PATHOLOGY

- SHEET NO. 12
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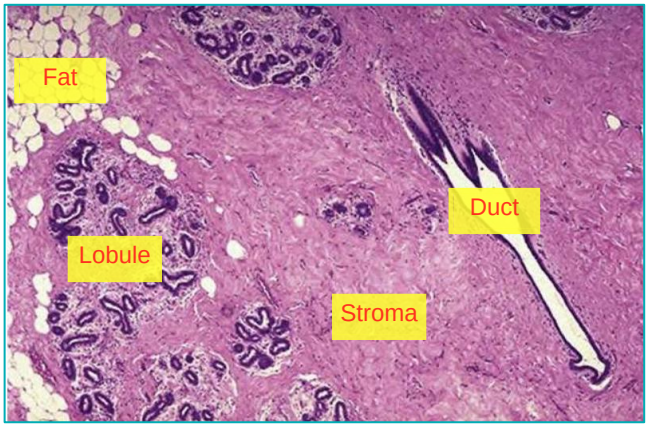
Breast Pathology

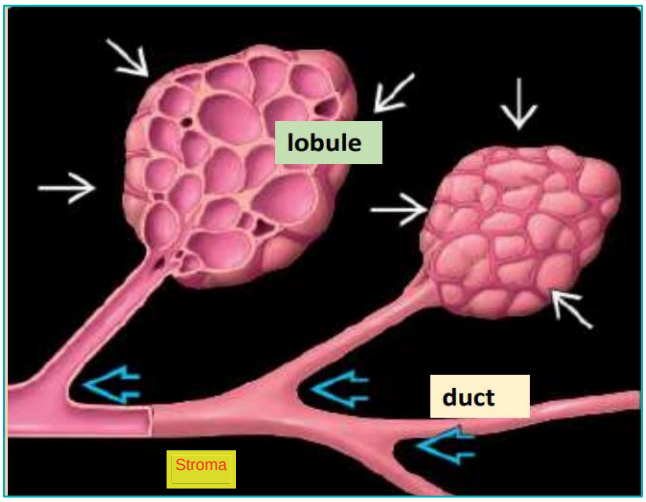
Breast Is a secretory gland, it produces secretions such as milk…



❖ **Normal breast, microscopic**

- **Lobule** is the secretory unit
- **The Duct** transfers the secretions from Lobules into the target
- The pinkish color is called **stroma**, and it's mesenchymal cells…

✓ Epithelial components: Lobules and ducts
✓ Non-epithelial components: Stroma and fat



Fibroadenoma: is a disease that affects the stroma

Epithelial lesions of the breast (to be discussed):

1- **Benign (proliferative and non-proliferative)**
2- **Malignant (in situ and invasive CA)**

✤ Clinical presentation of breast disease ✤

1. **Pain:** 90% of painful masses are benign
2. **Inflammation:**
   - ➔ Edema & erythema
   - ➔ Mostly associated with infections (during lactation and breastfeeding).
3. **Nipple discharge**
4. **Palpable masses:** all palpable masses require evaluation to rule out cancer
5. **Gynecomastia:** (this term isn't used in females)
   - ➔ The only common breast symptom in males.
   - ➔ Imbalance of estrogens, which stimulate breast tissue

❖ Regardless of the symptom:

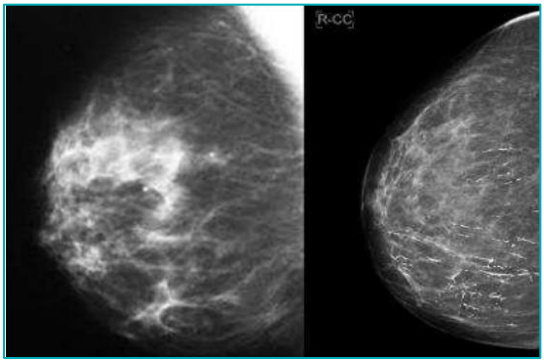
- ➔ The underlying cause is benign in >90% of cases.
- ➔ The likelihood of malignancy increases with age

