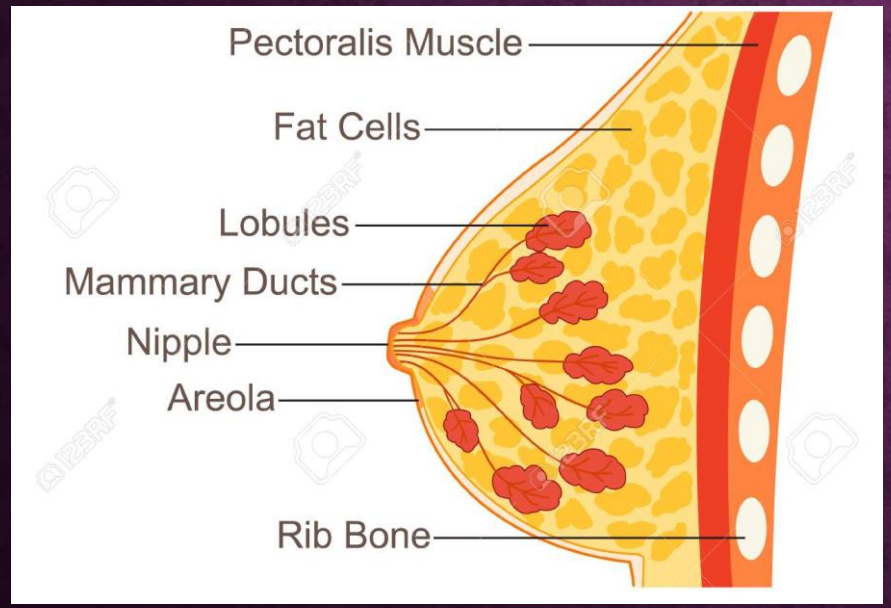
UROGENITAL SYSTEM-III.
BREAST

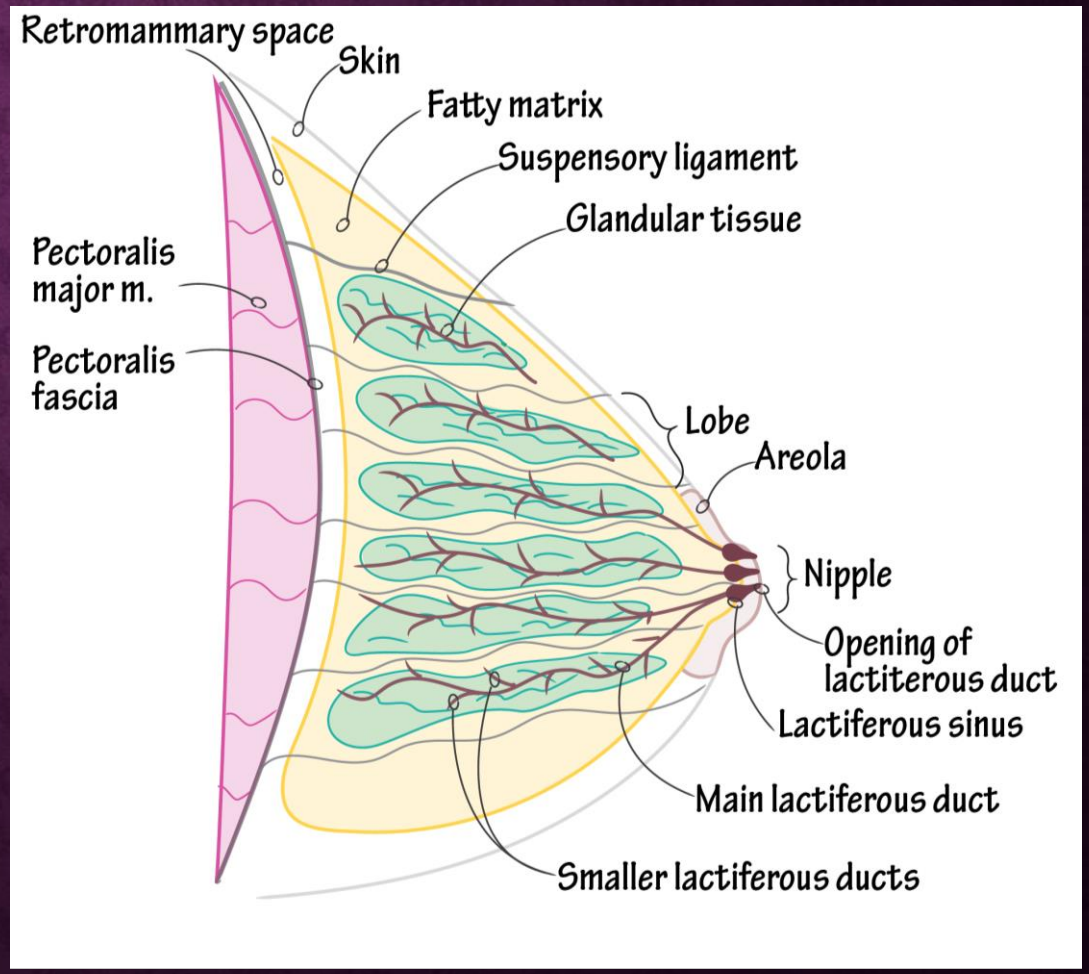
Dr.Eman Kreishan, M.D.

14/5/2023.

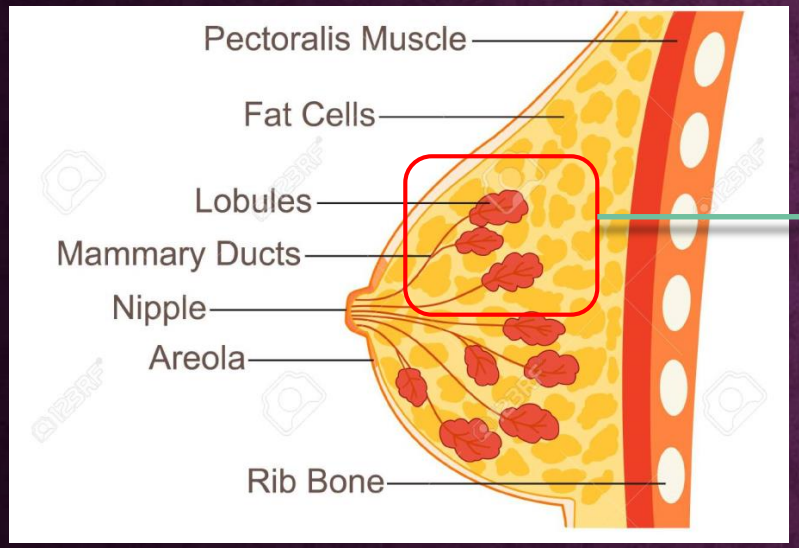
- Overview(anatomy, histology).
- Clinical Presentations of Breast Disease.
- Stromal Neoplasms.
- Benign Epithelial Lesions.
- Carcinoma.

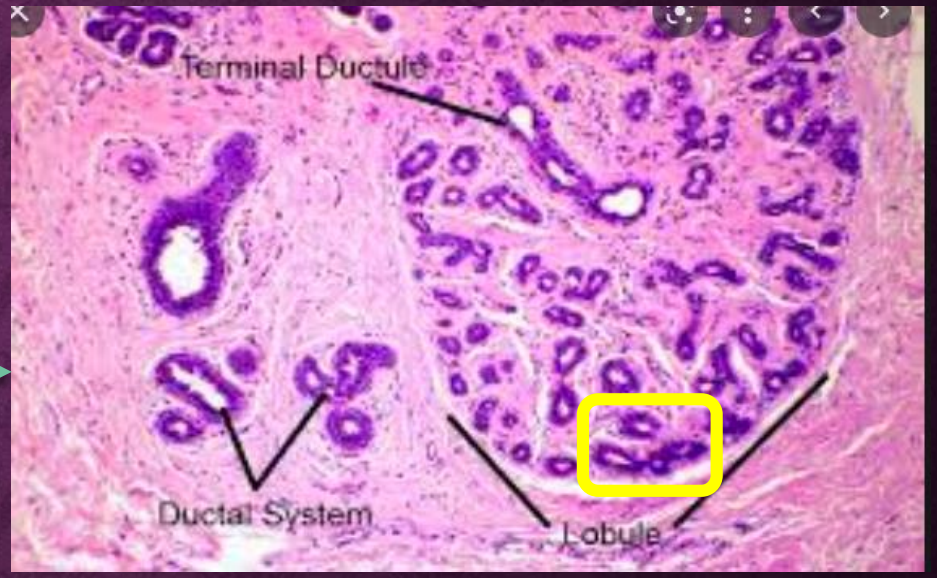
OVERVIEW …ANATOMY.

