Breast 2

(Pathology)

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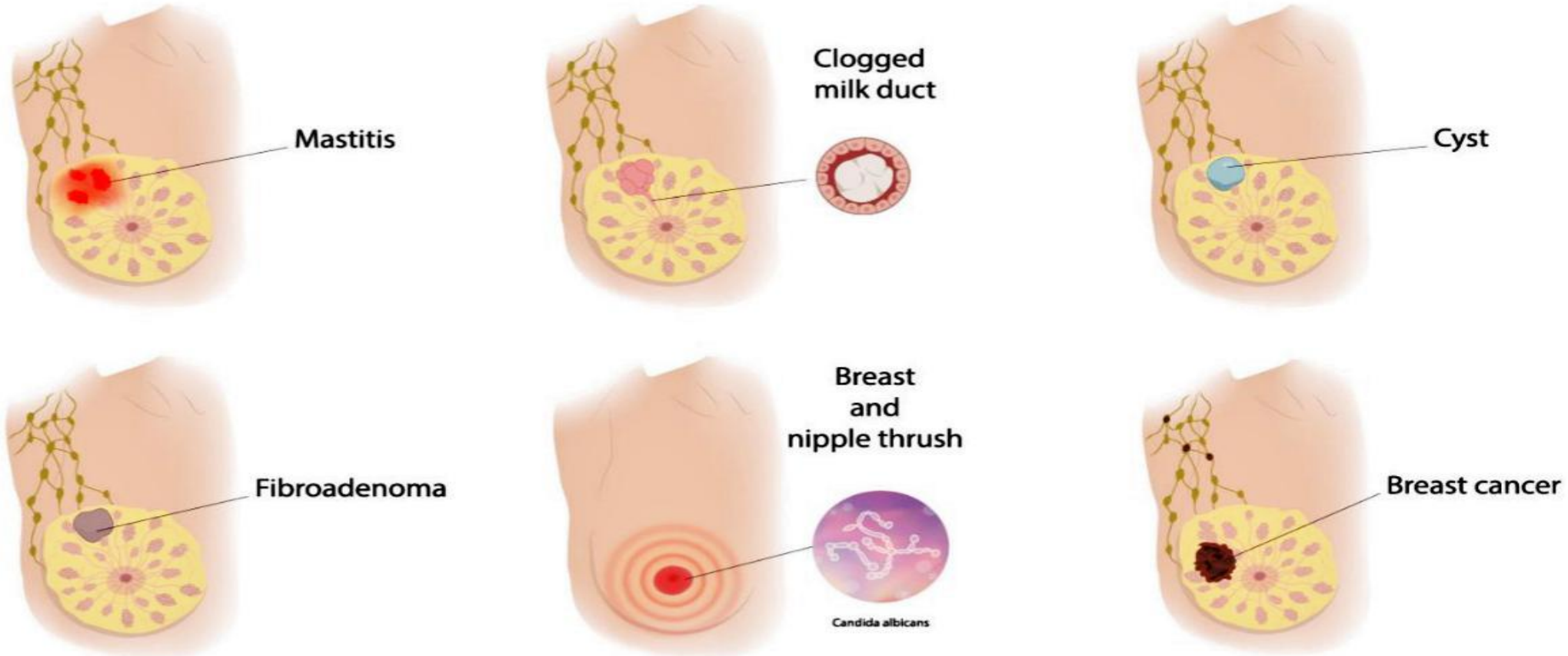
Breast Pathology

(Non-Neoplasmatic & Neoplasmatic Diseases)



Outlines:

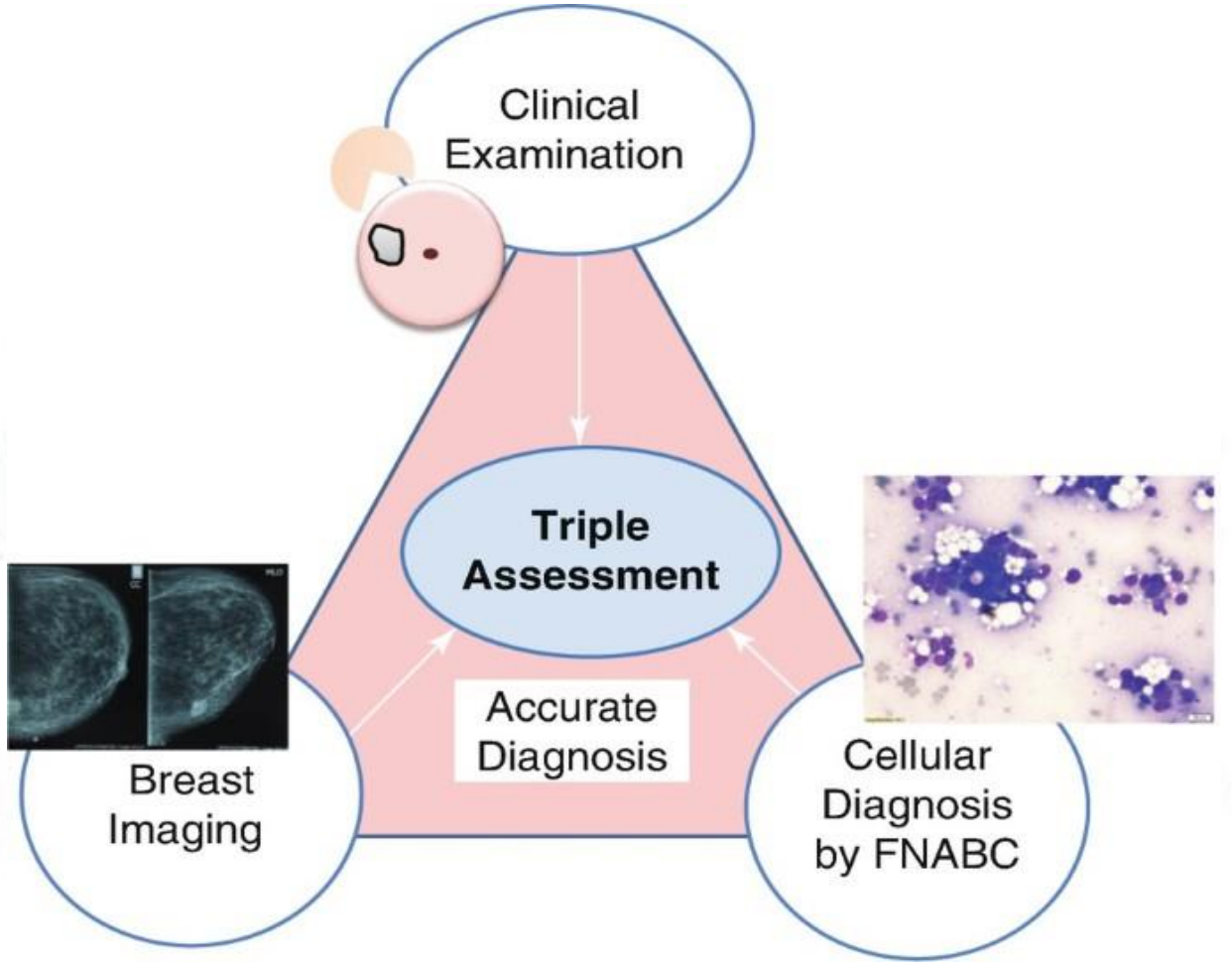
* *How to deal with Breast Symptoms " **Triple Assessment** "*

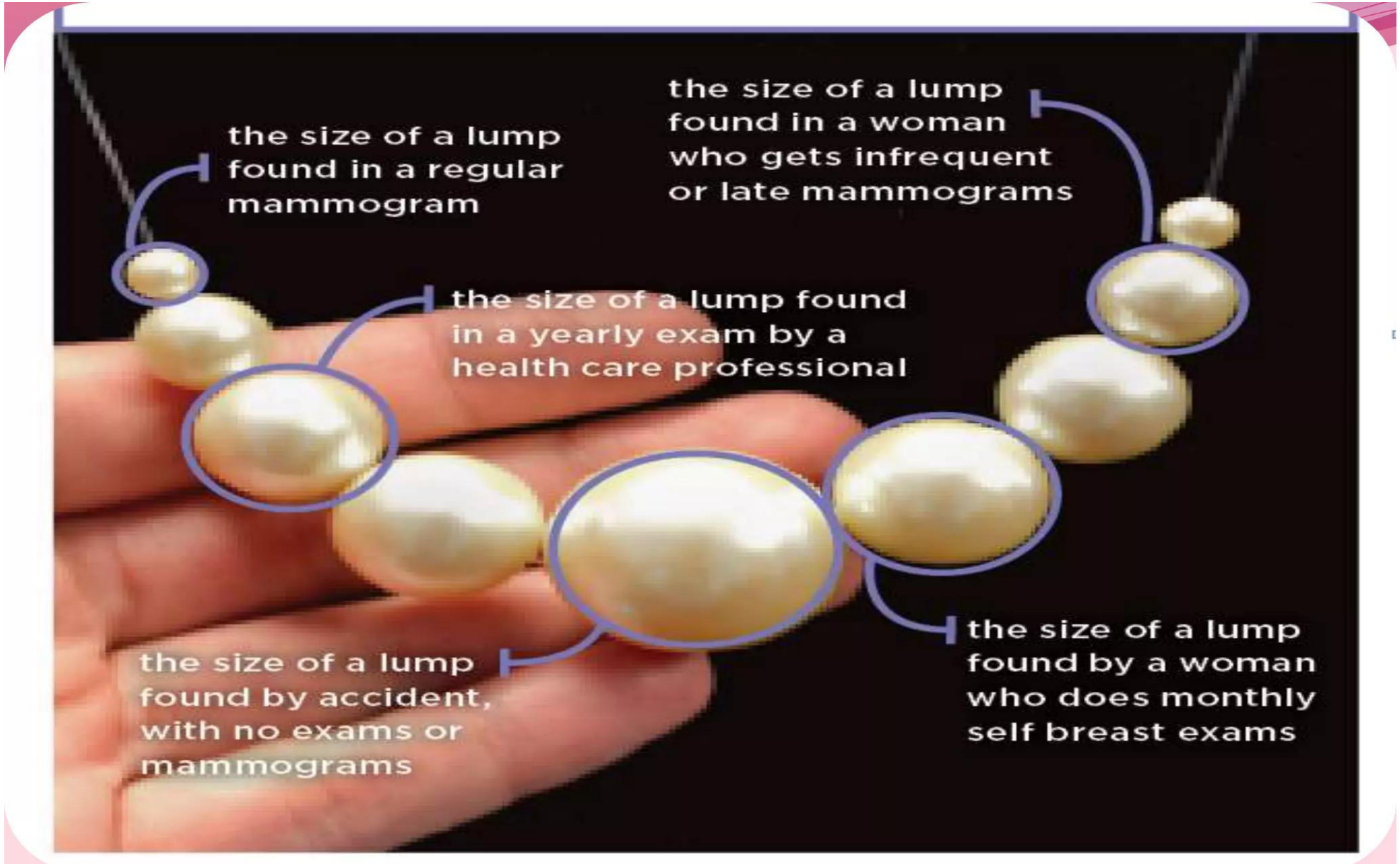
* *Investigations In Breast Diseases.*

* *Specific Benign and Malignant Breast Diseases.*

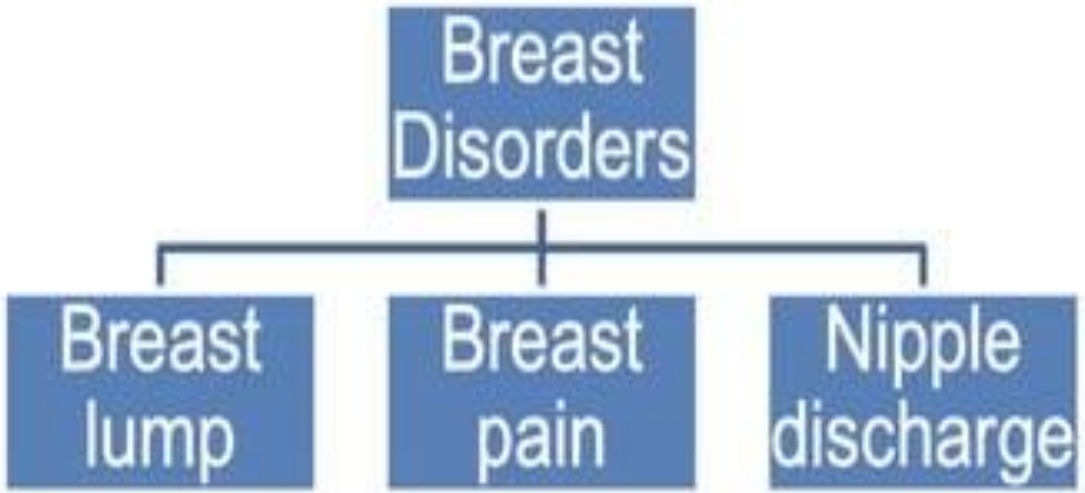
Dealing with Breast Symptoms(*Triple Assessment*):

- **Clinical assesment**
- **Imaging**
  - Ultrasonography
  - Mammography
  - MRI
- **Tissue sampling:**
  - FNAC
  - Biopsy
    - Core
    - Incisional
    - Excisional

