



Breast Pathology

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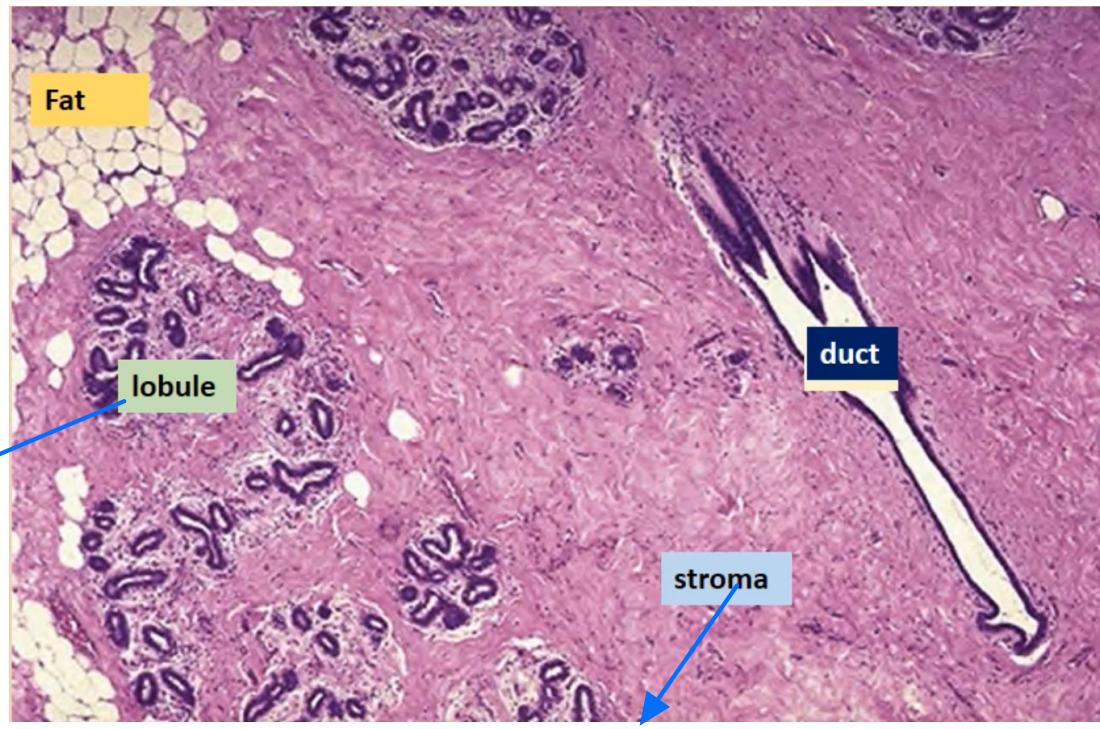
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تحرير: آمنة الأيوبيين

