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Study the Breast cancer

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Breast cancer is the most frequent malignancy in women worldwide and is curable in 70-80% of patients with early-stage, non- metastatic disease. Advanced breast cancer with distant organ metastases is considered incurable with currently available therapies. On the molecular level, breast cancer is a heterogeneous disease; molecular features include activation of human epidermal growth factor receptor 2 (HER2, encoded by ERBB2), activation of hormone receptors (oestrogen receptor and progesterone receptor) and/or BRCA mutations. Treatment strategies differ according to molecular subtype. Management of breast cancer is multidisciplinary; it includes locoregional (surgery and radiation therapy) and systemic therapy approaches. Systemic therapies include endocrine therapy for hormone receptor-positive disease, chemotherapy, anti-HER2 therapy for HER2-positive disease, bone stabilizing agents, poly(ADP-ribose) polymerase inhibitors for BRCA mutation carriers and, quite recently, immunotherapy. Future therapeutic concepts in breast cancer aim at individualization of therapy as well as at treatment de- escalation and escalation based on tumour biology and early therapy response. Next to further treatment innovations, equal worldwide access to the rapeutic advances remains the global challenge in breast cancer care for the future.

. Based on mRNA gene expression levels, BC can be divided into molecular subtypes (Luminal A, Luminal B, HER2-enriched, and basal-like). The molecular subtypes provide insights into new treatment strategies and patient stratifications that impact the management of BC patients. The eighth edition of TNM classification outlines a new staging system for BC that, in addition to anatomical features, acknowledges biological factors. Treatment of breast cancer is complex and involves a combination of different modalities including surgery, radiotherapy, chemotherapy, hormonal therapy, or biological therapies delivered in diverse sequences.

Keywords: BRCA mutations, Breast cancer

Breast Cancer Basics

RSTRACT

The breast is mostly made up of different types of tissue, ranging from very fatty tissue to very dense tissue. Within this tissue is a network of lobes, which are made up of small, tube-like structures called lobules that contain milk glands. Tiny ducts connect the glands, lobules, and lobes, carrying the milk from the lobes to the nipple. The nipple is located in the middle of the areola, which is the darker area that surrounds the nipple. Blood and lymph vessels also run throughout the breast. Blood nourishes the cells, and the lymphatic system drains bodily waste products. The lymph vessels connect to lymph nodes, which are small, bean-shaped organs that help fight infection.

Breast cancer development

Breast cancer begins when healthy cells in the breast change and grow out of control, forming a mass called a tumor. A tumor can be cancerous or benign. A cancerous tumor is malignant, meaning it can spread to other parts of the body. A benign tumor can grow but does not spread to other parts of the body, and it is rarely life-threatening.

Types of breast cancer

Breast cancer can be invasive or noninvasive. Invasive breast cancer is cancer that spreads into surrounding tissues. Noninvasive breast cancer does not go beyond the milk ducts or lobules in the breast. Most breast cancers start in the ducts, called ductal carcinoma, or in the lobules, called lobular carcinoma. A pathologist determines whether a tumor removed during a biopsy is ductal or lobular cancer. A pathologist is a doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease. If the disease has spread outside the duct or lobule and into the surrounding tissue, it is called invasive or infiltrating ductal or lobular carcinoma. Cancer that is located only in the duct or lobule is called in situ, meaning —in place,|| and is noninvasive. Most in situ breast cancers are ductal carcinoma in situ (DCIS). DCIS is often treated with surgery, radiation therapy, and hormonal therapy (see —Breast Cancer Treatment,|| p. 14). Lobular carcinoma in situ (LCIS) is not considered cancer and is usually monitored by a doctor with regularly scheduled examinations and imaging tests. LCIS in 1 breast is a risk factor for developing invasive breast cancer in both breasts. To reduce this risk, LCIS is sometimes treated with hormonal therapy.

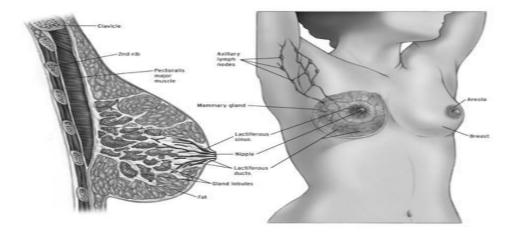


Figure (1)

Other less common types of breast cancer include medullary, mucinous, tubular, metaplastic, and papillary breast cancer, as well as other even rarer types. Inflammatory breast cancer is a faster growing type of cancer that accounts for about 1% to 5% of all breast cancers. At first, it may be misdiagnosed as a breast infection because there is often swelling of the breast and redness of the breast skin that starts suddenly, and there may be no breast mass or lump. Paget's disease is a type of cancer that begins in the ducts of the nipple. The skin often appears scaly and may be itchy. Although it is usually in situ, it can also be an invasive cancer.

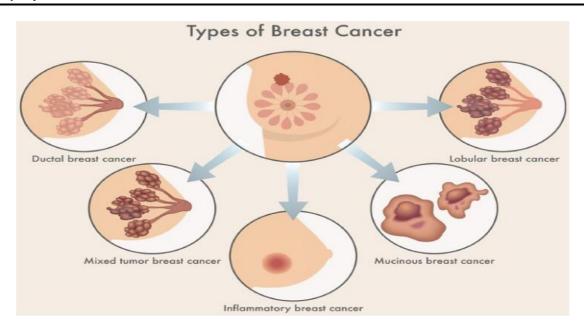


Figure (2)

Breast cancer spread

As a cancerous breast tumor grows, cancer cells may break away and be carried to other parts of the body through the bloodstream or lymphatic system. During this process, known as metastasis, the cancer cells can grow and develop in new locations in the body. One of the first places breast cancer usually spreads to is the regional lymph nodes located under the arm, in the neck, under the chest bone, or just above the collarbone. Breast cancer can also spread farther away from the breast to other parts of the body, such as the bones, lungs, and liver. Less often, breast cancer may spread to the brain. Breast cancer that has spread to a distant location in the body is referred to as stage IV or metastatic breast cancer. However, even if the cancer has spread, it is still named for the area where it began. For example, if breast cancer spreads to the lungs, it is called metastatic breast cancer, not lung cancer. No matter whether the cancer has spread or how far it has spread, breast cancer can be treated and/or managed.