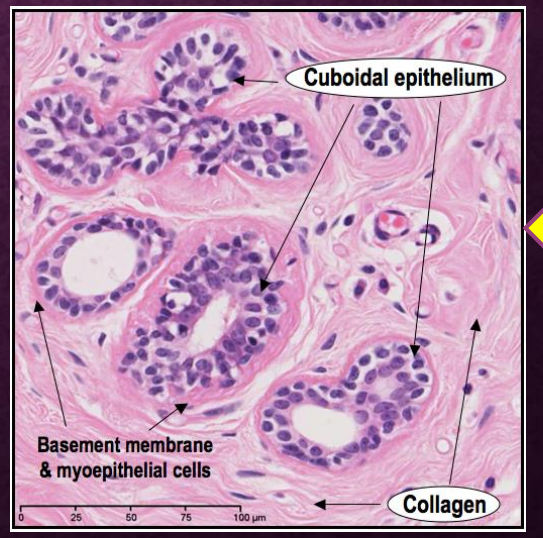


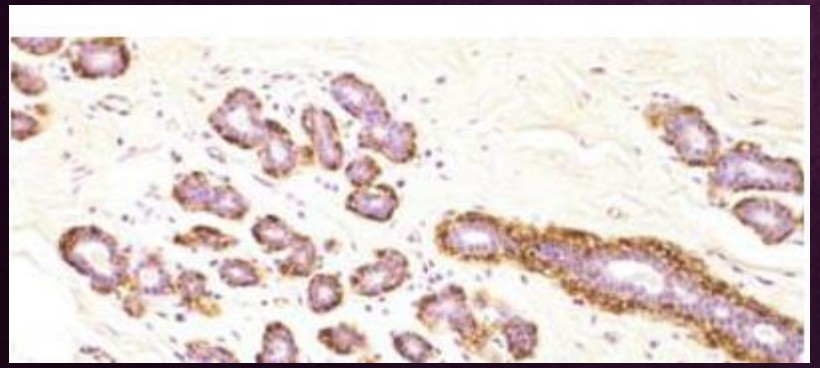


OVERVIEW …HISTOLOGY



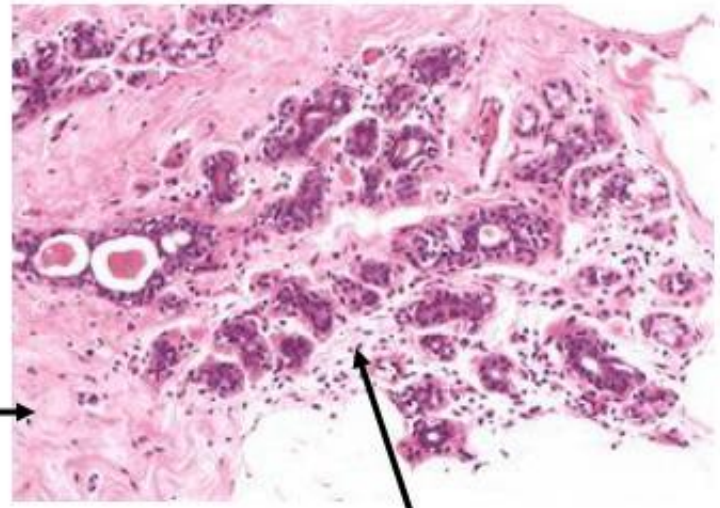






Higher magnification of a lobule

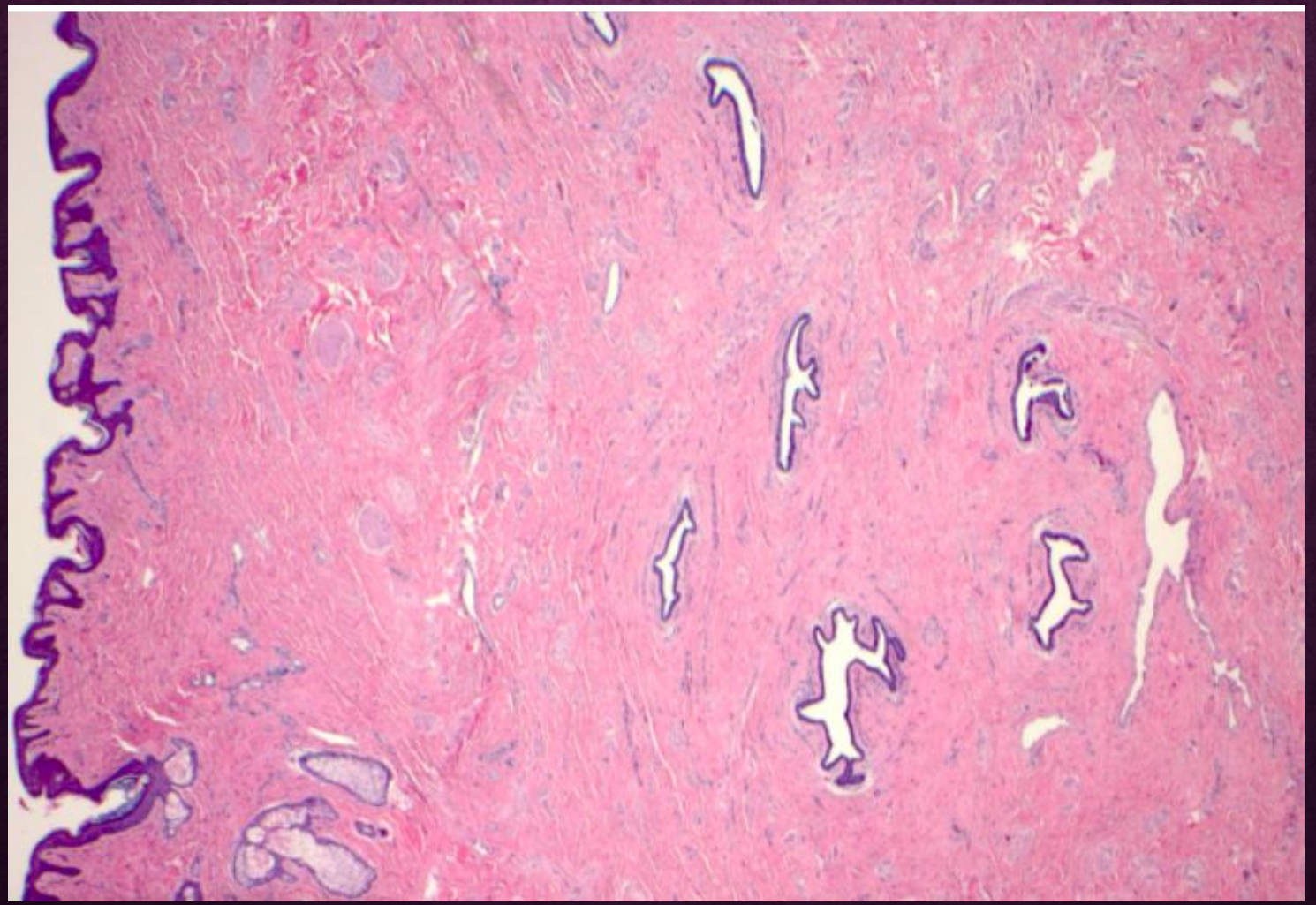
BM surrounds each alveolus



Interlobular
Dense CT

Intralobular
Loose CT

Nipple..histology

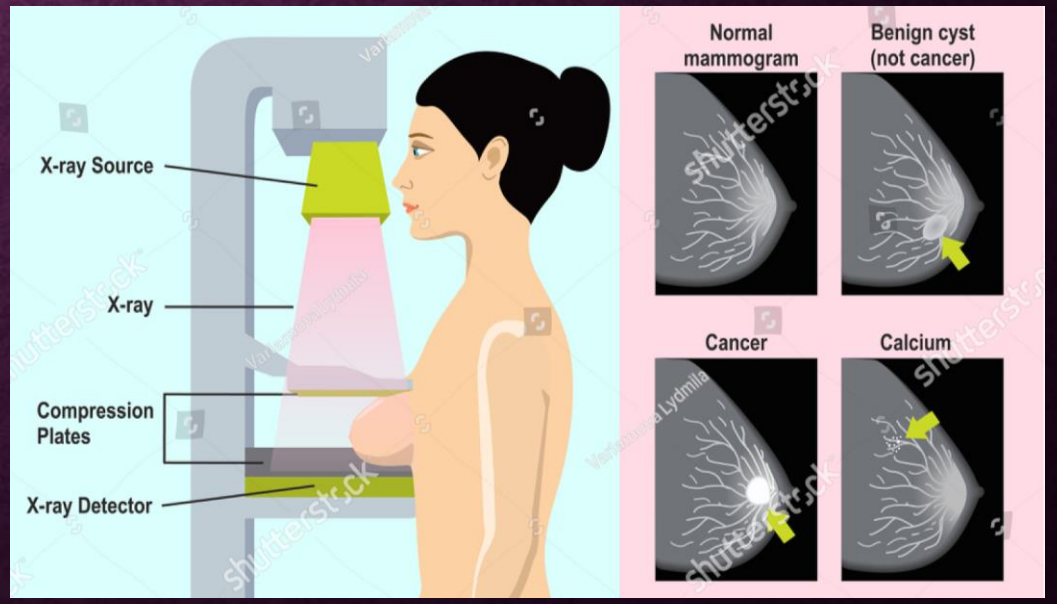


Common clinical presentation of breast disease

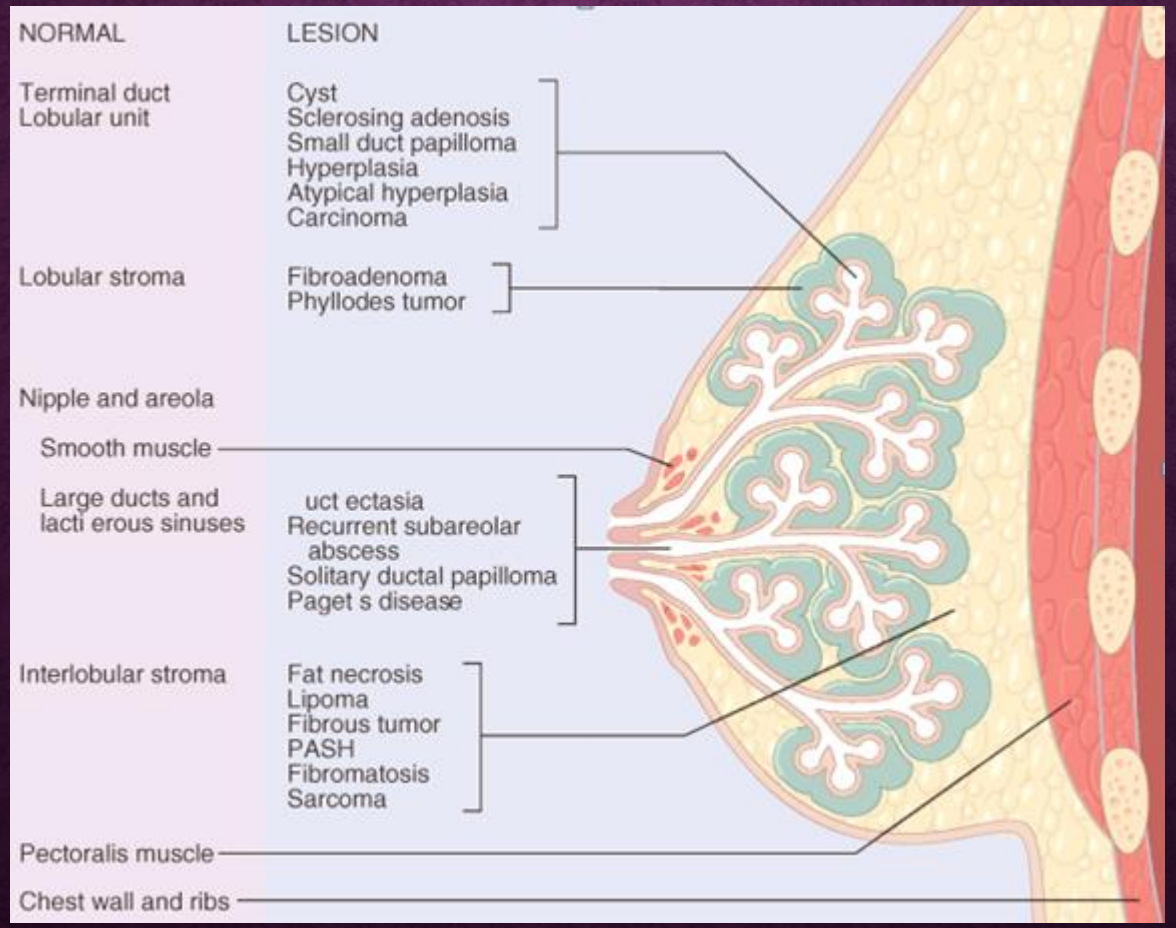
- Abnormal mammogram
- Generalized lumpiness and discomfort
- Palpable Mass
- Skin changes
  - Dimpling
  - Redness/induration
  - Peau d'orange
- Nipple discharge
  - Character – serous, bloody, milky
  - Onset – spontaneous vs expressed
  - Location – unilateral vs bilateral, single vs multiple ducts
- Axillary mass

ABNORMAL MAMMOGRAM

- Aimed to detect early, **nonpalpable asymptomatic breast** carcinomas before metastatic spread has occurred.
- average size of invasive carcinomas detected by mammography is about 1 cm.



