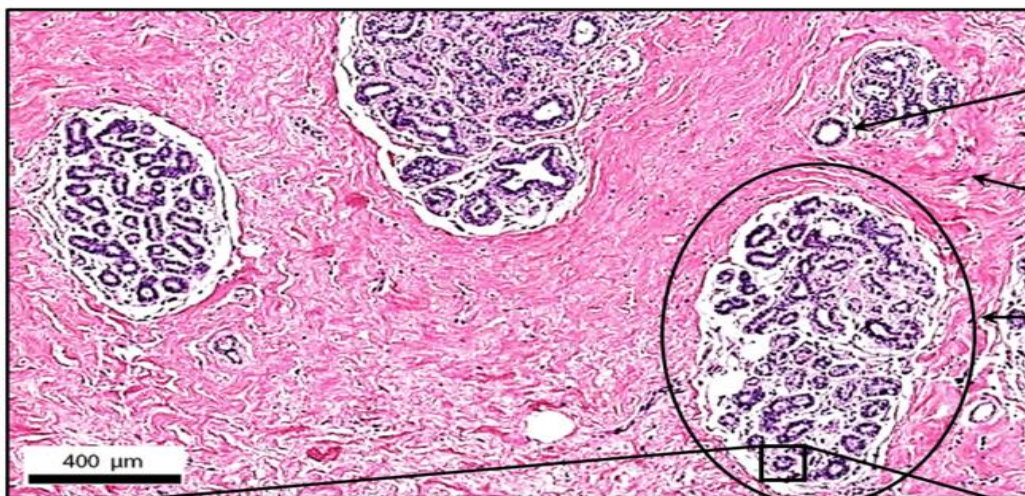


Breast pathology

Dr. Raghad Hanoon

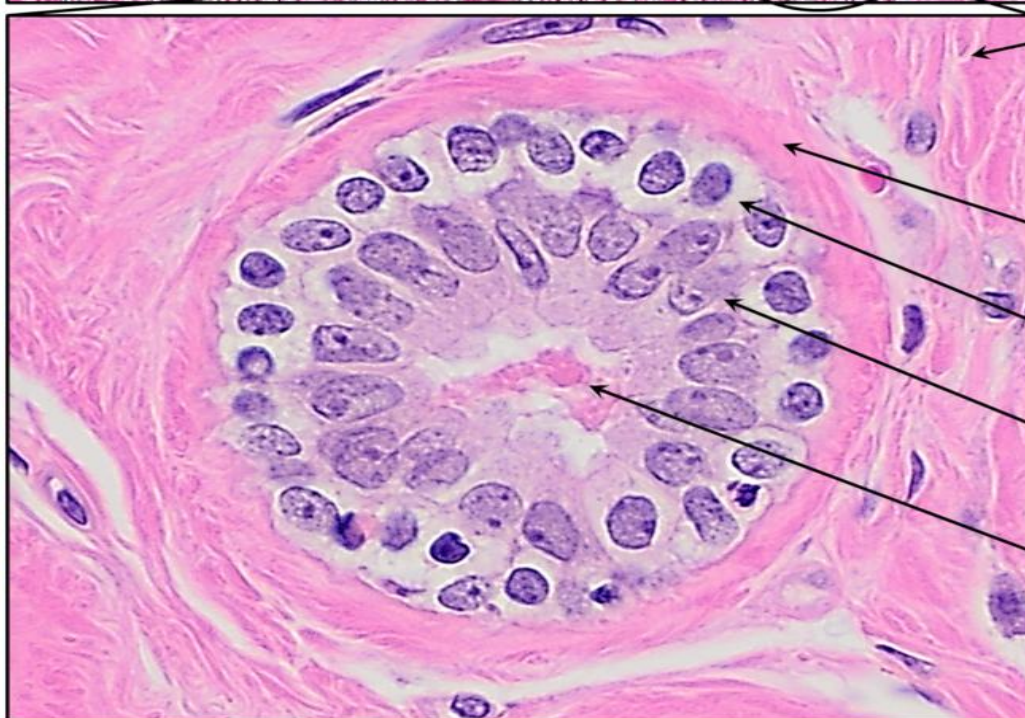
Breast histology



Duct

Interlobular stroma

Lobule



Intralobular stroma

Acinus:

Basement membrane

Myoepithelial cells

Luminal epithelial cells

**Lumen (with
eosinophilic secretions)**

Inflammatory lesions of the breast

- Inflammatory diseases of the breast are rare (accounting for <1% of breast symptoms)

A. Infective :

- 1- Acute mastitis (Acute pyogenic mastitis).
- 2- Chronic nonspecific mastitis.
- 3- Tuberculous mastitis.

B. Non-infective inflammatory lesions:

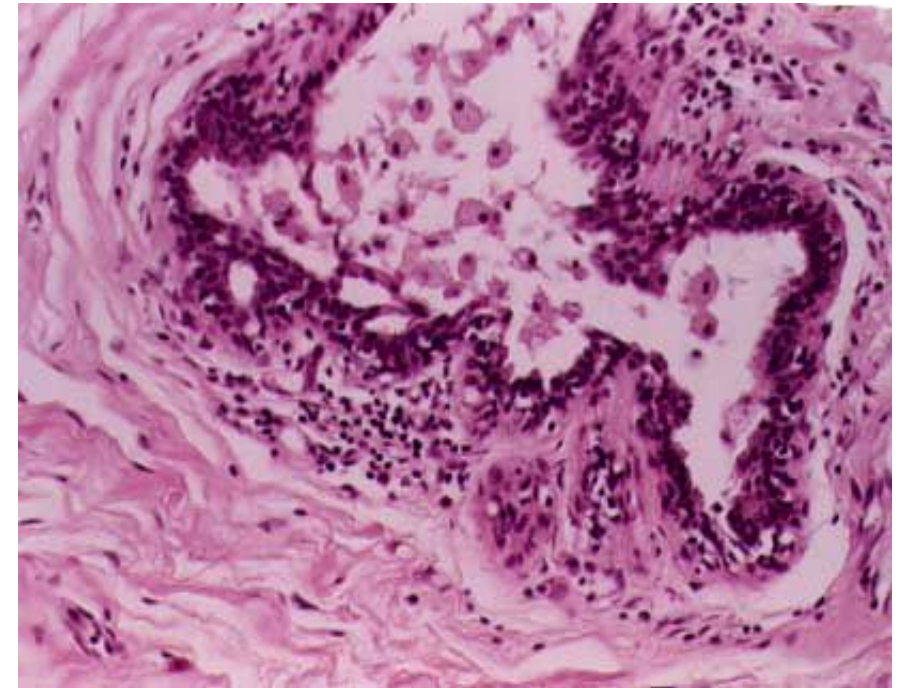
- 1- Mammary duct ectasia .
- 2- Fat necrosis of the breast .

Acute Mastitis

- It typically occurs **during the first month of breastfeeding** when the breast is most vulnerable due to cracks and fissures in the nipples.
- It is caused by a **local bacterial infection** (Staphylococcus aureus or, less commonly, streptococci).
- If not treated, it leads to multilocular abscess.
- **Gross:** there may be **generalized red, painful swelling** of the breast or a localized abscess may form in a single breast lobe. **The axillary lymph nodes are frequently swollen & show reactive hyperplasia.**
- **Microscopically:** there is an **acute suppurative inflammation** and with abscess formation.