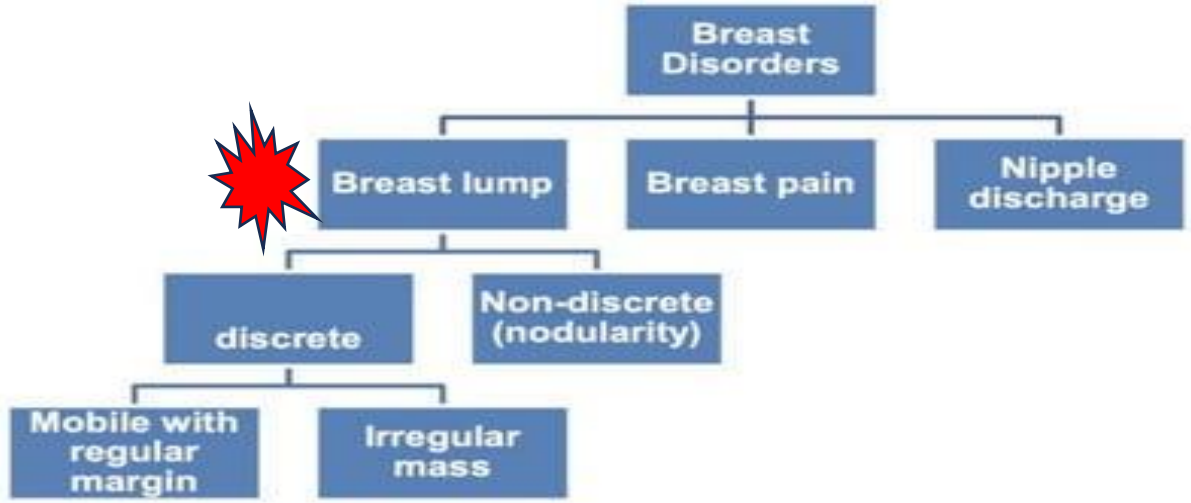



the size of a lump found in a regular mammogram
the size of a lump found in a woman who gets infrequent or late mammograms
the size of a lump found in a yearly exam by a health care professional
the size of a lump found by accident, with no exams or mammograms
the size of a lump found by a woman who does monthly self breast exams

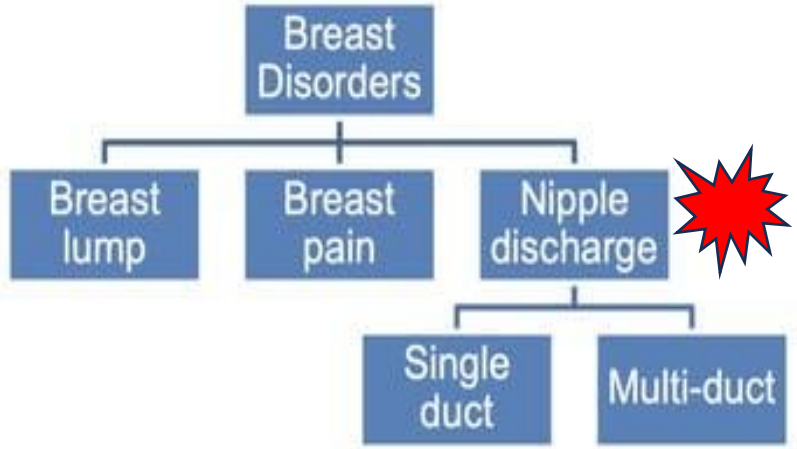
1. Clinical Assessment:
(History and Examination)



History:

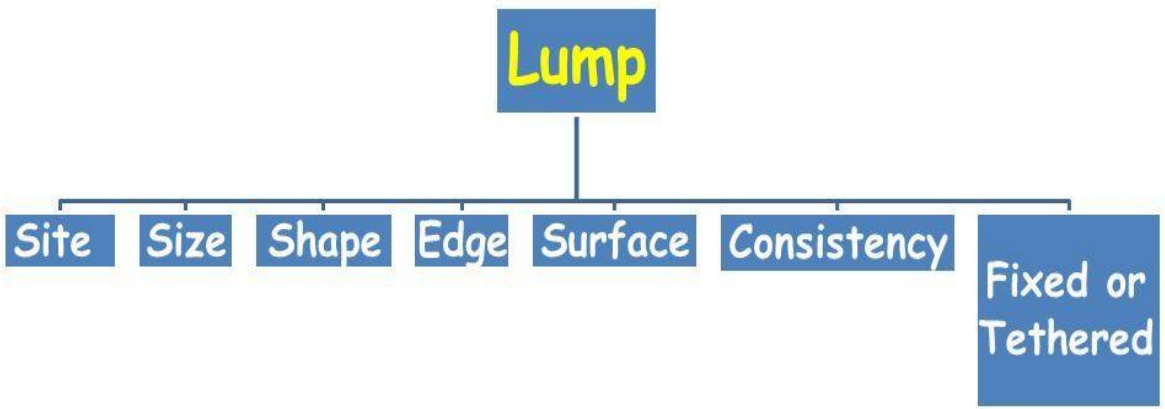

Breast Disorders
Breast lump
Breast pain
Nipple discharge
discrete
Non-discrete (nodularity)
Mobile with regular margin
Irregular mass


Breast Disorders
Breast lump
Breast pain
Nipple discharge
With signs of inflammation
Without signs of inflammation


Breast Disorders
Breast lump
Breast pain
Nipple discharge
Single duct
Multi-duct

Breast lump (Mass)

- When did the patient first notice it & how?
- Site
- Painful or not
- Hard or soft
- Single or multiple
- Changes in the size & shape of the mass
- Skin changes overlying the mass
- Relation to the menstrual cycle
- Other local symptoms :
  - Nipple discharge and inversion
  - Retroareolar pain or hotness & discoloration of skin



Breast pain

- Duration
- SOCRATES
- Relation with periods
- Nipple discharge
- Discoloration and hotness of skin
- Fever, fatigue, anorexia and weight loss
- History of trauma
- Pregnancy or lactation
- Last menstrual cycle

Nipple Discharge

- Site (nipple itself or adjacent area)
- Episodic or continuous
- Color
- Viscosity
- Passive or induced
- Uni/bilateral

Examination:

Position

Inspection

Palpation

position

- The patient must be fully undressed to the waist.
- sitting 45 degrees
- Patients sometimes say that their lump can only be felt when they adopt a certain posture and they should therefore be examined in this position as well.

Inspection

- Stand or sit **directly in front of the patient**, inspect both breasts and look for the following features

PALPATION

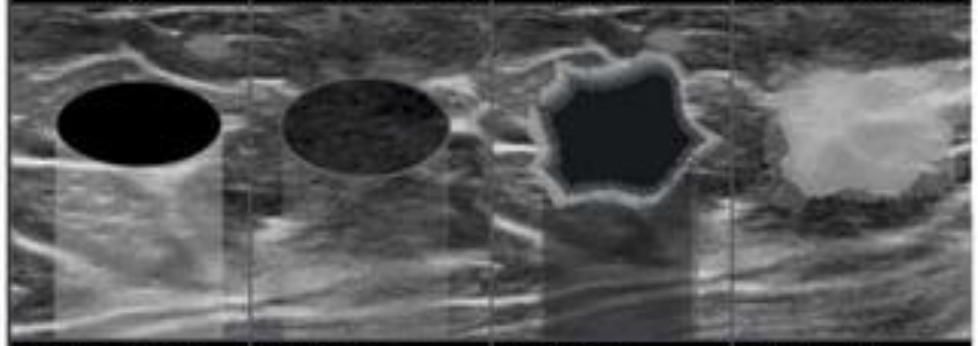
- Ask the patient to lay down with her hand ipsilateral to the breast.

- Ask where is the abnormality?
- Start with the normal breast, then abnormal, away from the tender area (for comparison and looking for separate pathology).

2. Imaging:

Ultrasonography

- Useful in young females with dense breast tissue.
- Distinguishes cysts and solid lesions.
- Localize impalpable areas of breast.
- Important in axillary evaluation and guided biopsy.
- Not great in screening, and is operator-dependent.

Cyst	Fibroadenoma	Cancer	Glandular tissue
			
Anechoic pattern	Hypoechoic	Hypoechoic	Hyperechoic
Oval or round shape	Most common: • oval or round Less frequent: • lobulated	Most common: • irregular shape Less frequent: • round or oval	Locally prominent glandular tissue
Circumscribed margin	Circumscribed margin	Margin is not circumscribed: • Indistinct • angular • microlobulated • spiculated	
Horizontal orientation	Horizontal orientation	Vertical orientation	
Posterior Enhancement	Sometimes minimal posterior enhancement	Frequently posterior shadowing	No feature
No calcifications	May have gross calcifications	May have small calcifications in or outside mass	No

Mammography

- Ultrasensitive film.
- Dose of radiation = 0.1cgy.
- Sensitivity increase with increasing age.
- ~5% of carcinoma missed in population screening.
- A normal mammogram doesn't exclude carcinoma.

Normal mammogram

Benign cyst (not cancer)

Cancer

BI-RADS classification

BI-RADS	Findings	Further management
0	**Incomplete** assessment	Need of additional imaging or prior examinations
1	**Negative**	Routine screening
2	**Benign**	Routine screening
3	**Probably** benign - risk of malignancy is lower than 2%,	Ultrasound imaging is necessary or a control mammography imaging and examination within 6 months
4	**Suspicious** - risk of malignancy is 2-94%,	Further cytology of pathohistology investigation is necessary
5	**Highly suspicious** - risk of malignancy is higher than 94%	Referral to a surgeon is necessary

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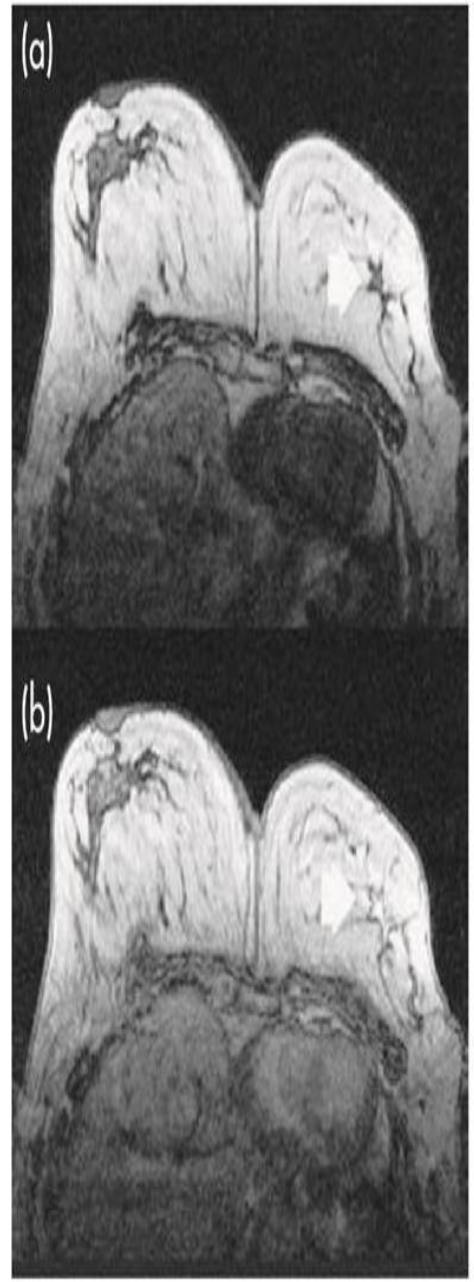
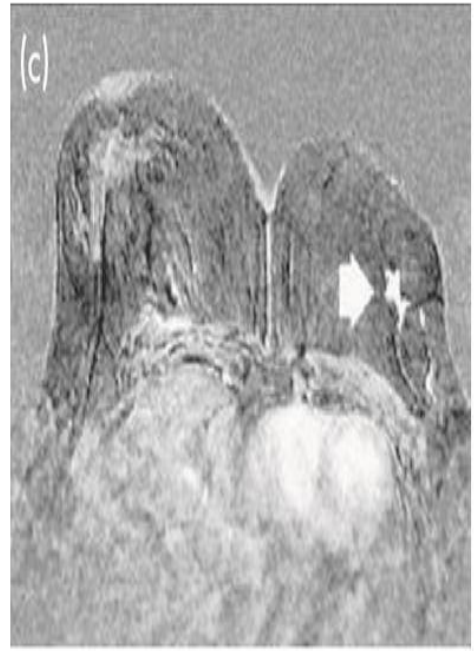
Magnetic Resonance Imaging

- Magnetic resonance imaging (MRI) is of increasing interest to breast surgeons in a number of settings:

1. It can be useful to distinguish scar from recurrence in women who have had previous breast conservation therapy for cancer.
2. It is becoming the standard of care when a lobular cancer is diagnosed to assess for multifocality and multicentricity.
3. It has proven to be useful as a screening tool in high-risk women (because of family history).





Magnetic resonance imaging scan of the breasts showing carcinoma of the left breast (arrows). (a) Pre-contrast; (b) post-gadolinium contrast; (c) subtraction image.

American Cancer Society Risk Criteria for Breast MRI Screening as an Adjunct to Mammography[218]

Women at high lifetime risk (~20%-25% or greater) of breast cancer include those who:

- Have a known *BRCA1* or *BRCA2* gene mutation
- Have a first-degree relative (mother, father, brother, sister, or child) with a *BRCA1* or *BRCA2* gene mutation, but have not had genetic testing themselves
- Had radiation therapy to the chest when they were between 10 and 30 years of age
- Have Li-Fraumeni syndrome or Cowden syndrome, or have a first-degree relative with one of these syndromes

Women at moderately increased (15%-20% lifetime risk) risk include those who:

- Have a lifetime risk of breast cancer of 15% to 20%, according to risk assessment tools that are based mainly on family history
- Have a personal history of breast cancer, ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), atypical ductal hyperplasia, or atypical lobular hyperplasia
- Have extremely dense breasts or unevenly dense breasts when viewed by mammograms

3. Tissue Sampling:

- **Core-cut biopsy**
  - Definitive diagnosis
  - Differentiate between In-situ and invasive diseases
  - Receptor status– important to start neoadjuvant therapy.
- **Cytology**
  - 21/ 23 G needle in 10ml syringe – multiple pass-through tissue with sustained negative suction.
  - Aspirate smeared over a glass slide and air dried and alcohol fixed.

