in the United States) [18], and carries slightly less risk of invasive cancer than DCIS. Also called lobular intraepithelial neoplasia, LCIS is actually considered by most medical experts to be neither cancer nor a premalignant lesion, but rather a marker that identifies women at increased risk of invasive breast cancer. Risk remains elevated beyond two decades and most subsequent breast cancers are ductal rather than lobular. LCIS typically includes multiple lesions and is frequently bilateral. It is usually discovered as an incidental finding from breast biopsy; there are rarely clinical or mammographic signs.

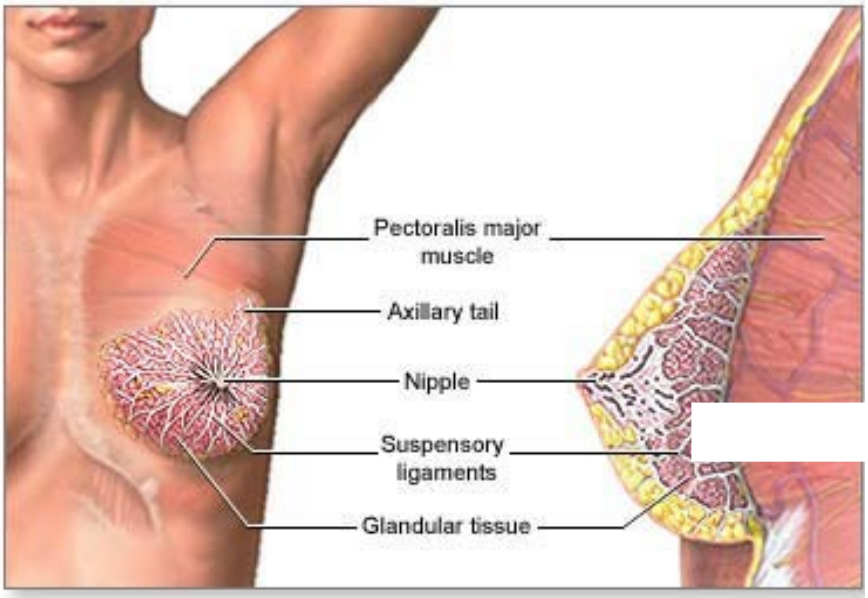


Figure (2- 3) Shows Noninvasive Breast Cancer (American Cancer Society, 2006)

Invasive Breast Cancer

Invasive (infiltrating) ductal carcinoma (IDC) is the most common type of breast cancer. About 80% of invasive breast cancers are classified as invasive ductal carcinoma (Unlu, 2008). Also called infiltrating ductal carcinoma, cancer cells have penetrated the ductal wall and invaded surrounding breast tissue. The cells may then metastasize to other parts of the body through the bloodstream or lymphatic system. IDC may present as a hard and firm palpable mass or as a mammographic abnormality. Tumors can cause skin and nipple retraction. IDC is most commonly encountered in pure form, although a substantial minority of IDC cases exhibits a combination of histologic types. As with all invasive breast cancers, it is important to detect and treat invasive ductal carcinoma early, before it has had an opportunity to metastasize. Invasive (infiltrating) lobular carcinoma (ILC) begins in the milk-producing lobules where it extends into the adipose tissue of the breast. It is relatively uncommon, comprising about 10% of invasive breast cancers (Unlu, 2008). As with IDC, ILC may present as a palpable mass, however, it tends to be less well-defined. Often, the only clinical evidence is that of a vague area of thickening. ILC can also be more difficult to detect by mammogram. Compared with IDC, patients with infiltrating lobular carcinoma are more often prone to bilateral disease (Santen, 2005).

Tubular carcinoma is a highly differentiated invasive carcinoma whose cells are regular and arranged in well-defined tubules. Before widespread use of mammography, tubular carcinomas were most often detected as palpable lesions. Now, most cases present as nonpalpable mammographic abnormalities, usually a mass lesion, and only occasionally associated with microcalcifications. Some are discovered incidentally in biopsies performed for unrelated reasons. Reported incidence in mammographically screened populations range from about 8% to as high as 27% (Santen, 2005). Pure tubular carcinoma has limited metastatic potential and better than average prognosis.

Medullary carcinoma is a relatively uncommon type of invasive carcinoma, accounting for less than 5% to 7% of all invasive breast cancers (Merajver, 2004). Lesions have well-defined boundaries and can be quite large and soft on palpation. Histologically, the tumor is characterized by larger than average cancer cells, and with immune system cells present on the edges of the tumor. The prognosis for this type of breast cancer is relatively favorable.

Mucinous carcinoma, also called colloid carcinoma, is an invasive form of breast cancer characterized by large amounts of extracellular mucin production. Less than 5% of invasive breast cancers show a mucinous component (Merajver, 2004). Usually occurring in postmenopausal women, tumors may or may not be palpable. Mammographically, pure mucinous carcinomas may mimic benign lesions with well-circumscribed and microlobulated margins. Like medullary carcinoma, mucinous carcinoma is associated with a relatively favorable prognosis.

Metaplastic carcinoma is uncommon, representing less than 5% of all breast cancers (Merajver, 2004). Lesions contain several different types of cells that are not typically seen in other forms of breast cancer. Clinical presentation is frequently a single palpable lesion often associated with rapid growth. Mammographically, most metaplastic carcinomas are fairly circumscribed, noncalcified lesions which, in some cases, appear benign. Prognostic implications of this type of breast cancer are variable.

