Breast disease

DR Ghada Nazar AL-Jussani

MBCHB, FRCPath (UK)

Assistant Professor , Faculty of medicine , Hashemite University

Breast Disease

Clinical presentation of breast disease

- **Pain**:

-cyclic: diffuse, premenstrual edema and swelling.
-noncyclic: Localized, ruptured cyst or physical trauma, or infection
-Almost all painful masses are **benign** except for 10% of cases that relates to cancers

- **Inflammation**:

-causes edematous and erythematous breast.
-most often caused by infections (during lactation and breastfeeding).
-An important mimic of inflammatory breast cancer

- **Nipple discharge:**
- **Normal:** when small in quantity and bilateral.
- **Milky discharges (galactorrhea):**

• are associated with elevated prolactin levels (pituitary adenoma), hypothyroidism, or endocrine anovulatory syndromes, patients taking OCPs, tricyclic antidepressants, methyldopa, or phenothiazines.

- **Bloody or serous discharges**:

▪ commonly due to large duct papillomas and cysts.

▪ During pregnancy, result from the rapid growth and remodeling of the breast.

▪ **BUT spontaneous, unilateral, and bloody discharge increases concern for malignancy**.

❑ Palpable masses:

-95% are benign

-all palpable masses require evaluation.

-**The most common palpable lesions are cysts, fibroadenomas, and invasive carcinomas**

-generally detected when they are 2 to 3 cm in size.

❑Gynecomastia:

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

-resulting from an imbalance between estrogens, which stimulate breast tissue, and androgens, which counteract these effects.

❑ General Consideration in Breast disease

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

▪the risk of nipple discharge being due to cancer increases from 7% in women <60 years vs. 30% in women >60.

▪only 10% of palpable masses in women <40 years are carcinomas vs. 60% in women >50.

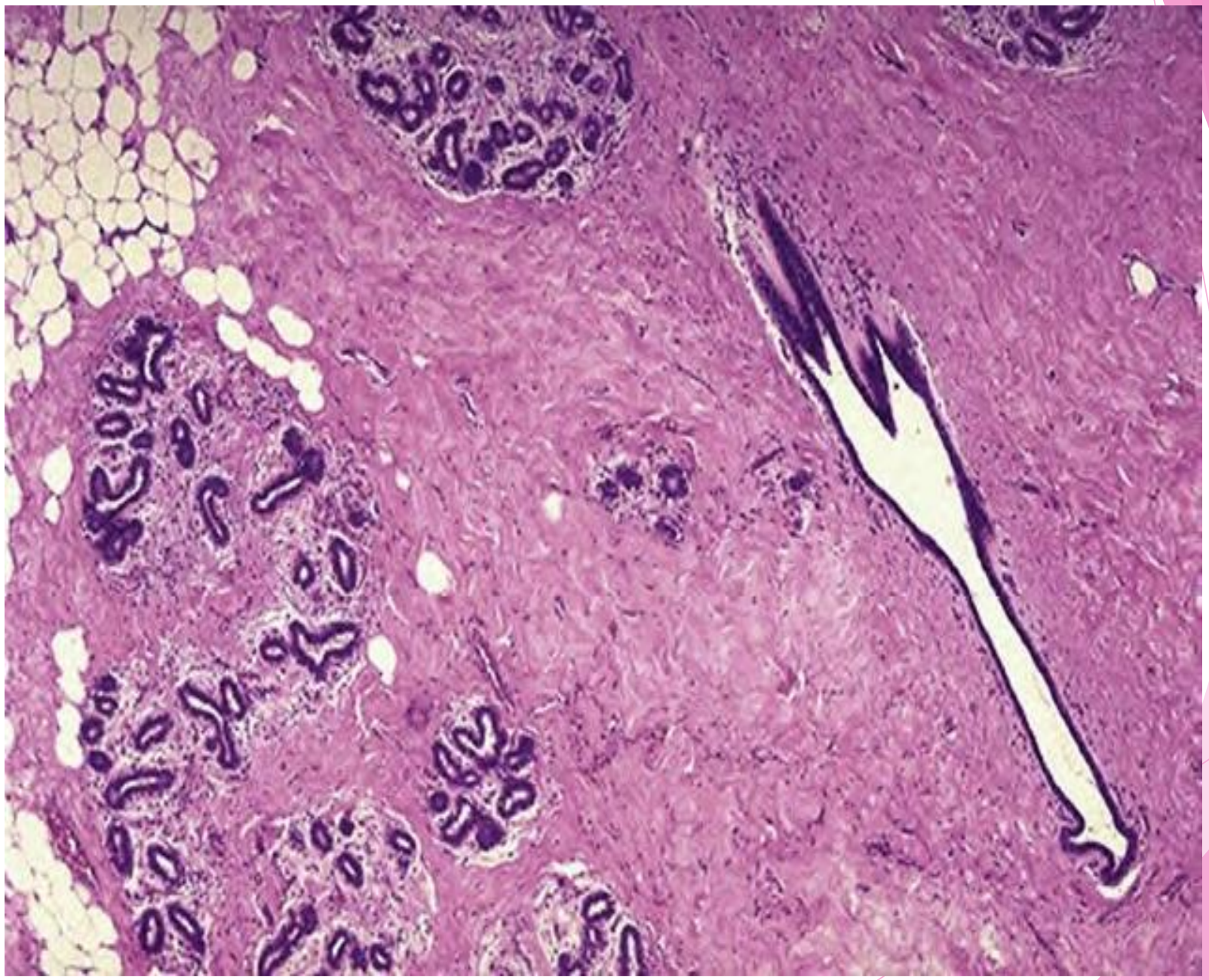
Of women with cancer:

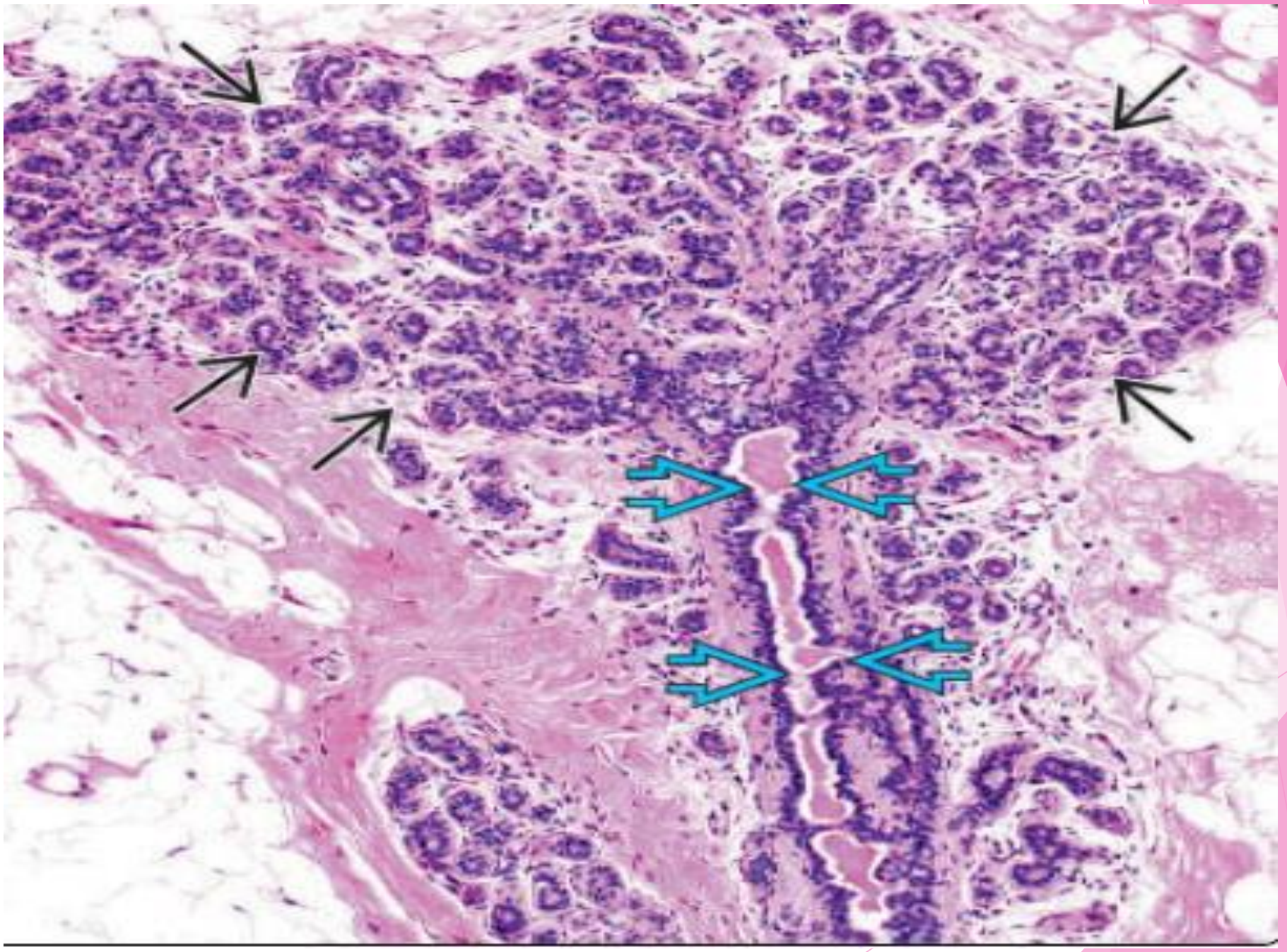
- ❑ about 45% have symptoms
- ❑ Palpable mass>>>> pain> nipple discharge > inflammatory changes
- ❑ the remainder come to attention through screening tests