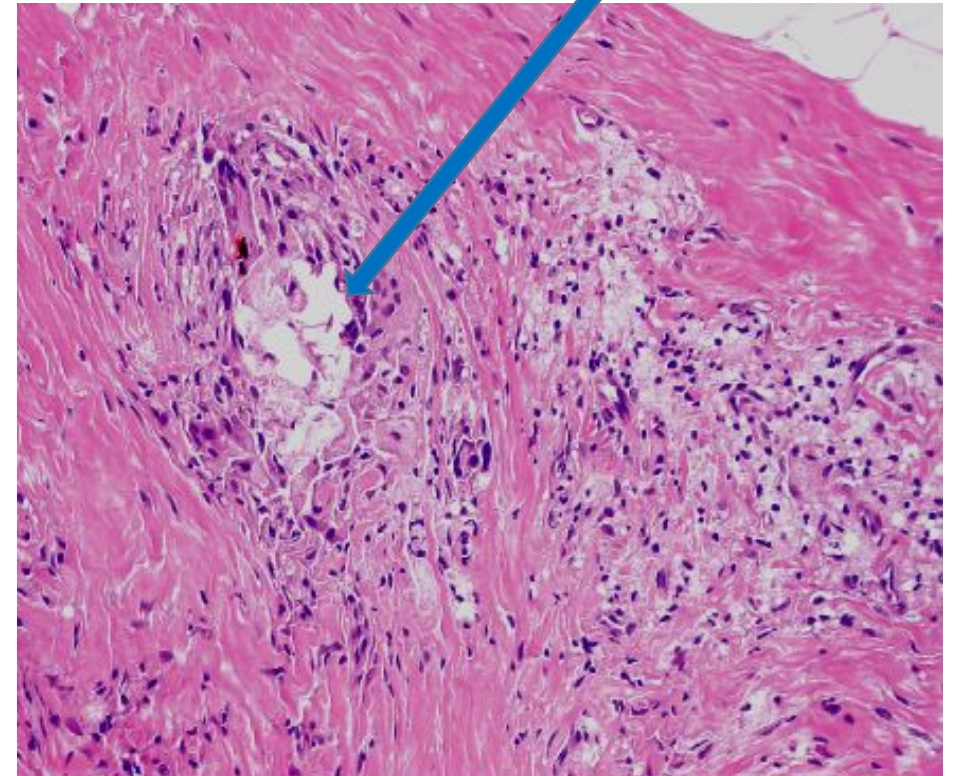
Duct Ectasia

- This disorder tends to occur **in the 5th or 6th decade of life**, usually in **multiparous** women.
- It presents as **a palpable periareolar mass** that is often associated with **thick, white nipple secretions**.
- **Grossly**, sectioning shows ropelike dilated ducts from which thick, cheesy secretions can be extruded.
- **Microscopically**, the **dilated ducts are filled by granular debris**, sometimes containing **lipid-laden macrophages** with **periductal plasma cell infiltration**.



Fat Necrosis

- The presentations of fat necrosis are **a painless palpable mass, skin thickening or retraction.**
- It is **caused by a trauma** to the breast which cause disruption of fat cells and allow the escape of fat globule into the surrounding tissue which cause foreign body giant cell reaction, with foamy cells and later dense fibrous tissue.
- **Clinically and mammographic** examination it may simulate carcinoma due to hard mass production and calcification.
- **Mic.;** There is a central focus of necrotic fat surrounded by inflammatory cells.



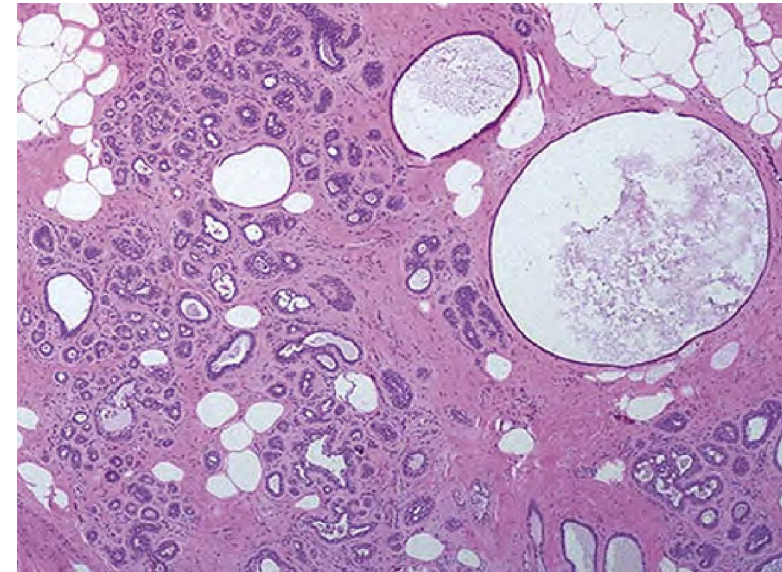
Benign Epithelial Lesions

They are classified into **three groups**, according to the subsequent risk of developing breast cancer:

- (1) **Non-proliferative breast changes**; not associated with an increased risk of breast cancer.
- (2) **Proliferative breast disease without atypia**; associated with a slightly increased risk of breast cancer (1.5- to 2 fold increased risk).
- (3) **Proliferative breast disease with atypia**; associated with a modest increase in the risk of breast cancer (4- to 5 fold increased risk of cancer).

1- Nonproliferative Breast Changes (Fibrocystic Changes)

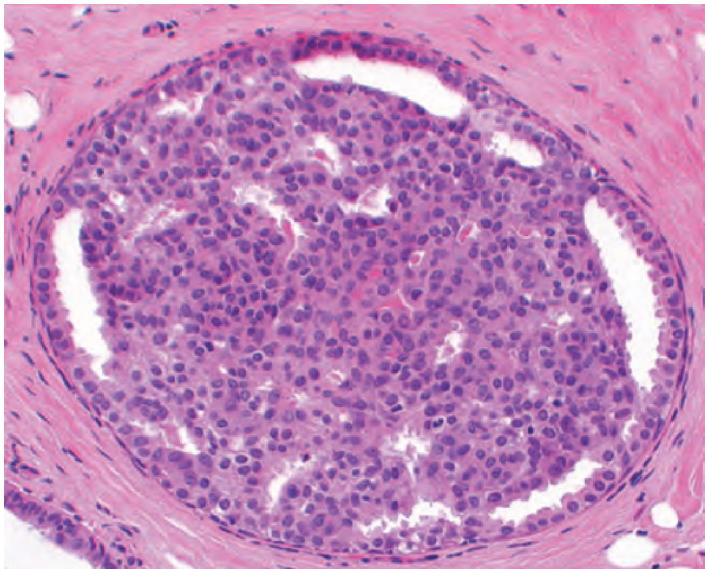
- **Not associated with an increased risk of breast cancer.**
- **Gross:** single large cyst appear brown to blue (blue dome cysts).
- **Mic.;** consists of **three** major morphologic changes; **Cysts:** Irregularly dilated ducts lined by uniform benign cuboidal to columnar epithelial cells, **Fibrosis:** Dense connective tissue located between the cysts, **Adenosis:** An increased number of acini (glands) within each lobule.



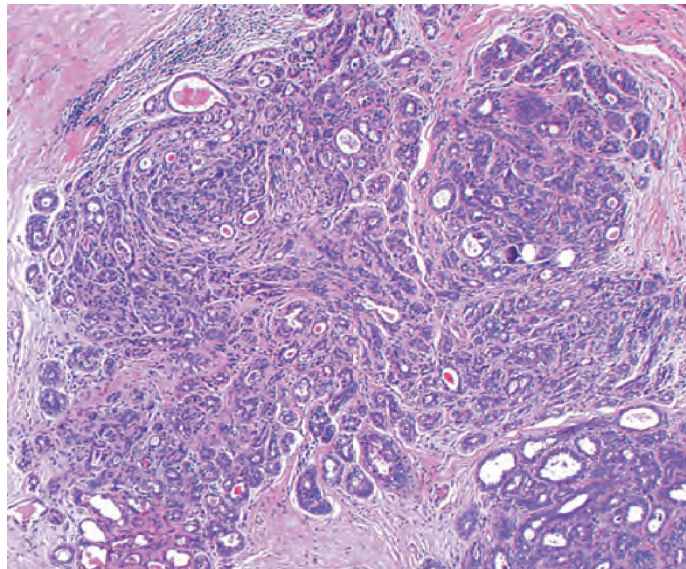
2- Proliferative Breast Disease Without Atypia

- These lesions are characterized by **epithelial proliferation, but without atypia**, associated with **a slightly increased risk of breast cancer**. Includes;
 - A. Epithelial hyperplasia:** increased numbers of both luminal and myoepithelial cell types, fill and distend ducts and lobules.
 - B. Sclerosing Adenosis:** increased number of acini that are compressed and distorted in the central portion of the lesion by dense stroma.
 - C. Papilloma:** reflect epithelial growth and associated fibrovascular cores within dilated ducts.

