Breast Pathology (Overview)

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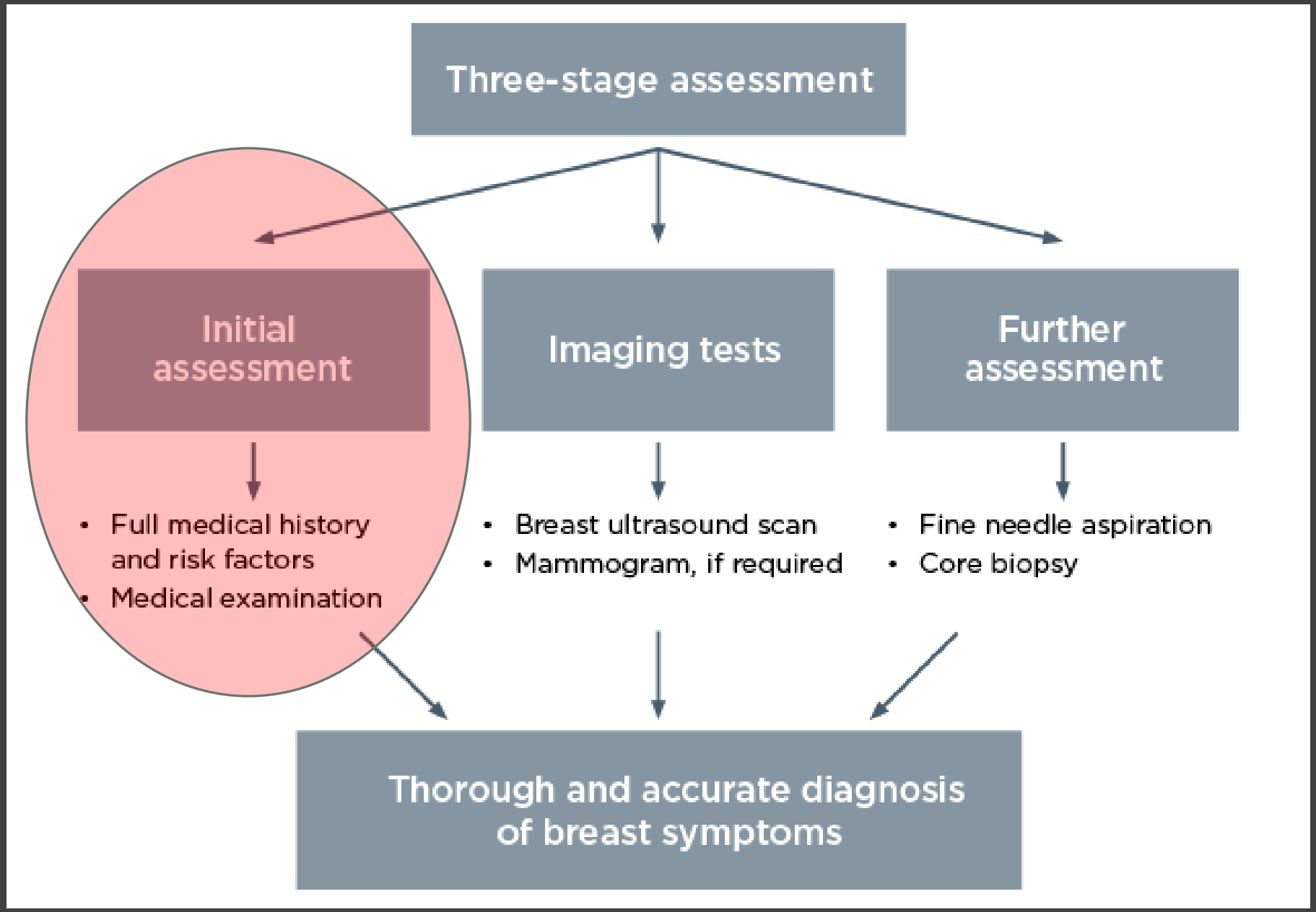
Three-stage assessment
Initial assessment
Imaging tests
Further assessment
• Full medical history and risk factors
• Medical examination
• Breast ultrasound scan
• Mammogram, if required
• Fine needle aspiration
• Core biopsy
Thorough and accurate diagnosis of breast symptoms

Benign Breast Diseases

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Objectives

- Identify wide range of benign breast disorders
- Understand clinico-pathological background of common disorders
- Diagnostic approach and findings to common breast disorders
- Management of common benign breast conditions

Introduction

- The vast majority of the lesions that occur in the breast are **benign**.
- The term “benign breast diseases” encompasses a ***heterogeneous group*** of lesions that may present a wide range of symptoms or may be detected as incidental microscopic findings.
- The incidence of benign breast lesions begins to rise during the **2nd decade** of life and peaks in the **4th-5th decades**

Targets of management of benign breast disorders

I. Distinguish **benign lesions** from in situ and invasive breast cancer

II. Assess a patient's risk of developing breast cancer

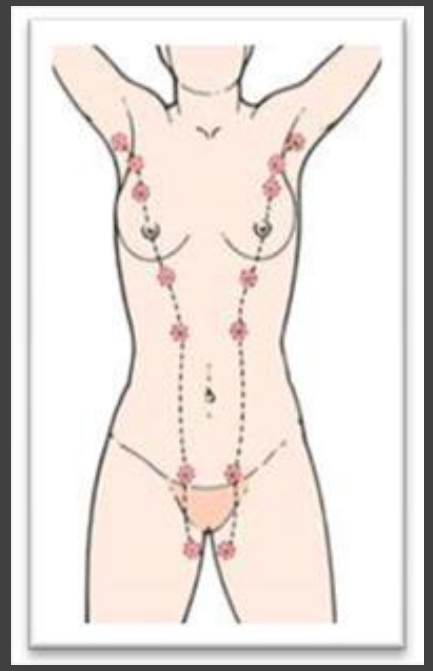
III. Avoid unnecessary surgical procedures

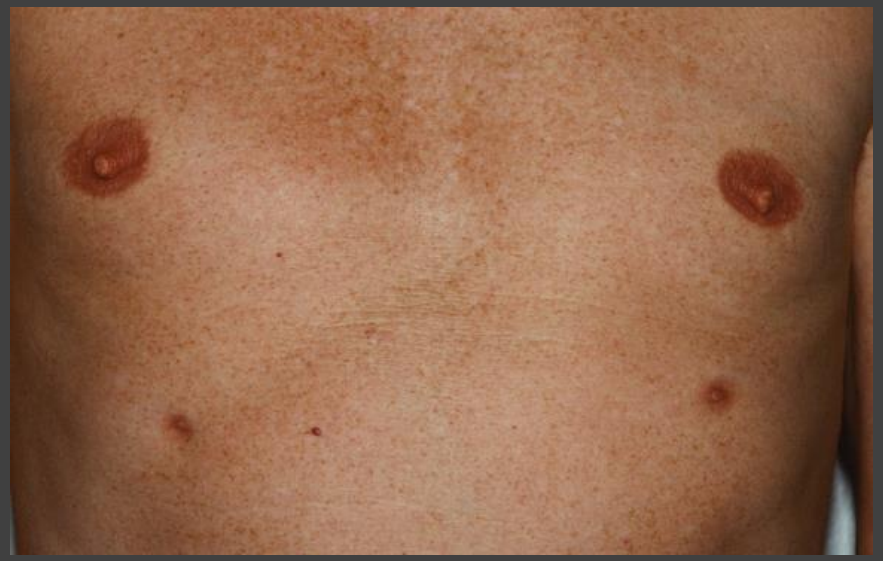
Category	Pathology / Disease	
Developmental Abnormalities	• **Ectopic breast (mammary heterotopia)** • **Underdevelopment of the breast (hypoplasia)** • **Amastia (complete absence of both breast and nipple)** • **Amazia (presence of only nipple without breast tissue)**	Nipple (polythelia), areola, glandular tissue (polymastia) Congenital Ulnar-mammary syndrome Poland's syndrome Turner's syndrome Congenital adrenal hyperplasia Acquired hypoplasia (iatrogenic) Trauma Radiotherapy
Inflammatory and related lesions	• **Mastitis** • **Mammary Duct Ectasia** • **Fat Necrosis**	Acute mastitis Granulomatous mastitis Foreign body reactions Zuska's disease
Fibrocystic Changes		
Breast Cysts		
Adenosis		

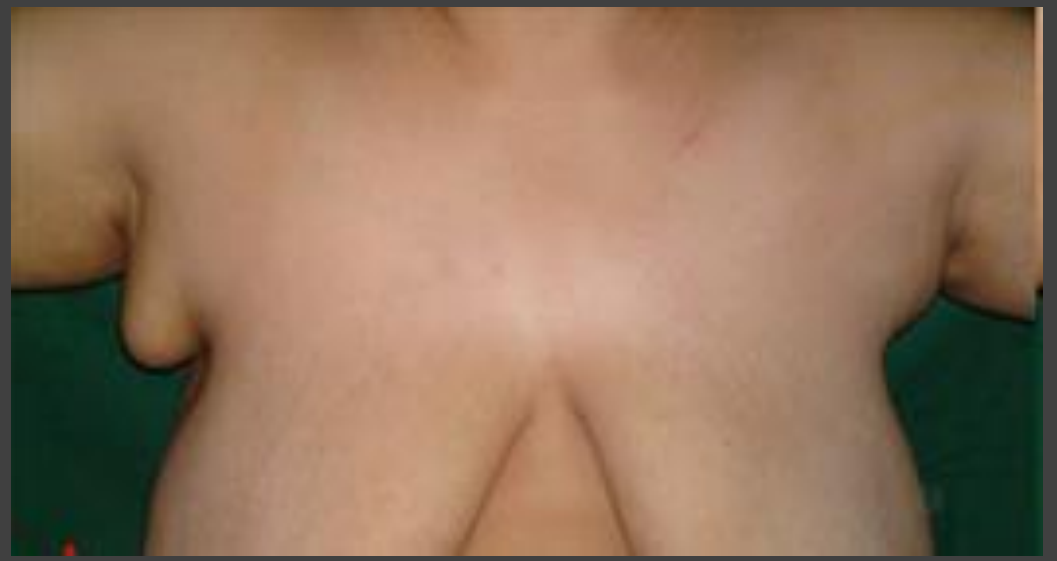
Developmental Abnormalities

1) Ectopic breast (mammary heterotopia)

- Described as both supernumerary and aberrant breast tissue
- The most common congenital abnormality of the breast.
- Location → mostly along the milk line; the most frequent sites are the chest wall, vulva, and axilla (i.e. most frequent site).
  - Can be seen in other areas (knee, thigh, buttock, face, ear, neck)
- It may vary in its components of nipple (polythelia), areola, and glandular tissue (Polymastia).
  - Absence of nipple makes the diagnosis of an accessory breast tissue difficult.
- The accessory breast tissue responds in the same way as normal breast tissue to physiological influences
- More common among Asians, especially Japanese







Clinical significance

- Recognition of ectopic breast tissue is important because it **can** develop a variety of ***benign and malignant lesions*** encountered in the normal breast.

- It has been reported that ectopic breast tissue is more prone to malignant change and that ectopic breast cancer occurs at an earlier age; however, it is rare

- Excessive breast growth (macromastia) can be seen in pregnancy as well as during adolescence.

2) Underdevelopment of the breast (hypoplasia)

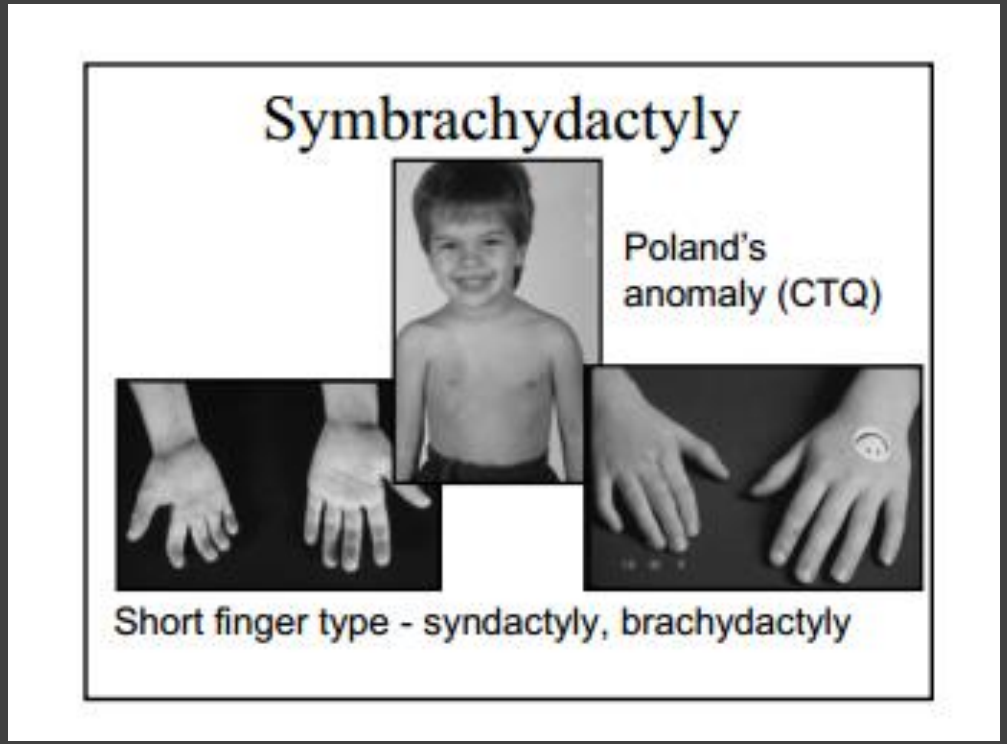
Congenital

- Usually associated with genetic disorders
  - Ulnar-mammary syndrome
  - Poland's syndrome
  - Turner's syndrome
  - Congenital adrenal hyperplasia

- Poland's syndrome has been reported to be associated with breast cancer most often.
- Some recent studies suggesting the association of ulnar-mammary syndrome and BC

Acquired

- Usually Iatrogenic
  - Most commonly subsequent to trauma or radiotherapy


Symbrachydactyly
Poland's anomaly (CTQ)
Short finger type - syndactyly, brachydactyly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Inflammatory Breast Disorders and Related Lesions

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1) Acute mastitis

- a.k.a "Puerperal or lactation mastitis"

- Defined as cellulitis of the interlobular connective tissue within the mammary gland, which can result in abscess formation and septicemia.

- Usually occurs during the first 3 months postpartum as a result of breast feeding
  - Occur in 2% to 24% of breastfeeding women from several weeks to up to 1 year after delivery in women who continue to breastfeed
  - 10% develop a breast abscess

Risk factors

Improper nursing technique

- Milk stasis and cracks or fissures of the nipple
- May facilitate entrance of microorganisms through the skin

Stress and sleep deprivation

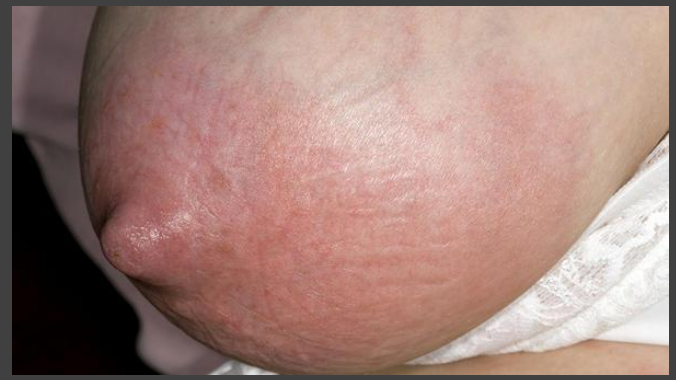
- Lower the mother’s immune status and inhibit milk flow, thus causing engorgement

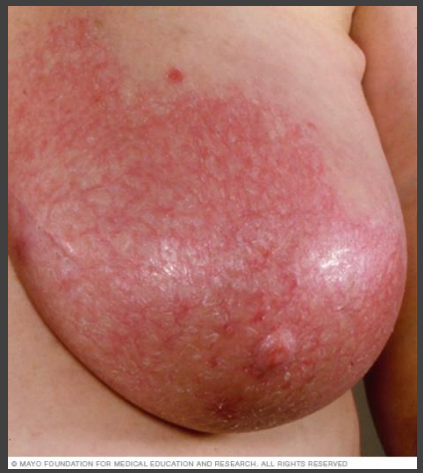
Causative agents

- ***S. aureus → most common pathogen***
- Coagulase-negative staphylococci
- β-hemolytic streptococci
- Other → Streptococcus faecalis, Escherichia coli

Presentation

- Pain – swelling – induration - redness – hotness – discharge
- Early diagnosis and early management of mastitis is of value
- The duration of symptoms before starting treatment is found to be the only independent risk factor for abscess development





Management

- Breast emptying with frequent nursing or manual pumping and
- **Empiric antibiotic therapy**
  - Little consensus on the type or duration of antibiotic therapy and when to begin antibiotics
- Abscess drainage
  - I&D
  - US guided aspiration

Breast feeding during mastitis ?

- Continue breastfeeding
  - Increasing the frequency of feeds
  - Manually emptying the breast between feeds.
- Initiate feeds on the unaffected breast and change the infant's position at different feeds.
- Continued breastfeeding is not harmful to the infant
  - Weaning / decrease feeding have an increased risk of developing a breast abscess.

- Analgesics (e.g. ibuprofen or acetaminophen)
- Increased fluid intake and adequate nutrition should be encouraged.
- Either cold or warm compresses may be used for comfort
  - Warm compresses may aid in breast drainage
- Wear some type of non-constricting breast support

Outpatient treatment

- Dicloxacillin 500 mg PO QID / 10-14 days
- Cephalexin 500 mg PO QID /10-14 days
- Amoxicillin-clavulanate 500 mg PO TID or 875 mg PO BID for 10-14 days
- If beta-lactam allergy:
  - Clarithromycin 500 mg PO BID for 10-14 days (or see following section)
- If suspected community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) infection:
  - Clindamycin 300 mg PO TID for 10-14 days
  - Doxycycline 100 mg PO BID for 10-14 days (pregnancy Category D and secreted in breast milk; do not use in pregnancy or if breastfeeding)

Inpatient treatment

- Nafcillin 2 g IV q4h **or**
- Oxacillin 2 g IV q4h

- If beta-lactam allergy or MRSA suspicion:
  - Clindamycin 600 mg IV q8h **or**
  - Vancomycin 15 mg/kg IV q12h

- For rare strains or refractory cases:
  - Tigecycline 100-mg IV infusion, then 50-mg IV infusion q12h for 5-14 days (pregnancy Category D and unknown if secreted in breast milk; do not use in pregnancy or if breastfeeding)

Clinical hints

Patients with recurrent mastitis

- Rule out abscess with ultrasonography.
- Consider choosing an antibiotic to cover (MRSA): clindamycin, trimethoprim-sulfamethoxazole, or vancomycin.