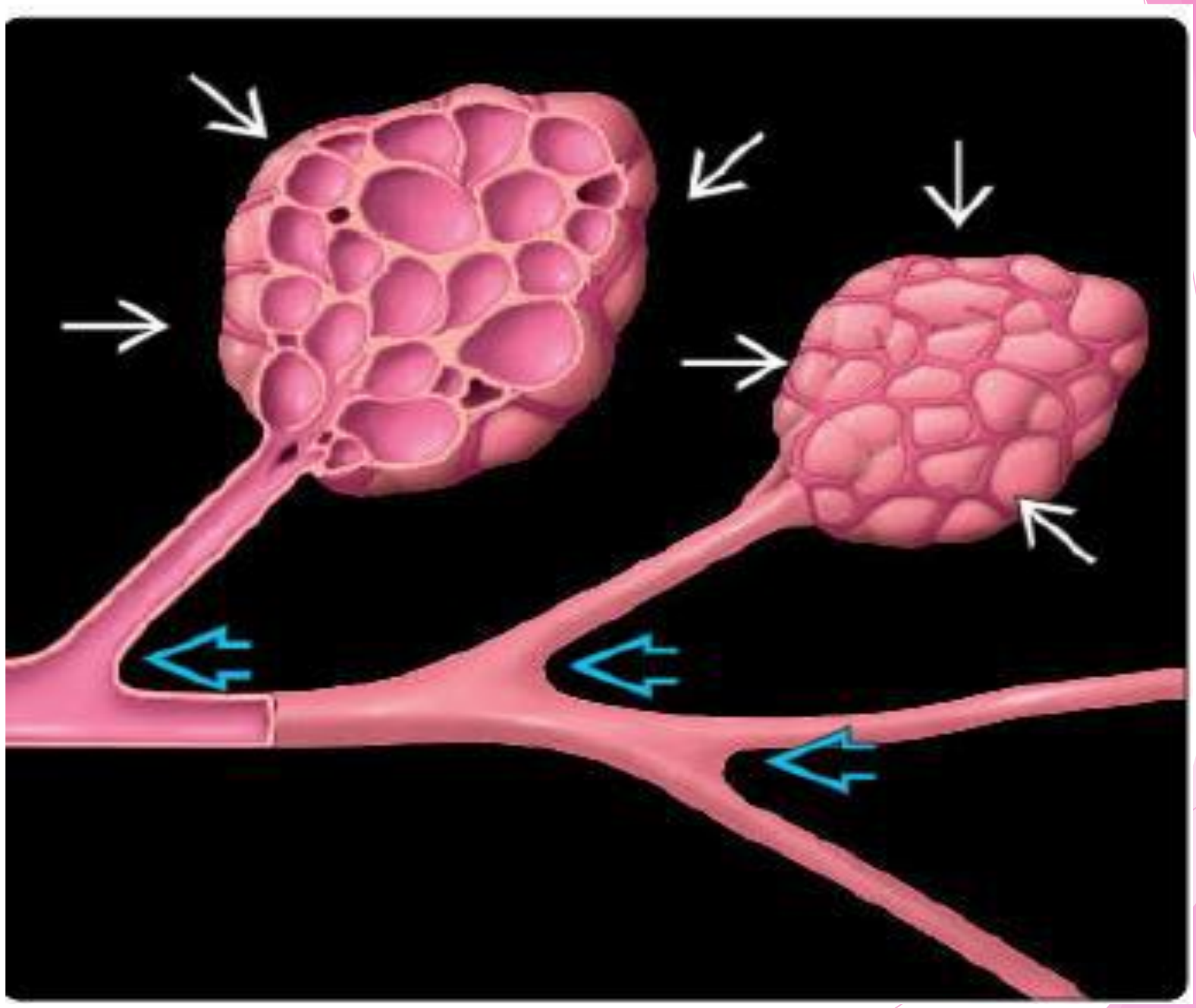
Mammographic Screening

- detects early, non palpable asymptomatic breast carcinomas before metastasis.
- the average size of invasive carcinomas detected by mammography is about 1 cm, at this stage only 15% will have metastasized to regional lymph nodes.

- The sensitivity and specificity of mammography increase with age→due to replacement of the fibrous, radiodense tissue of young women with the fatty, radiolucent tissue of older women







BREAST

Congenital anomalies

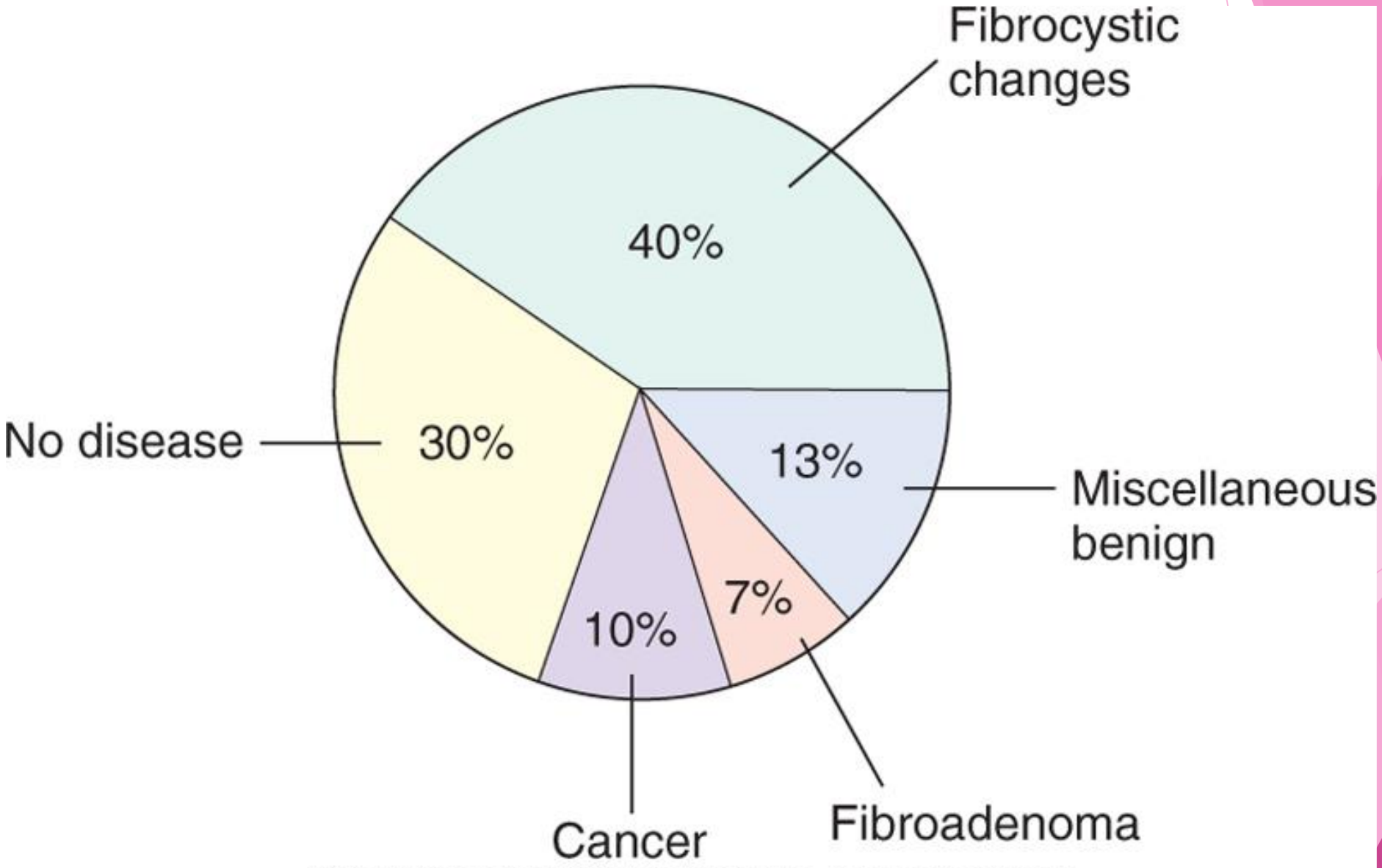
- Some women have sufficient irregularity of the normal breast tissue to cause them to seek clinical attention.

- Supernumerary nipples or breasts may be found along the embryonic ridge (milk line, especially the **axilla**) & are subject to the same diseases that affect the definitive breasts.

- Congenital inversion of the nipple is significant because similar changes may be produced by breast **ca**.

- Galactocele is painful cystic dilation of an obstructed ductthat arises during lactation, which may rupture, inciting a local inflammatory reaction & fibrosis that may arouse suspicion of breast **ca.**

The finding in **a** series of women seeking evaluation of apparent breast “lump”.



Inflammatory lesions of the breast

- rare
- caused by infections, autoimmune disease, or foreign body-type reactions.

- Clinically: erythema, edema, pain and focal tenderness.

- The only infectious agent is ***Staphylococcus aureus***

- Enters via fissures in nipple skin during the first weeks of breast feeding→lactational abscesses.

- If untreated, tissue necrosis →fistula tracks opening onto the skin.

- **Treatment**: antibiotics and continued expression of milk. Rarely, surgical incision and drainage is required.

- Note: Because inflammatory diseases are rare, the possibility that the symptoms are caused by inflammatory carcinoma **should always be considered.**

- INFLAMMATIONS OF THE BREAST

Includes: (1) acute mastitis, (2) mammary duct ectasia,& (3) traumatic fat necrosis, **none** of which are associated with ↑risk of ca.

- All three are uncommon & during the acute stages usually cause **pain & tenderness** in the involved areas

Acute mastitis

- Develops when bacteria gain access to the breast tissue through the ducts; when there is inspissation of secretions; through fissures in the nipples, which usually develop during the early weeks of nursing (lactation)or from various forms of dermatitis involving the nipple.

- **Grossly, staphylococcal infections induce single or multiple abscesses** accompanied by its typical clinical features. They are usually small, when large they may heal with residual foci of **scarring** that are palpable as localized areas of induration (that mimic ca).

- **Streptococcal infections** generally spread throughout the entire breast, causing pain, marked swelling, & breast tenderness, usually heal by resolution

Mammary duct ectasia (Periductal or Plasma Cell Mastitis)

- Is a **nonbacterial** chronic inflammation of the breast associated with
  - (1) **inspissation of breast secretions in the main excretory ducts**
  - **(2) ductal dilation& rupture** leading to reactive inflammatory changes in the surrounding tissue.
  - It is an **uncommon condition**, usually encountered in women in their 40s & 50s who have borne children.
- **Grossly,** usually the inflammatory changes are confined to an area drained by one or several major excretory ducts of the nipple with ↑firmness of the tissue. **O/S dilated rope like ducts** are seen from which thick, cheesy secretions can be extruded.
- Histopath, the **(1)dilated ducts are filled by granular debris**, WBCs, mainly **lipid-laden macrophages,**
- **(2)**the duct epithelium lining is generally destroyed, &

- **(3)**the most distinguishing features is the **prominence of a lymphocytic & plasma cell infiltration around the duct**
- Mammary duct ectasia is of principal importance because it leads to induration of the breast substance &, more significantly, to retraction of the skin or nipple, mimicking the changes caused by ca.

Traumatic fat necrosis

- Is an uncommon lesion, significant only because it produces a mass, mimicking ca.
- Most (but not all) women with this condition report some antecedent trauma to the breast.
- Grossly, the early lesion is sharply localized, small, often tender, less than 2 cm in ø.
- Histopath: a central focus of necrotic fat cells surrounded by neutrophils & lipid-filled macrophages, later enclosed by fibrous tissue& mononuclear leukocytes.
- Eventually, the focus is replaced by scar tissue, or the debris becomes cystic, surrounded by a scar.
- Calcifications

FIBROCYSTIC CHANGES (disease)

- **Very common condition**, in which changes in the female B range from innocuous, to patterns associated with an ↑ risk of ca.
- These changes have been called **fibrocystic disease**.
- **Most** of these changes have little clinical significance except that **some**(stromal fibrosis & microcysts or macrocysts) **produce palpable "lumps“,** which must be distinguished from cancer by examination of fine needle aspiration (FNA) material or, **more definitively by biopsy & histologic evaluation.**
- A **small minority** represents forms of epithelial hyperplasia that are clinically important.
- This range of changes is the **consequence of an** exaggeration & distortion of the cyclic breast changes that occur normally in the menstrual cycle.
- Estrogenic therapy & oral contraceptives do not seem to ↑the incidence of these alterations; indeed, oral contraceptives may decrease the risk.