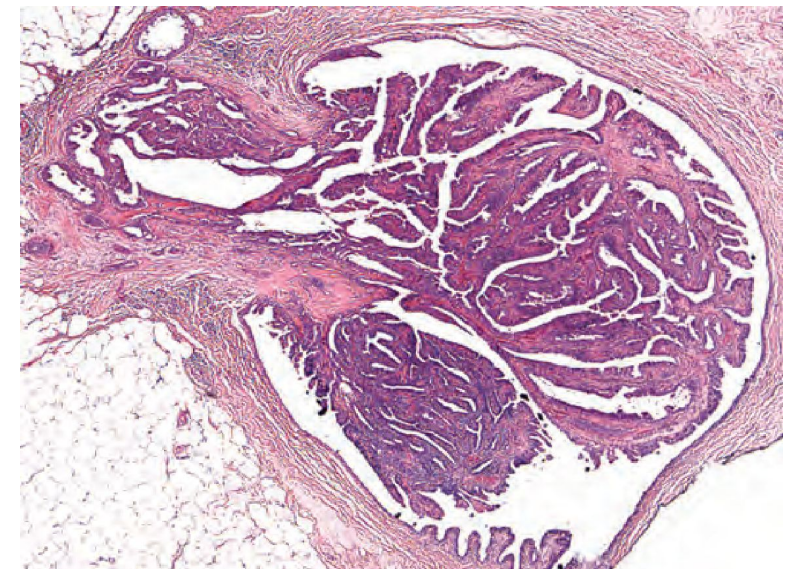
(A)



(B)



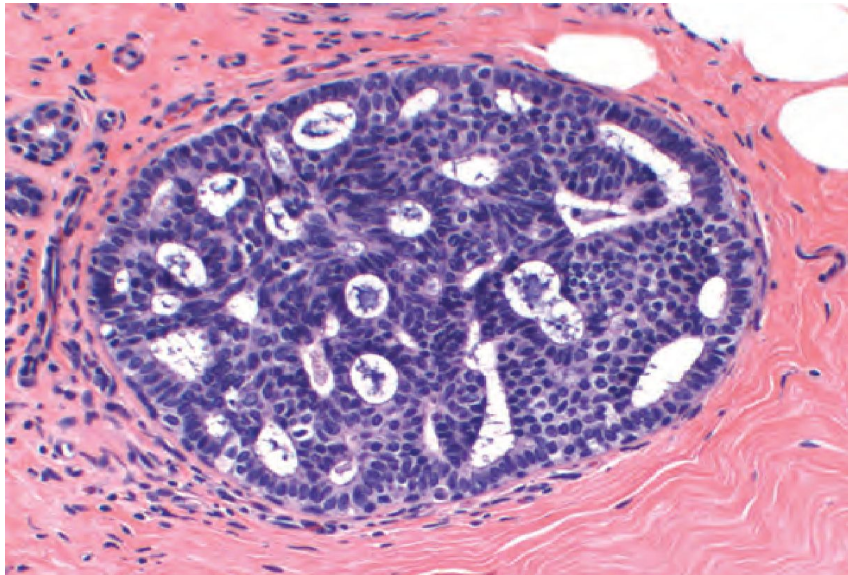
(C)



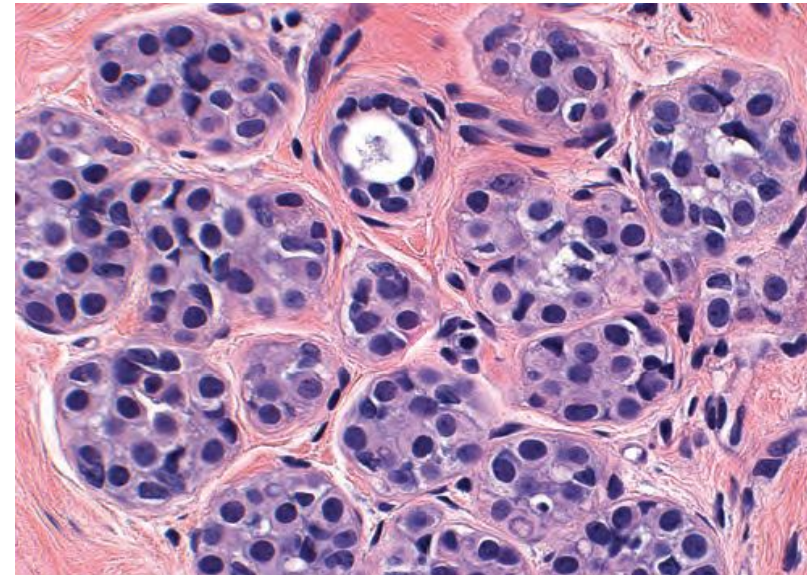
3- Proliferative Breast Disease with Atypia

- It is associated with a **moderately increased risk of carcinoma**.
- There are two types:
 - **Atypical ductal hyperplasia**; is recognized by its histologic resemblance to DCIS. It consists of a relatively monomorphic proliferation of regularly spaced cells, sometimes forming cribriform spaces. It is distinguished from DCIS in that it only **partially fills involved ducts**
 - **Atypical lobular hyperplasia**; consists of monomorphic small, round, loosely cohesive cells **partially fills a lobule**.

(A)



(B)



Tumors of the breast

- Tumor is the most important lesion of the female breast, it is classified in to :

1- Primary

A- Benign tumors:

Fibroadenoma.

Phyllodes tumors.

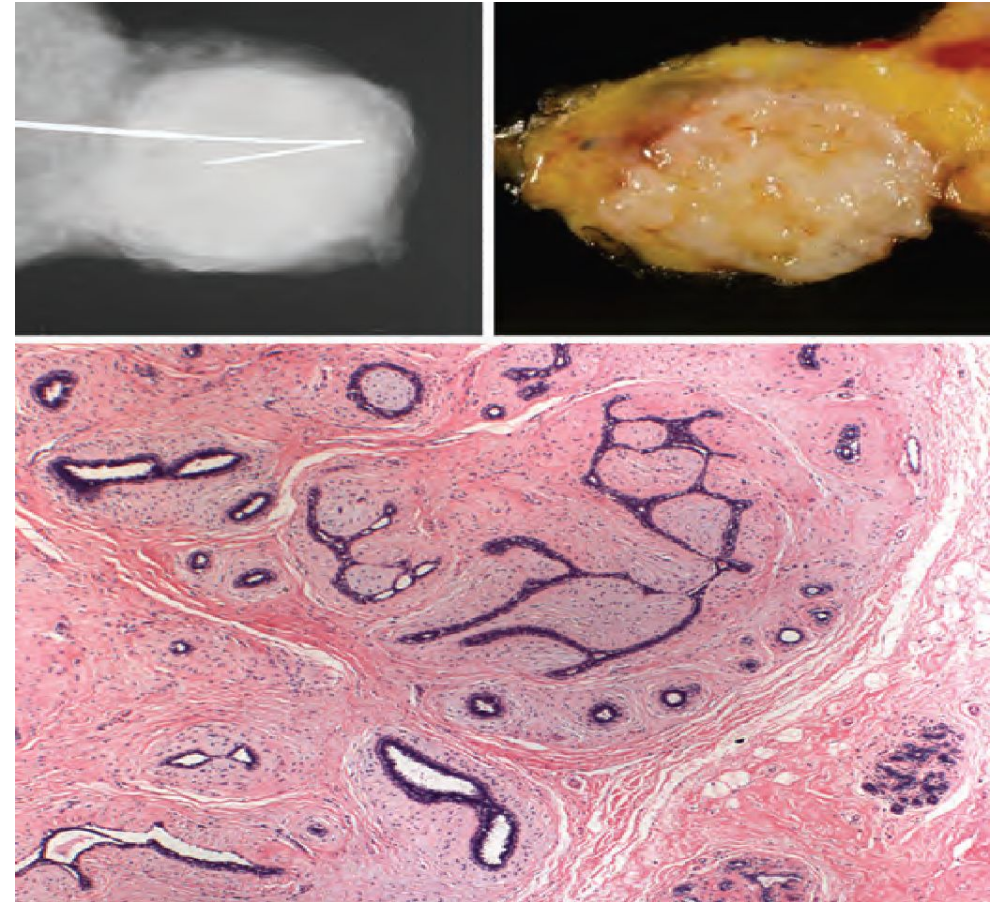
B- Malignant tumors:

Carcinoma of the breast (most important)

2- Secondary(Metastases) to the breast are rare.