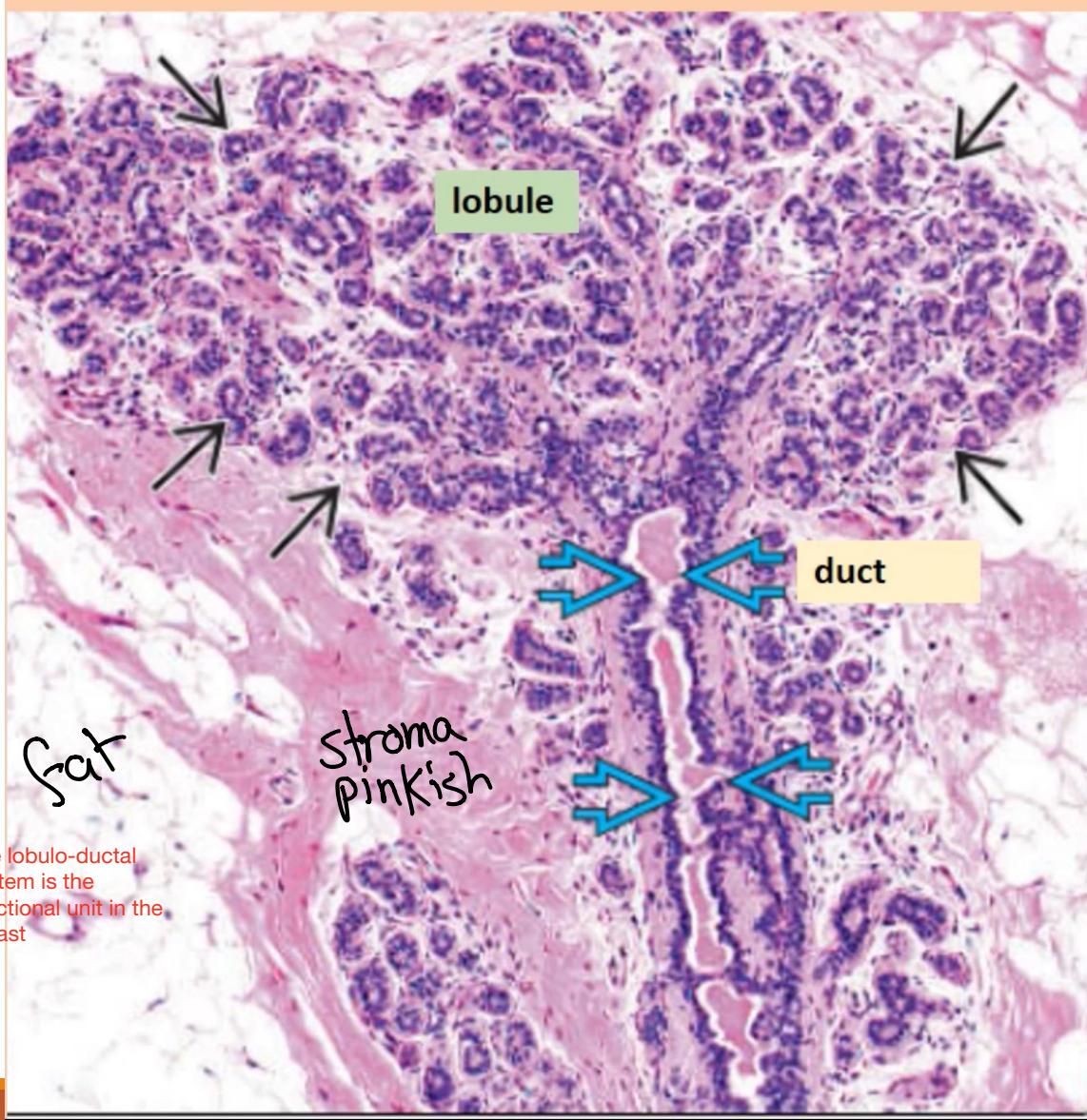
Normal breast, microscopic

Ducts and lobules are lined by epithelial cells



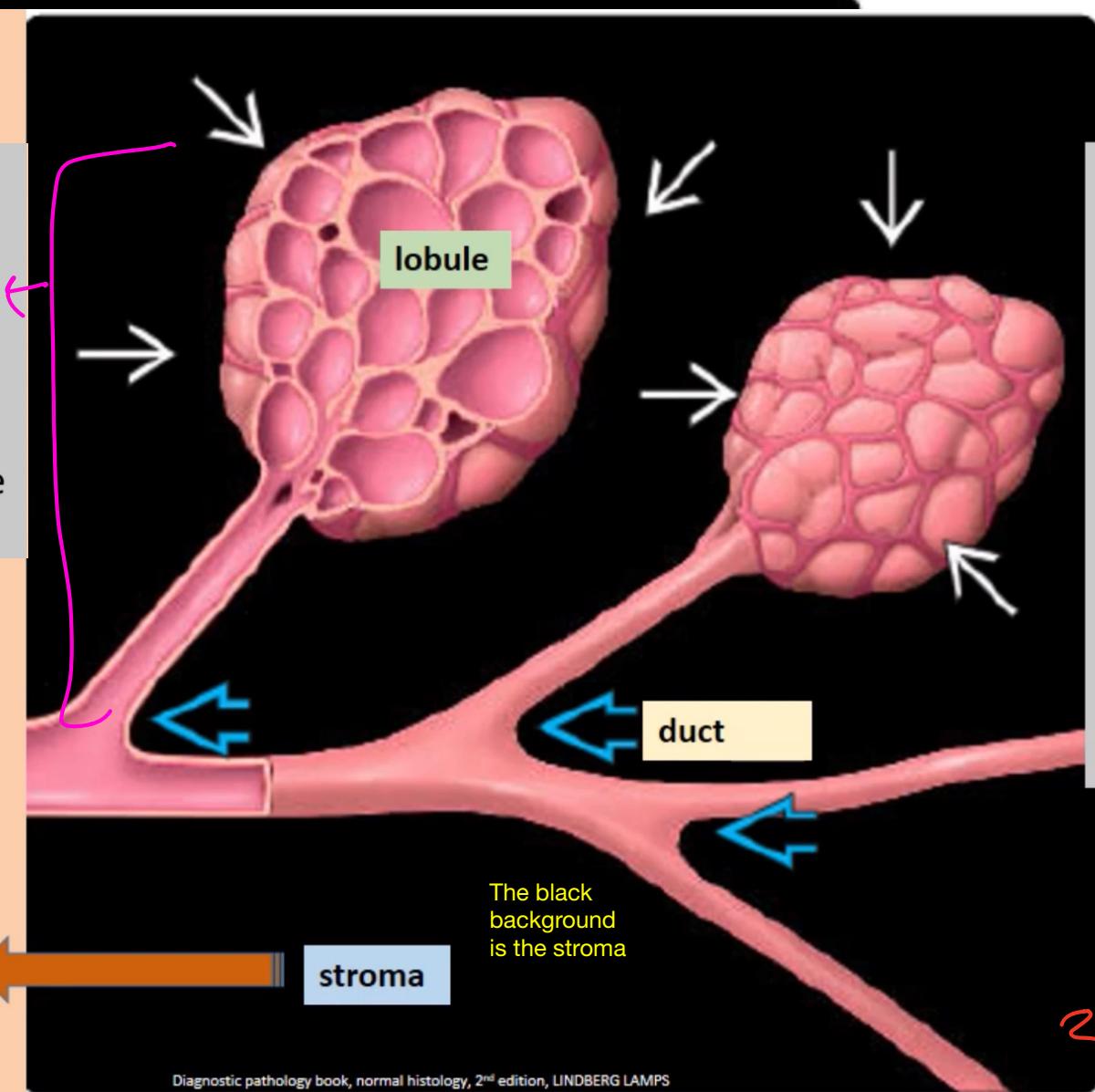
Where the
breast
secretions
are formed

mesenchymal cells (pinkish color)



Epithelial lesions:

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



Regardless of the symptom:

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

CLINICAL PRESENTATIONS OF BREAST DISEASE:

Pain: 90% of painful masses are benign

Inflammation:

- edema and **erythema**

- Mostly infections (during lactation and breastfeeding).

