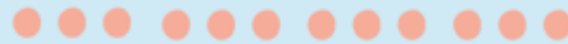# Pathology GUS

Done By Dana Alkhatib

Corrected By Dana Alkhatib
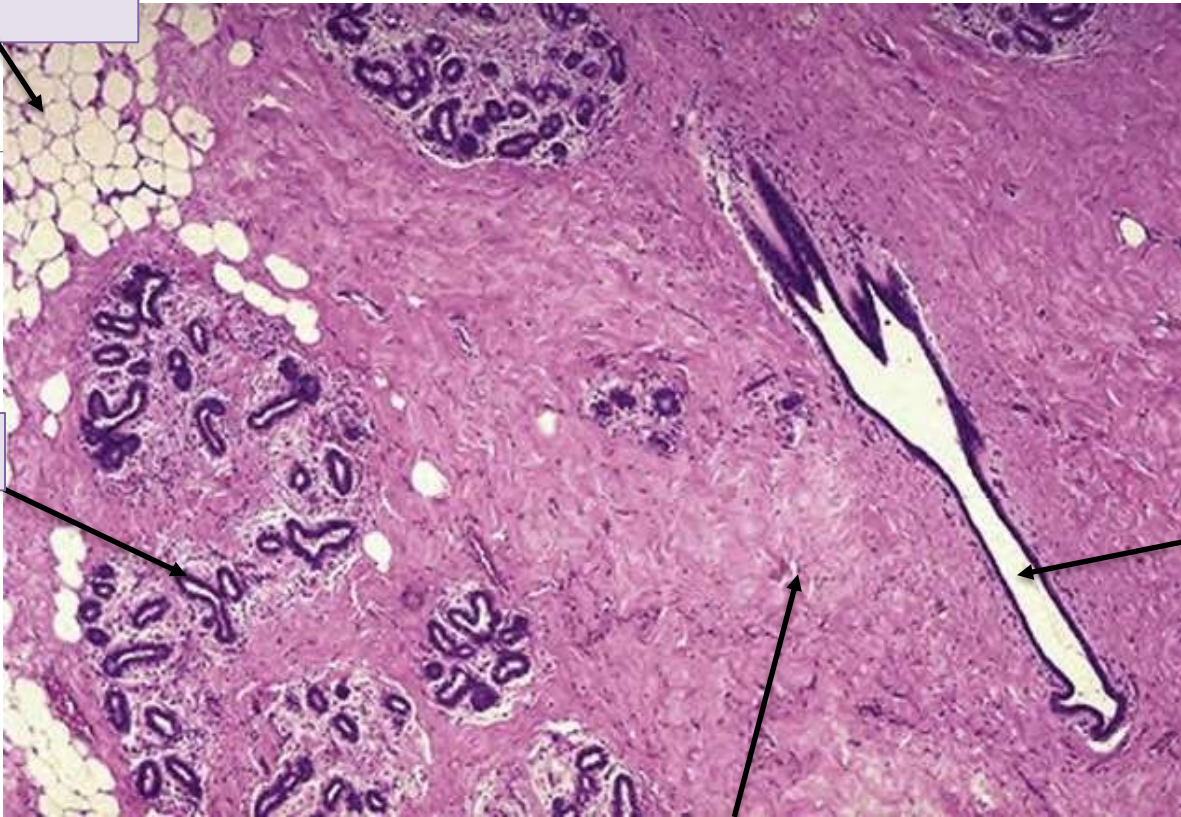
Breast Pathology

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Normal breast, microscopic

Fat (adipose tissue)

Lobules

Breast is a secretory gland , it produces secretions , the most important one is milk, because the breast is a secretory gland the basic structure of it resembles other secretory glands , constitutes of acini (lobules) or the production units and ducts which transfer the secretions from the secretory unit to the target location

This pinkish color is the stroma (mesenchyme) , fibroblasts and other non-epithelial cells , it's for support and other functions