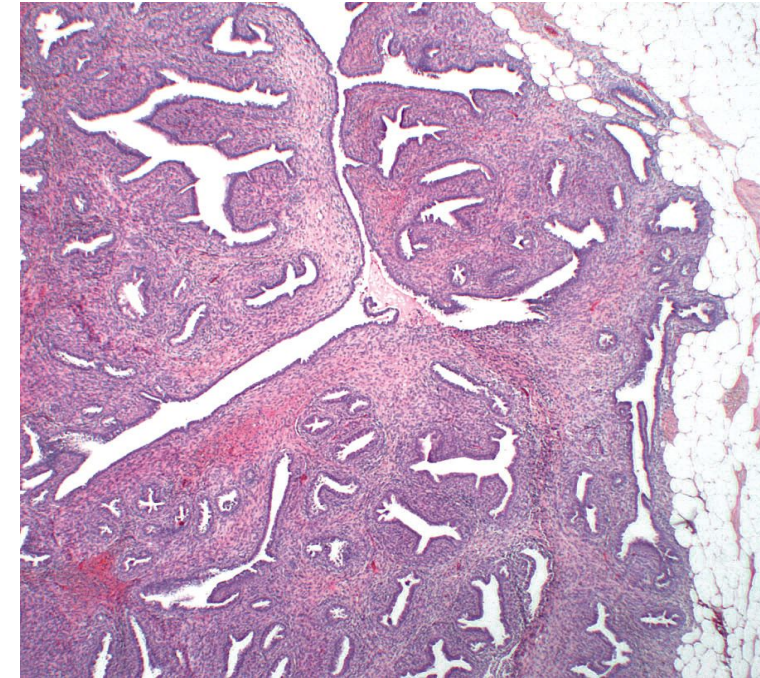
Fibroadenoma

- It is the **most common benign tumor** of the female breast.
- Derived from intralobular stroma and consist of of both stromal and epithelial cells (i.e., they are “biphasic”).
- **Clinically:** it is usually **solitary painless, well-demarcated** from adjacent breast tissue **freely movable mass**.
- **Grossly:** a **rubbery, white, well-circumscribed mass** is clearly demarcated from the surrounding yellow adipose tissue.
- **Microscopically:** The **proliferation of intralobular stroma surrounds, pushes, and distorts the associated epithelium**. The border is sharply delimited from the surrounding tissue.



Phyllodes tumors

- These tumors are much **less common** than fibroadenoma.
- Usually grow to **large**, possibly massive size (4-10 cm).
- They are thought to **arise from periductal stroma** and not from preexisting fibroadenoma
- **Clinically:** the patient typically has **a history of a rapidly growing palpable breast mass**.
- **Grossly:** the tumors are **lobulated and cystic and on sectioning exhibit leaf-like clefts and slits**.
- **Microscopically:** Like fibroadenomas, phyllodes tumors are **biphasic**, composed of **neoplastic stromal cells and epithelium-lined glands**. However, **the stromal element is more cellular and abundant**, giving rise to the typical leaf-like architecture.
- **Most** of these tumors remain localized "**benign**" and are cured by excision.
- **The malignant** changes in Phyllodes tumors occurs in **< 5% of cases**; however it usually remains localized and only 15% may metastasize.



Malignant tumors (Carcinoma) of the breast

- It is the most common malignancy of women globally and causes the majority of cancer deaths in women.

□ Epidemiology and Risk Factors

1. **Age & Gender:** Rare under 25; risk rises sharply after 30. Male incidence is only 1% of female incidence.
2. **Family History & Genetics:**
 - ****Greatest risk:** multiple first-degree relatives with early-onset breast cancer.
 - ****5–10%** of cases involve inherited tumor suppressor mutations: **BRCA1** and **BRCA2**.
 - ** **Lifetime risk with BRCA mutations:** >90%.
 - ** **BRCA carriers** are more likely to have: premenopausal, bilateral, or ovarian cancers; positive family history.
3. **Reproductive History:** Early menarche, nulliparity, no breastfeeding, and late first pregnancy increase risk (**due to prolonged estrogen exposure**).
4. **Ionizing Radiation:** Chest radiation during breast development (e.g., teens/20s for Hodgkin lymphoma) increases risk (25–30%); no elevated risk if treated later in life.

□ Pathogenesis

- Factors that contribute directly to the development of breast cancer can be grouped into genetic, hormonal, and environmental categories.

1. Genetic Factors:

- **Hereditary:** BRCA1/BRCA2 mutations.
- **Sporadic:** HER2/NEU overexpression (poor prognosis, in ~30% of invasive cancers); RAS/MYC amplification; RB and p53 tumor suppressor mutations.

2. Hormonal Factors: **Excess endogenous estrogen** (linked to long reproductive life, nulliparity, late first childbirth, estrogen-secreting ovarian tumors).

- Estrogen stimulates growth factors in breast cells. Estrogen/progesterone receptors may interact with growth promoters (e.g., TGF- α), creating an autocrine tumor development mechanism.

3. Environmental Factors: **Geographic differences** and variable incidence in genetically identical groups. **Irradiation and exogenous estrogens are** other important environmental variables

Morphology and histological subtypes of breast cancer (Classification):

- The most common location of tumors within the breast is in the **upper outer quadrant** (50%) followed by the central portion (20%).
- About **4% of women with breast cancer have bilateral primary tumors** or sequential lesions in the same breast.
- Breast cancers are classified morphologically **according to whether they have penetrated the basement membrane**. Those that remain within this boundary are termed *in situ carcinomas*, and those that have spread beyond it are designated *invasive carcinomas*. In this classification, the main forms of breast carcinoma are as follows:

A. Noninvasive

1. Ductal carcinoma in situ
2. Lobular carcinoma in situ

B. Invasive

1. Invasive ductal carcinoma (includes all carcinomas that are not of a special type)—70% to 80%
2. Invasive lobular carcinoma— ~10% to 15%
3. Medullary carcinoma— ~5%
4. Mucinous carcinoma (colloid carcinoma) — ~5%
5. Tubular carcinoma— ~5%
6. Other types (e.g. Inflammatory, papillary & metaplastic carcinoma).

❖ Noninvasive carcinoma (Carcinoma in situ)

- It is classified as **DCIS** (Ductal carcinoma in situ) or **LCIS** (Lobular carcinoma in situ) based on the resemblance of the involved spaces to normal ducts or lobules.
- DCIS and LCIS both arise from TDLU (terminal duct lobular unit) and both are **confined by a basement membrane and do not invade into stroma or lymphovascular channels**.

