CARCINOMA OF THE BREAST

★ Incidence:

♦ The commonest malignant tumour in females. (35% of malignancies in females).

♦ Age: The mean age of affection is above 50 years with a peak at 70 years.

★ High risk group of patients & predisposing factors: (GHHPIAS)

1. Genetic factor:

♦ In 5-10% of breast cancer, there is autosomal inheritance of a mutant gene.

♦ Two genes BRCA1 & BRCA2 on the chromosomes 17 & 13 respectively are incriminated. (BReast CAncer = BRCA)

♦ These cancers usually occur at a younger age and are bilateral & multifocal.

2. Family history of cancer breast, especially, in young, 1st degree
Breast disorders

relatives & bilateral breast cancer.

3. History **of previous carcinoma of breast** increase incidence of contralateral breast cancer.


5. **Hormonal** disturbance & Exogenous estrogens (Postmenopausal).

6. **Early menarche** (below 13) and **late menopause** (over 50).

7. Prolonged use of **contraceptive pills** (over 10 years).

8. **Infertile, nullipara & lack of lactation**.

9. Women who do not have their **1st pregnancy** until the age of 30 years.

10. **Obesity**: Steroidal hormones are converted to oestradiol in adipose tissues.

**11. Precancerous lesions:**
- Moderate or marked hyperplasia specially with cellular atypia.
- Duct papilloma.
- Lobular or duct carcinoma in situ increase the risk of development of invasive carcinoma by 8 – 10 times.
12. Exposure to **irradiation**.

13. **Excess smoking & alcohol intake**.
★ Pathology:

- **Site**: 60% in the upper outer quadrant as it contains the largest part of the mammary gland.
- **Origin**: Carcinoma of breast usually develops from the epithelium of duct (90%) or rarely from lobular epithelium (10%).
Carcinoma of the breast *is Classified into*:

I) Carcinoma in situ:

- It is Carcinoma of breast remain **localized** within the **basement membrane** without any lymphatic or blood spread.

- Carcinoma in situ is classified into:
  
  A) Duct carcinoma in situ:

  - It is **20-30 %** of newly diagnosed breast cancer which appears as **breast lump or micro-calcification** by mammography.
If not excised, it will progress to invasive duct carcinoma.

B) Lobular carcinoma in situ:

- It is usually discovered accidentally after pathological examination of excised breast lump.
- This patient has an increased risk to develop breast cancer in either breast.

II) Invasive breast cancer:

- It is Carcinoma of breast penetrate the basement membrane & divide into the stroma with tendency for lymphatic & blood spread.

- Invasive breast cancer is classified into:

  A) Invasive duct carcinoma: In the past, it is divided into:
Breast disorders 1

1- Not otherwise specified carcinoma: (Scirrhus carcinoma)
   ♦ The commonest, more than 75% of cases.
   ♦ Usually females above 50 years.
   ♦ **Fibrous tissue is predominant**.
   ♦ **Slowly growing** small hard mass.
   ♦ **Cut section**: Gritty sensation on cutting, greyish white in colour with concave cut surface.
   ♦ It invades & fixed to surrounding structures by white processes.
   ♦ **Microscopically**: Irregular groups of spheroidal cells separated by excess fibrous tissues.

2- Papillary carcinoma: Rare, (1-2%).
   ♦ Develops in the **large ducts** near the nipple, either *de novo* or *on top* of duct papilloma, slowly growing & circumscribed.
   ♦ **Microscopically**: A papillary growth which has a fibrous tissue core covered with many layers of malignant cells.

3- Comedo carcinoma: Rare, (1-2%).
   ♦ It has **comedos** i.e. necrotic sebaceous like material extruded from cut surface of the tumor.

4- Encephaloid carcinoma: Rare, (1-2%).
   ♦ Usually female 20-40 years.
   ♦ **Rapidly growing**, greyish white, large, soft mass (**brain like**).
   ♦ **Cut section**: Soft on cutting, bulging cut section with areas of hge & necrosis.
Breast disorders 1

- **Microscopically:** Large masses of spheroidal cells separated by minimal delicate vascular fibrous stroma markedly *infiltrated with lymphocytes* (good host immune reaction).
- It has **better prognosis** than scirrhus carcinoma.

5- **Medullary carcinoma:** Rare, (1-2%).

- **Microscopically:** Large masses of anaplastic malignant cells separate by fibrous stroma heavily infiltrated with *lymphocytes & plasma cells* (good host immune reaction).
- It is usually high-grade malignancy in their appearance but low-grade in their behavior as its lymphatic & blood spread are delayed and has good prognosis.

6- **Colloid (mucinous) carcinoma:** Rare, (1-2%).

- Soft gelly-like tumour, with *mucin* (produced by tumour cells) in present intra & extracellular.

