Pathology of breast cancer

- **Structure of the breast:**
  * It rests on the chest wall (pectoralis major muscle and fascia).
  * From the 2nd to the 6th rib, and from the lateral aspect of the sternum to the midaxillary line.
  * It is composed of 15-20 lobules and each lobule has its own lactiferous duct which will open in lactiferous sinuses in the nipple.

- **Histology of the breast:**
  * The duct are composed of 2 layers:
    # The epithelium: which give rise to ductal carcinoma.
    # The myoepithelial cells.
  * Lobular carcinoma arises from the acini (alveoli which secrete milk).
  * Intralobular connective tissue (stroma) will give rise to benign tumor fibroadenoma.

- **Inflammatory lesions:**
  * **Acute mastitis:** due to bacterial infection (Staphylococcus aureus) which might result in the formation of abscess.
  * **Fat necrosis:**
    # It is a benign lesion which presents as a lump in the breast & appear calcified in x-ray.
    # Characterized by the formation of foam cells, presence of giant cells, neutrophils, blood, fibroses & calcification.
  * **Granulomatous mastitis:**
    # It is caused by hypersensitivity reaction & presented clinically as a lump.
    # Formation of granuloma which is also seen in other disease such as Tb and sarcoidosis.
    # Characterized by the presence of epithelioid cells + infiltration of lymphocytes.
- **Fibrocystic changes:**
  * Presented clinically as a lump associated sometimes with brownish discharge from the nipples.
  * **Cause:** hormonal effect of estrogen.
  * **Classified to:**
    # **Simple:** no hyperplasia.
    # **Proliferative:** hyperplasia with increased risk of malignancy. (note: atypical hyperplasia is associated with increased risk of malignancy more than normal hyperplasia ≈5 times compared with 1.5-2).
  * **Grossly:** cyst (filled with fluid or solid material) + fibrosis (appear white in color).
  * **Histologically:** formation of cysts + apocrine metaplasia + fibrosis in stroma + adenosis.

![Image of fibrocystic changes](image)

- **Neoplasia:**

  1) **Benign tumors:**

  * **Fibroadenoma:**
    # Presents clinically as a mobile breast lump especially in young women.
    # It increases in size during pregnancy and lactation (hormonal effect).
    # **Grossly:** defined margins with whitish appearance and slit like spaces.
    # **Histologically:** proliferation of the intralobular connective tissue (stroma) which will push the ducts and thus they will lose their normal shape.

![Image of fibroadenoma](image)

* **Phyllodes tumor:**
  # Majority are benign. Some can be malignant spreading through hematogenous route (blood stream) to distant sites.
  # It is resembling fibroadenoma but characterized by stromal proliferation (in a leaf-like pattern) + mitosis and the margins of the tumor are not well-defined.
* **Intraductal papilloma:**
  # Arising usually in the main ducts (lactiferous ducts)
  # It is a tumor with finger-like processes.
  # Presented clinically as a small subareolar tumor with bloody discharge (and rarely nipple retraction).
  # Histologically: a mass with finger-like processes inside the lumen of the duct

![](image1.png)

2) *Malignant tumors (50% in the upper outer quadrant of the breast):*

* Non-invasive carcinoma of the breast (tumors limited by the basement membrane):
  # Ductul carcinoma in situ:
    ✓ **Comedo:** large high-grade tumor with necrosis and calcification.
    ✓ **Non-comedo:** low-grade tumor with no necrosis. It includes solid, papillary and cribriform tumors.

![](image2.png)

# Lobular carcinoma in situ:
  ✓ Monomorphic population of small, rounded loosely cohesive cells fills and expands the acini of a lobule.

![](image3.png)

# Paget’s disease:
  ✓ The skin of the nipple is eroded with the formation of ulcers & it indicated the presence of ductul carcinoma.

![](image4.png)
* Invasive carcinoma (infiltrating to surrounding tissues):

# Invasive ductul carcinoma:
- Strong hard mass with large amount of fibrous stroma.
- It can be fixed to the overlying skin of the breast or to the chest wall.
- Grossly: necrotic centers with no well-defined margins.
- Histologically: malignant cells in tubules in a fibrous stroma.

# Invasive lobular carcinoma:
- More than one mass and it can be bilateral.
- Histologically: small cells arranged in chains or cords (Indian-file) with no formation of tubules.

# Medullary carcinoma:
- Grossly: large, well-defined soft mass.
- Histologically: high-grade tumor cells with pleomorphic nuclei and lymphocytes infiltrating at the periphery of the tumor.
- Better prognosis compared with invasive ductul carcinoma.

# Mucinous (colloid carcinoma):
- Grossly: soft gelatinous circumscribed mass found in post-menopausal women.
- Histologically: tumor cells floating in mucin.
- Good prognosis.
# Tubular carcinoma:
- Small circumscribed hard tumor.
- Histologically: well formed tubules in a dense stroma with little pleomorphism.
- Good prognosis.

# Inflammatory carcinoma:
- Presents clinically as an inflammatory lesion
- Breast is edematous and red.
- Aggressive with poor prognosis.

- Spread of carcinoma
  - Lymphatic: to axillary, internal mammary or subcalvicular lymph nodes
  - Hematogenous (distant metastasis): lung, liver, bone, adrenals, brain
  - Local infiltration: resulting in nipple retraction. Orange-peel skin, fixation to skin or muscle

- Prognostic factors:
  - Stage of tumor (size, nodes, metastasis).
  - Histologic grading (well, moderately or poorly differentiated). Grading is done using 3 criteria: tubule formation, frequency of cell mitosis and nuclear pleomorphism.
  - Histologic type.
  - Presence of estrogen and progesterone receptors: denotes better prognosis and respond to the treatment by tamoxifen.
  - Nottingham prognostic index.

- Staging of breast cancer

| STAGE-I | < 2 cm / no lymph node / no metastasis |
| STAGE-II | > 2 cm - < 5 cm / 1-3 lymph nodes / no metastasis |
| STAGE – III | > 5 cm / 1-3 lymph nodes / no metastasis |
| STAGE – IV | Any size / ± lymph nodes / distant metastasis |

- Her-2-neu:
  - Cell surface receptor expressed by tumor cells.
  - Overexpression is associated with poor prognosis.
  - Respond to the treatment with herceptin.