Figure 53.6 Corecut biopsy of breast.

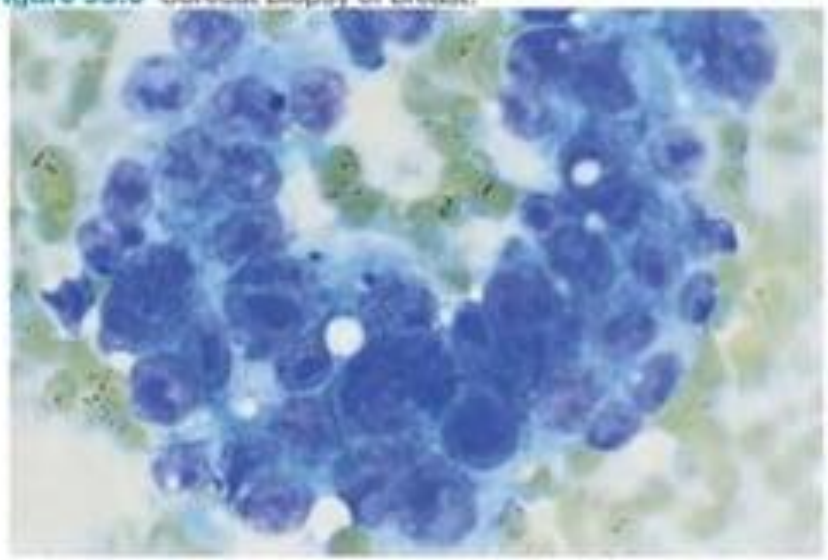


Figure 53.7 Fine-needle aspiration cytology showing grade III ductal carcinoma cells.

Common Benign Breast Diseases:

Congenital Abnormalities:

- **Amazia :** absence of u/l or b/l breasts.
- **Polymazia**: accessory breasts, sites: axilla, groin; functioning during lactation
- **Mastitis of infants**
  - true mastitis uncommon
  - "witch's milk"– few days after birth disappears after 3rd week.
  - Caused by stimulation of the fetal breasts by prolactin in response to drop in maternal estrogen.

Diffuse Hypertrophy:

- Sporadic in otherwise healthy girls during puberty; aka benign virginal hypertrophy.
- Rarely unilateral.
- Tremendous growth due to alteration in sensitivity of breasts to estrogenic hormones.
- T/T– antiestrogens, Reduction mammoplasty.

Breast Injuries (Trauma) :

a. **Hematoma**

- Resolving hematoma – lump
- If overlying bruising absent– difficult in diagnosis unless biopsied.

b. Traumatic fat necrosis

- Acute or chronic; middle-aged women.
- Blow, or even indirect violence (e.g. contraction of the pectoralis major).
- Lump, often painless.
- Mimic a carcinoma– skin tethering – nipple retraction.
- Biopsy is required for diagnosis.
- History of trauma – not diagnostic – merely draw the patient's attention to a pre-existing lump

Acute/Subacute inflammation of breast

- **Bacterial mastitis**
  - The most common variety of mastitis.
  - Associated – lactation in the majority of cases.
  - *Staphylococcus aureus* and *Streptococcus* species.
- Staph. Infections –more localized, may be deep seated.
- Strept. infections – diffuse superficial involvement

Breast abscess

- Staphylococcal infections
- Point tenderness, erythema, and hyperthermia.
- Related to lactation – usually the first few weeks of breastfeeding.
- Progression – may result in subcutaneous, subareolar, interlobular. (periductal), and retromammary abscesses .

- Previously: treated by operative incision and drainage.
- Now the initial approach is antibiotics and repeated aspiration of the abscess, usually ultrasound-guided aspiration.
- **Epidemic puerperal mastitis**
  - Highly virulent MRSA – suckling neonate.
  - Substantial morbidity and occasional mortality.
  - Purulent fluid – expressed from the nipple – breastfeeding is stopped, antibiotics are started, and surgical therapy is initiated.

- **Operative drainage** reserved for
  - Non resolving with repeated aspiration and antibiotic therapy.
  - Some other indications for incision and drainage (e.g., thinning or necrosis of the overlying skin).

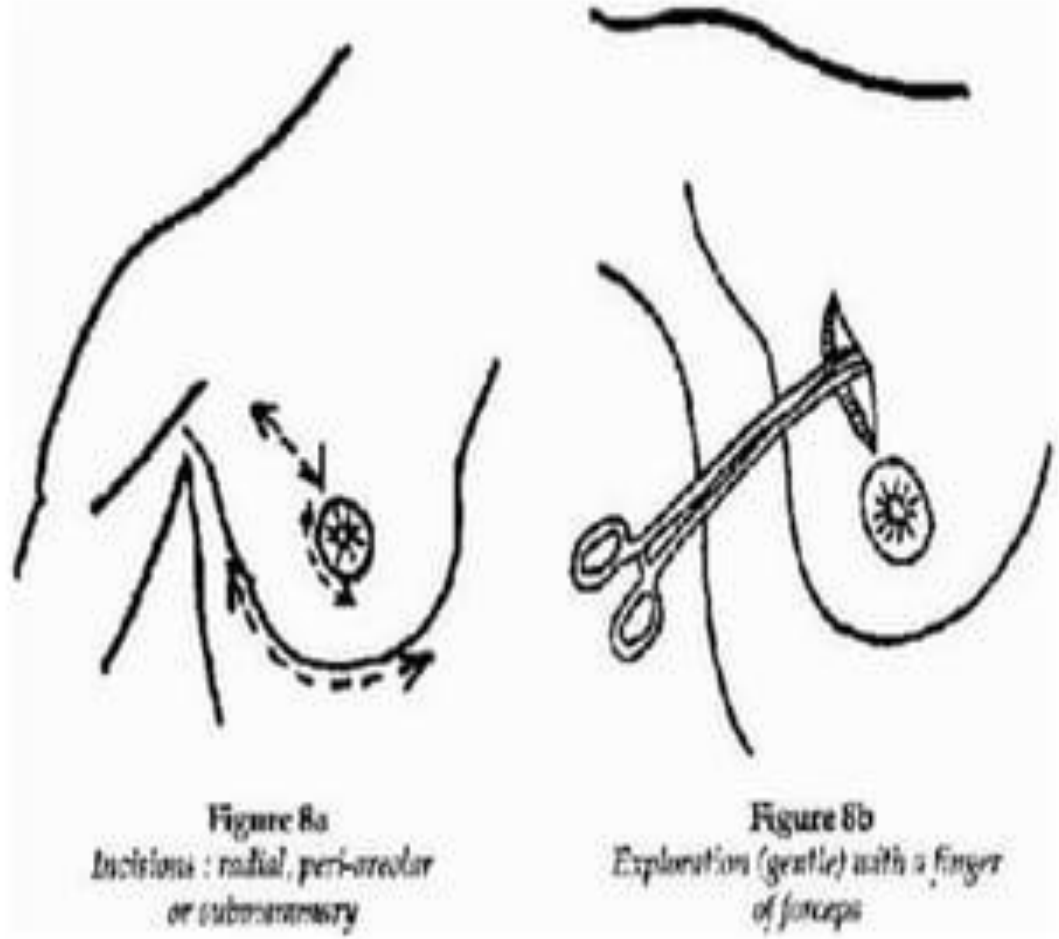


Figure 8a
Incisions : radial, peri-areolar or submammary

Figure 8b
Exploration (gentle) with a finger of forceps

Classification of Mastitis

- **SIMPLE MASTITIS:**
  - -Lactational
  - -Non lactational
- **COMPLICATED MASTITIS:**
  - -Abscess
  - -Draining sinus tracts
  - -Infected cysts
  - -Infected galactoceles
  - -Infected postinterventional collections
- **SPECIFIC MASTITIS:**
  - -Tuberculosis
  - - Fungal

- **PERIDUCTAL MASTITIS/ DUCT ECTASIA**
- **PLASMA CELL MASTITIS.**
- **GRANULOMAT. MASTITIS**
- **DIABETIC MASTOPATHY**
- **POST IRRADIATION**
- **SECONDARY MASTITIS**
  - - Vascular diseases
  - - Collagen disorders
  - - Post traumatic fat necrosis
  - - Foreign bodies

- **INFLAMMATORY CARCINOMA**
- **MALIGNANT ABSCESS**

Mondor's disease

- Superficial thrombophlebitis – breast and chest wall.
- Thrombosed subcutaneous cord, attached to the skin.
- When stretched by raising the arm, a narrow, shallow, subcutaneous groove alongside the cord becomes apparent
- **D/D** :lymphatic permeation from an occult carcinoma.
- **T/T** :restrict arm movements, NSAIDS, warm compresses, rarely excision of the affected vein.

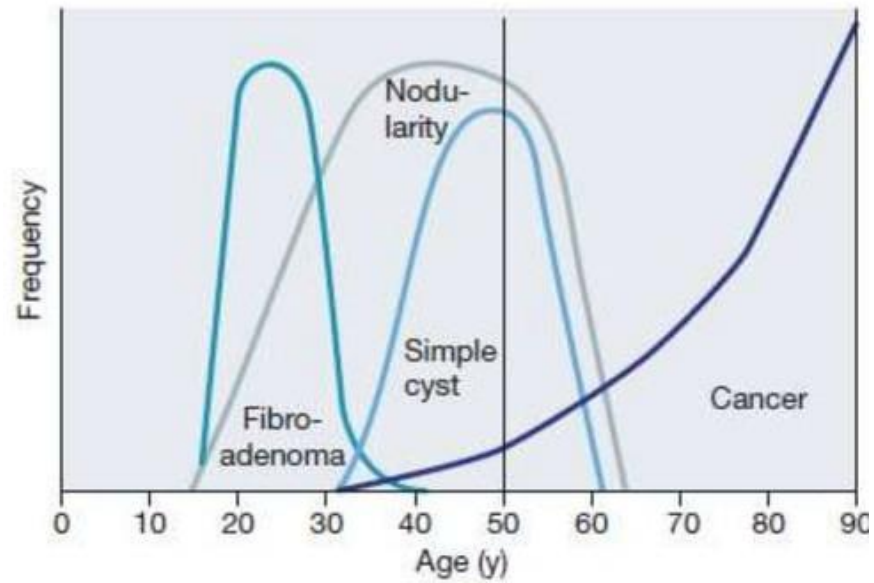
Aberrations of Normal Development and Involution (ANDI)

- The basic principles – ANDI classification of benign breast conditions :
  - Benign conditions – normal processes of reproductive life and involution.
  - The spectrum ranges from normal – >disorder –> disease
  - Encompasses all aspects of the breast condition: pathogenesis and the degree of abnormality.

- **Essentially 4 features:**
  - **Fibrosis** – the disappearance of fat and elastic tissue; interstitium with chronic inflammatory infiltrate.
  - **Cyst formation**:almost inevitable and vary in size.
  - **Hyperplasia** of epithelium in ducts and acini – with or without atypia.
  - **Papillomatosis** :with ingrowth from epithelial hyperplasia.

ANDI classification of benign breast disorders

	NORMAL	DISORDER	DISEASE
Early reproductive years (age 15–25 y)	Lobular development	Fibroadenoma	Giant fibroadenoma
	Stromal development	Adolescent hypertrophy	Gigantomastia
	Nipple eversion	Nipple inversion	Subareolar abscess
			Mammary duct fistula
Later reproductive years (age 25–40 y)	Cyclical changes of menstruation	Cyclical mastalgia	Incapacitating mastalgia
		Nodularity	
	Epithelial hyperplasia of pregnancy	Bloody nipple discharge	
Involution (age 35–55 y)	Lobular involution	Macrocysts	—
		Sclerosing lesions	
	Duct involution		
	Dilatation	Duct ectasia	Periductal mastitis
	Sclerosis	Nipple retraction	—
	Epithelial turnover	Epithelial hyperplasia	Epithelial hyperplasia with atypia



Specific Benign Breast Diseases:

- Fibroadenoma
- Cyclical mastalgia
- Breast cysts
- Periductal Mastitis
- Papillomas and Papillomatosis
- Sclerosing Adenosis
- Phylloides' tumor

a. Fibroadenoma

- Benign solid tumors – stromal and epithelial elements.
- 2nd most common tumor (after carcinoma).
- Most common tumor in women <30 years.
- Late teens and early reproductive years.

Normal	Disorder	Disease
Small fibroadenoma <1 cm in size	Larger fibroadenoma 1 to 3 cm	Fibroadenoma larger than 3 cm

Clinical features

- Firm masses – easily movable – increase in size over several months.
- Surface: Lobulated or smooth.
- Usually grow 1-2 cm in diameter and stabilizes.

- On excision:
  - well-encapsulated masses – detach easily from surrounding breast tissue.

- Two subtypes
  - **Giant** fibroadenoma – fibroadenoma >5cm.
  - **Juvenile** fibroadenoma –histologically more cellular than the usual fibroadenoma.