- **Microscopically:** Spheroidal cells distended with mucin → *signet ring* appearance.

7- **Tubular carcinoma:** Rare (1-2%), tends to form tubes of malignant cells

8- **Inflammatory carcinoma:** (Acute mastitis carcinomatosa, acute or lactational carcinoma). Rare (1-2%)

- It occurs usually during *lactation or pregnancy*.
- Very rapidly growing large soft mass.
- The breast is enlarged with *rapid onset* of pain, redness, hotness & dilated veins.
- **D.D:** *from acute mastitis* (mention in short).
9- **Paget's disease of the nipple:** Rare (1-2%)

- **Definition:** A disease of the breast characterised by *nipple eczema* associated with or followed within 2 years by breast carcinoma.

- **Pathology:**
  
  a. **Origin:** It is regarded as primary *carcinoma of a main lactiferous* duct which extends *outwards* affecting the skin of nipple & areola and inwards spreads into the breast substance to produce an underlying carcinoma.

  b. **Gross picture:**

     1. **Nipple eczema:** which has the character mentioned in D.D later on.

     2. **Breast carcinoma:** of scirrhous type develops within 2 years after the onset of the eczema.

  c. **Microscopically:**
• Epidermis shows hyperplasia.
• Among the deep layers of epidermis there are Paget's cells which are large, rounded vaculated giant cells with dark small nuclei.
• Rounded cells & plasma cells infiltrate the dermis.


PAGET'S DISEASE OF THE NIPPLE
Breast disorders 1

- **Origin of Carcinoma**
- **Paget’s disease**
  - Papillary Carcinoma
  - Tumour with excessive F.T
  - Not otherwise specified carcinoma
  - Inflammatory carcinoma
  - Atrophic serous carcinoma
  - Tumour with excessive cells
  - Encephaloid carcinoma
II. **Invasive lobular carcinoma**: (5-10%)

- It arises from the epithelium of the lobules.
- It may be multicentric & bilateral in

  20% of cases.

★**Grading system in cancer breast:**

<table>
<thead>
<tr>
<th>Grade I</th>
<th>Grade II</th>
<th>Grade III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well differentiated</td>
<td>Moderate differentiated</td>
<td>Poorly differentiated</td>
</tr>
<tr>
<td>breast cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cells appears normal</td>
<td>Cells not normal</td>
<td>Cells appears abnormal</td>
</tr>
<tr>
<td>Low grade malignancy</td>
<td>Moderate malignancy</td>
<td>Highly malignant</td>
</tr>
<tr>
<td>with slow rate of growth &amp; spread</td>
<td>with moderate rate of growth &amp; spread</td>
<td>grow rapidly with aggressive spread</td>
</tr>
</tbody>
</table>

![Prognosis and Grade Diagram]

- **Grade 1**: Low grade malignancy with slow rate of growth & spread.
- **Grade 2**: Moderate malignancy with moderate rate of growth & spread.
- **Grade 3**: Highly malignant, grow rapidly with aggressive spread.
Breast disorders 1

★ Hormone receptors:
- About 60% of breast cancers have oestrogen receptors in the tumour cells & their metastases and termed ER positive. These tumors are oestrogen dependent tumors ie. become more active in presence of oestrogen and regress on its deprivation of oestrogen or blocking of oestrogen receptors by anti-oestrogen.
- Breast cancers may have also progesterone (PR) receptors.
- 20% of breast cancer have Human Epidermal growth factor Receptor 2 or also called neu (HER2/neu) which involved in regulation of cell growth. HER2/neu is present on the long arm of chromosome 17.
- 30% of breast cancers are triple negative i.e do not have ER, PR or HER2/neu.
- Over expression of HER2/neu or triple negative breast cancers are high risk tumours i.e. grow rapidly & metastasize early.

Estrogen & progesterone receptors

HER2/neu
Complications:

A. Spread:

I. Direct spread:

a) To the surrounding breast stroma, Cooper’s ligaments & lactiferous ducts.

b) To the deeper structures (to pectoral facia, pectoral muscles, serratus muscle, ribs, intercostals muscles). Spread to pleura & malignant pleural effusion are rarely due to direct spread but usually occur 2ry. to lung metastases.

c) To the skin, nipple and areola leading to the followings manifestations:

1. **Skin tethering** due to invasion of cooper’s ligament, where the mass can be moved within a certain range without affection of the skin, but outside this range the skin is dimpled.

2. **Skin fixation** is caused by direct infiltration of the skin with the tumor can not be moved at all without moving the skin.

3. **Dimpling and puckering** of the skin overlying the tumour:

   ♦ This is the earliest manifestation of pathology in the breast with excess fibrosis but it is not pathognomonic of carcinoma.
   