Histology of breast
1. epithelial structures : lobules and ducts
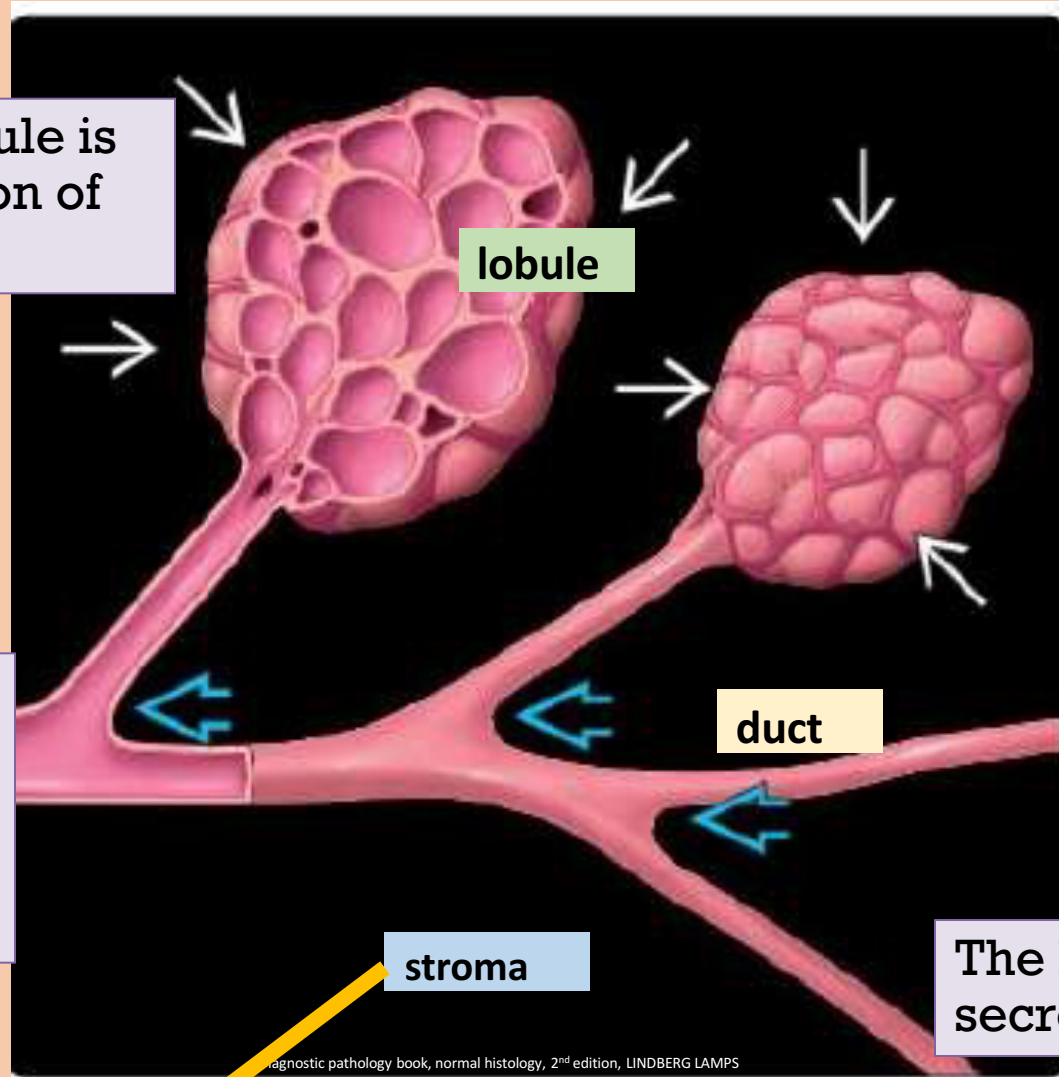2. Non-epithelial (stromal) structures: stroma and fat (adipose tissue)
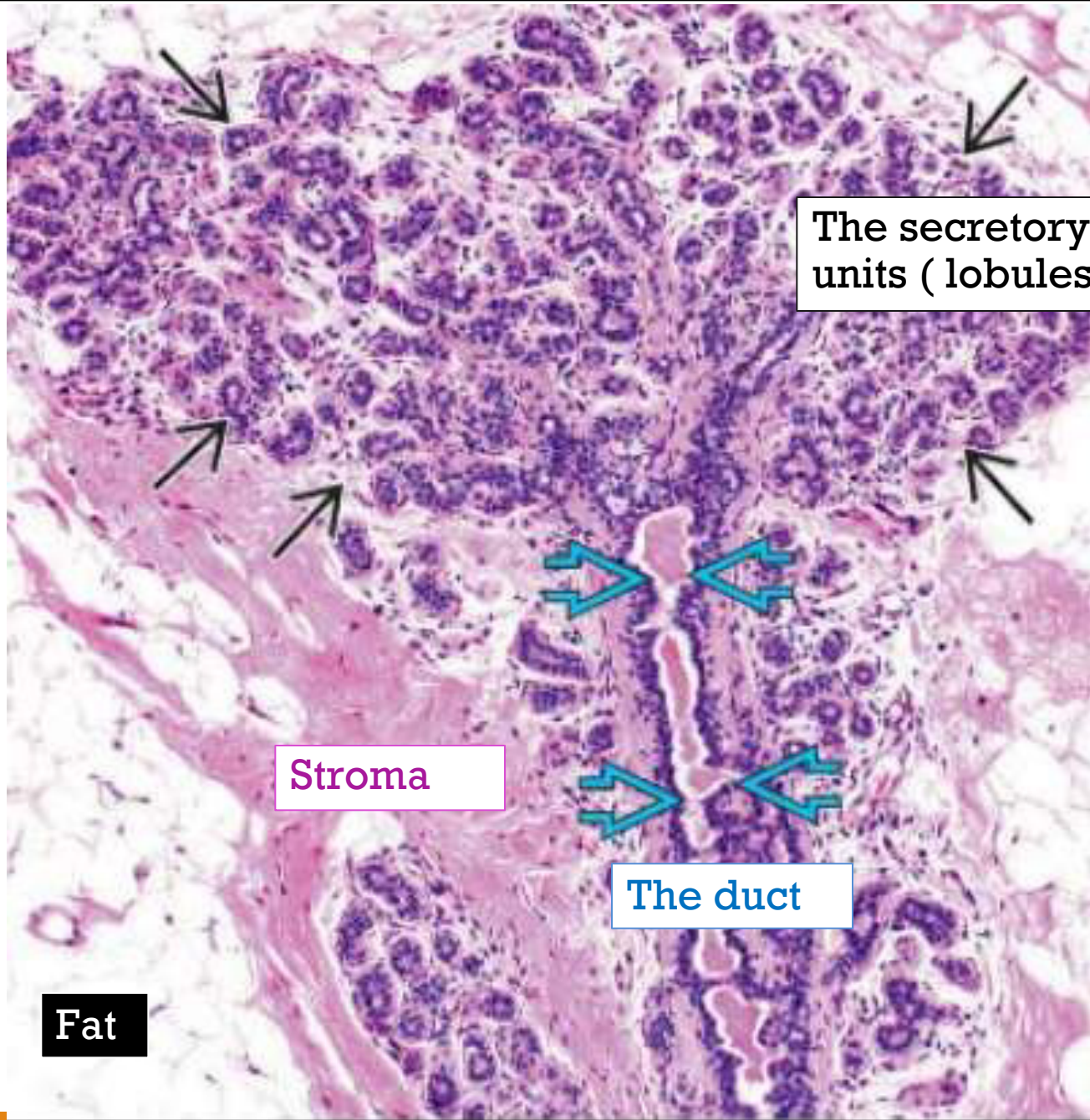
The secretory units (lobules

Stroma

The duct

Fat

The lobule is collection of acini

lobule

Then the ductal system will transfer the secretions into the nipple

duct

stroma

Diagnostic pathology book, normal histology, 2nd edition, LINDBERG LAMPS

The lobules will give the secretions into the ducts

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

Fibroadenoma

A disease that affects the stroma of the breast

CLINICAL PRESENTATIONS OF BREAST DISEASE:

❑**Pain**: 90% of painful masses are benign

❑**Inflammation**:

-edema and erythema

-Mostly infections (during lactation). Benign

❑*Nipple discharge* Secretions coming out of the nipple , related to benign lesions , rarely related to malignancy

❑*Palpable masses:* all palpable masses require evaluation. To rule out cancer

❑*Gynecomastia*: Physiological or pathological enlargement of the breast tissue in male

-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**

Of women with cancer:

◦ about 45% have <u>symptoms</u>

◦ Palpable mass>>>> pain> nipple discharge > inflammatory changes

◦ the remainder come to attention through <u>screening</u> tests
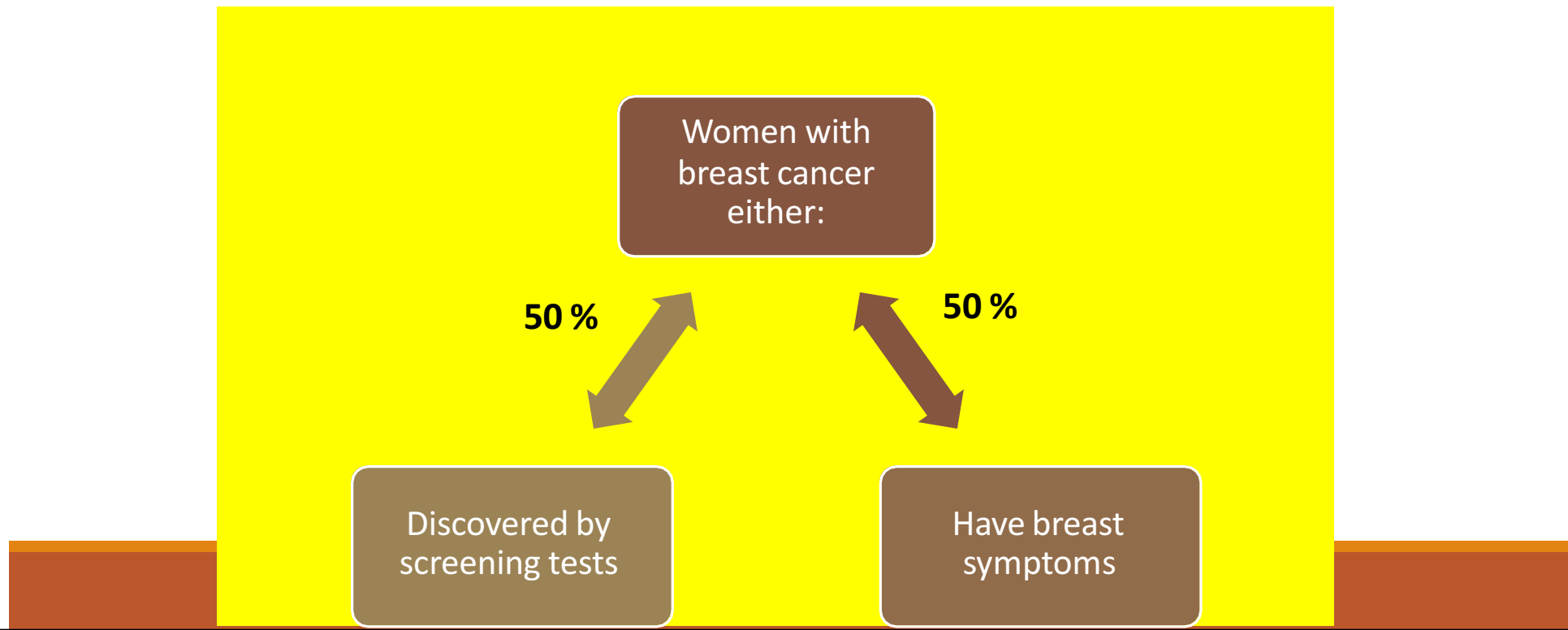
Women with breast cancer either:

50 %

50 %

Discovered by screening tests

Have breast symptoms

Mammographic screening:

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

- average size of cancer detected by mammography is ≈ **1 cm** (lower chance for metastasis to regional lymph nodes)

So helped to reduce morbidity & mortality associated with breast cancer
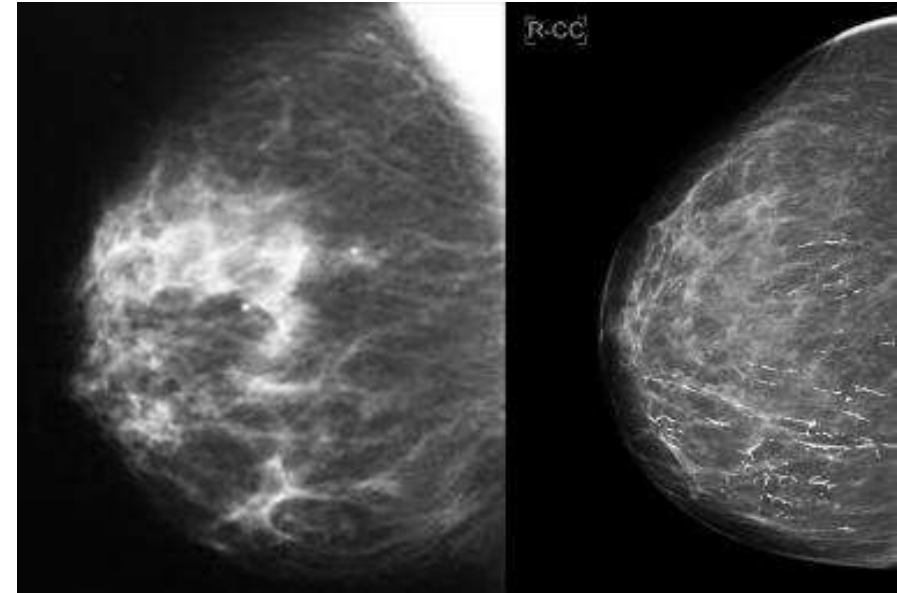
From the important things wanted to be evaluated is whitish densities & micro calcifications (not our topic)

Topics covered in this lecture

- **Benign stromal lesions**

  - Fibroadenoma

- **Benign epithelial lesions**
  - **Nonproliferative changes**
  - **Proliferative disease without atypia**
  - **Proliferative disease with atypia**

- **Malignant epithelial lesions**

  - in situ carcinoma

  - invasive carcinoma

Fibroadenoma

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

o Related to **estrogen activity**:
  ◦ may enlarge during pregnancy.
  ◦ After menopause usually regress and calcify.

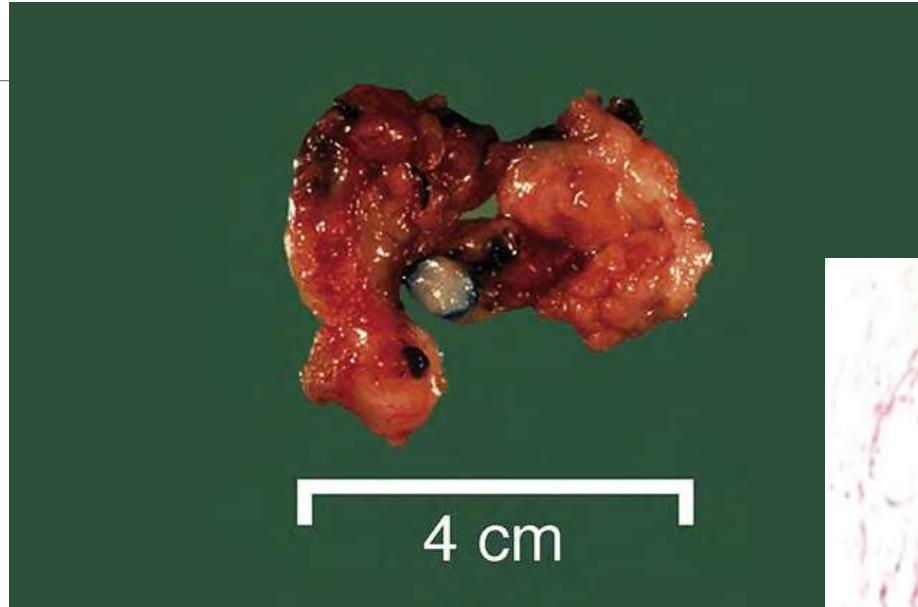o Peak: 20s and 30s | Young females in their productive period of life |