Breast cancer genetics

Although most women who develop breast cancer have no known risk factors and no family history of breast cancer, about 5% to 10% of breast cancers occur when gene changes, called mutations, are passed down in a family from 1 generation to the next. Breast cancer may run in a family if other close relatives have been diagnosed with breast, ovarian, or other cancers, especially before age 50. If 2 first-degree relatives developed breast cancer, a person's risk is 5 times the average risk.

There are several genes linked to an increased risk of breast cancer, but 2 of the most common are breast cancer genes 1 and 2. These are commonly shortened to BRCA1 and BRCA2. A mutation in either of these genes gives a person an increased risk of developing breast and/or ovarian cancer, as well as other types of cancer. Men who inherit these gene mutations also have an increased risk of developing breast cancer, as well as prostate cancer. Other gene mutations or hereditary conditions can increase a person's risk of breast cancer. They are far less common than BRCA1 or BRCA2, and they do not increase the risk of breast cancer as much:

- flynch syndrome, associated with the PMS2, MLH1, and MSH2 genes
- Cowden syndrome (CS), associated with the PTEN gene
- ☐ Li-Fraumeni syndrome (LFS), associated with the TP53 gene
- Peutz-Jeghers syndrome (PJS), associated with the STK11 gene
- Ataxia telangiectasia (A-T), associated with the ATM gene
- ☐ Hereditary diffuse gastric cancer (HDGC), associated with the CDH1 gene fPALB2 gene fCHEK2 gene

Genetic testing is available to check for known mutations in these genes. Your doctor may recommend a test called a panel test, which looks for mutations in several different genes at the same time. But this testing is not recommended for everyone. It is only recommended after a person has received appropriate genetic counseling.

4. Understanding Your Diagnosis

The process of diagnosing breast cancer usually begins when a person or their doctor discovers an abnormality in the breast during a clinical or self-examination or when a mass or tiny spots of calcium appear on a screening mammogram. After this, the doctor will use a number of tests and procedures to determine whether the mass is cancerous and, if it is, to figure out if the cancer has spread. Not every test is right for every person. Your doctor may consider factors such as your age, medical condition, signs and symptoms, and previous test results when deciding whether a specific diagnostic test is right for you.

Imaging tests

4.1 Diagnostic mammography

Mammography is a type of x-ray designed to view the breast. The x-ray films produced by mammography, called mammograms, help doctors find small tumors or irregularities in the breast. Diagnostic mammography is similar to screening mammography except that more pictures are taken, and it is often used when a person is experiencing signs, such as nipple discharge or a new lump. Diagnostic mammography may also be used if something suspicious is found on a screening mammogram. A 3-dimensional version of mammography called digital breast tomosynthesis may also be used for breast cancer screening, especially for people who have dense breasts. However, it is not

always covered by medical insurance, so talk with your provider about whether it may be covered for you.



Figure (3)

4.2 Ultrasound

An ultrasound uses high-frequency sound waves to create an image of the breast tissue. An ultrasound can distinguish between a solid mass, which may be cancer, and a fluid-filled cyst, which is usually not cancer.

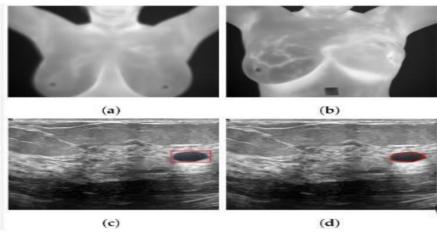


Figure (4)

4.3 Magnetic resonance imaging (MRI)

An MRI uses magnetic fields, not x-rays, to produce detailed images of the body. An MRI can also be used to measure a tumor's size. A special dye called a contrast medium is injected into a patient's vein before the scan to help create a clearer picture of the possible cancer. A breast MRI may be used after a woman has been diagnosed with cancer to check the other breast for cancer or to find out how much the disease has grown throughout the breast. It may also be used before surgery to find out if chemotherapy is working to shrink the tumor.



Figure (5)

4.4 Biopsy

A biopsy is the removal of a small amount of tissue for examination under a microscope.

Other tests can suggest that cancer is present, but only a biopsy can make a definite diagnosis. There are different types of biopsies, classified by the technique and/or size of the needle used to collect the tissue sample.



Figure (6)



Figure (7)

✓ Fine needle aspiration biopsy

This type of biopsy uses a thin needle to remove a small sample of cells from a suspicious lump.

✓ Core needle biopsy

This procedure uses a thicker needle to remove a larger sample of tissue. It is usually the preferred biopsy technique to find out whether an abnormality discovered during a physical examination or on an imaging test is cancer. A vacuum-assisted biopsy removes several large cores of tissue. Medication to block the awareness of pain, called local anesthesia, is used to reduce a person's discomfort during the procedure.

✓ Image-guided biopsy

This test is done when a distinct lump can't be felt, but an abnormality is seen with an imaging test, such as on a mammogram. An image-guided biopsy can be done using a fine needle, core needle, or vacuum-assisted needle, depending on the amount of tissue that needs to be removed. During the procedure, the needle is guided to the best location with the help of an imaging technique, such as mammography, ultrasound, or MRI. A stereotactic biopsy is done using mammography to help guide the needle. A small metal clip may be put into the breast to mark where the biopsy sample was taken in case the tissue is cancerous and more surgery is needed. This clip is usually titanium so it will not cause problems with future imaging tests, but check with your doctor before you have any additional tests or scans.