   ♦ It is due to infiltration & shortening of Cooper’s ligaments.
Breast disorders 1

- by the tumour → pulling the skin inwards.
  - It is **demonstrated early** by asking the patient to **elevate her arms**.

**Clinical Present**

- **Dimpling or puckering of the skin**

4. **Dilated veins** on the skin due to increased vascularity of the breast

5. **Ulceration & fungation** (mention characters of malignant ulcer).

6. **Peau d’orange:**
  - A hard **thick non-pitting oedema of the skin** which is marked in the dependent part i.e the lower 1/2 of the breast.
It is due to **obstruction of the skin lymphatics** by malignant cells & fibrosis.

Skin swells except at **the points of** attachment of hair follicles, sweat & sebaceous glands producing pits that give the skin the orange appearance.

- It is **not pathognomonic** for carcinoma.
- It becomes **more obvious** by squeezing the skin gently.
7. *Skin nodules*: near or far from the tumour due to *retrograde lymphatic spread*.
   ♦ This is *pathognomonic* for carcinoma but it is a very *late* sign.

   ♦ The skin is *very hard, thick, fixed and pigmented*. It is not localized to the breast but it may extend to the chest, trunk, arms and neck.
   ♦ This is *due to* malignant infiltration and fibrosis of the skin as well as hard lymphatic oedema due to obstruction of skin lymphatics.
9. **Nipple is retracted and elevated:** This *not pathognomonie* of carcinoma as it may occur in any fibrotic process entangling main milk ducts.
10. **Paget's disease** of the nipple. ( Mention in details).


II- **Lymphatic Spread**: By both permeation and embolization.

- **The lymph nodes draining the breast:**
  - Recent description of lymphatic drainage of breast & the skin overlaying suggest that lymph vessels accompany the major blood vessels directly to the following draining L.Ns.:
  1. **75% to axillary** L.Ns mainly pectoral, basal & apical L.Ns.
  2. **20% to internal thoracic** (parasternal) L.Ns. (along internal thoracic vessels) Via lymphatics passing along perforating branches of internal thoracic vessels.
  3. **5% to infra-clavicular, supra-clavicular, subscapalar** ( drain the tail ) or posterior intercostal L.Ns.
The lymphatic drainage passes along the following pathways:

a. **Laterally:** Most of breast drains to pectoral L.Ns. → basal → apical L.Ns → supraclavicular LNs

b. **Medially:** The medial part of the breast drains to:
   1. The internal thoracic (parasternal) L.Ns by lymphatics enter the thorax along the perforating branches of internal thoracic.
   2. The opposite breast & axilla (some authors deny this)

c. **Upwards:** Some lymphatics pass from the upper part of breast directly to infra-clavicular & supra-clavicular L.Ns.

d. **Downwards:** (usually occur when the main lymphatic pathways are obstructed)
   1. The lower inner part of breast communicates with the lymphatics in the rectus sheath leading to malignant nodule in the umbilicus (sister Joseph nodule) & falciform ligament → L.Ns metastases in the porta hepatis (may lead to obstructive jaundice).
   2. The lower inner part of breast communicates with the Subdiaphragmatic, liver and peritoneal lymphatics.
Sister Joseph nodule

- **Significance of lymphatic spread of carcinoma of breast:**

  1. By the time the *L.Ns.* are histologically affected by malignancy, *distal organ micrometastases* are likely to be present. Therefore *L.Ns* affection is an important prognostic factor.

  2. Patients with histologically negative axillary nodes have better prognosis than patients with histological positive nodes.

  3. The prognosis is *inversely related to the number* of involved axillary nodes.
4- Pathological staging of axillary nodes is performed after postoperative exam. suggesting the prognosis:

a) **Histologically negative:** disease free survival at 10 years is over 70%.

b) **Histologically positive:**
   - 1-3 nodes: disease free survival at 10 years is about 35%.
   - More than 3 nodes: disease free survival at 10 years is 17%.

5- The axillary L. Ns are divided into **3 levels**.
   - I. L.Ns. *inferior* to lower border of pectoralis minor.
   - II. L Ns directly *deep* to pectoralis minor.
   - III. L.Ns *superior* to pectoralis minor.

6- Prognosis is **inversely related to the level** of axillary L.Ns involvement.

7- Metastatic involvement of axillary nodes progress regularly from level I to II then to III; skip metastases are recorded only in 2% of cases.
8) **Sentinel lymph node** is the first node receiving lymph from the primary tumour.

9) **Parasternal L.Ns** involvement are more common from inner or central tumours or with large tumours.

10) **Axillary L.Ns** involvement are much more common than parasternal nodes involvement (even inner and central regions).

11) The incidence of **positive axillary or parasternal nodes** increases with the size of the tumour and with the local invasiveness of the neoplasm.