discrete, usually solitary, freely movable nodule, (<10 cm).
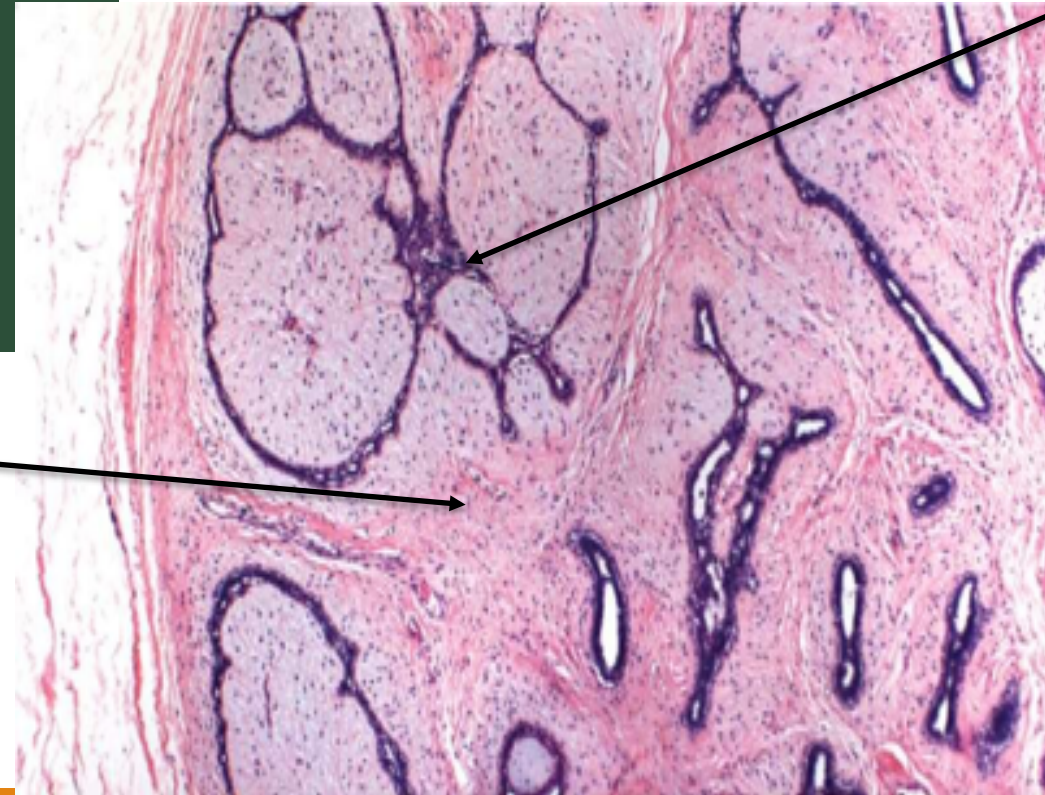
- usually easily "shelled out" surgically. | Without more invasive surgery |

Fibroadenoma

The neoplastic structure is the stroma

Entrapped ducts, not part of the tumor , they're normal epithelial structures that have been trapped in the growing stroma

4 cm

The stroma is growing having mitosis & proliferation—> enlargement in size
The lesion is discrete & circumscribed with sharp borders

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ممكن تيجي بالعملي

Benign Epithelial Lesions

This classification is to estimate the risk of having breast cancer, they're benign lesions but they may increase the risk of breast cancer
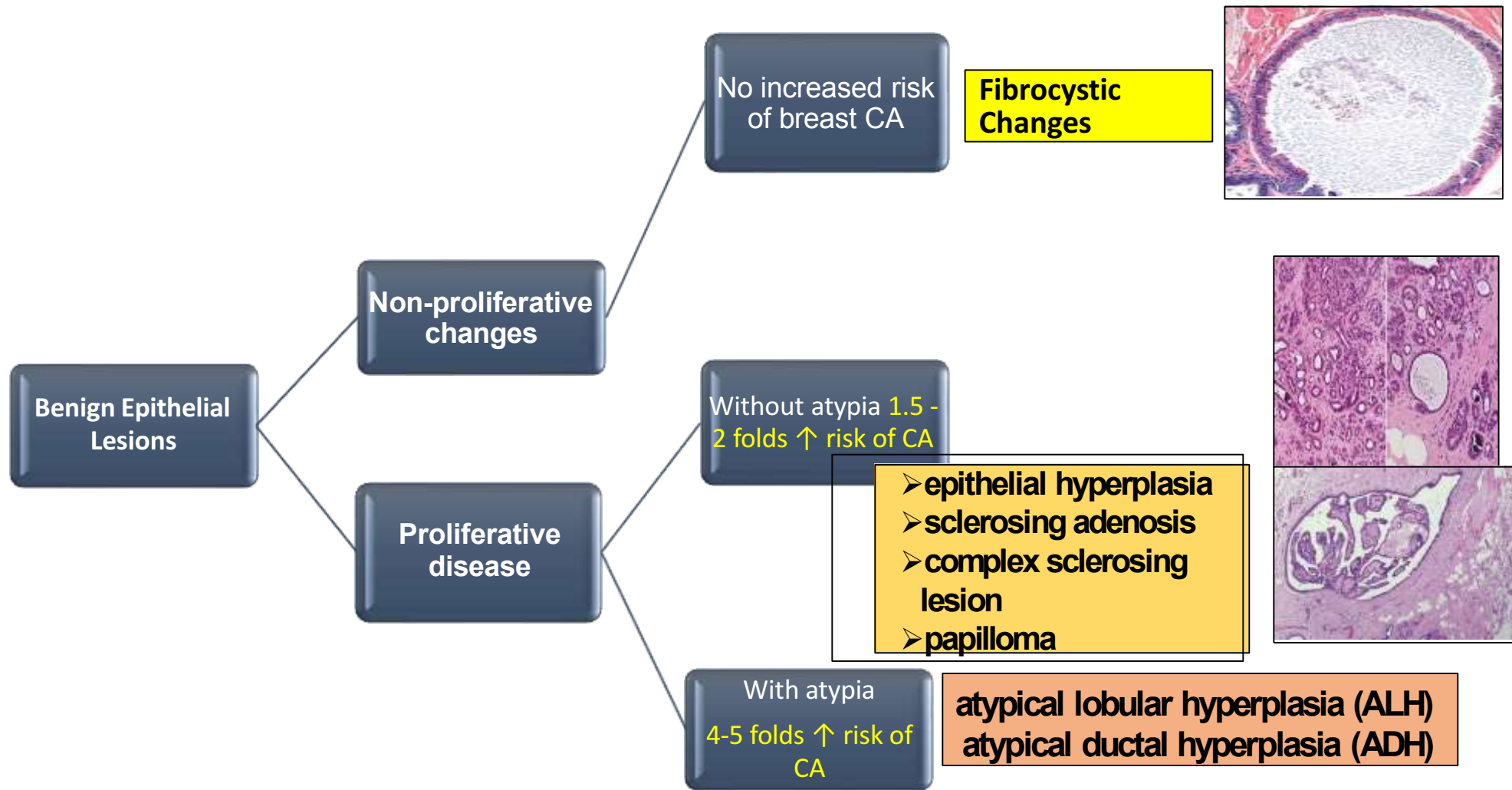
Divided into three groups:

1Nonproliferative changes: (no associated increased risk of breast cancer)

Without significant epithelial cells proliferation

2Proliferative disease without atypia: (1.5-2 folds increase risk of breast cancer)

There's proliferation without atypia

3Proliferative disease with atypia: (4-5 folds increase risk of breast cancer)

Benign Epithelial Lesions

Non-proliferative changes

No increased risk of breast CA

Fibrocystic Changes

Proliferative disease

Without atypia 1.5 - 2 folds ↑ risk of CA

➤epithelial hyperplasia
➤sclerosing adenosis
➤complex sclerosing lesion
➤papilloma

With atypia
4-5 folds ↑ risk of CA

atypical lobular hyperplasia (ALH)
atypical ductal hyperplasia (ADH)

# Non-proliferative Breast Changes (Fibrocystic Changes)

-Common

Symptoms: tenderness and pain usually cyclical with the menstruation

-3 principal morphologic changes:

(1) cystic change: with apocrine metaplasia (most common)

(2) Fibrosis

(3) Adenosis (lobules look more prominent without increased number of layers of cells)

No cell proliferation & no increased risk for breast cancer
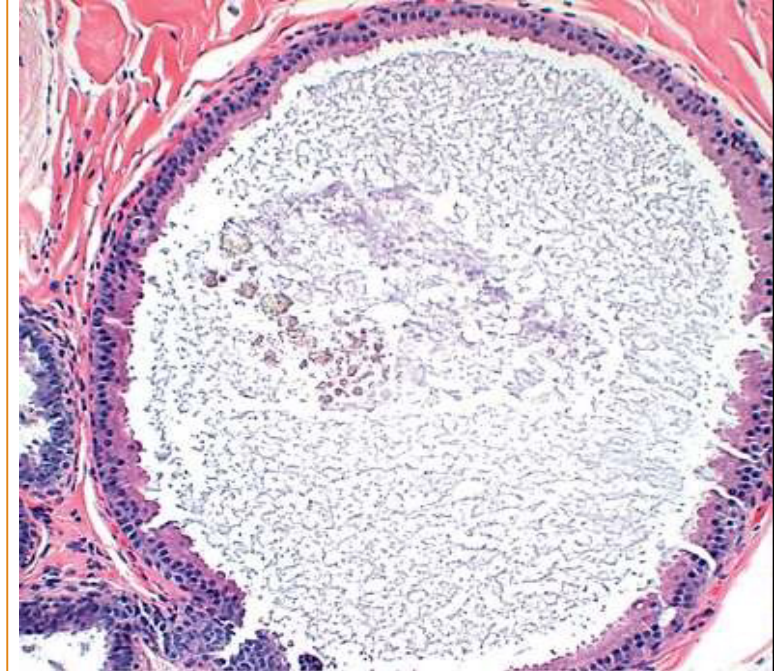
Proliferative lesions without atypia

Includes:

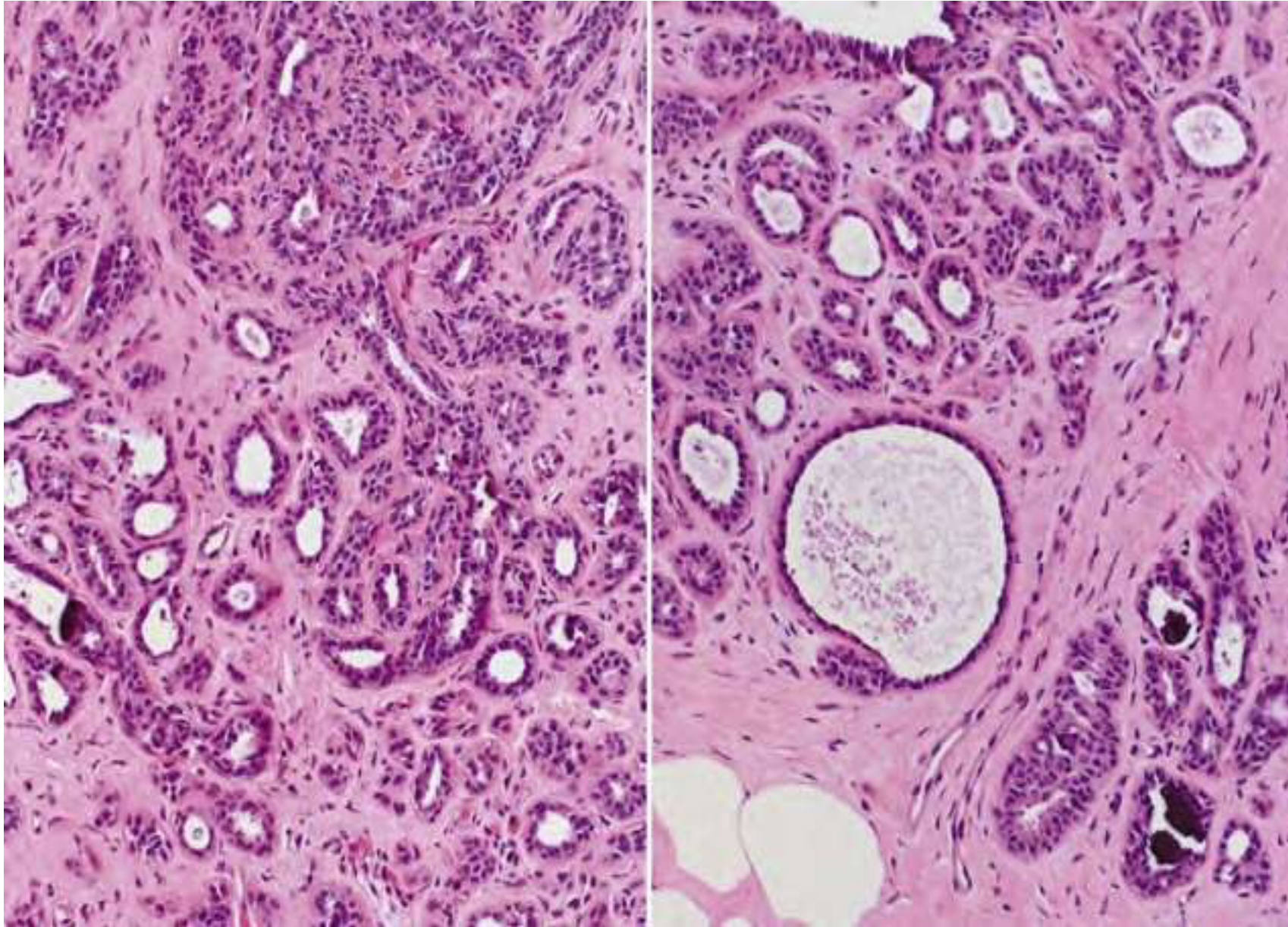epithelial hyperplasia

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

Glands are prominent (the number of lobules is increased but the structure is normal)
no. of layers is normal without atypia surrounded by stromal reaction and fibrosis

intraductal papilloma in a breast duct

Finger like growth inside the duct

Proliferative Disease With Atypia

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

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

Breast Cancer...Epidemiology

The most common malignancy of women

Among the most common causes of cancer deaths in women

mortality rate dropped dramatically (improved screening and more effective treatment) Chemotherapy, radiotherapy, immunotherapy & hormonal therapy

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 <u>first-degree</u> relatives with <u>early-onset</u> breast cancer.

To be significant family history = first degree + early onset (30s to 40s)

Pathogenesis

Factors contributing directly can be grouped into:

Genetics: BRCA1 and BRCA2; TP53; PTEN (loss) ; 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 increased exposure to estrogenic stimulation.

Estrogen is implicated but progesterone is protective

Environmental

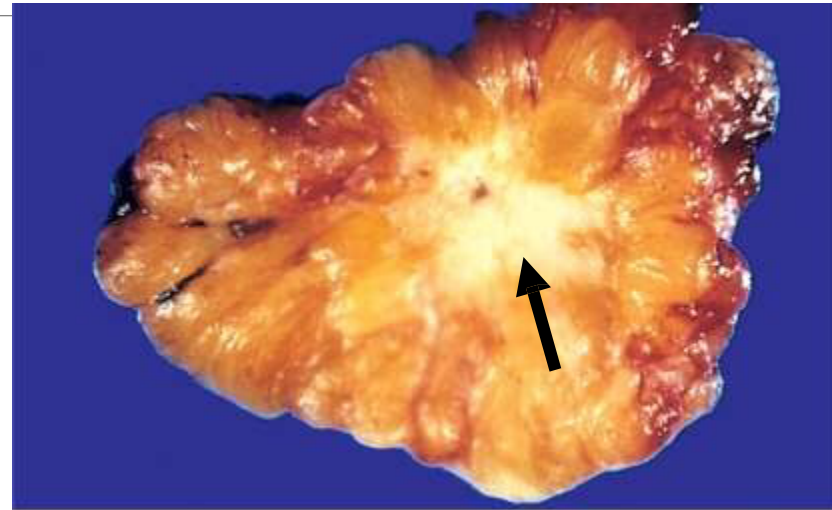Cigarettes smoking , morbid obesity, lifestyle

Morphology:

Location:

upper outer quadrant (50%)

central portion –subareola (20%)

Lower outer quadrant 10%

Upper inner quadrant 10%

Lower inner quadrant 10%

Breast Carcinoma- Histologic Types

A. Noninvasive (insitu) :(the presence of malignant glands inside the ducts or lobules 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): | Histologic variants |
1. Invasive ductal carcinoma- NOS (not otherwise specified) (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

LOBULAR carcinoma in-situ (LCIS)

- Malignant clonal proliferation of cells within lobules

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

Regarding the material that is produced inside these ducts which come from necrosis

Ranges from low to high nuclear grade (pleomorphic).

In Situ Carcinoma - Management:

A patient came to the clinic suffering from a palpable mass in her right breast, the Dr did a physical examination to the mass then ordered a mammogram to look for the abnormalities, the Dr noticed ill-defined whitish irregularities in the outer upper quadrant , so she is suspecting breast cancer, what is the next step?
Biopsy using true cut procedure, under microscope the pathologist saw the pic to the right so what is the diagnosis? Comedo DCIS ….Is it cancer or not? Yes it's cancer but not invasive

excellent prognosis (97% long-term survival after simple mastectomy)

So using mammogram and detecting the lesions as early as possible is very important

treatment strategies: surgery (eg; wide local excision) ; irradiation tamoxifen ,

Significance: adjacent invasive CA; become invasive if untreated (1/3 of cases)

Depending on the case we decide the best treatment, among the used treatments in breast cancers: radical mastectomy (removal of the breast + ipsilateral lymph nodes) , chemotherapy, hormonal therapy , immunotherapy
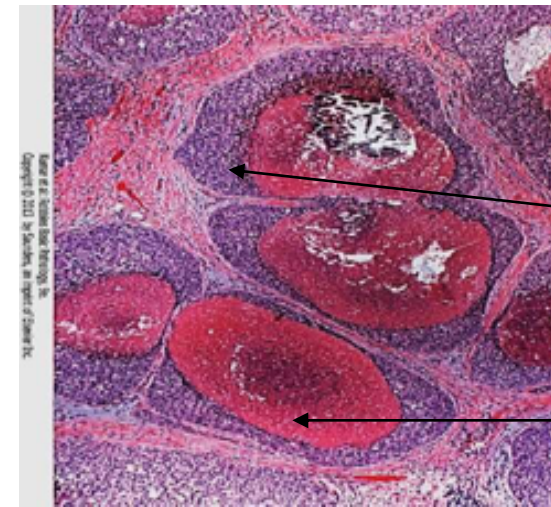
The duct is swollen, dilated and full of cells with producing of pinkish material from necrosis