Benign Epithelial lesions

- The majority are incidental findings detected by mammography.
- Benign changes are divided into three groups:
- **Non proliferative changes**: is not associated with an increased risk of breast cancer.
- **Proliferative disease without atypia**: polyclonal hyperplasias& associated with 1.5-2 folds increase risk of breast cancer.
- **Proliferative disease with atypia**: monoclonal "**precancers**" & associated with 4-5 folds increase risk of breast cancer in **both** breast

Non Proliferative breast changes (fibrocystic changes).

- Common
- There are three principal morphologic changes:

(1) cystic change, often with apocrine metaplasia (most common)

- Although it may present as a single large cyst within one breast, the disorder is usually multifocal& often bilateral,

(2) Fibrosis.

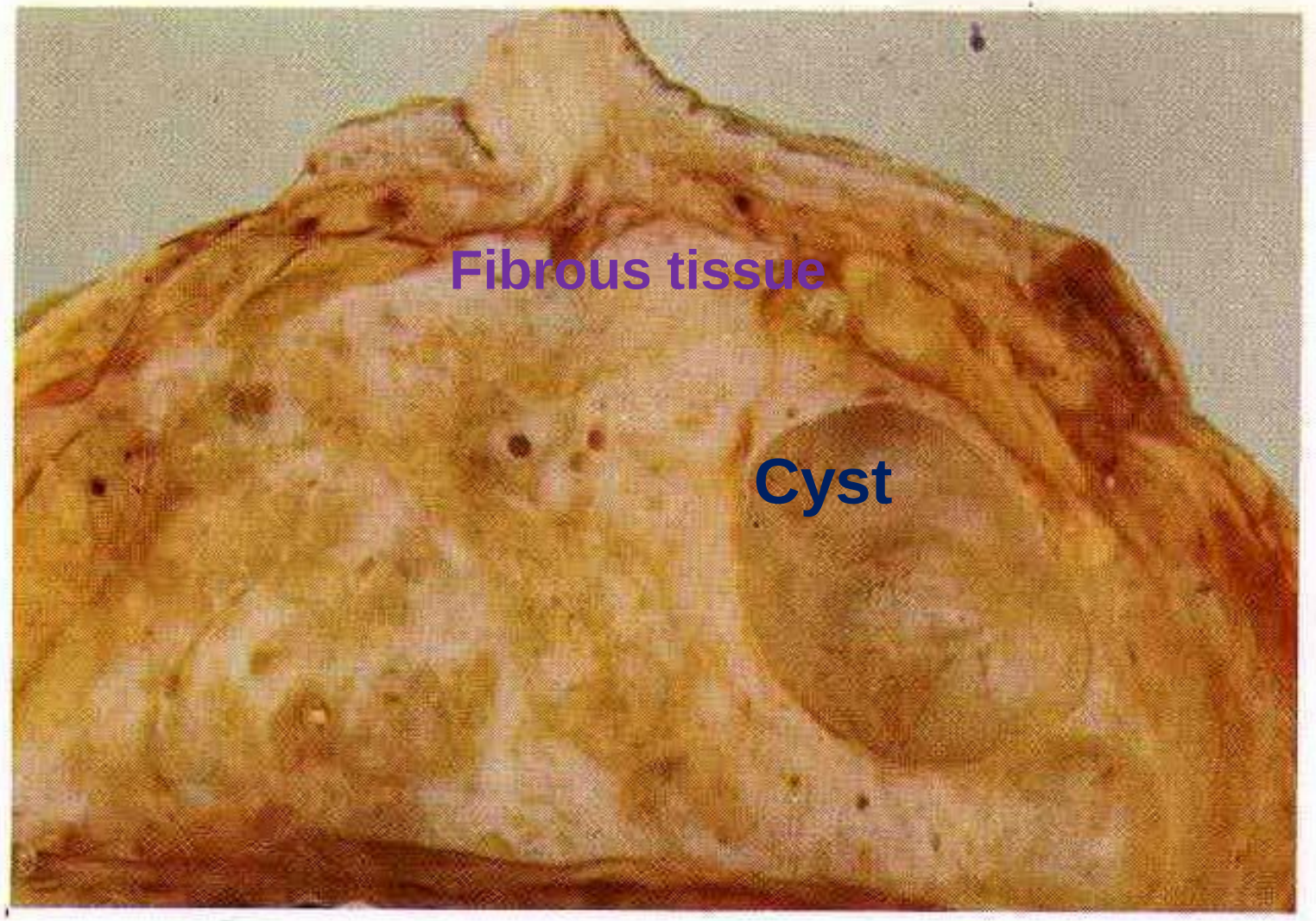
(3) Adenosis

- H/P:The smaller cysts epithelium is cuboidal to columnar & is sometimes multilayered in focal areas.

- In larger cysts it may be flattened or even totally atrophic .

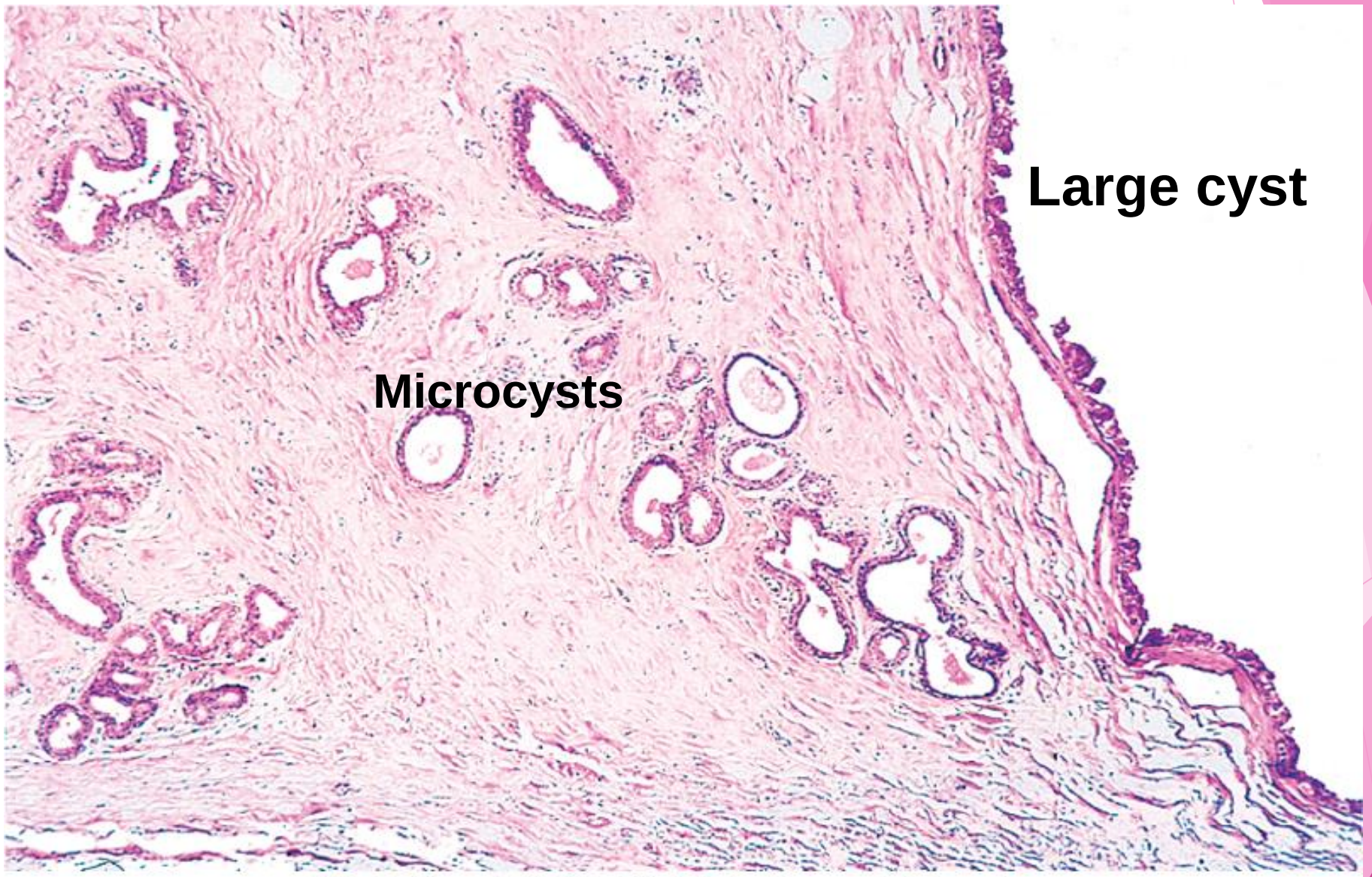
- Frequently, cysts are lined by large polygonal cells, with abundant granular eosinophilic cytoplasm & small, round, deeply chromatic nuclei, called **apocrine metaplasia ;this is virtually always benign.**
- The stroma surrounding the cysts consist of compressed fibrous tissue.
- A stromal **lymphocytic infiltrate is common** in all variants of fibrocystic change (proliferative & non proliferative)

Fibrocystic disease: breast. Replacement of the normal breast tissue by greyish-white**fibrous**tissue, within which are multiple small & large **cysts**.