Patients with nonpuerperal mastitis

- Consider the possibility of cancer.
- A ruptured cyst may be associated with inflammation.
- The mastitis may be self-limited, and antibiotics therefore of questionable benefit.
- If antibiotic treatment is needed, provide it as for lactating women

2) Granulomatous mastitis

- A **rare** benign inflammatory breast disease of variable etiologies
  - Infectious etiology (e.g. TB)
  - Foreign material
  - Systemic autoimmune diseases (e.g. sarcoidosis and Wegener's granulomatosis)
  - ***Idiopathic***

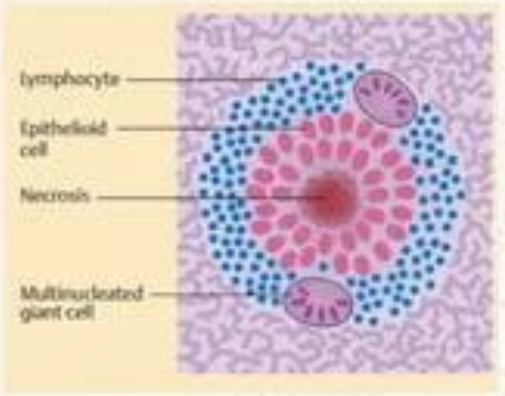
- Identification of the etiology requires microbiologic and immunologic testing in addition to histopathologic evaluation

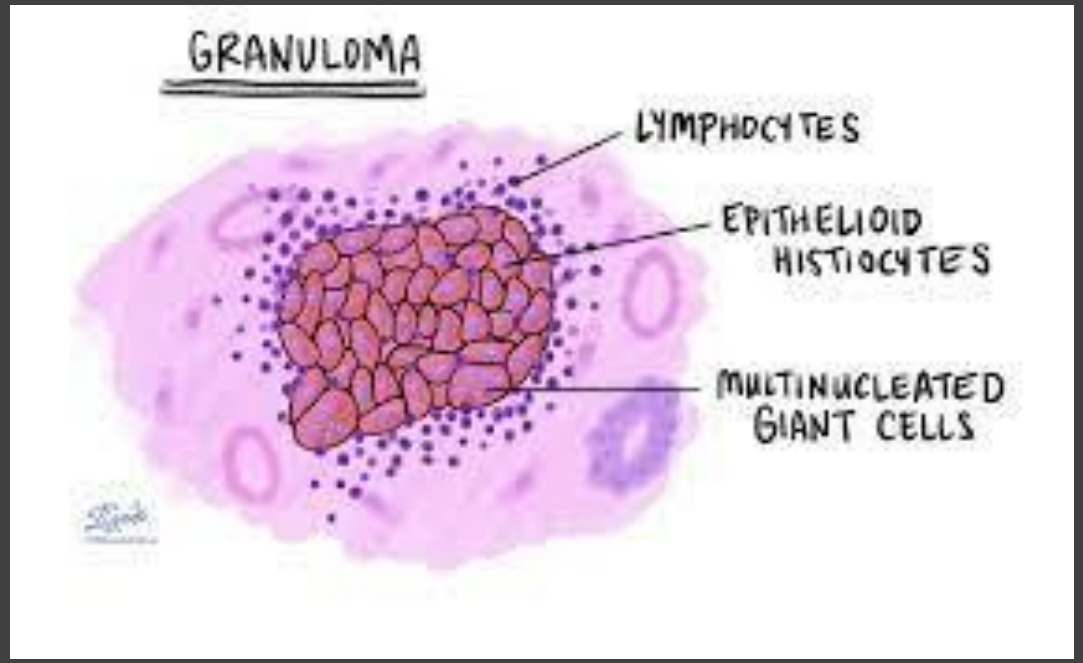
Idiopathic granulomatous mastitis

- A **non-caseating granulomatous** lesions without an identifiable cause.
- Diagnosis by excluding other possible causes
- Cause is unknown;
  - may be attributed to a localized autoimmune response to retained and extravasated fat- and protein-rich secretions in the duct
- Histologically
  - chronic non-caseating granulomatous inflammation typically limited to lobuli.

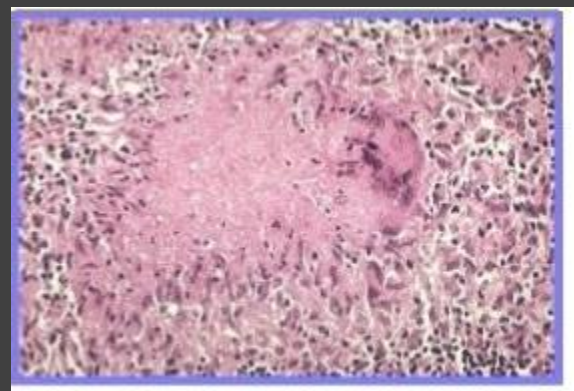
COMPOSITION OF GRANULOMA

- Following structural components
  - Epitheloid cells
  - Multinucleate giant cells
  - **Lymphoid cells** - cell mediated immune reaction
  - Necrosis & Fibrosis.

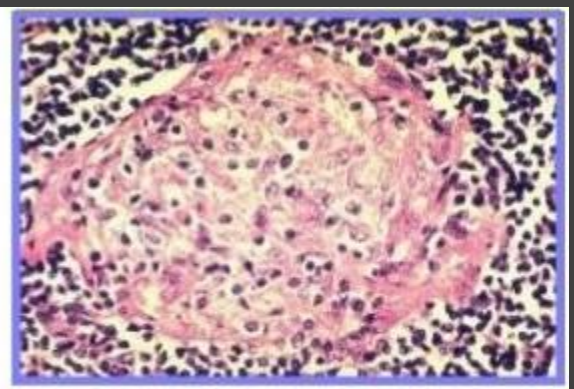




CASEATING GRANULOMA	NONCASEATING GRANULOMA
A granuloma with such a center that has undergone caseous necrosis is known as a caseating granuloma.	All granulomas that do not have a center that has undergone caseating necrosis are called noncaseating granulomas.
Occurs typically in tuberculosis.	Occurs in disease conditions such as sarcoidosis, Crohn's disease, and leprosy.



Caseating granulomas

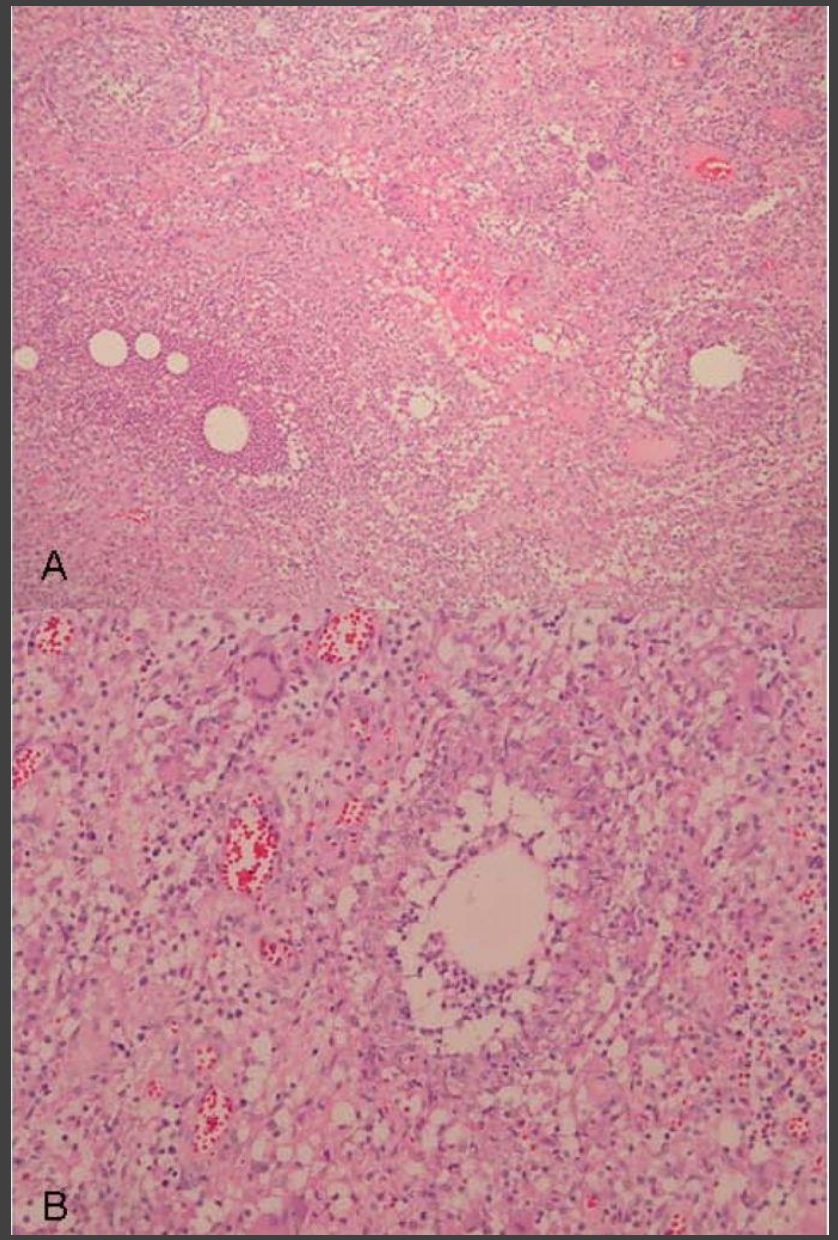


Non caseating granulomas

Granulomatous Lobular Mastitis	Sarcoidosis
Centered on lobules	Widespread distribution
Granulomas may not be well formed	Well formed tight granulomas
Associated inflammtion may be extensive	Frequently lacks extensive accompanying inflammation (naked granulomas)
May have associated fat necrosis and abscess	Necrosis and abscess rare

Granulomatous Lobular Mastitis	Mammary Duct Ectasia
Centered on lobules	Centered on ducts
Granulomatous inflammation	May have giant cells but usually lacks formed granulomas
Nearly all cases postpartum	May occur without associated pregnancy

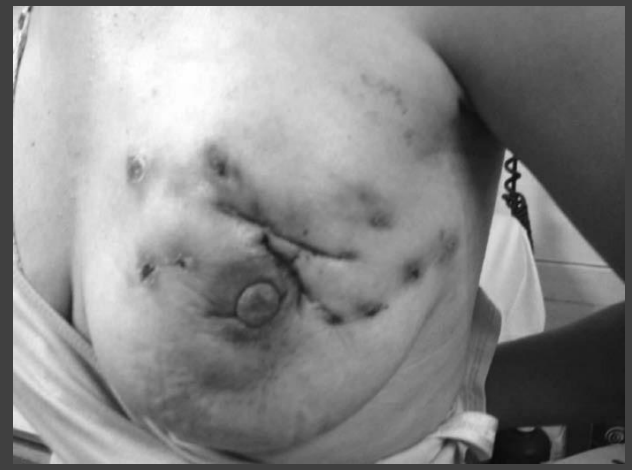
Granulomatous Lobular Mastitis	Puerperal Mastitis
No infectious organisms	Bacterial infection
Mean interval two years from delivery	Recent delivery



Microscopic findings of idiopathic granulomatous mastitis. 2A Empty spaces of varying sizes surrounded by granulomatous inflammation and micro-abscess formation (H & E, 40×) 2B Epithelioid granuloma admixed with polymorphonuclear cells and multinucleated giant cells

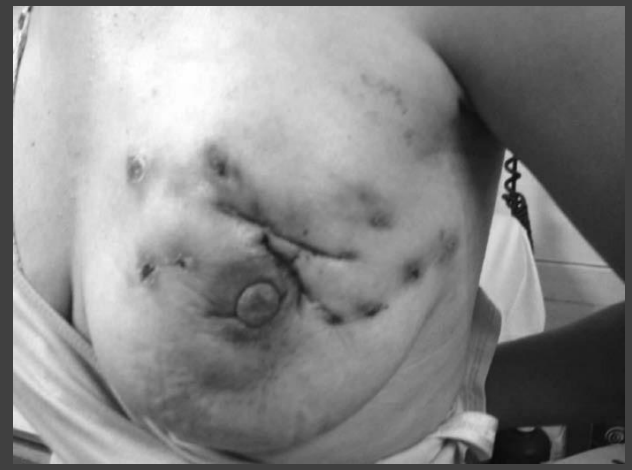
Presentation

- Ill defined painful mass in the breast
  - Can involve any quadrant
  - Bilateral involvement is rare
- Skin thickness, sinus and abscess formation
- Axillary lymphadenopathy
- Nipple retraction
- May be mistaken with breast carcinoma



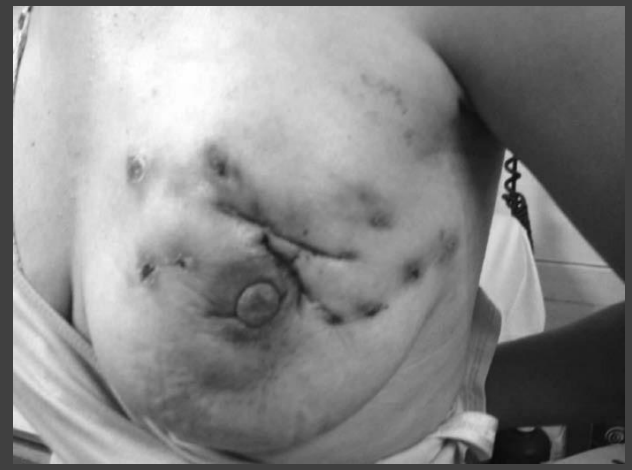
Diagnosis

- Triple assessment
- Breast Imaging → Breast ultrasound +/- mammogram
- Tissue biopsy?



Treatment

- Complete surgical excision whenever possible plus steroid therapy.
- Abscess I&D
- Spontaneous resolution occur



Prognosis

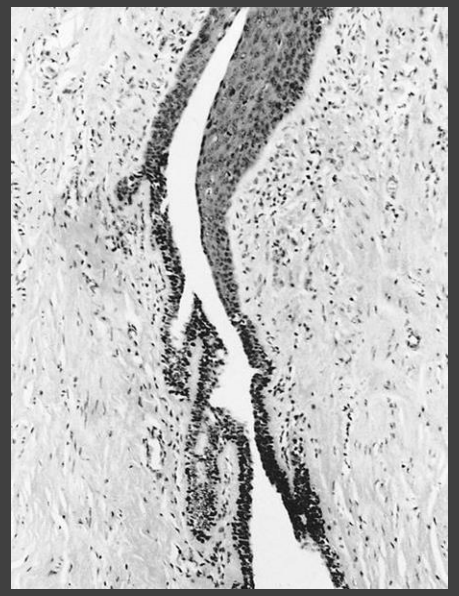
- 5-50% of the cases have
  - Persistence
  - Recurrence
  - Complications (e.g. abscess formation, fistulae, and chronic suppuration)
- long-term follow up is necessary in these patients

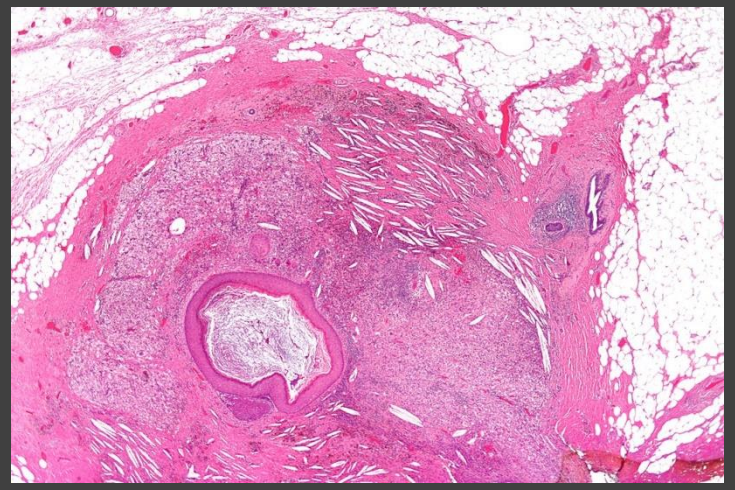
3) Recurring subareolar abscess (Zuska's disease)

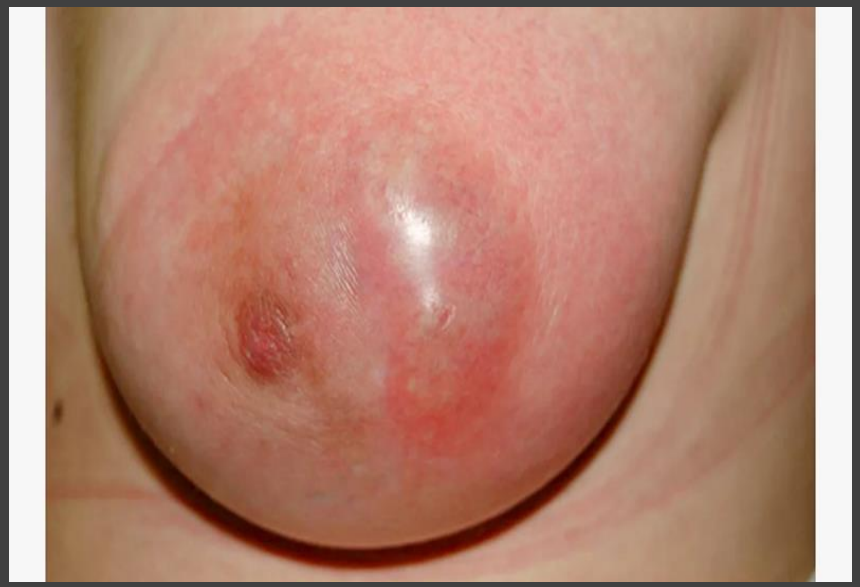
- **Rare, benign bacterial infection of the breast**
- **90% of patients are *smokers***
- **A triad of:**
  - **Draining cutaneous fistula from the subareolar tissue**
  - **Chronic thick, pasty discharge from the nipple**
  - **History of multiple, recurrent mammary abscesses**

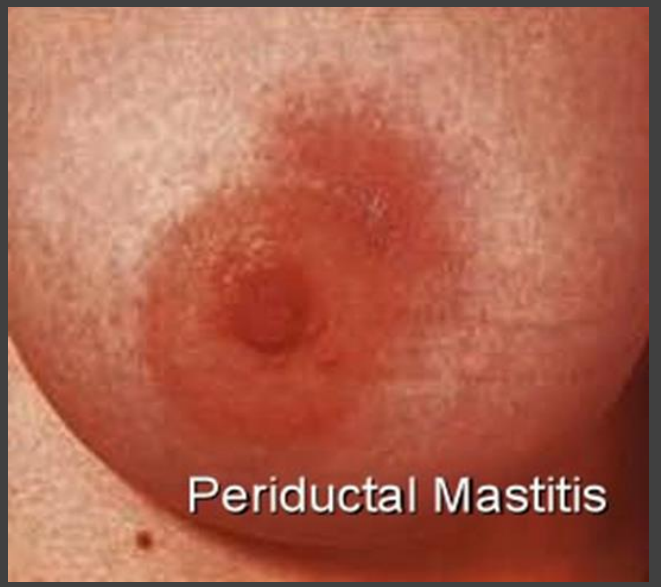
Pathology

- **Squamous metaplasia** of one or more lactiferous ducts in their passage through the nipple (i.e. probably induced by smoking)
- **Keratin plugs** obstruct and dilate the proximal duct, which then becomes infected and ruptures.
- **Abscess** formation beneath the nipple, and fistula opens at the margin of the areola for drainage.








Periductal Mastitis

Treatment

- Surgical drainage → the acute inflammation resolves
- Complete excision of the affected duct and sinus tract ***(fistulectomy [Hadfield operation])***
- ***Smoking cessation***
- Abscesses may recur when the process develops in another duct

4) Mammary Duct Ectasia

- Also called ***periductal mastitis***
- Distinctive clinical entity that **can mimic invasive carcinoma** clinically.
- Age → middle-aged to elderly parous women

Presentation:

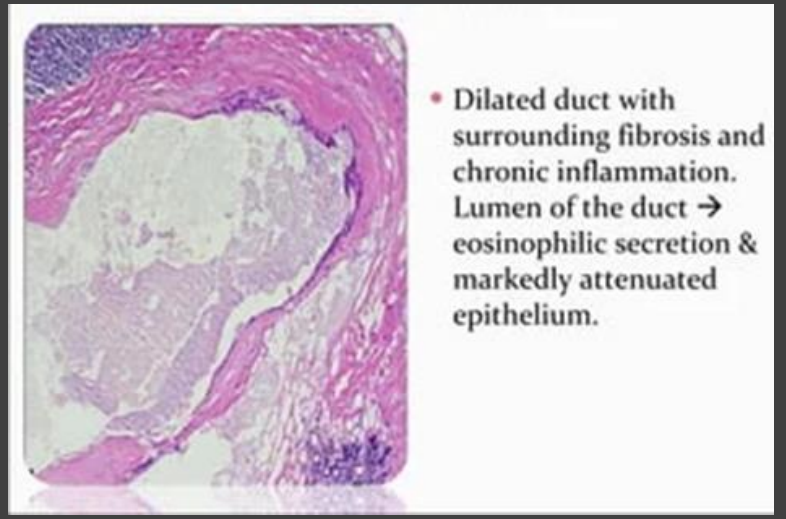
- Nipple discharge (bloody, serous, creamy white, yellow)
- Palpable subareolar mass
- Noncyclical mastalgia
- Nipple inversion or retraction.

