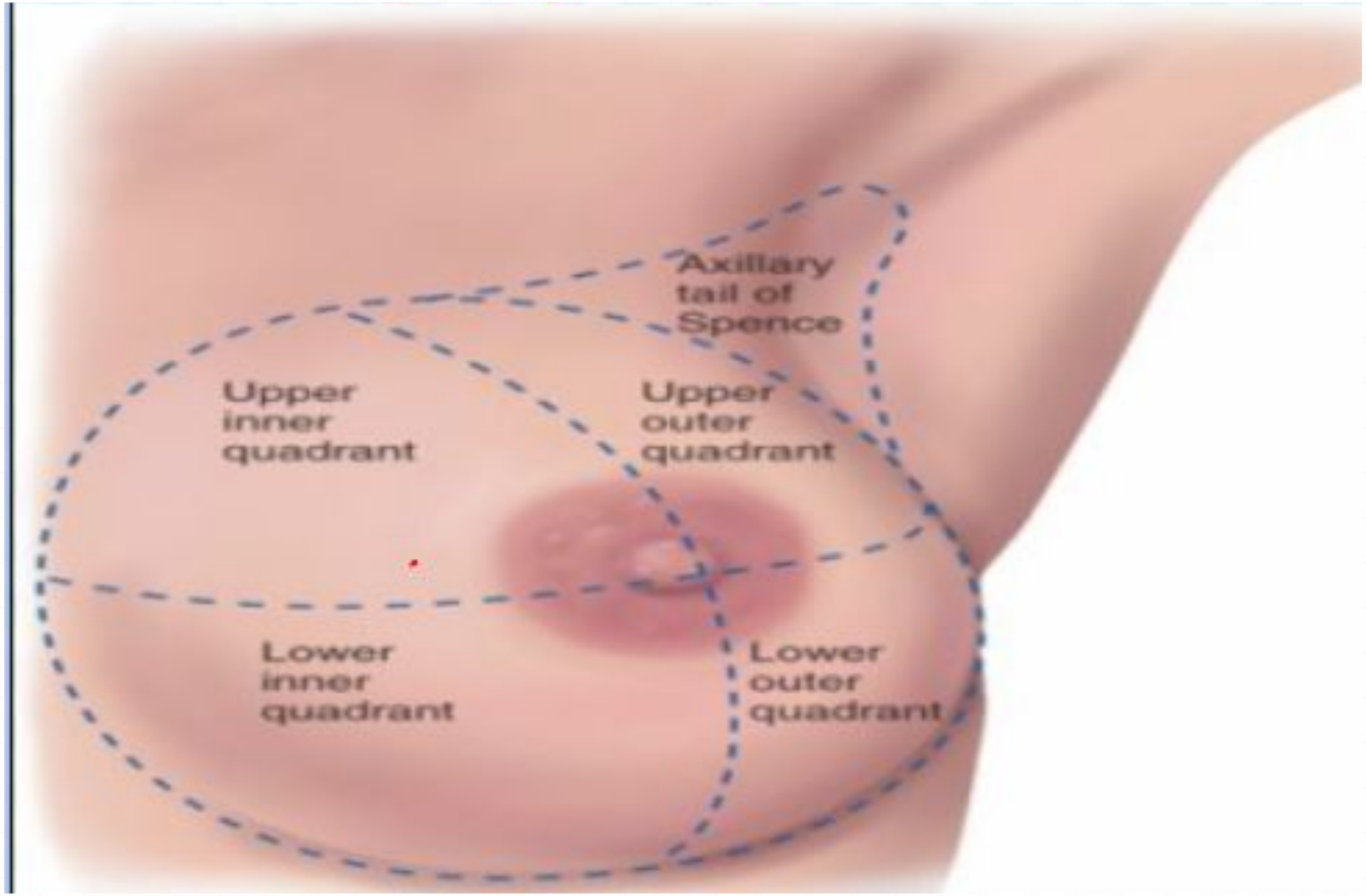
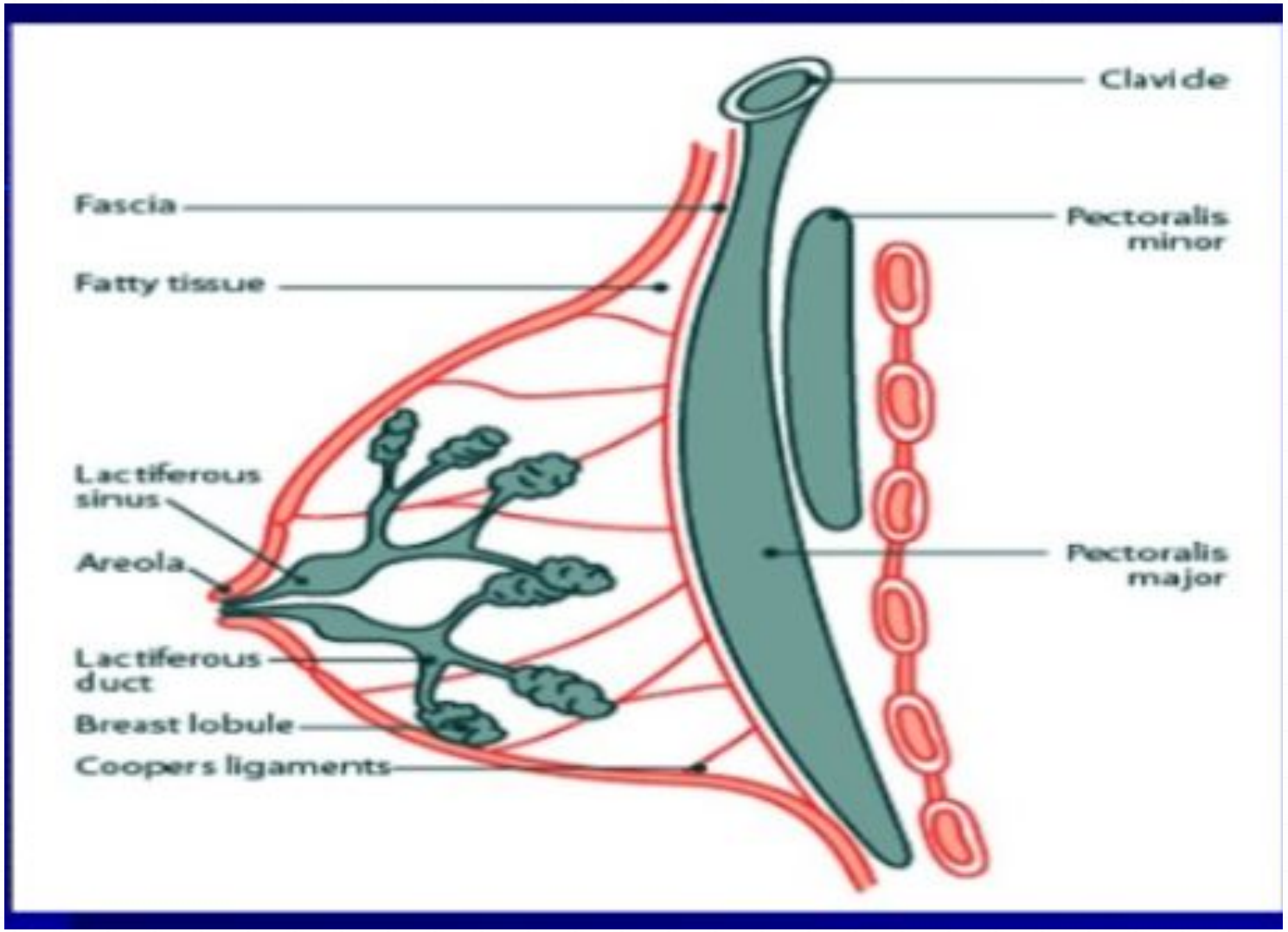
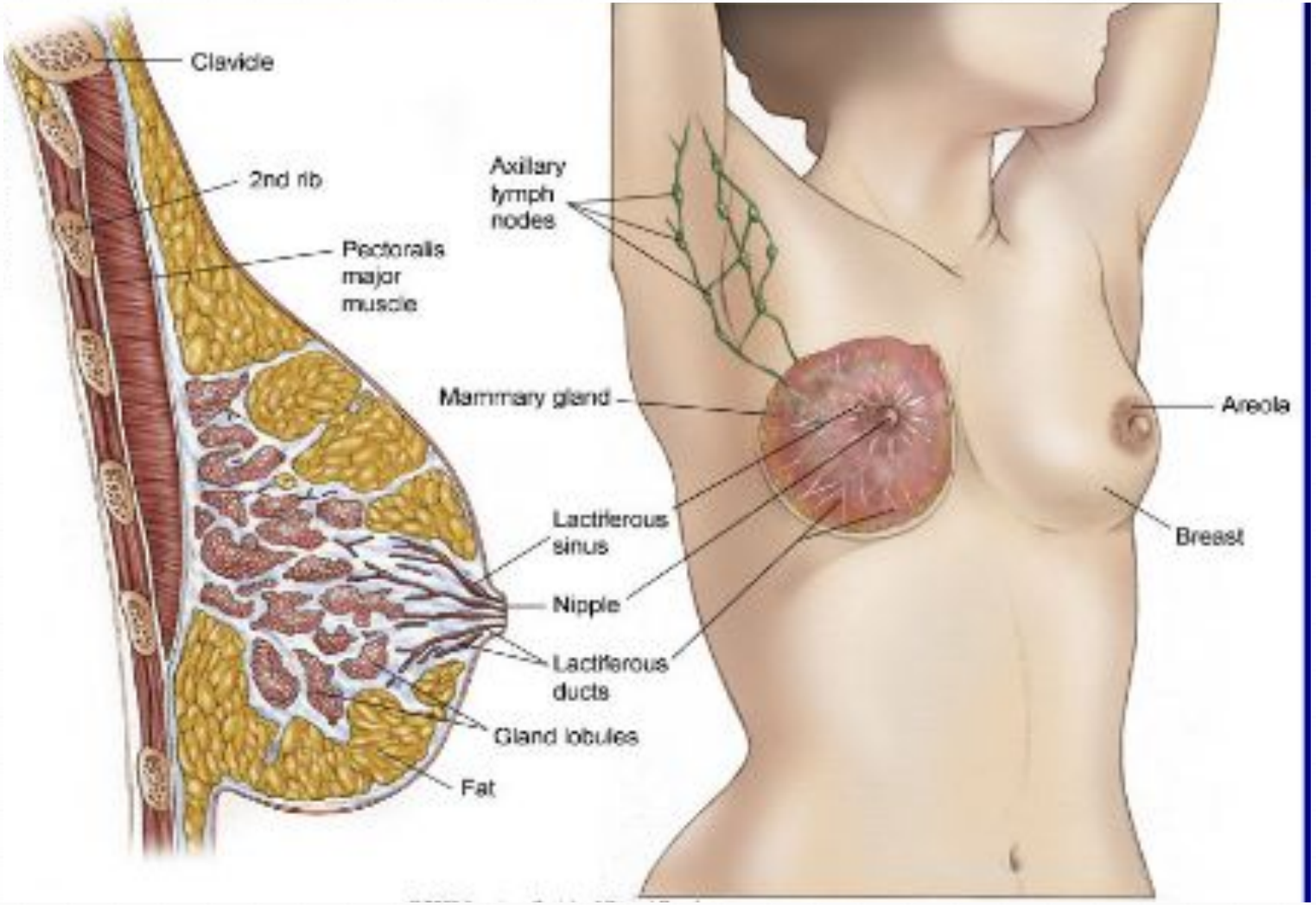
Breast Pathology