Breast lesion can be classified according to the anatomical location



I. STROMAL NEOPLASMS

- The two types of stroma in the breast, intralobular & interlobular, give rise to different types of neoplasms.

❖Intralobular (specialized)stroma:

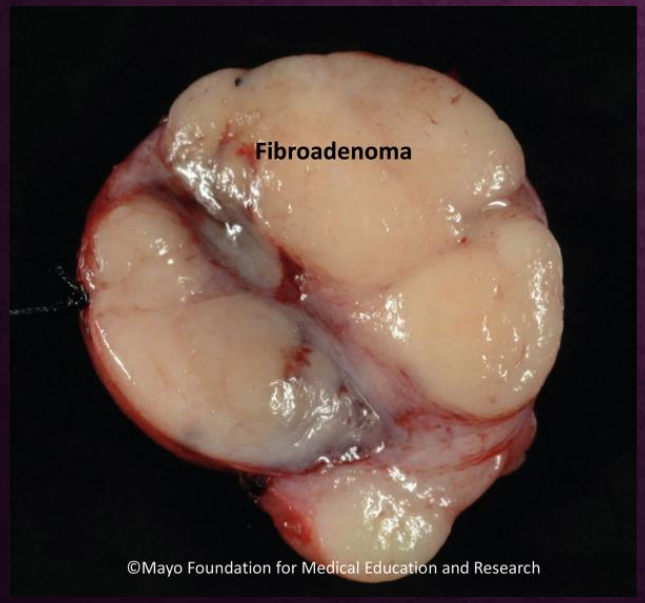
- (1) benign fibroadenomas
  (2) phyllodes tumors

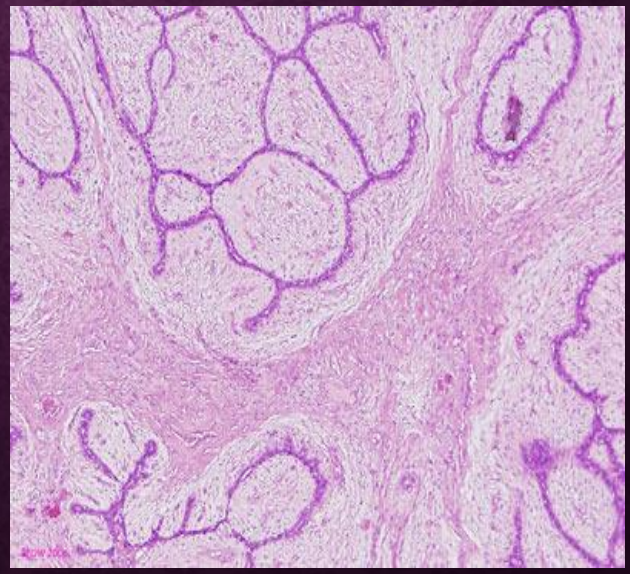
❖Interlobular stroma:

- Same connective tissue tumors in other body sites (hemangiomas & angiosarcomas)

A. FIBROADENOMAS

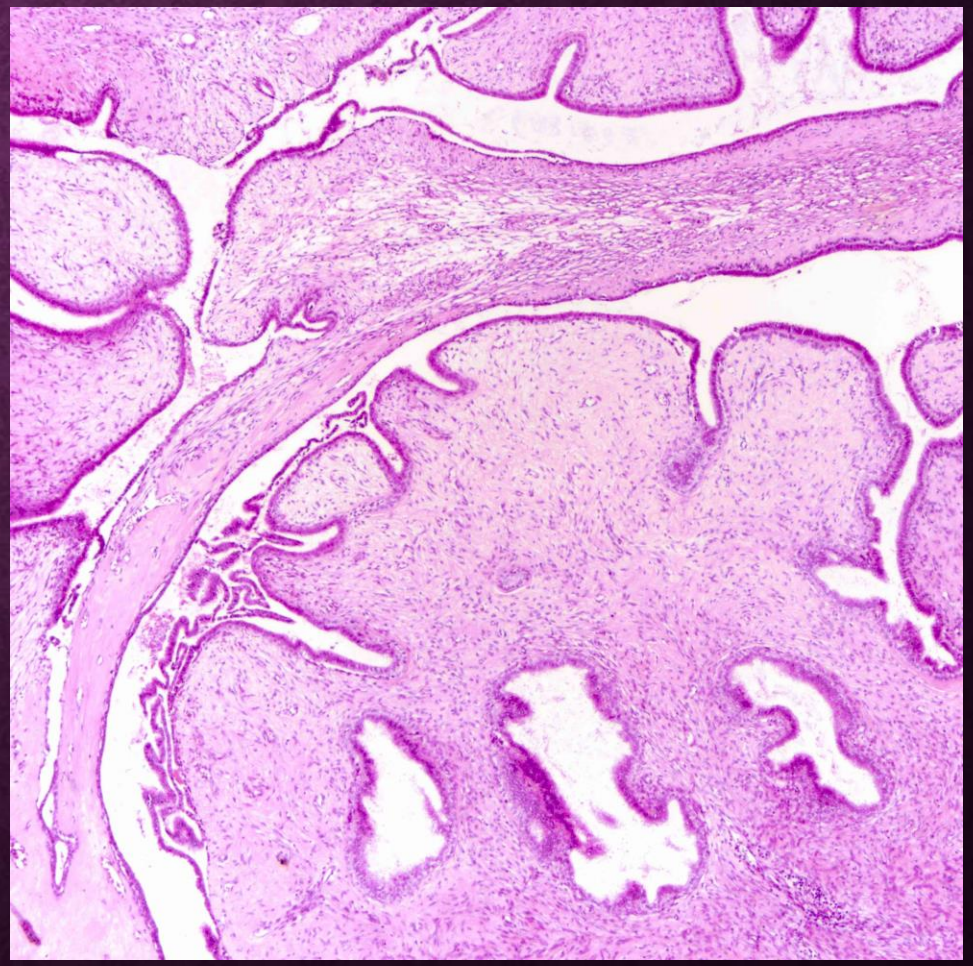
- The most common benign tumor of the breast.
- Affecting reproductive age.
- Estrogen sensitive.
- **Gross**: well-circumscribed & freely mobile (breast mouse).
- **Microscopic**: Low cellularity, intralobular fibroblasts proliferate →push & distort epithelial cells (elongated slitlike structures instead of round acini) & rare mitoses.





B. PHYLLODES TUMORS

- Less common, older age group.
- Microscopic: Highly cellular -stromal cells outgrow epithelial cells- resulting in bulbous nodules stromal cells covered by epithelium (leaflike morphology (Greek: phyllodes)
- Mitoses can be seen, & Infiltrative borders , Tends to recur locally.
- High grade forms : sarcoma like & ass with metastasis 2%.

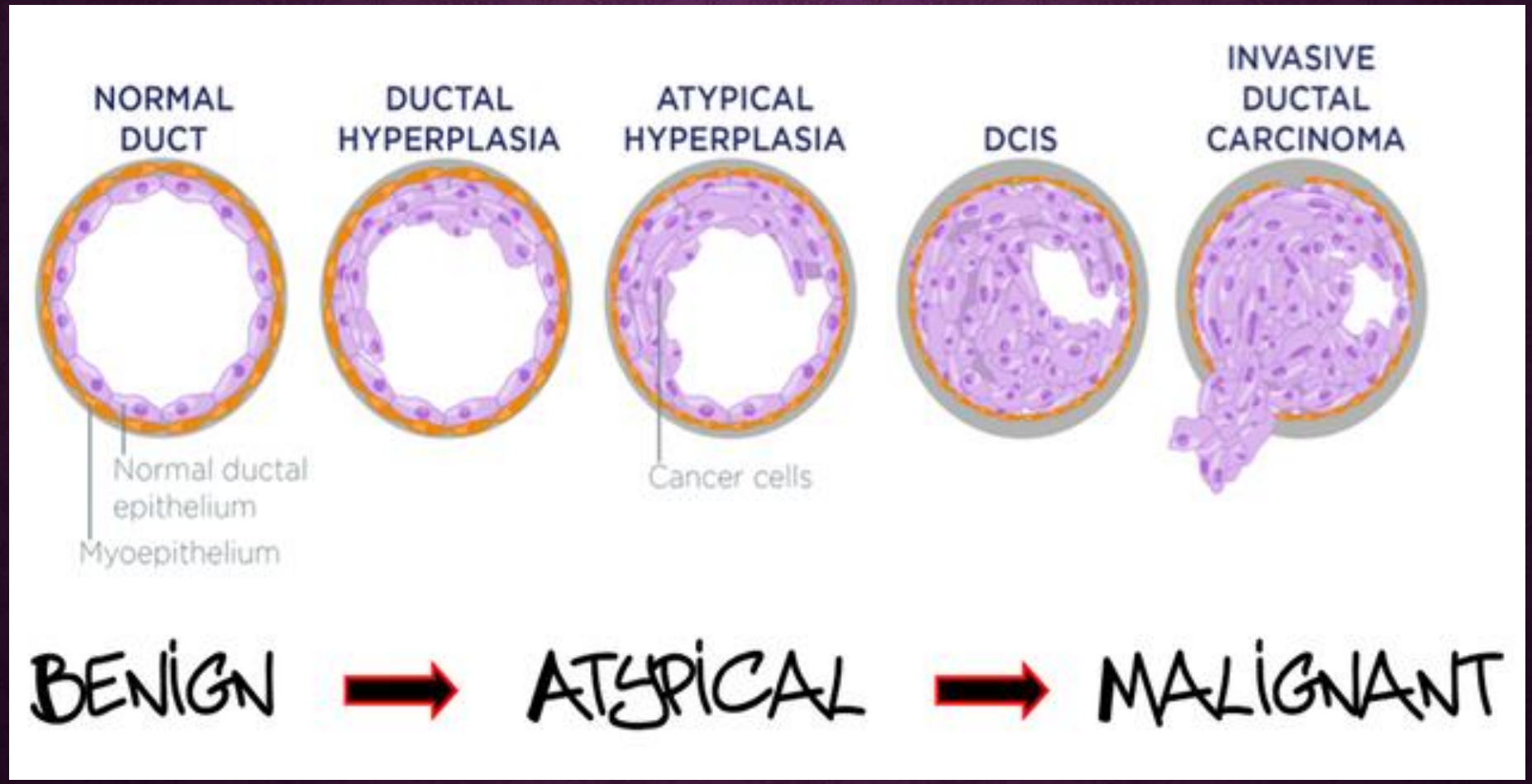


II. BENIGN EPITHELIAL LESIONS

- Divided into three groups each associated with a different degree of breast cancer risk :

1. **Nonproliferative disease**: no ↑ in breast cancer risk.
2. **Proliferative disease without atypia**: polyclonal hyperplasia with minimal ↑ risk of breast cancer.
3. **Proliferative disease with atypia**: monoclonal precancers, a modest ↑ in breast cancer risk in both breasts.