❖ Patients with breast cancer:

- ➔ **about 45% have symptoms**: Palpable mass>>>> pain> nipple discharge >inflammatory changes
- ➔ **The remainder come to attention through screening test**

❖ Mammographic screening:

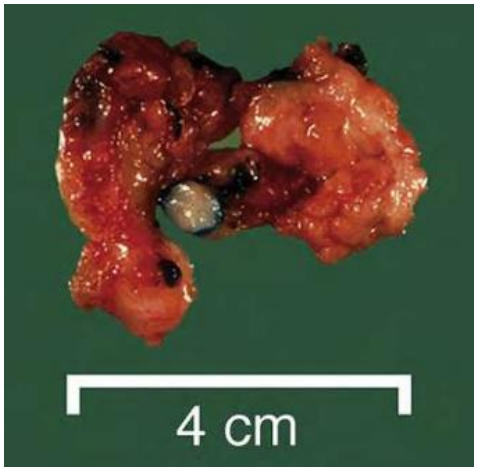
- ➔ Detects early, nonpalpable asymptomatic breast cancer before metastasis.
- ➔ average size of cancer detected by mammography is ≈ 1 cm (lower chance for metastasis to regional lymph nodes)

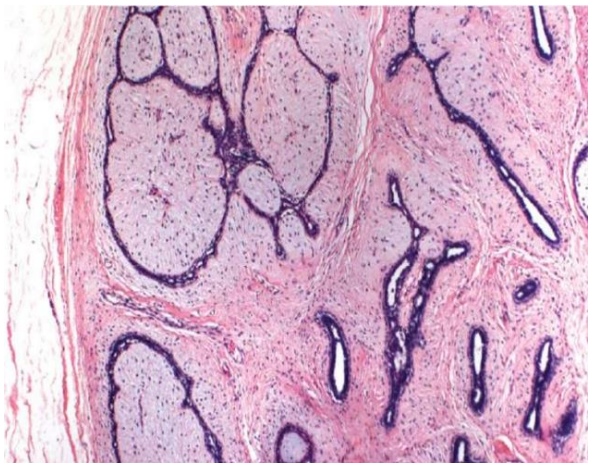


✤ Fibroadenoma: a stromal disease ✤

- **The most common benign neoplasm of female breast.**
- The presence of fibroadenoma is **related to estrogen activity**:
  - ➔ That's why they tend to enlarge during pregnancy
  - ➔ They regress and calcify after menopause
- The peak age is: **20s and 30s** (young females in their reproductive period of life)
- These lesions are discrete, usually solitary, freely movable nodule, (<10 cm).
- Usually easily "shelled out" surgically. (they can be removed easily during surgery)

شكلها مميز ، بالعادة بتيجي بأسئلة العملي

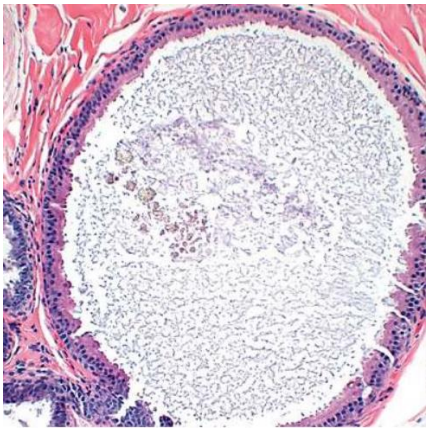




✤ Benign epithelial lesions ✤

- **Divided into 3 groups:**
  1. **Non-proliferative changes (fibrocystic changes)**: (no associated increased risk of breast cancer)
  2. **Proliferative disease without atypia**: (1.5-2 folds increase risk of breast cancer)
  3. **Proliferative disease with atypia**: (4-5 folds increase risk of breast cancer) أسوء وحدة فيهم