Anatomy of the breast

- Modified apocrine sweat gland.
- Develop along milk line ,axilla to groin .
- Located in superficial fascia
- (15-20) lobes .
- Each lobe has its own lactiferous duct.
- Cooper's ligaments (fibrous bands of CT) that run perpendicular to dermis of skin.
- 2^{nd} 6^{th} rib, sternum to mid Axillary line.
- *Axillary Tail of Spence :* pierce the deep fascia to enter axilla.

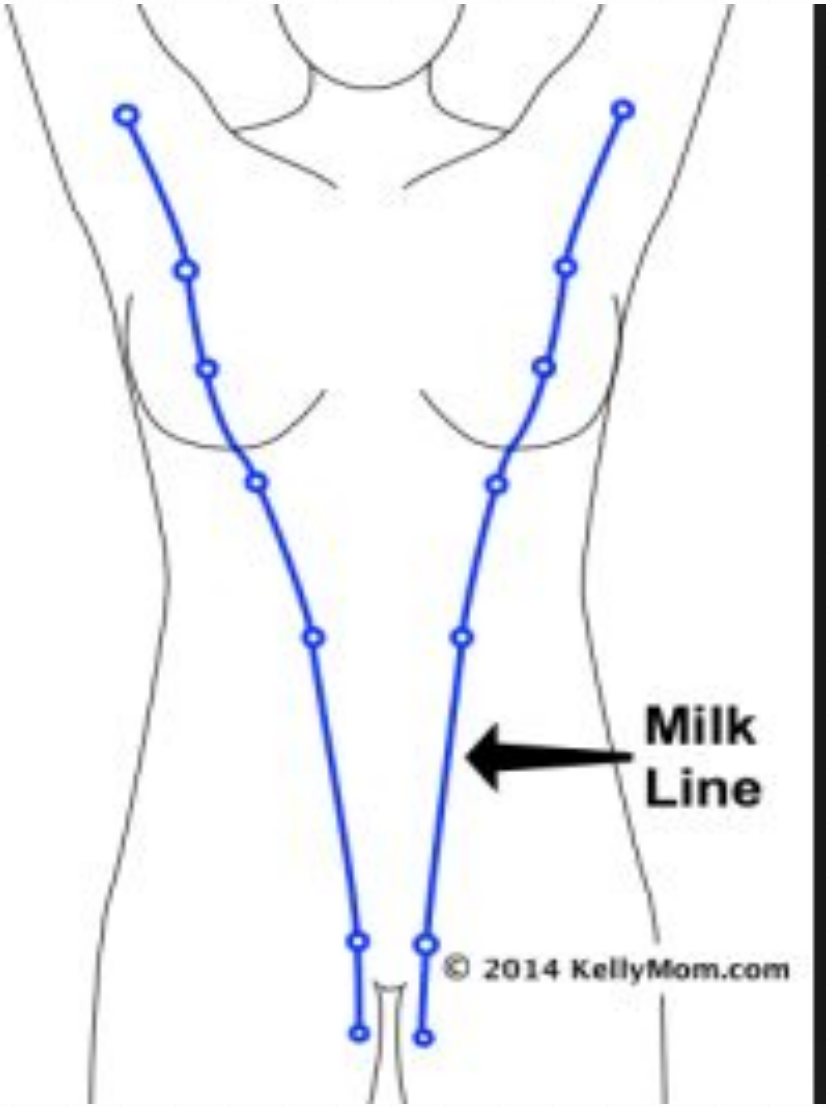

Axillary
tail of
Spence
Upper
inner
quadrant
Upper
outer
quadrant
Lower
inner
quadrant
Lower
outer
quadrant


Clavicle
Fascia
Pectoralis minor
Fatty tissue
Lactiferous sinus
Areola
Pectoralis major
Lactiferous duct
Breast lobule
Coopers ligaments


Clavicle
2nd rib
Pectoralis major muscle
Axillary lymph nodes
Mammary gland
Areola
Breast
Lactiferous sinus
Nipple
Lactiferous ducts
Gland lobules
Fat

Development of the breast

- **Milk line.**
- **Polythelia**
- **Polymastia**
- **Gynaecomastia**
- **Micromastia**
- **Macromastia**



Polymastia









Amastia

Polythelia












alamy

Polymastia





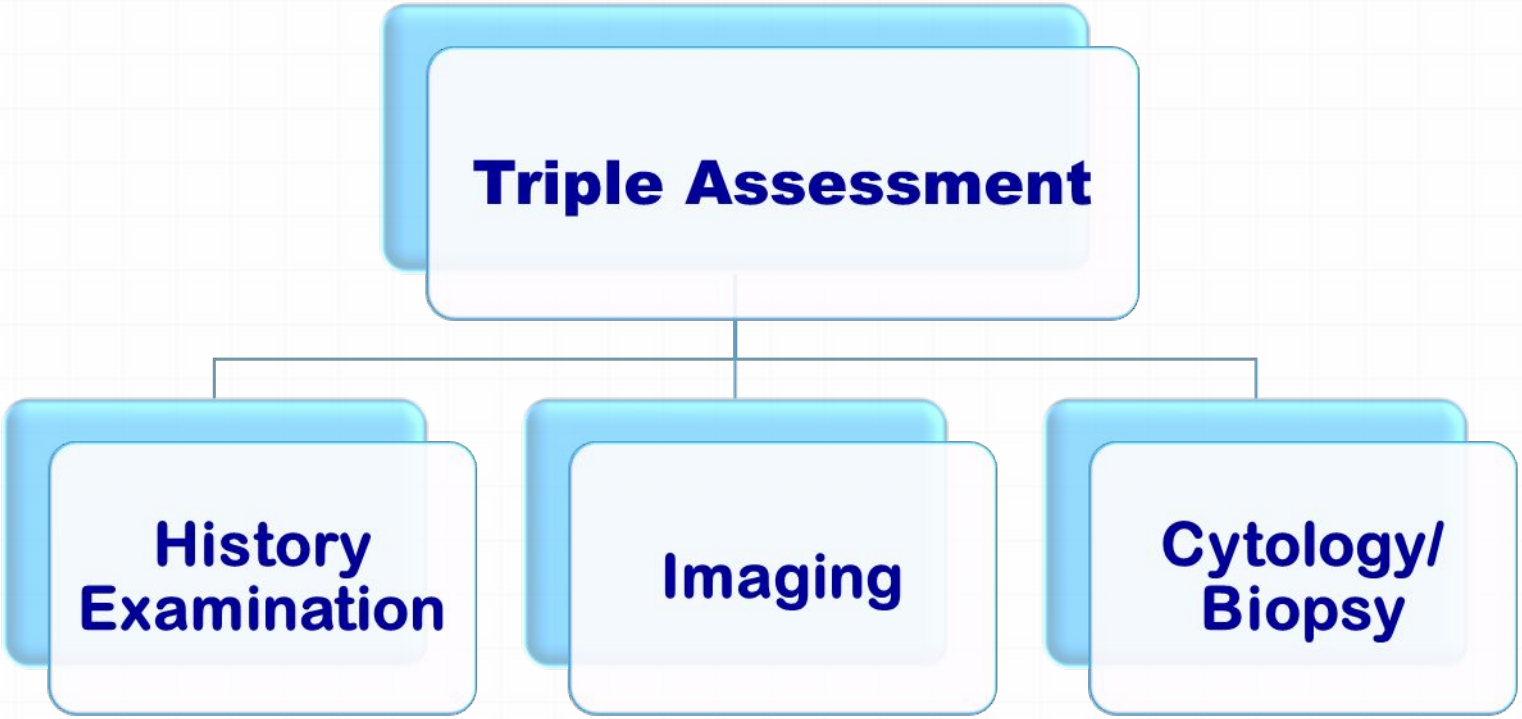
Benign breast disease

- **Universal phenomenon among women.**
- **Half the female population will seek medical attention .**
- **6-10% will have cancer.**
- **Aberrations of normal development and involution *(ANDI) .***
- **Very common occurrence , no clinical correlation .**