✓ Surgical biopsy

This type of biopsy removes the largest amount of tissue. A surgical biopsy is either —incisional|| if it removes part of the lump or —excisional|| if it removes the entire lump. Because surgery is best done after a cancer diagnosis has been made, a surgical biopsy is usually not the recommended procedure for diagnosing breast cancer. Most often, nonsurgical core biopsies are recommended to diagnose breast cancer. This means that only 1 surgical procedure is needed to remove the tumor and to take samples of the lymph nodes.



Figure (8)

4.5 Examining the tissue

After a biopsy, a pathologist will look very closely at the tissue that was removed using a microscope. Based on this examination, the pathologist can tell which area of the breast the cancer started in (ductal or lobular), whether the tumor has spread outside this area (invasive or in situ), and how different the cancer cells look from healthy breast cells (the grade). If the tumor was removed, the healthy tissue around the edges of the tumor, called the margins, will also be examined to see if cancer cells are present and to measure their distance from the tumor, which is referred to as the margin width.

ER and PR status

About 60% to 75% of breast cancers have estrogen and/or progesterone receptors. Breast cancer cells with these receptors depend on the hormones estrogen and/or progesterone to grow. The presence of these receptors helps determine the risk of the cancer coming back after treatment and the type of treatment most likely to lower this risk. Generally, hormonal therapy works well for ER-positive and/or PR- positive cancers, also called hormone receptor-positive cancers. Two commonly used types of hormonal therapy are tamoxifen (Nolvadex, Soltamox) and aromatase inhibitors (see —Hormonal therapy,|| p. 21).

✓ HER2 status

About 20% to 25% of breast cancers have more copies than usual of a gene called the human epidermal growth factor receptor 2 (HER2). Because this gene makes a protein that fuels tumor cell growth, HER2-positive cancers may grow more quickly. The tumor's HER2 status also helps determine whether drugs that target HER2 might help treat the cancer. These drugs include trastuzumab (Herceptin), pertuzumab (Perjeta), ado-trastuzumab emtansine (Kadcyla), lapatinib (Tykerb), and neratinib (Nerlynx). About 50% of HER2positive tumors also have hormone receptors, so people with breast cancer can benefit from both types of treatment.

✓ Triple-negative

If a tumor does not express ER, PR, or HER2, the tumor is called —triple-negative.|| Triplenegative breast cancer makes up about 15% of invasive breast cancers. Triple-negative breast cancer may be more common among younger patients, particularly younger Black women. Triple-negative cancer is also more common in people with a mutation in the BRCA1 gene. Experts recommend that all people under age 60 with triple-negative breast cancer be tested for BRCA gene mutations.

4.6 Grades

Doctors may use the term —grade|| when talking about breast cancer. The grade describes how much cancer cells look like healthy cells when viewed under a microscope. Knowing the grade of the cancer may help your doctor predict how quickly the cancer will spread. If the cancer looks similar to healthy tissue and contains different cell groupings, it is called differentiated or a low-grade tumor. If the cancerous tissues look very different from healthy tissue, it is called poorly differentiated or a high-

grade tumor. In general, the lower the tumor's grade, the better the prognosis.

4.7 Grades

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- GX—Cannot be evaluated; undetermined.
- ❖ G1—Similar to healthy breast tissue, well differentiated, low grade.
- G2—Still has some features of healthy breast tissue, moderately differentiated, intermediate grade.
- ❖ G3—Very different from healthy breast tissue, poorly differentiated, high grade .

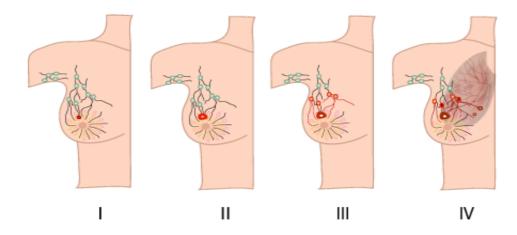
2.1 Breast Cancer Stages

The stage of your cancer is based on the size of the tumor and if it has spread to other areas.14 It is also based on the type of tumor cells (genes and biomarkers—see Genetic and Biomarker Testing).

There are five stages of breast cancer, including zero through four, written as 0, I, II, III, and IV. The higher the number, the more the cancer has spread. The cancer is staged when you are first diagnosed. If you have Stage II breast cancer and the cancer comes back and spreads to your bone, you will still be Stage II breast cancer with metastasis (spread) to the bones.¹³

The stage of breast cancer is also described by the "TNM" system:

- **T: Tumor** size (in centimeters)
- N: Number of near by lymph nodes with cancer
- **M:** Whether the cancer has **metastasized** or spread to other organs of the body (0 = no spread, 1 = it has spread)



The Stages of Breast Cancer

2.1.1 The Clinical Stages of Breast Cancer

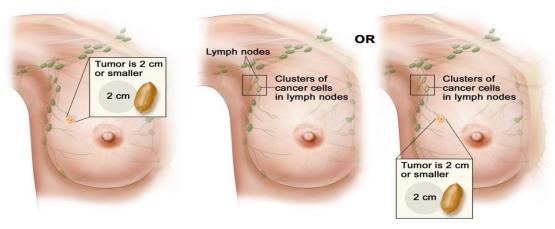
Stage 0: The disease is only in the ducts and lobules of the breast. It has not spread to the surrounding tissue. It is also called noninvasive cancer (Tis, N0, M0).

Stage I: The disease is invasive. Cancer cells are now in normal breast tissue. There are 2 types:

- **Stage IA:** The tumor is up to 2 centimeters (cm). It has not spread to the lymph nodes (T1, N0, M0).
- **Stage IB:** The tumor is in the breast and is less than 2 cm. Or the tumor is in the lymph nodes of the breast and there is no tumor in the breast tissue.