Nipple discharge

Palpable masses: all palpable masses require evaluation.

Gynecomastia: Enlargement of male breast

- The only common breast symptom in **males**.

- imbalance of estrogens, which stimulate breast tissue.,

affect & grow

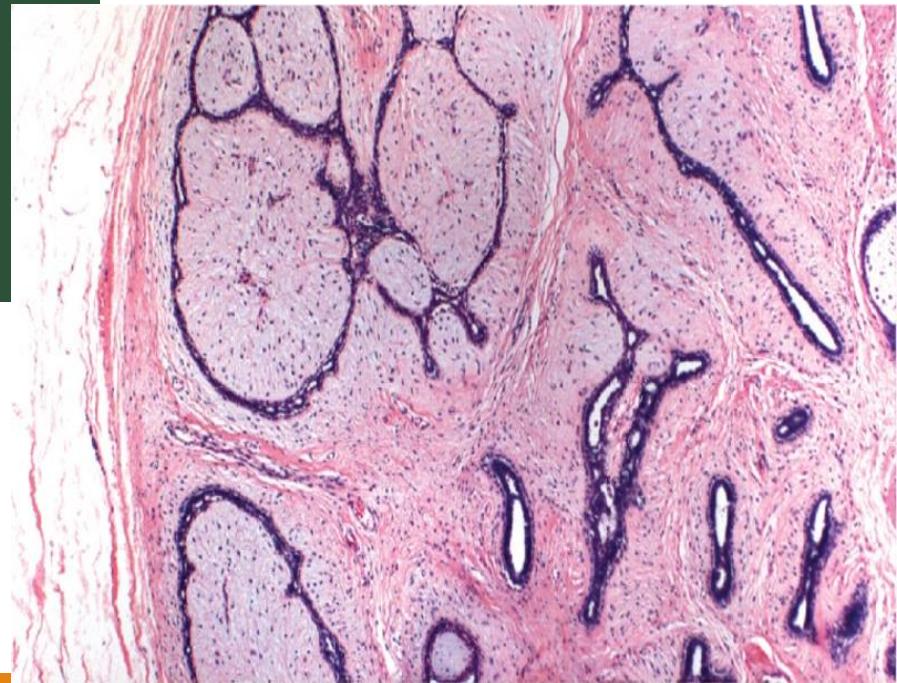
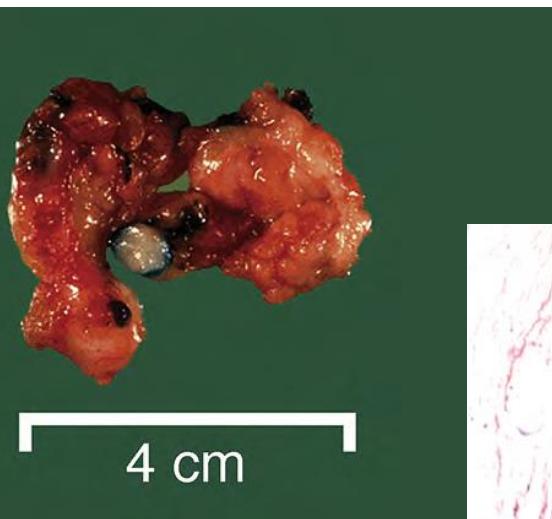
Fibroadenoma

The **most common benign neoplasm** of the female breast.

○ Related to **estrogen activity**:

- may enlarge during pregnancy. And during the late phase of menstrual cycle
- After menopause usually regress and calcify.
- Peak: 20s and 30s
- discrete, usually solitary, freely movable nodule, (<10 cm). Sharp borders
- usually easily "shelled out" surgically.

