# Breast Pathology

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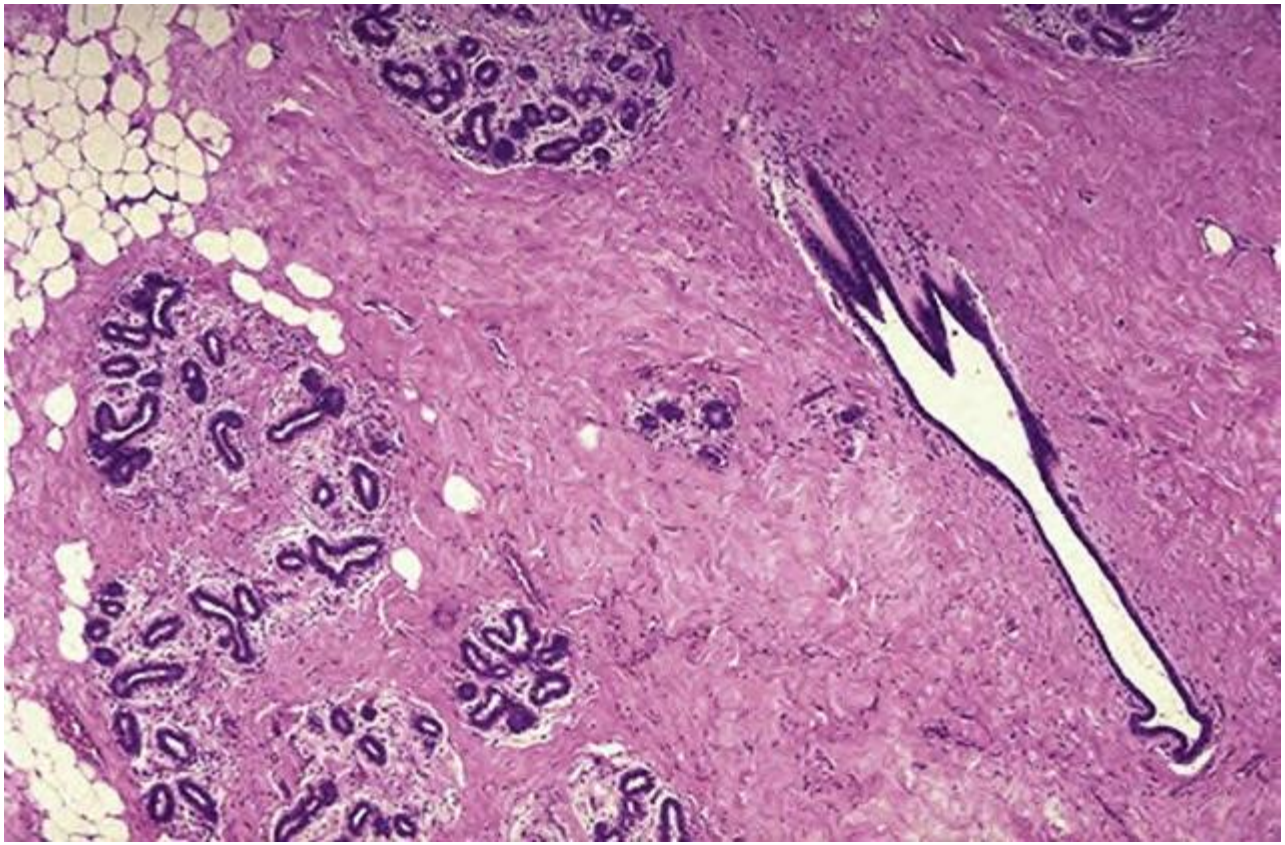