Pathologic Lesion	Relative Risk (Absolute Lifetime Risk)*
Nonproliferative Breast Changes (Fibrocystic changes)	1.0 (3%)
Proliferative Disease Without Atypia	1.5 to 2.0 (5% to 7%)
Proliferative Disease With Atypia	4.0 to 5.0 (13% to 17%)
Carcinoma *in situ*	8.0 to 10.0 (25% to 30%)


NORMAL DUCT
DUCTAL HYPERPLASIA
ATYPICAL HYPERPLASIA
DCIS
INVASIVE DUCTAL CARCINOMA
Normal ductal epithelium
Myoepithelium
Cancer cells
BENIGN
ATYPICAL
MALIGNANT

A. NONPROLIFERATIVE DISEASE - FIBROCYSTIC CHANGES

- Nonproliferative →contain single layers of epithelial cells.
- Presentation: breast lumpiness (palpable nodularity.)

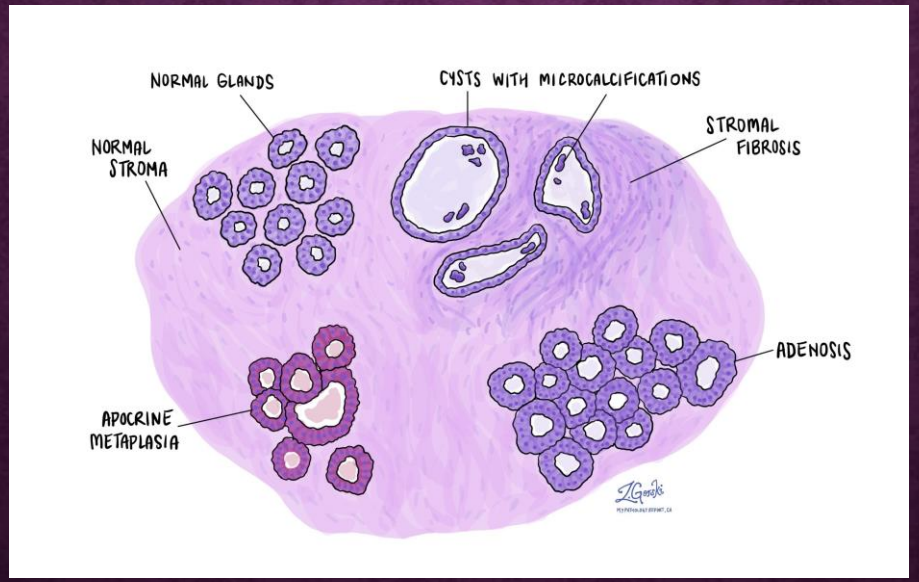
- characterized by :

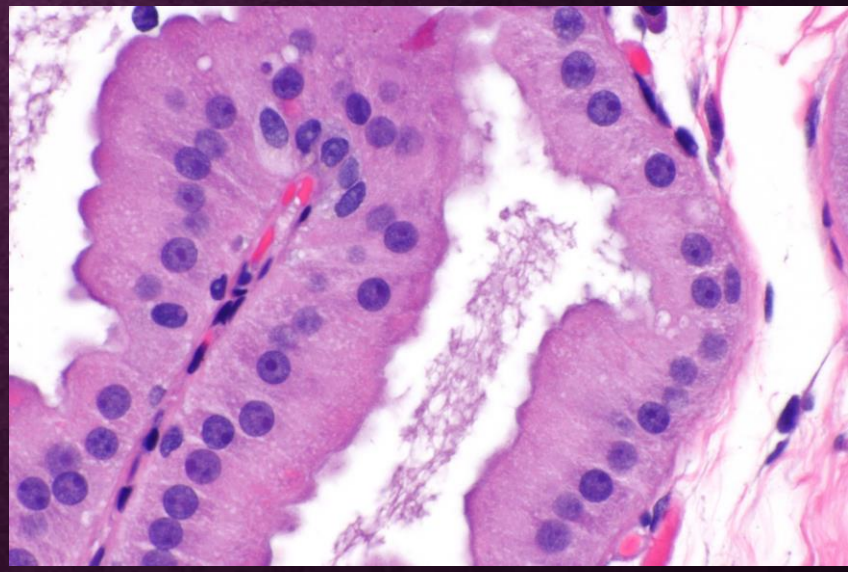
❖Adenosis.

❖fibrosis .

❖cyst formation.

❖Apocrine mataplasia.





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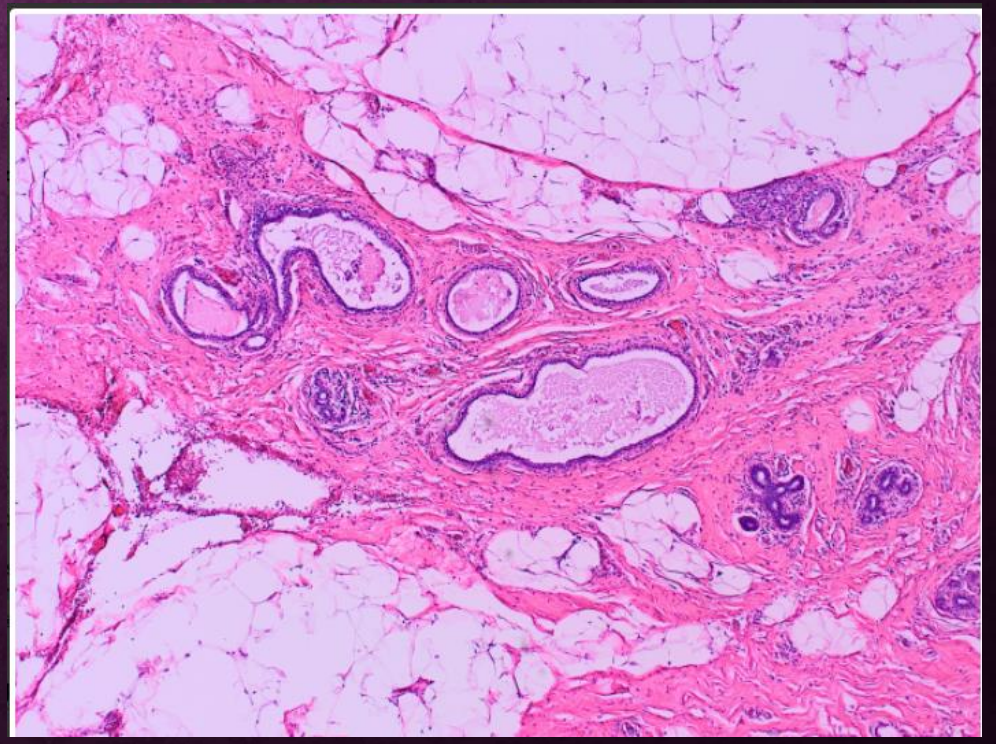
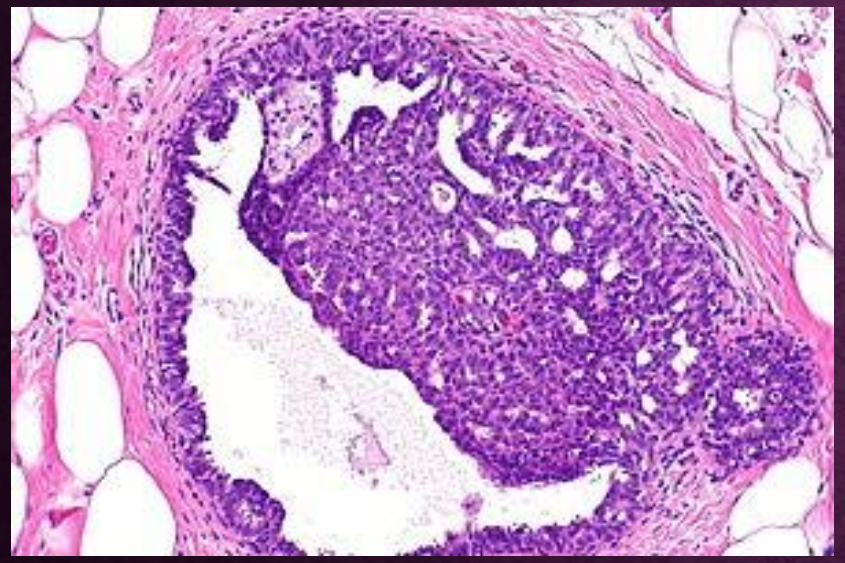
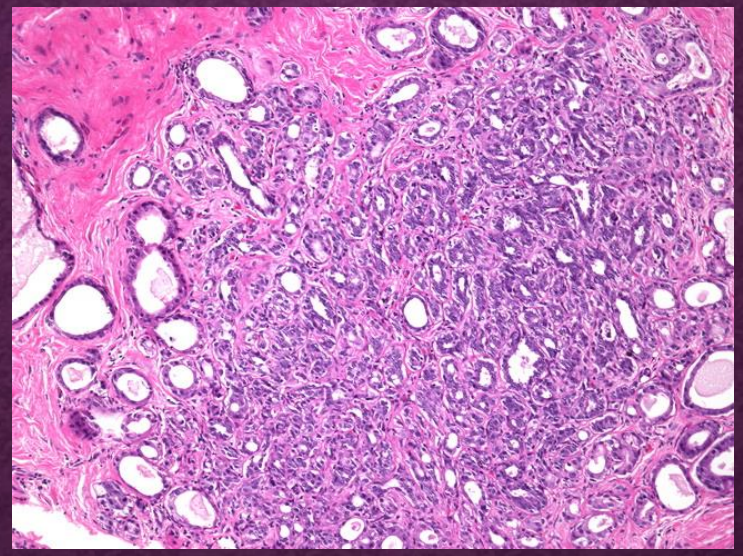