Role of dietary factors

- **Deficiency of essential fatty acids.**
- **Low consumption of vegetables.**
- **Low vitamin A .**
- **Increase consumption of red meat.**
- **Higher levels of saturated fatty acids.**
- **Cigarette smoking .**
- **Alcoholic drinks .**

Recommendations for Evaluation of breast lump or change in breast texture



Can Identify the Cause in Most of Cases

Clinical examination CBE

Inspection (Skin Changes)



- color
  - Redness
  - Eczema
- Edema, thickening (peau d'orange)
- infiltration, Ulceration
- Venous pattern

Infiltration ulceration









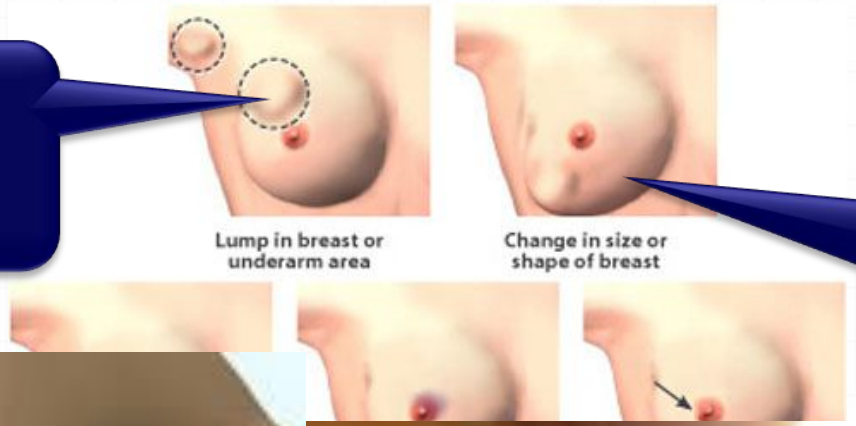
Erythema

Figure 1: Left Inflammatory Breast Cancer—Left breast is enlarged with evidence of erythema.

Edema and peau d orange

Clinical examination inspection (breasts)

Masses or thickening in breast



- Size (symmetry)
- breast shape (Dimpling)





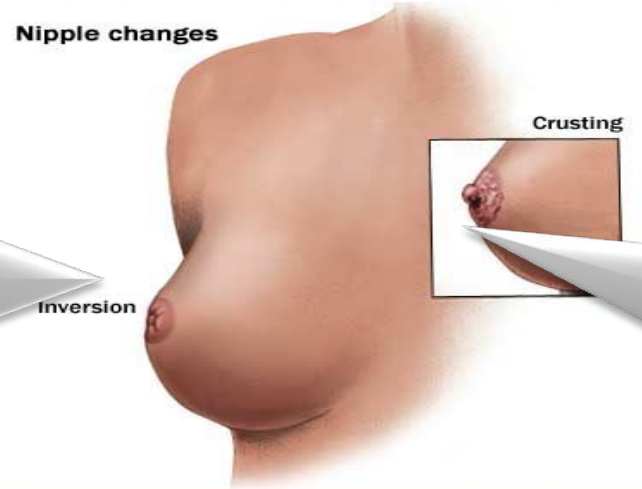
Dimpling seen by skin

Clinical examination

Inspection (Areola, Nipple changes)

Change in appearance of nipple

- Inversion, (turning inward into the breast)
- retraction



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Change in color of nipple and areola

- Erythema,
- Erosion
- ulceration

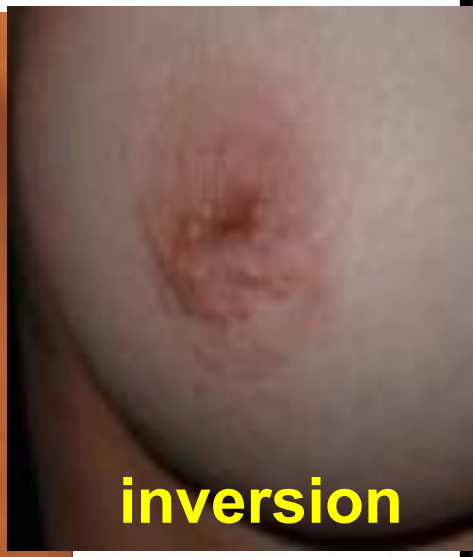
Discharge




Erosion
&ulceration


Erythema

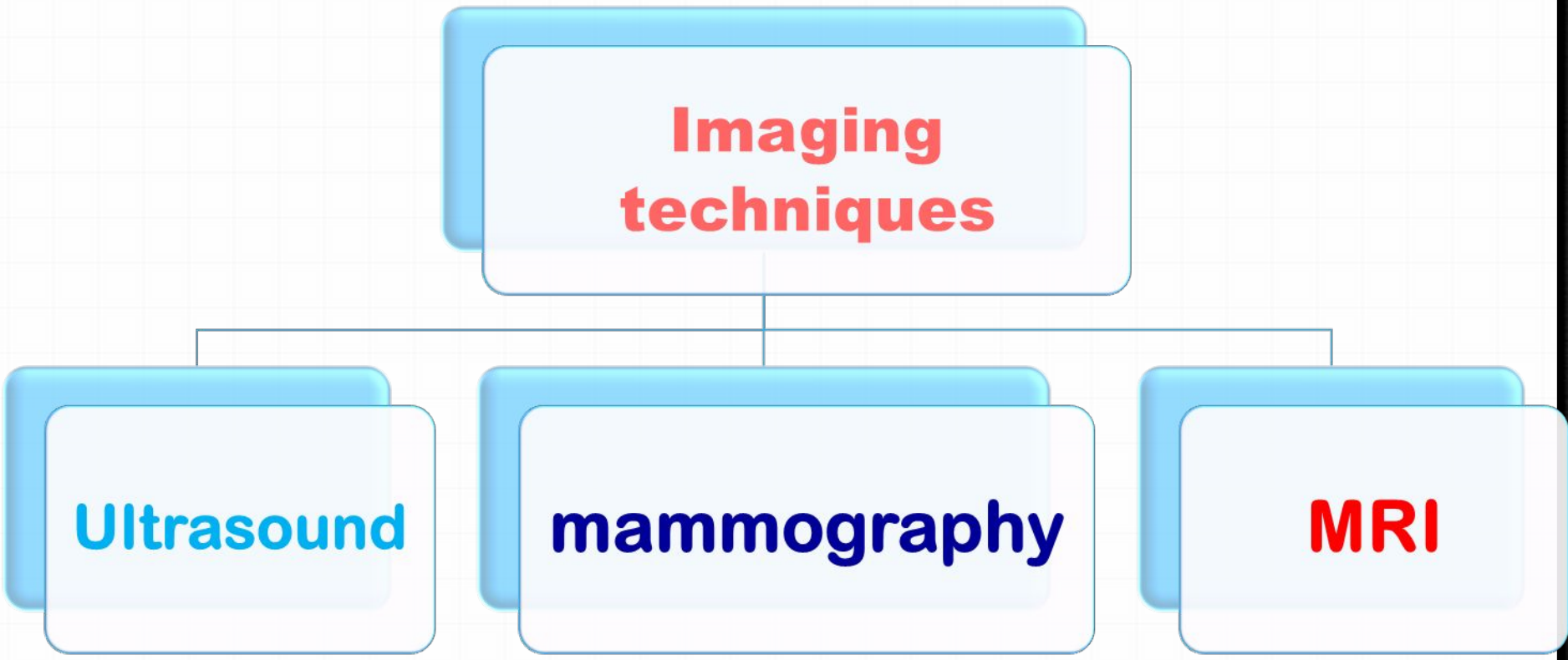

Retraction


inversion








Imaging techniques
Ultrasound
mammography
MRI

Mammography and ultrasonography are the **Primary** imaging studies for evaluating palpable breast masses.

Ultrasound is the first or the only test ordered in women under *Age 30,*

Mammography is the first test ordered in women *Age 30 or older*

MRI no role in the workup of a *Palpable* abnormality

FIBROCYSTIC CHANGES

- changes in the female breast that consist predominantly of cyst formation and fibrosis.
- In the past, these lesions were called **fibrocystic disease**
- However, since most of these changes have little clinical significance beyond the need to distinguish them from cancer, the term fibrocystic change is preferred
- fibrocystic changes are the most common breast abnormality seen in premenopausal women. The changes tend to arise during reproductive age and are most likely a consequence of the cyclic breast changes that occur normally in the menstrual cycle

- This is the most common “condition" of breast
- Always multifocal
- The cause is obscure;
  - Estrogen is a known factor,
  - Women on the estrogen-progesterone balanced pills get less fibrocystic change.