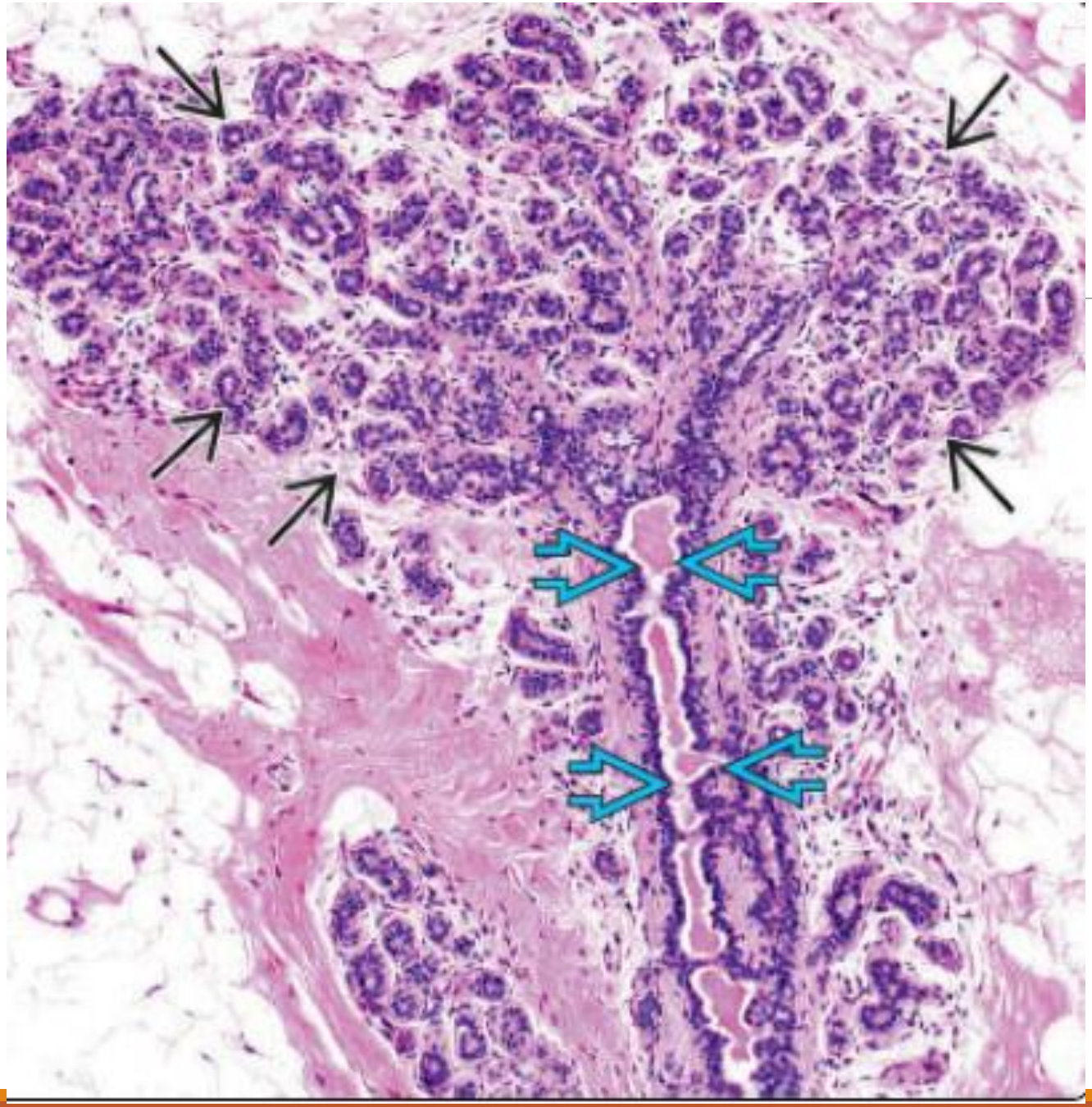
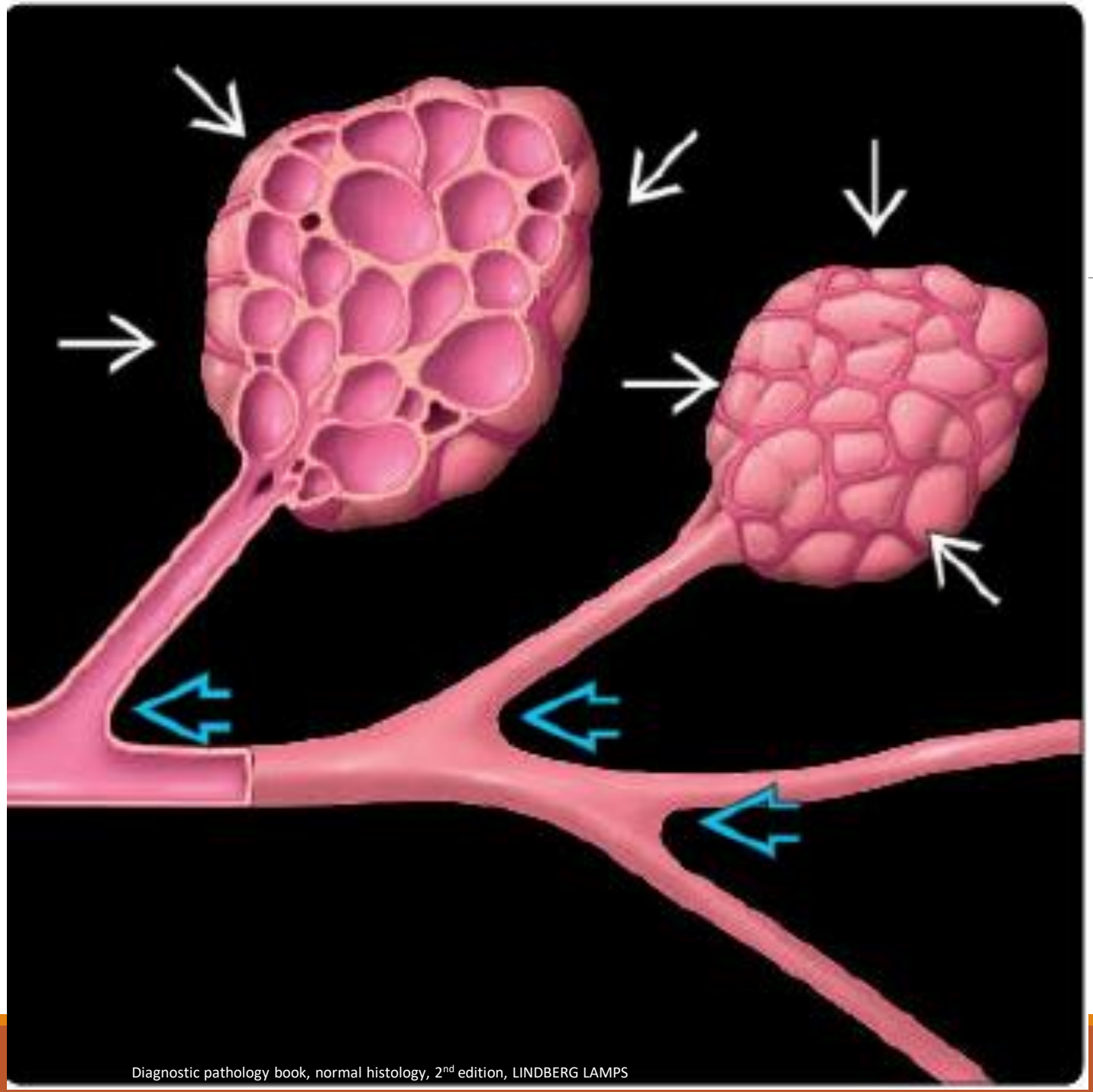
# Normal breast, microscopic