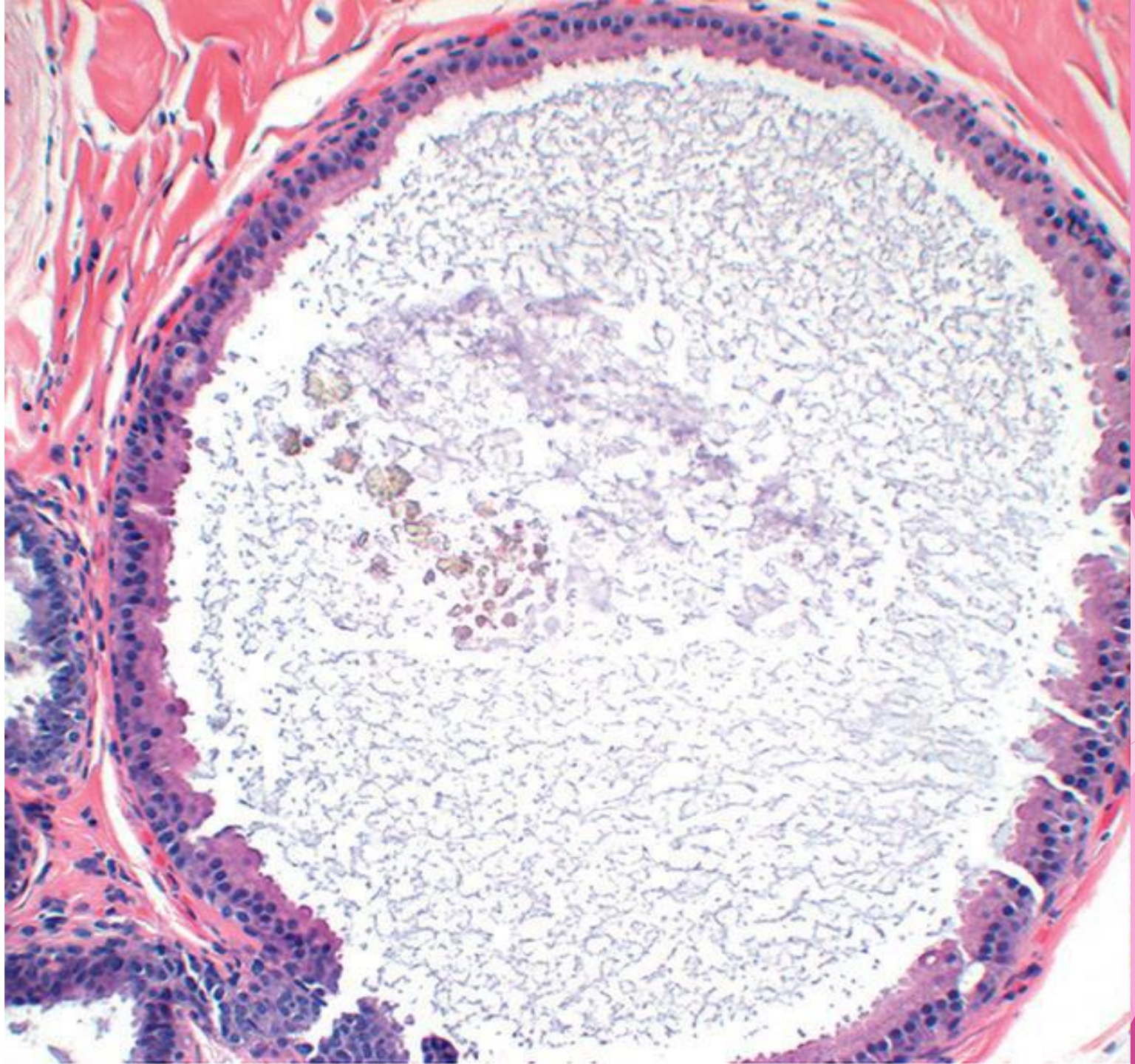


12.1 Fibroepithelial hyperplasia: breast

Histology of fibrocystic change of the breast revealing dilatation of the ducts producing **microcysts**&, at right, the wall of a **large cyst** with visible lining epithelial cells



Non-Proliferative Disease .Apocrine Cyst



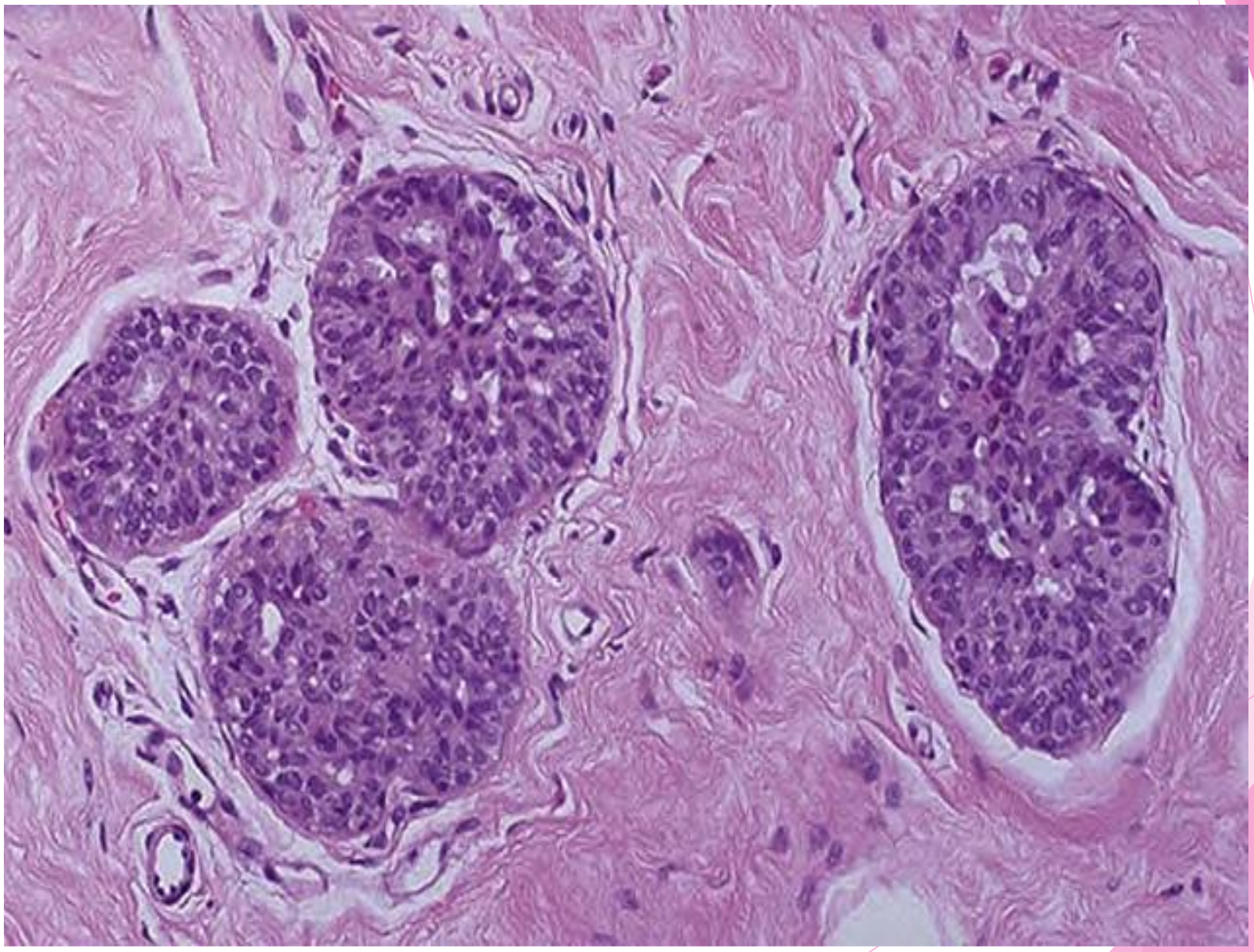
Proliferative disease without Atypia

Includes:

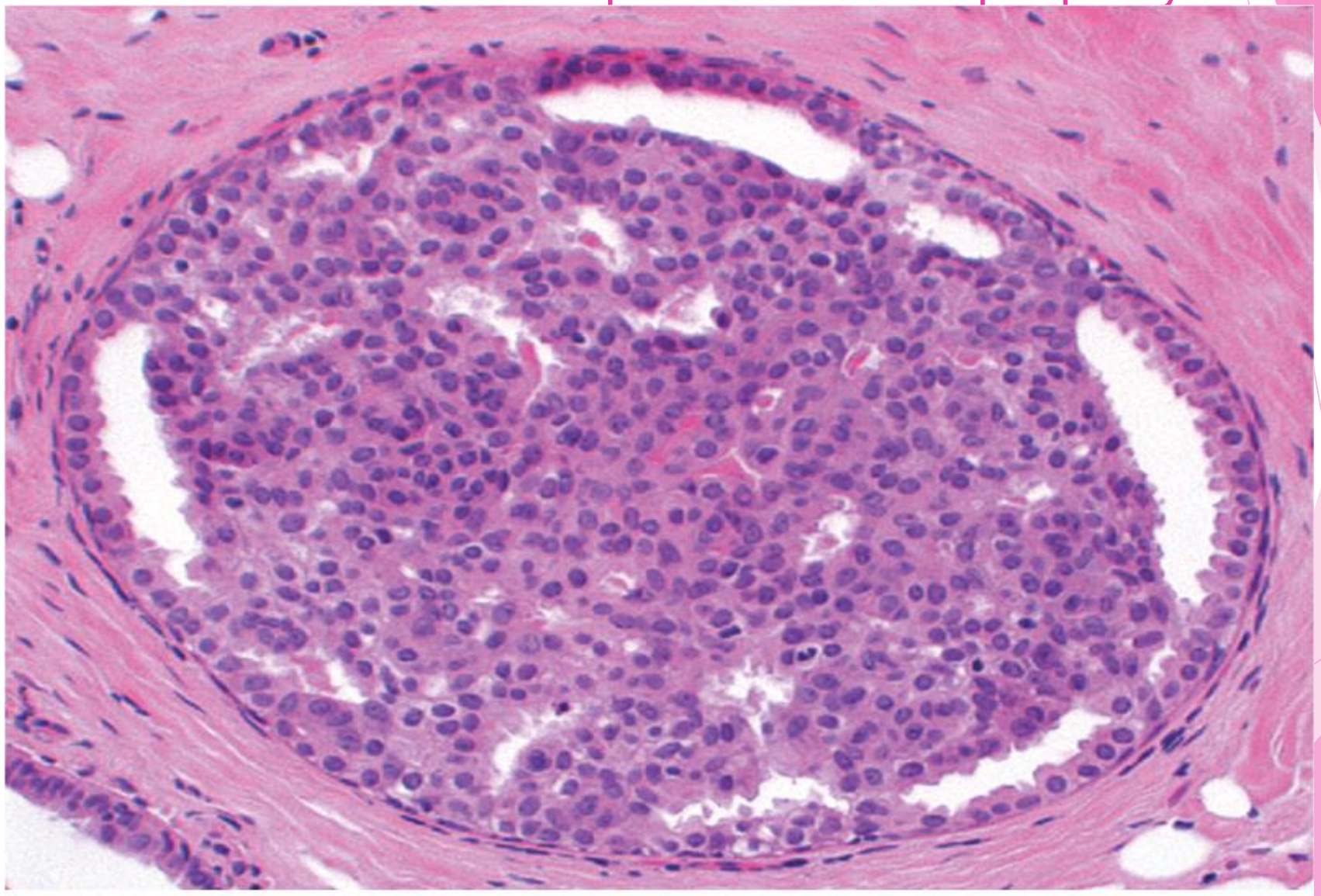
- epithelial hyperplasia
- sclerosing adenosis
- complex sclerosing lesion
- papilloma

- associated with varying degrees of epithelial cell proliferation.
- **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.
- are predictors of risk but unlikely to be true precursors of carcinoma.