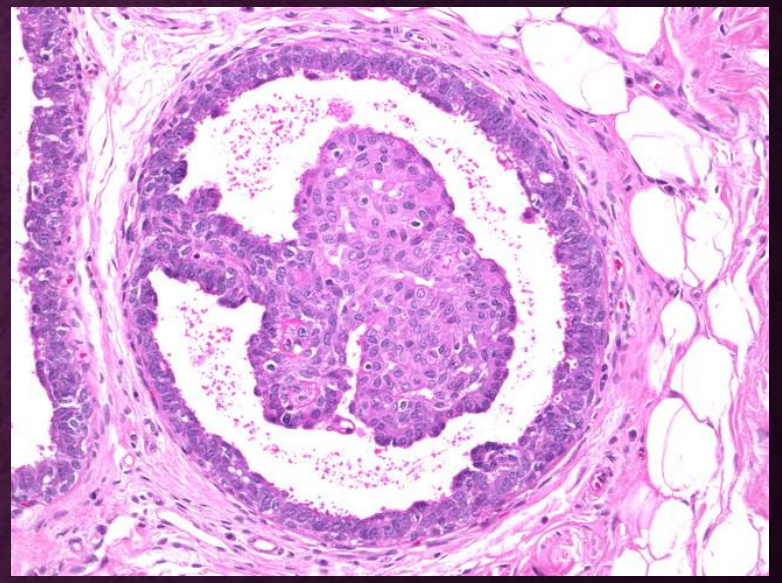
B. PROLIFERATIVE DISEASE WITHOUT ATYPIA

1. Epithelial hyperplasia.
2. Sclerosing adenosis
3. Papilloma.

B. Proliferative disease without atypia



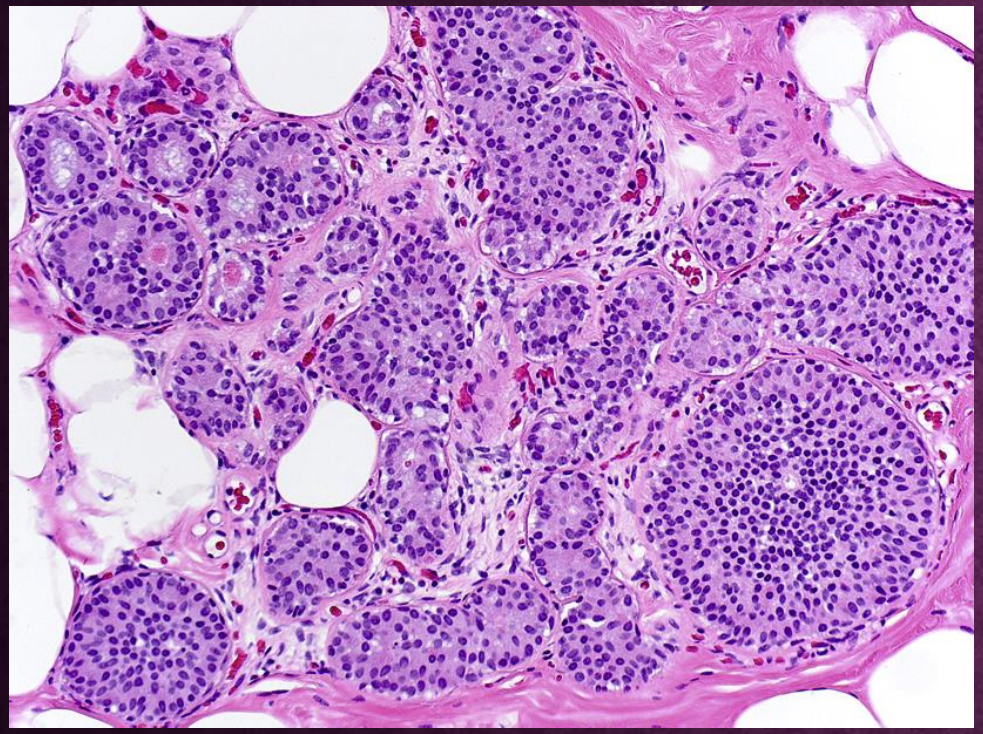




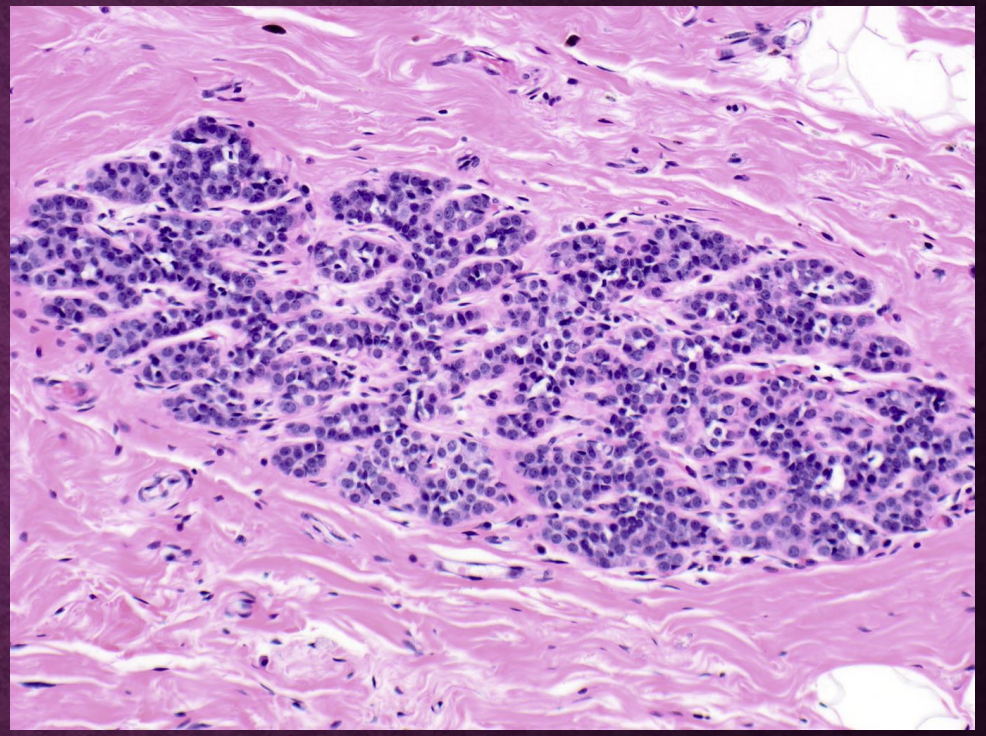
C. PROLIFERATIVE DISEASE WITH ATYPIA

1. Atypical lobular hyperplasia (ALH) resembles lobular carcinoma in situ (LCIS).
2. Atypical ductal hyperplasia (ADH) resembles ductal carcinoma in situ (DCIS)

- Clonal proliferations having some, but not all, histologic features that are required for the diagnosis of carcinoma in situ (LCIS or DCIS)