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

# Regardless of the symptom:

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

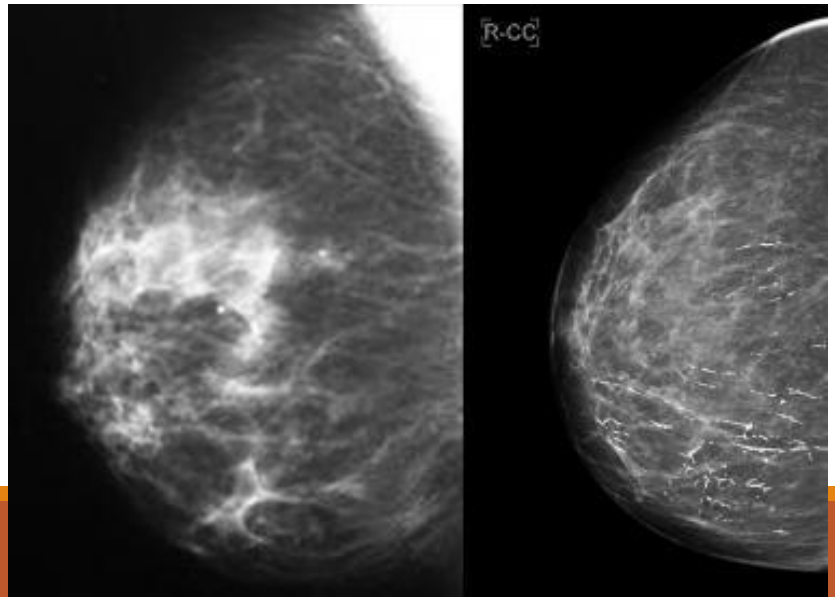
# Of women with cancer:

- about 45% have symptoms
  - Palpable mass>>>> pain> nipple discharge > inflammatory changes
- the remainder come to attention through screening tests

# Mammographic screening:

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

the average size of cancer detected by mammography is **≈ 1 cm** (<15% have mets to regional lymph nodes)



# 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****:*

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

-imbalance of estrogens, which stimulate breast tissue,.

# Fibroadenoma

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

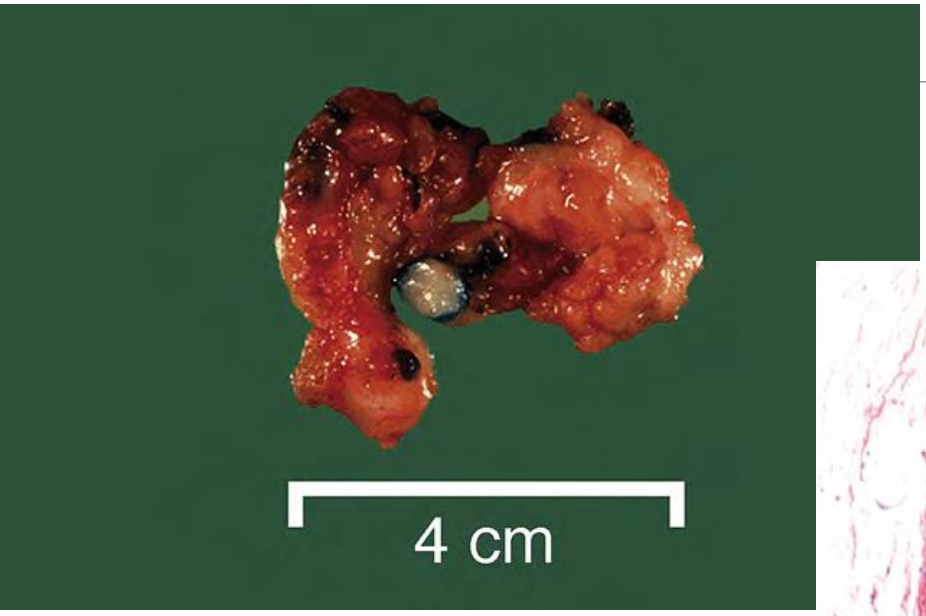
- Related to **estrogen activity**:
  - may enlarge during pregnancy.
  - After menopause usually regress and calcify.