The pathogenesis and the etiology of the disease are still being debated.

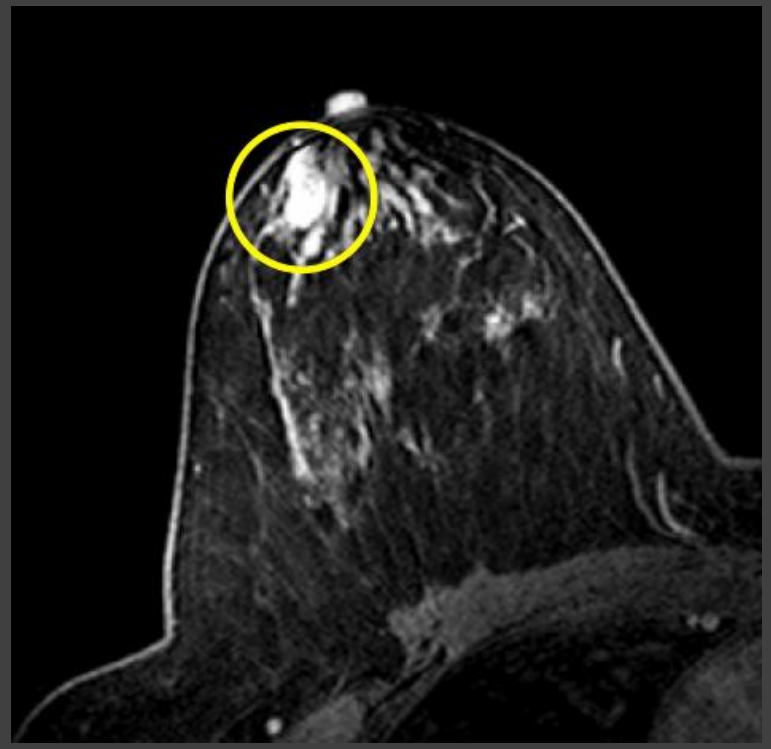
- ***Smoking*** has been implicated as an etiologic factor in mammary duct ectasia. More association with young smokers

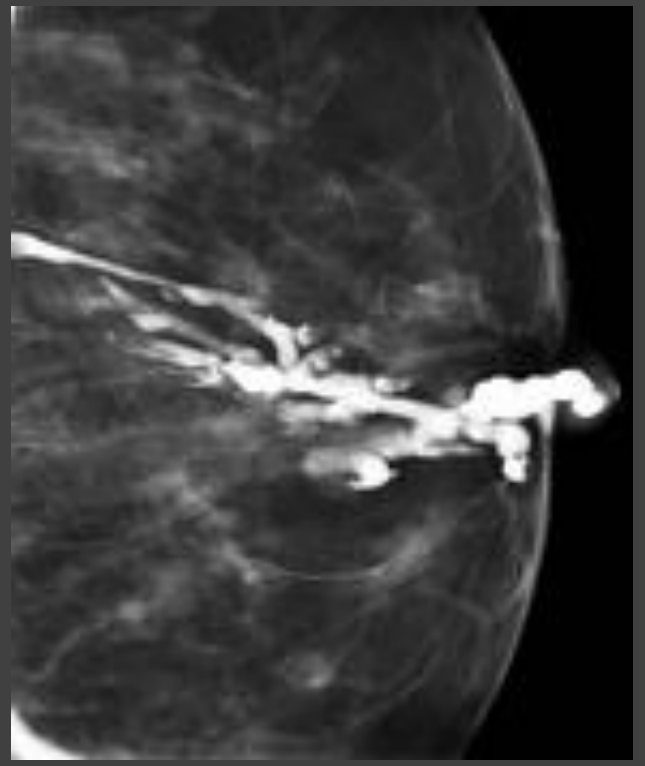
Pathologic findings

- Dilatation of major ducts in the subareolar region.
- Accumulation of eosinophilic, granular secretions and foamy histiocytes within the duct epithelium and the lumen.
- The inspissated luminal secretions may undergo calcifications



- Usually an asymptomatic lesion and is detected mammographically because of microcalcifications.





Management

- There is no evidence in the literature indicating that mammary duct ectasia is associated with an increased risk for breast cancer.
- CNB → if clinical presentation and mammographic findings are suggestive for malignancy
- Generally does not require surgery and should be managed conservatively
- *Failed conservative txn → Surgical excision of the main duct*

5) Fat necrosis

- Is a benign nonsuppurative inflammatory process of adipose tissue.

- Causes:
  - Secondary to trauma
    - Accidental
    - Surgical
    - Radiation therapy
  - Associated with breast pathology
    - Carcinoma
    - Lesion with suppurative or necrotic degeneration (e.g. mammary duct ectasia, fibrocystic disease with large cyst formation)

Clinically

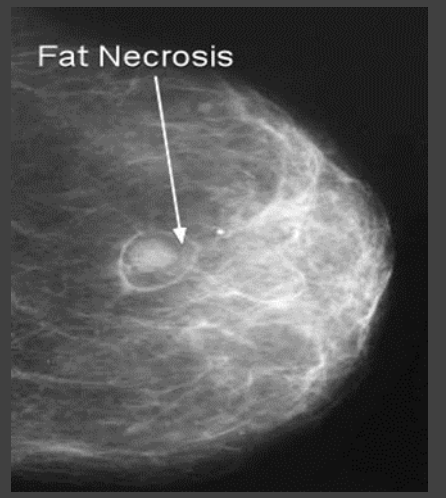
- Ill-defined or spiculated dense mass
- Skin retraction
- Ecchymosis
- Erythema
- Skin thickness

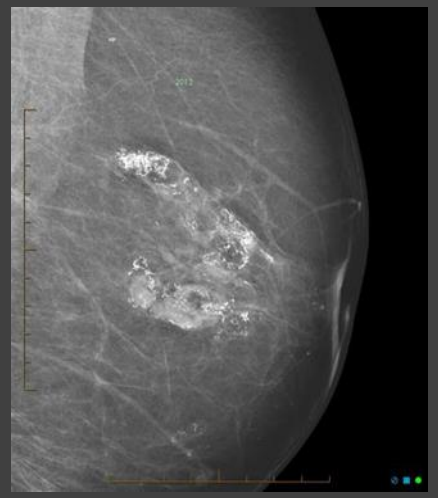
❑Radiologic workup for evaluation and to distinguish it from a malignant lesion → Breast U/S +/- Mammogram

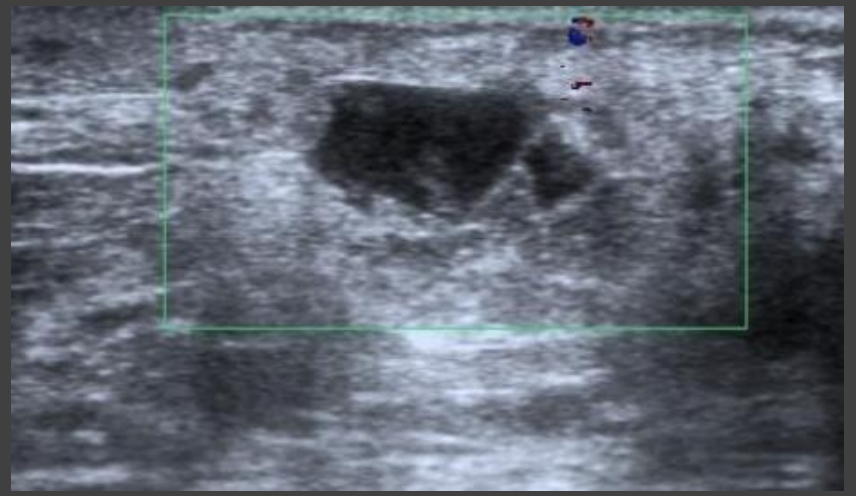
Mammogram →

- ill-defined and irregular, spiculated mass-like area +/- calcifications
- More defined with time (oil cyst)

US → hypoechoic mass with well-defined margins +/- mural nodule(s

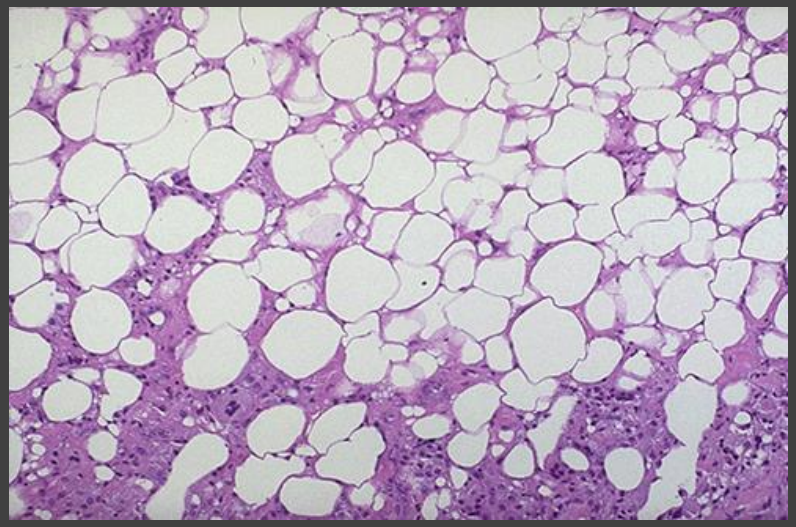






Histologically:

Anuclear fat cells often surrounded by histiocytic giant cells and foamy phagocytic histiocytes



Management:

- Conservative management
- Short interval follow up ?!
- Excisional biopsy is required if carcinoma cannot be excluded preoperatively

Fibrocystic Breast Changes

Fibrocystic Breast Changes

- The most frequent benign disorder of the breast.
- Generally affect premenopausal women between 20 and 50 years of age
- Observed clinically in up to 50% and histologically in 90% of women
- May be multifocal and bilateral.

Fibrocystic Breast Changes

- The most common presenting symptoms are breast pain (mastalgia) and tender nodularity in breasts.

- The exact pathogenesis of the entity is not clear
  - (i.e. Hormonal imbalance, particularly estrogen predominance over progesterone)

FCC: Dupont and Page Classification

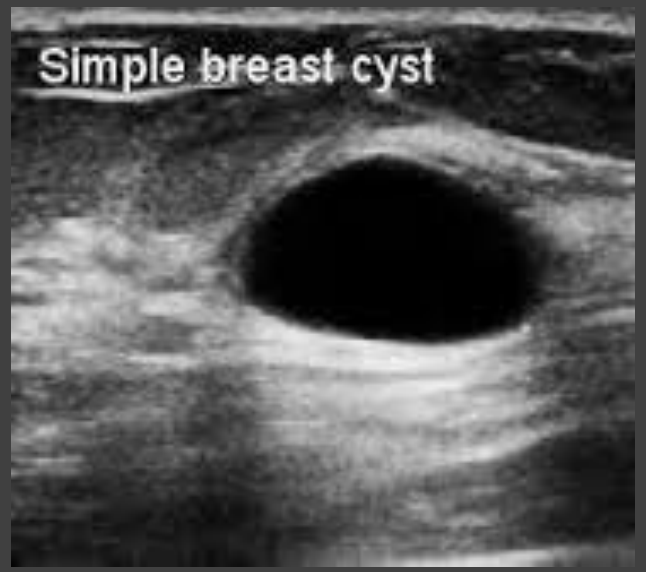
Nonproliferative lesions	• Cysts • Papillary apocrine changes • Epithelial-related calcifications • Mild epithelial hyperplasia • Ductal ectasia • Nonsclerosing adenosis • Periductal fibrosis	• 70% of cases • No increase in risk of BC
Proliferative lesions without atypia	• Moderate or florid ductal hyperplasia of the usual type • Sclerosing adenosis • Radial scar • Intraductal papilloma or papillomatosis	• BC RR increase 1.3-1.9 times
Proliferative lesions with atypia (atypical hyperplasia)	• Atypical ductal hyperplasia (ADH) • Atypical lobular hyperplasia (ALH)	• BC RR increase 3.9-13 times • > 80% of patients with atypical hyperplasia do not develop invasive cancer during their lifetimes

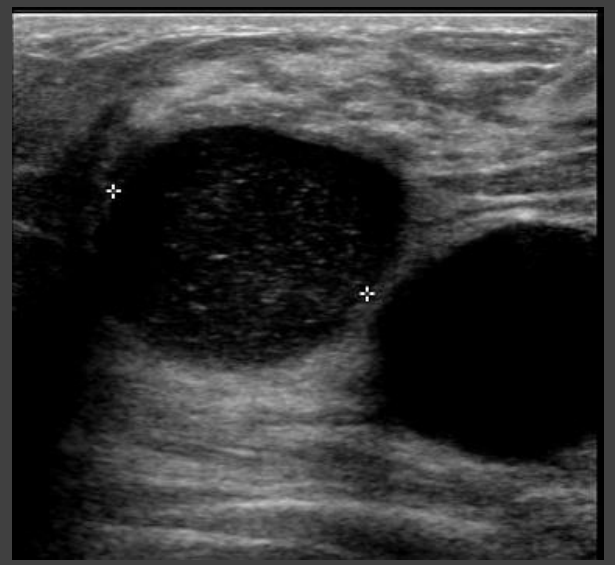
Determinants of breast cancer risk after the diagnosis of benign breast disease

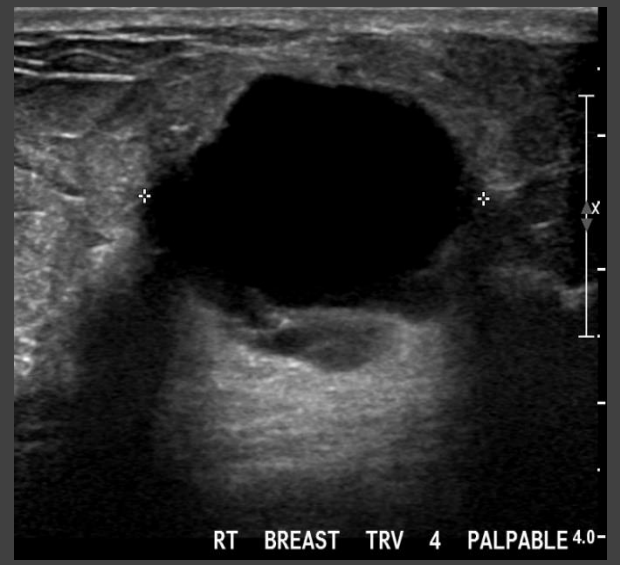
- **Histologic features**
- **Age at biopsy**
  - **In comparison to women > 55 years old, the risk for breast cancer in young women with a diagnosis of atypical epithelial proliferation is twice.**
- **Degree of family history of BC**
  - **Strong family history** may increase breast cancer risk even in patients with nonproliferative lesions

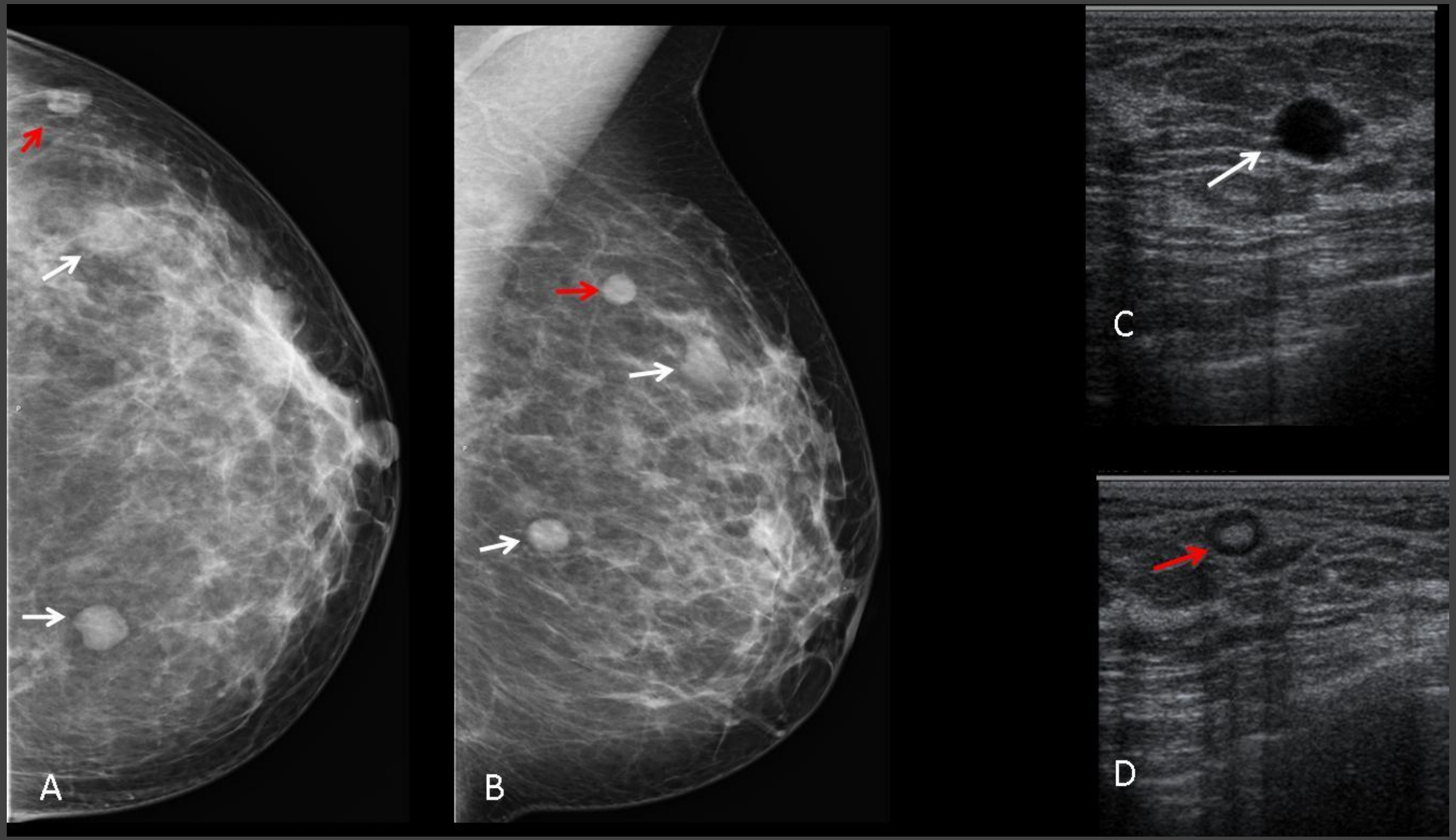
1) Breast Cysts

- Fluid-filled, round or ovoid structures
- 1/3 of women between 35 and 50 years old
- Classification
  - **Size**
    - Subclinical (microcysts) → majority of cases
    - Palpable (gross) cysts → 20%–25% of cases, generally are simple cysts
  - **Structure**
    - Simple cysts
    - Complex / atypical cysts → 5-5.5% of all breast US examinations
      - Internal echoes – thin septations – thickened/irregular wall – absent posterior enhancement