□ DCIS;

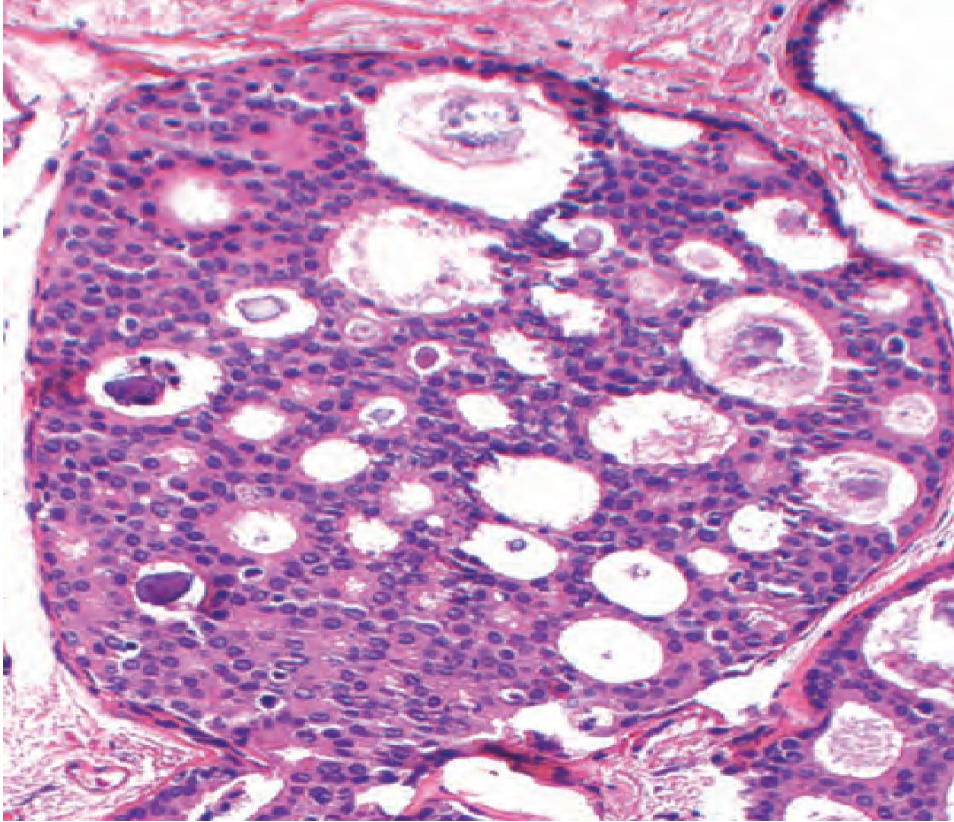
*Has wide variety of histological appearances: **solid, comedo, cribriform, papillary, micropapillary**.

***Nuclear appearance** ranges from bland and monotonous (low nuclear grade) to pleomorphic (high nuclear grade).

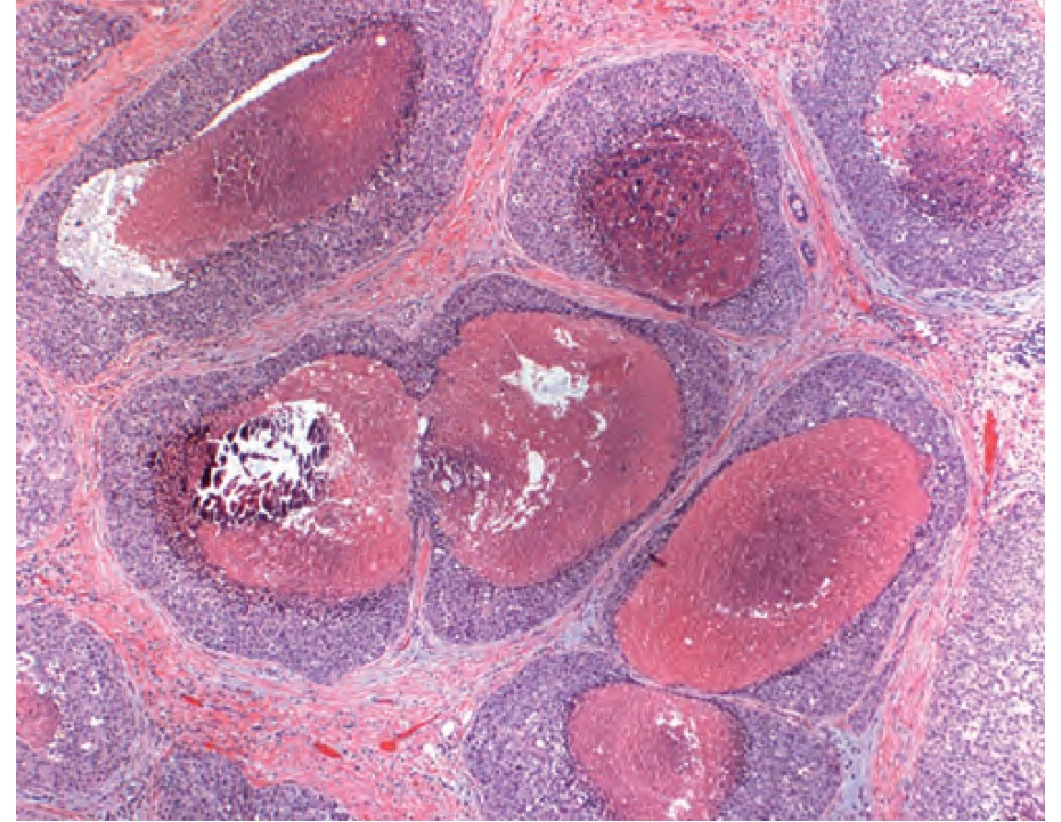
***Calcifications frequently are associated with DCIS.**

***Comedo type** (more aggressive) ;the tumor cells lined the dilated ducts are highly pleomorphic , high grade nuclei with extensive central necrosis.

- **The prognosis is excellent**, with greater than 97% long-term survival.
- **If untreated, DCIS progresses to invasive cancer** in roughly one-third of cases, usually in the same breast and quadrant as the earlier DCIS.



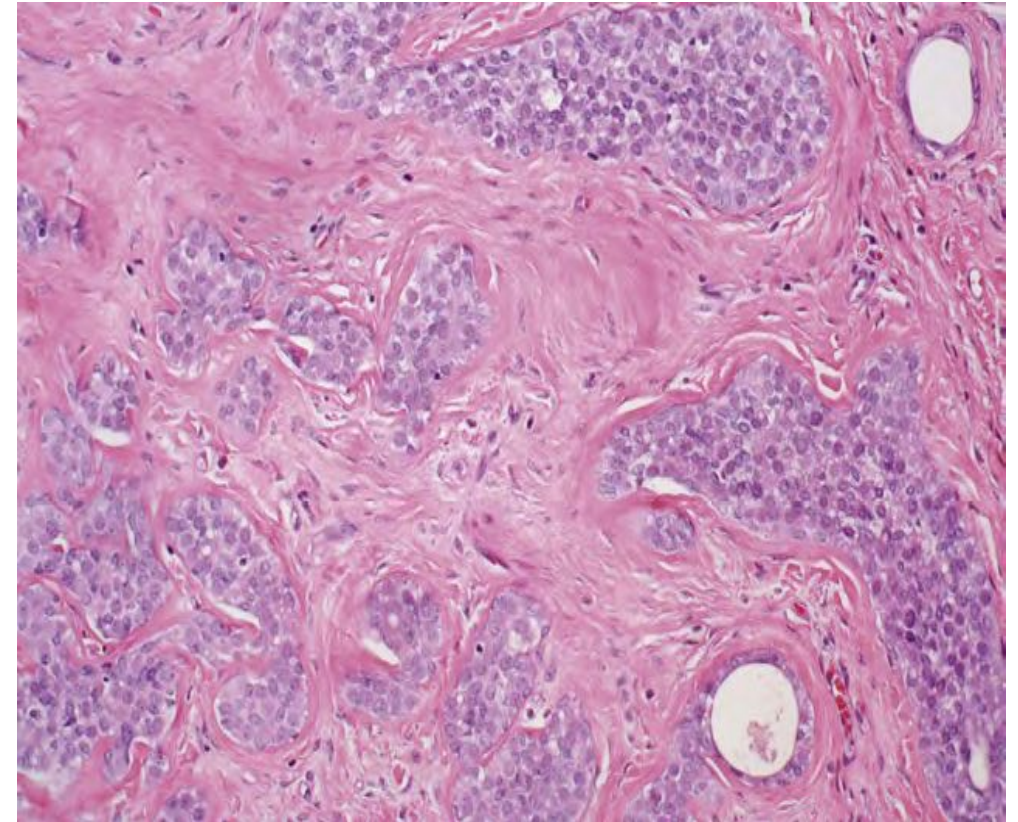
- ❑ **Cribriform DCIS.** Neoplastic cells with the round, regular (cookie cutter) spaces containing **calcifying secretory material**



- ❑ **The comedo pattern of DCIS.** Is characterized by the presence of rapidly proliferating, high grade malignant cells with prominent central necrosis in these ducts.