Epithelial hyperplasia ,,the epithelial cells are multilayered filling the duct and the acini,myoepithelial cells are increased , no epithelial atypia



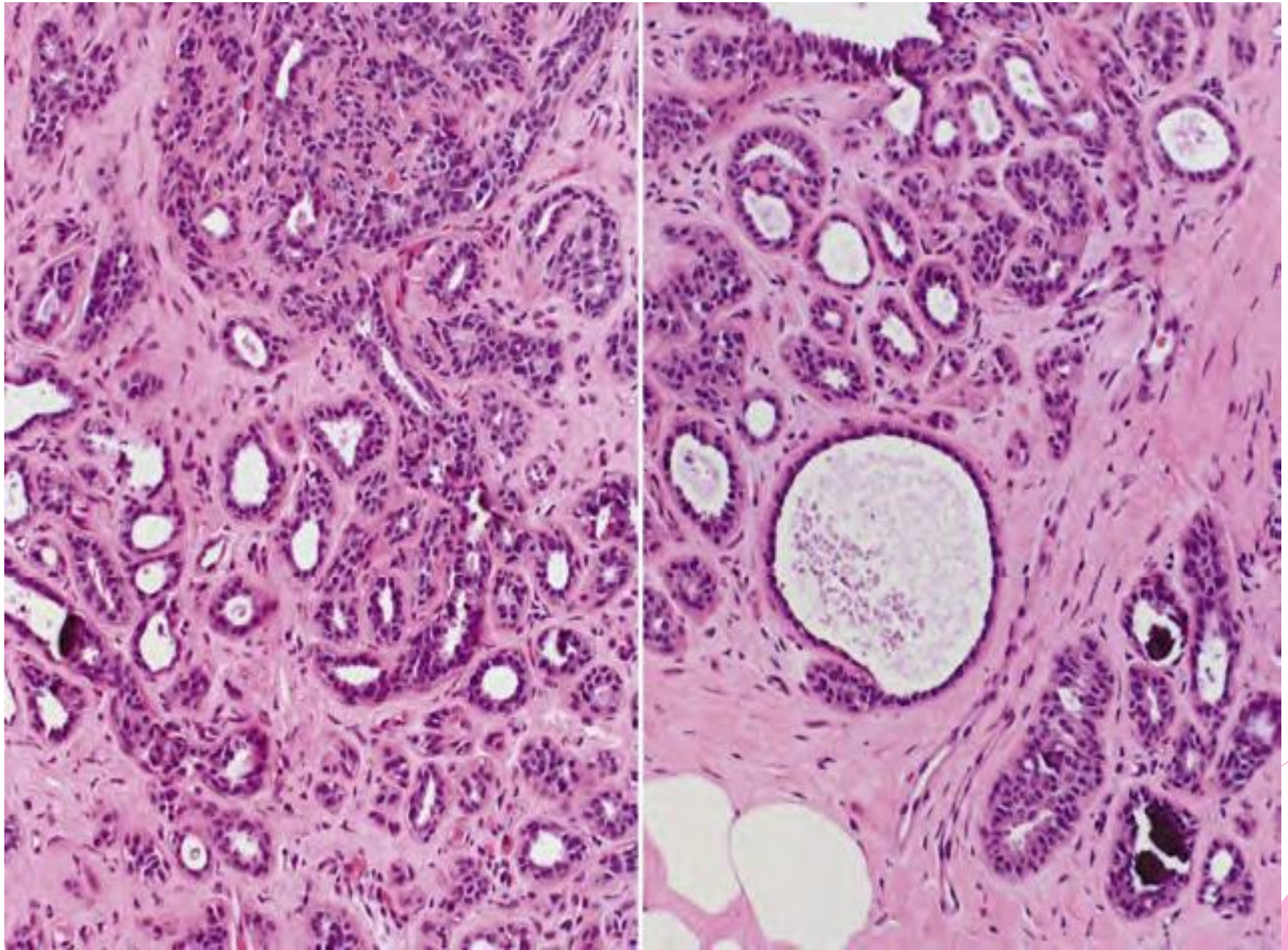
Epithelial hyperplasia . The duct lumen is filled with a heterogeneous population of cells of different morphologies. Irregular slit-like fenestrations are prominent at the periphery.



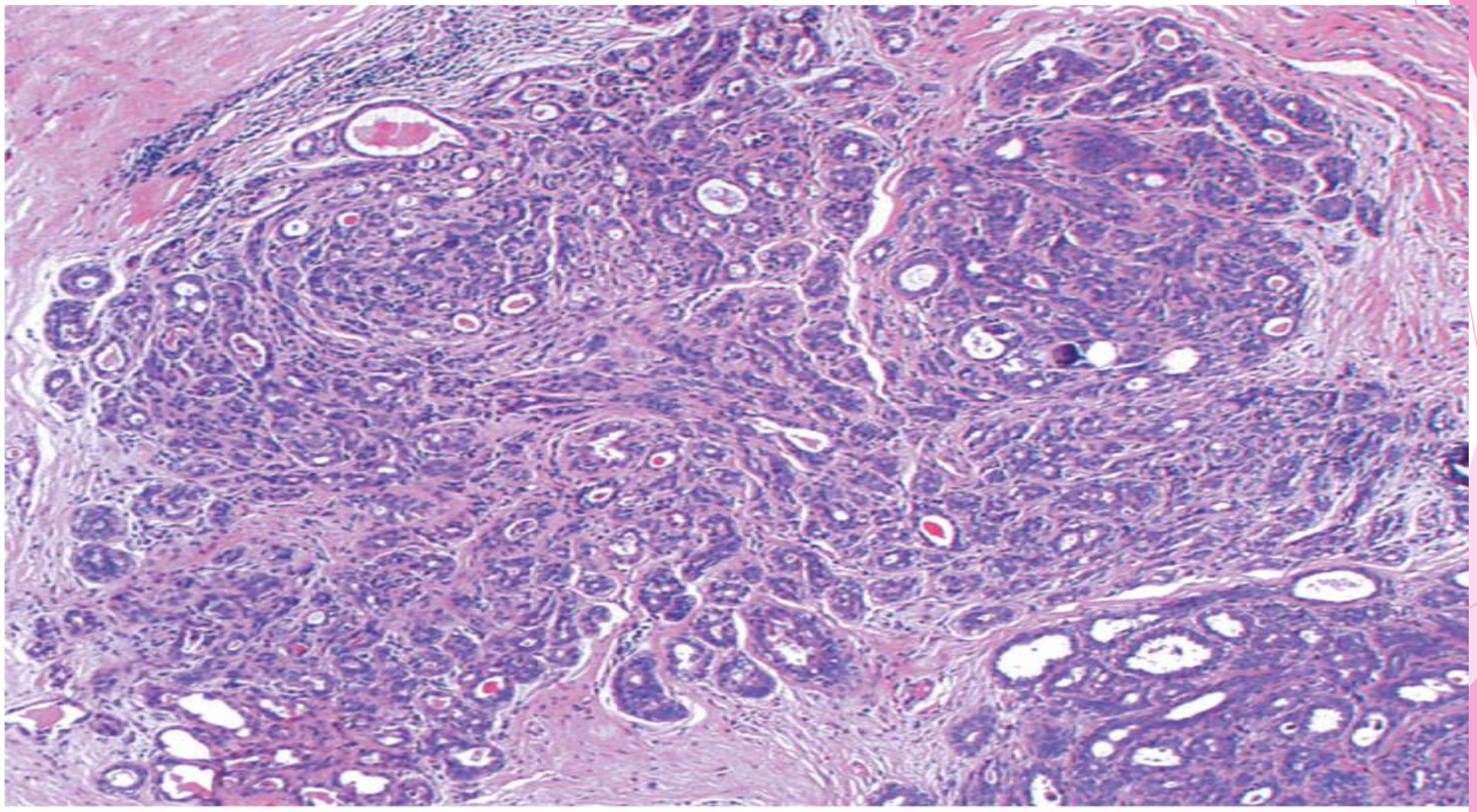
Sclerosing adenosis

- Aggregated glands or proliferating ductules may be virtually back to back, with single or multiple layers of cells in contact with one another **(adenosis).**
- Marked stromal **(sclerosing fibrosis)**compress & distort the proliferating epithelium, is always associated with the adenosis; hence, the designation **sclerosing adenosis.**
- **This overgrowth of fibrous tissue may completely compress the lumina of the acini & ducts, so that they appear as solid cords of cells**, a pattern may be difficult to distinguish histologically from an invasive scirrhous **ca**.
- The presence of double layers of epithelium & the identification of **myoepithelial elements** are helpful in suggesting a **benign diagnosis**.
- Although sclerosing adenosis is sometimes difficult to differentiate clinically & histologically from ca, it is associated with only a minimally ↑risk of progression to ca.

Sclerosing Adenosis

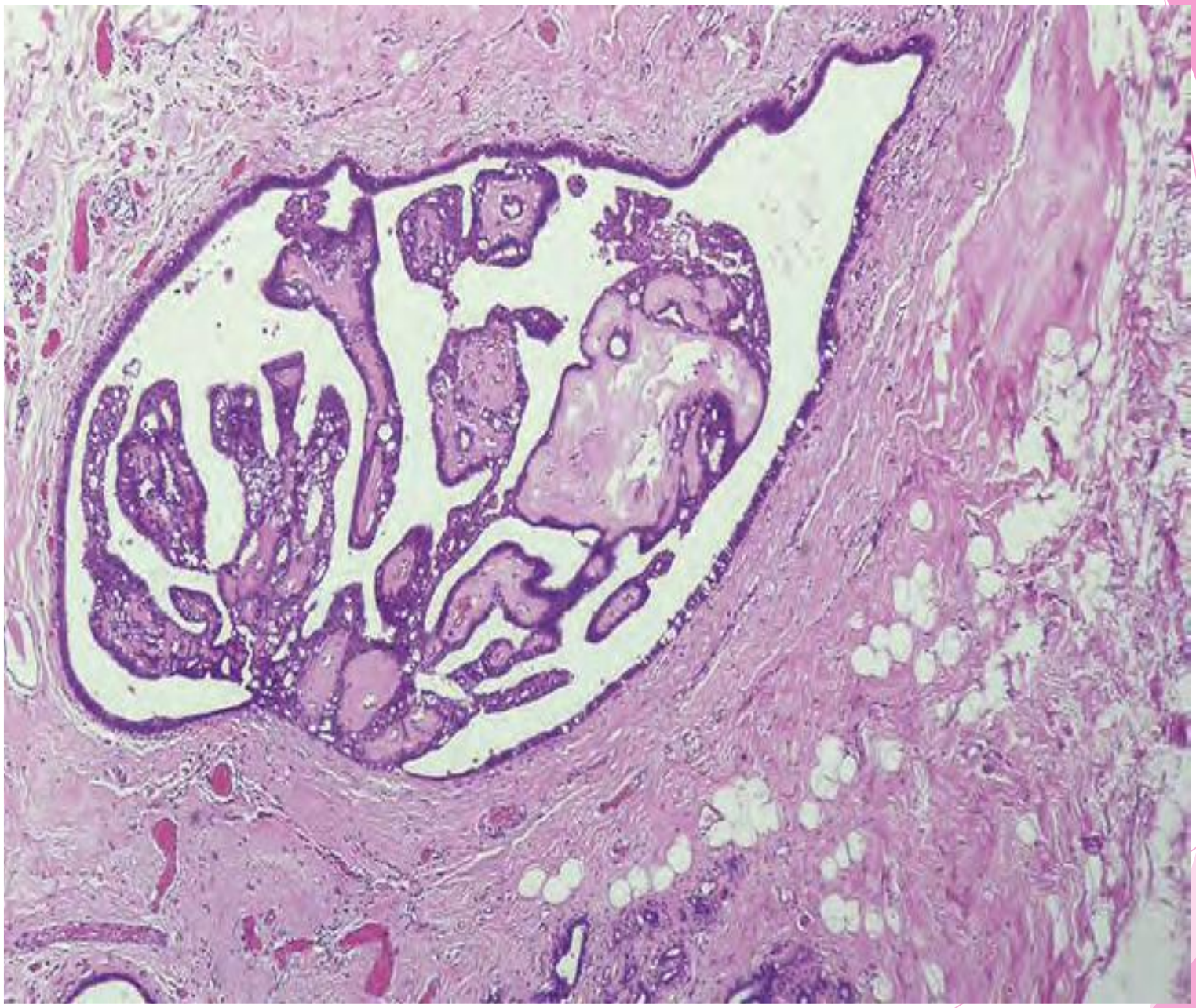


Sclerosing adenosis . Enlarged terminal duct lobular unit. The acini are compressed & distorted by the surrounding dense stroma. **Unlike carcinomas**: •the acini are arranged in a swirling pattern, & •the outer border is usually well circumscribed.