12) **Supraclavicular or infraclavicular L.Ns** involvement represents a late stage of axillary L.Ns involvement, systemic disseminated disease and carries a grave prognosis. (i.e. Stage IV).

13) **Oedema of arm** represents a late stage of axillary node involvement with affection of supraclavicular or infraclavicular L.Ns (Stage IV).

**Supraclavicular lymph nodes**
Breast disorders 1

III- Blood spread: ( 2L & 2B or LBLB )

- Blood spread to the lungs, liver, brain, bones (mainly to ribs, sternum, thoracic spines, skull & long bones).
- Previously it was thought that breast cancer spreads locally at first, then by lymphatics & lastly by blood stream.
- This view is no longer accepted, and it is now well established that carcinoma of the breast may spread by the blood stream very early producing micrometastases in distant organs.
- The tendency of breast cancer to metastasize to the spine is explained by the free communication of posterior intercostal veins with vertebral venous plexus.

IV ) Transperitoneal spread:

- By seeding or from liver metastases or peritoneal lymphatics → malignant ascites, Krukenberg’s tumour (malignant cells implanted on the ovaries → bulky tumour), nodules in the Douglas pouch, omentum and parietal peritoneum.
B. Hge, anaemia, infection, malignant cachexia & death .

★ Clinical Picture:

I. Incidence: (mention high risk group)

II. Symptoms:

A) Early:

1) **Painless accidentally discovered lump** in the breast is the commonest presentation. An accidental trauma to the breast may call the attention of the patient to the presence of the lump.

2) **Pricking pain in the breast**.

3) Changes in the *level, shape and size* of the breast

4) Recent changes in *Skin, areola & Nipple changes*.

5) **Nipple discharge**: May be blood (in duct carcinoma), necrotic discharge (in degenerated cancer) or pus (in case of associated infection).

6) The disease may be discovered by routine **screening** mammography that is done for the high risk asymptomatic women.

B) Late: **Manifestations of metastases**:

1. *In L.Ns.*: Axillary or supraclavicular swellings & edema of arm.

2. *In bone*: Bony pain, swelling or pathological fracture.

3. *In lung*: Chest pain, cough, dyspnea, haemoptysis ... etc.

4. *In liver*: Pain & swelling in right hypochondrium & Jaundice.

5. *In peritoneum*: Abdominal masses (peritoneal nodules) or ascitis.
6. **In brain:** Headache, vomiting, blurring of vision, mental changes, motor & sensory manifestations.

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**Early Symptoms & Signs of Breast Cancer**
Signs of Breast Cancer
III. Examination:

A) **General:** To detect manifestations of metastases.

B) **Local:** Both sides should be examined starting by the normal side.

   a) **Breast as a whole:** As a result of neoplastic fibrosis:
      1. **The size** of the breast is small, atrophic & shrunken, (if there is no fibrosis, the breast is enlarged).
      2. The breast is **elevated,** puckered, deformed & displaced.
      3. The above mention signs are more evident on **raising the arms or on leaning forwards.**

b) **Nipple & areola:**
   1. **Recent unilateral acquired retraction** of the nipple (D.D congenital retraction which dates since birth and usually bilateral).
   2. **Mal-directed** nipple (normal: forewords, lateral & slightly downwards).
   3. Squeeze the nipple to detect **nipple discharge**
   4. **Malignant eczema** (paget's disease) with erosion of the nipple and areola (D.D. ordinary eczema). (Mention in short)

c) **Skin:** Show dimpling, puckering, dilated Vs, peau d’orange, tethering, fixity to the tumour, malignant nodules, malignant ulceration, fungation and cancer en cuirasse. Redness, oedema of the skin may suggest inflammatory carcinoma which should be differentiated from breast abscess (Mention in short).

d) **Breast mass:** A malignant breast lump is usually by the flat of the hand as stony hard, irregular with restricted mobility & fixed to surrounding structures.

e) **Draining lymph nodes:** palpate the axillary, infraclavicular & supraclavicular L.Ns. on both sides. Malignant deposits are painless, hard, discrete first mobile but in advanced cases become painful, matted & fixed.
IV- Special forms of breast cancer:

1. Paget’s disease of the nipple:
   - The first symptom is pricking sensation in the nipple with superficial erosion.
   - The diagnosis is established by biopsy.
   - D.D.: from ordinary eczema of the nipple.