Fibrocystic changes can be subdivided into nonproliferative and proliferative patterns:

Nonproliferative Changes

- cysts and Fibrosis Nonproliferative changes are the most common type of fibrocystic lesions, characterized by an increase in fibrous stroma associated with dilation of ducts and formation of variably sized cysts.

Three patterns occur separately or together:

- 1. fibrosis
- 2. cyst formation (>3 mm)
- 3. adenosis.

FIBROCYSTIC CHANGE OF THE BREAST

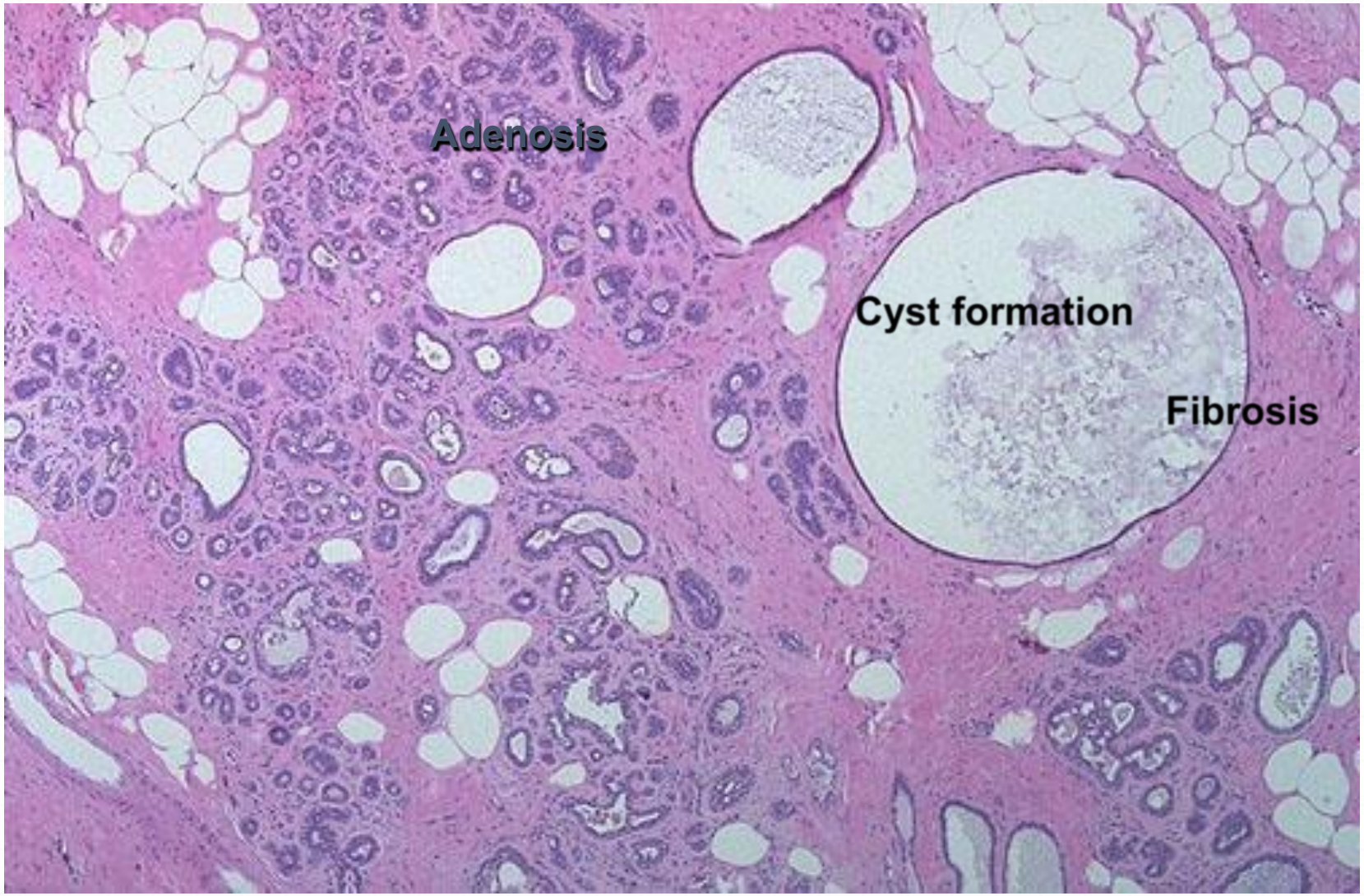
- **1. Fibrosis**
  - Dense collagenization distorting and compressing the epithelial structures.
  - This is most common in upper outer quadrants, patients in 30's.

OF FIBROCYSTIC CHANGE THE BREAST

- **2. Cyst formation** (>3 mm) :
  - Dilated dusts containing cloudy serous fluid (sometimes bloody or infected)
  - All breasts, during childbearing, contain microscopic cysts.
    - They are abnormal when they got larger than 2 mm or so.
  - Grossly, the blue-dome cyst is very familiar.
  - Epithelium may be flattened, cuboidal, columnar, or even show **apocrine metaplasia**.
  - Surrounding stroma likely to be fibrous.
  - Cysts likely to be tender before menses.

FIBROCYSTIC CHANGE OF THE BREAST

- **3. Adenosis:**
  - This extremely common change means extra, crowded ductules in some of the lobules.
  - Often the lumens are a bit distended ("blunt duct adenosis"), but they are not deformed, compressed or distorted.


Adenosis
Cyst formation
Fibrosis

MORPHOLOGY

- A single, large cyst may form within one breast, but changes usually are multifocal and often bilateral. The involved areas appear as ill-defined, diffusely increased densities and discrete nodularities on mammography.
- The cysts range from less than 1 cm and up to 5 cm in diameter. Unopened, they are **brown to blue (blue dome cysts)**

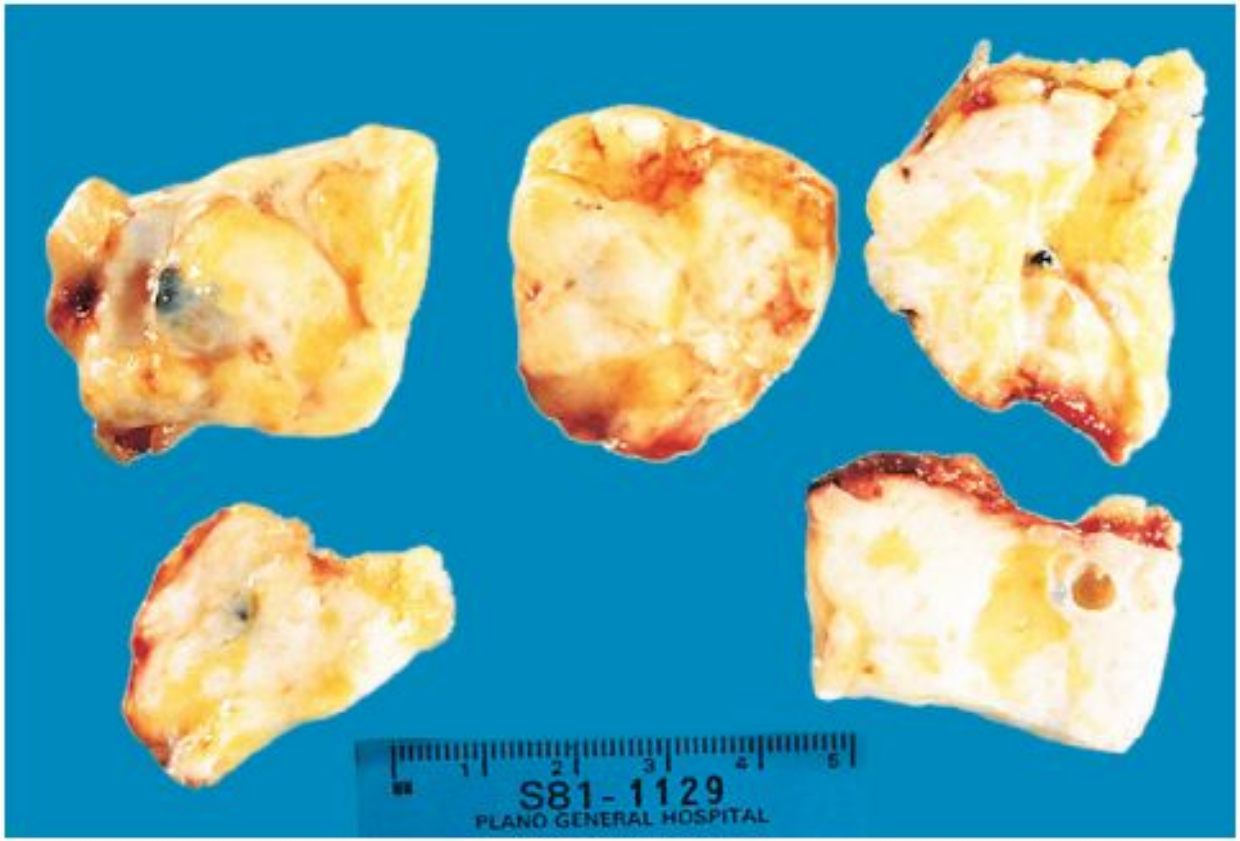


Figure 18–23 Fibrocystic change seen in breast biopsy specimens. The scattered, poorly demarcated white areas represent foci of fibrosis. In the specimen at the *lower right*, a transected empty cyst is evident; in the two specimens on the *left*, unopened blue dome cysts are seen.