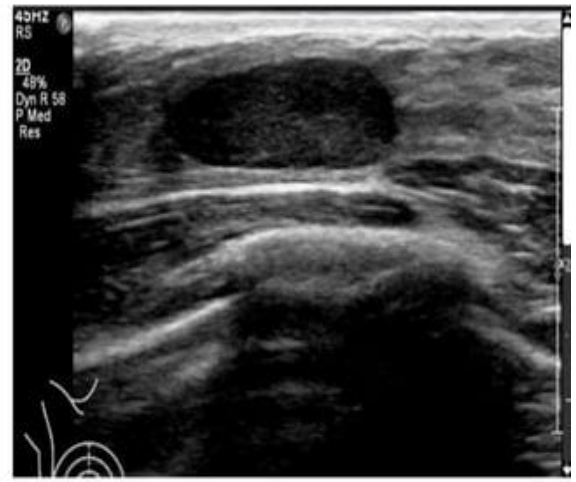
- Neoplasia is extremely rare.

- Surgery only if:
  - Suspicious cytology.
  - Very large.
  - Patient desires removal.
  - Increasing size on f/u.

Typical USG picture: Fibroadenoma

- Hypoechoic
- Oval shaped
- Circumscribed margin
- Orientation parallel to the skin

  (Wider than taller).
- May have gross calcification



b. Cyclical mastalgia

- In later reproductive years (25-40 years).
- Pain fluctuates with the menstrual cycle.
- **Pronounced** if interferes with daily life, affects sleep or impairs sexual activity.

TABLE 53.1 Treatment of breast pain.	
Exclude cancer	
Reassure	Use pain chart if unsure if cyclical or non-cyclical. Also allows time for reassurance to become active!
Adequate support	Firm bra during the day and a softer bra at night
Exclude caffeine	Works for some although not very efficacious in author's practice
Consider medication	
Evening primrose oil (GLA)	Better effect in women over 40 years old than in younger women
Danazol, 100 mg three times a day	Start at 100 mg per day and increase (seldom used these days)
Tamoxifen	Not licensed for this indication but occasionally very helpful

Meta-Analysis > Breast. 2007 Oct;16(5):503-12. doi: 10.1016/j.breast.2007.03.003.
Epub 2007 May 16.

Evidence-based management of Mastalgia: a meta-analysis of randomised trials

A Srivastava [1], R E Mansel, N Arvind, K Prasad, A Dhar, A Chabra

Affiliations + expand

PMID: 17509880 DOI: 10.1016/j.breast.2007.03.003

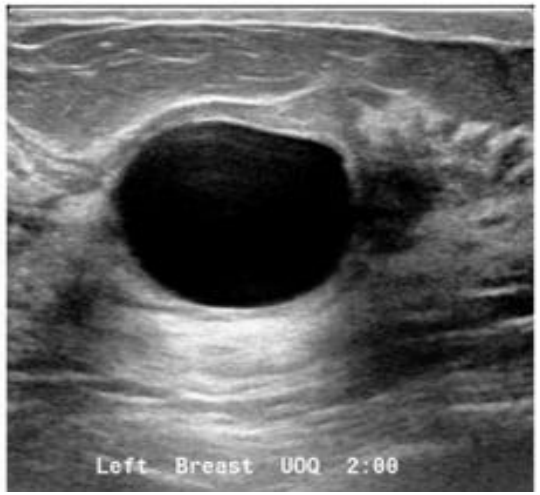
Abstract

Several agents have been utilised for therapy of mastalgia based on data from small trials. No meta-analysis of trials on mastalgia exists. We have conducted a meta-analysis on trials on mastalgia published in the English language. Study was restricted to randomised controlled trials comparing Bromocriptine, Danazol, Evening primrose oil (EPO) and Tamoxifen with placebo. The analysis was carried out on the REVMAN statistical package. Weighted mean difference in the pain score in favour of Bromocriptine was -16.31(95% CI -26.35 to -6.27). Danazol produced a significant benefit with a mean pain score difference -20.23(95% CI -28.12 to -12.34). EPO did not offer any advantage over placebo in pain relief, mean pain score difference being -2.78 (95% CI -7.97 to 2.40). Tamoxifen achieved a relative risk (RR) of pain relief of 1.92 (95% CI 1.42-2.58). Tamoxifen is associated with least side effects and should be the drug of first choice.

- ✓ **Bromocriptine, Danazol and Tamoxifen offered significant relief from mastalgia.**
- ✓ **Tamoxifen had the least side effects.**
- ✓ **Evening primrose oil is ineffective and shouldn't be used.**

c. Breast cyst

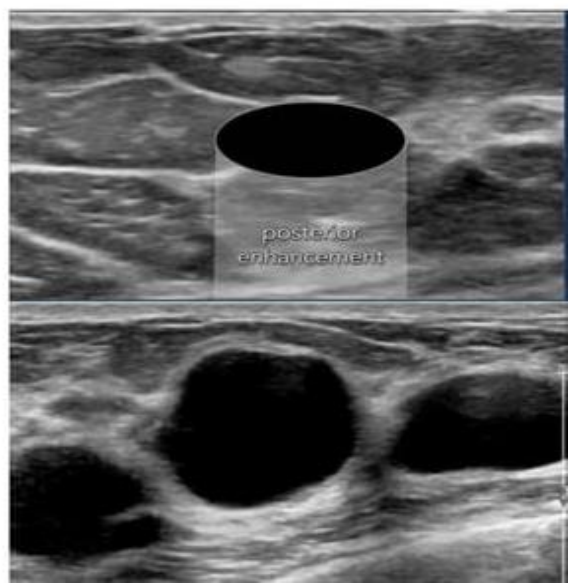
- Fluid-filled – epithelial lined cavities – microscopic to large palpable masses – 20 to 30 mL of fluid.
- Palpable cyst : 1:14 women.
- 50% - multiple or recurrent.
- Influenced by ovarian hormones – variation with the menstrual cycle.
- Last decade of reproductive life.
- No evidence of increased risk for breast cancer.



- Confirmed: Ultrasonography or direct needle aspiration
- If the mass resolves after aspiration and the cyst contents are not grossly bloody, the fluid does not need to be sent for cytologic analysis.
- If mass is noted on initial ultrasound or residual mass post aspiration, then tissue specimen is obtained by core biopsy.

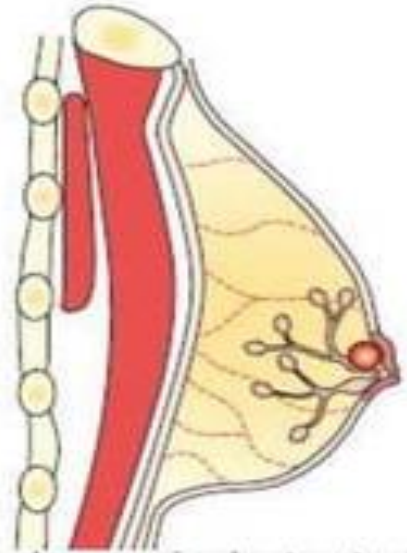
Typical USG picture: Cyst

- Echolucent (or black) pattern.
- Round or oval shaped.
- Sharp circumscribed margin.
- Posterior enhancement.
- No calcification.



d. Ductal ectasia and periductal mastitis

- Chronic relapsing form of infection may develop in the subareolar ducts of the breast.
- Dilatation of breast ducts –>associated with periductal inflammation.
- Marked association with smoking.



Subareolar abscess in duct ectasia.

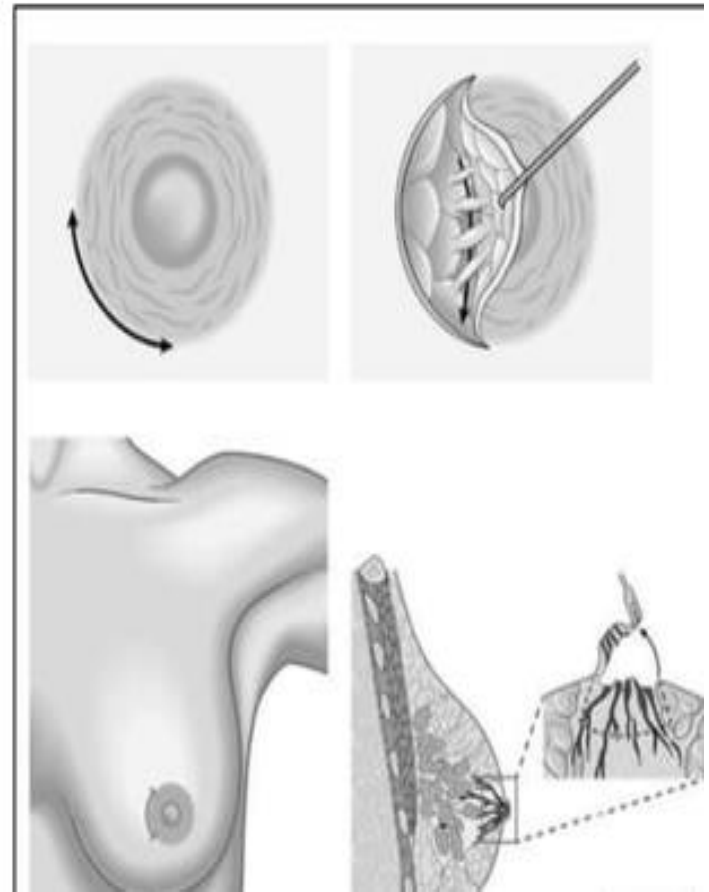
Pathogenesis

- Dilatation of ducts. → Stagnation of secretions containing chemically irritating fatty acids → epithelial ulceration → leakage. → periductal fibrosis.
- Alternate theory: Periductal fibrosis. → Weakening of ducts. → Secondary dilatation.
- Most likely, both process occurs together.

- **Clinical features**
  - Nipple discharge (any color).
  - Subareolar mass/ abscess/ mammary duct fistula.
  - Nipple retraction.
- **Treatment**
  - If mass/ nipple retraction: 1st exclude carcinoma.
  - Antibiotics.

Surgical treatment

Treatment of recurrent subareolar sepsis	
SUITABLE FOR FISTULECTOMY	SUITABLE FOR TOTAL DUCT EXCISION
Small abscess localized to one segment	Large abscess affecting >50% of the areolar circumference
Recurrence involving the same segment	Recurrence involving a different segment
Mild or no nipple inversion	Marked nipple inversion
Patient unconcerned about nipple inversion	Patient requests correction of nipple inversion
Younger patient	Older patient
No discharge from other ducts	Purulent discharge from other ducts
No prior fistulectomy	Recurrence after fistulectomy



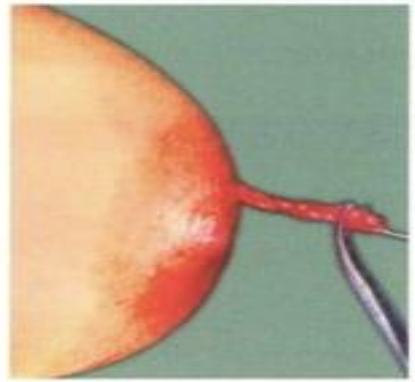


Fig. 21.33: Papilloma excision

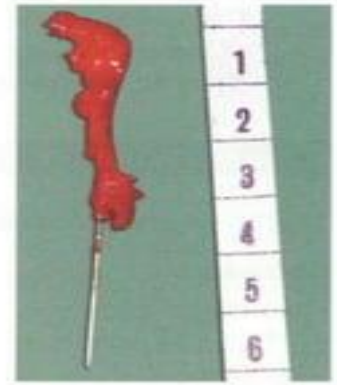


Fig. 21.34: Specimen of papilloma

e. Papilloma

- Solitary intraductal papillomas – true polyps of epithelial-lined breast ducts.
- The most common cause of pathological nipple discharge (52-57%).
- Mostly located close to the areola but may be present peripherally.
- Most are smaller than 1 cm but can grow up to 4 to 5 cm.
- Not associated with an increased risk for breast cancer.
- T/t: Excision through circumareolar incision.

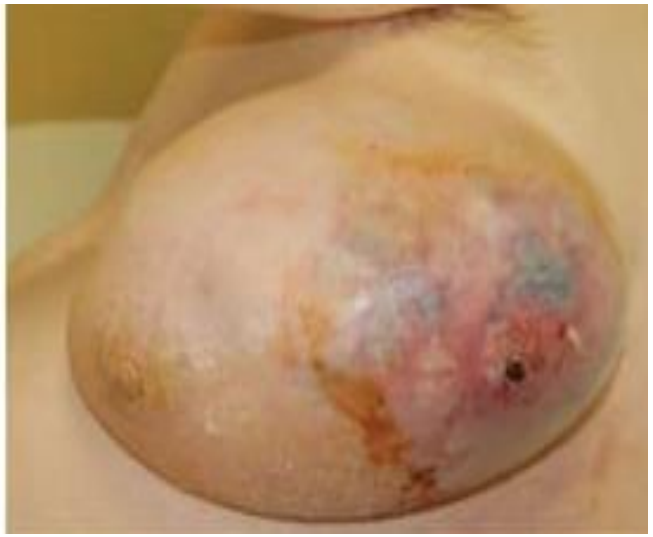
g. Phyllodes' tumor

- Fibroepithelial tumors composed of epithelial and stromal component.
- > Prediliction to attain massive size and recur locally after lumpectomy.
- Types:

a. **Benign**: More than 60% in younger women.

b. **Borderline**: Depends on mitotic activity and cellularity.

c. **Malignant**: Infiltration at edge of tumor



Diagnosis

- Often, clinical diagnosis.
- USG helps detect size of tumor, solid and cystic areas.
- Trucut biopsy reveals mitotic figure s/o malignancy.