Comedo type DCIS

Important

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:

✓ ER positive (HER2 negative; ≈ 60%) | Estrogen antagonists could be used as a treatment

✓ HER2 positive (ER positive or negative; 20%)

✓ Triple negative (ER, PR, and HER2 negative; 10%) | Aggressive, needs other methods of treatments
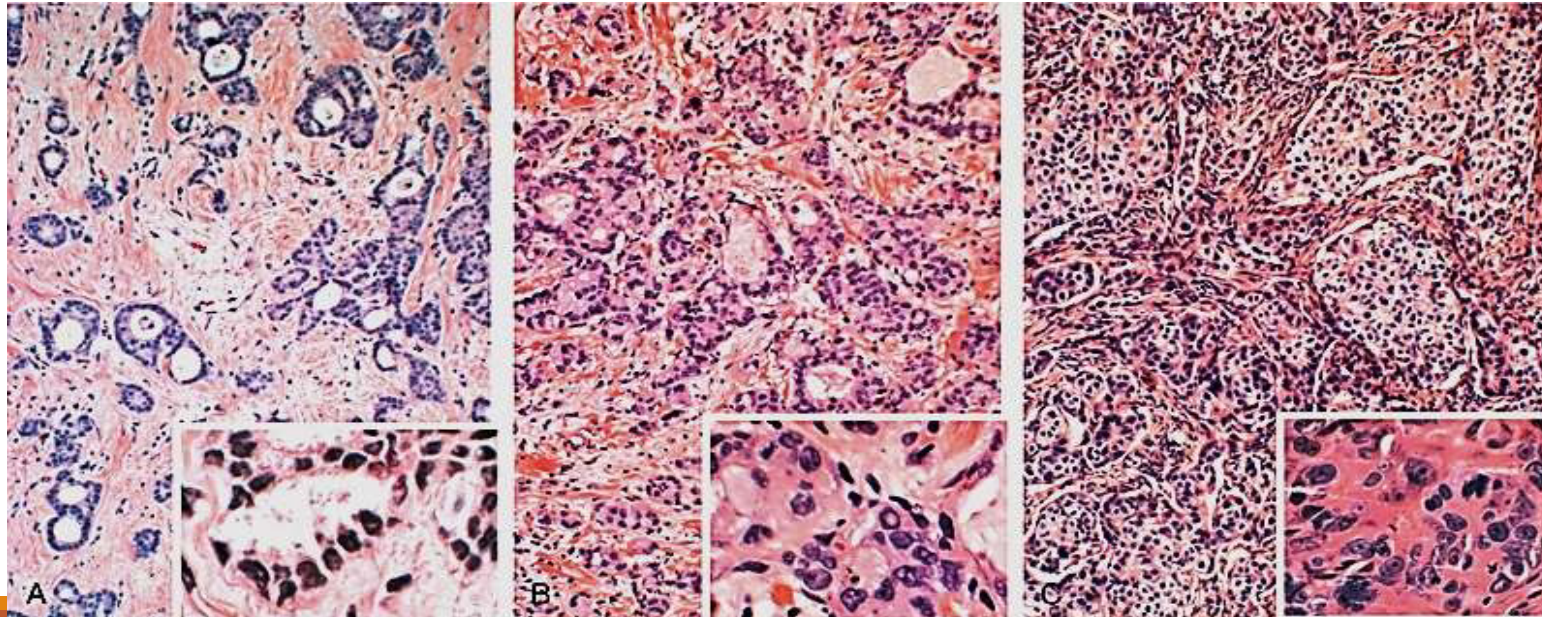
Invasive Ductal Carcinoma

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

Precancerous lesion: usually DCIS

Receptor profile:

Usually: ER (+), PR (+); HER2 (-); wide range of differentiation(grades)

Kumar et al: Robbins Basic Pathology, 9e.
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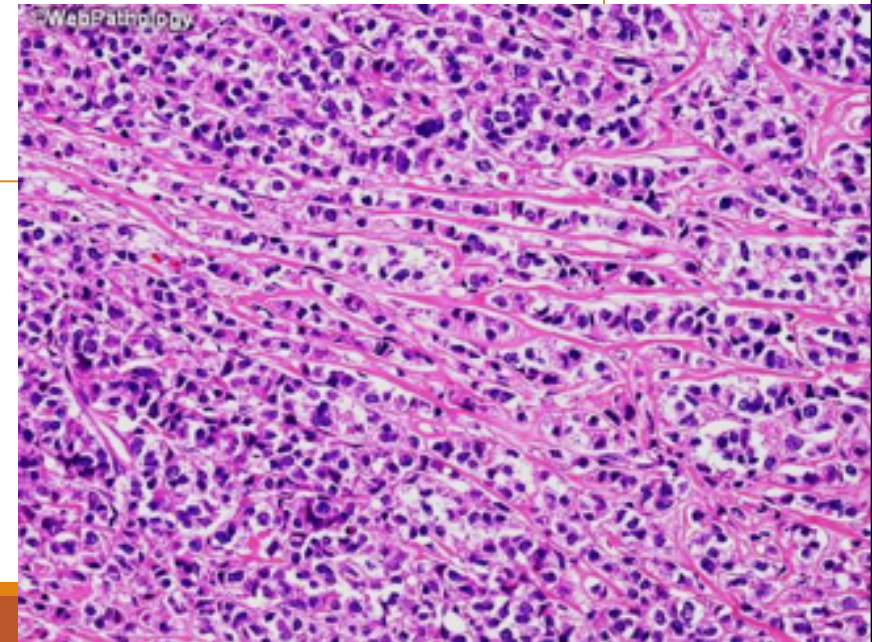
Invasive lobular carcinoma

≈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.