PROLIFERATIVE BREAST DISEASES

- Three entities have been removed from the "fibrocystic change" category because they confer a significant cancer risk:
- **1. Epithelial hyperplasia**
  - Totally benign-looking hyperplasias
  - Atypical ductal hyperplasias
  - Atypical lobular hyperplasia
- **2. Sclerosing adenosis**
- **3. Small duct papillomas**

Proliferative Change

- **Epithelial Hyperplasia:**
- Normal ducts and lobules of the breast are lined by two layers of cells—a layer of luminal cells overlying a second layer of myoepithelial cells. Epithelial hyperplasia is recognized by the presence of more than two cell layers. The spectrum of epithelial hyperplasia ranges from mild and orderly to atypical hyperplasias with features that resemble those of in situ carcinoma.

PROLIFERATIVE BREAST DISEASES

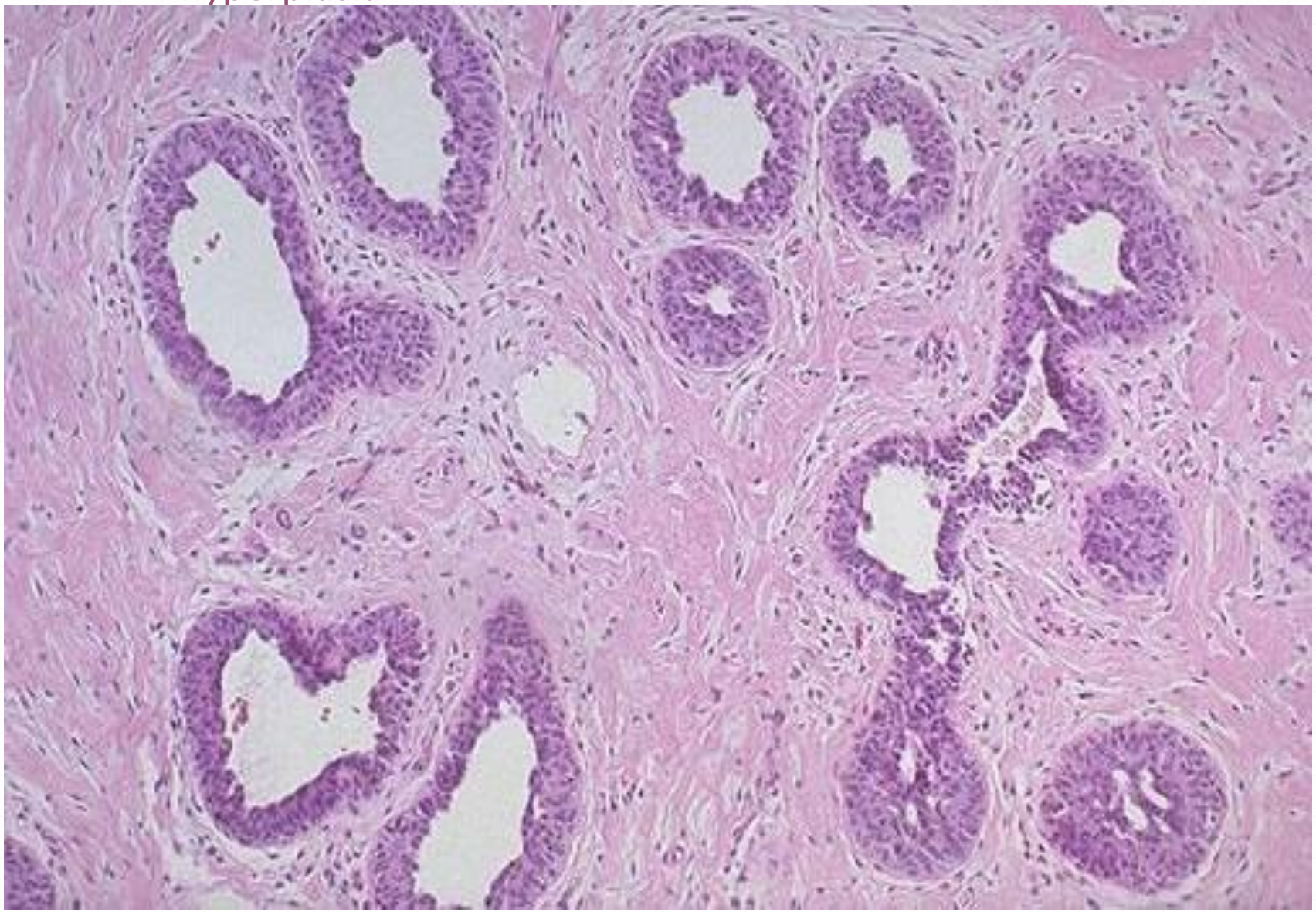
Epithelial hyperplasia

- More than the usual two layers of cells in ducts and/or lobules.
  - At least one layer will be myoepithelial cells.
- Epithelial hyperplasia is usually an incidental finding, and does not produce a mass.
- Cells are piled up and may even fill ducts and/or ductules.
- Most often, there is a mixed population of cells.
  - Epithelial cells,
  - Myoepithelial cells.

ALERTS

- Atypical hyperplasia:
  - If there is some anaplasia of architecture (swiss cheese) or cells (with ugly nuclei).
  - The cells do not fill the ducts or acini ("in-situ cancer“).
- Carcinoma in situ (CIS):
  - CIS is only slightly more likely to progress to invasive cancer than is "atypical hyperplasia."

Epithelial hyperplasia



MORPHOLOGY

- The ducts, ductules, or lobules may be filled with orderly cuboidal cells within which small gland patterns (called **fenestrations**) can be discerned
- Sometimes, the proliferating epithelium projects as multiple small papillary excrescences into the ductal lumen (ductal papillomatosis).
- The degree of hyperplasia, judged in part by the number of layers of intraductal epithelium, can be mild, moderate, or marked.
- In some instances the hyperplastic cells have features bearing some resemblance to ductal carcinoma in situ Such hyperplasia is called atypical ductal hyperplasia. Atypical lobular hyperplasia is used to describe hyperplasias that exhibit changes that approach but do not meet diagnostic criteria for lobular carcinoma in situ. Both atypical ductal and lobular hyperplasia are associated with an increased risk of invasive carcinoma.

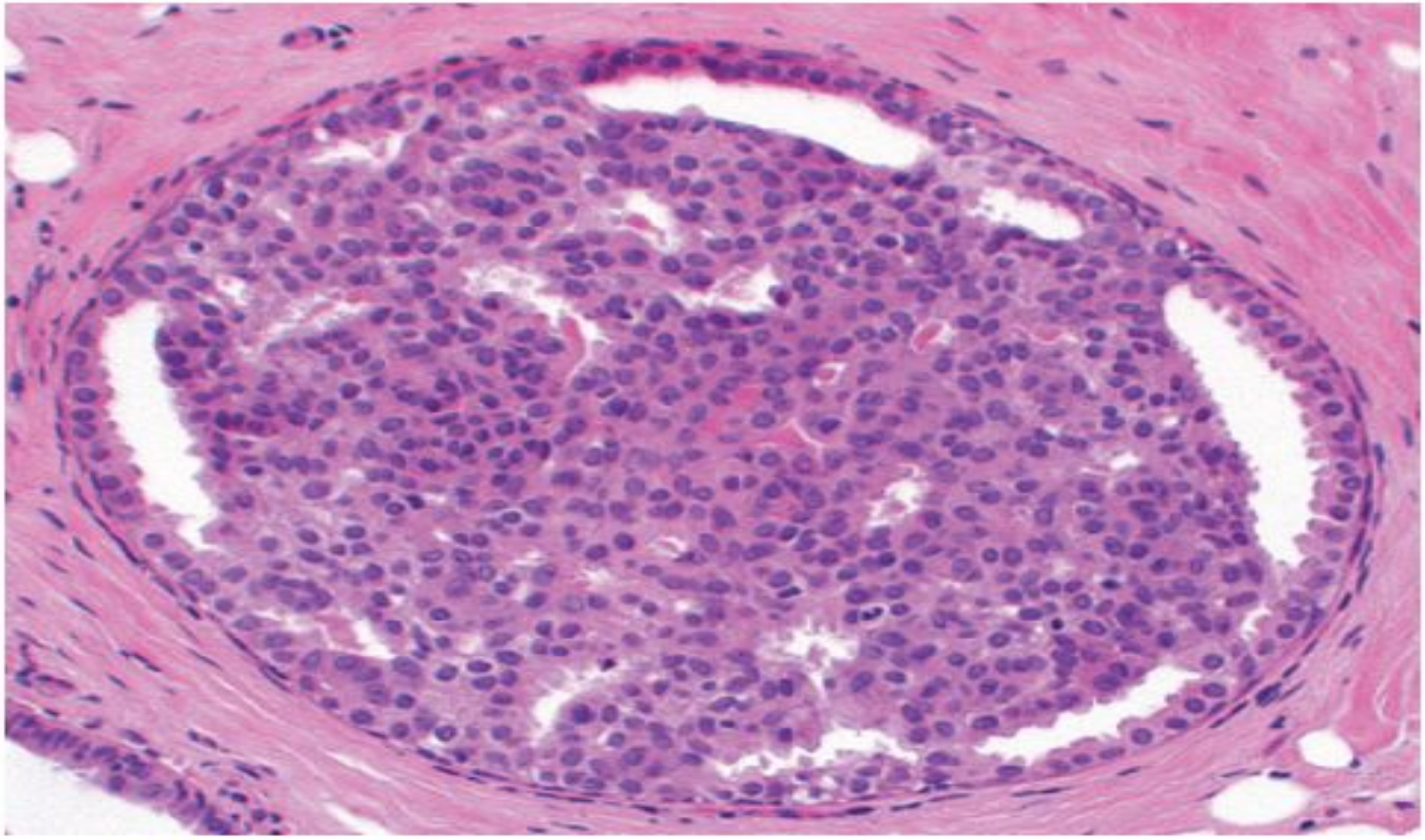


Figure 18–25 Epithelial hyperplasia in a breast biopsy specimen. The duct lumen is filled with a heterogeneous population of cells of differing morphology. Irregular slitlike fenestrations are prominent at the periphery.