Invasive cribriform carcinoma is a well-differentiated cancer comprised of small and uniform cells. It shares some features with tubular carcinoma and is also associated with better than average prognosis. Roughly 5% to 6% of invasive breast cancers show

at least a partial invasive cribriform component (Santen, 2005). Invasive papillary carcinoma is very rare, comprising less than 1% to 2% of invasive breast cancers [22]. Found predominantly in postmenopausal women, it is characterized by nodular densities that may be multiple and are frequently lobulated. Limited data suggests relatively favorable prognosis.

Invasive micropapillary carcinoma is a distinct but poorly recognized variant of breast cancer, usually presenting as a firm, immobile mass. Findings on mammography are of a spiculated, irregular or round, high density mass with or without associated microcalcifications. Pure micropapillary carcinoma is uncommon, with an incidence of less than 3% (Santen, 2005). Limited research suggests that this type of cancer may be associated with a relatively poor prognosis.

Figure (2- 4) Shows left Breast Cancer (Reaney, 1999)

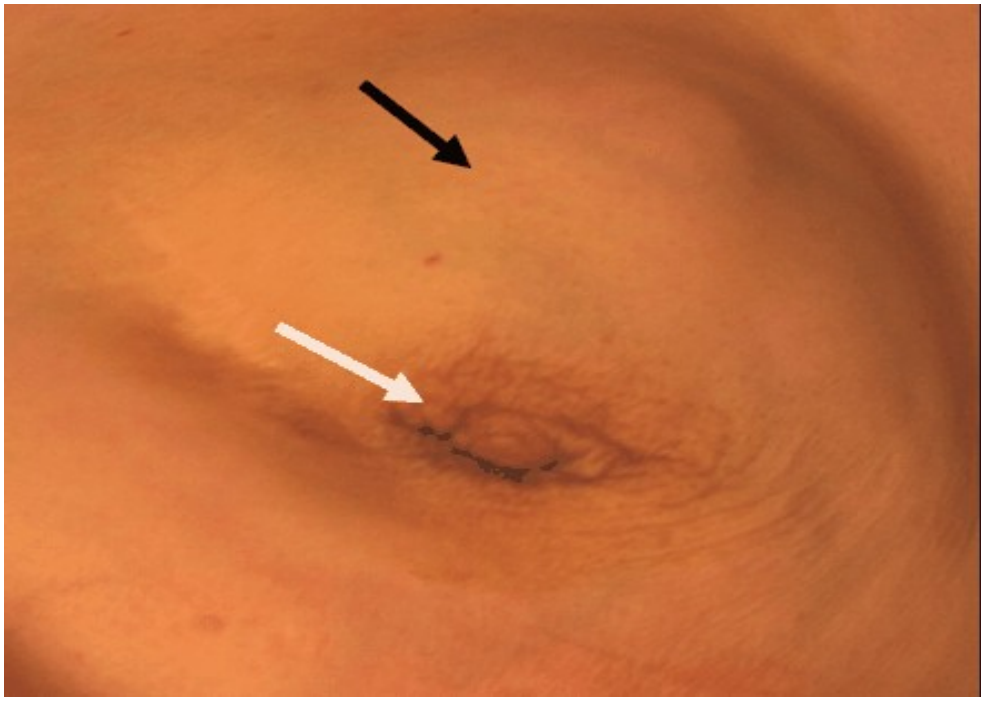


Figure (2- 5) Shows Nipple displacement and retraction due to poorly differentiated infiltrating ductal carcinoma with necrosis in a 75-year-old woman(Rees, 1994)

Other Types of Breast Cancer

Inflammatory breast cancer is a form of locally advanced breast cancer associated with a rapid onset of clinical features including breast inflammation, warmth, thickening or dimpling (peau d' orange), and a palpable ridge at the margin of induration. Often mistaken as an infection, symptoms result from the blocking of lymphatic vessels near the surface of the skin by cancer cells. Inflammatory breast

cancer is relatively rare, representing about 1% to 5% of all breast cancers in the United States (Web, 2010) and has a less favorable than average prognosis.

Paget's disease of the nipple begins in the milk ducts as either an in situ or invasive cancer; prognosis is excellent when associated with carcinoma in situ. Early stage symptoms include erythema and mild scaling of the nipple skin. Symptoms of more advanced disease may include nipple tingling, itching, increased sensitivity, burning, pain or oozing. Diagnosed by biopsy, Paget's disease of the nipple must be differentiated from eczema, contact dermatitis, basal cell carcinoma, and a number of other conditions. Paget's disease of the nipple accounts for approximately 1% of all breast cancers (Thin, 1881).

Phylloides tumors (also spelled phyllodes) can be benign, borderline or malignant. Malignant tumors are very rare. Phylloides tumors are biphasic and composed of benign epithelial elements and cellular connective tissue stroma. The stroma dictates whether the tumor will be benign, borderline or malignant. They can grow to a relatively large size within a few months, although rapid growth does not necessarily indicate malignancy. The gross appearance of most phylloides tumors, particularly those that are benign, is not distinctly different from fibroadenomas. They can also be difficult to distinguish from fibroadenomas on fine-needle aspiration and on core biopsy. Phylloides tumors are often painless (Thin, 1881).

.

Figure (2- 6) Shows Inflammatory Breast Cancer (Web, 2010).

Figure (2- 7) Shows Breast Cancer – Paget's disease (Thin, 1881).