Fibroadenoma

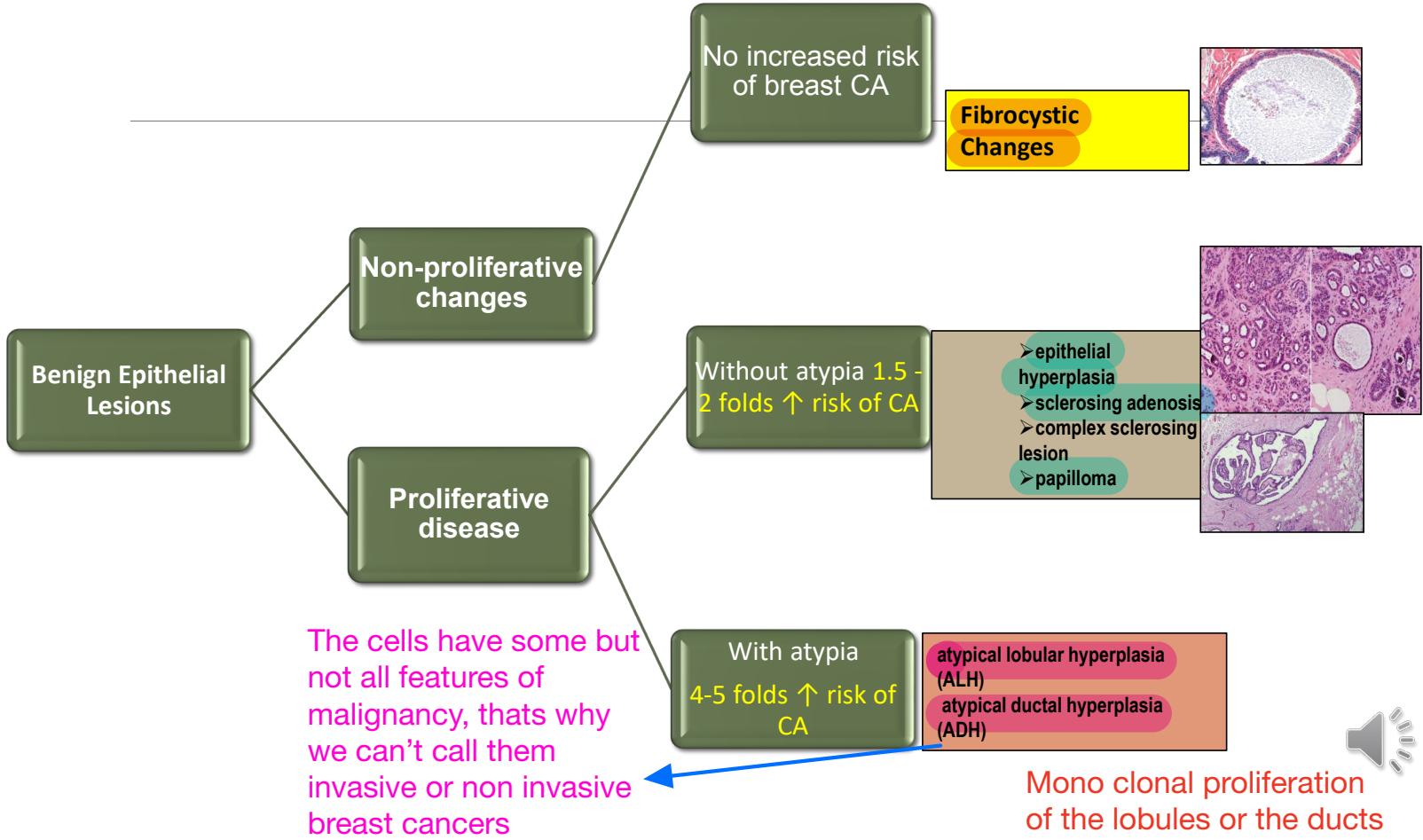




benign epithelial lesions:

divided into three groups:

- **Nonproliferative changes:** not associated with an increased risk of breast cancer
- **Proliferative disease without atypia:** (1.5-2 folds increase risk of breast cancer)
- **Proliferative disease with atypia:** (associated with 4-5 folds increase risk of breast cancer)



Non-proliferative Breast Changes (Fibrocystic Changes)

-Common

-3 principal morphologic changes:

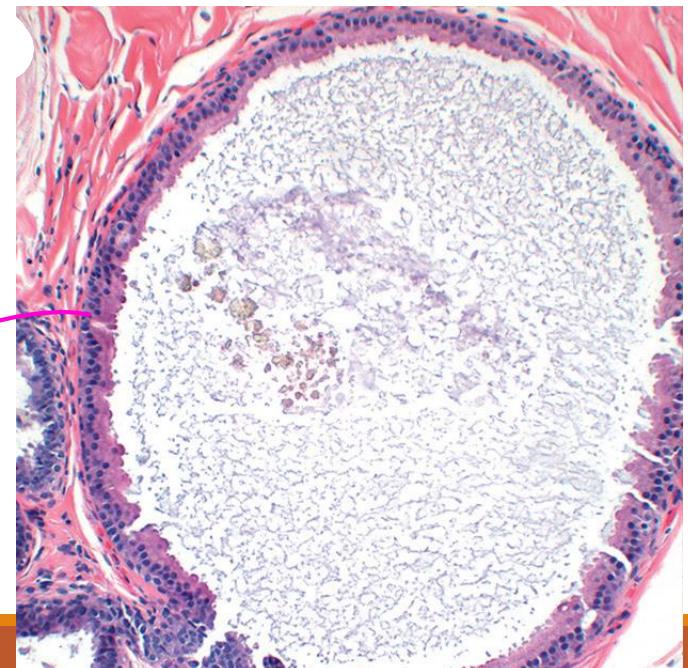
(1) **cystic change:**

apocrine metaplasia
(most common)