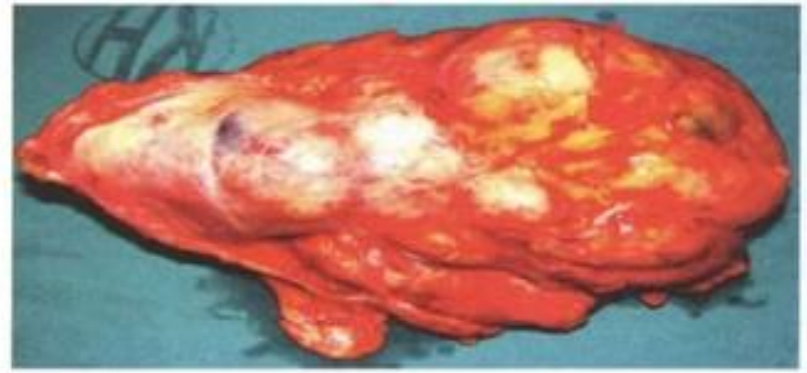
Clinical features

- Age group: 30-40 years.
- Rapid growth.
- Stretchy shiny skin.
- Red, dilated veins over surface.
- Bosselated surface (big nodules).
- Undergoes necrosis resulting in cystic areas with serous discharge.

Treatment

- **Small**: Wide excision (1-2 margins). Lumpectomy shouldn't be done as it can cause recurrence.
- **Giant**: More wider excision.
- **Malignant**: Simple mastectomy may be necessary.

Fig. 21.15: Phylloides tumour of the left breast at surgery



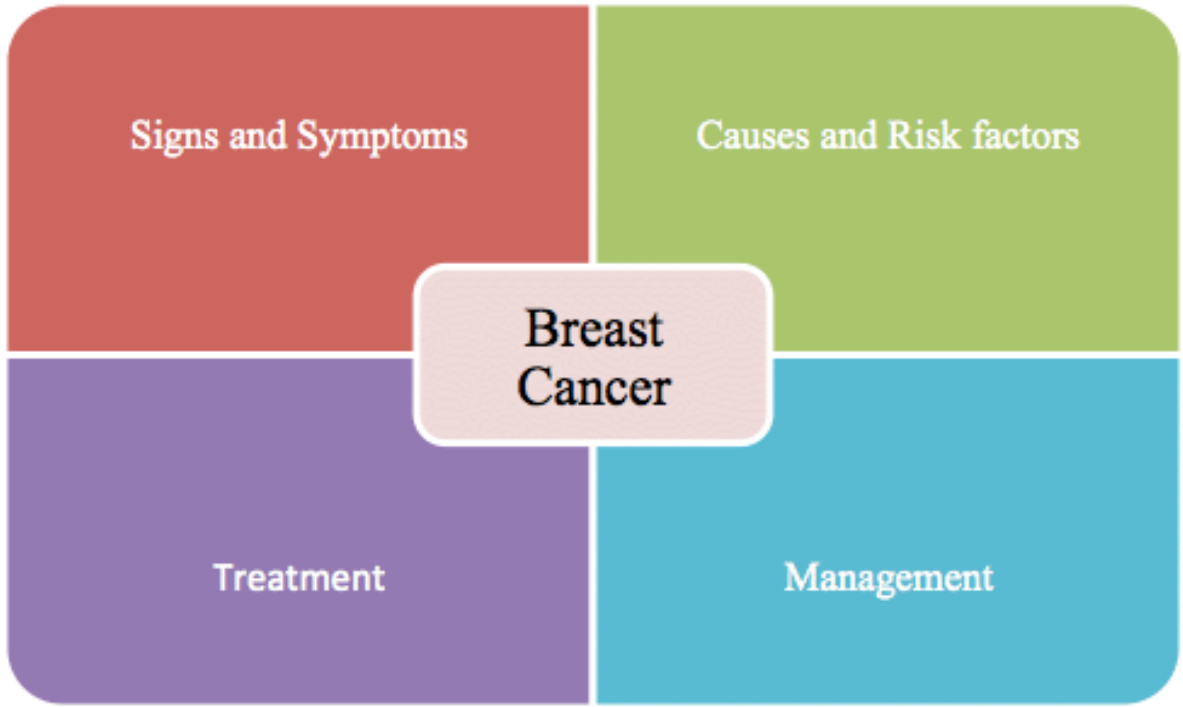
Differentiation from carcinoma

- No fixity to the skin.
- No fixity to underlying pectoralis.
- Lymph nodes will not be involved.
- No nipple retraction.

Breast Cancer

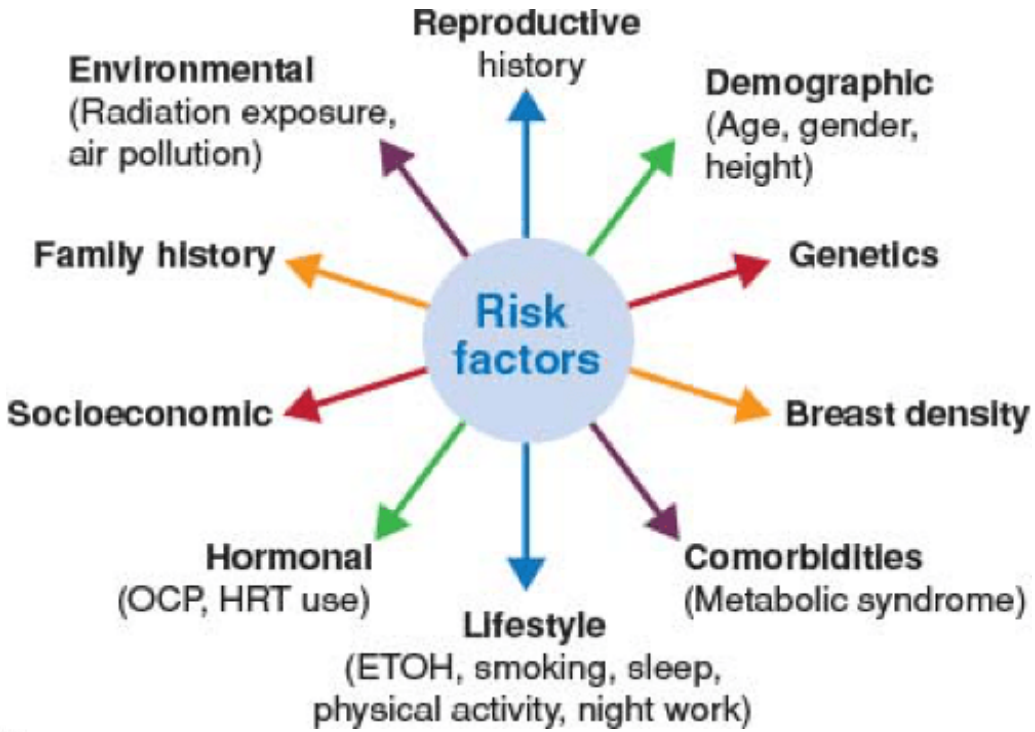
Breast Cancer Facts

- 2nd leading cause of death
- 2nd most common cancer
- Incidence increases with age
- **All** women are at risk



Presentation

- Hard lump
- Nipple retraction
- Discharge
- Peau d'orange
- Fixation of breast
- Ulcerating mass



Breast factors

- High breast density – more glandular tissue, less fatty tissue.
- Previous breast cancer.
- Atypical ductal hyperplasia (ADH) and atypical lobular hyperplasia (ALH). These confer fivefold increased risk.
- Lobular in situ neoplasia (LISN) . Up to 11 times greater risk of developing cancer in either breast.
- Previous breast irradiation early in life.

Genetic factors

- Family history - A woman with one affected first degree relative (mother or sister) has double the risk. This risk increases when two or more relatives are affected.
- Gene mutations :Mutations in the breast cancer susceptibility genes BRCA1 and BRCA2 account for the majority of families with four or more affected members. Mutations show autosomal dominant inheritance.

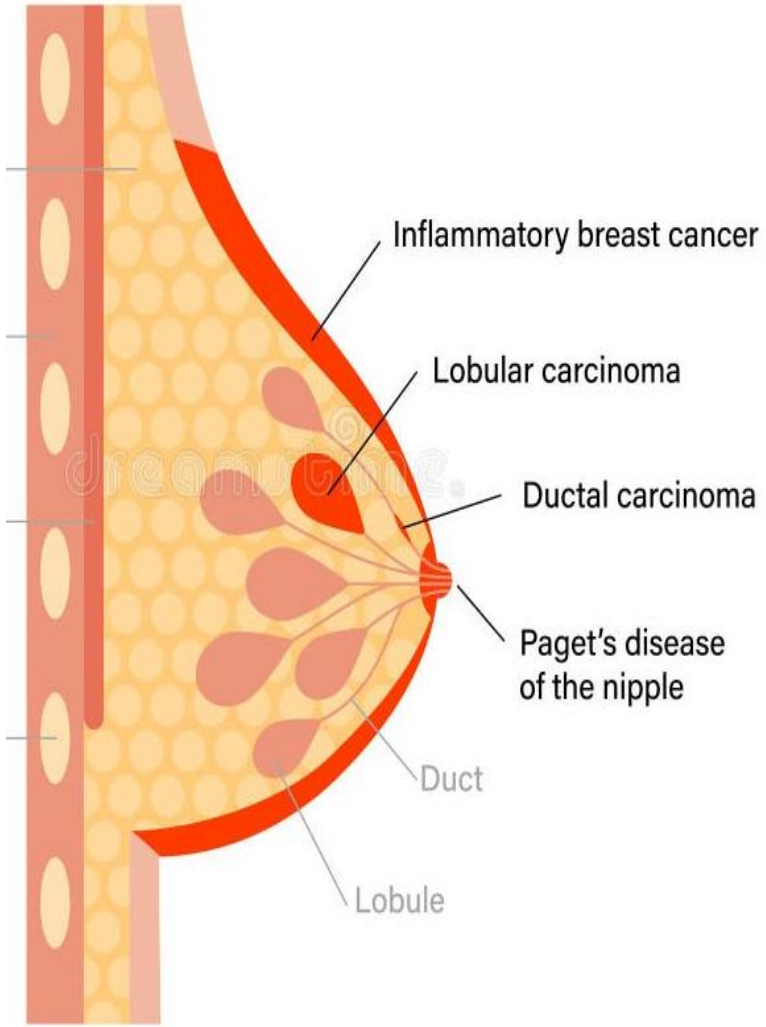
Other factors

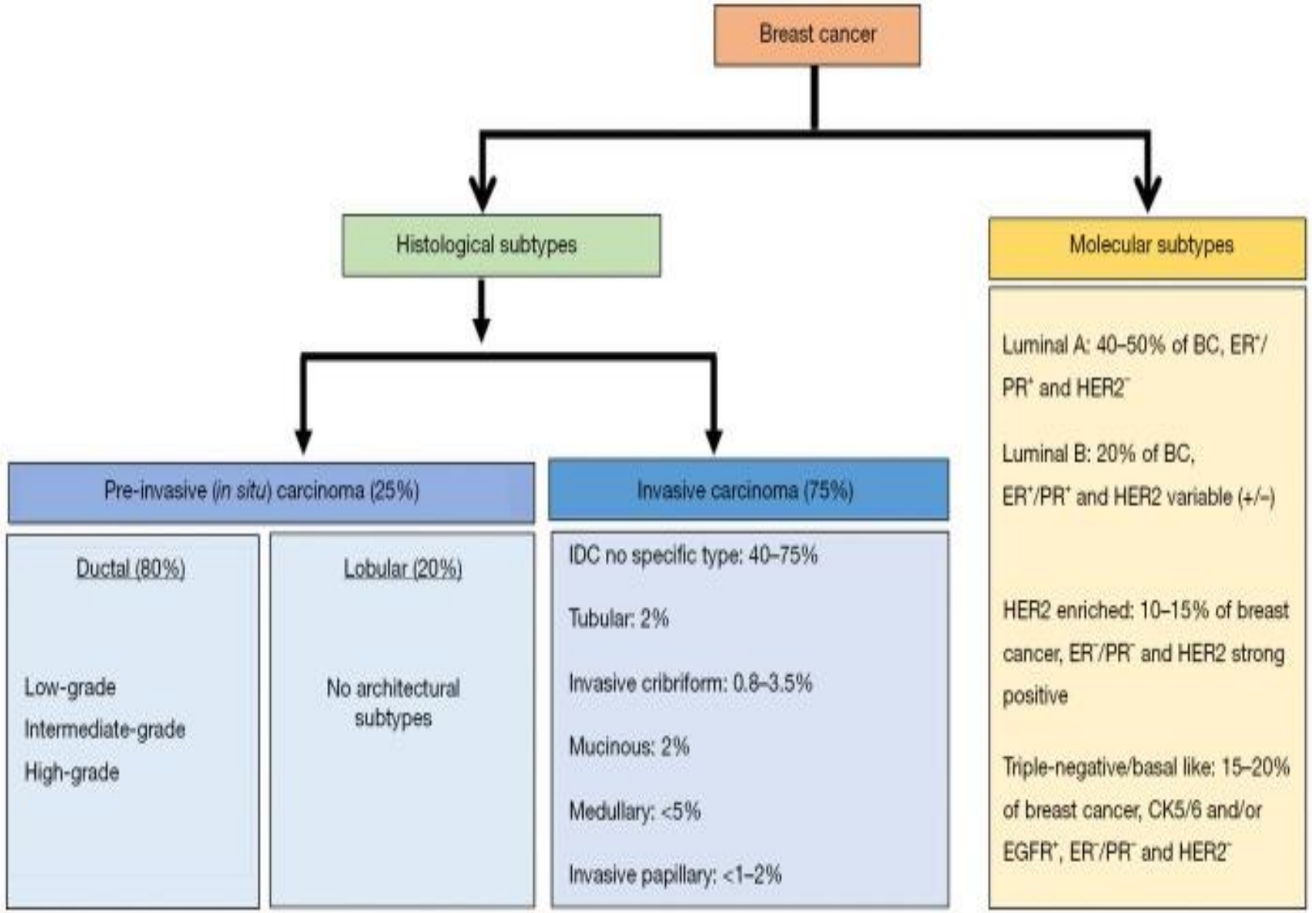
- Age – the older the woman, the higher the risk. 80% of new breast cancer cases occur in women >50 years.
- Increased body weight
- Lack of physical activity
- Excess alcohol consumption
- Caucasian race.