Ductal papillomatosis

- with proliferating epithelium projecting in multiple small **papillary projections** into the ductal lumen.
- The degree of hyperplasia, manifested in part by the number of layers of intraductal epithelial proliferation, can be mild, moderate, or severe;

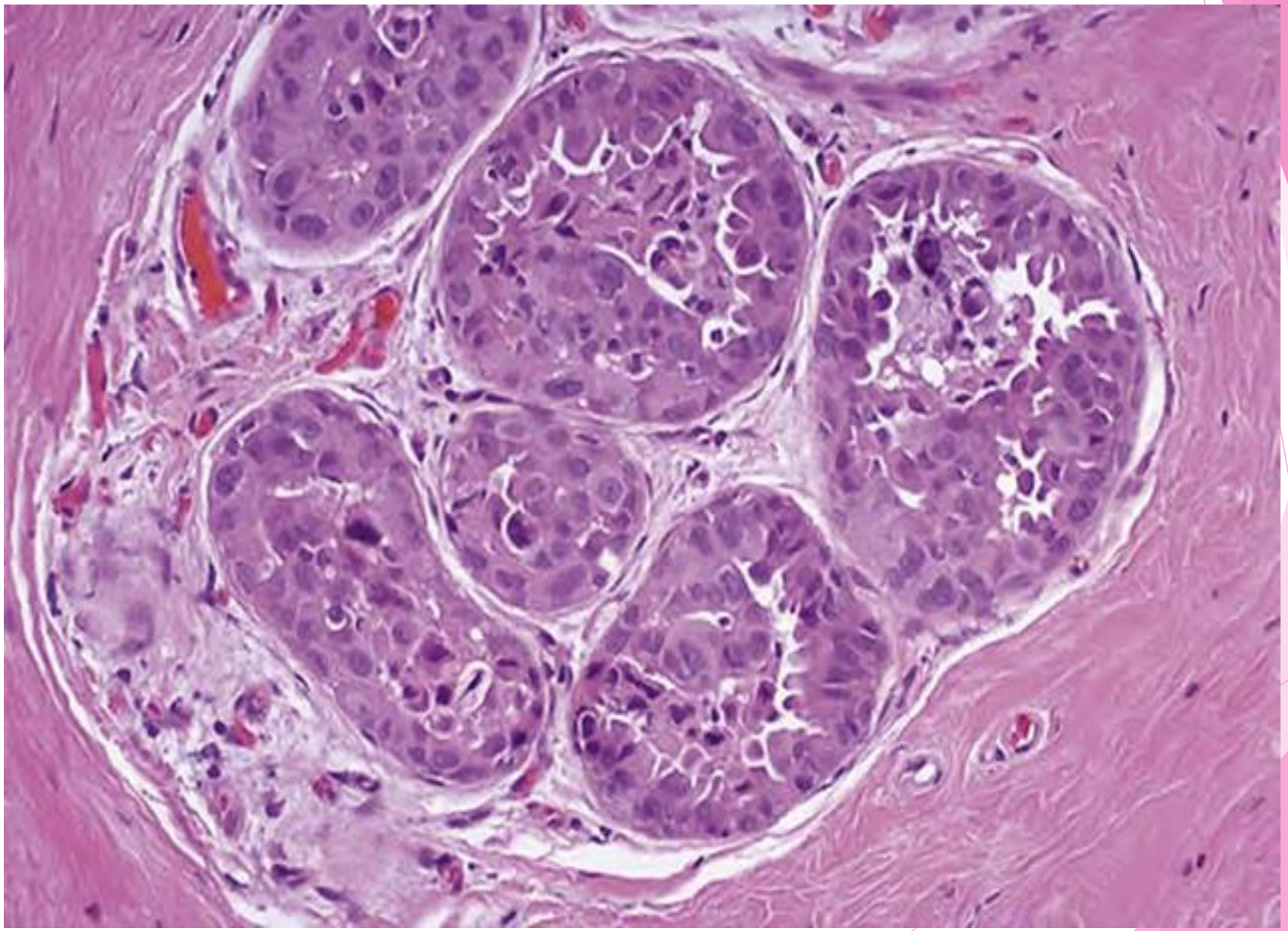


Proliferative Lesions with atypia

- **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

- Atypical Hyperplasia in which the hyperplastic cells become monomorphic with complex architectural patterns, having changes approaching those of ductal ca in situ (**DCIS**) such hyperplasia is called **atypical.**
- The line separating the epithelial hyperplasias without atypia from atypical hyperplasia is important but difficult to define, just as it is difficult to clearly distinguish between atypical hyperplasia & ca in situ.
- Immunohistochemical (IHC) stains provide information and aid in the differential diagnosis of challenging epithelial lesions of the breast.

Atypical Ductal Hyperplasia



Non-Invasive In-situ Carcinoma

- **include:**
- 1. Ductal carcinoma in situ, DCIS
- 2. Lobular carcinoma in situ, LCIS

◉both types arise from cells in the terminal duct that give rise to lobules.

◉LCIS usually expands involved lobules, whereas DCIS distorts lobules into duct like spaces

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

Lobular carcinoma in Situ

- Malignant clonal proliferation of cells within ducts and lobules.

⦿Cells grow in a discohesive fashion→an **acquired loss of the tumor suppressive adhesion protein E-cadherin**.

⦿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

- malignant clonal proliferation of epithelial cells within ducts and lobules.
- DCIShas a wide variety of histologic appearances including:
  - 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

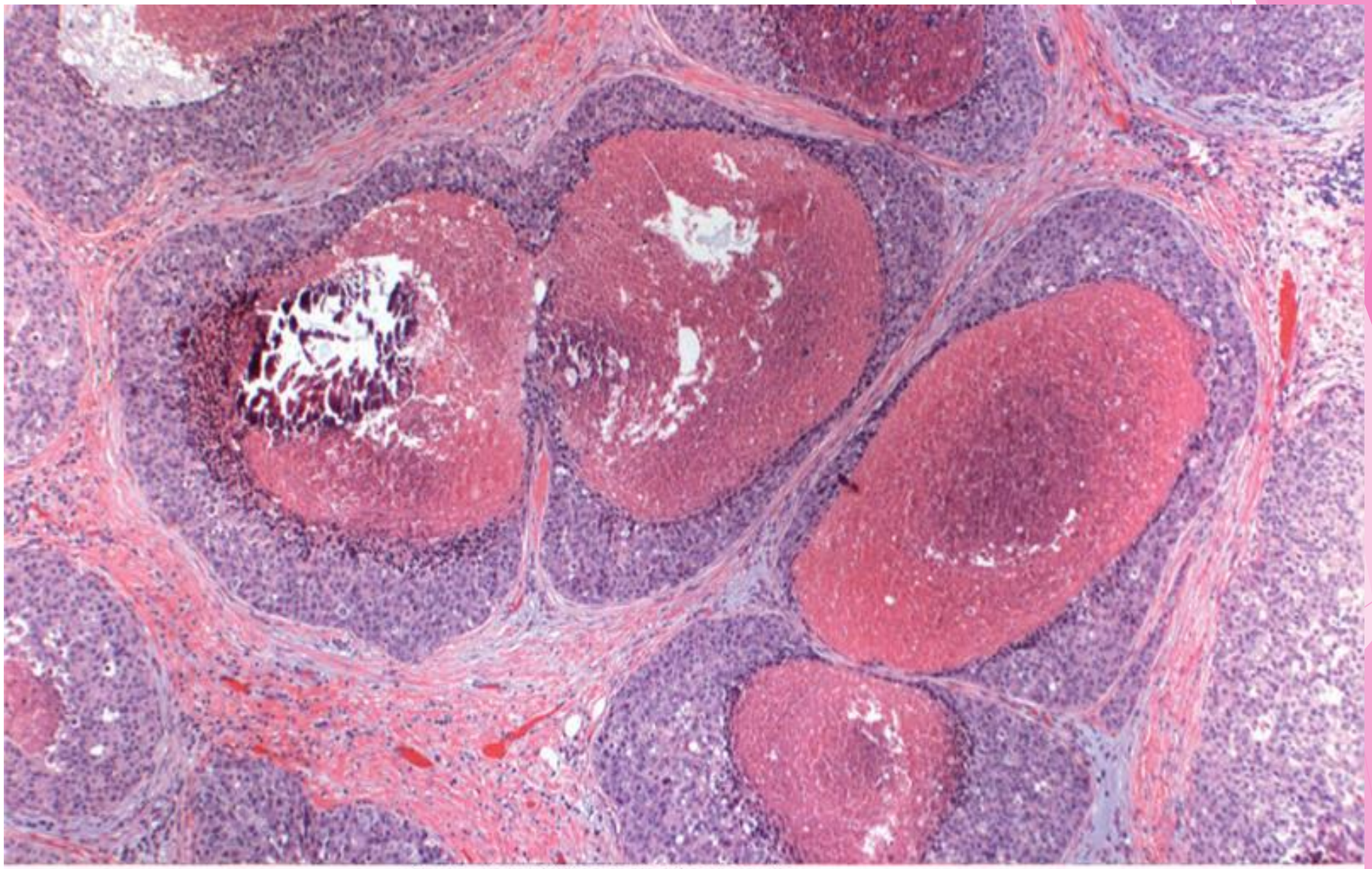
Management DCIS

- The prognosis : excellent (97% long-term survival **afte**r simple mastectomy).

- Current treatment strategies: surgery and irradiation, tamoxifen

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

COMEDO DCIS , High Grade Proliferation associated with central zone of necrosis and calcification



Kumar et al: Robbins Basic Pathology, 9e.