Stage IA Breast Cancer

Stage IB Breast Cancer



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Breast Cancer Stage IA and IB

Stage II describes invasive breast cancer. There are 2 types:

- **Stage IIA:** A tumor may not be found in the breast, but cancer cells have spread to at least 1 to 3 lymph nodes. Or Stage IIA may show a 2 to 5 cm tumor in the breast with or without spread to the axillary lymph nodes.
- **Stage IIB:** The tumor is 2 to 5 cm and the disease has spread to 1 to 3 axillary lymph nodes. Or the tumor is larger than 5 cm but has not spread to the axillary lymph nodes.

Stage III describes invasive breast cancer. There are 3 types:

- **Stage IIIA:** The tumor is in the breast and any size or no tumor is found in the breast but is in the lymph nodes. The disease has spread to more than 4 lymph nodes in the breast or axilla. It has not spread to other parts of the body.
- **Stage IIIB:** The tumor may be any size and the disease has spread to the chest wall. It may cause swelling of the breast and may be in up to 9 lymph nodes. Inflammatory breast cancer is considered Stage IIIB.
- **Stage IIIC**: There may be no sign of cancer in the breast or a tumor may be any size and may have spread to the chest wall or breast skin. The disease has spread to 10 or more axillary lymph nodes, or nodes above or below the collarbone or next to the breastbone.

Stage IV (metastatic): The tumor can be any size and the disease has spread to other organs and tissues, such as the bones, lungs, brain, liver, distant lymph nodes, or chest wall (any T, any N, M1).

2.2 Breast Cancer treatment

If you have breast cancer, you should be assigned a multidisciplinary team (MDT), which is a group of specialists who work together to provide the best treatment and care.

The main treatments for breast cancer are:

- surgery
- radiotherapy
- chemotherapy
- hormone therapy
- targeted therapy

You may have one of these treatments, or a combination. The type or combination of treatments you have will depend on how the cancer was diagnosed and the stage it's at.

Breast cancer diagnosed at routine screening may be at an early stage, but breast cancer diagnosed when you have symptoms may be at a later stage and require a different treatment.

Your MDT should discuss with you which treatments are most suitable.

Choosing the right treatment for you

When deciding what treatment is best for you, your doctors will consider:

• the stage and grade of the cancer (how big it is and how far it has spread)

- your general health
- whether you have experienced the menopause

You should be able to discuss your treatment with your care team at any time and ask questions.

Treatment overview

Surgery is usually the first type of treatment for breast cancer. The type of surgery you have will depend on the type of breast cancer you have.

Surgery is usually followed by chemotherapy or radiotherapy or, in some cases, hormone or targeted therapies.

Again, the treatment you'll have will depend on the type of breast cancer. Your doctor will discuss the most suitable treatment plan with you. Chemotherapy or hormone therapy will sometimes be the first treatment. Treatment aims to achieve remission, where cancer shrinks or disappears, and you feel able to enjoy a good quality of life.

Secondary breast cancer

Most breast cancers are discovered at an early stage.

A small proportion of women discover they have breast cancer after it has already spread to other parts of the body (metastasis), and for some women breast cancer may come back after initial treatment. In these cases, the type of treatment you have may be different. Secondary cancer, also called "advanced" or "metastatic" cancer, is not curable.

Want to know more?

- Macmillan Cancer Support: treatments for breast cancer
- Breast Cancer Now: secondary (metastatic) breast cancer

Surgery

There are 2 main types of breast cancer surgery:

- breast-conserving surgery, where the cancerous lump (tumour) is removed
- mastectomy, where the whole breast is removed

In many cases, a mastectomy can be followed by reconstructive surgery to try to recreate a breast. Studies have shown that breast-conserving surgery followed by radiotherapy is as successful as total mastectomy at treating early-stage breast cancer.

Breast-conserving surgery

Breast-conserving surgery ranges from a lumpectomy or wide local excision, where the tumour and a little surrounding breast tissue is removed, to a partial mastectomy or quadrantectomy, where up to a quarter of the breast is removed.

If you have breast-conserving surgery, the amount of breast tissue that is removed will depend on:

- the type of cancer you have
- the size of the tumour and where it is in your breast
- the amount of surrounding tissue that needs to be removed
- the size of your breasts

Your surgeon will always remove an area of healthy breast tissue around the tumour, which will be tested for traces of cancer.

If there's no cancer present in the healthy tissue, there's less chance that the cancer will return.

If cancer cells are found in the surrounding tissue, more tissue may need to be removed from your breast.

After having breast-conserving surgery, you'll usually be offered radiotherapy to destroy any remaining cancer cells.

Mastectomy

A mastectomy is the removal of all the breast tissue, including the nipple.

If there are no obvious signs that the cancer has spread to your lymph nodes, you may have a mastectomy, where your breast is removed, along with a sentinel lymph node biopsy.

If the cancer has spread to your lymph nodes, you'll probably need more extensive removal (clearance) of lymph nodes from the area under your arm (axilla).

Reconstruction

Breast reconstruction is surgery to make a new breast shape that looks as much as possible like your other breast.

Reconstruction can be done at the same time as a mastectomy (immediate reconstruction), or it can be done later (delayed reconstruction).

It can be done either by inserting a breast implant or by using tissue from another part of your body to create a new breast.

Lymph node surgery

To find out if the cancer has spread, a procedure called a sentinel lymph node biopsy may be done.

The sentinel lymph nodes are the first lymph nodes that the cancer cells reach if they spread. They're part of the lymph nodes under your arms (axillary lymph nodes).

The position of the sentinel lymph nodes varies. They're identified using either a combination of a radioisotope and a blue dye, or a magnetic liquid (Magtrace).