Simple breast cyst




RT BREAST TRV 4 PALPABLE 4.0

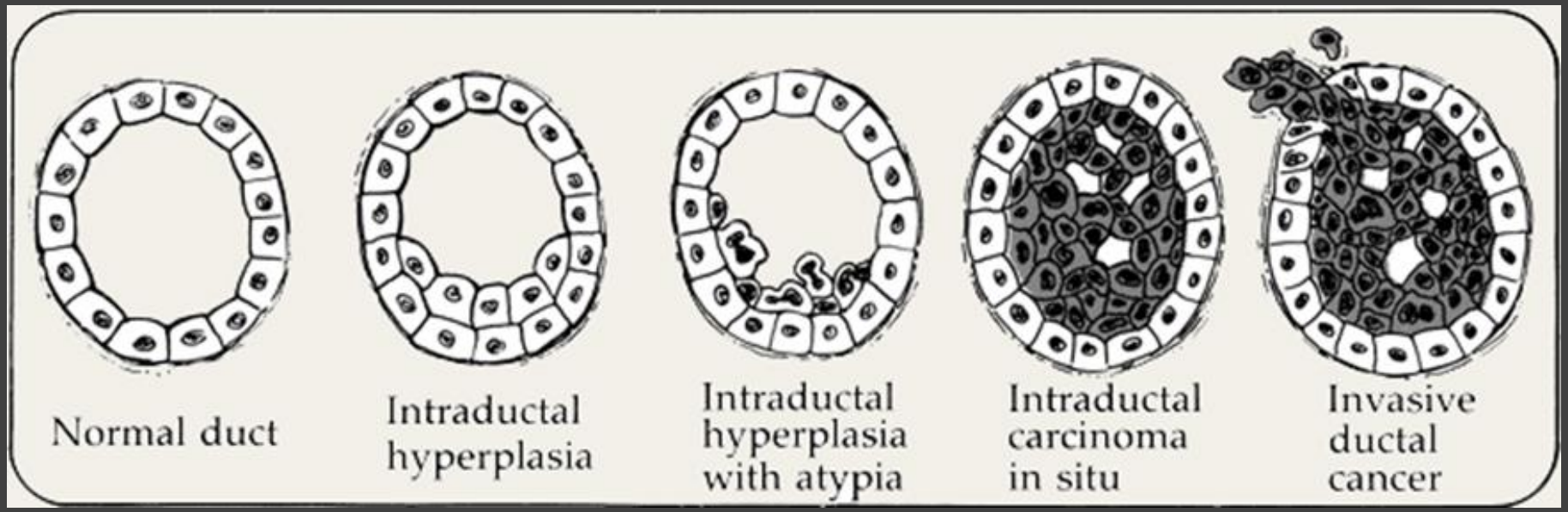

A
B
C
D

Clinical significance and management

- Gross simple cysts are not associated with increased risk of malignancy
  - Routine follow up
- Malignancy rate of complex cysts 0.3%
  - Follow up with imaging studies
- **Complex cysts with intracystic mass/nodule are suspicious for malignancy**
  - **CNB or surgical biopsy**

2) Epithelial Hyperplasia

- Epithelial hyperplasia is one of the most challenging FCCs to diagnose properly.
- The most common form of proliferative breast disease
- **Classified into:**
  - **Ductal Lesions**
  - **Lobular Lesions**


Normal duct
Intraductal hyperplasia
Intraductal hyperplasia with atypia
Intraductal carcinoma in situ
Invasive ductal cancer

2. A) Ductal hyperplasia

- Increase the number of cell layers lining of breast ducts > 2 layers

- More frequently diagnosed with the use of mammogram and detection of microcalcifications

i. Usual (simple) ducal hyperplasia

- Mild hyperplasia → 3-4 cell layers, no luminal distention
- Moderate hyperplasia → > 4 cell layers thickness, bridging of luminal space
- Florid hyperplasia → distended and possible obliterated lumen

ii. Atypical Hyperplasia

- Uniform population of cells
- Mimic low grade DCIS

Usual Ductal Hyperplasia (UDH)	Atypical Ductal Hyperplasia (ADH)
30% of breast biopsies	10% of breast biopsies
Late premenopausal age	Late premenopausal age
No Atypia	Atypia
RR for BC increase slightly (1.5-2X)	RR increase by (4-5X) over 10-15 years
	Represent low grade intraductal carcinoma in 1-3 ducts, size less than or equal 2 mm

- For ADH; risk of cancer decreases after 15 years
- Premenopausal with ADH have higher risk for developing BC than postmenopausal women.

Management of ductal hyperplasia?

- Typical vs. Atypical
- Follow up vs. Surgical Excision

Upgrade rate?

The pooled upgrade rate for atypical ductal hyperplasia was 29%

2. B) Lobular hyperplasia

- A description include ALH and cLCIS
- Both ALH and LCIS have very similar histologic features, except for extent & degree of proliferation
- Considered as risk factors for BC (not precursors)
- Rarely clinically detected
  - Diagnosed during breast biopsies (i.e. 0.5-4% of all benign breast biopsies)
- More common in premenopausal women
- Multicentric (85%) and bilateral in (30-67%)

	ALH	cLCIS
Extent of proliferation	Proliferation not occluding the lumen	Lumen is occluded
Risk of BC	RR 4-5 X	RR 8-10 X
Site of BC	Ipsilateral : contralateral = 3:1	Risk is equal in both breasts

Management

- **ALH**
  - Systemic follow-up and appropriate risk assessment

- **cLCIS**
  - WLE to role out synchronous DCIS or invasive carcinoma
    - Upgrade rate 3-30%
    - Negative margins are required for pLCIS
    - LRR risk 6% with positive margins and 1-2% in negative margins
  - Other options
    - Chemoprevention
    - Bilateral risk reducing mastectomy → preserved for patients with additional risk of BC

3) Intraductal papilloma

- Benign tumor of the epithelium of mammary ducts
- Multiple branching papillae lined by epithelium and myoepithelium within one or more dilated ducts.
- Shows predilection for extreme ends of the ductal system: lactiferous sinuses and terminal ductules
- May be associated with hyperplasia (usual or atypical) or metaplasia (apocrine or squamous)

	Solitary intraductal papilloma (SIP)	Multiple intraductal papilloma (MIP)
Age	50-60 years	Young age More likely bilateral
location	MC → subareolar	MC → peripheral Subareolar At least 5 clearly separate papillomas within localized breast segment
RR for BC	2X Significant correlation between ADH within SIP and BC risk	3X
Prognosis	ADH or DCIS confined to SIP have no prognostic significance or impact	
Treatment	Excisional biopsy Follow up	Excisional biopsy Follow up

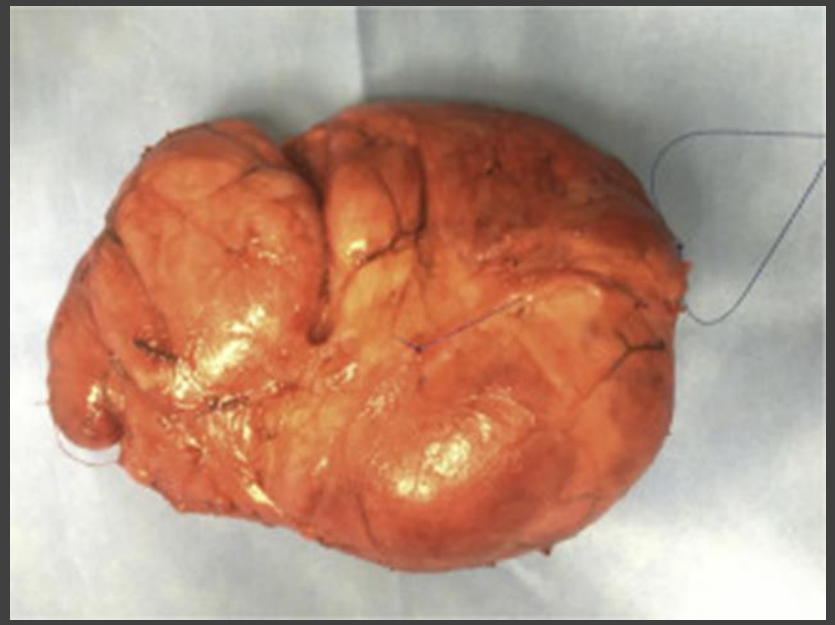
Benign Breast Tumors

DR. MAHMOUD AL-BALAS; CONSULTANT BREAST AND GENERAL SURGERY

Introduction

- Fibroadenoma
- Intraductal Papilloma
- Gynecomastia
- Phyllodes Tumor
- Lipoma
- Hamartoma
- Granular Cell Tumor
- Radial Scar

Fibroadenoma



Fibroadenoma

- Benign Tumor
- Incidence: 8-10% (1955) BUT recent studies estimate it as high as 25% in Asymptomatic Women.
- Any age; mainly 20-30 yrs. Old
- Composed of epithelial and stromal elements.
- Arise form TDLU
  - Might arise from bcl-2 positive mesenchymal cells similar to solitary fibrous tumors.

Fibroadenoma

Pathogenesis

- Unknown
- Hormonal stimulation (increased estrogen sensitivity, OCP in young age)
- EBV in immunosuppressed women

Fibroadenoma

Clinical Presentation:

- Most are asymptomatic

- If symptomatic:
  - Firm, movable mass.
  - Painless BUT may be associated with discomfort when large or in pressure area (i.e. wire of female brassiere)
  - Multiple, bilateral in 20% of cases

- Medical attention ? Pain – Rapid growth – Cosmetic effect – Fear of malignancy

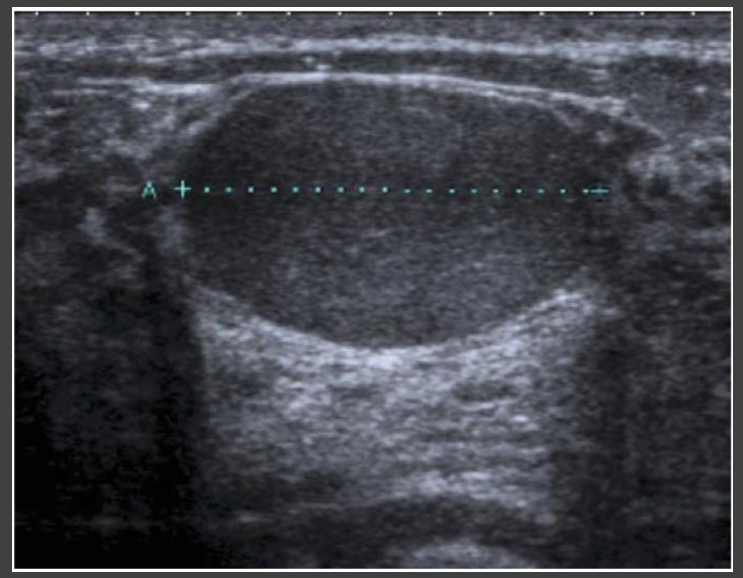
- Fibroadenoma is a small,solitary, well-encapsulated, spherical or discoid mass measuring 2-4 cm diameter.
- The cut surface is firm, grey-white, slightly myxoid and may show slitlike spaces.

Fibroadenoma

Radiologic Findings:

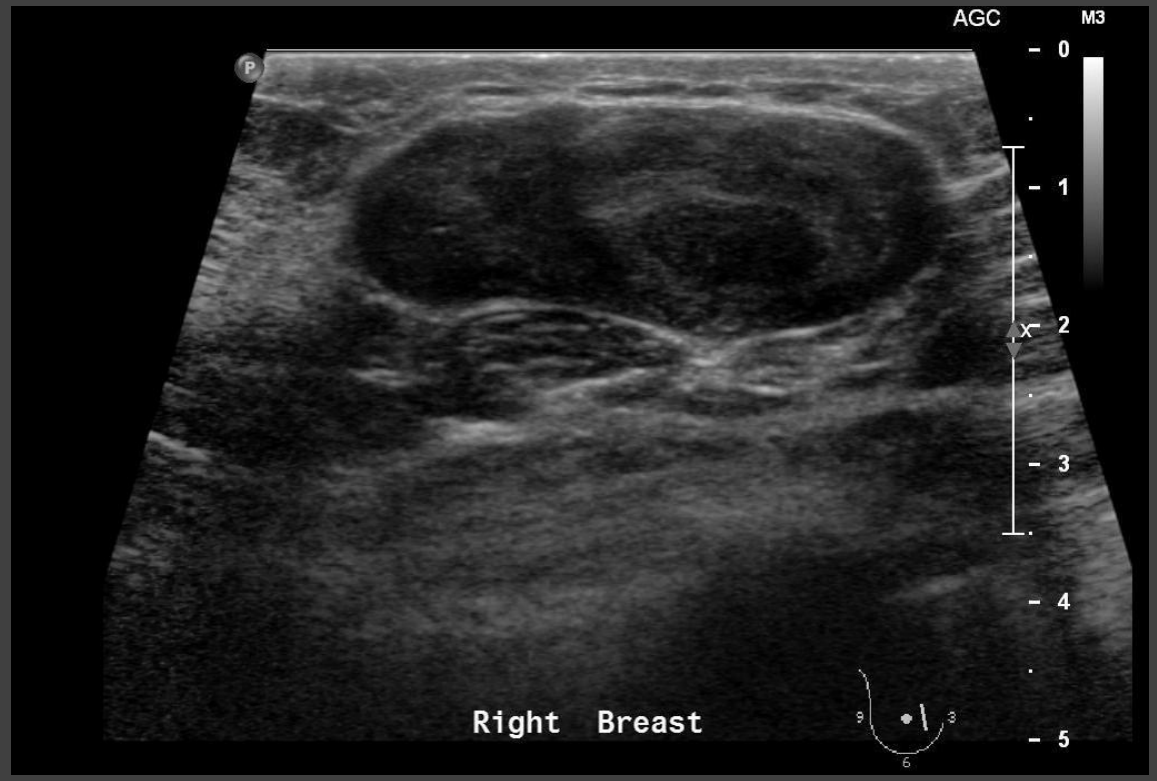
Ultrasound:

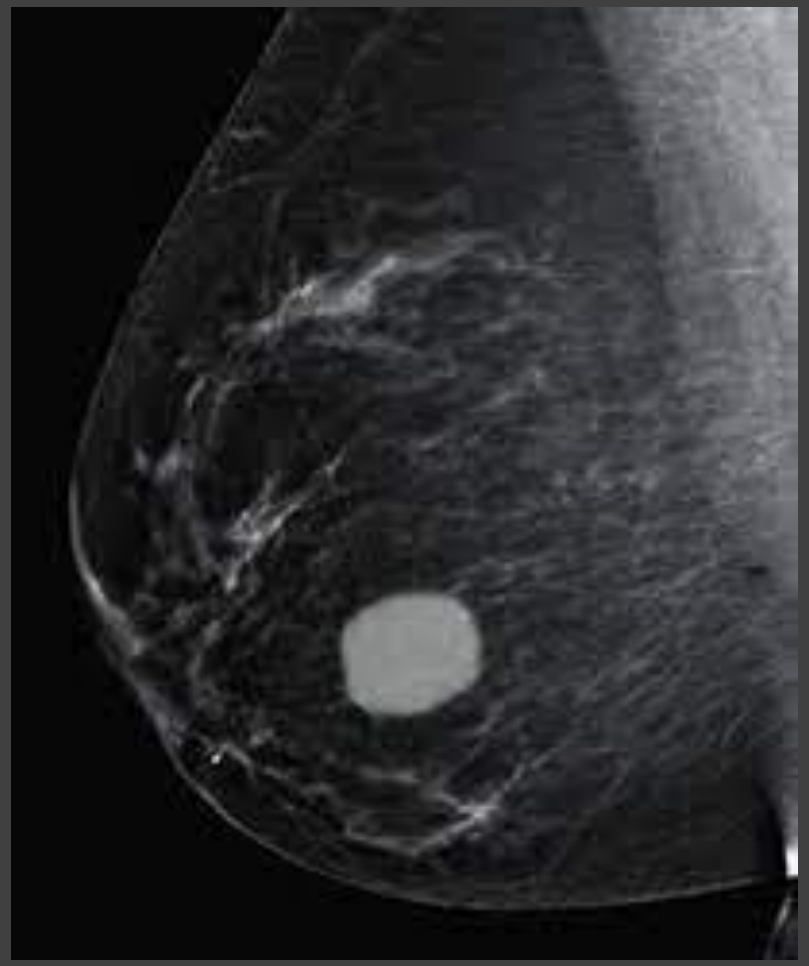
- Usually the first radiologic modality of diagnosis.
- Round, oval, or lobular well circumscribed hypoechoic mass.



Mammogram:

- Female > 35 years old
- Personal or Family history of BC.
- Clinically suspicious lesion


AGC
M3
0
1
2
3
4
5
Right Breast



Pathologic Classification

Size:

- < 5 cm
- > or equal 5 cm (Giant fibroadenoma or Juvenile giant fibroadenoma in young age)

Microscopic architecture of ductal elements:

- Pericanalicular.
- Intracanalicular.
- Simple Vs. Complex (i.e. with hyperplasia, metaplasia or sclerosing adenosis)

Rare types:

- Tubular (pure) adenoma → prominent adenosis with very little stroma
- Lactational adenoma → lactational changes in secretory glands in fibroadenoma of pregnant or breast feeding women.