(2) **Fibrosis**

(3) **adenosis**

apocrine cyst



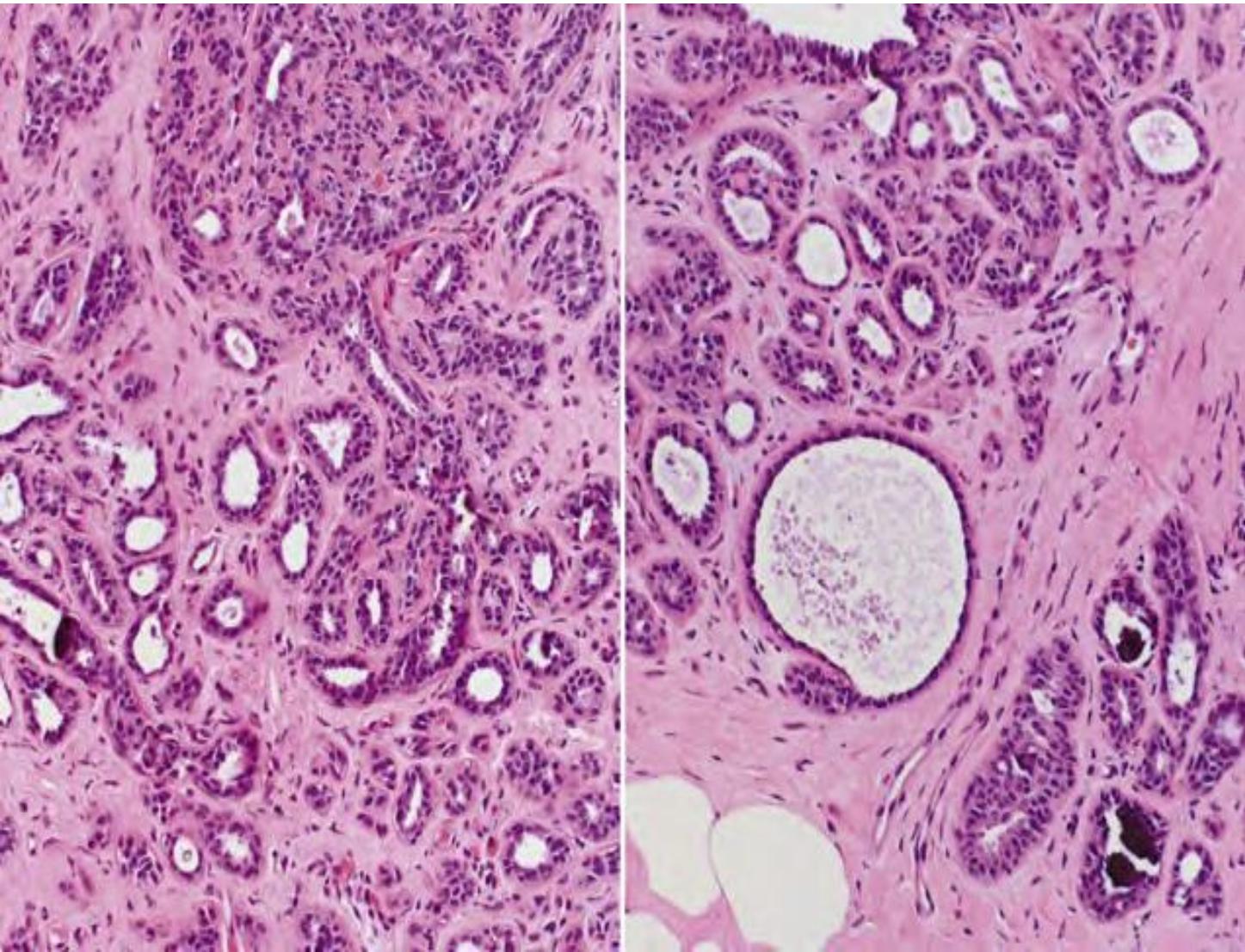
Proliferative disease **without atypia**

Includes:

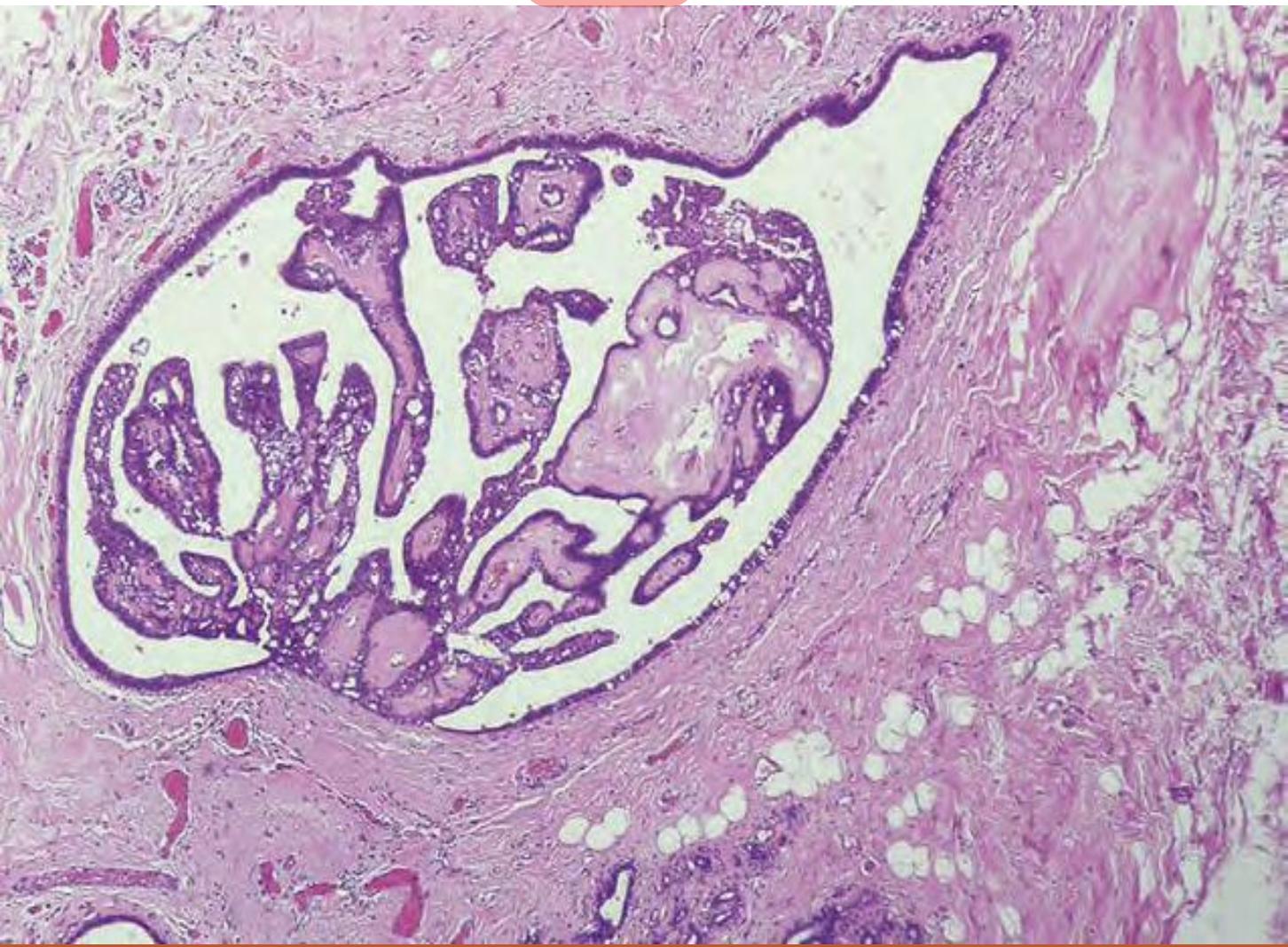
- **epithelial hyperplasia**
- **sclerosing adenosis**
- **complex sclerosing lesion**
- **papilloma**