Reproductive factors

- Early menarche; late menopause.
- Age >30 at first childbirth.
- Parity – childbearing reduces breast cancer risk.
- Breastfeeding reduces risk.
- Exogenous hormones -Increased risk with oral contraceptive pill and HRT.

Types of breast cancer





Receptor status

- Determined by immunohistochemistry (IHC) or fluorescence in situ hybridisation (FISH).
- Helps target treatment with specific adjuvant therapy and provides prognostic information.
- **Oestrogen receptor (ER)**
  - ➢ 70% of invasive breast cancers are ER positive.
  - ➢ ER positive cancer cells depend on oestrogen for growth.
  - ➢ Targeted by drugs that interfere with oestrogen activity.
- **Progesterone receptors (PR) -** PR status influences likelihood of recurrence.
- **Human epidermal growth factor receptor 2 (HER2/neu)**
  - ✓HER2 positivity (determined by protein overexpression or gene amplification) is found in 15% of early stage invasive breast cancers. Associated with poor prognosis.
  - ✓ Tumours with high levels of these receptors may respond to drugs such as trastuzumab (Herceptin®).
- **Triple negative breast cancer**
  1. Tumours not expressing ER, PR or HER2/neu are known as triple negative tumours.
  2. They have a relatively poor prognosis.

Biological tools

- Newer biological tumour analysis techniques look at all these factors together.
- Commercially available gene profiling kits include MammaPrint® and Oncotype DX®.
- These categorise breast cancer into a number of molecular subtypes, which have different prognoses and different responses to treatments.
- Four distinct molecular subtypes have been described so far: ◦ Luminal A (42–59%) ◦ Luminal B (6–19%) ◦ Triple negative/basal-like (14–20%)

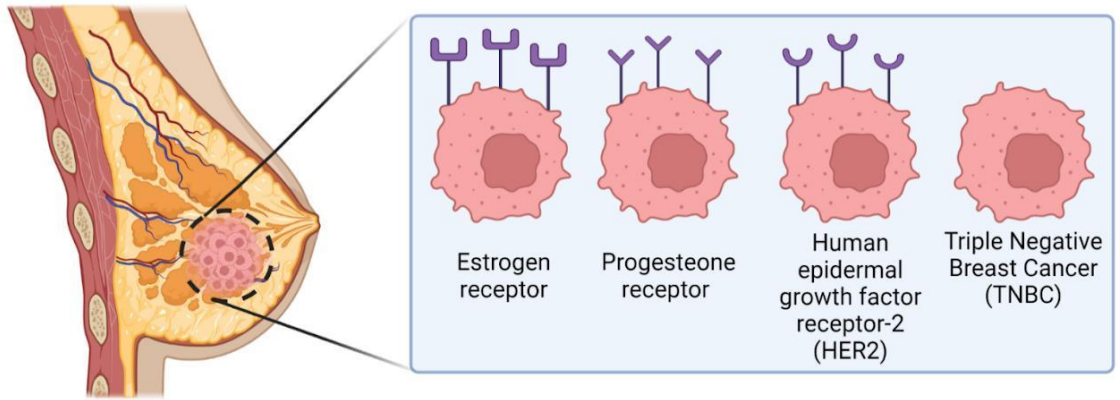
Intrinsic Subtypes of Breast Cancer

Luminal A
(ER+ &/or PR+, HER2-)
- Most common subtype
- Less aggressive
- Lower histological grade
- Good prognosis
- Hormone responsive
- Associated with increasing age

Basal-Like
(Triple Negative, cytokeratin 5/6+ &/or EGFR+)
- Aggressive Subtype
- High grade histology, and high mitotic rate
- Risk at younger age (<40)
- More likely premenopausal African American women

Luminal B
(ER+ &/or PR+, HER2+)
- Similar to Luminal A
- More frequently ER+/PR-
- Worse Outcome than Luminal A

HER2+ (ER-)
- Less common, highly aggressive subtype
- High grade histology
- Risk at young age (<40) greater than luminal subtypes
- African American ethnicity may be a risk factor
- Outcome improved with HER2

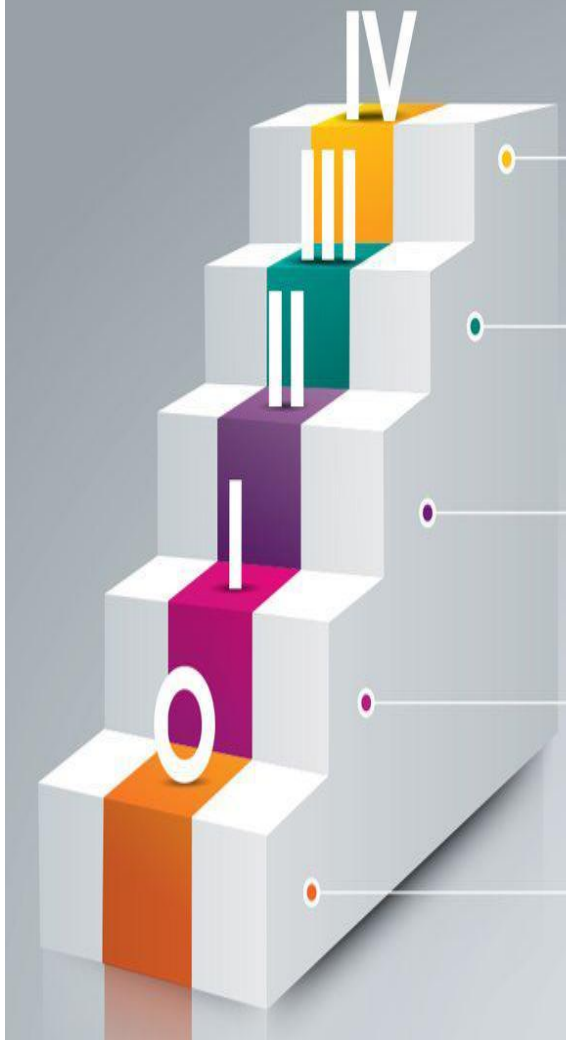


TNM stage

TNM stage groupings			
STAGE 0	TIS	N0	M0
Stage IA	T1[a]	N0	M0
Stage IB	T0	N1mi	M0
	T1[a]	N1mi	M0
Stage IIA	T0	N1[b]	M0
	T1[a]	N1[b]	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1[a]	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
Stage IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
Stage IIIC	Any T	N3	M0
Stage IV	Any T	Any N	M1

Tumor size **T**	Tumor size < 2 cm  	Tumor size 2-5 cm  	Tumor size > 5 cm  	Tumor extends to skin or chest wall 
Lymph Nodes **N**	**N0** No lymph node metastasis	**N1** Metastasis to ipsilateral, movable, axillary LNs	**N2** Metastasis to ipsilateral fixed axillary, or IM LNs	**N3** Metastasis to infraclavicular/ supraclavicular LN, or to axillary and IM LNs
Metastasis **M**	**M0** No distant metastasis	**M1** Distant metastasis		

THE STAGES OF BREAST CANCER



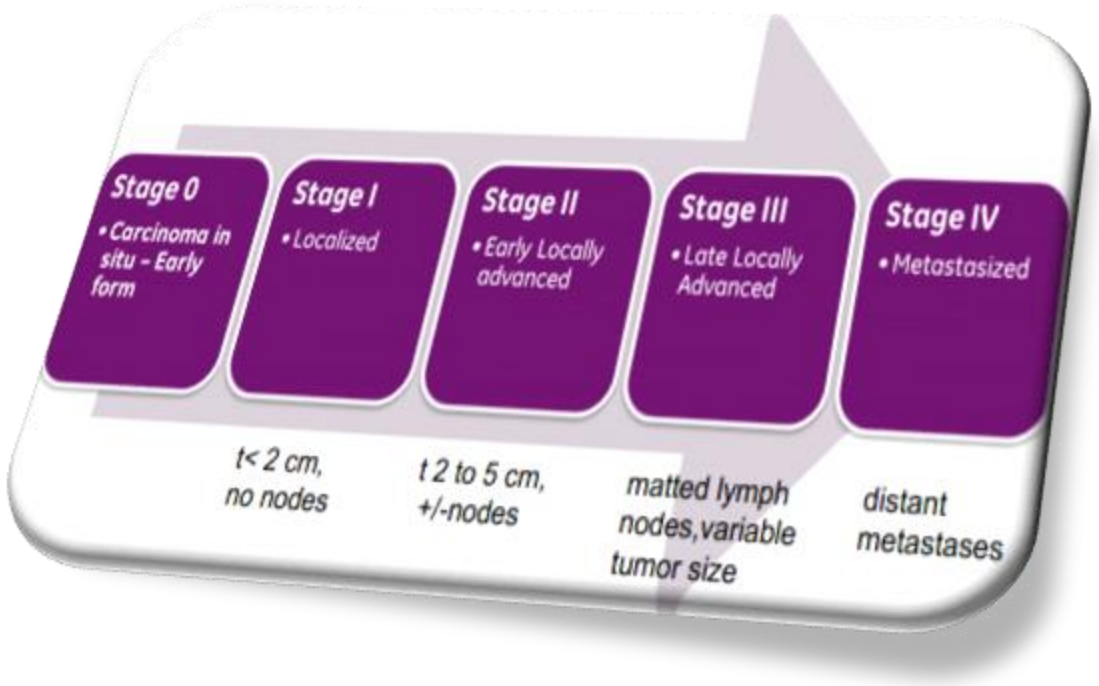
IV. **Distant Spread:** Cancer has spread beyond the breast to other parts of the body.

III. **Regional Spread:** Tumor is larger than 50mm, with more lymph nodes involved across a wider region. In some cases, there is no tumor present at all. Cancer may have spread to skin or chest wall.

II. **Localized:** Tumor is between 20-50mm and some lymph nodes are involved or a tumor larger than 50mm with no lymph nodes involved.

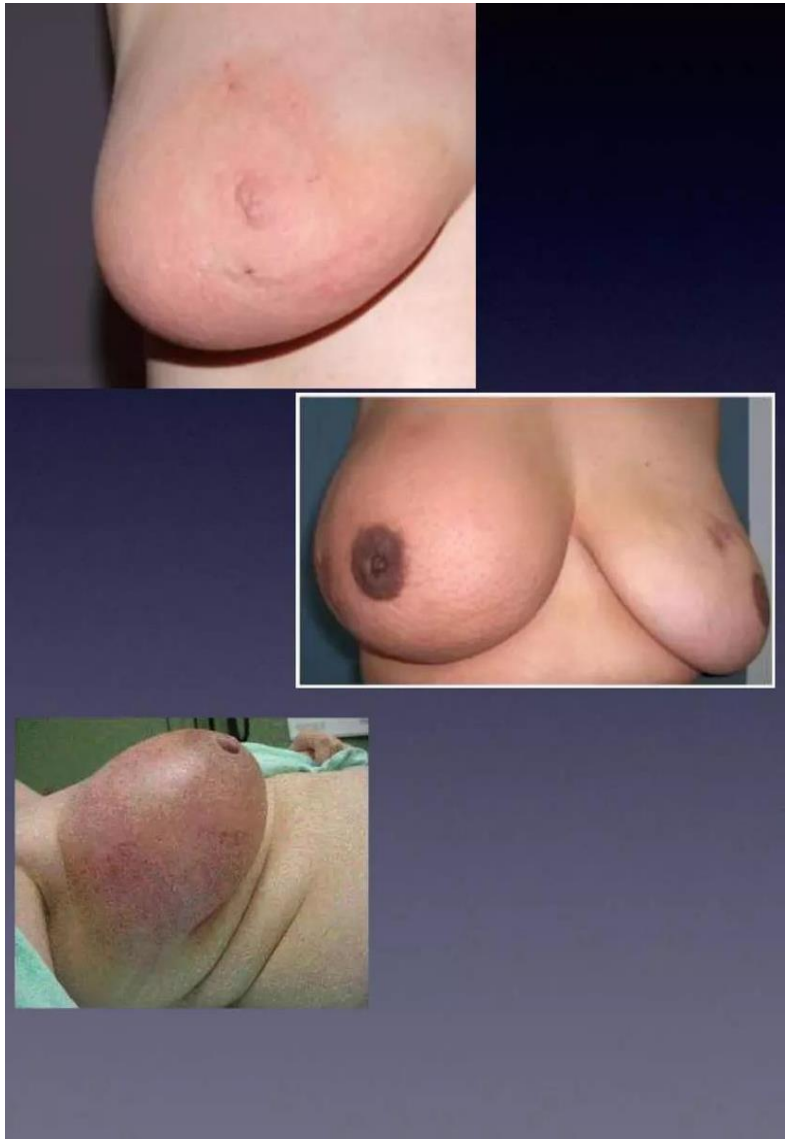
I. **Early Stage:** Cancer has spread to other tissue in small area.