Sclerosing Adenosis

- The type of fibrocystic change termed sclerosing adenosis is less common than cysts and hyperplasia but is significant because its clinical and morphologic features may mimic those of carcinoma. These lesions contain marked intralobular fibrosis and proliferation of small ductules and acini

PROLIFERATIVE BREAST DISEASES

Sclerosing adenosis

- Proliferation of small ductules and sometimes even acini in a fibrous stroma
- Usually it's a tender lump in the upper outer quadrant.
- Patients are usually around age 30-40.
- This mimics cancer both clinically and microscopically:
  - (1) There'll always be myoepithelium, expressing smooth-muscle actin, S100, high MW keratin and P63 antigens.
  - (2) The normal lobular architecture is preserved, though lobules may be expanded (under low-magnification).

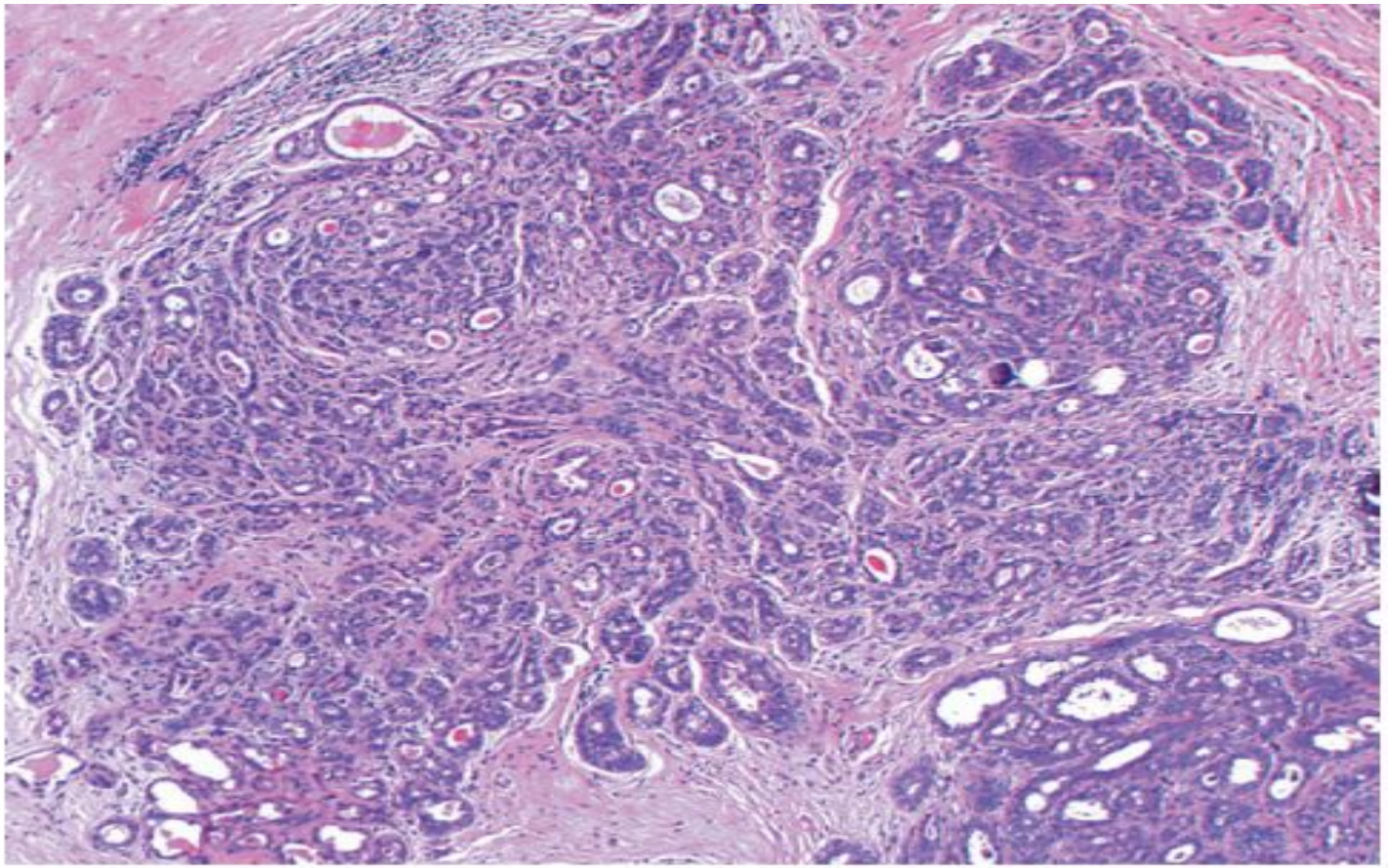


Figure 18–26 Sclerosing adenosis, breast biopsy. The involved terminal duct lobular unit is enlarged, and the acini are compressed and distorted by surrounding dense stroma. Unlike in breast carcinoma, the acini are arranged in a swirling pattern, and the outer border is well circumscribed.

Relationship of Fibrocystic Changes to Breast Carcinoma

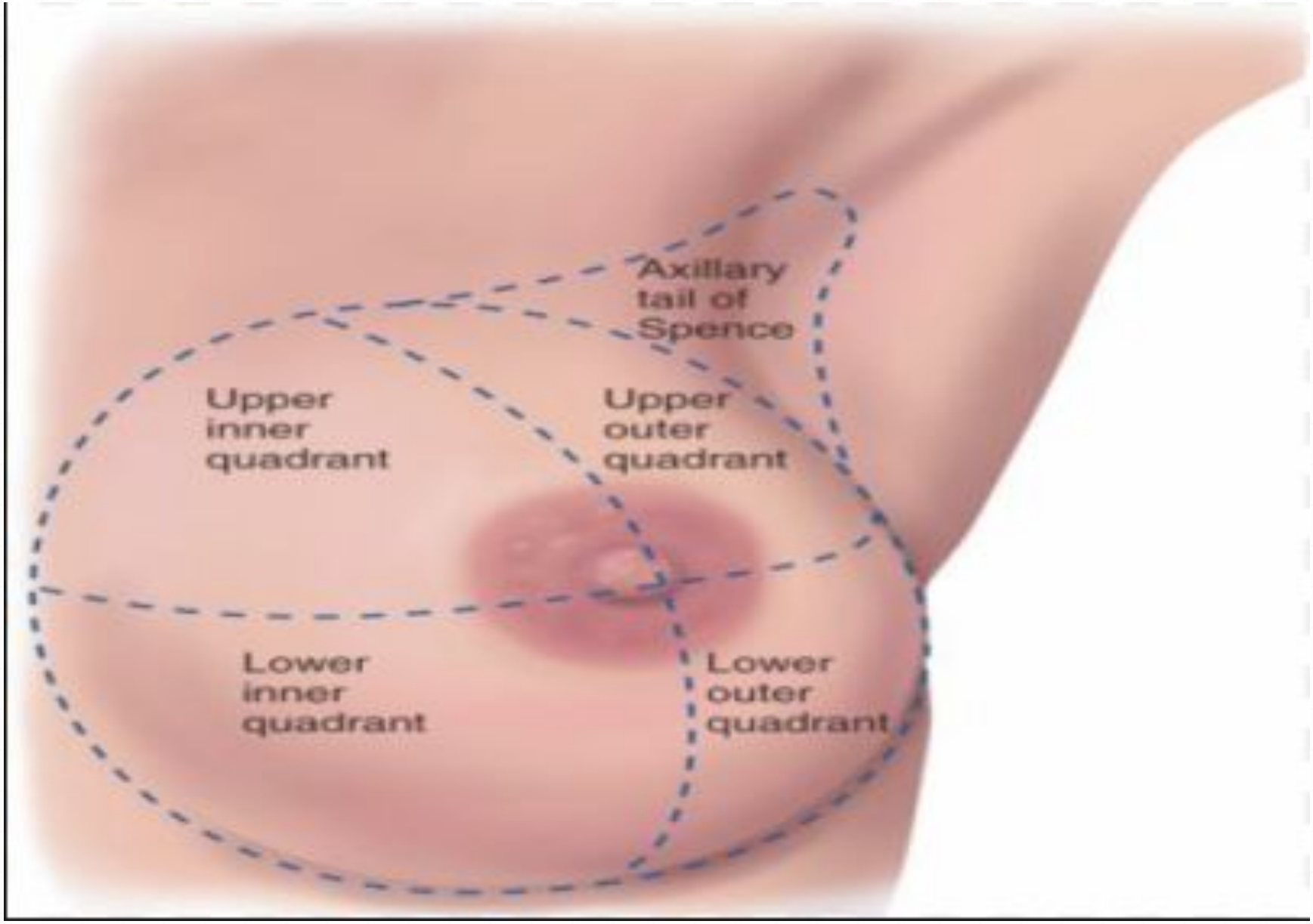
- Although fibrocystic changes are benign, some features may confer an increased risk for development of cancer:
- Minimal or no increased risk of breast carcinoma: fibrosis, cystic changes, apocrine metaplasia, mild hyperplasia
- Slightly increased risk (1.5- to 2-fold): moderate to florid hyperplasia (without atypia), ductal papillomatosis, sclerosing adenosis
- Significantly increased risk (5-fold): atypical hyperplasia, whether ductular or lobular