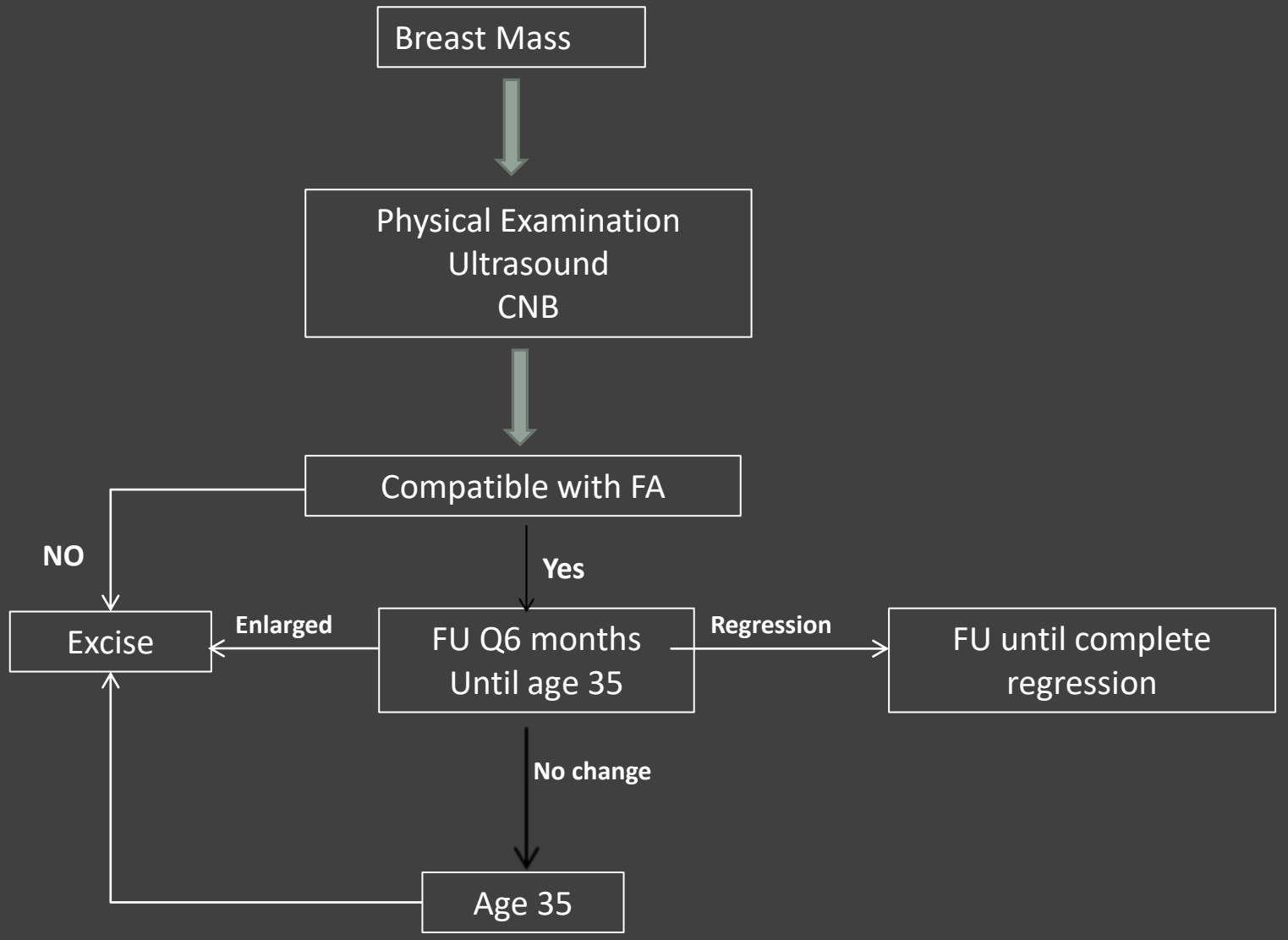
Management:

- Follow up if → < 2.5 cm , low growth, no personal or family history of BC

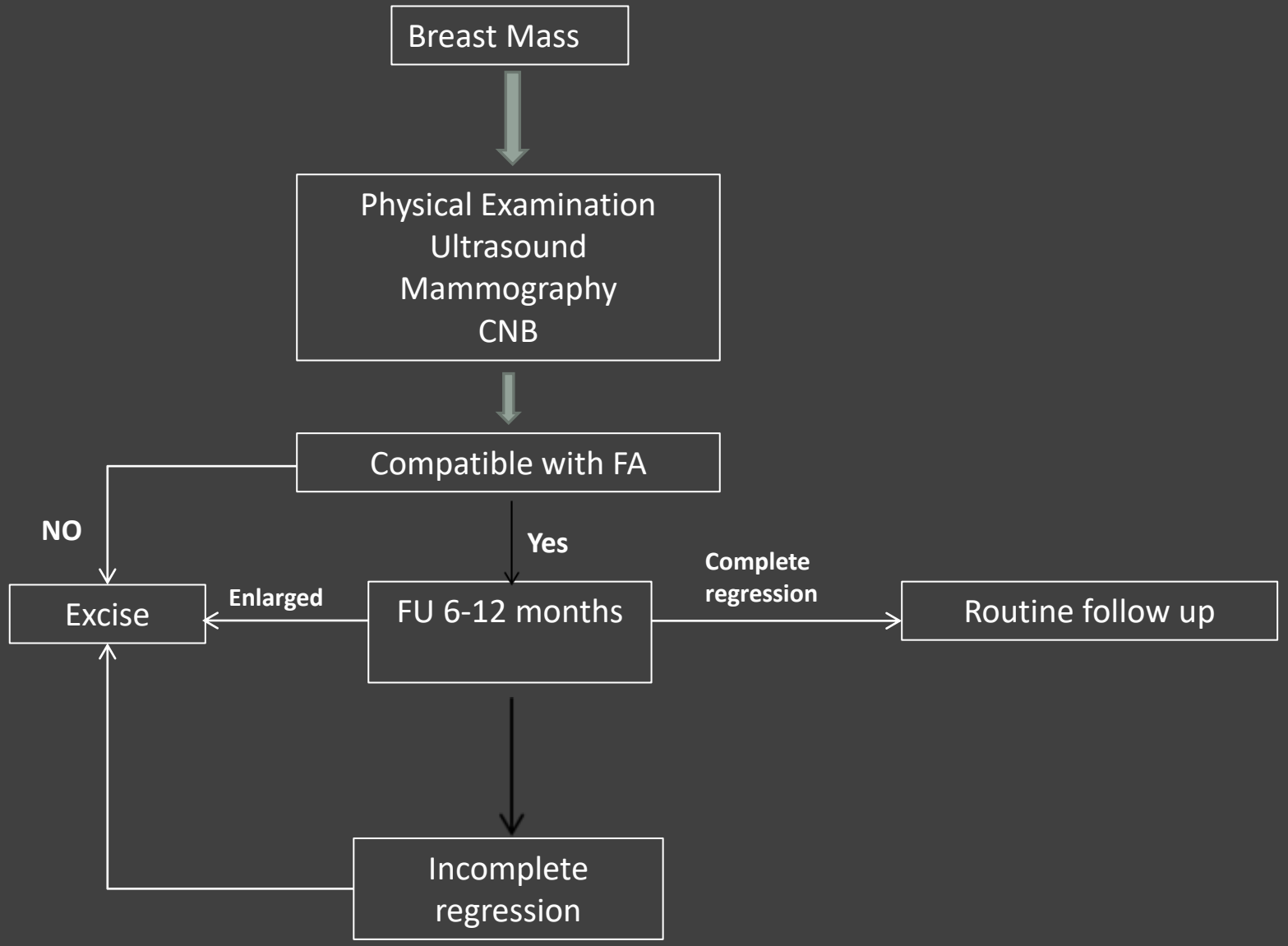
- Excision
  - High growth rate
  - Fibroepithelial lesion
  - Complex lesions (i.e. may have slightly higher risk for BC)
  - Patient desire, pain, cosmetics
  - Older women
  - FH of BC

- Surgical excision vs. US-Guided vacuum-assisted biopsy device (i.e. ling term data for recurrence not yet available)

Management of Fibroadenoma in women younger than 35 years old



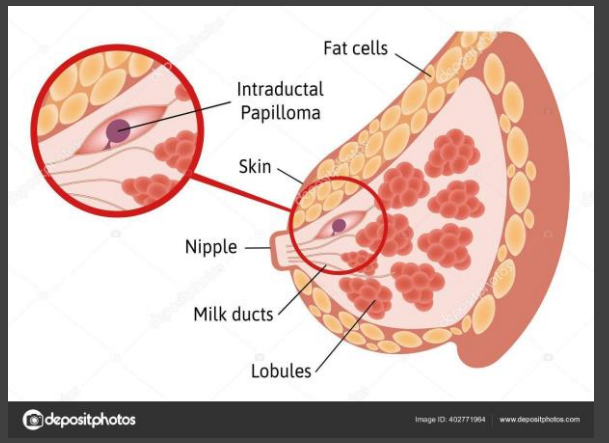
Management of Fibroadenoma in women older than 35 years old

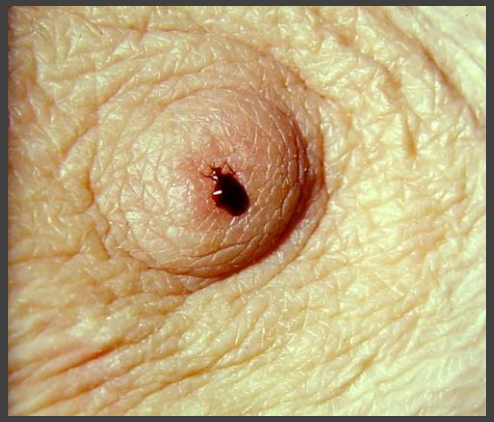


Intraductal Papilloma

Intraductal Papilloma

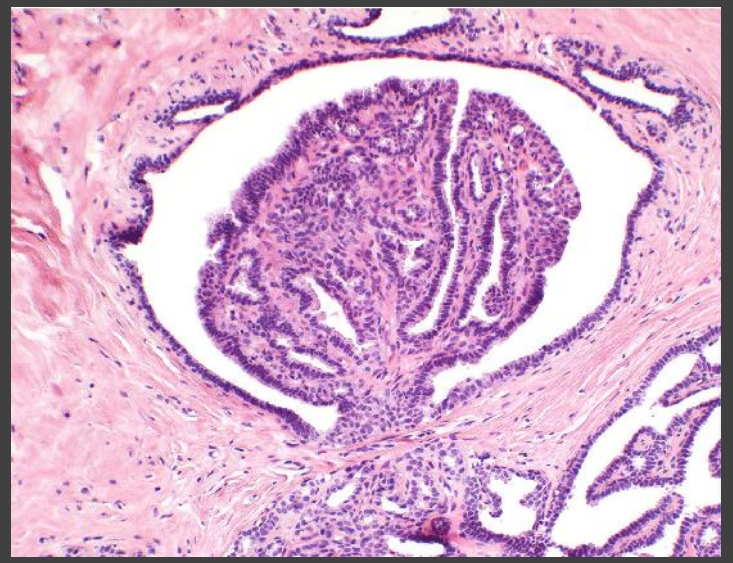
- Benign rare neoplasms.
- Incidence 2-3% of population.
- Usually age 30-55
- Develop within the mammary duct; ***most common cause of bloody nipple discharge***
- Typically small (few mm) and may grow to several centimeters. ***80% of them cause nipple discharge***





Pathology

- Composed of breast epithelium supported by underlying stroma and a branching fibrovascular core.
- May be associated with ductal epithelial hyperplasia, ADH or DCIS.
- Atypical features associated with Intraductal papilloma carry higher risk of malignancy.
- Upgrading rate for CIS or IC was variable reported 0-29%



Classification:

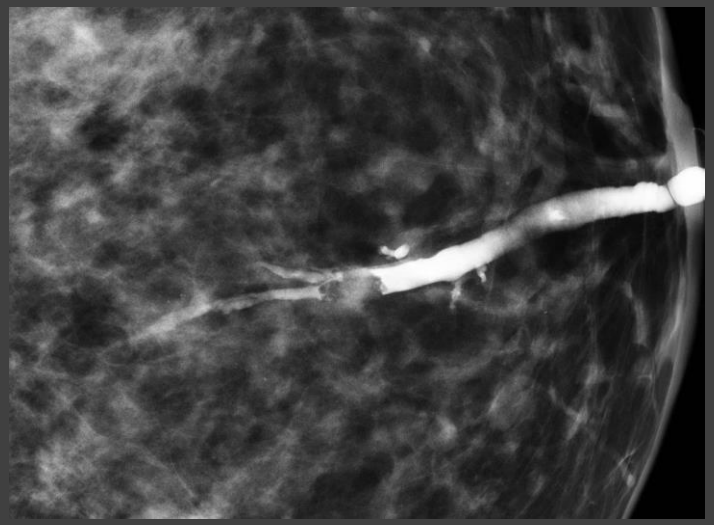
- Solitary or Multiple (papillomatosis)
- Central (subareolar) or peripheral.

Clinical presentation:

- Central:
  - Spontaneous nipple discharge, serous, greenish or bloody (30%)
  - Mass (rare)

- Peripheral:
  - More frequently are asymptomatic
  - Incidentally discovered on imaging studies.
  - Higher association with malignancy (specially when multiple and Atypia is found)

Imaging Modality	Central Intraductal Papilloma	Peripheral Intraductal Papilloma
Mammography	• Frequently Occult	• Architectural distortion • Nodular densities • Mass +/- calcifications • Calcifications alone
Ultrasound	• Intraductal mass • Complex cystic lesion with dilated duct	
Ductogram	• Completely obstructed duct • Duct expansion and distortion • Intraductal filling defects • Wall irregularity	



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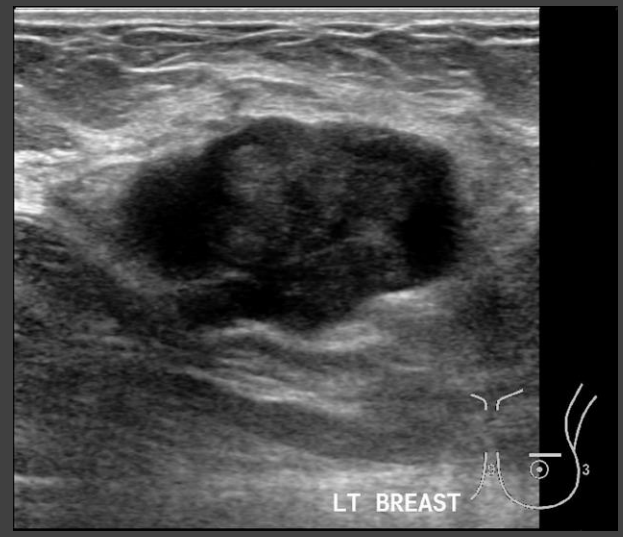

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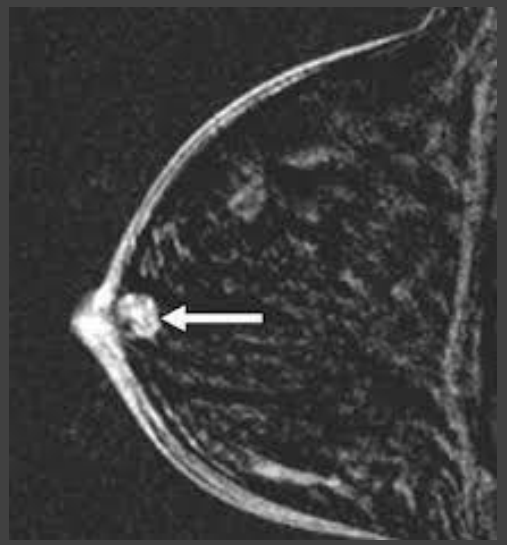


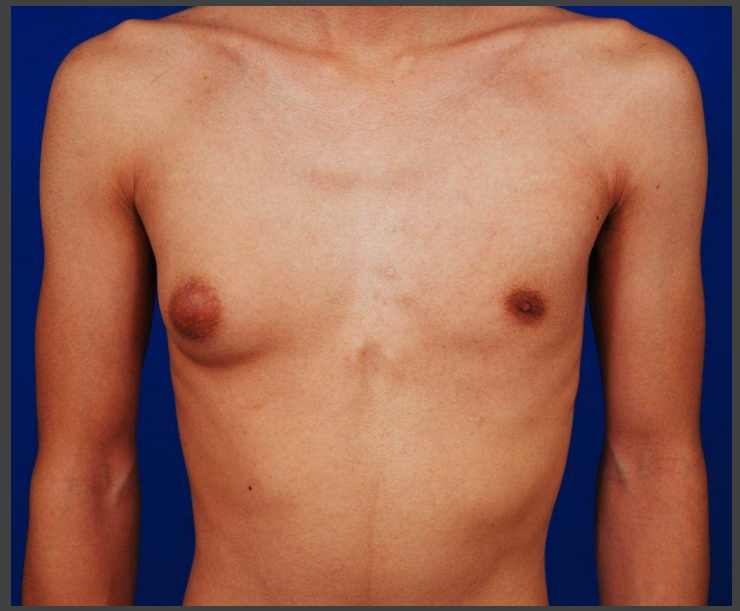
C

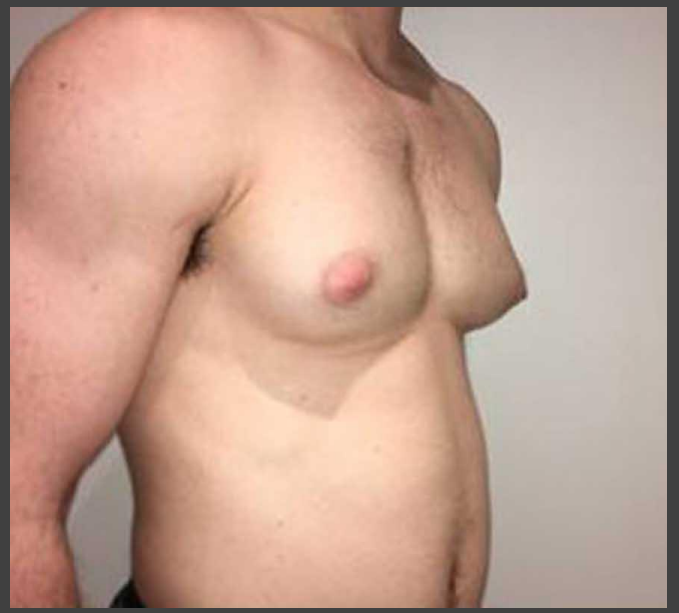
Treatment:

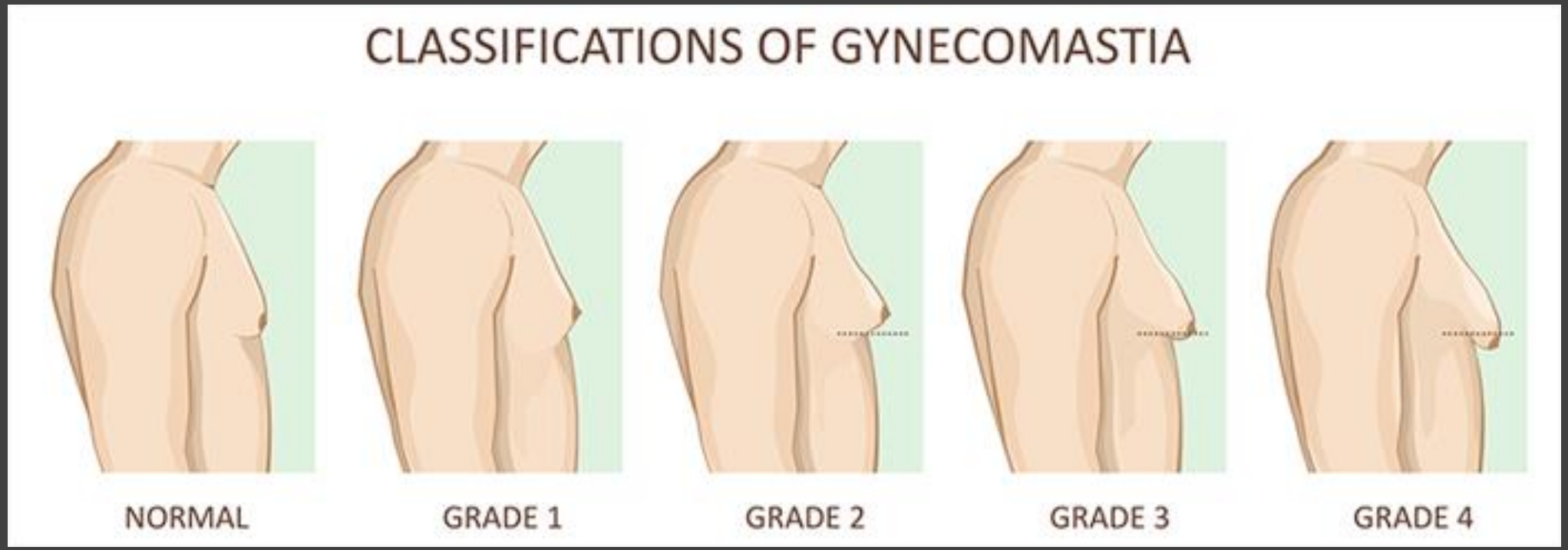
- Surgical excision

- Low risk lesions for upgrading:
  - No microcalcifications
  - Absence of atypia
  - Microscopic size lesions
  - Sufficient amount of tissue on core biopsy.