The Relationship of Fibrocystic Changes to Breast Ca

The following statements represent opinion of the relationship:

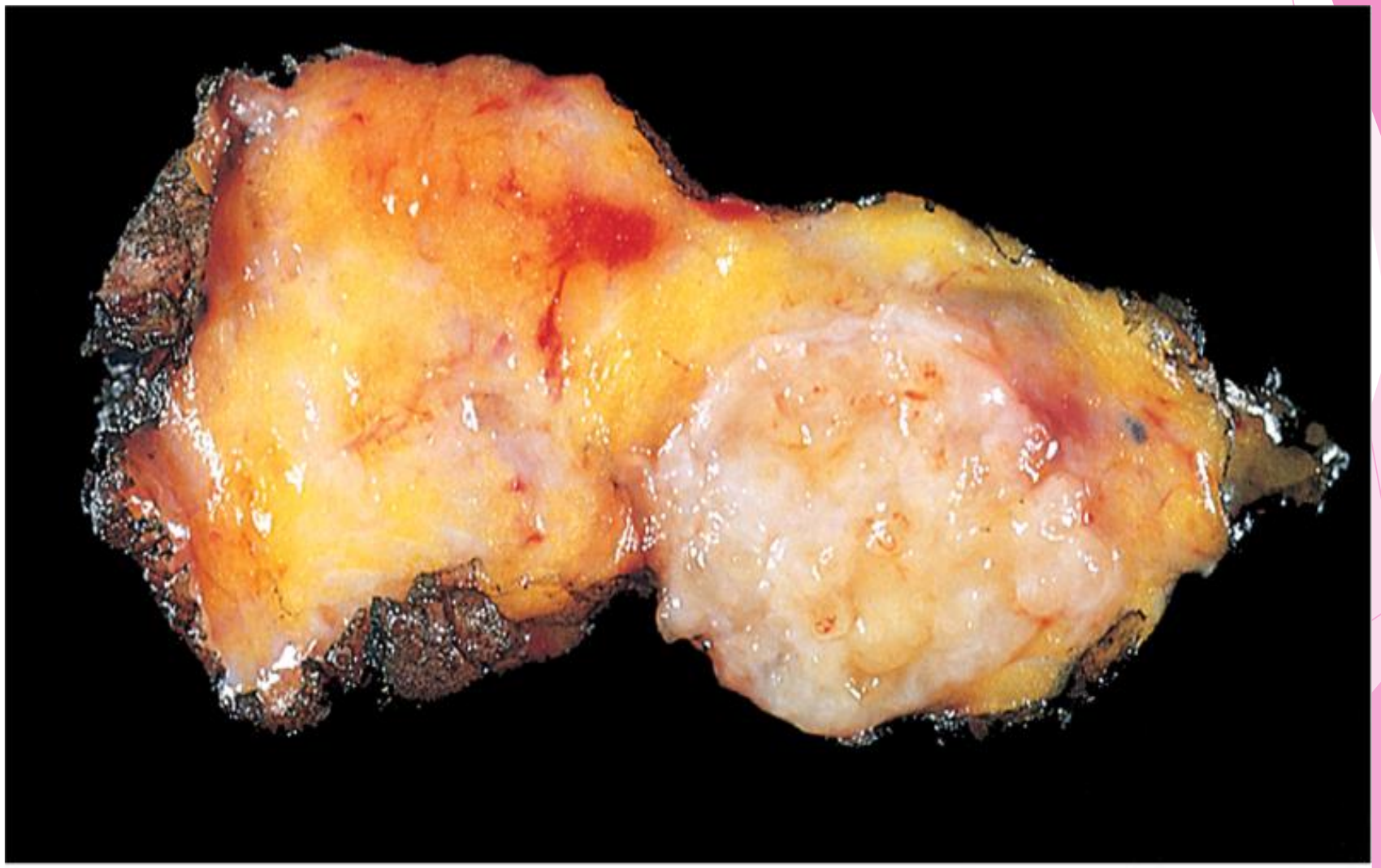
- Minimal or no ↑riskof breast ca:fibrosis, microscopic or macroscopic cysts, apocrine metaplasia, mild hyperplasia, fibroadenoma.
- Slightly ↑risk(X1.5-2 times):hyperplasia without atypia, ductal papillomatosis & sclerosing adenosis.
- Significantly ↑risk(X5 times):ductular or lobular **atypical hyperplasia**(seen in 15% of biopsies). Proliferative lesions may be multifocal, & the risk of subsequent ca extends to both breasts.
- A family history of breast ca may ↑the risk in all categories(e.g., to X10-fold with atypical hyperplasia).
- Fortunately,most women who have lumps related to fibrocystic change can be reassured that there is little or no ↑predisposition to ca.

The most important lesions of the female breast are TUMORS

Fibroadenoma (FA)

- Most common benign tumor of the female breast.
- An absolute or relative increase in estrogen activity is thought to contribute to its development. It may enlarge late in the menstrual cycle & during pregnancy; while it may regress & calcify after menopause.
- Usually appear in young women; the peak incidence is in the 3rd decade (21 to 30 years) of life.
- Clinically as solitary, discrete, freely movable nodule (so-called Breast mouse), 1-10 cm in ∅. Rarely, multiple fibroadenomas are encountered &, Rarely, they exceed 10 cm in ∅(giant fibroadenoma).
- Whatever their size, they are usually easily "shelled out."

Fibroadenoma. A rubbery white, well-circumscribed mass, clearly demarcated from the surrounding yellow fatty adipose breast tissue. **On mammogram ,** fibroadenoma appears **densert** han the surrounding tissue because it does not contain adipose tissue.



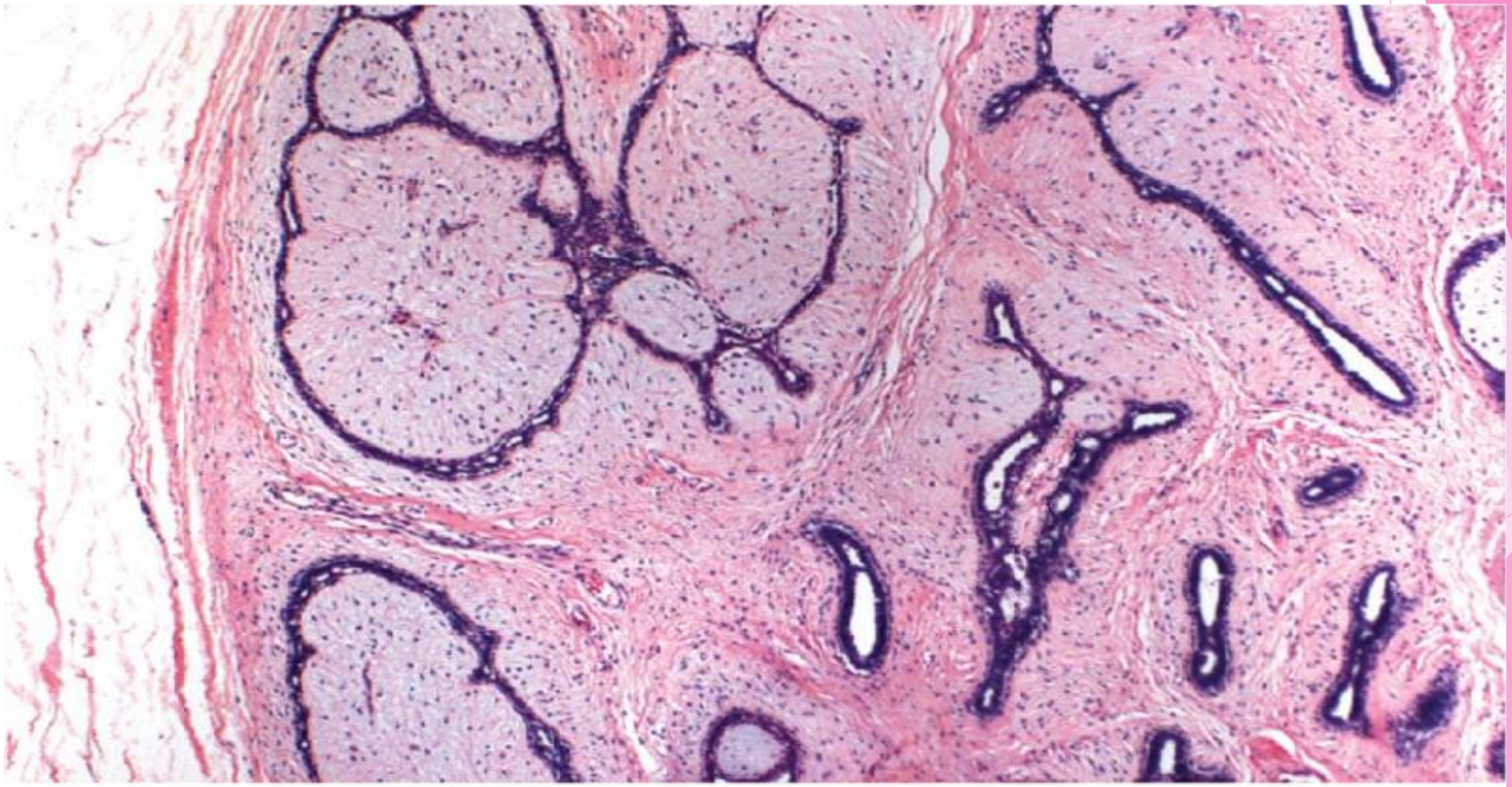
- Grossly, all FA are firm, with a uniform white cut section .
- H/P, there is (I) a loose fibroblastic stroma containing
- (II) duct-like, epithelium-lined spaces of various forms & sizes, lined with single or multiple layers of cells that are regular & have a well-defined, intact basement membrane.
- The ductal lumens or spaces are either:

•open, round to oval, & fairly regular, this type is called (pericanalicular FA) ,while in others…

•the lumens are compressed by extensive proliferation of the surrounding stroma, so they appear as slits or irregular star-shaped structures (intracanalicular FA),type .

- Fibroadenomas almost never become malignant.

Fibroadenoma, consisting of a proliferating intralobular stroma surrounding, pushing & distorting the associated epithelium. The border is sharply delimited, by a capsule from the surrounding tissue.



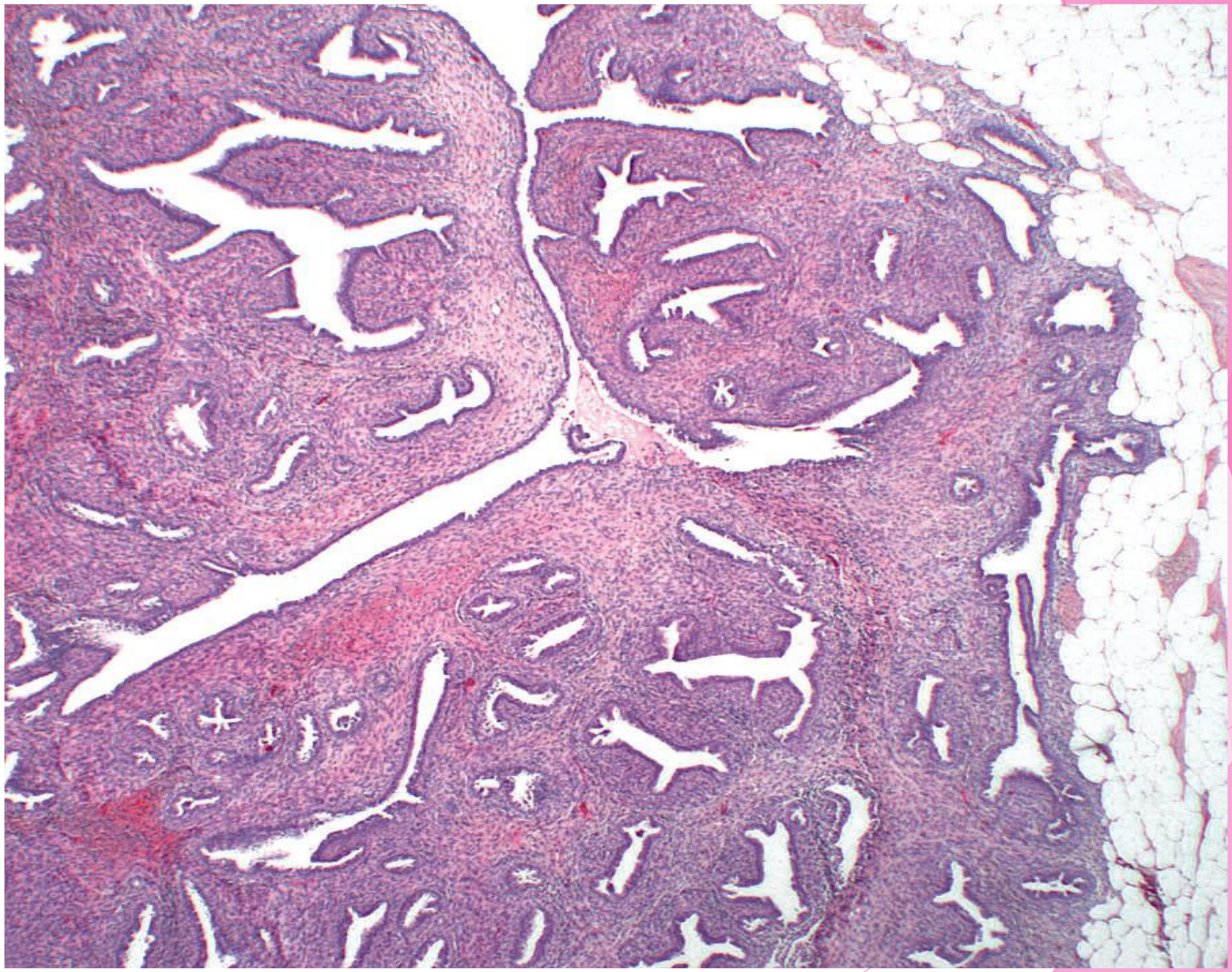
Phyllodes Tumor (T)