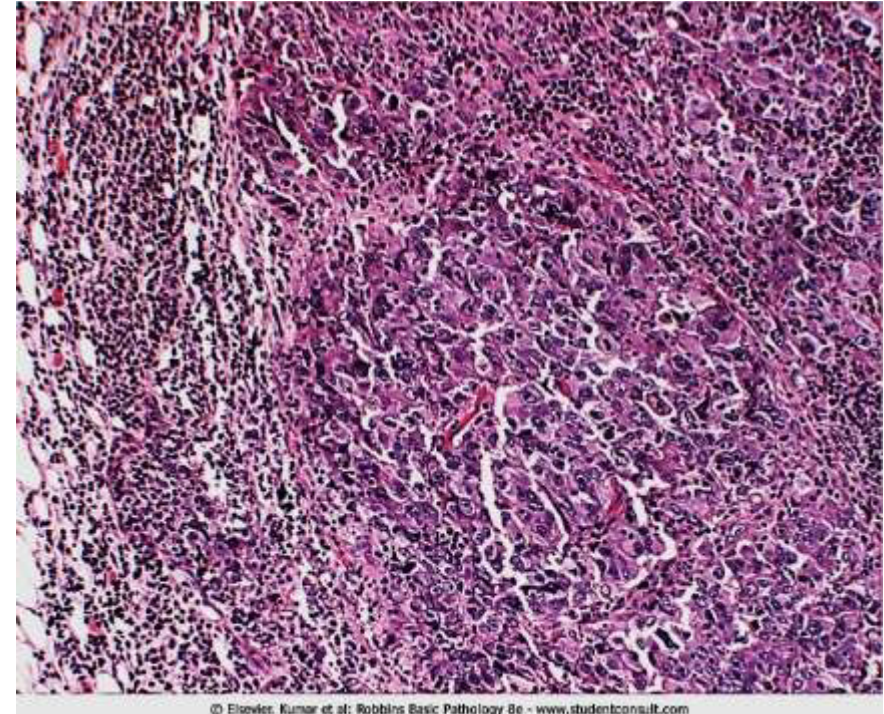# Carcinoma with Medullary features:

5%

Triple negative (ER, PR, and HER2 all negative).

large anaplastic cells with lymphocytic infiltrate.

usually **absent** Precancer
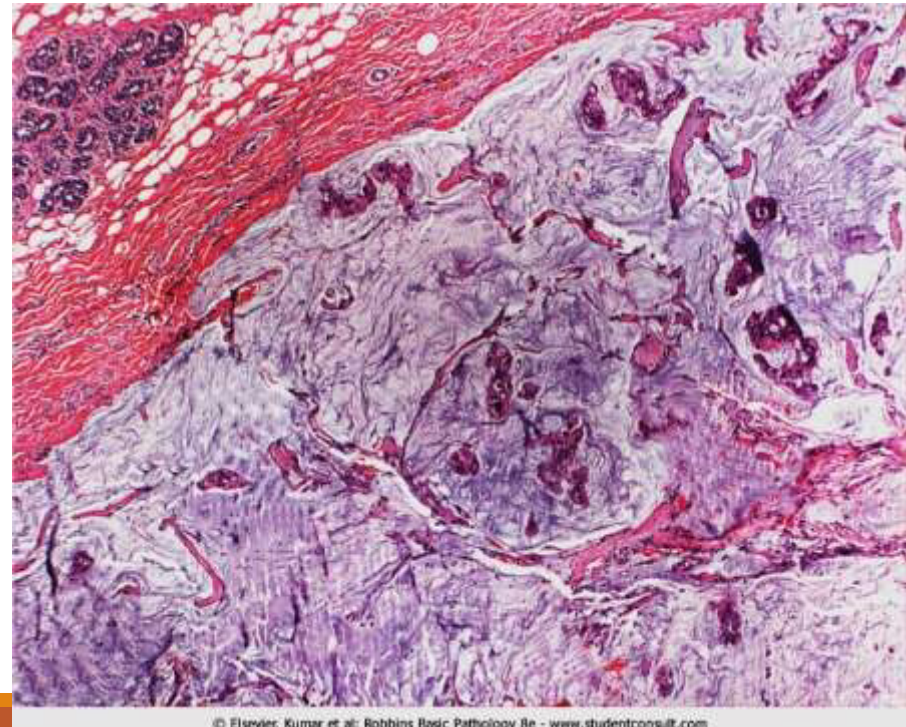
↑in women with **BRCA1** mutations.

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Colloid (Mucinous) Carcinoma

Rare

abundant extracellular mucin (blue)

soft and gelatinous mass

ER-positive

HER2- negative

Tubular carcinomas
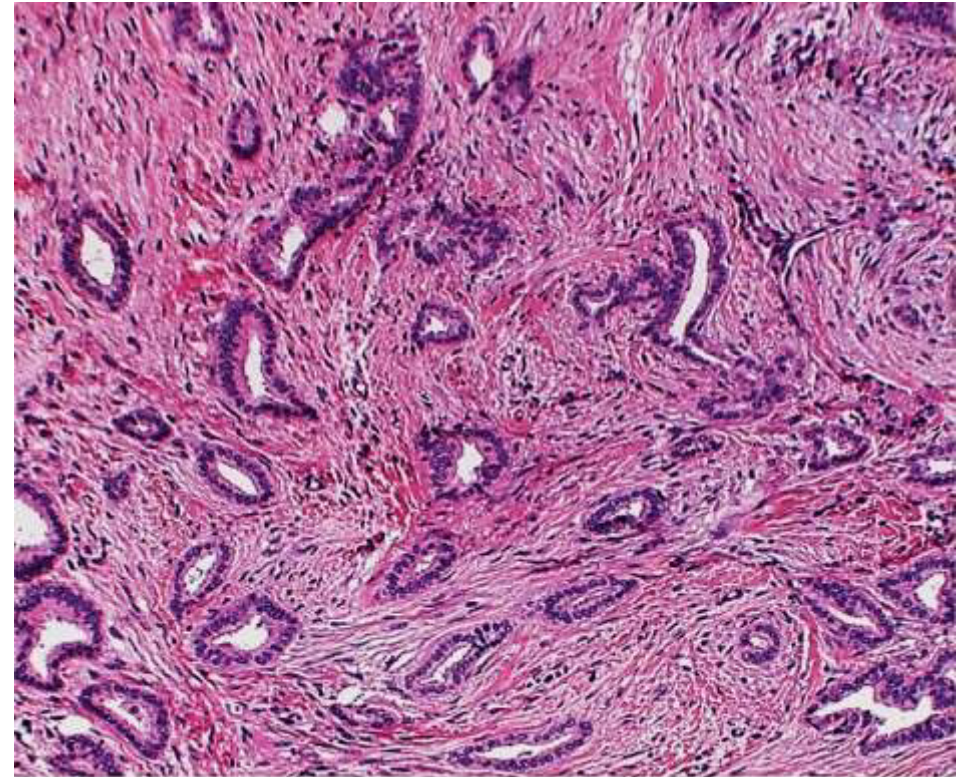
< 5 % (the least common)

irregular mammographic densities.

well-formed tubules;low-grade nuclei

Lymph node mets: rare

Prognosis: excellent.

ER-positive

HER2- negative

through **lymphatic** (starting from ipsilateral axillary lymph nodes) **and hematogenous** channels.

So Removal of the axillary lymph nodes is a crucial part of the radical mastectomy procedure

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 (patients need follow up)

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**