ADH

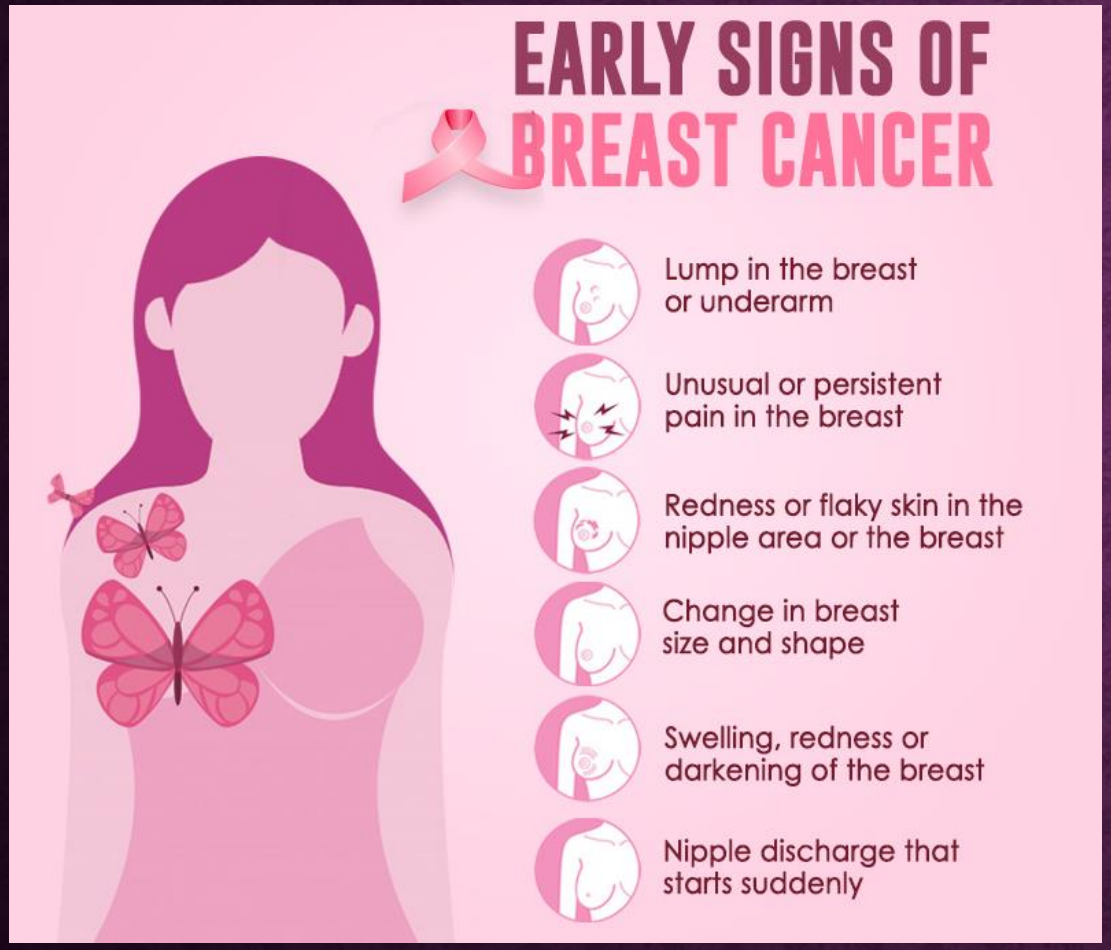


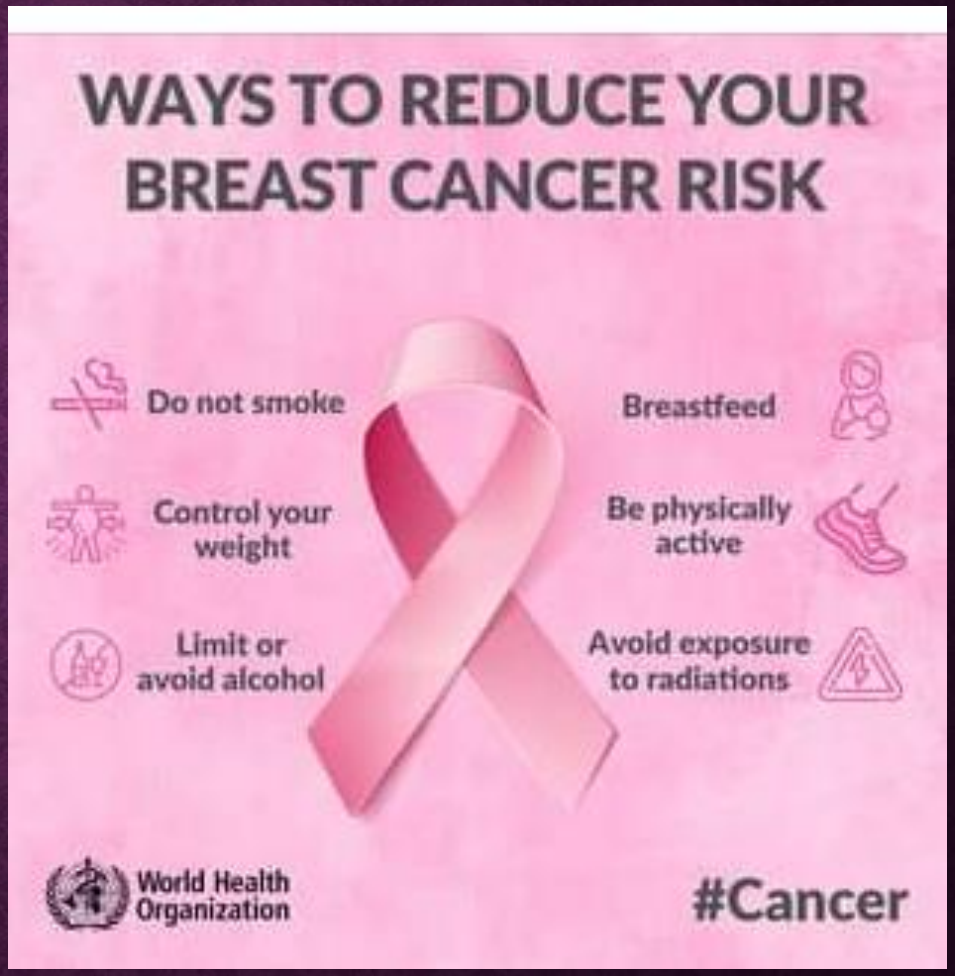
ALH

BREAST CARCINOMA

- The most common malignancy of women globally. (excluding nonmelanoma skin cancer)
- 2nd most common cause of cancer deaths in women. (2nd to lung cancer)
- Worldwide incidence and mortality is increasing at an alarming rate.

Risk factors



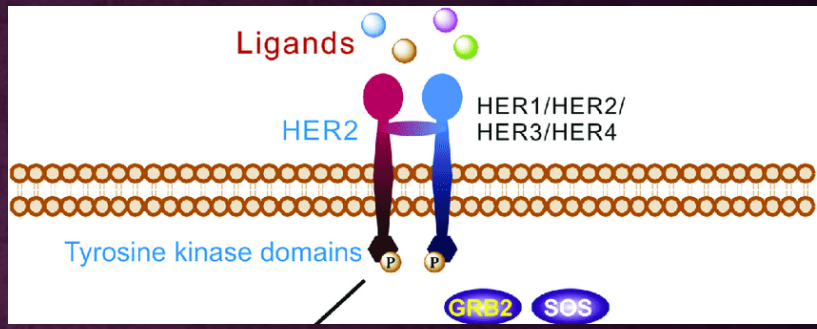


The most common location of tumors in breast is upper outer quadrant (50%), followed by the central portion (20%).

PATHOGENESIS/GENETICS

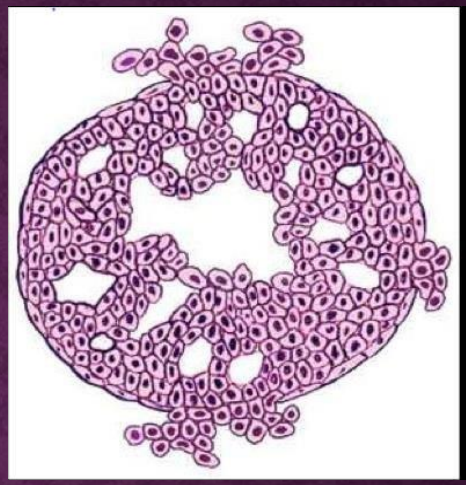
- Some Familial cases are ass with mutations of :
- BRCA1 & BRCA2 tumor suppressor genes (susceptibility to breast Ca. & ovarian serous Ca).
- familial germiline mutations; TP53 & PTEN.
- The pathways in which familial breast cancer genes function also are often disturbed in sporadic breast cancers.

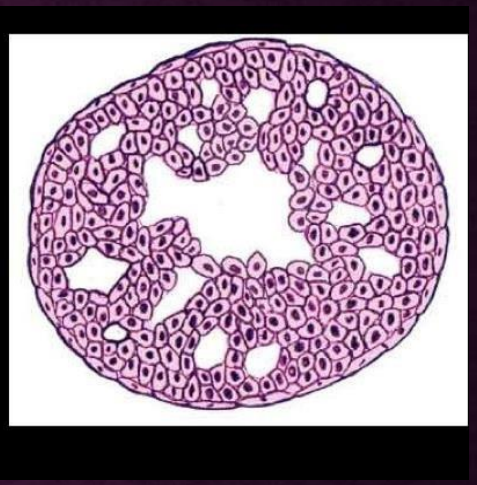
PATHOGENESIS/HER2 GENE



- **A common clinically important driver mutation in breast Ca is the amplification of the HER2 gene.**
- HER2 is a receptor tyrosine kinase that promotes cell proliferation & opposes apoptosis.
- Cancers overexpress HER2 are distinct & highly proliferative.
- **Used** to have poor prognosis → the availability of HER2 targeting therapeutic agents → markedly improved prognosis in patients w HER2-amplified tumor

MORPHOLOGY





- the main forms of breast carcinoma are as follows:(depend on B.M status):
- **Noninvasive**

1. Ductal carcinoma in situ (DCIS)
2. Lobular carcinoma in situ (LCIS)

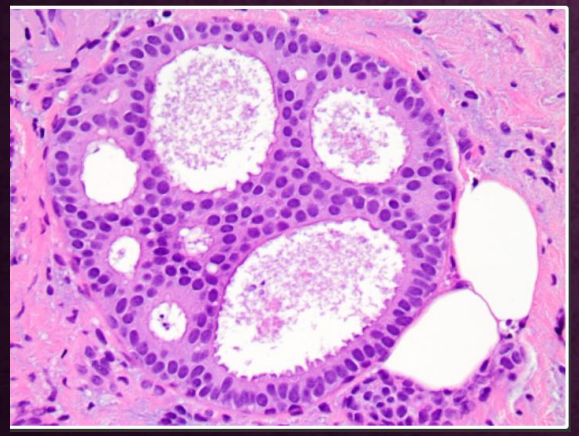
- **Invasive**

1. Invasive mammary carcinoma , NOS(70-80%).
2. Invasive carcinoma of special type (lobular, medullary, secretory, mucinous)

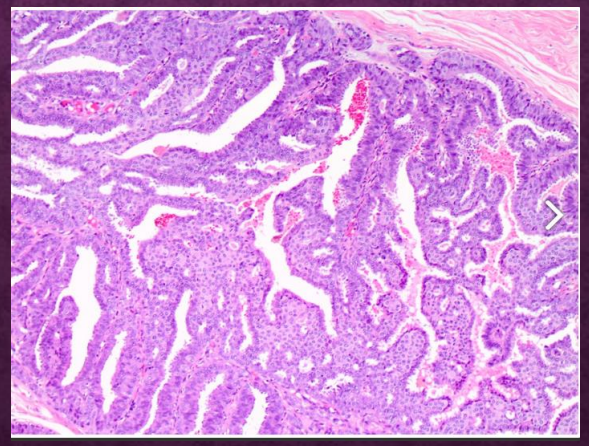
NONINVASIVE (IN SITU) CARCINOMA

- Malignant clonal proliferation of epithelial cells within the lobules & ducts.
- Both types of CIS arise from cells in the terminal duct
- Both “respect” the basement membrane & do not invade into stroma or lymphovascular channels.

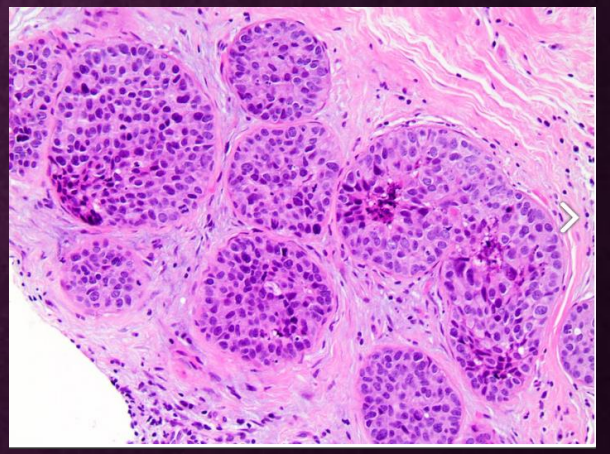
Ductal carcinoma in situ (DCIS) is a neoplastic proliferation of mammary ductal epithelial cells confined to the ductal-lobular system without evidence of invasion through the basement membrane into the surrounding stroma