Gynecomastia






CLASSIFICATIONS OF GYNECOMASTIA
NORMAL
GRADE 1
GRADE 2
GRADE 3
GRADE 4

Neonatal gynecomastia:

- Placental transfer of maternal estrogen into fetal circulation
- Transient process
- Resolve spontaneously

Adolescent gynecomastia:

- Peak age 13 – 14
- Peripheral aromatization of circulation androgen
- Transient process; resolves with 1-3 years
- 8% of cases continue into adulthood
- Reassurance and surveillance
- Impact: psychological (embarrassment) and fear of malignancy

Adult gynecomastia:

- ***Idiopathic***

- Physiological
  - Also called senile gynecomastia
  - Due to decreased levels of circulating androgens either to decreased production or increased peripheral conversion to estrogen

- Medication related

- Chronic diseases (liver failure, renal failure, testicular tumors, adrenocortical tumors, pituitary adenoma, hypogonadism, hyperthyroidism, obesity, ectopic hormone release, etc.)

Gynecomastia

Etiology	%
Idiopathic	25%
Acute / persistent in puberty	25%
Medications	10-20%
Cirrhosis / Malnutrition	8%
Hypogonadism	8%
Renal diseases	1%
Testicular tumors	3%

Gynecomastia (Clinical valuation and Workup)

- **Clinical history and Physical exam**
- **Assessment of regional lymph nodes**
- **Distinguishing clinical feature is → concentric enlargement**
- **Frequently bilateral**

Pseudogynecomastia

- ***Excess fat deposition without concomitant ductal proliferation***
- ***Soft bilaterally enlarged breast***

Gynecomastia

Alarming features

- Unilateral
- Eccentric growth pattern
- Skin or nipple changes
- Nipple discharge
- lymphadenopathy
- Family history of breast cancer

Mammogram in male BC	
Sensitivity	92%
Specificity	90%

Laboratory Work up
LFT
KFT
TSH
Prolactin
Beta-HCG
LH
Testosterone

Gynecomastia

Gynecomastia Stages		
Nodular Pattern	• Recent onset < 1 year • Fan shaped subareolar density • Appear as hypoechoic subareolar mass with fat tissue surrounding	• Reversible stage / no fibrosis established
Dendritic Pattern	• In more chronic stage • Flame (or cone) shaped density infiltrate deeper, surround fat	• Irreversible fibrosis
Diffuse glandular pattern	• US / Mammogram similar to female breast • In patient treated with high doses of estrogen	

Gynecomastia (Pathology)

Florid phase (reversible)	• **In 1st year of onset** • **Proliferation of ductal epithelium and stromal elements** • **Periductal inflammation and edema** • **No fibrosis**	• **Non surgical treatment might be successful**
Fibrotic phase (irreversible)	• Start after 6 months • Minimal ductal proliferation • Hyalinized periductal tissue	• **Only surgical treatment**

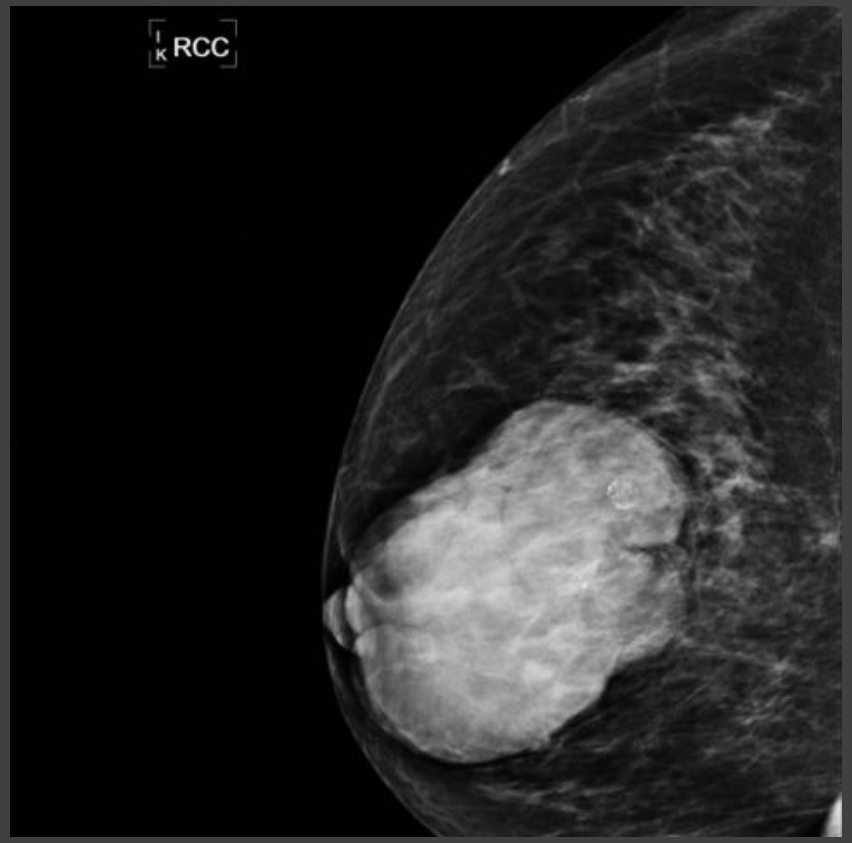
Gynecomastia (Management)

- Look for possible underlying cause.

- Surgery
  - Mainstay of treatment in long standing cases
  - Subcutaneous mastectomy
  - Liposuction

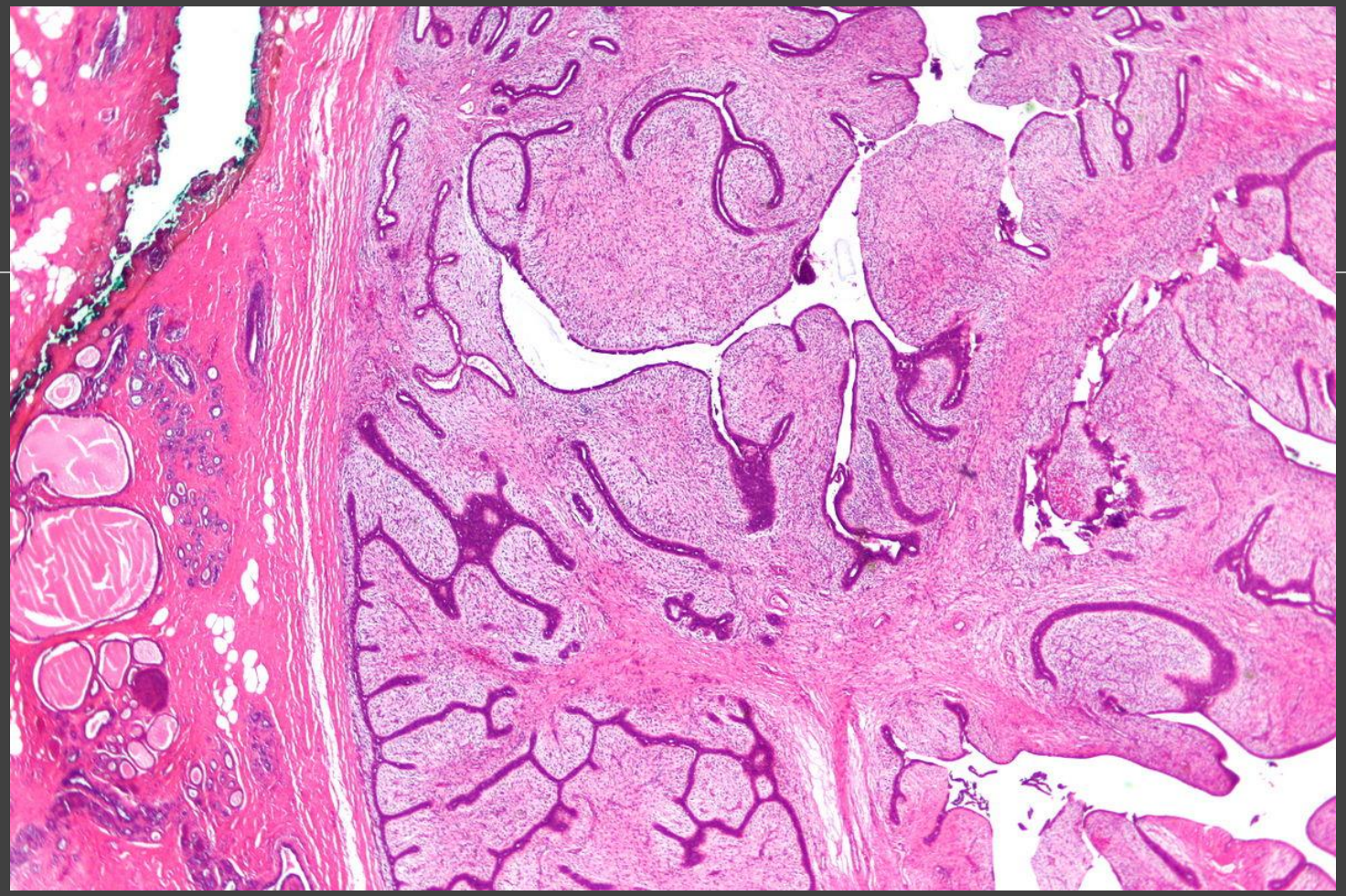
- Prophylaxis strategy in high risk patients (e.g. prostate cancer)
  - Radiotherapy
  - Tamoxifen ?! Not yet FDA approved

Phyllodes tumor



Phyllodes tumor

- phyllodes tumor (PT) of the breast is a rare fibroepithelial neoplasm, accounting for 0.3% to 1% of all breast tumors
- The term cystosarcoma phyllodes was first introduced by M¨uller in 1838. It is derived from the Greek words sarcoma, meaning flesh appearance, and phyllon, meaning leaflike
- Phyllodes tumor presents a morphologic continuum from benign to malignant. The classification of PT proposed by the World Health Organization (WHO) into benign, borderline, and malignant variants
- Biphasic tumors, histologically characterized by a leaflike architecture resulting from an enhanced intracanalicular growth pattern, cleftlike spaces lined by epithelium, and hypercellular stroma



Micrograph of a phyllodes tumor (right of image) with the characteristic long clefts and myxoid cellular stroma. Normal breast and fibrocystic change are also seen (left of image). H&E stain.

Phyllodes tumor

- Most of the tumor arises in women aged between 35 and 55 years (approximately 20 years later than fibroadenoma)
- More prevalent in the Latin American white and Asian populations
- Few cases have been reported in men and these have invariably been associated with the presence of gynaecomastia.
- It usually presents as a rapidly growing but clinically benign breast lump. In some patients a lesion may have been apparent for several years, with clinical presentation precipitated by a sudden increase in size.
- The skin over large tumors may have dilated veins and a blue discoloration but nipple retraction is rare.

Phyllodes tumor

- Fixation to skin and pectoralis muscles has been reported, but ulceration is uncommon.
- More commonly found in upper outer quadrant with an equal propensity to occur in either breast.
- Rarely bilaterally
- The median size is around 4 cm. 20% of tumors grow larger than 10 cm (giant phyllodes tumor).

Phyllodes tumor

Clinical findings
- (i) Sudden increase in size in a longstanding breast lesion
- (ii) Apparent fibroadenoma > 3 cm diameter or in patient >35 years

Imaging findings
- (i) Rounded borders/lobulated appearance at mammography
- (ii) Attenuation or cystic areas within a solid mass on Ultrasonography

FNAC findings
- (i) Presence of hypercellular stromal fragments
- (ii) Indeterminate features

ANY 2 features mandate core biopsy

Phyllodes tumor

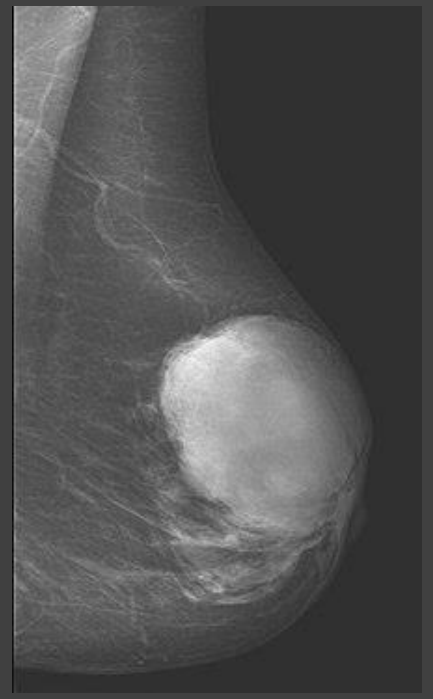
Criteria	Benign	Borderline	Malignant
Stromal cellularity and atypia	Minimal	Moderate	Marked
Stromal overgrowth	Minimal	Moderate	Marked
Mitoses/10 high power fields	0-4	5-9	≥10
Tumor margins	Well circumscribed with pushing tumor margins	Zone of microscopic invasion around tumor margins	Infiltrative tumor margins

WHO Classification[63]	*Benign PT*	*Borderline PT*	*Malignant PT*
Stromal cellularity	Modest	Modest	Marked
Cellular pleomorphism	Little	Moderate	Marked
Mitoses	Few, if any	Intermediate	Numerous (>10/ HPF)
Margins	Well circumscribed (Pushing)	Intermediate	Invasive
Stromal pattern	Uniform stromal distribution	Heterogenous stromal distribution	Marked stromal overgrowth
Heterologous stromal distribution	Rare	Rare	Not uncommon
Overall average distribution (%)	60	20	20

Phyllodes tumor

- Tumor should be resected with at least 1 cm margins particularly in the borderline and malignant phyllodes tumors
- Re-excision of borderline and malignant phyllodes tumors identified after local excision should be considered.
- Local recurrence in phyllodes tumors has been associated with *inadequate local excision* and various histological characteristics, including mitotic activity, tumor margin, and stromal cellular atypia (range from 15 to 20%).
- As malignant phyllodes tumors undergo mainly hematogenous spread, lymph node metastases are only <1% (lymph node enlargement in about 10%). Axillary dissection is required, when histologically positive for malignant cells.

A



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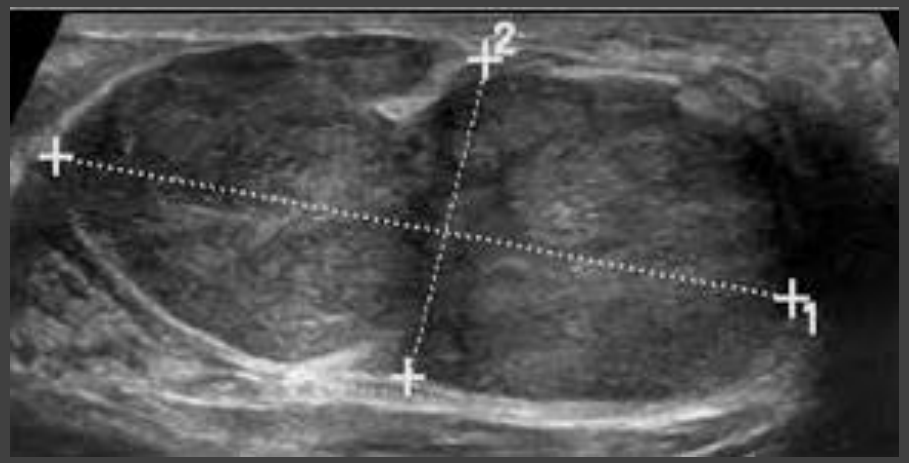
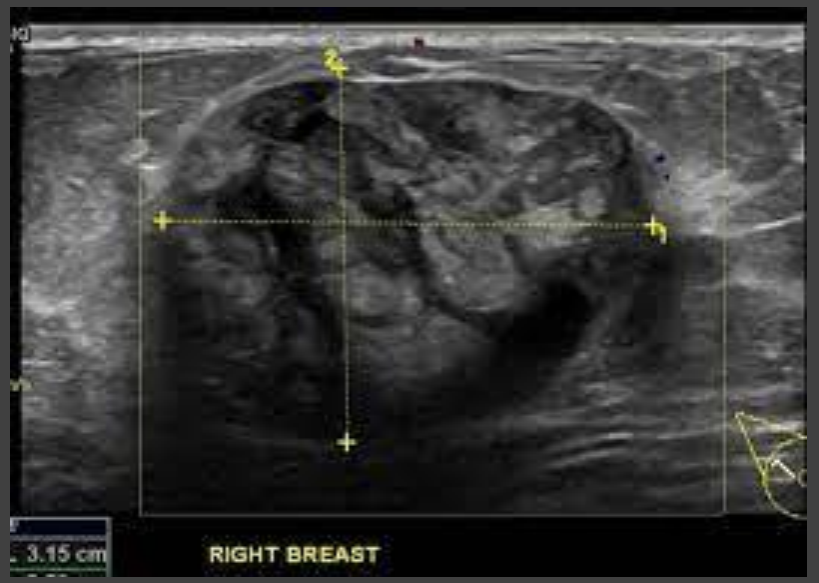
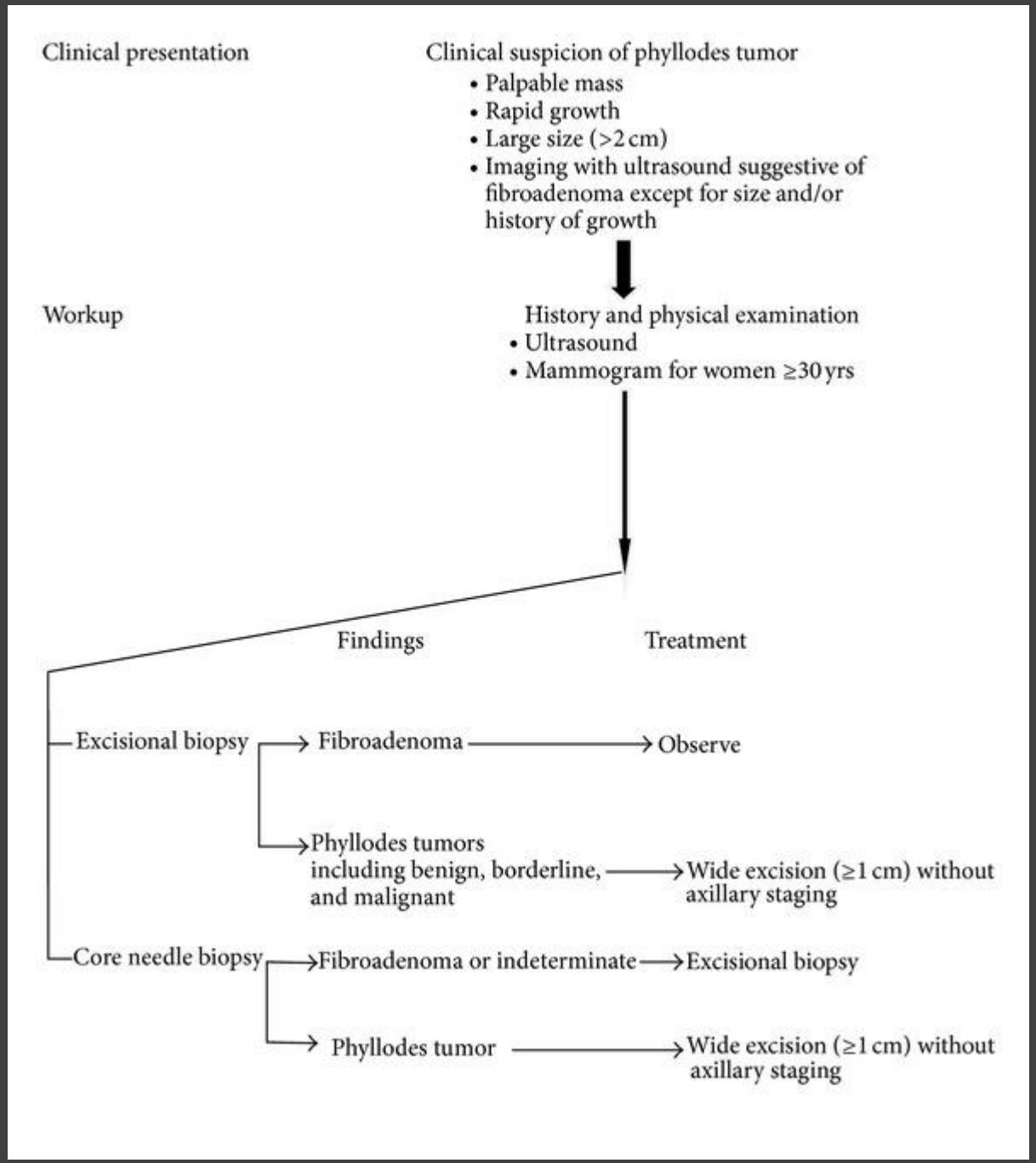




C

Ultrasound demonstrates a solid 4.25 x 3.3 x 2.4 cm well-circumscribed lobulated mass with a heterogeneous mixed echopattern and, casting a posterior shadow.