<table>
<thead>
<tr>
<th>* Paget’s eczema *</th>
<th>* Ordinary eczema *</th>
</tr>
</thead>
<tbody>
<tr>
<td>◆ Around menopause</td>
<td>◆ During lactation.</td>
</tr>
<tr>
<td>◆ Unilateral</td>
<td>◆ Usually bilateral</td>
</tr>
<tr>
<td>◆ Start in the nipple</td>
<td>◆ Start in the areola</td>
</tr>
<tr>
<td>◆ Non-itchy, no oozing, no</td>
<td>◆ Itchy, oozing and vesicles are</td>
</tr>
<tr>
<td>vesicles.</td>
<td>common.</td>
</tr>
<tr>
<td>◆ Nipple is eroded</td>
<td>◆ Intact nipple.</td>
</tr>
<tr>
<td>◆ Well-defined margin</td>
<td>◆ Ill-defined margin</td>
</tr>
<tr>
<td>◆ Followed by carcinoma</td>
<td>◆ Followed by acute mastitis.</td>
</tr>
<tr>
<td>◆ A breast lump may be felt</td>
<td>◆ No lump.</td>
</tr>
<tr>
<td>◆ Does not respond to eczema</td>
<td>◆ Responds to treatment eczema.</td>
</tr>
<tr>
<td>treatment.</td>
<td></td>
</tr>
</tbody>
</table>
2. **Inflammatory carcinoma:**

- It is highly malignant tumour occurs during *pregnancy or lactation*.
- It is a rapidly growing painful tumour which infiltrate the breast diffusely.
- The overlying skin is *red, oedematous & warm*.
- **D.D.:** from *acute bacterial mastitis*.

<table>
<thead>
<tr>
<th><strong>Inflammatory carcinoma</strong></th>
<th><strong>Acute bacterial mastitis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>♦ Less redness i.e dusky red</td>
<td>♦ More redness i.e fiery red.</td>
</tr>
<tr>
<td>♦ Affects more than 1/3 the breast</td>
<td>♦ Affect one sector of the breast</td>
</tr>
<tr>
<td>♦ No or mild fever or leucocytosis</td>
<td>♦ There are high fever &amp; leucocytosis</td>
</tr>
<tr>
<td>♦ Gradual onset &amp; progress is slower.</td>
<td>♦ Acute onset &amp; rapidly progress.</td>
</tr>
<tr>
<td>♦ Not or mild tenderness</td>
<td>♦ Markedly tenderness.</td>
</tr>
<tr>
<td>♦ No tender axillary L.Ns.</td>
<td>♦ Tender axillary L.Ns.</td>
</tr>
<tr>
<td>♦ No response to antibiotics within 1 week is indication for biopsy.</td>
<td>♦ Curred by antibiotics or form acute abscess.</td>
</tr>
</tbody>
</table>
3. **Breast cancer during pregnancy or lactation:**

- The *diagnosis may be delayed* due to physiological changes in the breast.
- Pregnancy or lactation are not contraindication to operation & treatment is based on the stage of the disease as in non-pregnant females.
- **In the first 6 months**, termination of pregnancy is essential to cut down estrogen secretion.
- **In the last 3 months**, pregnancy may be allowed to proceed to full term.

4. **Carcinoma in situ:**

- It is *frequently diagnosed* nowadays due to the use of mammographic screening.
- It represent *20%* of cancer breast detected by screening.

<table>
<thead>
<tr>
<th>Duct carcinoma in situ</th>
<th>Lobulal carcinoma in situ</th>
</tr>
</thead>
<tbody>
<tr>
<td>- More common</td>
<td>- Less common</td>
</tr>
<tr>
<td>- Rare .</td>
<td>- May be bilateral &amp; multicentric</td>
</tr>
<tr>
<td>- Presence of microcalcification or breast lump .</td>
<td>- Absent .</td>
</tr>
<tr>
<td>- Early detection is possible</td>
<td>- Less likely</td>
</tr>
<tr>
<td>- Turn to invasive cancer in 50%</td>
<td>- It is a mark of increase risk of cancer in both breasts .</td>
</tr>
<tr>
<td>- Treated as invasive carcinoma</td>
<td>- careful follow up .</td>
</tr>
</tbody>
</table>
but no axillary resection.

★ N.B : **Triple assessment for sure diagnosis of breast cancer :**

- **Comparing the results** of the followings :
  1. Clinical examination
  2. Digital mammography or U/S .
  3. Tru-cut needle biopsy.
- If the results of the three parameters are concordant , diagnosis of breast cancer is established .
- If the results of the three parameters are not concordant , further investigations as excision biopsy is needed .

**V. Early detection of breast cancer:**

- Screening programs have been established in order to detect early silent cancer breast to give the patient a better chance for cure.
- These *screening programs* include:
  1. **Breast self examination:**
     - All women over 20 years should be taught to examine their breast monthly.
     - Menopausal women should perform this examination every week.
     - The patient is instructed to ask for medical evaluation if any abnormality is noted. *(mention early symptoms).*
  2. Screening program : High risk patients are subjected to
    a. *Regular mammography* every 1-3 years according to the
age & program.
- It is the only reliable mean to detect early lesions.
- **Mention features of malignancy in mammography**

b. Careful regular *clinical examination* by a well trained surgeons every 1-3 years according to the age & the program. *(Mention examination in short).*

c. Any suspicious lesion must undergo biopsy *(Mention).*
Investigations:

- **Aim:**
  a. *Diagnosis* of carcinoma by mammography, ultrasound & biopsy.
  b. *Metastatic work up*.