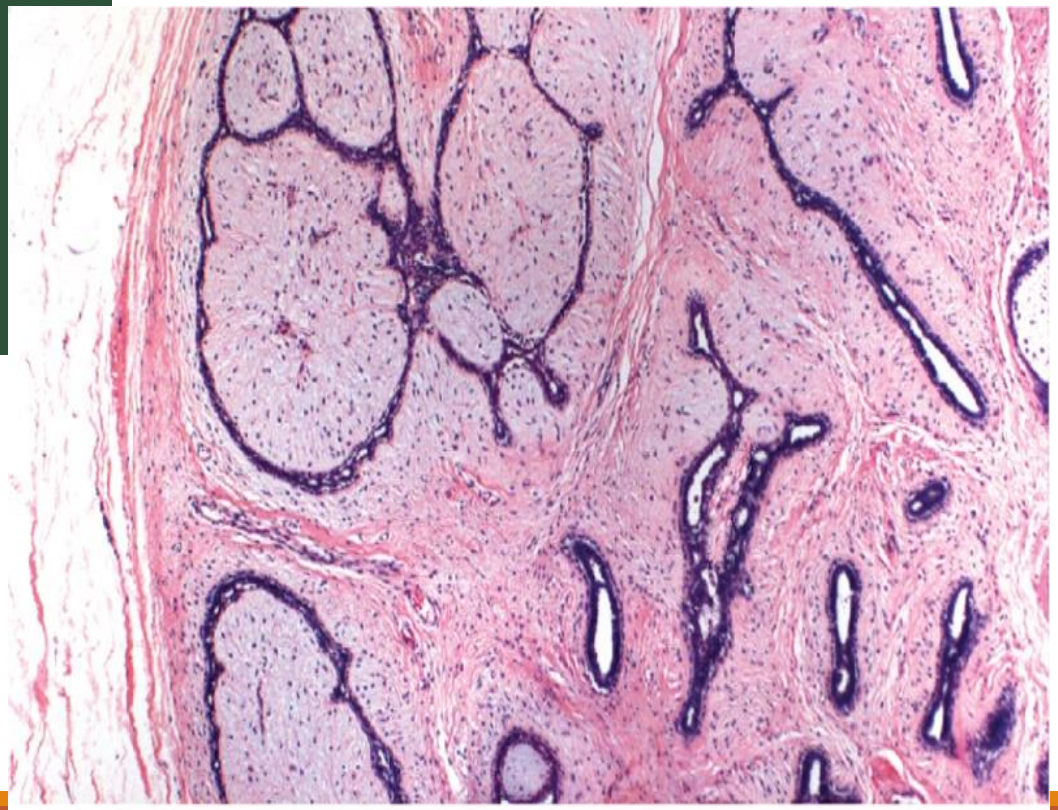
- Peak: 20s and 30s

discrete, usually solitary, freely movable nodule, (<10 cm).

- usually easily "shelled out" surgically.

# Fibroadenoma



# benign epithelial lesions:

divided into three groups:

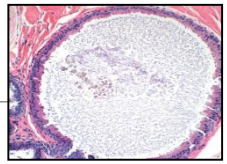
- **Nonproliferative changes**: not associated with an increased risk of breast cancer

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

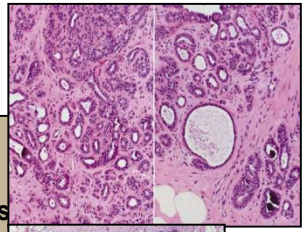
- **Proliferative disease with atypia**: (associated with 4-5 folds increase risk of breast cancer)

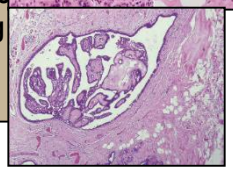
**Benign Epithelial Lesions**

- **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)

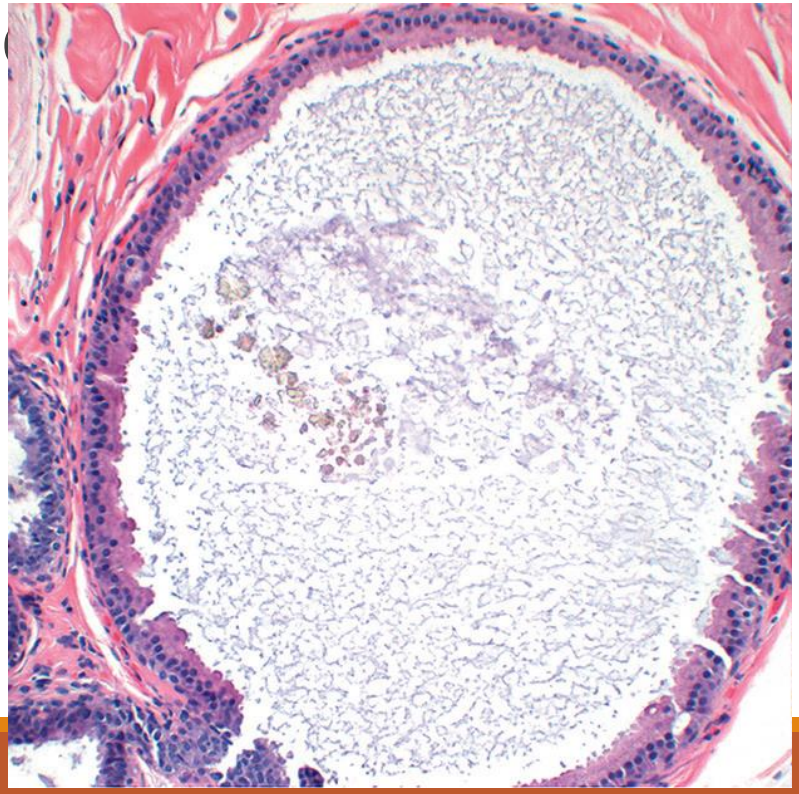
-Common

-3 principal morphologic changes:

(1) cystic change: with apocrin common)