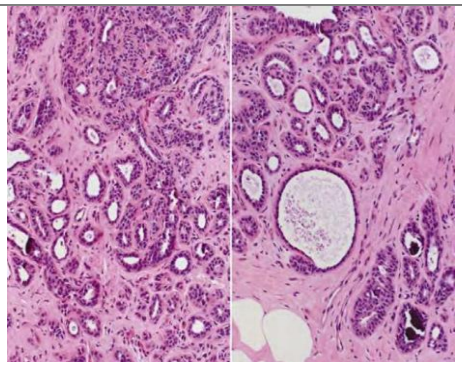
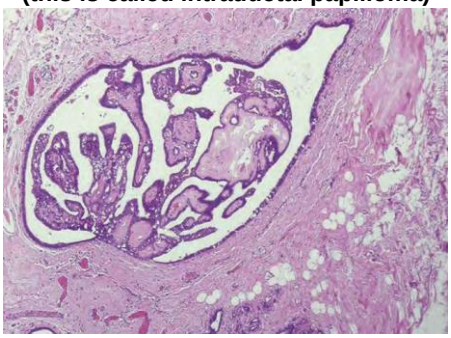
1. Non-proliferative changes (Fibrocystic changes):



- **Common**
- **3 principal morphologic changes**:
  1. Cystic change: with apocrine metaplasia (most common)
  2. Fibrosis
  3. Adenosis (lobules look more prominent, but there's no abnormal growth or more number of layers inside those lobules and ducts, if the number of cells is increased, then this is proliferative lesion without atypia)

2. Proliferative lesions without atypia:

- **includes 4 types:**

epithelial hyperplasia	sclerosing adenosis	complex sclerosing lesion	papilloma
			**(this is called intraductal papilloma)** 

- **associated with a small increase in the risk of subsequent carcinoma in either breast.**
- not clonal and are not commonly found to have genetic changes.

3. Proliferative lesions with atypia:

- **includes 2 types:**
  1. **atypical lobular hyperplasia (ALH):** resembles lobular carcinoma in situ (LCIS)
  2. **atypical ductal hyperplasia (ADH):** resembles ductal carcinoma in situ (DCIS)

- are clonal proliferations having some, but not all, histologic features that are required for the diagnosis of carcinoma in situ.
- Associated with a moderately increased risk of carcinoma

✤ Breast Cancer ✤

❖ **Epidemiology**:

- **The most common malignancy of women**
- **Among the most common causes of cancer deaths in women**
- Mortality rate dropped to dramatically (improved screening and more effective treatment)
- Almost all breast malignancies are **adenocarcinomas (>95%)**

❖ **Risk factors:**

- **Age**: incidence increases rapidly after age 30
- **Gender**: The incidence in men is only 1% of that in women
- **Family History of Breast Cancer**: multiple affected first-degree relatives with early-onset breast cancer.

❖ **Pathogenesis:**

Factors contributing directly can be grouped into:

- **Genetics**: BRCA1 and BRCA2; TP53; PTEN; and HER2 gene amplification
- **Hormonal**: Estrogens & Estrogen agonists:
  - ➔ Reproductive History: Early age of menarche, nulliparity, absence of breastfeeding, and older age at first pregnancy are all associated with increased risk due to <u>increased exposure to estrogenic stimulation.</u>
- **Environmental**

❖ **Morphology:**

Location:

- **upper outer quadrant (50%)**
- **central portion –subareola (20%)**
- **Lower outer quadrant 10%**
- **Upper inner quadrant 10%**
- **Lower inner quadrant 10%**