Mastalgia

- **70% of female will experience breast pain.**
- **Cyclic in two thirds , non cyclic in the rest .**
- **Unilateral , bilateral, multi-centric , multifocal.**
- ***Only 7% of Breast Cancer present with pain.***
- ***Cyclic Mastalgia :*** **start at *34 y* relieved by menopause exercise increase pain.**
- ***Non cyclic Mastalgia:*** **start at older age *43y* in chest wall or breast itself.**

Diagnosis of breast pain

Physiological	*Pathological*
Bilateral	Unilateral
Symmetrical	Asymmetrical
Cyclic	Non cyclic
Diffuse	Focal
Upper outer quadrant	Any quadrant
Radiate to axilla	No radiation


Axillary
tail of
Spence
Upper
inner
quadrant
Upper
outer
quadrant
Lower
inner
quadrant
Lower
outer
quadrant

Mastalgia CONT

- Avoid caffeine.
- Decrease fat intake and chocolates.
- Will fitting bra.
- Stop HRT.
- Stop smoking, exercise.
- Increase vegetables and carrots.
- Hot compressors.
- NSAIDS topical and systemic.
- Vitamin E 400 U/day.
- Evening primrose oil.
- Tamoxifen 20mg/day for 3 month

Medical treatment

- Mastalgia
- Evaluate for mass
- Exclude cancer
- Reassurance
- Pattern of discomfort

	Cyclical	Non-cyclical
Evening primrose oil	70%	40%
Danazol	50%	35%
Bromo-criptine	50%	20%
Tamoxifen		

INFLAMMATORY PROCESSES

- Included in this category are several forms of mastitis and traumatic fat necrosis, none of which increase the risk of cancer.

Lactational breast abscess:

- Arise from entry of bacteria through the nipple into the duct system and are characterized by fever, leukocytosis, erythema, and tenderness.
- *Uni-organism:* Staph aureus.
- Usually during first 6 weeks of lactation or during weaning in glandular tissue.
- Mastitis : inflammation and swelling.
- Treatment : Aspiration & antibiotics If failed I&D



Mammary duct ectasia (plasma cell mastitis)

- is a nonbacterial chronic inflammation of the breast associated with inspissation of breast secretions in the main excretory ducts. Ductal dilation and eventual rupture leads to reactive changes in the surrounding tissue that may present as a poorly defined **periareolar mass** with **nipple retraction**, mimicking the changes caused by some cancers.
- It is an uncommon condition usually encountered in parous women between 40 and 60 years of age.

Non-lactational breast abscess:

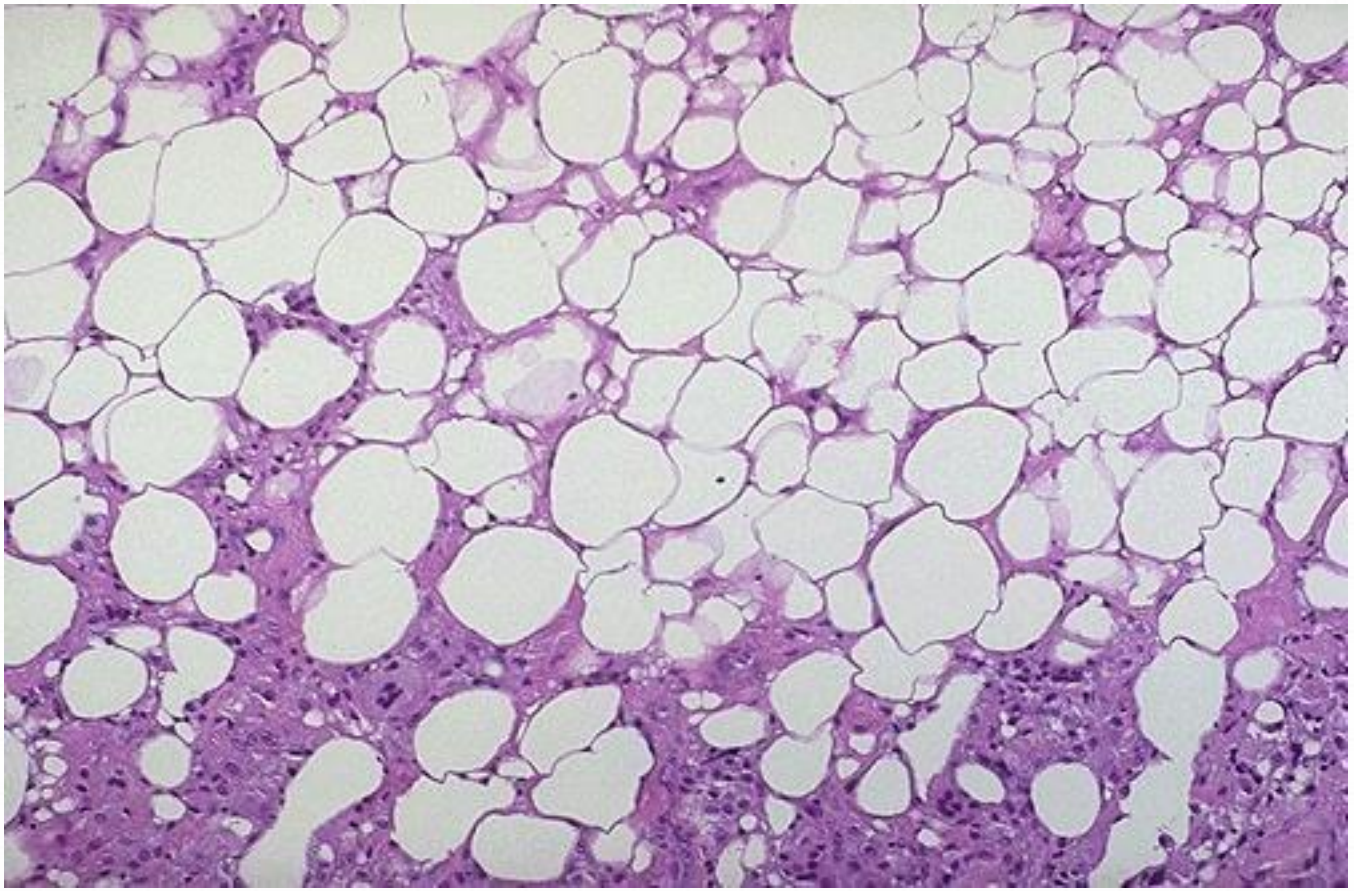
- **Chronic Sub-areolar Infections associated with duct ectasia or peri-ductal mastitis.**
- **Mean Age 32 Y.**
- **Smoking and Diabetes is common.**
- **The infections are most often *Mixed organisms* that include aerobic and anaerobic skin flora.**
- **Warm soaks and oral antibiotics may be effective treatment at this stage.**
- **Aspiration and I&D Late cases *Hadfield's operation .***


A

Fat necrosis

- Fat necrosis is an uncommon, innocuous lesion that is significant only because it often produces a mass. Most women with this condition report some antecedent trauma to the breast.