The sentinel lymph nodes are examined in the laboratory to see if there are any cancer cells present. This provides a good indicator of whether the cancer has spread.

If there are cancer cells in the sentinel nodes, you may need further surgery to remove more lymph nodes from under your arm.

Chemotherapy

Chemotherapy involves using anti-cancer (cytotoxic) medicine to kill cancer cells.

It's usually used after surgery to destroy any cancer cells that have not been removed. This is called adjuvant chemotherapy.

In some cases, you may have chemotherapy before surgery, which is often used to shrink a large tumour. This is called neo-adjuvant chemotherapy.

Several different medicines are used in chemotherapy, and 2 to 3 are often given at once.

The choice of medicine and the combination will depend on the type of breast cancer you have and how far it has spread.

Chemotherapy is usually given as an outpatient treatment, which means you will not have to stay in hospital overnight.

The medicines are usually given through a drip straight into a vein.

In some cases, you may be given tablets that you can take at home. You may have chemotherapy sessions once every 2 to 4 weeks and then have a break. Each treatment session is known as a cycle. You may have up to 8 cycles of chemotherapy.

The main side effects of chemotherapy are caused by its influence on normal, healthy cells, such as immune cells.

Side effects of chemotherapy include:

- infections
- loss of appetite
- feeling sick
- being sick
- tiredness
- hair loss
- sore mouth

Many side effects can be prevented or controlled with medicines that your doctor can prescribe.

Chemotherapy medicine can also stop the production of oestrogen in your body, which is known to encourage the growth of some breast cancers.

If you have not experienced the menopause, your periods may stop while you're having chemotherapy treatment.

After you have finished the course of chemotherapy, your ovaries should start producing oestrogen again.

But this does not always happen and you may enter an early menopause. This is more likely in women over 40, as they're closer to menopausal age.

Your doctor will discuss with you the impact that treatment will have on your fertility.

Tamoxifen

Tamoxifen stops oestrogen from binding to oestrogen-receptor-positive cancer cells. It's taken every day as a tablet or liquid.

Targeted therapies

Targeted therapies are medicines that change the way cells work and help to stop cancer from growing and spreading. Not all types of breast cancer can be treated with targeted therapies

The targeted therapy most commonly used to treat breast cancer is trastuzumab (also known by the brand name herceptin).

Other targeted therapies include abemaciclib (brand name Verzenios), and palbociclib (brand name, Ibrance). These are used alongside hormone therapy treatments such as fulvestrant to treat certain types of breast cancer. You may be offered them if the cancer has spread to other parts of your body. Abemaciclib is also used for primary breast cancer if it's likely to come back after treatment such as surgery.

Targeted therapies come as tablets or injections or are given through a drip into a vein. Side effects of targeted therapies include:

- shivering and feeling unwell
- diarrhoea
- feeling and being sick
- headache
- cough
- skin rash

Psychological support

Dealing with cancer can be a huge challenge for you and your family and friends. It can cause emotional and practical difficulties.

Many women with breast cancer will have to cope with the removal of part or all of a breast, which can be very upsetting.

It often helps to talk about your feelings or other difficulties with a trained counsellor or therapist. You can ask for this kind of help at any stage of your illness.

Your hospital doctor, specialist nurse or GP can refer you to a counsellor. If you're feeling depressed, talk to a GP. A course of antidepressants may help, or a GP can refer you to see a counsellor or psychotherapist.

It can also help to talk to someone who's been through the same thing as you. Many breast cancer charities have helplines and online forums and staff can also put you in touch with other women who have had cancer treatment.

The practical side of research

Introduction:

75 samples were taken from patients with breast cancer whose ages rafged from 25-45 years, and they include a number of residential areas: Nader the First, Nader the Second, Nader the Third, Al-Iskan, Al-Akrameen, Al-Muhandiseen, Al-Jamiya, Al-Bakrli, Al-Sahha District, Al-Jazair, Al-Thawra, Al-Ustadha, and the Teachers' District, as mentioned in the table above. The samples were collected from Imam Al-Sadiq Hospital and Babylon Oncology Center.

Sampl	Notes	Continuo	Radiati	Gene	Тур	Diagnos		Occupati			th
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numb		nttreat	treatm	facto			Center -		statu	ht	ag
er		me	en t	r					S		e
1.	White	Arimide	Gy	both	D	right	Healt	Housewif	marrie	105	35
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2.	=	=	=	=	D	=	Rare-2	=	=	95	28
3.	=	=	=	Yes	D	left	Professors	=	=	65	44
4.	=	=	=	both	С	=	Al-Akramin neighborho o d	=	=	78	38
5.	=	=	=	=	D	=	Bakrli-Al	employee	=	64	45
6.	=	=	=	Yes	В	=	Nader -3	=	=	86	41
7.	=	=	=	Yes	D	=	Algeria	Housewif e	=	58	30
8.	=	=	=	both	D	=	Nader -1	employee	=	60	42
9.	=	II	nothing	=	D	=	Health district	=	=	63	35
10.	=	=	Gy	=	С	right	Nader -3	=	=	74	43
11.	=	=	=	Yes	A	=	Al-Akramin	Housewif e	=	88	28
12.	=	=	=	both	D	left	Engineers	=	=	67	33