- 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.

Sclerosing adenosis



intraductal papilloma in a breast duct



Proliferative disease with atypia

1- atypical lobular hyperplasia (ALH): resembles lobular carcinoma in situ (LCIS)

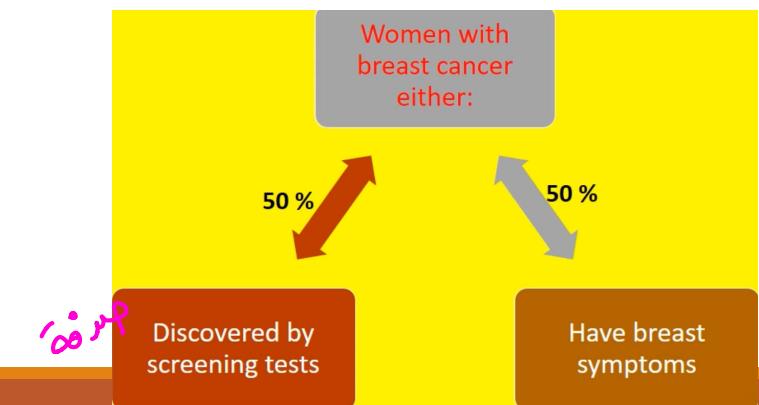
2- atypical ductal hyperplasia (ADH): resembles ductal carcinoma in situ (DCIS)

- 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

Of women with cancer:

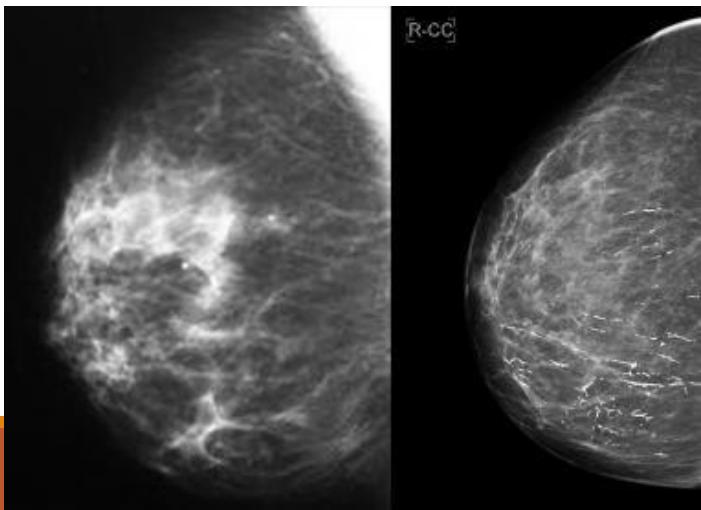
- ① ○ about 45% have symptoms
 - Palpable mass>>> pain> nipple discharge > inflammatory changes *نار*
- ② ○ the remainder come to attention through screening tests
 - Self physical examination
 - Clinical physical examination
 - Radiology associated test (mammography)



Mammographic screening:

detects early, **non-palpable** **asymptomatic** breast carcinomas before metastasis.

the average size of cancer detected by mammography is $\approx 1 \text{ cm}$ ($<15\%$ have mets to regional lymph nodes)



Breast cancer...Epidemiology:

- The most common malignancy of women
- Among the most common causes of cancer deaths in women
- mortality rate dropped to <20% (improved screening and more effective treatment)
*↓
and earlier*
- Almost all breast malignancies are adenocarcinomas (>95%)

 Aries from the epithelial components of the breast

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:

- ER positive (HER2 negative; $\approx 60\%$)
- HER2 positive (ER positive or negative; 20%)
- Triple negative (ER, PR, and HER2 negative; 10%)

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 that contribute directly to the development of breast cancer can be grouped into:

- **Genetic:** include: *BRCA1* and *BRCA2*; *TP53*; *PTEN*; and *HER2* gene amplification

Hormonal: Estrogens & Estrogen antagonists:

Reproductive History.

- Early age of menarche, nulliparity, absence of breastfeeding, and older age at first pregnancy are all associated with increased risk → due to increased the exposure to estrogenic stimulation.