(2) Fibrosis

(3) adenosis



# Proliferative disease without atypia

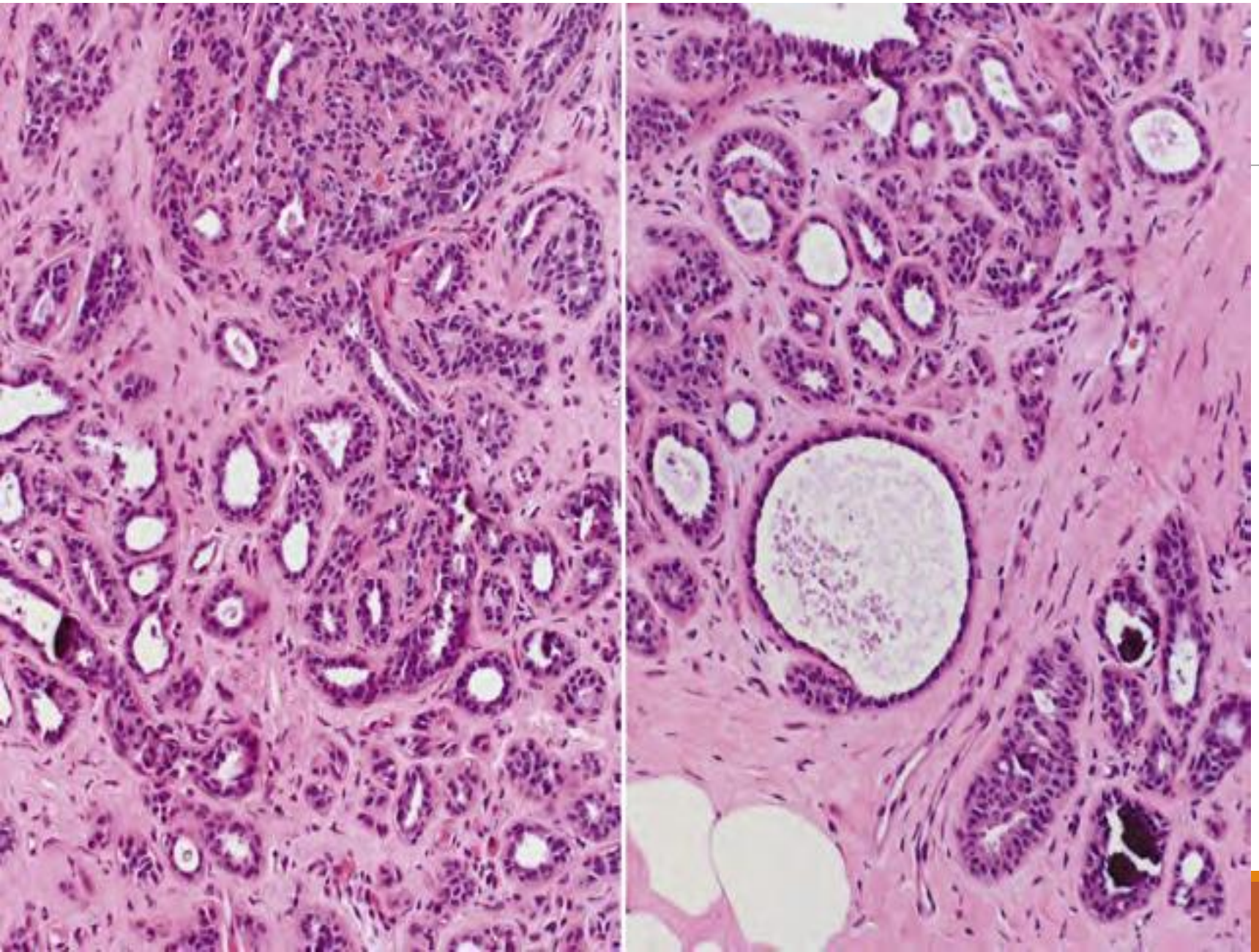
Includes:

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

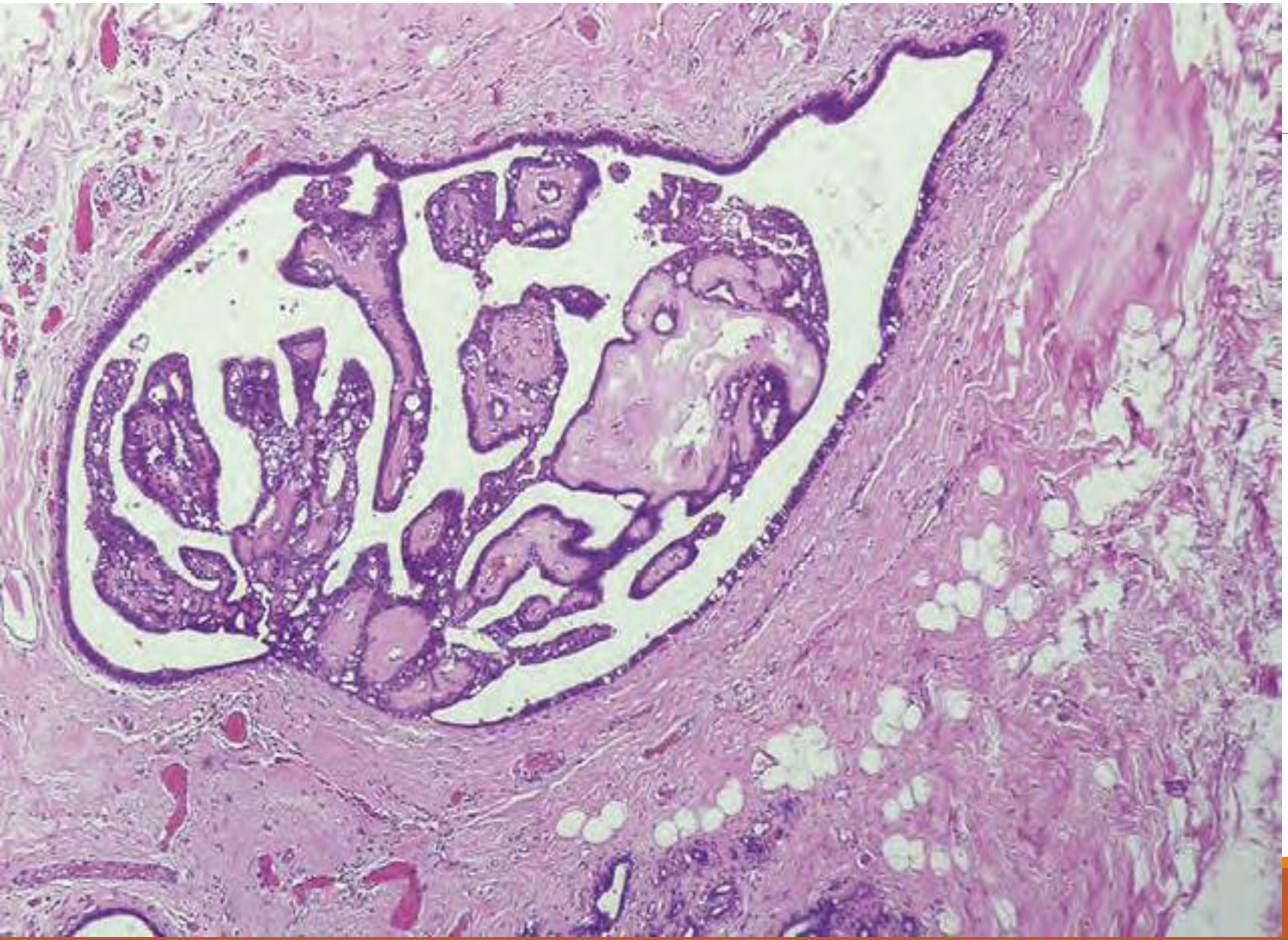
**- associated with a small increase in the risk of subsequent carcinoma in either breast.**

- 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

# 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

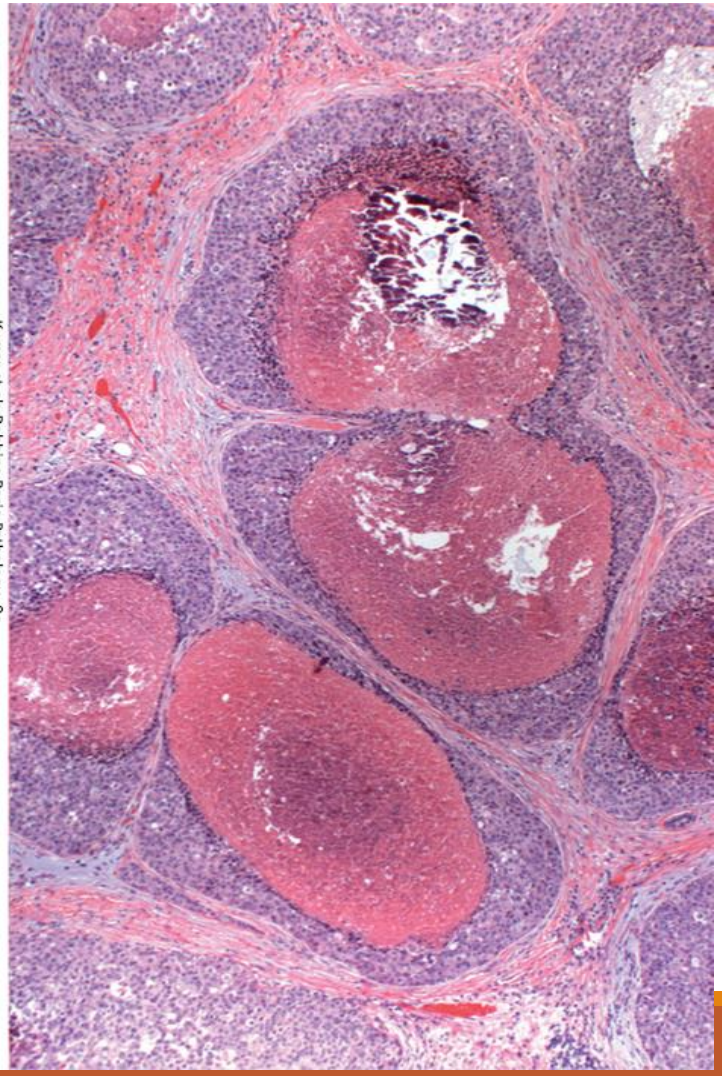
- Ranges from low to high nuclear grade (pleomorphic).