CRIBRIFORM

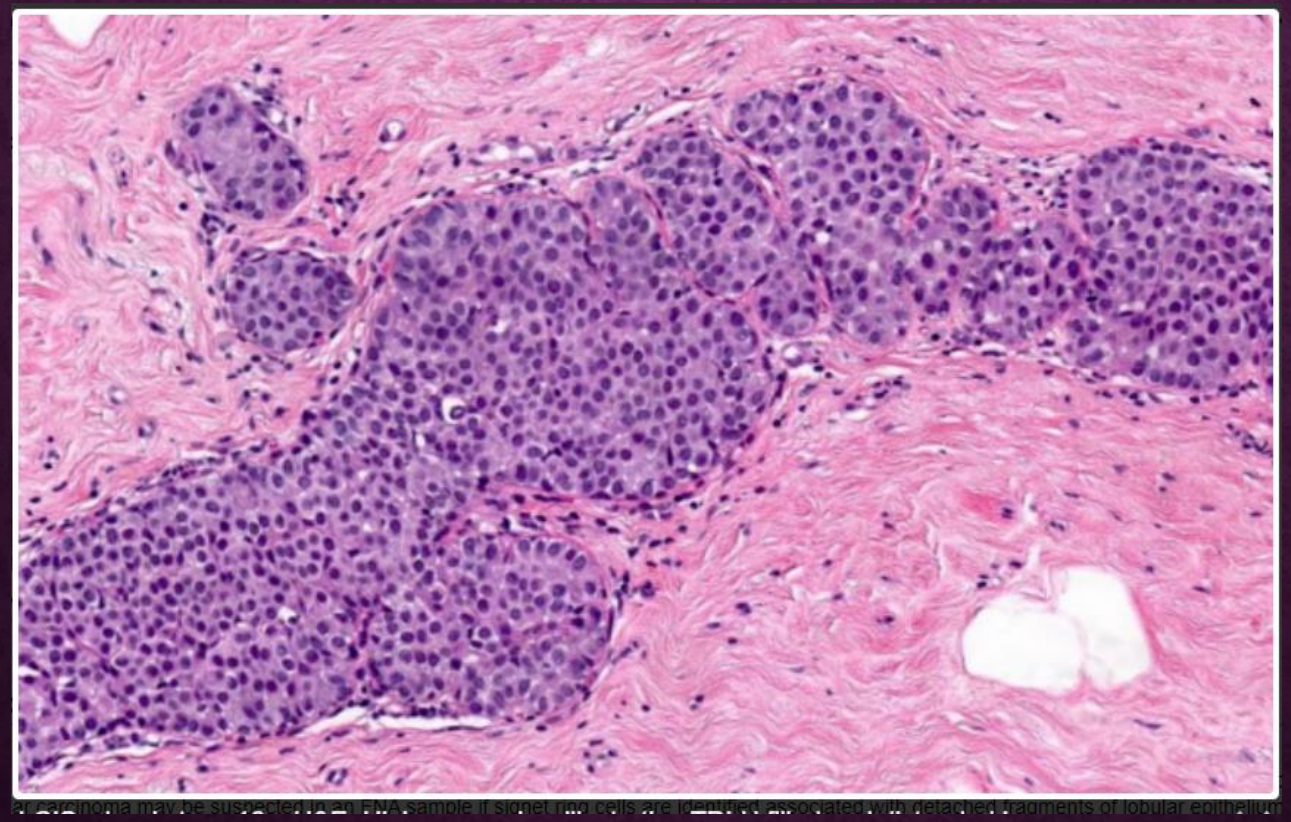


PAPILLARY



SOLID

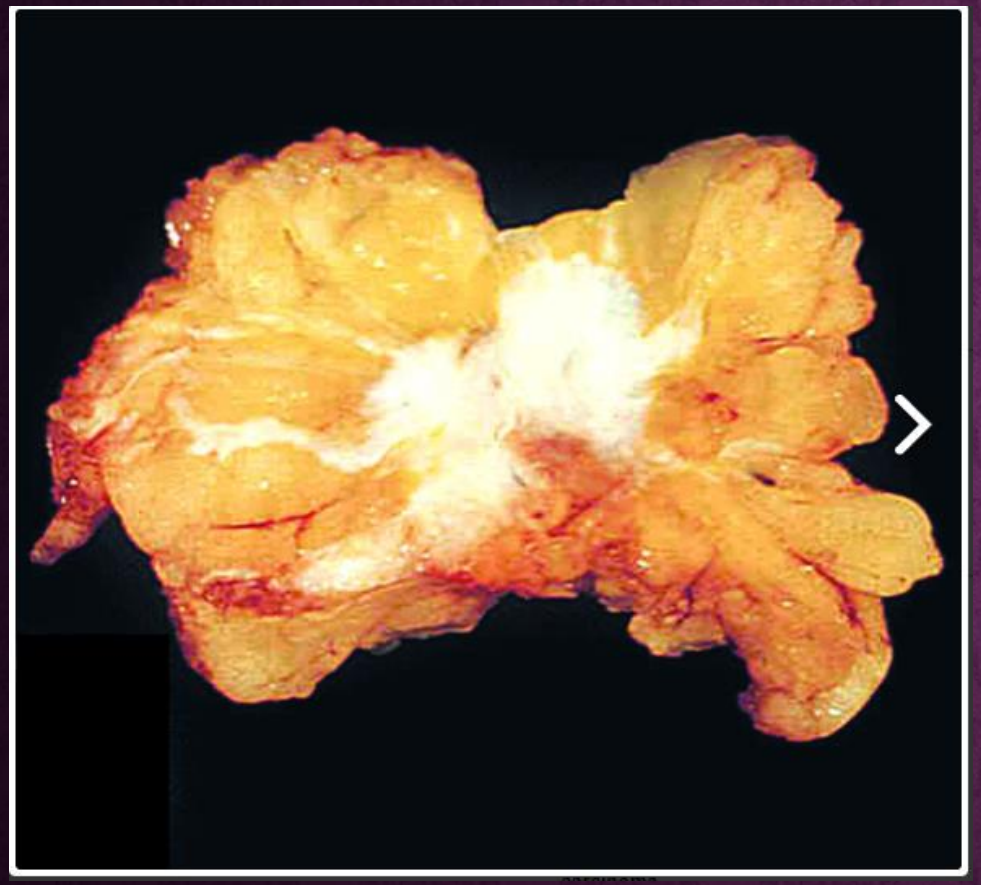
•Lobulocentric proliferation of small uniform cells which fill and distend most of the acini in the involved lobule

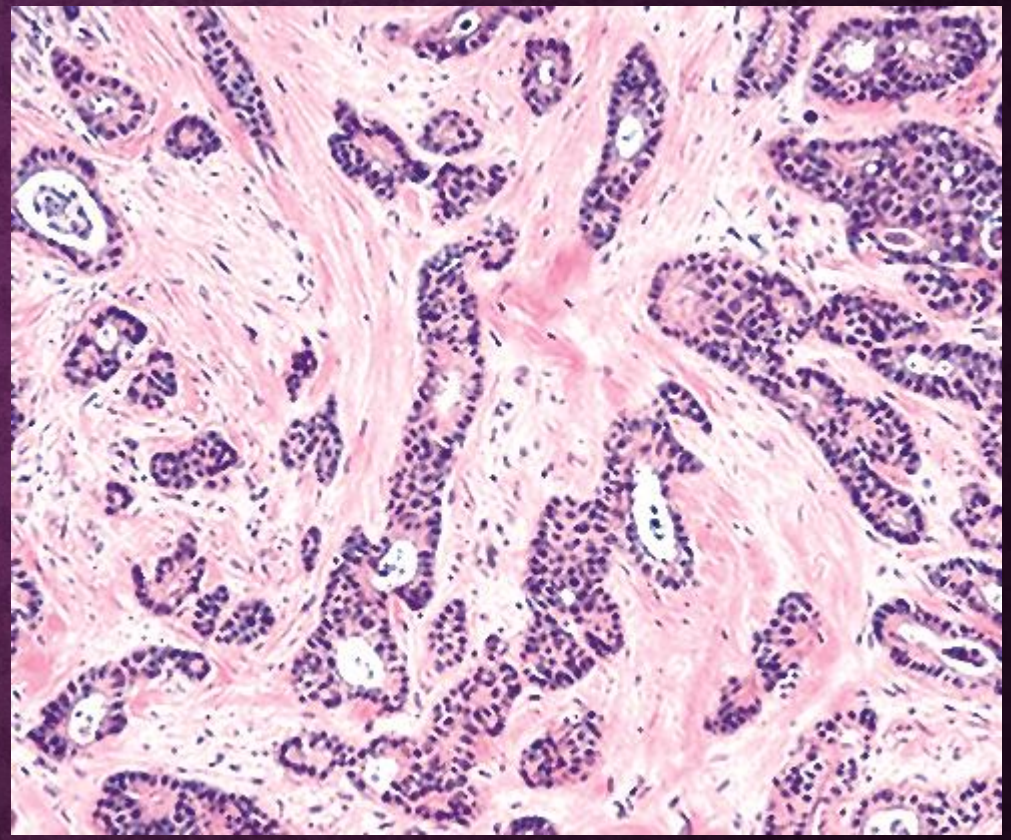


LCIS

INVASIVE DUCTAL CARCINOMA (IDC)

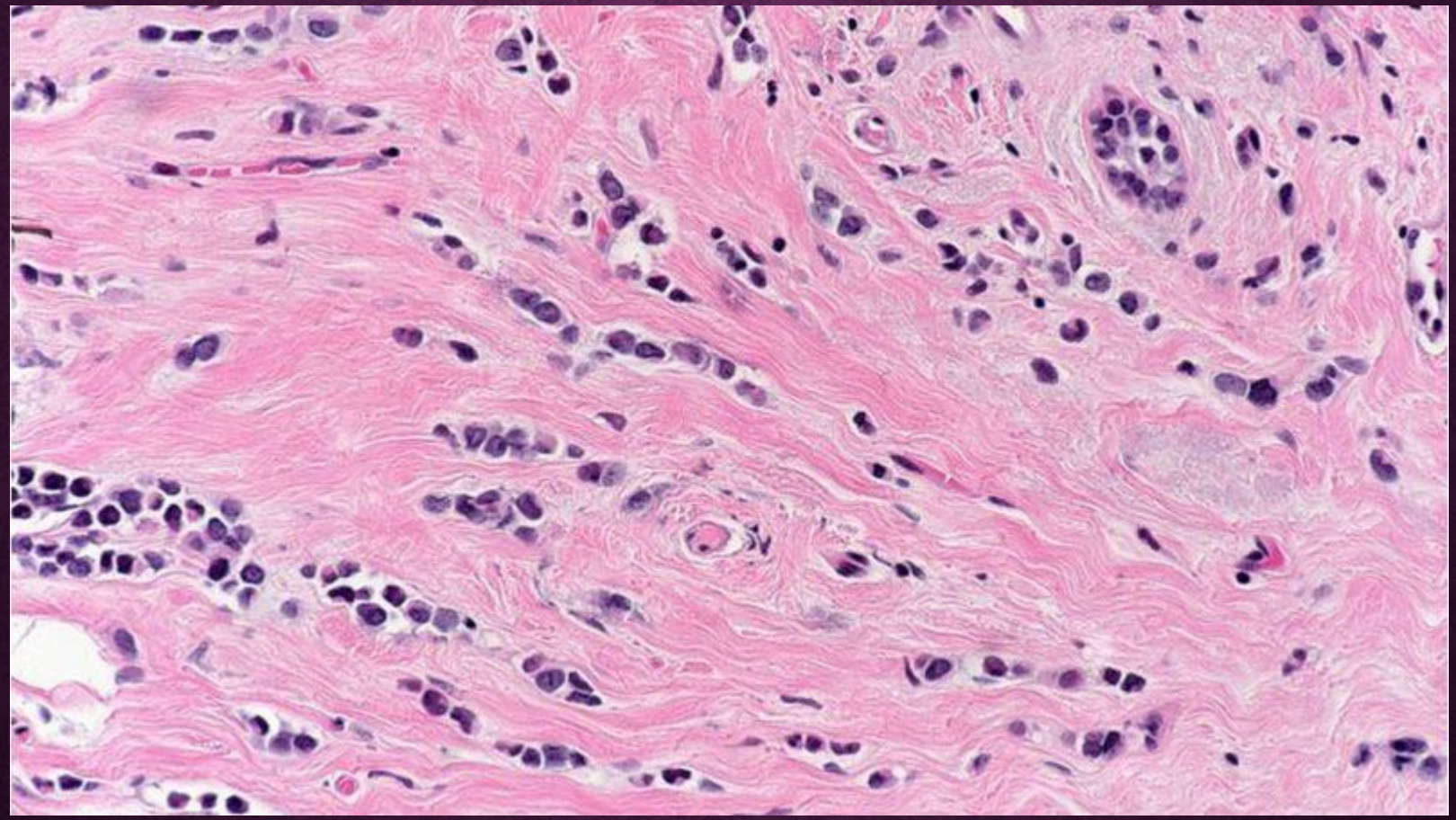
- All carcinomas that cannot be subclassified into one of the specialized types, 70-80%.
- Associated with DCIS (precursor).
- **Gross**: Mostly produce a desmoplastic response that replaces normal breast fat (& a mammographic density) & appear as a hard, palpable infiltrative mass.
- **Microscopic**: ranging from well-developed tubules & low-grade nuclei to tumors consisting of sheets of anaplastic cells.