Clinical presentation
Clinical suspicion of phyllodes tumor
• Palpable mass
• Rapid growth
• Large size (>2 cm)
• Imaging with ultrasound suggestive of fibroadenoma except for size and/or history of growth
Workup
History and physical examination
• Ultrasound
• Mammogram for women ≥30 yrs
Findings
Treatment
Excisional biopsy
Fibroadenoma
Observe
Phyllodes tumors including benign, borderline, and malignant
Wide excision (≥1 cm) without axillary staging
Core needle biopsy
Fibroadenoma or indeterminate
Excisional biopsy
Phyllodes tumor
Wide excision (≥1 cm) without axillary staging

Adjuvant Therapy

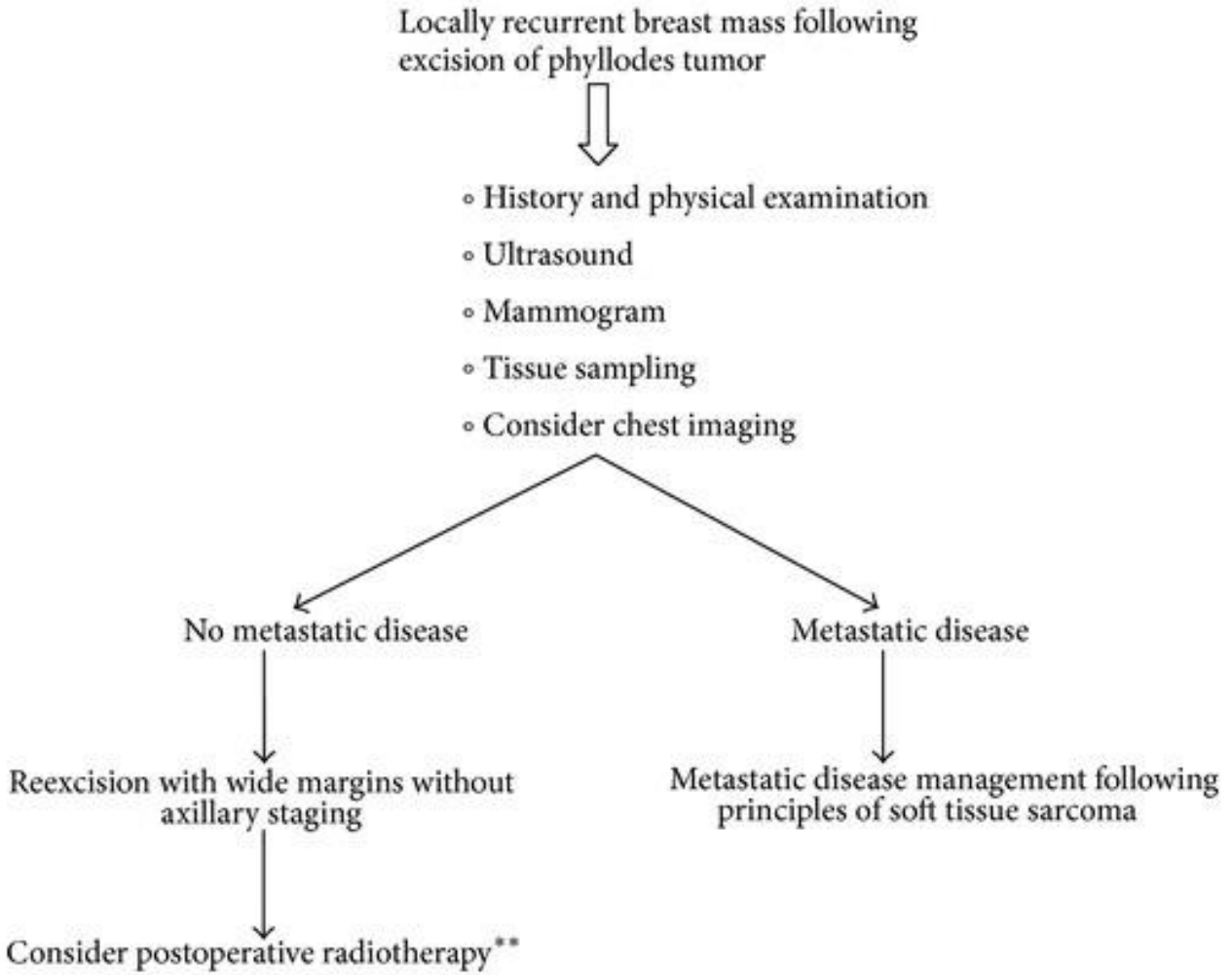
- The role of adjuvant radiotherapy remains uncertain
- Chaney et al. found adjuvant radiotherapy to be beneficial in patients with adverse features (e.g., bulky tumors, close or positive surgical margins, hypercellular stroma, high nuclear pleomorphism, high mitotic rate, presence of necrosis, and increased vascularity within the tumor and tumor recurrence) but the use is controversial.
- In MD Anderson Cancer Center, radiotherapy is recommended only for cases with positive or near-positive surgical margins and selected cases for whom further surgical procedures cannot be performed.

Chemotherapy

- including anthracyclines, ifosfamide, cisplatin, and etoposide, has been mentioned in various studies but with no survival advantage.

Hormonal therapy (e.g. tamoxifen)

- Estrogen and progesterone receptor expression has been shown in 43% and 84%, respectively, of the epithelium and less than 5% of the stromal cells.
- Still, the use of endocrine therapy in either the adjuvant or palliative setting has not been extensively studied.



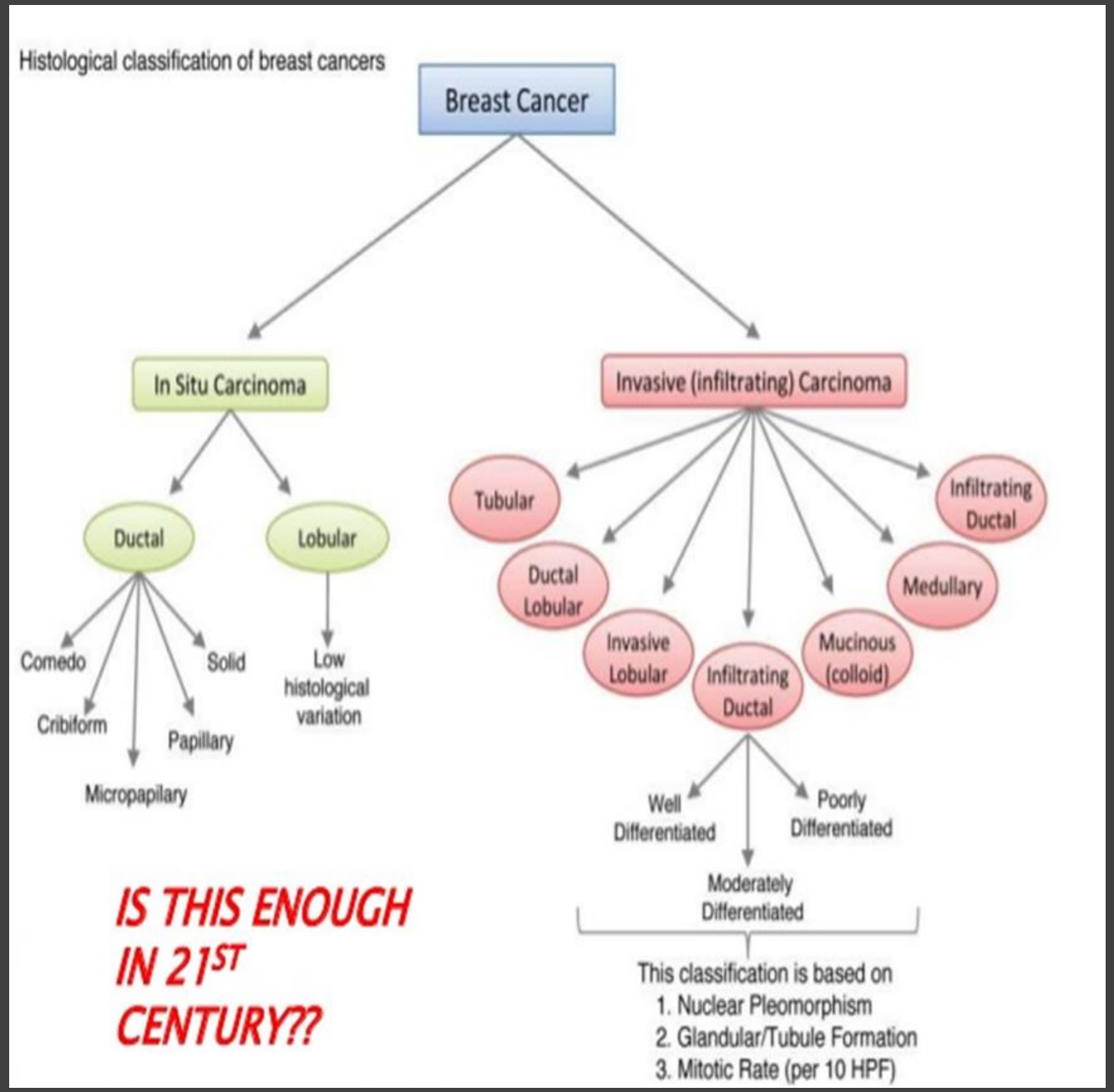
** There is no prospective randomized data supporting the use of radiation treatment with phyllodes tumors. However, in the setting where additional recurrence would create significant morbidity, e.g., chest wall recurrence following salvage mastectomy, radiation therapy may be considered, following the same principles that are applied to the treatment of soft tissue sarcoma.

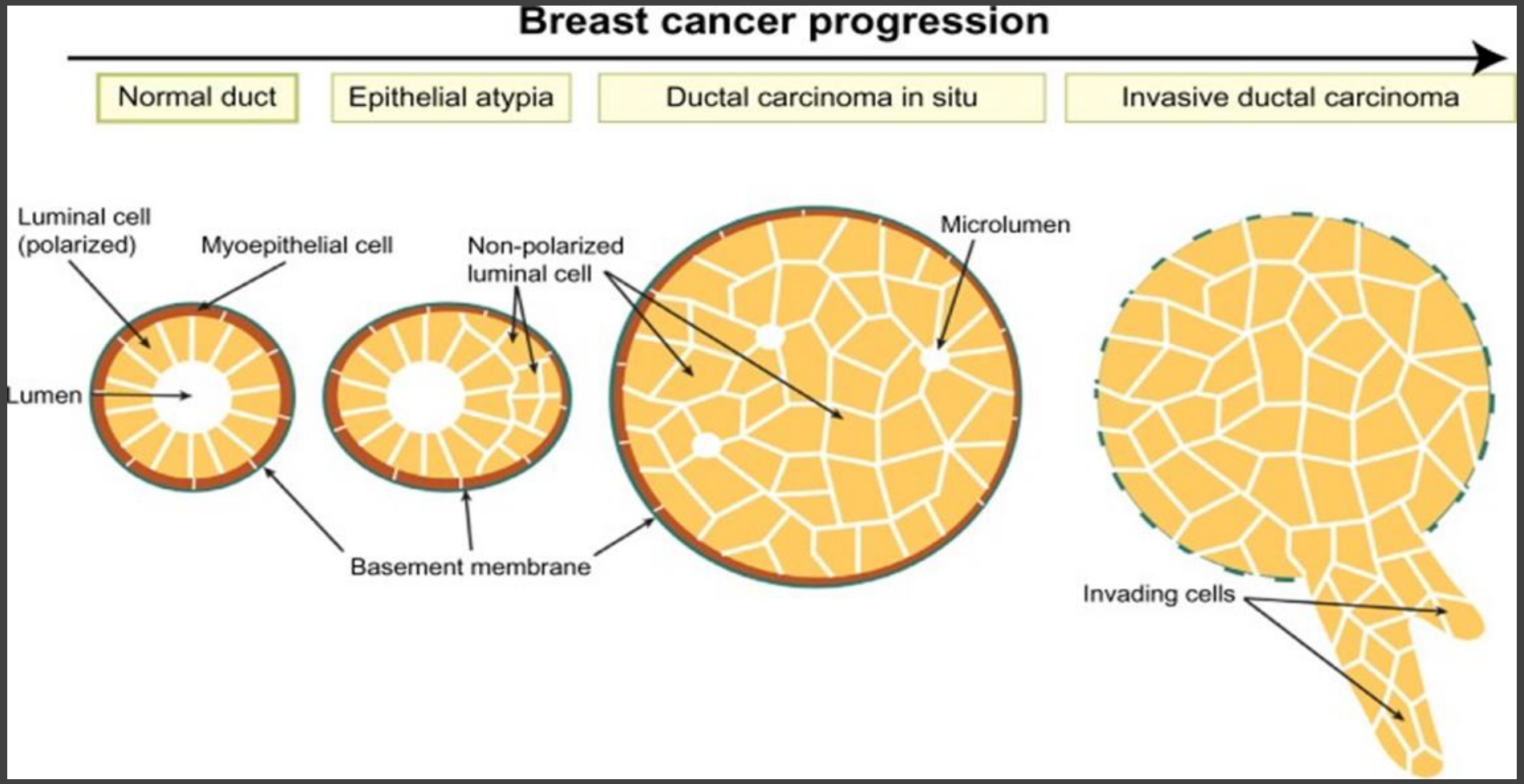
Malignant Breast Tumors

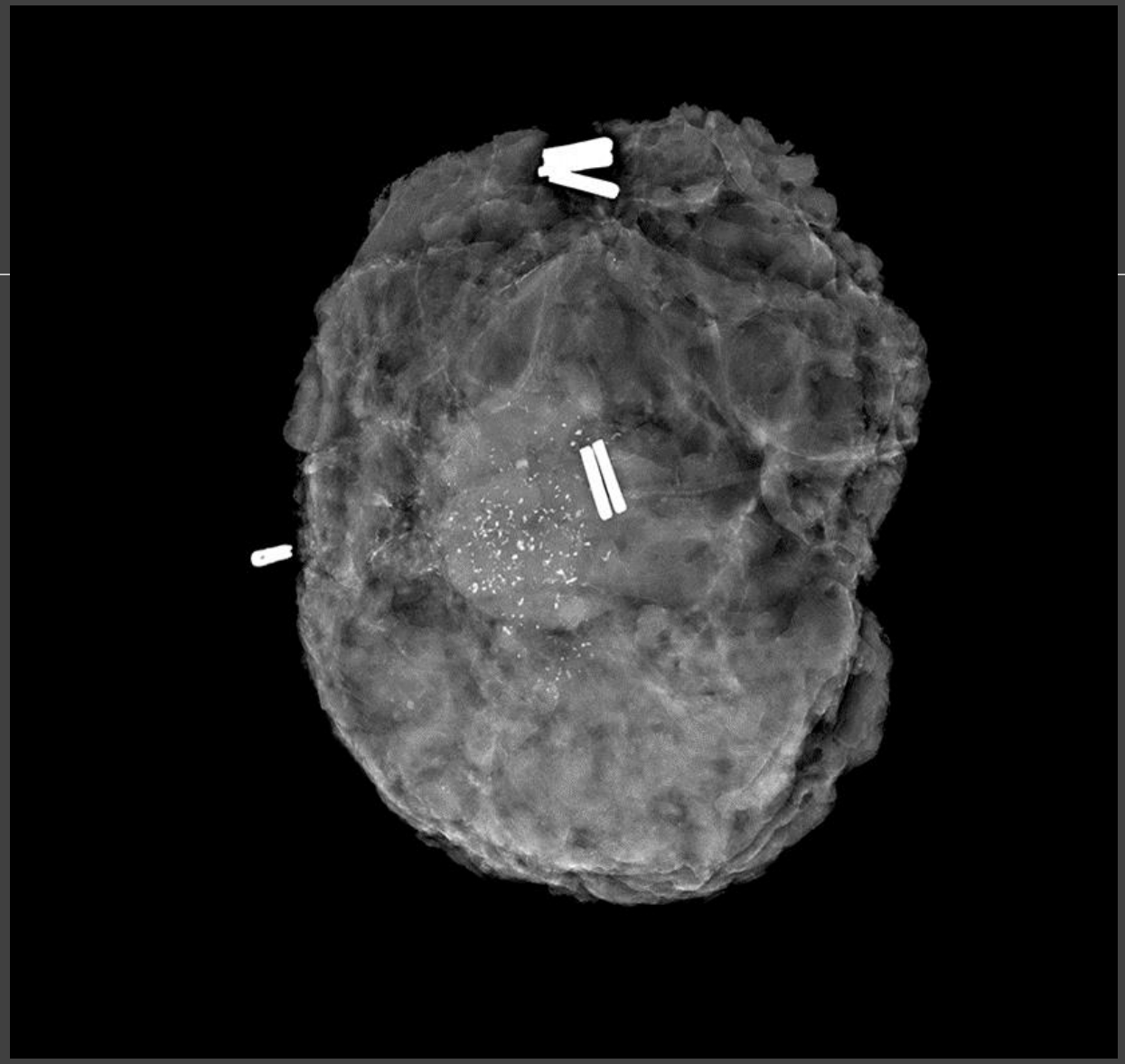
DR. MAHMOUD AL-BALAS; CONSULTANT BREAST AND GENERAL SURGERY

Factors that Increase the Relative Risk (RR) for Breast Cancer in Women

RR>4.0	❑ Female ❑ Age (65+) ❑ Inherited genetic mutations associated with breast cancer such as BRCA1/BRCA2 ❑ Two or more first-degree relatives with breast cancer diagnosed at an early age ❑ Personal history of breast cancer ❑ Biopsy-confirmed atypical hyperplasia ❑ DCIS, LCIS
2.1<RR<4.0	❑ One first-degree relative with breast cancer ❑ High-dose radiation to chest ❑ High bone density (post-menopausal) ❑ Breast density > 50%
1.1<RR<2.0	**Factors affecting circulating hormones:** ❑ Late age at first full-term pregnancy (>30 yrs) ❑ Early menarche(<12 yrs) ❑ Late menopause ❑ No full-term pregnancies ❑ No breastfeeding ❑ Recent oral contraceptive use ❑ Recent and long-term hormone replacement therapy ❑ Obesity ❑ Breast density 26-50% **Other factors:** ❑ Personal history of endometrium, ovary or colon cancer ❑ Alcohol consumption ❑ Height (tall) ❑ High socioeconomic status ❑ Jewish heritage


Histological classification of breast cancers
Breast Cancer
In Situ Carcinoma
Invasive (infiltrating) Carcinoma
Ductal
Lobular
Comedo
Solid
Cribiform
Papillary
Micropapilary
Low histological variation
Tubular
Infiltrating Ductal
Ductal Lobular
Medullary
Invasive Lobular
Mucinous (colloid)
Infiltrating Ductal
Well Differentiated
Poorly Differentiated
Moderately Differentiated
IS THIS ENOUGH IN 21ST CENTURY??
This classification is based on
1. Nuclear Pleomorphism
2. Glandular/Tubule Formation
3. Mitotic Rate (per 10 HPF)