**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 **afte**r simple mastectomy)
- treatment strategies: surgery; irradiation tamoxifen
- Significance: adjacent invasive CA; become invasive if untreated (1/3 of cases)



# 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)
- Almost all breast malignancies are adenocarcinomas (>95%)

# 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% )
- 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%)
- central portion –subareola (20%)
- Lower outer quadrant 10%
- Upper inner quadrant 10%
- Lower inner quadrant 10%

# Breast carcinoma- histotypes

## 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

# Invasive ductal carcinoma

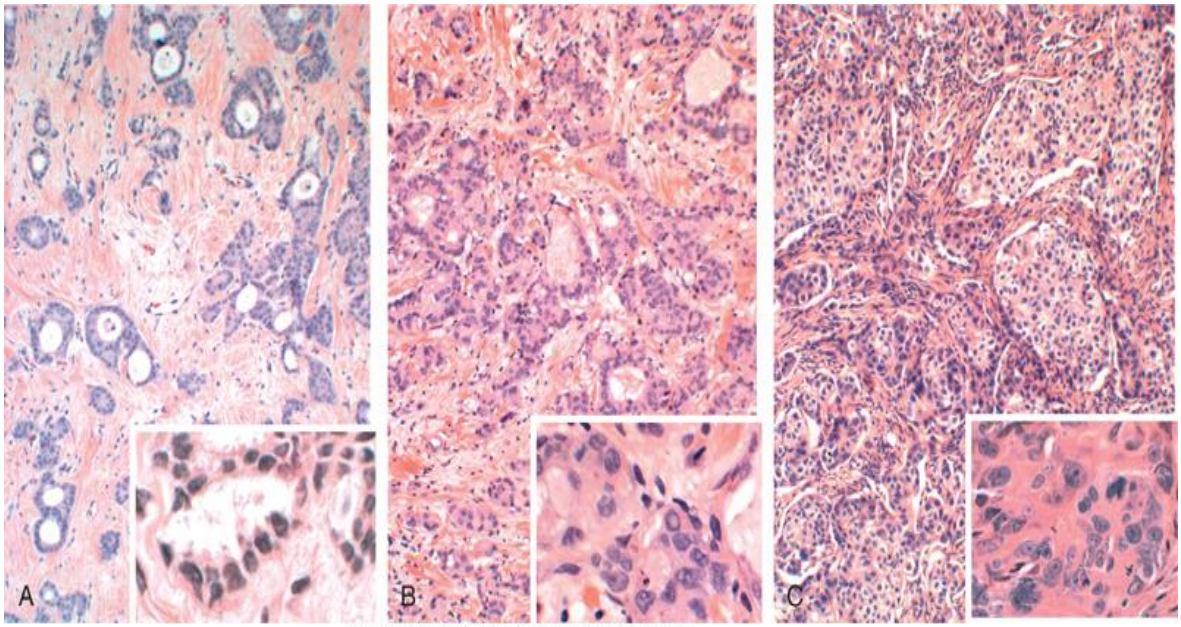
Also called **Carcinomas "not otherwise specified"**

**Precancerous lesion**: usually DCIS

**Receptor profile**:

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

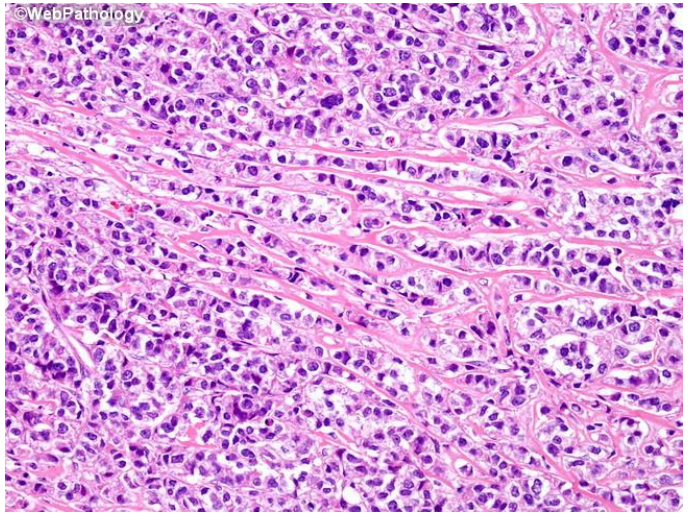
A wide range of differentiation (grades)




Kumar et al: Robbins Basic Pathology, 9e.

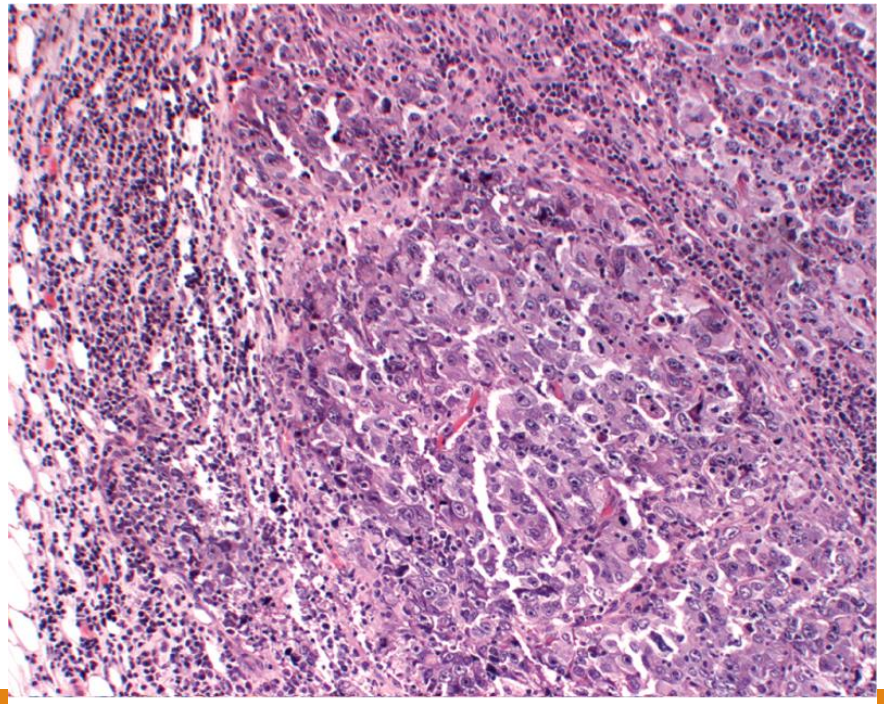
# Invasive lobular carcinoma

- ≈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:

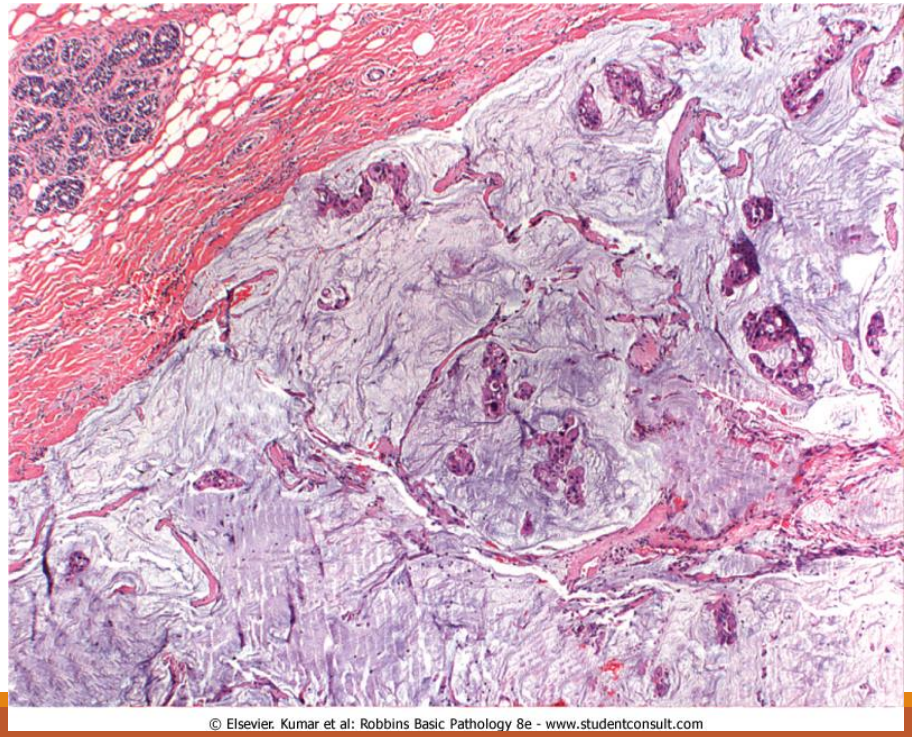
- 5%
- **Triple negative (ER, PR, and HER2 all negative).**
- large anaplastic cells with with lymphocytic infiltrate.
- usually **absent** Precancer
- ↑in women with *BRCA1* mutations.



# Colloid (mucinous) carcinoma

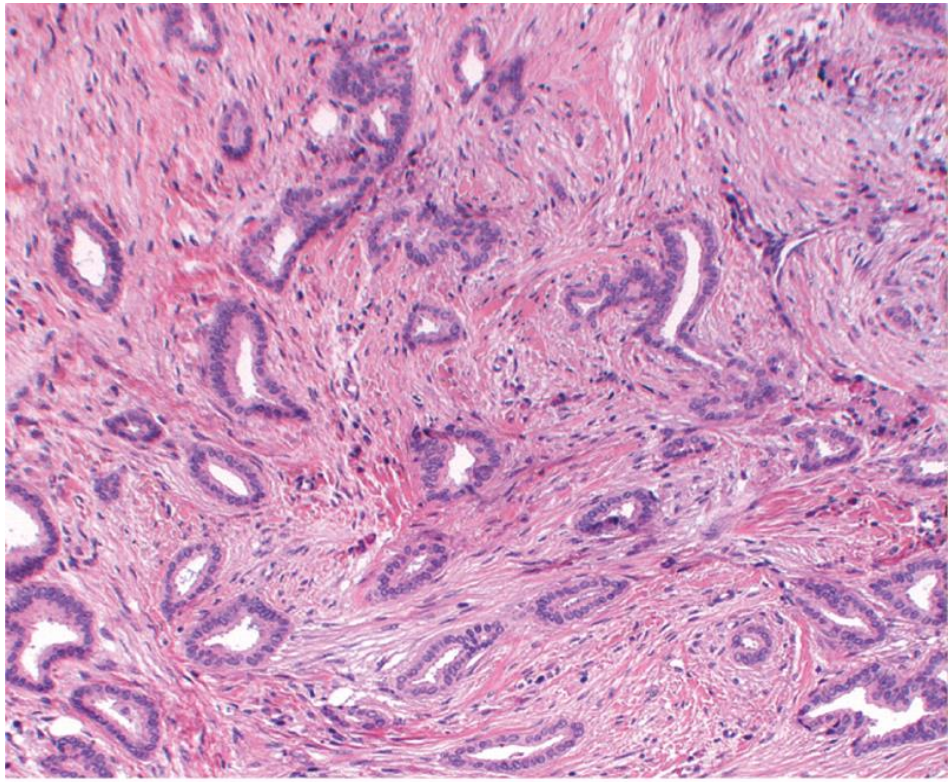
- rare
- abundant extracellular **mucin**
- soft and gelatinous mass

- 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:

- ***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***