0. Abnormal cells are present but **have not spread** to nearby tissue.



What is inflammatory breast cancer?

- An aggressive subset of breast cancer diagnosed clinically (no current molecular definition!)
- 2-5% of total BC incidence, but ~10% of mortality
- 2 types of IBC
  - **Primary IBC** - IBC developing in a previously normal breast (MOST CASES)
  - **Secondary IBC** - IBC features (and biopsy-proven invasive cancer) on the chest wall post mastectomy for non-IBC or a recurrence with inflammatory features in a breast that already had cancer
- A palpable lump is present in only a third of IBC patients at diagnosis
  - Hence the IBC Network's slogan -"No lump still cancer" slogan



- Classical signs of primary IBC
  - Warm, rapidly enlarging swollen breast (due to the blockage of lymph vessels with tumor clumps)
  - Redness (or pinkness) covering **1/3 or more** of the breast, with a history of no more than 6 months
    - (Impt: neglected non-IBC can invade skin and appear like IBC)
  - Peau d'orange (orange peel) appearance of the skin overlying the breast
  - Breast can be painful
  - Nipple changes (e.g. retraction, flattening, crusting)

NCCN® Practice Guidelines in Oncology – v.1.2009

Inflammatory Breast Cancer

CLINICAL PRESENTATION[a] WORKUP

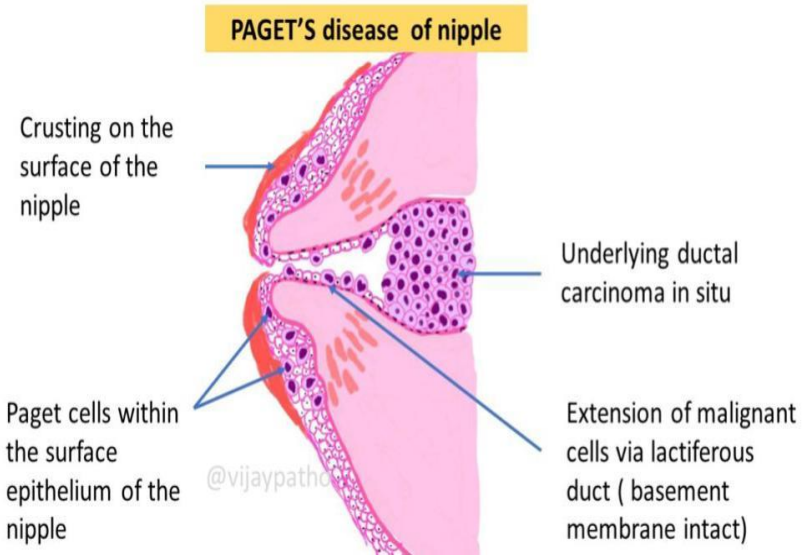
Clinical pathologic diagnosis of IBC Stage T4d, N0-N3, M0

- History and physical exam
- CBC, platelets
- Liver function tests
- Pathology review
- Determination of tumor ER/PR status and HER2 status
- Bilateral diagnostic mammogram, ultrasound as necessary
- Breast MRI (optional)
- Bone scan (category 2B)
- CT scan chest/abd/pelvis (category 2B)
- Chest imaging (if pulmonary symptoms are present)

TREATMENT

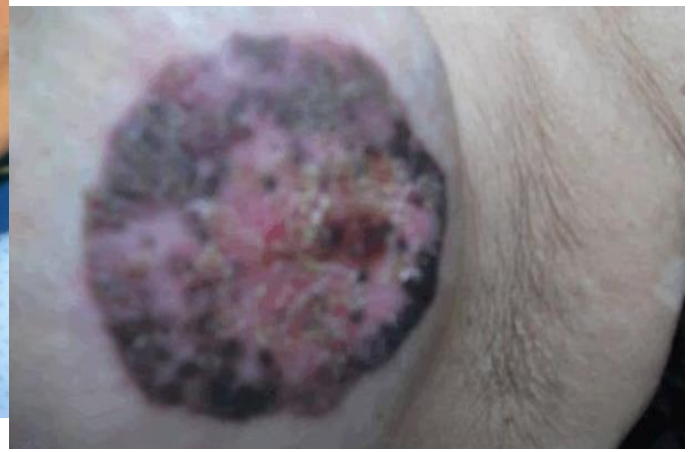
Preoperative chemotherapy, anthracycline ± taxane[b] If tumor HER2 positive, trastuzumab containing regimen but not concurrent with anthracycline

- Response → Total mastectomy + level I/II axillary dissection + radiation therapy to chest wall and supraclavicular nodes (plus internal mammary nodes if involved, consider internal mammary nodes if not clinically involved [category 3]) ± delayed breast reconstruction → Complete planned chemotherapy regimen course if not completed preoperatively plus endocrine treatment if estrogen receptor positive (sequential chemotherapy followed by endocrine therapy). Complete 1 year of trastuzumab if tumor HER2-positive
- No response → Consider additional systemic chemotherapy and/or preoperative radiation
  - Response - See above pathway
  - No response → Individualized treatment



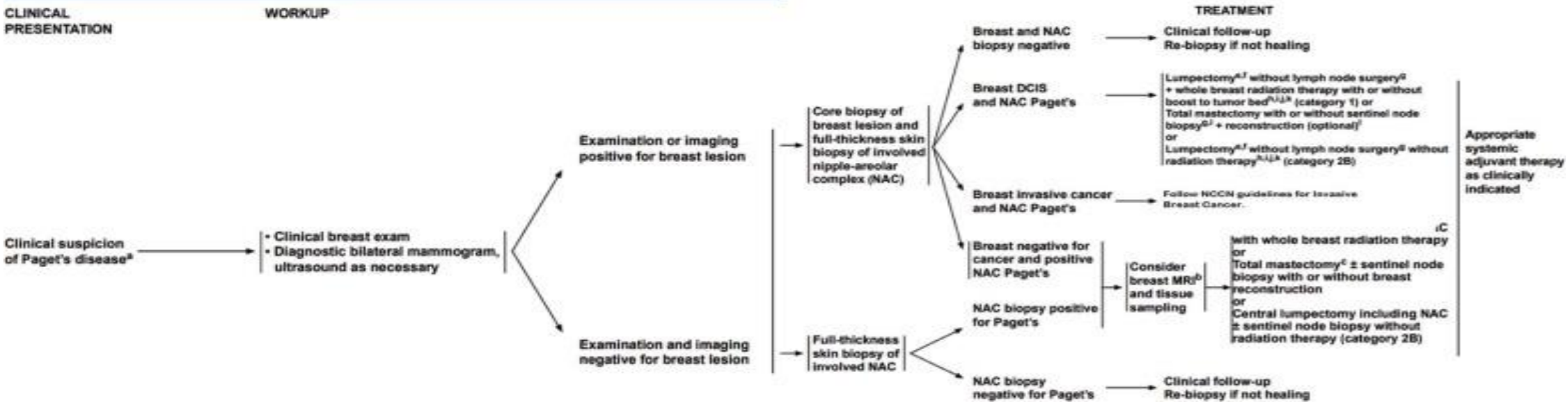
Early Stage

Late stage



National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2017
Paget's Disease

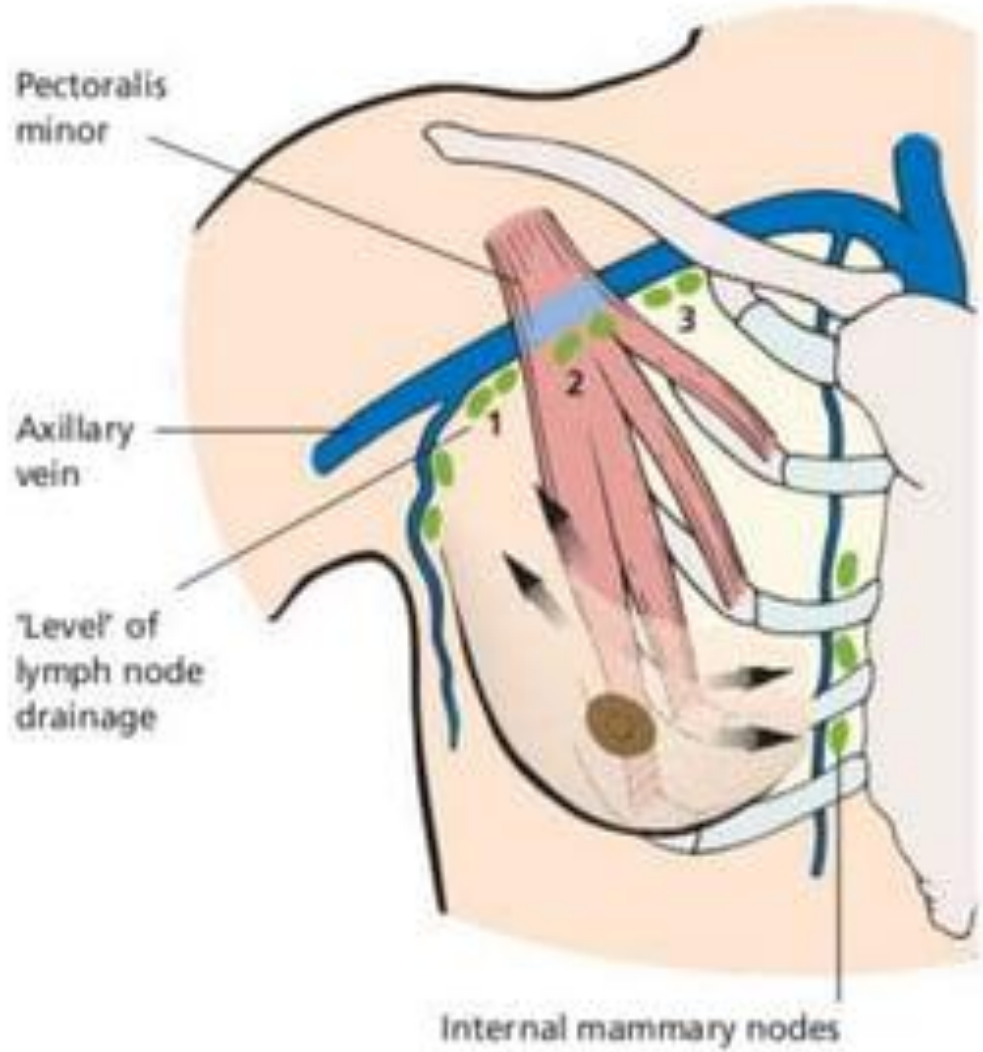


Investigation

- FHG, LFT, CXR
- Triple assessment = clinical, radiologic, biopsy
  - Histology should include E2, P2, HER2
- Ultrasound if <35 years
- Mammogram
  - Irregular diffuse margins, spiculated
  - Clustered microcalcifications
  - Large nodes
  - Assess for multifocal/multicentric disease
- MRI breast
- Staging CT
- Abdominal Ultrasound
- Bone scan

Management

- Surgery
  - Breast conservation
  - MRM
  - Palliative mastectomy
- Chemotherapy
  - Neoadjuvant, adjuvant or sandwitch
  - CDF, CMF, second line: taxanes
- Radiotherapy
  - In combination with chemo – if <2mm
  - Local vs axillary (extensive nodal disease)
- Endocrine therapy
- Targeted therapy



Surgical treatment

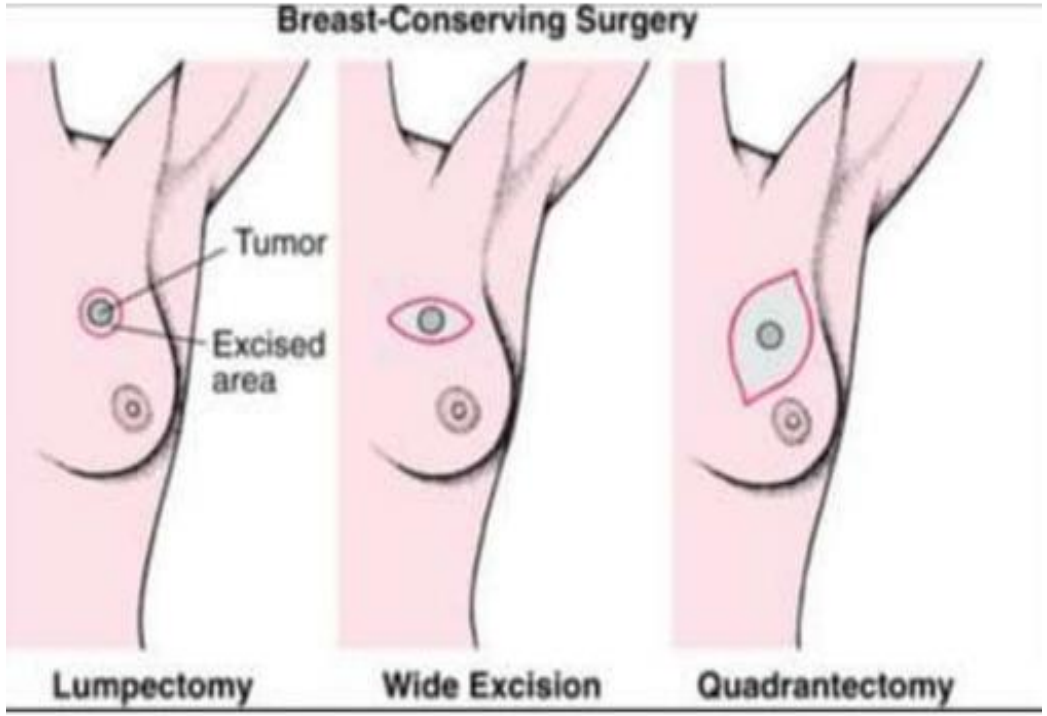
Primary tumours

- **Breast conserving surgery**

1. Wide local excision (WLE) ◦
2. Quadrantectomy

- **Mastectomy**

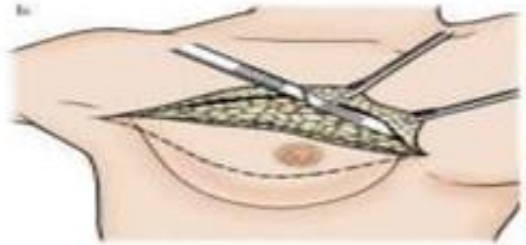
1. Radical
2. Extended radical
3. Modified radical
4. Simple
5. Skin sparing
6. Nipple sparing