- Environmental

Morphology:

Location:

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



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Hard, in-defined and whitish or yellowish area inside the breast tissue

Breast carcinoma- histotypes

in situ

A. Noninvasive:(confined by a basement membrane and do not invade into stroma or lymphovascular channels), include:

1. Ductal carcinoma in situ (DCIS) More common
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

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NONINVASIVE (IN SITU) CARCINOMA

include:

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

By definition both confined by a basement membrane and do not invade into stroma or lymphovascular channels

LOBULAR carcinoma in-situ (LCIS)

- Malignant clonal proliferation of cells within lobules
- The term “lobular” was used to describe this lesion because the cells expand but do not distort involved spaces and, thus, the underlying lobular architecture is preserved.

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).

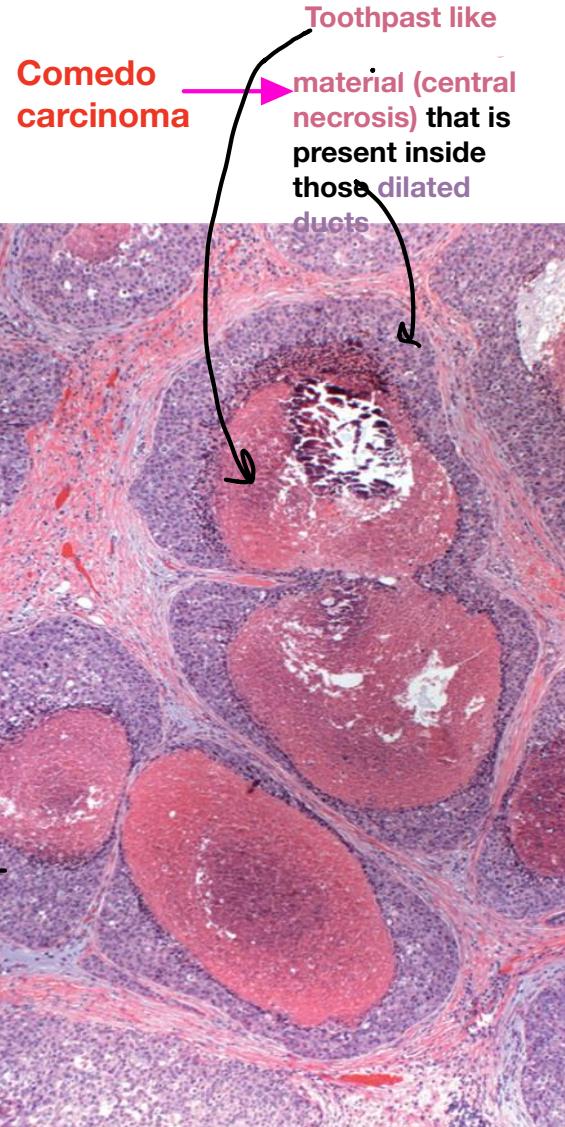
comedo subtype:

- extensive central necrosis. (The name derives from the toothpaste-like necrotic tissue).
- Frequently associated with Calcifications → detected by mammography

DCIS - management:

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

These malignant cells are confined by the basement membrane



Invasive ductal carcinoma

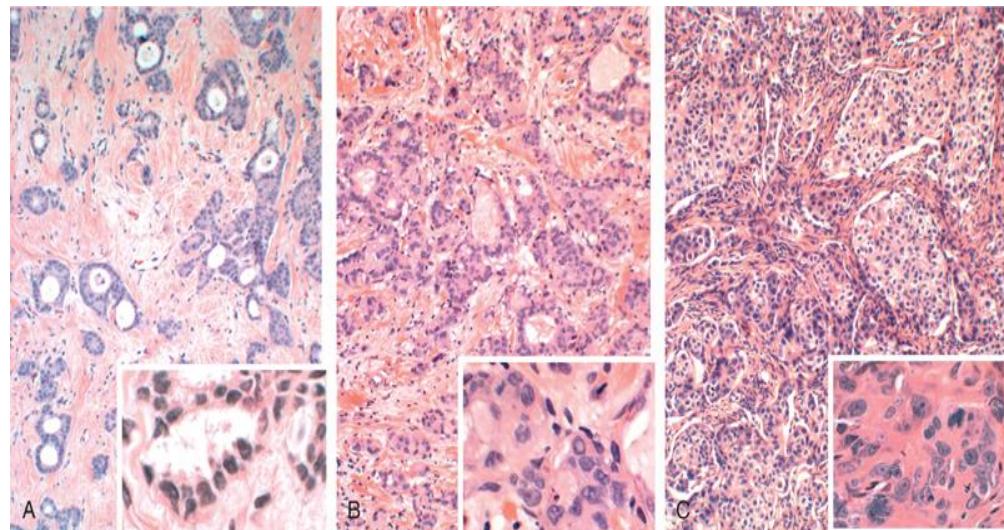
Also called **Carcinomas "not otherwise specified"**

Precancerous lesion: usually DCIS

Receptor profile:

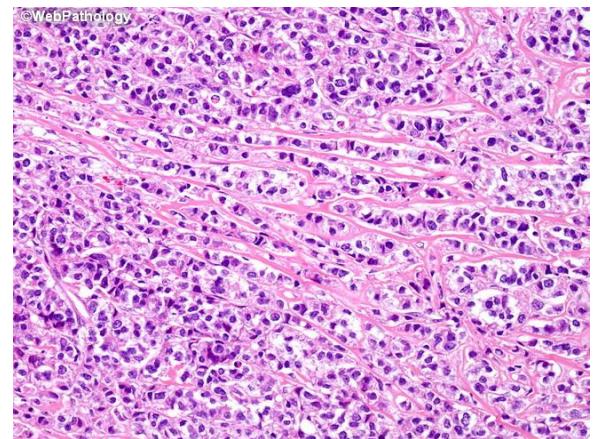
Usually: ER, PR (+), HER2 (-)