- **Methods:**

  I) Radiological investigations:

  1- *Digital Mammography*:

  - It is a plain X-ray of the breast obtained on a computer system.
  - In expert hands, it is 95% accurate in diagnosing breast cancer.
  - Malignant lesions appear as ill-defined shadow, irregularly penetrating the surrounding structure, irregular opacity, microcalcification shows pleomorphic dots.
  - In young age, it is difficult to differentiate the density of the lesion from the normal breast tissue. In these cases contrast enhanced digital mammography or *tomosynthesis* (3D digital mammography) can be used.
Breast disorders 1

Mammogram

Cancer, deep in the right breast

2D  3D slice 43  2D contrast
Breast disorders 1

2- Ultrasonography:

- It can differentiate **cystic from solid** lesions.
- In addition, **Duplex ultrasound** identify the vasculariry of the lesion:
  
  C) **Malignancy** receive blood flow from all around with turbulent speed.
  
  D) **Benign** lesions receive blood flow from one side with low speed.

- **U/S guided tru-cut needle biopsy is the standard method for diagnosis** of breast cancer nowadays.

3- **MRI with contrast** may be indicated in certain situation eg. Before & after **neoadjuvant** therapy to monitor the response.

II) **Biopsy:** The **most important** investigation. It may be:

1- **U/S guided Tru-cut thick needle biopsy** is the standard & **most popular method** for diagnosis of breast cancer nowadays.

- It is done under local anaesthesia with a special needle that cuts a core of the tumour for **histological** exam. and for assessment of the receptors.
2- **Fine needle aspiration cytology**: (FNAC) this method depends on exam. of cells to detect criteria of malignancy.

- **Indication**: cystic swelling.

- **Malignancy is suspected** in bloody aspirate, residual mass after aspiration, rapid reaccumulation after aspiration or malignant cells are discovered.

- In the **outpatient** clinic. The mass is fixed between the fingers of one hand & the needle is passed in it while keeping constant suction by the other hand.

- False negative results may occur in 10% of cases.

- **Criteria of malignancy** include hyperchromatosis, pleomorphic cells & nuclei, ill-defined cytoplasm & abnormal nuclear chromatin ratio.

- It is very simple, **inexpensive & accurate**.
3- Excision biopsy & *paraffin sections*:

- Under local anaesthesia, the whole lump is excised through circumareolar or transverse incision & definitive surgery is postponed.
- Paraffin sections are stained, examined & result is obtained in few days.
- It is the *most reliable* method to obtain sure diagnosis.

4- **Excision biopsy and frozen sections** of the tissues obtained under general anaesthesia to proceed to definitive surgery if histological exam. show malignancy.

- 3 & 4 are gradually *loosing popularity* in favour of the simpler needle biopsy.

5- **Stereotactic core biopsy** ie. Mammographic guided biopsy.

- It is used for *non-palpable mammographically detected* lesions such as microcalcification that can not to be seen by U/S
6- Biopsy from non-palpable breast mass:

- The radiologist insert a **hook wire** inside the lesion under mammographic or U/S guidance.
- At operation, the mass is removed with the wire for histological exam.

![Insertion of a hook wire inside the lesion](image)

7- Sentinel lymph node biopsy:

- Identification of sentinel node by injection of methylene blue or radioactive sulphur colloid in the subareolar or peritumour area before the operation. During the operation through axillary incision, the sentinel node is identified (the blue coloured node or by radiation detection probe), excised with immediate pathological exam.
III. Metastatic work up: (investigations to detect distant metastases should be mentioned in any malignancy).

- In early breast cancer: The following is enough
  1- **X-ray chest** for invasion of the ribs, lung metastasis, pleural effusion.
  2- **Abdominal ultrasound**.

- If positive nodes, locally advanced tumor or suggestive symptoms the following investigations can be done:
  1- CT brain, chest & abdomen.
  2- Radioactive isotopic scan of bone.
  3- **PET scan & PET-CT**.
  4- **Serum alkaline phosphatase** is elevated in early liver or bone metastases.
  5- If pleural effusion or ascites aspiration show hemorrhagic fluid containing malignant cells and rapidly reaccumulate.
IV) Detection of tumor maker:

- Cancer Antigen 15-3 (CA15-3) is the tumor marker for breast cancer.
- It is elevated in large or disseminated tumors.
- It is not useful for diagnosis but it is used to monitor response to breast cancer treatment and disease recurrence.