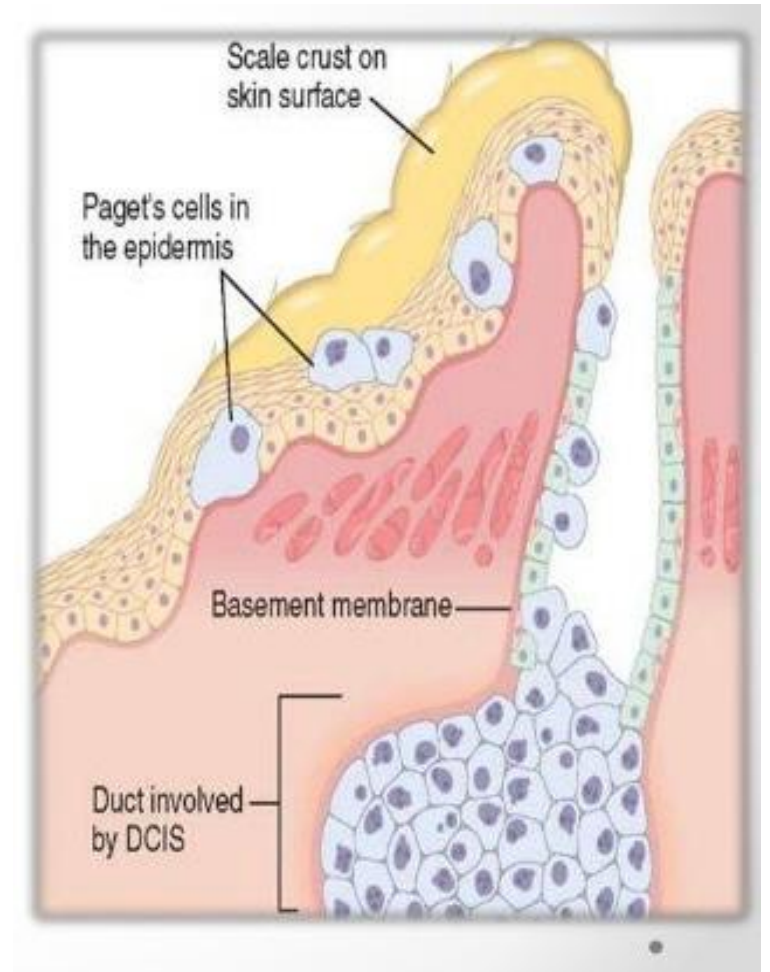
□ LCIS:

- The neoplastic cells expanding the lobules, but **not invading** the stroma.
- LCIS is unlikely to form a palpable mass or radiologic density, but it can be **multicentric** and is **bilateral** in 20% to 40% of cases.
- LCIS does **not usually form microcalcifications**.
- LCIS consists of a **proliferation of small, round, monomorphic epithelial cells within the terminal breast ducts and acini**.
- Although low grade, there is an increased risk for development of invasive carcinoma in the same or the opposite breast.



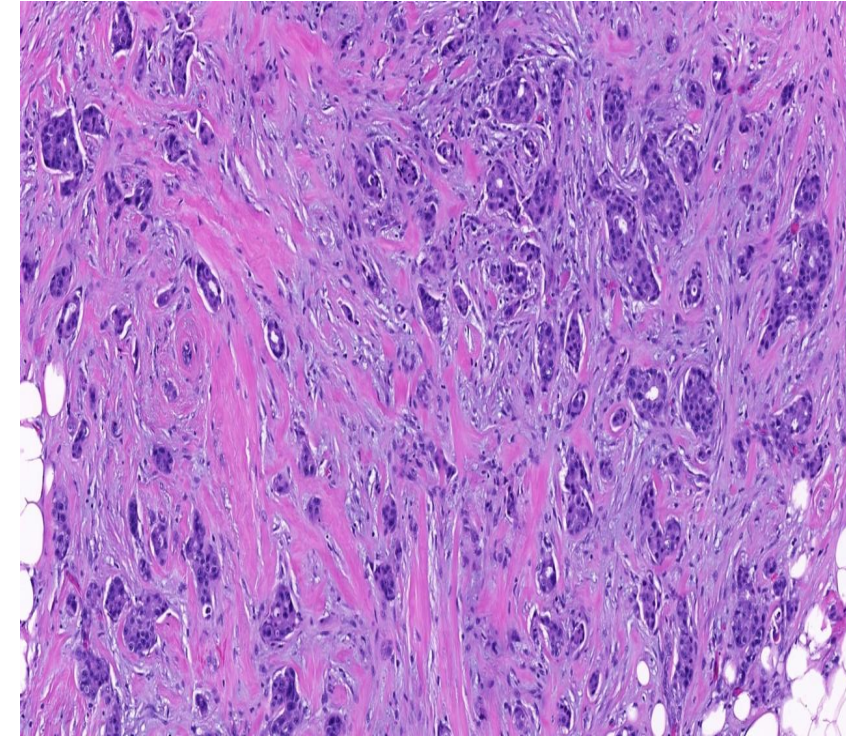
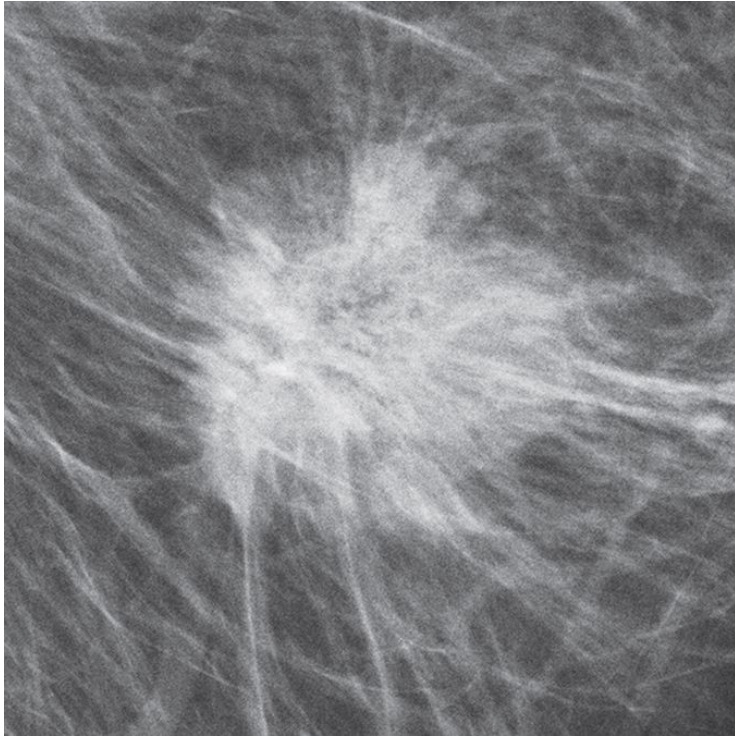
□ Paget's disease of the nipple

- It is a rare **manifestation** of breast cancer, that presents as a **unilateral erythematous eruption**, a **scale crust with pruritus**, the lesion may be **mistaken for eczema**.
- The malignant cells (Paget cells) extend from DCIS within the ductal system via the lactiferous duct into nipple skin **without crossing the basement membrane**.
- A palpable mass is present in 50% to 60% of women with Paget disease, and **almost all of these women have an underlying carcinoma (in situ or invasive)**.
- The prognosis is not worsened by the presence of Paget's disease.