Fat
necrosis



TUMORS OF THE BREAST

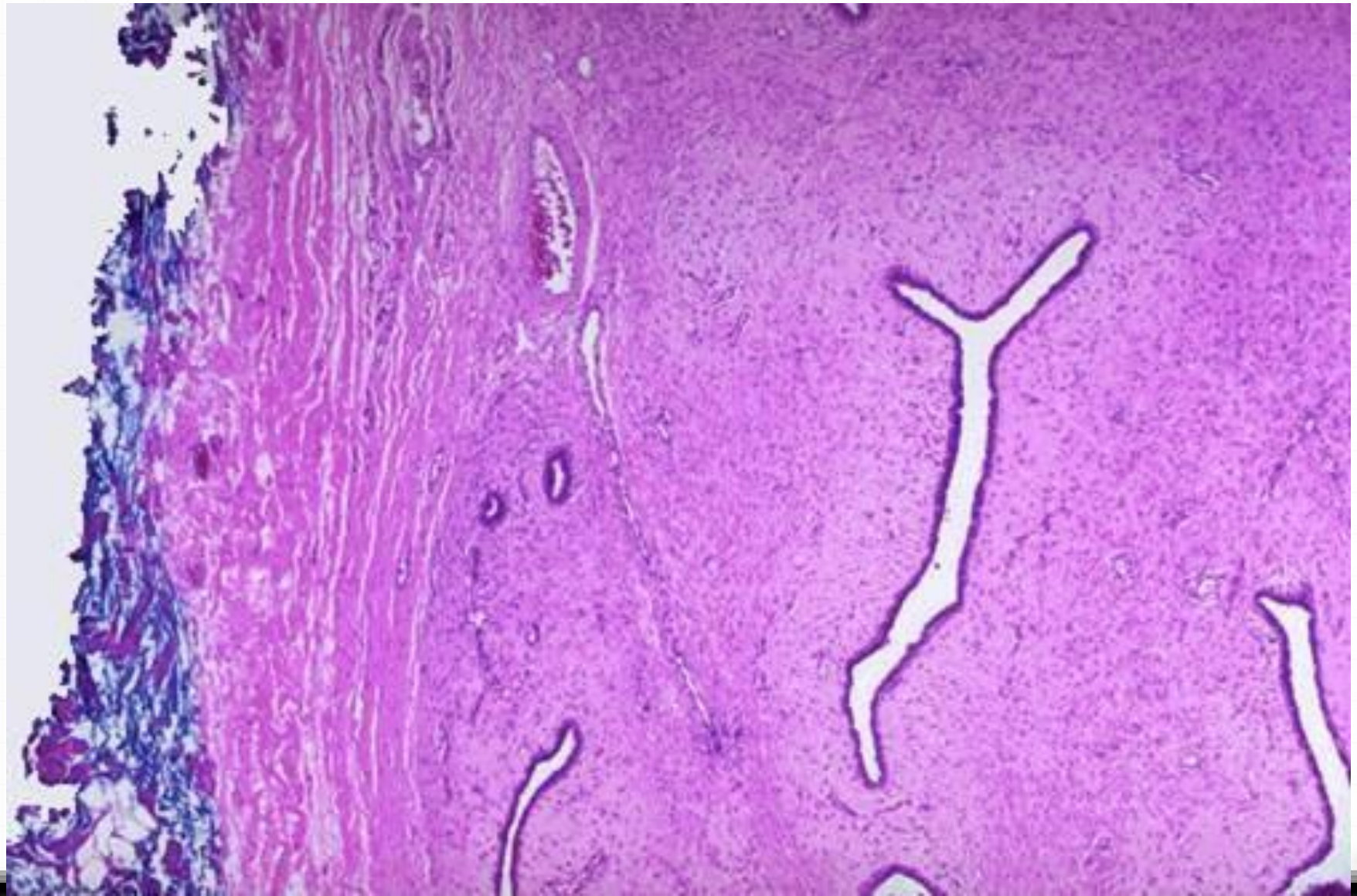
Fibroadenoma

- Fibroadenoma is by far the most common benign neoplasm of the female breast. It is a biphasic tumor composed of fibroblastic stroma and epithelium-lined glands

STROMAL TUMORS FIBROADENOMA

- The most common benign breast tumor,
- Occurs at any time during reproductive life,
  - most often under age 30.
- It presents a small, sharply circumscribed, freely movable nodule within the breast substance.
- A loose stroma surrounds ducts that are often crushed flat.

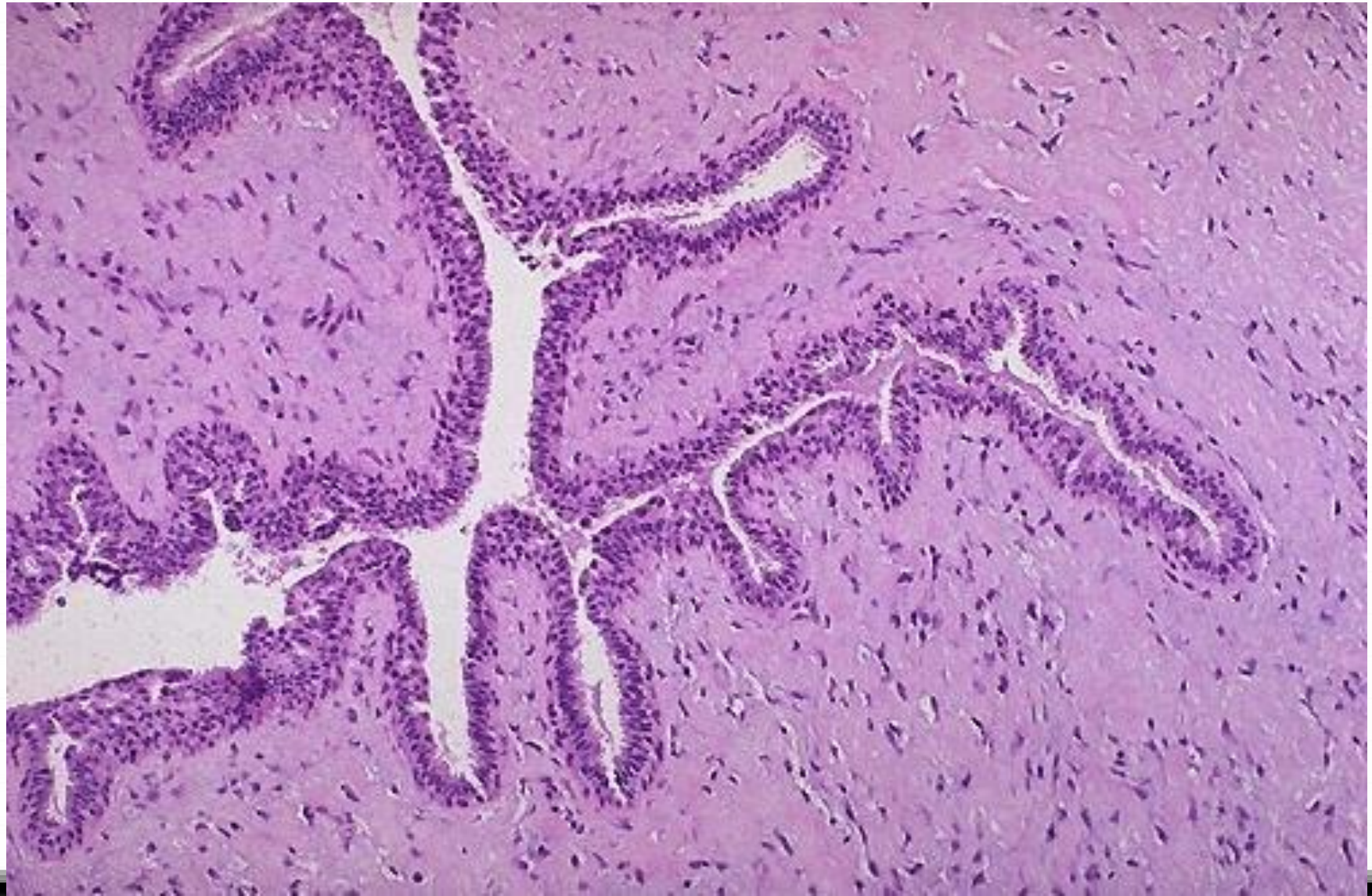
Fibroadenoma



Phylloides tumor

- Cystosarcoma phylloides
- "Phylloides" means "leaves", referring to the artichoke-like appearance of many of these tumors
- Phyllodes tumor, like fibroadenoma, arises from intralobular stroma but is much less common. Cystosarcoma phyllodes is a term sometimes used for these lesions, but phyllodes tumor is preferred, since most behave in a benign fashion and are not cystic. Like fibroadenomas, the majority of phyllodes tumors have MED12 mutations. Benign-appearing phyllodes tumors that have only a slight propensity to recur often have MED12 mutations and few other genetic changes. In contrast, tumors that display malignant behavior are more likely to have mutations in additional genes, such as TERT, the gene that encodes telomerase
- Exhibits metaplastic and/or anaplastic stroma and supposedly rapid growth
- If it metastasizes, it will be as a sarcoma

Phylloides tumor



CARCINOMA OF THE BREAST

- This is the most common cancer in women
- It is rare before age 25,
  - more common with increasing age.
- Around 1 in 9 women will develop breast cancer during their life.
- Breast cancer usually presents as a dominant, painless mass.
- Nowadays it is often found on mammography long before symptoms appear.

Risk factors

- **Female gender**
  - 100x as common as in men
- **Ethnic group**
  - Ashkenazi (a Jewish ethnic group) ancestry (the effect is explained by the high prevalence of BRCA1 mutations in the Ashkenazi population)
  - Every ethnic group has a high incidence of breast cancer; American Indians have the least.
- **Geography**
  - The US and Northern Europe have the highest rates
- **Increasing age**
  - breast cancer is rare before age 25
- **Obesity**
  - supposedly; "synthesis of estrogens in fat deposits"
- **Longer reproductive life: Estrogen ↑**
  - menarche before age 13 or menopause after 50

- Nulliparous women or those having their first child at a late age (over 30)
- Family history of breast cancer
- father's side as well as mother's
- History of high-dose radiation
  - atom bomb survivors, women radiated for breast abscesses
  - Hodgkin's disease treatment only in younger women
- History of epithelial hyperplasia (especially Atypical)
- Previous breast cancer
- Previous cancer of the endometrium

- Alcoholism
  - because of folic acid deficiency
- Previous fibroadenoma
  - triples the risk
- Genetic Factors: Germ line mutations in BRCA1 and BRCA2, p53 (Hereditary breast-ovarian cancer syndrome) ATM gene(Ataxia Talengiectasia), 10q locus in Cowden Syndrome.
- Estrogen replacement
  - as a risk factor for breast cancer after menopause remains controversial.