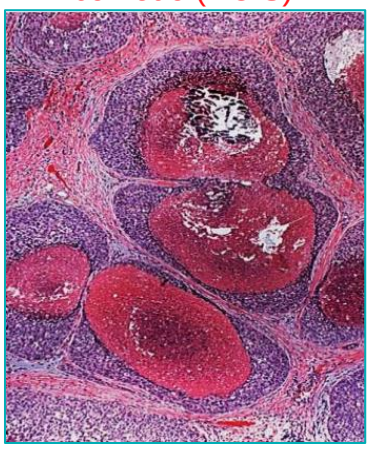
✤ Breast Caircnoma – Histologic types ✤

A. Noninvasive: confined by a basement membrane and do not invade into stroma or lymphovascular channels, include: 1. Ductal carcinoma in situ (DCIS) 2. Lobular carcinoma in situ (LCIS)	***B. Invasive*** *(infiltrating):* *1. Invasive ductal carcinoma- NOS (not of a special type) → 70%* *2. Invasive lobular carcinoma → 10%* *3. Carcinoma with medullary features< 5%* *4. Mucinous carcinoma (colloid carcinoma) <5%* *5. Tubular carcinoma< 5%* *6. Other types*

✪ NONINVASIVE (IN SITU) CARCINOMA:

1. **Lobular carcinoma in situ (LCIS):** Malignant clonal proliferation of cells within lobules
2. **Ductal carcinoma in situ (DCIS):**
   - malignant clonal proliferation of epithelial cells within ducts
   - has a wide variety of histologic appearances: solid, comedo, cribriform, papillary, and micropapillary
   - Ranges from low to high nuclear grade (pleomorphic).
   - Comedo subtype:
     1. extensive central necrosis. (The name derives from the toothpaste-like necrotic tissue).
     2. **<u>Frequently associated with Calcifications</u>**

comedo (DCIS)



❖ **Management:**

- excellent prognosis (97% long-term survival after simple mastectomy)
- treatment strategies: surgery; irradiation; tamoxifen, hormonal therapy
- Significance of DCIS: adjacent invasive CA; become invasive if untreated (1/3 of cases)

✪ INVASIVE CANCERS:

❖ Classification Systems:

Receptors that are examined in any breast cancer tissue are:

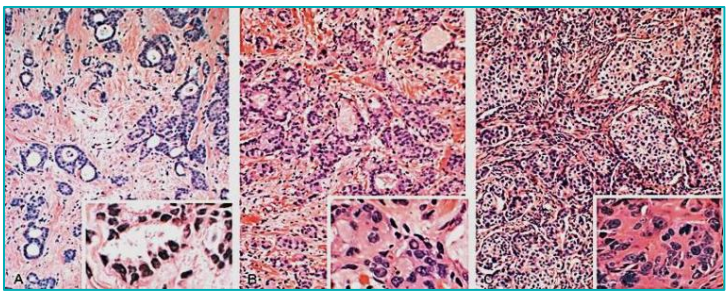
Estrogen receptor (ER); progesterone receptor (PR); & human epidermal growth factor receptor 2 (HER2/neu)

Cancer can be classified according to expression of hormone receptors into three major groups:

1. ER positive (HER2 negative; ≈ 60%)
2. HER2 positive (ER positive or negative; 20%)
3. Triple negative (ER, PR, and HER2 negative; 10%)

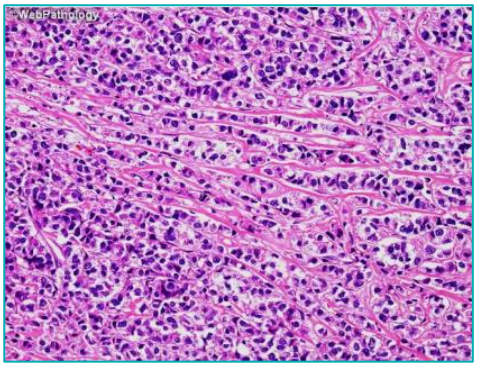
❖ Invasive Ductal Carcinoma:

- **Also called Carcinomas "not otherwise specified"**
- **Precancerous lesion**: usually DCIS
- **Receptor profile**:
  Usually: ER, PR (+), HER2 (-); A wide range of differentiation (grades)