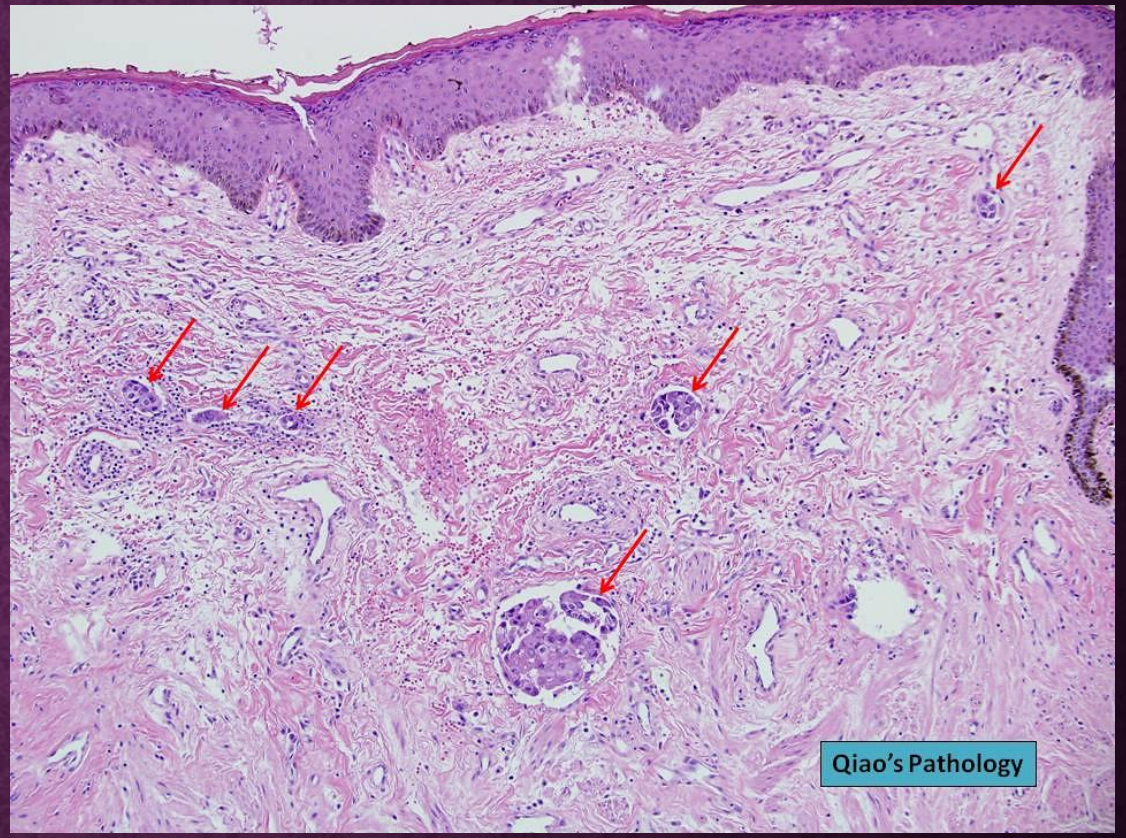
INVASIVE LOBULAR CARCINOMA

- Infiltrating cells similar to tumor cells in LCIS, ~10-15%.
- Associated with LCIS (precursor),
- Cells invade stroma individually.
- Most manifest as palpable masses or mammographic densities (as IDC).
- Commonly multicentric or bilateral.
- Almost all lobular carcinomas express hormone receptors, HER2 overexpression is rare.



INFLAMMATORY CARCINOMA

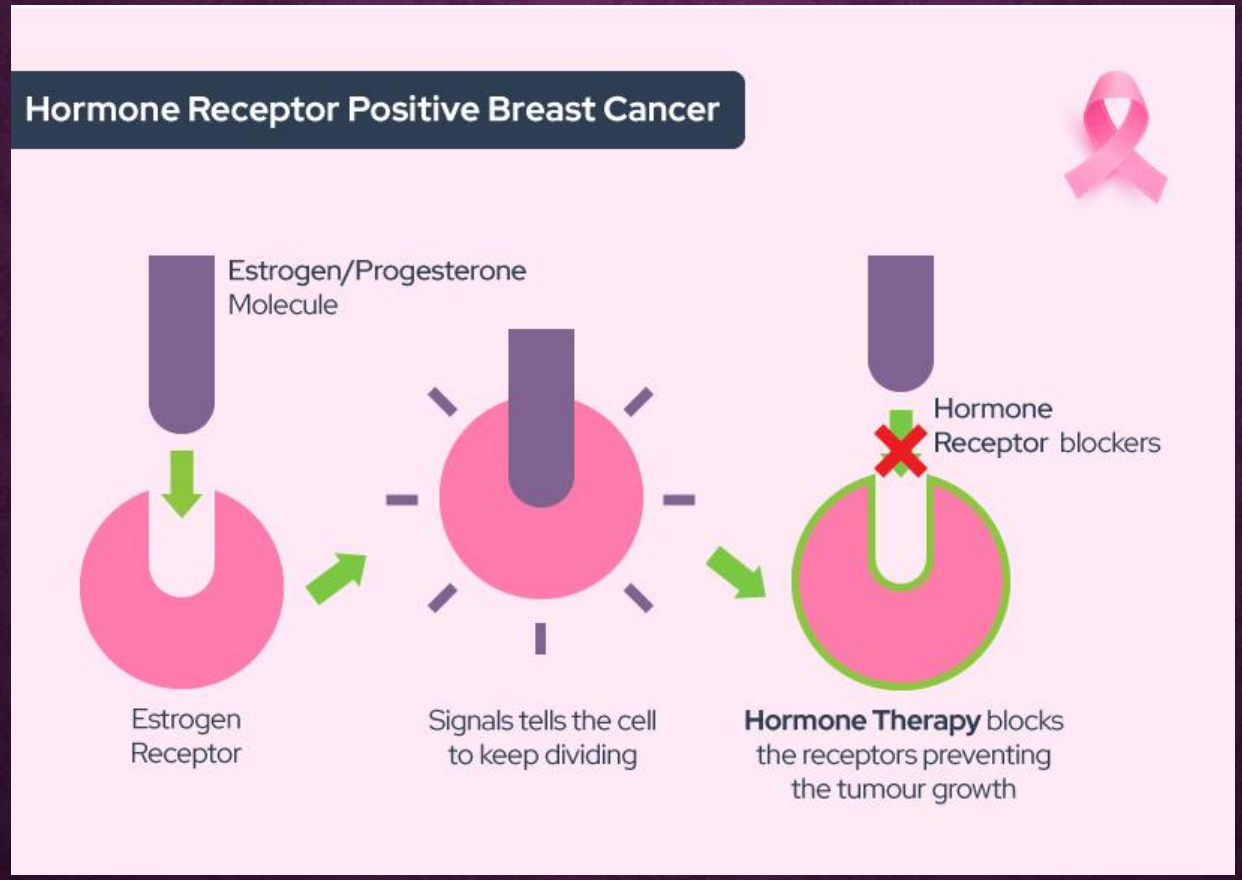
- Defined by its clinical presentation.
- **Presentation**: breast swollen & erythematous, skin thickening → **Peau d'orange**
- **Microscopic**: Invasive carcinoma, generally poorly differentiated & diffusely infiltrates **and obstructs dermal lymphatic spaces,** causing the “inflamed” appearance; true inflammation is absent.
- Most of these have distant metastases & the prognosis is extremely poor.


Qiao's Pathology

The most clinically useful classification of breast cancers → based on expression of hormone receptors {estrogen (ER) & progesterone (PR) receptors & the expression of the human epidermal growth factor receptor 2 (HER2, ERBB2):

1. ER positive (HER2 –ve ; 50%–65% of cancers).
2. HER2 positive (ER +ve or –ve ; 10-20% of cancers).
3. Triple negative (ER, PR, & HER2 –ve ; 10-20%of cancers).

HORMONAL THERAPY



•Hormone receptor positive breast carcinomas may be treated with neoadjuvant endocrine therapy with lower toxicity and cost than the alternative of neoadjuvant chemotherapy

CLINICAL OUTCOME

- ✓ Patients with distant metastases have very poor survival.
- ✓ Favored metastasis are the bone, lungs, skeleton, liver.
- ✓ Axillary lymph node status is the most important prognostic factor for invasive carcinoma in the absence of distant (risk ↑with ↑ size of the primary tumor).

CLINICAL OUTCOME

- predicted based on:

1. **Biologic type**: evaluated by a combination of histologic appearance, grade, expression of hormone receptors, & expression of HER2.
2. **Tumor stage:** a measure of the extent of tumor at time of diagnosis. (primary tumor (T), involvement of regional lymph nodes (N),& presence of distant metastases (M))
   + The majority of cancers first metastasize to regional (axillary) nodes

CLINICAL OUTCOME

3. **The availability of treatment modalities**: 80% of women with breast cancer who receive **optimal** therapy will survive.