❖ Invasive ductal carcinoma

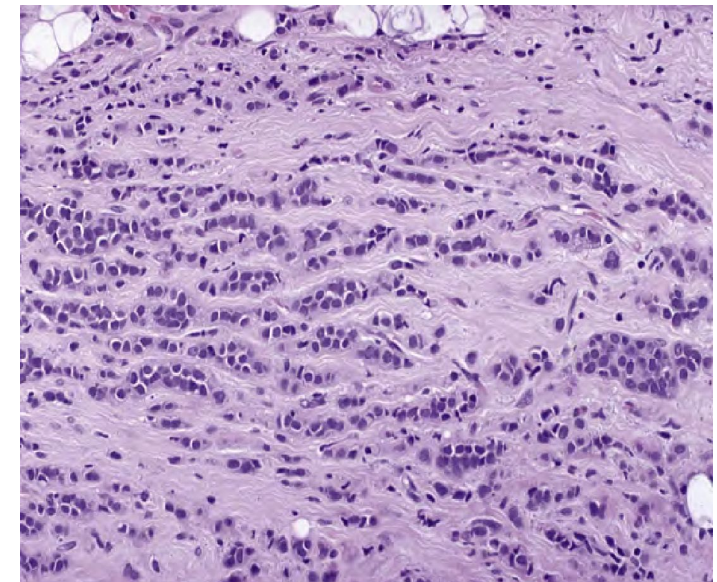
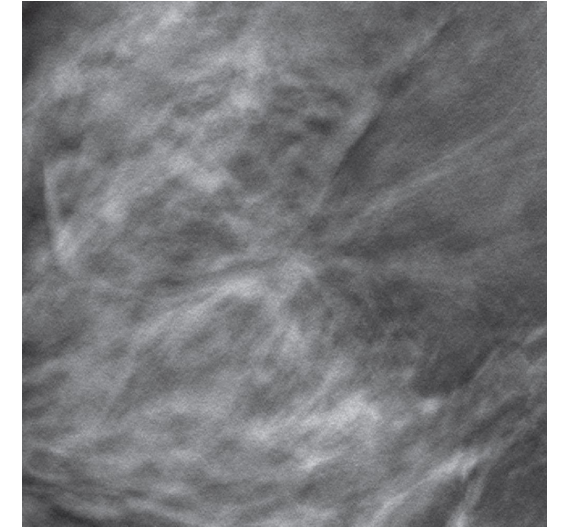
- Is a term used for all carcinomas that cannot be subclassified into one of the specialized types so called of no special type (NST).
- A majority (70%–80%) of cancers falls into this group.
- This type of cancer usually is associated with DCIS.
- **Microscopically;** consists of infiltrative small nests, strands and tubules of neoplastic cells with enlarged nuclei and prominent desmoplastic stroma.
- Most invasive ductal carcinomas produce a desmoplastic response, which replaces normal breast fat (resulting in a mammographic density) and eventually leads to the appearance of a hard, palpable irregular mass.
- About 50% to 65% of ductal carcinomas are ER positive, 20% are HER2 positive, and 15% are negative for both ER and HER2.



- ❑ **Invasive ductal carcinoma.** (A) **on mammogram**; carcinomas appear as dense masses with spicular margins resulting from invasion of adjacent radiolucent breast tissue. (B) **gross examination**; irregular, stellate, firm, palpable mass. (C) **Microscopically**; infiltrative small nests and tubules of tumor cells with enlarged nuclei and prominent desmoplastic stroma.

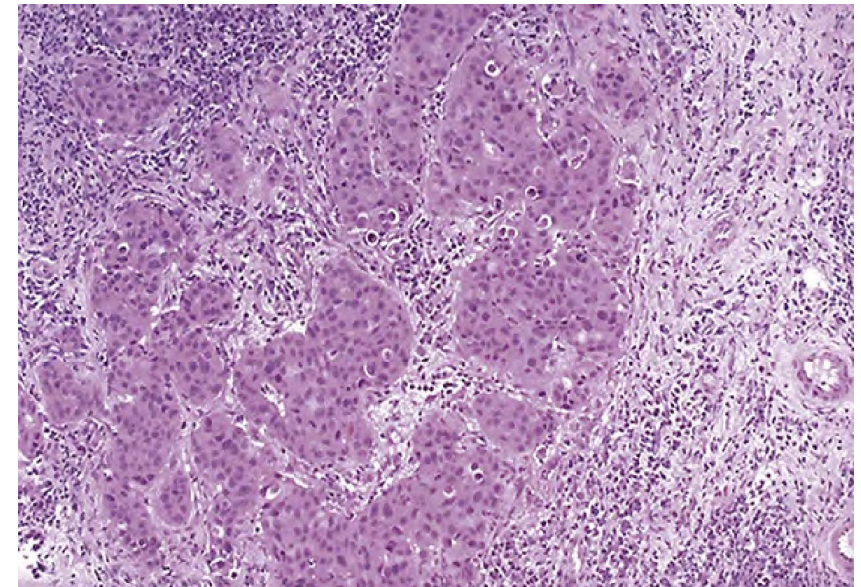
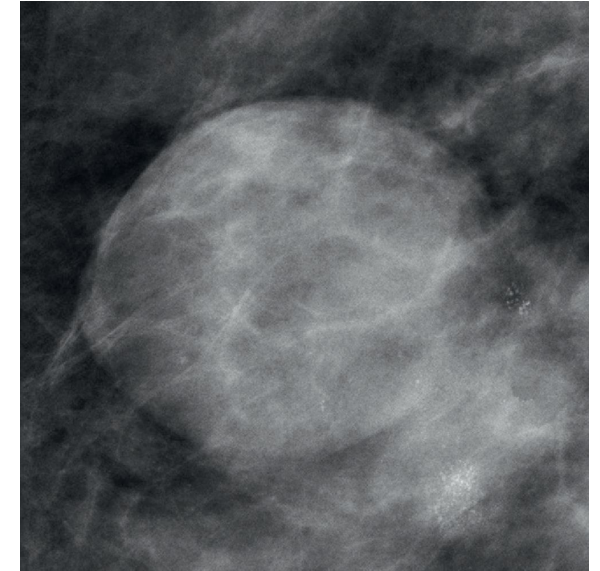
❖ Invasive lobular carcinoma

- Lobular carcinomas make up **10–15%** of breast cancers, often linked to **LCIS**.
- They are frequently **multicentric and bilateral (10–20%)**.
- While some form palpable masses, others **lack desmoplastic response** and are hard to detect via imaging.
- **On mammogram**; often appear as relatively subtle, irregular masses.
- **Microscopically**; composed of **noncohesive tumor cells that invade as linear cords “single-file” of cells and induce little stromal response**.
- Metastasis targets unusual sites: CSF, serosa, GI tract, ovaries, uterus, and bone marrow.
- Most express hormone receptors (ER, PR), but HER2 overexpression is rare.