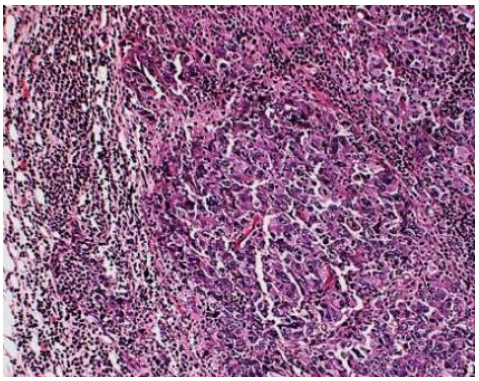
❖ Invasive lobular carcinoma:

- ≈10%
- **Precancerous lesion**: LCIS.
- 10% -20% multicentric and bilateral
- palpable masses or mammographic densities
- Usually express hormone receptors ER, PR
- HER2 overexpression is rare or absent.



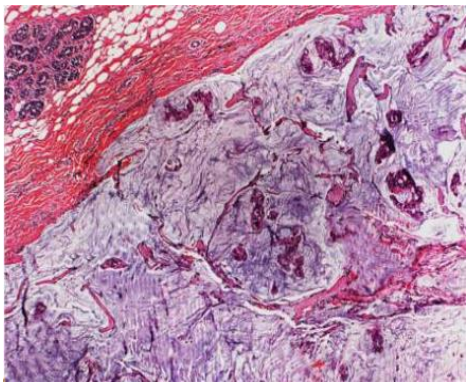
❖ Carcinoma with Medullary features:

- 5%
- **Triple negative (ER, PR, and HER2 all negative).**
- large anaplastic cells with lymphocytic infiltrate.
- usually **absent** Precancer
- ↑in women with BRCA1 mutations.



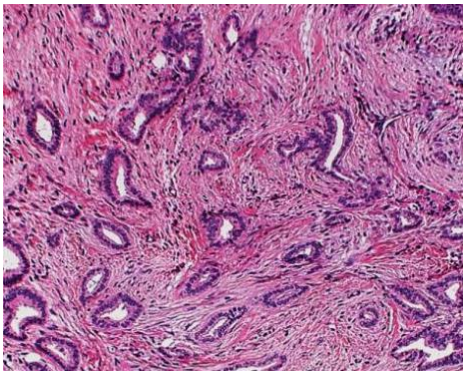
❖ Colloid (Mucinous) Carcinoma:

- Rare
- abundant extracellular **mucin**
- soft and gelatinous mass
- ER-positive
- HER2- negative



❖ **Tubular carcinomas:**

- **< 5 %**
- irregular mammographic densities.
- well-formed tubules; low-grade nuclei
- **Lymph node mets: rare**
- **Prognosis: excellent.**
- ER-positive
- HER2- negative



✤ Spread of breast cancer ✤

- through **lymphatic** and **hematogenous** channels.
- Favored metastasis: **bone**, **lungs**, **liver**, and **adrenals**,,, and (less commonly) brain, spleen, and pituitary.
- **Metastases may appear many years after apparent therapeutic control of the primary lesion**

❖ **Screening:**

- **mammographic screening: most frequently used**
- **Magnetic resonance imaging, MRI**

❖ **Prognostic factors:**

- Tumor stage:
  - ➔ Invasive carcinoma versus carcinoma in situ
  - ➔ Distant metastases.
  - ➔ Lymph node metastases (significant poor prognostic factor)
  - ➔ Tumor size.
  - ➔ Locally advanced disease
- Lymphovascular invasion
- Molecular subtype.
- Special histologic types.
- Histologic grade
- ER; PR; and HER2 expression

Past Papers?!

Take this short quiz!

https://forms.gle/9P8ShpDezv6c7YbCA

لَهُ الْحَمْدُ فِي الأُولَىٰ وَالآخِرَةِ ۖ وَلَهُ الْحُكْمُ وَإِلَيْهِ تُرْجَعُونَ ﴿٧٠ القصص﴾