13.	=	=	=	=	D	right	srofessors	=	=	66	37
14.	=	=	=	=	D	=	Teachers area	=	=	54	41
15.		Arimidex tab	Gy	Yes	В	left	Association	Housewife	Single	66	26
16.	=	=	=	both	D	left	Nader -3	=	Single	90	30
17.	=	Ш	=	=	С	right	=	II	married	84	39
18.	П	Ш	=	=	D	left	Ш	Ш	=	105	40
19.	White secretions 2. Red spots on the breast Choose the size Continuous heat Pain sometimes	II	=	=	D	right	II	II	married	91	26
20.	=	=	=	=	D	left	=	=	Single	86	30
21.	=	=	=	Yes	D	left	Algeria	=	married	58	42
22.	=	=	=	both	В	left	Nader -3	employee	=	65	38
23.	=	=	=	=	С	right	Imam	=	Single	93	31
24.	=	ш	=	=	D	left	Housing	Ш	riedmar	52	42
25.	=	Ш	=	=	D	left	Engineers	II		99	31
26.	=	Ш	=	=	A	left	Nader -3	Ш	Single	59	25
27.	=	Ш	=	=	D	left	=	Ш	married	65	32
28.	=	=	=	=	В	left	Housing	=	=	74	40
29.	=	ш	=	=	С	right	revolution	Ш	Single	77	34
30.	=	=	=	=	D	right	Khasrawiya	=	married	86	44
31.	=	=	=	=		left	Nader -3	=	=	58	41
32.	=	=	=	both	A	left		Housewife	=	65	31

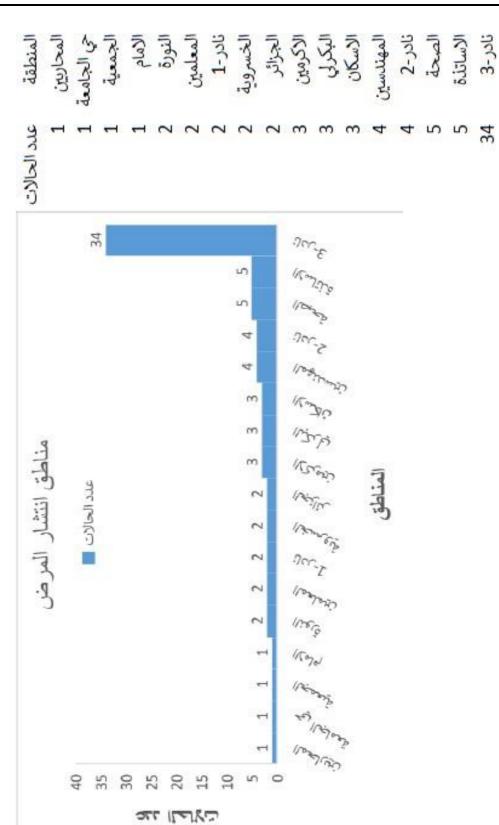
33.	=	=	=	both	D	right	Professors	employee	married	115	25
34.	=	=	=	Yes	D	right	Health district	employee	=	55	30
35.	=	=	=	=	D	right	enerous The g ones	Housewife	=	54	28
36.	=	=	=	=	D	right	Nader -2	employee	=	62	45
37.	=	=	=	=	D	right	Nader -3	employee	=	92	41
38.	=	=	=	=	С	right	=	employee	Single	60	26
39.	=	=	=	=	A	left	=	Housewife	married	110	26
40.	=	=	=	=	A	right	=	=	=	98	42
41.	=	=	=	=		right	=	=	=	69	35
42.	=	=	=	=	D	right	Professors	employee	=	92	28
43.	=	Arimidex	Gy	both	В	right	Nader -3	employee	married	78	45
	=	tab									
44.	=	=	Gy	both	D	=	Nader -2	=	=	66	44
45.	White secretions 2. Red spots on the breast Choose the size Continuous heat Pain sometimes	=	Gy	=	D	=	Health district	=	married	85	31
46.	=	=	Gy	=	С	=	Bakrli-Al	=	=	98	28
47.	=	=	Gy	=	D	left	Nader -3	=	=	68	38
48.	=	=	Gy	Yes	D	right	Nader -1	Housewife	Single	92	35
49.	=	=	Gy	both	В	=	Nader -2	employee	=	52	40
50.	=	=	Gy	=	A	=	Professors	Housewife	=	74	25

51.	=	=	Gy	=	D	=	Teachers	=	=	55	25
							area				
52.	=	=	=	=	D	left	Nader -3	=	=	87	28
53.	=	=	=	=	D	=	=	=	married	59	37
54.	=	=	=	=	D	right	=	=	=	66	445
55.	=	=	=	=	A	=	=	=	=	90	30
56.	=	=	=	both	A	left	=	ifeHousew	Single	105	44
57.	=	=	=	Yes	В	=	=	employee	Single	71	43
58.	=	=	=	both	D	right	=	Housewife	married	82	28
59.	=	=	=	=	D	right	=	Housewife	=	98	41
60.	=	=	=	=	D	left	=	Housewife	Single	88	32
61.	=	=	=	=	Α	right	=	Housewife	_	60	27
62.	=	=	=	Yes	D	left	Health district	employee	=	64	39
63.	=	=	=	both	В	=	Bakrli-Al	employee	=	84	34
64.	=	=	=	=	Α	=	revolution	employee	=	75	44
65.	=	=	=	=	D	right	Khasrawiya		=	77	38
66.	=	=	=	=	D	right		Housewife		52	32
67.	=	=	=	Yes	A	left	=	employee	ngleSi	61	25
68.	=	Arimidex tab	Gy	Yes	D	right	Nader -3	Housewife	married	64	44
69.	=	Arimidex tab	Gy	both	В	right	Housing	employee	married	62	39
70.	=	=	=	both	D	right	Engineers	Housewife	Single	58	28
71.	White secretions 2. Red spots on the breast	=	=	Yes	D	left	e th university	employee			38

	Choose the size Continuous heat Pain sometimes										
72.	=	=	=	both	C	left	Nader -3	Housewife	=	58	34
73.	=	=	=	Yes	С	left	Warriors	Housewife	Single	96	29
74.	=	=	=	both	С	right	Nader -3	employee	married	79	42
75.	=	=	=	both	D	left	Engineers	employee	=	95	45

It has emerged that the highest area in the center of Al Hilla with breast cancer cases is (Nader 3rd) and its case count is (34 cases), some of which are hereditary cases (4) and the latter are non-hereditary (30). Through studying the area, it was found A radioactive source in the area, which is called (the industrial district), which contains a high amount of car oils and other waste, and this is considered one of the causes of breast cancer. The World Health Organization also indicated that this area is radioactively contaminated due to its exposure to wars, especially in the year 2003, and it was bombed with materials. The radioactive..