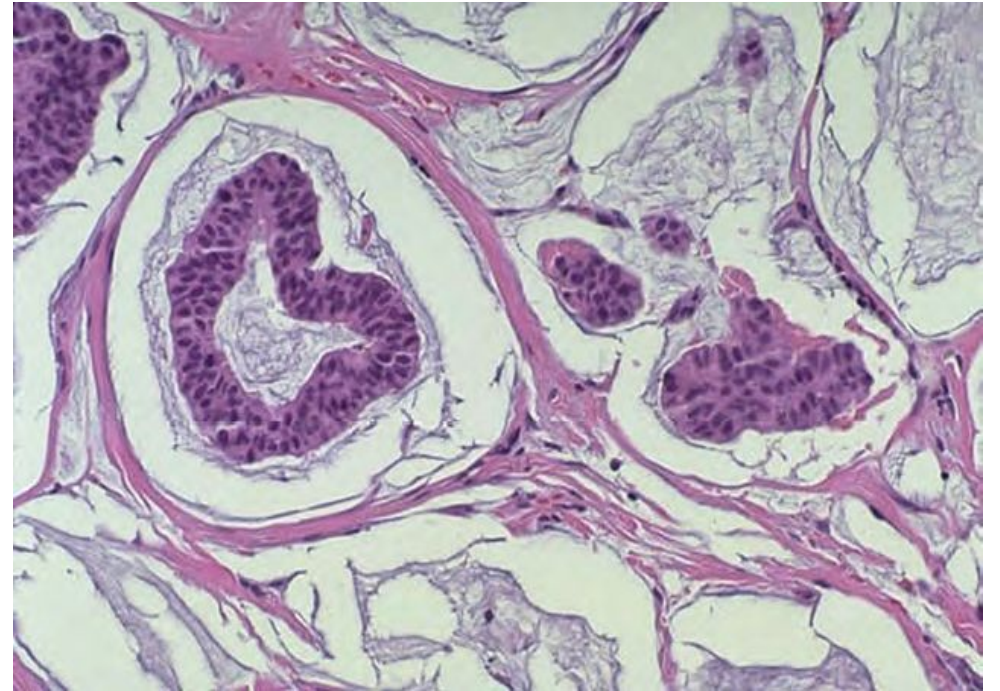
◆ Medullary carcinoma

- Are a special type of **triple-negative cancer** comprising about 5% of all breast cancers.
- **On mammogram;** well-circumscribed masses mimicking the appearance of a benign lesion.
- **Mic.:** consist of **sheets of large anaplastic cells associated with pronounced lymphocytic infiltrates composed predominantly of T cells**, The presence of lymphocytes is associated with a favorable prognosis, at least in part due to a better response to chemotherapy compared to poorly differentiated carcinomas without lymphoid infiltrates.



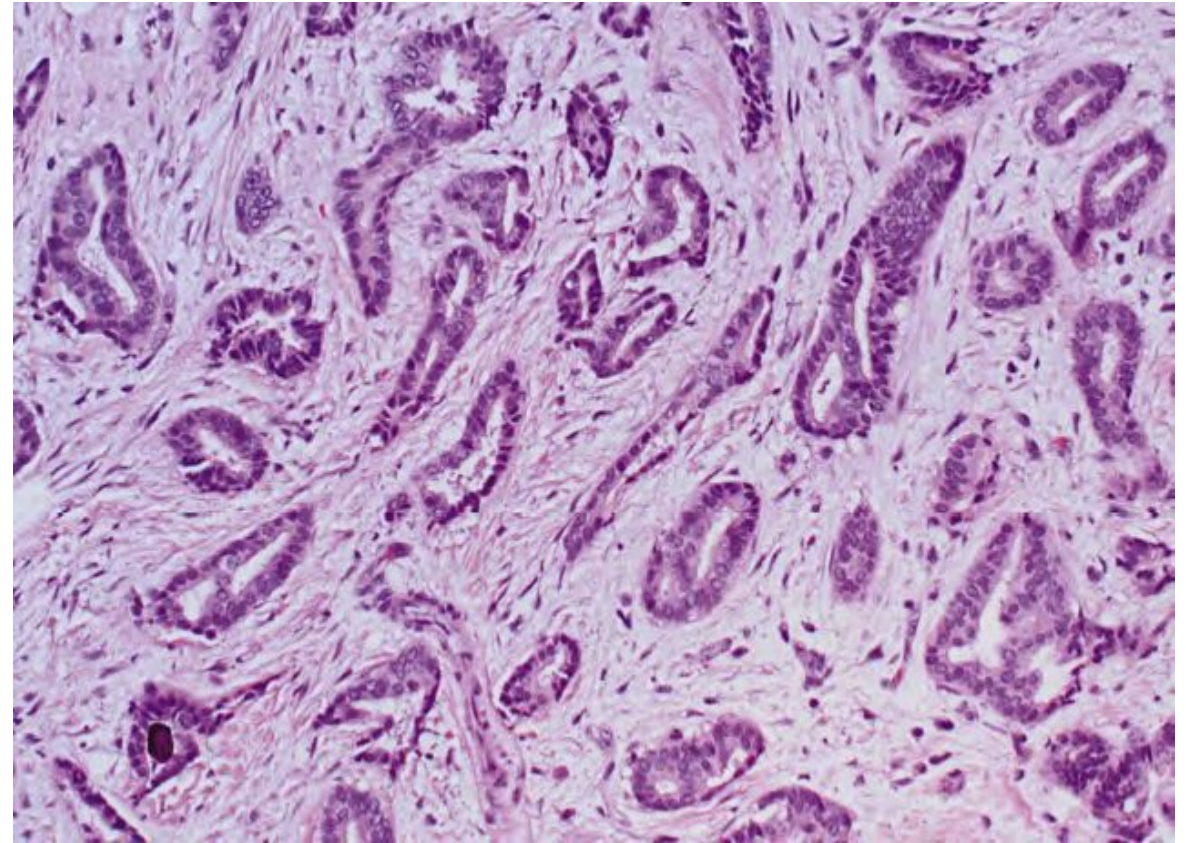
❖ Mucinous (Colloid) carcinoma

- Is a rare subtype.
- **Grossly;** the tumors are usually soft and gelatinous.
- **Mic.;** The tumor cells produce abundant quantities of extracellular mucin that dissects into the surrounding stroma.



❖ Tubular carcinoma

- Rarely presents as palpable masses but account for 10% of invasive carcinomas smaller than 1 cm found with mammographic screening.
- **Mic.;** Consists of well-formed tubules of neoplastic cells with low-grade nuclei.
- Lymph node metastases are rare, and prognosis is excellent.



◆ Inflammatory carcinoma

- Is defined clinically by an enlarged, swollen, erythematous breast, usually without a palpable mass.
- The underlying carcinoma is generally poorly differentiated and diffusely invades the breast parenchyma.
- The blockage of numerous dermal lymphatic spaces by malignant cells results in the clinical appearance. True inflammation is minimal or absent.
- Most of these tumors have distant metastases, and the prognosis is extremely poor.

Spread of breast cancer

- **Direct:** it invades the breast tissue and overlying skin with ulceration and nipple retraction, it may invade underlying muscle and chest wall.
- **Lymphatics:** Permeation of the local dermal lymphatics by tumor causing blockage of lymphatics and edema of the skin producing a **Peau d'orange skin appearance**.
 - Invasion of axillary L-nodes.
 - Invasion of internal mammary L-nodes.
 - Invasion of supraclavicular L-nodes .
- **Blood:** spread to lung, liver, long bones, and brain.

Prognosis

1. **Histologic grade:** All types of invasive breast carcinoma graded based on nuclear pleomorphism, tubule formation, and mitotic into **grade I** (well differentiated), **grade II** (moderately differentiated), and **grade III** (poorly differentiated) types. **Grade I has the better prognosis.**
2. **The staging of the breast carcinoma (TNM):**
 - ***T:** size of the primary Tumor, the smaller size the better the prognosis.
 - ***N:** extent of lymph Node involvement: Without L-node involvement the 5 year survival rate is close to 90%.
 - ***M:** Metastasis, Cancer with Hematogenous spread rarely curable.
3. **Histologic type:** Special types (tubular, medullary, mucinous) have better prognosis than NST; A major exception is inflammatory carcinoma, which has a poor prognosis.
4. **ER/PR status:** Positive = slightly better prognosis and predicts response to tamoxifen (80% if both positive).
5. **HER2/neu overexpression:** Poor prognosis but predicts response to Herceptin.

The Male Breast

❖ Gynecomastia (enlargement of the male breast):

*It occurs as a result of an imbalance between estrogens, which stimulate breast tissue, and androgens, which counteract these effects.

*It may appear during puberty or at any time during adult life when there is cause for hyperestrinism (e.g. liver cirrhosis, drugs (such as heroin and anabolic steroids), alcohol or in association estrogen secreting tumors) .

Microscopically: an increase in the stroma (dense collagenous connective tissue) with duct enlargement and sometimes epithelial hyperplasia, a Lobule formation is almost never observed.

*Gynecomastia may be **associated with a small increased risk of breast cancer.**

❖ Male Breast Cancer

*The incidence is < 1% of that in women.

*The typical age at diagnosis is between **60 and 70 years**

*The pathology of male breast cancer is remarkably similar to that of cancers seen in women. However, ER positivity is more common.



JOIN THE **FIGHT**

TO END BREAST CANCER