- Phyllodes T are much less common than fibroadenomas & are thought to arise from the periductal stroma & not from preexisting fibroadenomas.
- Types: Most of these phyllodes **T** are benign, may be small (3-4 cm in ∅, **but most grow to large, possibly massive size,**distending the breast.
- **Some** become lobulated & cystic (because their section grossly exhibit leaflike clefts & slits, they have been designated phyllodes, from Greek, for "leaflike" T.

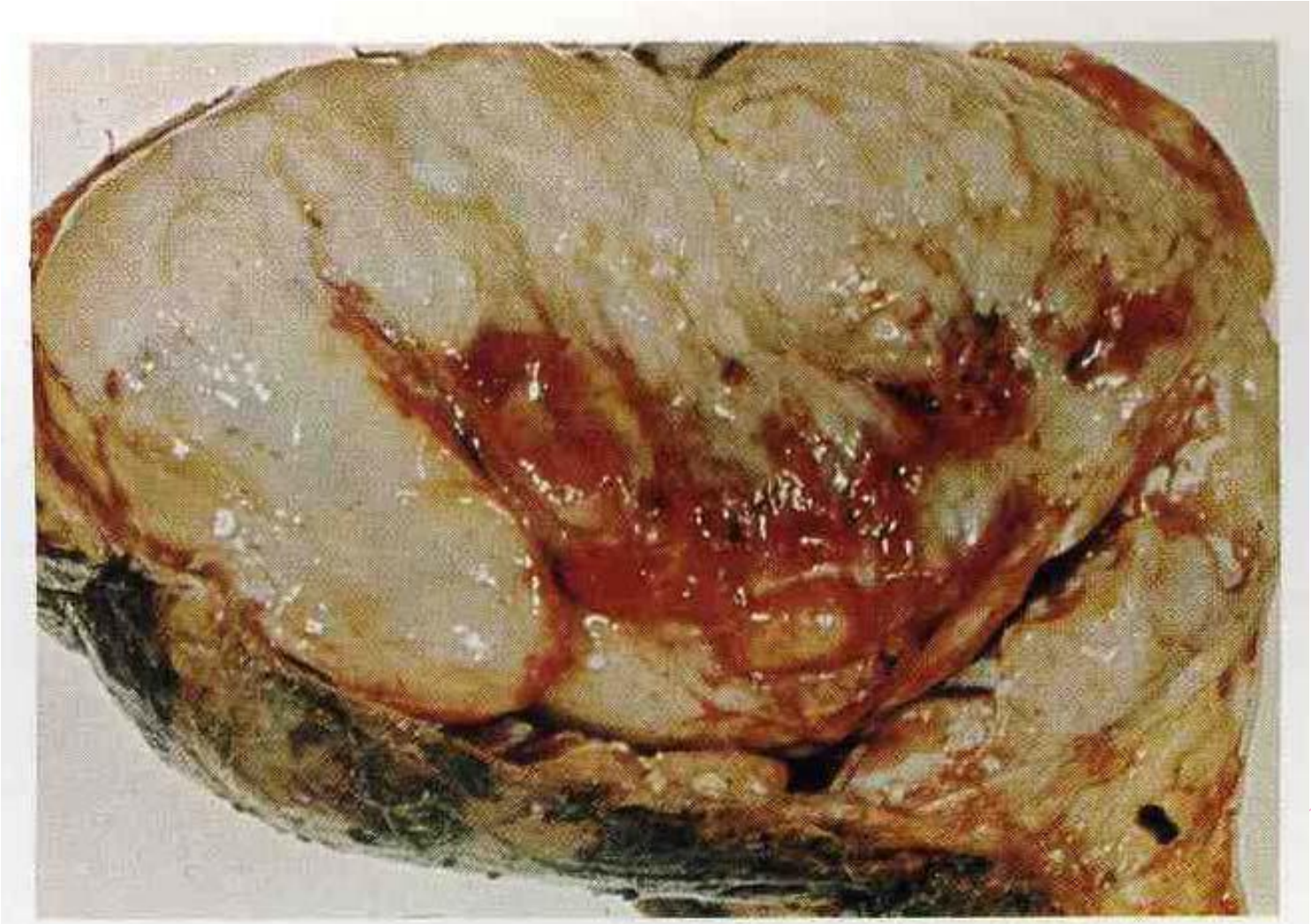
- Some of the phyllodes **T** show ↑stromal cellularity, anaplasia & high mitotic activity, accompanied by rapid ↑in size, usually with **invasion** of adjacent breast tissue.

- Most of these T remain localized & are cured by excision;
- Malignant phyllodes T (cystosarcoma phyllodes, may recur, but they tend to remain localized.
- Only the most malignant, (15% of cases), metastasize to distant sites

Phyllodes Tumor



Cystosarcoma phylloides breast. The Greek term is derived from the leaf like clefts & slits pattern of the tumor. C/S showing myxomatous tumor with extensive recent hemorrhage.



12.7 Cystosarcoma phylloides: breast

Intraductal Papilloma

- A benign papillary tumor growth within a duct**.**
- Most are solitary, found within the main lactiferous ducts or sinuses.
- They **present clinically** as a result of:

(1) the appearance of serous or bloody nipple discharge,

(2) the presence of a small **subareolar mass a few mm inØ,**

(3) **nipple retraction**.

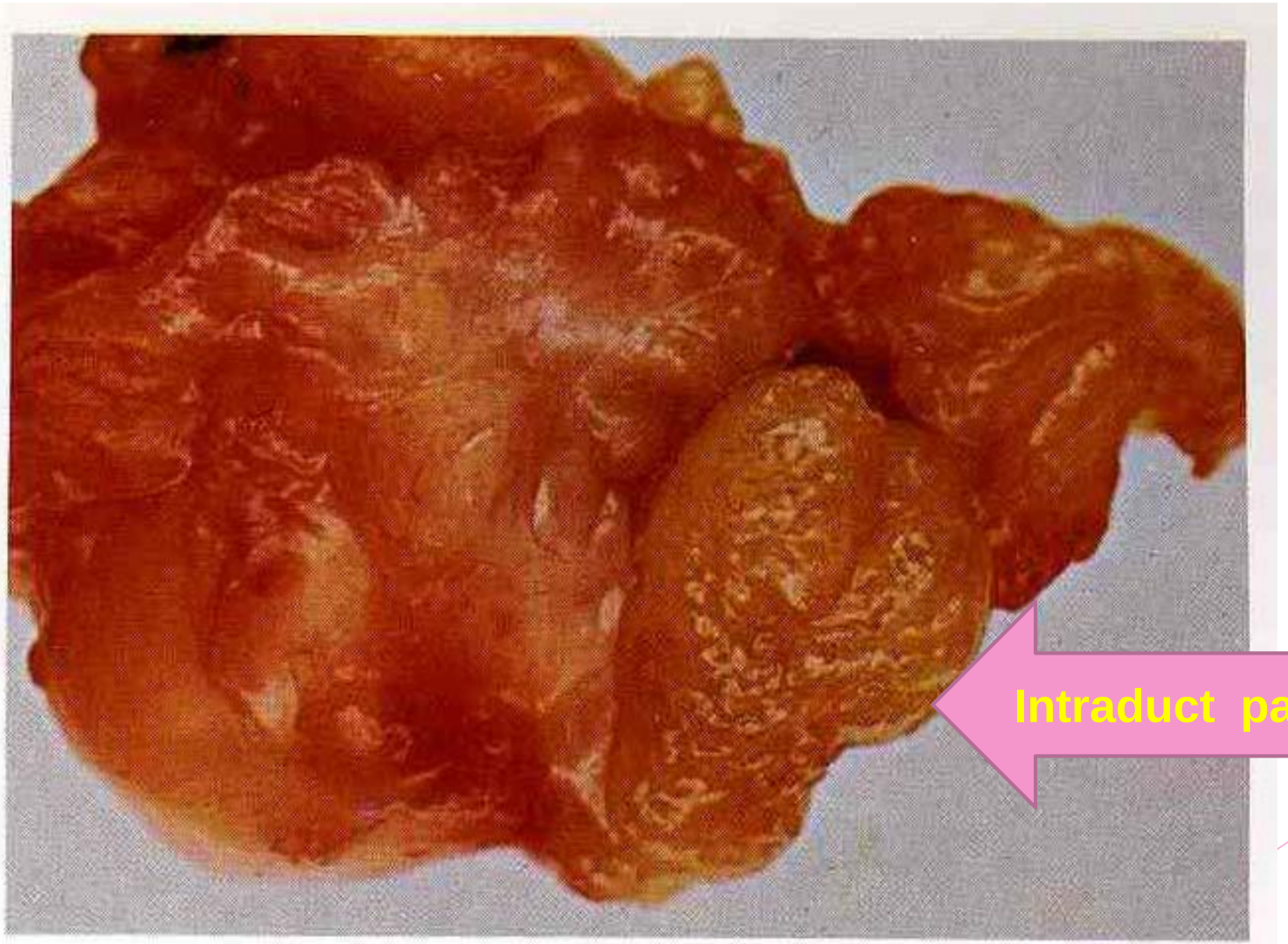
- **Grossly, T** usually **solitary**, less than 1 cm in Ø, consisting of delicate, branching papillae within a dilated duct or cyst.

H/P:the multiple papillae have connective tissue stromal axis covered by cuboidal epithelial cells that are frequently **double layered** **(**epithelial layer overlying a myoepithelial layer).

- **Solitary papilloma** almost always remains **benign**, but if **multiple papillomas**, (intraductal papillomatosis), they sometimes become malignant.

- **Papillary carcinoma** must be excluded; it often lacks a myoepithelial component & shows either monotonous ductal epithelium or severe cytologic atypia.

Intraduct papilloma; breast. A firm, lobulated pale yellow papilloma (1.5 cm in ø) is present within a dilated duct. It has granular surface & forms a raspbeery-like nodule.



12.2 Intraduct papilloma: breast