Breast cancer progression
Normal duct
Epithelial atypia
Ductal carcinoma in situ
Invasive ductal carcinoma
Luminal cell (polarized)
Myoepithelial cell
Lumen
Non-polarized luminal cell
Basement membrane
Microlumen
Invading cells



Molecular subtype	Biomarker profile
Luminal A	ER+ and/or PR+, HER2−, and low Ki67 (<14%)
Luminal B	ER+ and/or PR+ and HER2+ (luminal-HER2 group) ER+ and/or PR+, HER2−, and high Ki67 (>14%)
HER2 enriched	ER−, PR−, and HER2+
Basal-like	ER−, PR−, HER2−, and CK5/6 and/or EGFR+

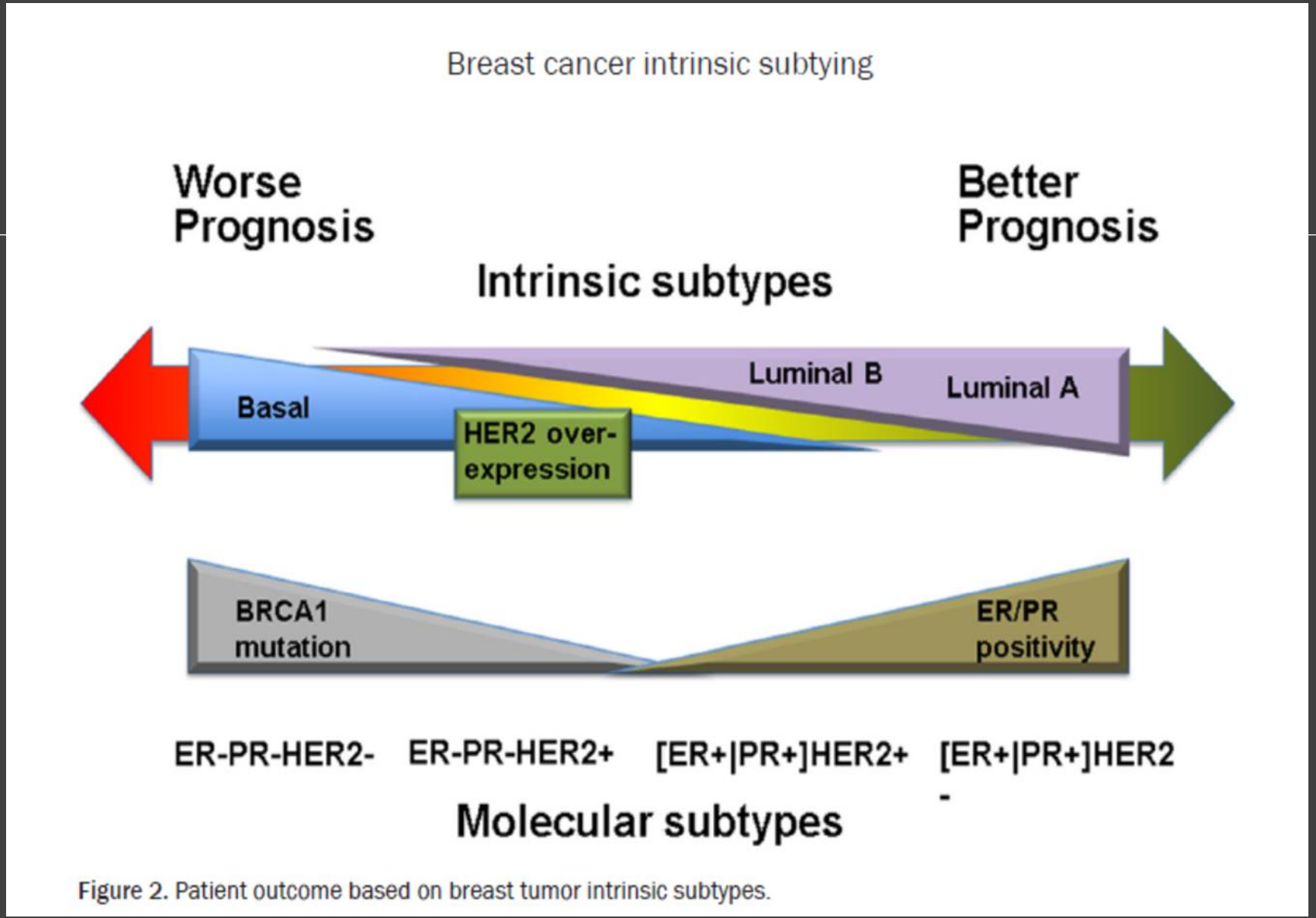
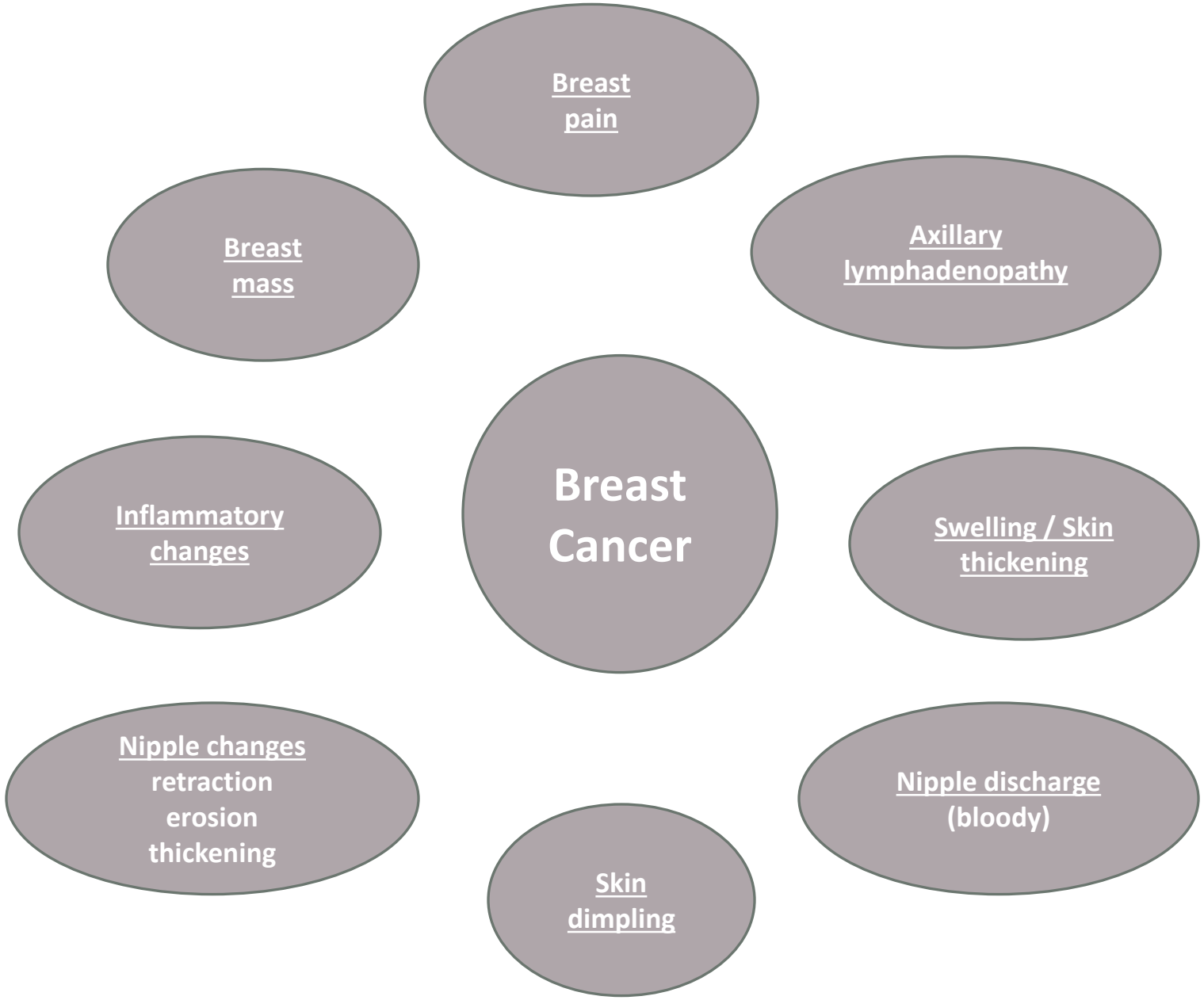


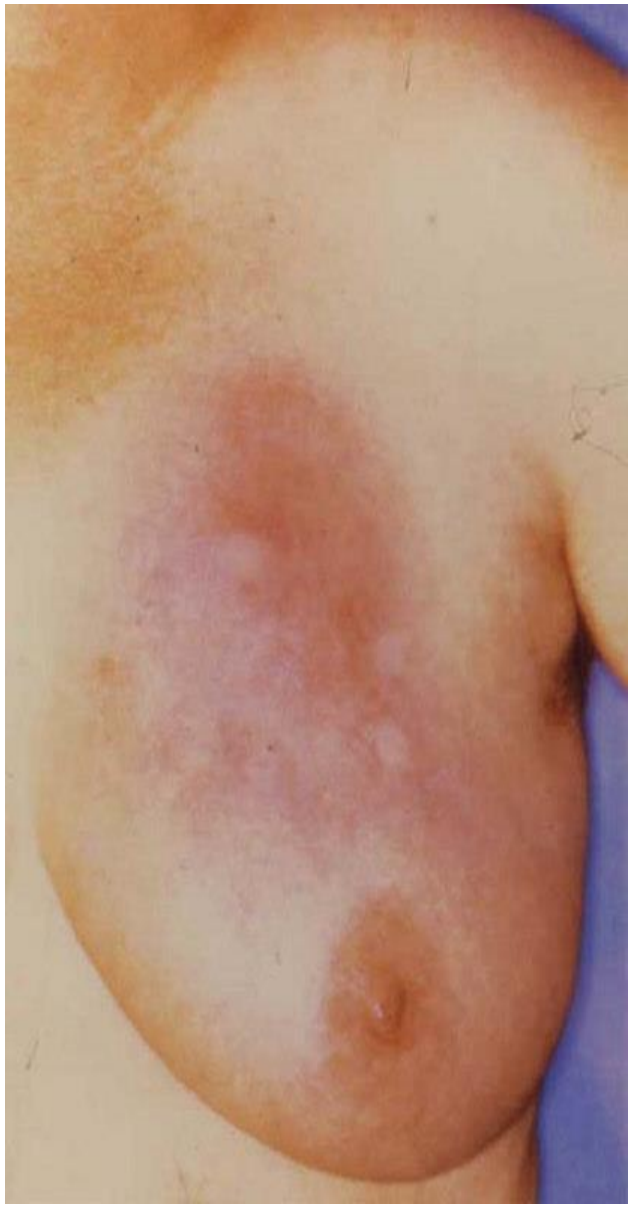
Figure 2. Patient outcome based on breast tumor intrinsic subtypes.

CLINICAL PRESENTATION OF BREAST CANCER

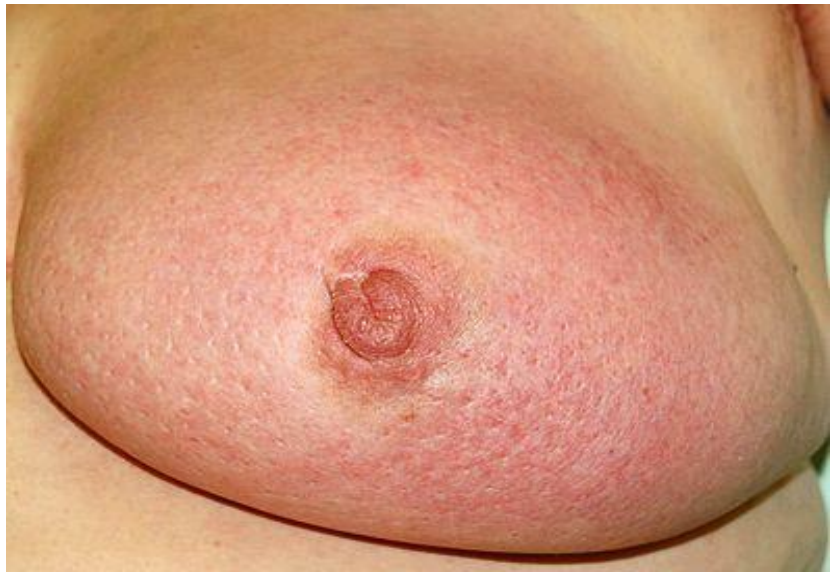
- Typically; small tumors are asymptomatic and usually discovered during screening.

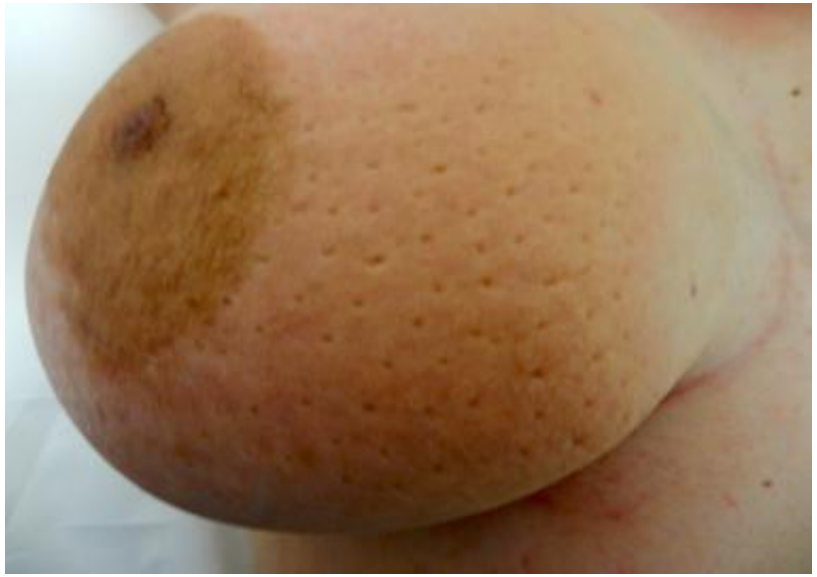
- Symptomatic or palpable tumors are generally present in advanced stage.
  - Generally, more aggressive treatment will be required

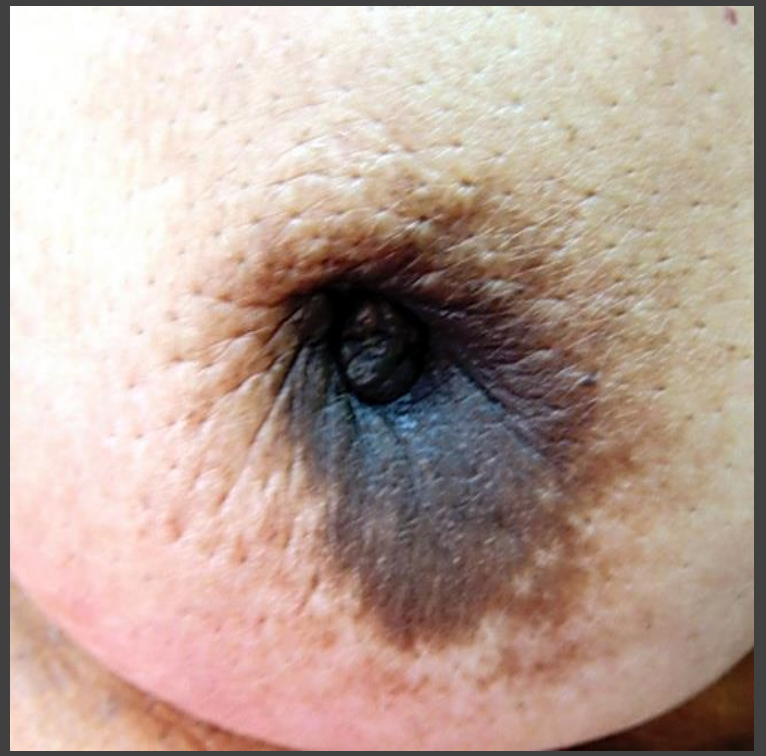

Breast pain
Breast mass
Axillary lymphadenopathy
Breast Cancer
Inflammatory changes
Swelling / Skin thickening
Nipple changes
retraction
erosion
thickening
Nipple discharge
(bloody)
Skin dimpling

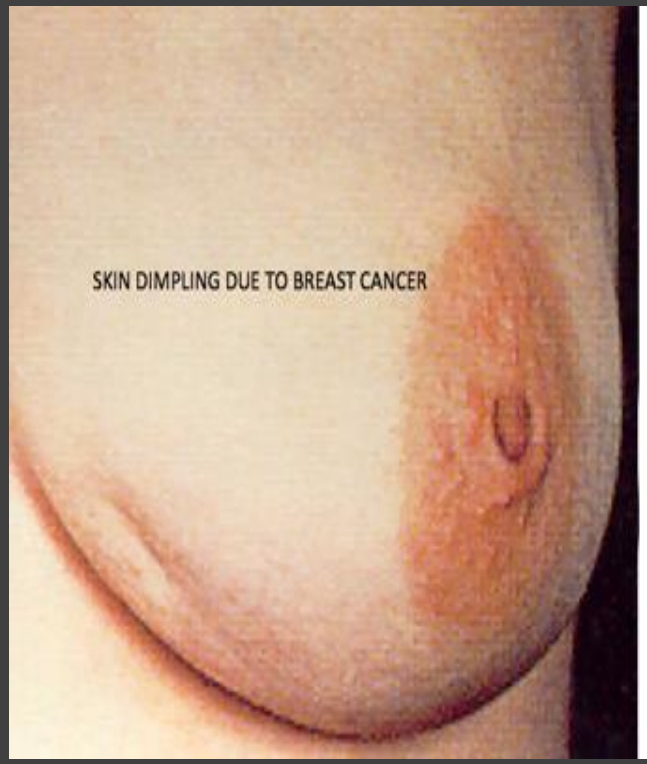


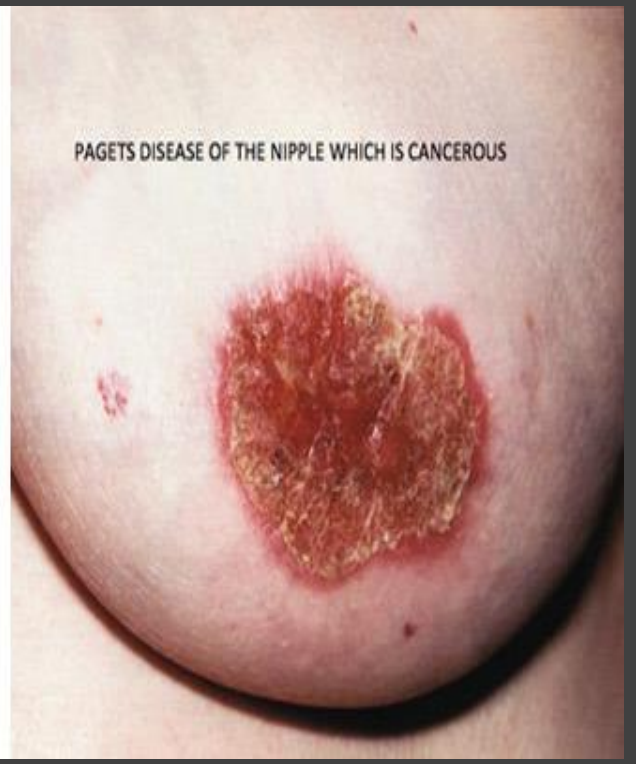
https://bugswong.smugmug.com/Medical-slides/Breast-disease/








SKIN DIMPLING DUE TO BREAST CANCER


PAGETS DISEASE OF THE NIPPLE WHICH IS CANCEROUS

Questions?