A wide range of differentiation
(grades)



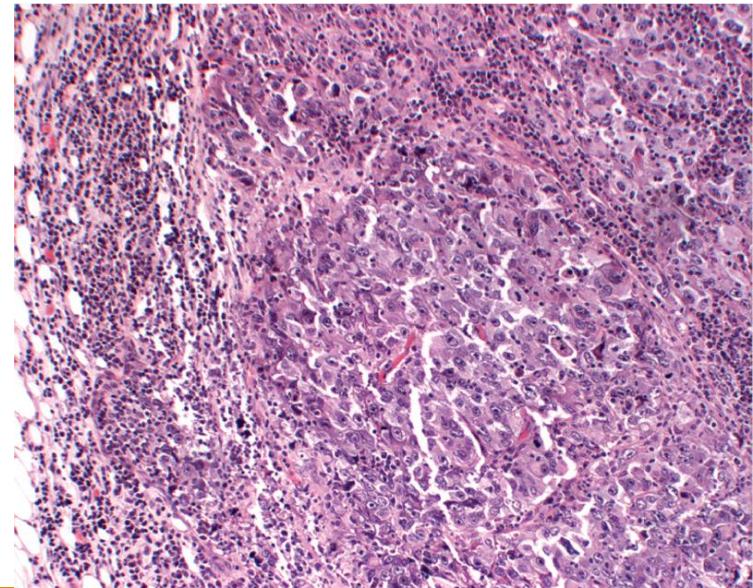
Invasive lobular carcinoma

- ≈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.



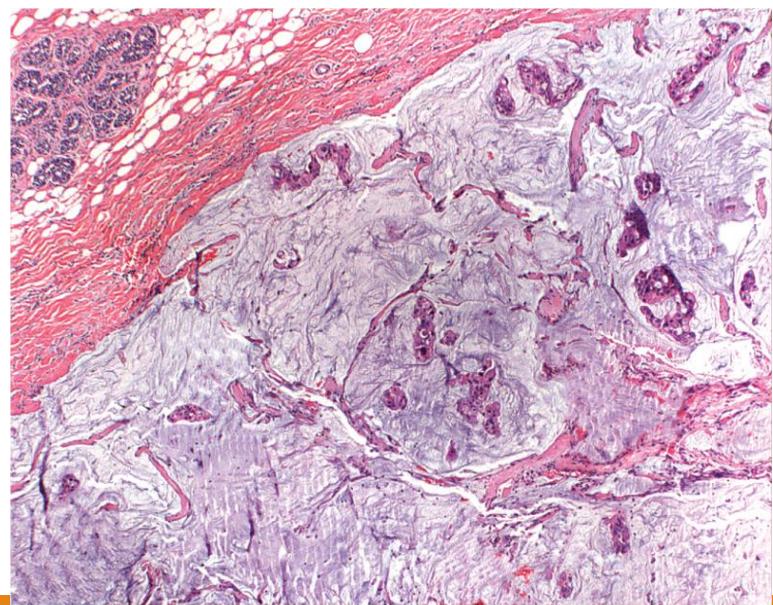
Carcinoma with Medullary features:

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



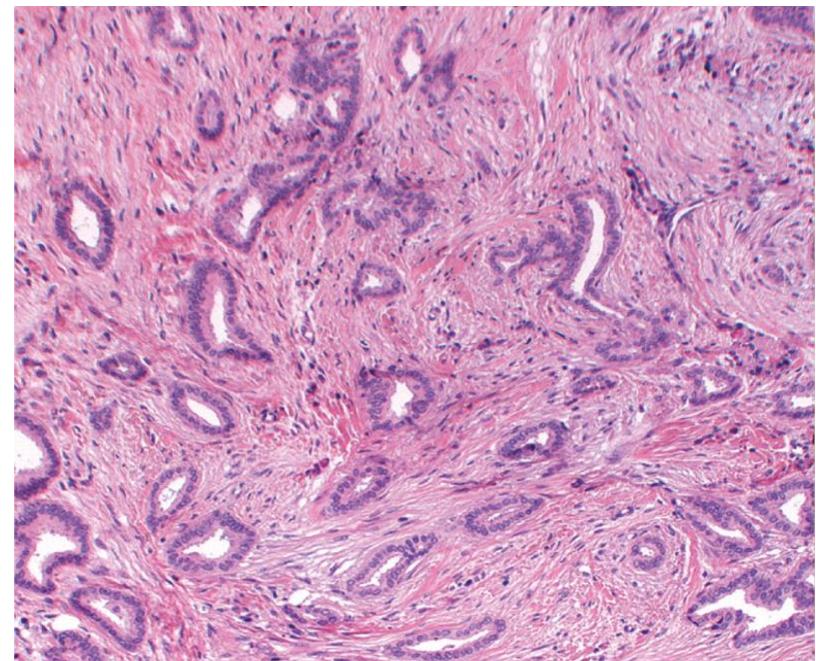
Colloid (mucinous) carcinoma

- 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
 - Magnetic resonance imaging, MRI

PROGNOSTIC FACTORS:

The most important 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

Important in the management and therapy

The larger size the tumor is the larger number of lymph node that contain mets of the tumor.