- 2-The least infected area is (Al-Ustadah neighborhood) (5) cases 3-13-33-42-50. Then followed by the Al-Saha district (5) cases.
- 1-9-34-45-62. Then followed by (Al-Mohandiseen District) 4 cases 12-25-70-75. Then followed by (Nader Al Thani) 4 cases
- 2-36-44-49. Then followed by (Hayy al-Akramin) 3 cases 11-4-35, then followed by (Al-Bakrli neighborhood) 3 cases 5-46-63. Then (the warriors) is followed by one case
- 73. Then (Hay Al-Jameaa) was followed by one case
- 71. Then (Hay Al-Jazair) was followed by two cases
- 7-21. Then (Al-Khusrawiyah) is followed by two cases
- 65-30. Then it is followed by (Nadir Al-Awwal) two cases
- 8-48. Then it was followed by (Al-Iskan neighborhood) 3 cases 69-28-24. Then it was followed by (Hayy al-Tameen) two cases 14-51. Then (the revolution) is followed by two cases
- 26-64. Then (the association) is followed by one case.15 Then (Al-Imam neighborhood) was followed by one case.



Conclusions

- 1. The highest number of infections was observed in the (Nader Al- Thalatha) area (34). The reason is either a genetic factor or an environmentally polluted area.
- 2. The highest number of cases of type D breast cancer was found in the (Nader Al-Thalatha) area, numbering (12).
- 3. The highest number of cases of breast cancer, type B, was observed in this area (Nader Al-Thalatha), numbering (3).
- 4. Cases of type A breast cancer were observed in the (Nader Al- Thalatha) area, and their number is (8).
- 5. The highest number of cases of type C breast cancer was observed in the (Nader Al-Thalatha) area, numbering (4).

In this review, we aimed to summarize and update the current knowledge about breast cancer with an emphasis on its current epidemiology, risk factors, classification, prognostic biomarkers, and available treatment strategies. Since both the morbidity and mortality rates of breast cancer have significantly increased over the past decades, it is an urgent need to provide the most effective prevention taking into account that modifiable risk factors might be crucial in providing the reduction of breast cancer incidents. So far, mammography and sonography is the most common screening test enabling quite an early detection of breast cancer. The continuous search for prognostic biomarkers and targets for the potential biological therapies has significantly contributed to the improvement of management and clinical outcomes of breast cancer patients.

Periodic inspection:-

All people who have previously had breast cancer are at risk of the disease recurring, even after removal and recovery Especially if it is detected in its final stages,

Therefore, the importance of early detection has become apparent because the earlier the disease is discovered, the greater the chances of surviving it. One of the important tips to avoid contracting breast cancer or its return is regular self-examination at least once a month to notice any possible changes that may occur in the breast.

The relationship between herbs and cancer treatment:

Some herbs interact with chemotherapy and radiation for cancer Some medicinal herbs affect the way the body reacts to chemotherapy and radiation therapy. Some herbs increase the body's sensitivity to light and must be completely avoided before radiation therapy. Other herbs also work to reduce or increase the availability of chemotherapy in the body, including the following:

Ginkgo. Kava. Saint John.

References

- 1. D. Hanahan and R. A. Weinberg (2000). The hallmarks of cancer. *Cell* **100:**57–70.
- 2. M. Malumbres and M. Barbacid (2001). To cycle or not to cycle: A critical decision in cancer. *Nat. Rev. Cancer* **1**:222–231.
- 3. C. J. Ormandy, E. A. Musgrove, R. Hui, R. J. Daly, and R. L. Sutherland (2003). Cyclin D1, EMS1 and 11q13 amplification in human breast cancers. *Breast Cancer Res. Treat.* **78:**323–335.
- 4. M. F. Buckley, K. J. Sweeney, J. A. Hamilton, R. L. Sini, D. L. Manning, R. I. Nicholson, A. deFazio, C. K. W. Watts, E. A. Musgrove, and
- 5. R. L. Sutherland (1993). Expression and amplification of cyclin genes in human breast cancer. *Oncogene* **8**:2127–2213.
- 6. K. Keyomarsi and A. B. Pardee (1993). Redundant cyclin overexpression and gene amplification in breast cancer cells. *Proc. Natl. Acad. Sci. U.S.A.* **90:**1112–1116.
- 7. C. Gillett, V. Fantl, R. Smith, C. Fisher, J. Bartek, C. Dickson, *et al.* (1994). Amplification and overexpression of cyclin D1 in breast cancer detected by immunohistochemical staining. *Cancer Res.* **54:**1812–1817.

8. K. M. Alle, S. M. Henshall, A. S. Field, and R. L. Sutherland (1998). Cyclin D1 protein is overexpressed in hyperplasia and intraductal carcinoma of the breast. *Clin. Cancer Res.* **4**:847–854.