V) Hormone receptor determination in breast carcinoma:

- Immunohistochemical techniques using monoclonal antibodies.

VI) Routine investigations: (before surgery or chemotherapy)

1. Full blood picture: for anaemia
2. ESR is elevated in disseminated tumors.
4. ECG & echocardiography.
5. Chest x-ray
6. Liver functions: are impaired in advanced liver metastases.

★ Treatment:

- Multidisciplinary assessment involving surgical, medical, radiotherapy and oncology opinions to plan the best treatment for each case. The patient and her family should be involved in decision making.
- Breast cancer has 2 compartments:
1) **Loco-regional disease**:  
- It is formed of the primary tumor and regional lymph nodes.
- Surgery and radiotherapy are effective in treatment of loco-regional disease.

2) **Systemic disease**:  
- It is formed of occult distal micro-metastases.
- Hormonal therapy, chemotherapy and target therapy are effective in treatment of systemic disease.

Treatment of breast cancer **depends mainly** on staging and presence of high risk factors.

- Recently the patients are classified into **3 categories** as follows:

**I - Early breast cancer:**

- Those are cases of **Stage I & IIA in UICC Staging** i.e less than or equal to $T_2 N_1 M_0$.

**Methods:**

**A) Surgical treatment:**

1) **Breast conservative therapy:**

   - **Advantage**: minimizing psychological trauma.
   - **Indication**: Recent it is the **most popular** procedure for solitary, *small* (less than 4 cm) *peripheral* tumour in *large* breast.
   - **Contraindications** : ( as indications of modified radical mastectomy ) + pregnancy ( radiotherapy is contraindicated).
   - **Methods**: The following 3 steps should be done.
a- Management of the 1ry. tumor by **lumpectomy** (wide local excision of the tumor with 1cm safety margin)

(*Axillary dissection* if indicated + *Postoperative radiotherapy* to the remaining breast and axilla.)

b- Management of axillary lymph nodes:

- In case of early small tumors with clinically impalpable axillary lymph nodes (**N0**), **sentinel lymph node biopsy**:
  - If negative node, this usually means that other axillary nodes are also clear and the patient can be saved from unnecessary axillary dissection with reduction of incidence of lymphedema.
  - If positive node, axillary lymph nodes dissection should be done.

- **Clinically palpable mobile axillary lymph nodes** (**N1**), axillary lymph nodes dissection should be done.
  - In axillary lymph nodes dissection, remove level I & II nodes and if they are grossly affected, level III nodes should be excised.
  - In axillary lymph nodes dissection, 10 or more should be removed.

*c- Postoperative radiotherapy*: to the whole breast with a boost at the site of the operation.
- **Indication:** Small breast, large, central, multicentric or local recurrence after breast conservative surgery. High risk patients as positive family history with BRCA1 & BRCA2 mutant genes.

- **Method:**

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**Modified Radical Mastectomy:**

- **Indication:** Small breast, large, central, multicentric or local recurrence after breast conservative surgery. High risk patients as positive family history with BRCA1 & BRCA2 mutant genes.

- **Method:**
Through elliptical **skin incision**, the following structures are removed en block:

- A **wide ellipse** of skin include the skin over the tumour with at least 5 cm safety margin, **nipple & areola**.
- The **whole breast** include the tumor.
- It differs from radical mastectomy in **preserving pectoralis major** & pectoralis **minor is either** removed or its insertion is cut → better appearance.

**Axillary dissection**: All fat and L.Ns **medial to axillary** vein are removed.

- During operation, axillary vessels, cephalic vein & brachial plexus, nerve to serratus anterior & nerve to latissimus dorsi should be preserved.
3) Breast Reconstruction:

- **Timing**: Either early at the time of mastectomy or delayed after 3 - 6 months after mastectomy.

- **Methods**:
  1. This can be performed by implantation of prosthesis deep to the pectoralis major or
  2. Transvers rectus abdominis (most popular) or latissimus dorsi myocutaneous flap.
Transvers rectus abdominis myocutaneous flap (TRAM)

Latissimus dorsi myocutaneous flap
B) **Postoperative radiotherapy:**

- **Indication:** Post-operative radiotherapy for the followings:
  a) After breast conservative surgery
  b) 4 or more positive axillary L. Ns.
  c) Tumours more than 4cm.
  d) Tumour within the medial ½ of breast.

- **Site:** Remaining part of the breast after breast conservative surgery, axilla, supraclavicular & parasternal (tumor in the medial half of the breast)

C) **Adjuvant therapy:**

- **Indication:** It is *recommended for all patients with positive axillary L.Ns* to eliminate occult distal micrometastases, responsible for late recurrence.