- 9. K. Keyomarsi, N. O'Leary, G. Molnar, E. Lees, H. J. Fingert, A. B. Pardee, and E. Cyclin (1994). A potential prognostic marker for breast cancer. *Cancer Res.* **54**:380–385.
- 10. M. Loden, M. Sighall, N. H. Nielsen, G. Roos, S. O. Emdin, H. Ostlund, *et al.* (2002). The cyclin D1 high and cyclin E high subgroups of breast cancer: Separate pathways in tumorigenesis based on pattern of genetic aberrations and inactivation of the pRb node. *Oncogene* **21**:4680–4690.
- 11. R. Hui, A. L. Cornish, R. A. McClelland, J. F. Robertson, R. W. Blamey, E. A. Musgrove, *et al.* (1996). Cyclin D1 and estrogen receptor messenger RNA levels are positively correlated in primary breast cancer. *Clin. Cancer Res.* **2:**923–928.
- 12. Y. Geng, W. Whoriskey, M. Y. Park, R. T. Bronson, R. H. Medema, T. Li, et al. (1999). Rescue of cyclin D1 deficiency by knockin cyclinE. *Cell* **97**:767–777.
- 13. D. O. Morgan (1995). Principles of CDK regulation. *Nature* **374:**131–134.
- 14. C. J. Sherr and J. M. Roberts (1999). CDK inhibitors: Positive and negative regulators of G1-phase progression. *Genes Dev.* **13:**1501–1512.
- 15. N. Dyson (1998). The regulation of E2F by pRB-family proteins. Genes Dev. 12:2245–2262.
- 16. J. LaBaer, M. D. Garrett, L. F. Stevenson, J. M. Slingerland, C. Sandhu, H. S. Chou, *et al.* (1997). New functional activities for the p21 family of CDK inhibitors. *Genes Dev.* **11:**847–862.
- 17. E. A. Musgrove, J. A. Hamilton, C. S. Lee, K. J. Sweeney, C. K. Watts, and R. L. Sutherland (1993). Growth factor, steroid, and steroid antagonist regulation of cyclin gene expression associated with changes in T-47D human breast cancer cell cycle progression. *Mol. Cell. Biol.* 13:3577–3587.
- 18. J. Lukas, J. Bartkova, M. Welcker, O. W. Petersen, G. Peters, M. Strauss, *et al.* (1995). Cyclin D2 is a moderately oscillating nucleoprotein required for G1 phase progression in specific cell types. *Oncogene* **10**:2125–2134.
- 19. R. J. Fiddes, P. W. Janes, S. P. Sivertsen, R. L. Sutherland, E. A. Musgrove, and R. J. Daly (1998). Inhibition of the MAP kinase cascade blocks heregulin-induced cell cycle progression in T-47D human breast cancer cells. *Oncogene* **16**:2803–2813.
- 20. G. A. Colditz (1998). Relationship between estrogen levels, use of hormone replacement therapy, and breast cancer. *J. Natl. Cancer Inst.* **90**:814–823.
- 21. O. W. Prall, B. Sarcevic, E. A. Musgrove, C. K. Watts, and R. L. Sutherland (1997). Estrogen-induced activation of Cdk4 and Cdk2 during G1-S phase progression is accompanied by increased cyclin D1 expression and decreased cyclin-dependent kinase inhibitor association with cyclin E- Cdk2. *J. Biol. Chem.* 272:10882–10894.
- 22. J. S. Foster and J. Wimalasena (1996). Estrogen regulates activity of cyclin-dependent kinases and retinoblastoma protein phosphorylation in breast cancer cells. *Mol. Endocrinol.* **10**:488–498.
- 23. L. Altucci, R. Addeo, L. Cicatiello, S. Dauvois, M. G. Parker, and M. Truss *et al.* (1996). 17b-Estradiol induces cyclin D1 gene transcription, $p36^{D1}$ - $p34^{cdk4}$ complex activation and $p105^{Rb}$ phosphorylation during mitogenic stimulation of G1-arrested human breast cancer cells. *Oncogene* **12:**2315–2324.
- 24. M. D. Planas-Silva and R. A. Weinberg (1997). Estrogen-dependent cyclin E-cdk2 activation through p21 redistribution. *Mol. Cell. Biol.* **17:**4059–4069.
- 25. J. Lukas, J. Bartkova, and J. Bartek (1996). Convergence of mitogenic signalling cascades from diverse classes of receptors at the cyclin D-cyclin-dependent kinase-pRb-controlled G1 checkpoint. *Mol. Cell. Biol.* **16:**6917–6925.
- 26. O. W. Prall, E. M. Rogan, E. A. Musgrove, C. K. Watts, and R. L. Sutherland (1998). c-*Myc* or cyclin D1 mimics estrogen effects on cyclin E-Cdk2 activation and cell cycle reentry. *Mol. Cell. Biol.* **18**:4499–4508.
- 27. O. W. Prall, J. S. Carroll, and R. L. Sutherland (2001). A low abundance pool of nascent p21^{WAF1/Cip1} is targeted by estrogen to activate cyclin E-Cdk2. *J. Biol. Chem.* **276**:45945–45951.
- 28. A. L. Gartel, X. Ye, E. Goufman, P. Shianov, N. Hay, and F. Najmabadi et al. (2001). Myc represses

the p21WAF1/CIP1 promoter and interacts with Sp1/Sp3. *Proc. Natl. Acad. Sci. U.S.A.* **98:**4510–4515.

- 29. E. A. Musgrove, A. Swarbrick, C. S. Lee, A. L. Cornish, and R. L. Sutherland (1998). Mechanisms of cyclin-dependent kinase inactivation by progestins. *Mol. Cell. Biol.* **18**:1812–1825.
- 30. A. Swarbrick, C. S. Lee, R. L. Sutherland, and E. A. Musgrove (2000). Cooperation of p27^{Kip1} and p18^{INK4c} in progestin-mediated cell cycle arrest in T-47D breast cancer cells. *Mol. Cell. Biol.* **20**:2581–2591.
- 31. R. L. Sutherland, R. E. Hall, and I. W. Taylor (1983). Cell proliferation kinetics of MCF-7 human mammary carcinoma cells in culture and effects of tamoxifen on exponentially growing and plateau-phase cells. *Cancer Res.* **43:**3998–4006.