- **Methods:**
  1) **Hormonal therapy:**
     - **Indication:** for all cases with estrogen positive receptors.
     - **Effect:** it reduces ipsioateral & contralateral breast recurrence by 40% & improve survival rate.
     - **Methods:**
       - In *premenopausal & postmenopausal* patients:
         - **tamoxifen** block estrogen receptors. It is not given for more than 5 years (to avoid development of endometrial carcinoma and thromboembolic disease).
       - In *premenopausal* patients: Ovarian suppression by **Zoladex** which stop the ovaries from making estrogen plus
Anastrazole.

➢ In **postmenopausal** patients: **Anastrazole** is an aromatase inhibitor which inhibits peripheral conversion of androgen to estrogens.

2) Chemotherapy:

• **Indications**:
  a) Positive axillary lymph nodes.
  b) Aggressive tumors eg. Negative hormones receptor or triple negative tumor or over expression of HER2/neu.
  c) Tumors more than 5 cm.

• **Methods**:
  ▪ Drugs commonly used nowadays are **anthracyclines and taxanes**.

3) Target therapy:

• **Indications**: HER2/neu positive tumors.

• **Method**:
  ▪ **Trastuzumab (Herceptin)** is a monoclonal antibody 
    against HER2/neu receptors, decrease incidence of local recurrence & improve survival rate.

*D) Follow up of the patient* at regular intervals for life is required to:

 a) Detect **local** or distal **recurrence**.

 b) Detect carcinoma in the **contralateral breast** by annual mammography.

 c) Detect & treat complications of mastectomy which are:

  1. **Psychiatric morbidity**.
2. **Arm oedema:**
   
   - **Aetiology:**
     a. Excision of lymphatics or their obstruction by radiotherapy.
     b. By lymphangitis due to infections.
     c. Malignant recurrence in the axilla.
     d. Thrombosis of axillary V.
   
   - **Treatment**
     a. **Prophylaxis:** Avoid radiotherapy to fully resected axillary L.Ns, avoid minor trauma to the hand, wearing gloves during manual working, avoid infection & lymphangitis.
     b. **Curative:** Arm elevation, massage & elastic compression.
     d) **Patients are instructed** not to get pregnant for at least 3 years and to use non-hormonal contraception.

II- **Locally advanced breast cancers:**

- Those are cases of **Stage IIB & III in UICC Staging** i.e equal to T_{3-4} N_{2-3} M_0 .
- **Methods :**
  
  A) **Neo-adjuvant therapy :**
    - **Pre-operative chemotherapy** (same drugs as before) to reduce the size of the tumor and allows surgery.
  
  B) **Surgical treatment :**
    - Usually by **modified radical mastectomy**.
  
  C) **Post-operative radiotherapy :** for all patients.
III- Advanced breast cancers:

- Those are cases of *Stage IV in UICC Staging* i.e $M_1$.
- **Aim**: Palliation & improving quality of life.
- **Methods**:
  - Mainly hormonal therapy, chemotherapy & target therapy but radiotherapy or surgery are of secondary value.

1) **Hormonal therapy**:

- **Indication**: for all cases with estrogen positive receptors.
- **Methods**:
  - Tamoxifen is the primary hormonal therapy. It is not given for more than 5 years.
  - If no response to tamoxifen, aromatase inhibitor (anastrozole) is used.

2) **Chemotherapy**:

- **Indication**:
  1. Failure of hormonal treatment.
  2. If the tumour is triple negative.
  3. Visceral metastasis (brain, lung or liver).
- **Methods**:(same drugs mention before in early breast caners )

4) **Target Therapy**:

- **Indications**: Her2/neu positive patients
- **Method**: In addition to chemotherapy, target therapy is taken in the form of Trastuzumab (Herceptin) plus Pertuzumab as first line.
5) **Radiotherapy:**
   - **Indication:** Palliative radiotherapy is indicated in stages III & IV to control pain, ulceration, brain & bone metastases, spinal metastases with cord compression.

6) **Surgery:**
   - **Indications & methods:**
     1- **Simple mastectomy** is mainly used to remove unpleasant, malodorous, fungating tumor.
     2- **Internal fixation** of pathological fractures.

7) **Management of specific problems:**
   - **Hypercalcaemia:**
     - It occurs in widespread bone metastases.
     - The patient is dehydrated, thirst with drowsiness & constipation.
     - Treatment: correct dehydration by IV fluid, frusemide, prednisolone & bicarbonates.
   - **Pathological fracture:** internal fixation & radiotherapy.
   - **Spinal cord compression:** urgent cord decompression, fixation followed by radiotherapy.
   - **Pleural effusion:** chemotherapy & chest tube.
   - **Liver metastases:** chemotherapy.
   - **Cerebral metastases:** corticosteroids & radiotherapy.