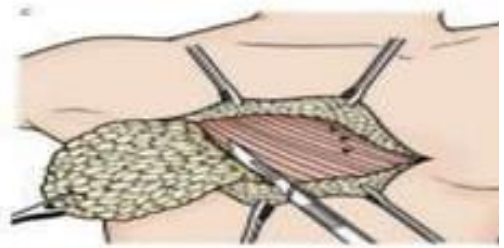


Simple (total) mastectomy

- Removes the entire breast without axillary nodes.
- Usually done for:

1. T2 tumours in patients with small breasts
2. Multicentric tumours
3. Small invasive breast cancer but with widespread DCIS

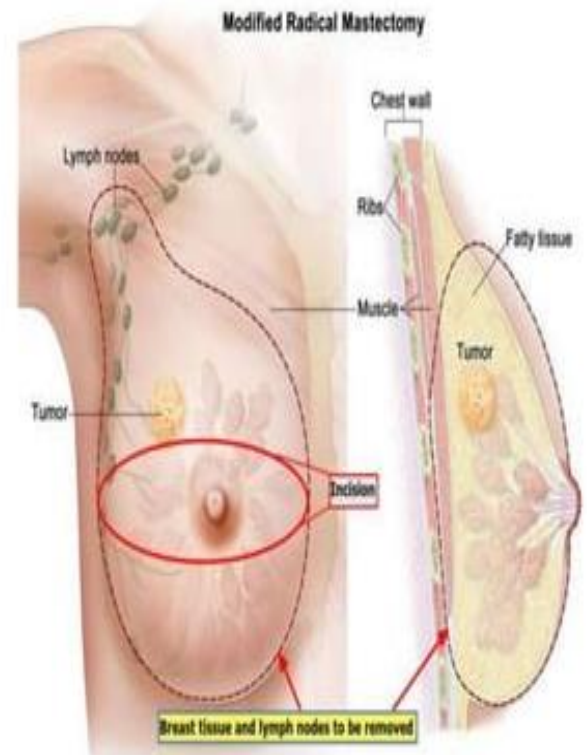




Modified radical mastectomy

- Removes the entire breast and axillary lymph nodes with preservation of pectoralis muscles.

1. Pateys
2. Scanlon
3. Auchincloss



- The main concern is local recurrence in the NAC and retroareolar area
  - Many advocate biopsy from under the NAC to ensure clear margins.
- NSM can be used for 'prophylaxis' and selected therapeutic cases.
- Most suited to patients with tumours <3 cm, located far from the nipple with favourable pathological features and no axillary disease.
- Women are counselled about nipple necrosis and potential for local recurrence.

Mastectomy

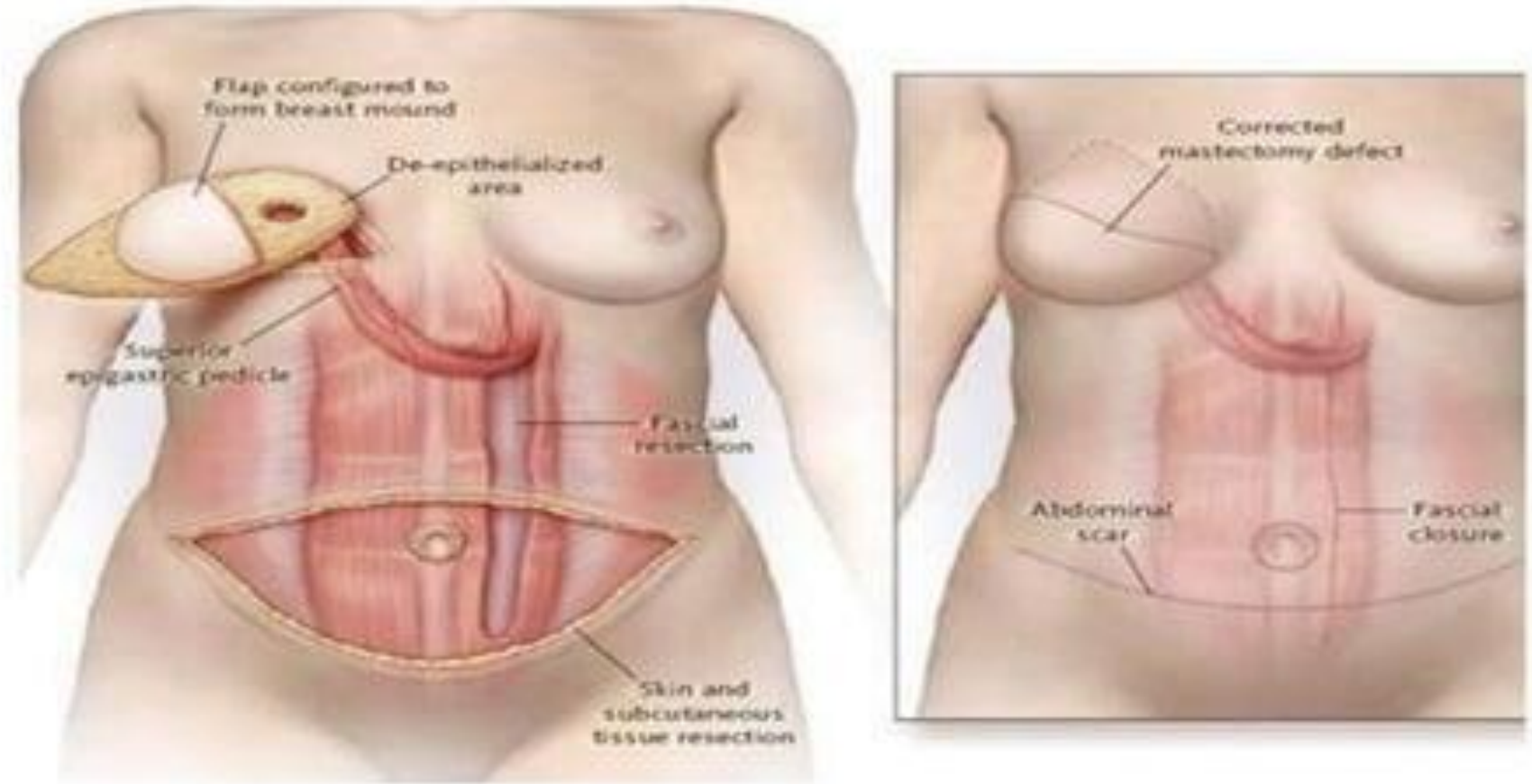
Skin-sparing Mastectomy

- Preserves most breast skin
- Removes nipple and areola
- Implant or tissue flap replaces breast tissue

Nipple-sparing Mastectomy

- Preserves most breast skin, nipple, areola
- Implant or tissue flap replaces breast tissue

De-epithelialised transverse rectus abdominis myocutaneous (TRAM) or deep inferior epigastric perforator (DIEP) flap



Staging the axilla

- Pre-operative axillary ultrasound with, if appropriate, FNAC or core biopsy.
- If metastatic disease is not confirmed pre-operatively, the axilla should be staged operatively by one of these methods:

1 Sentinel lymph node biopsy (SLNB) using a combined radioisotope and blue dye technique. – This is the preferred technique in early breast cancer.

2 Axillary node sampling. – Removes part of level 1, including at least four lymph nodes

Treatment of the axilla

- Indications for axillary clearance:

1 Positive pre-operative FNAC or ultrasound-guided biopsy.

2 Positive SLNB, either macrometastases or micrometastases.

Treatment involves either axillary clearance or radiotherapy.

Radiotherapy

Indicated in

- Breast : Primary invasive breast cancer treated with breast conserving surgery.
- Chest wall radiotherapy for high risk disease, such as:

1. Large tumour
2. High grade tumour
3. ≥4 positive axillary lymph nodes
4. Involved resection margins.

Chemotherapy

1. Lymph node positive breast cancer
2. Large primary tumour
3. High grade (grade 3) tumour
4. ER negative, HER2 positive.
5. Neoadjuvant treatment – to reduce the size of tumour prior to surgery.
6. Adjuvant therapy – to prolong disease-free survival in patients with early breast cancer, especially pre-menopausal women with ER negative tumours.
7. Treatment for recurrence

Hormonal therapy

- All patients with ER positive cancer potentially benefit from hormonal therapy:
- **Tamoxifen** : ER antagonist in breast tissue via its active metabolite, hydroxytamoxifen. Partial agonist in endometrial tissue. Linked to endometrial cancer in some women
- Aromatase inhibitors (**anastrozole**, exemestane, letrozole) : Prevent conversion of androgens to oestrogen in peripheral tissues .Considered in postmenopausal women with ER positive tumours.
- Progestogens
- Luteinising hormone releasing hormone (LHRH) analogues
- Oophorectomy by radiotherapy, laparoscopy or open surgery.

Biological therapy

- Trastuzumab (Herceptin) is a monoclonal antibody to HER2 receptor.
- Reduces relapse of HER2 positive breast cancer by 50% and mortality by 30%. Can cause cardiac toxicity.

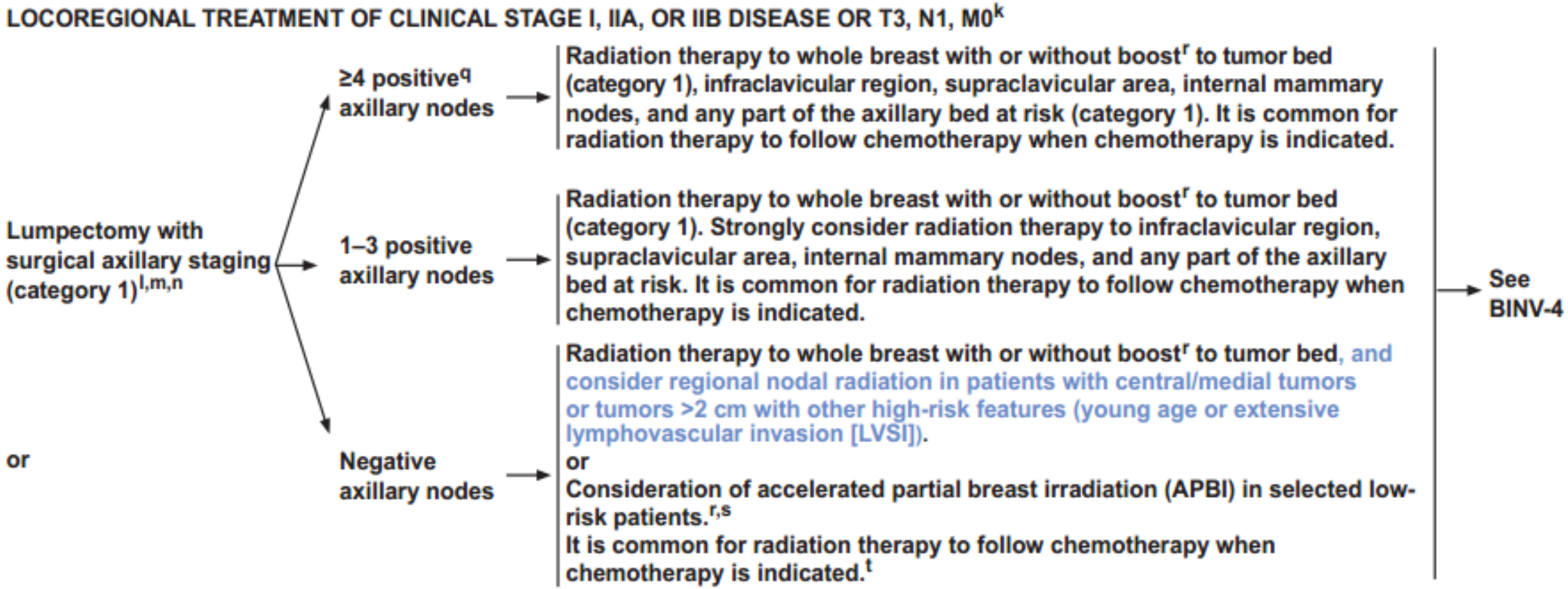
Prognostication

- Axillary spread
- Tumor size
- Tumor grade

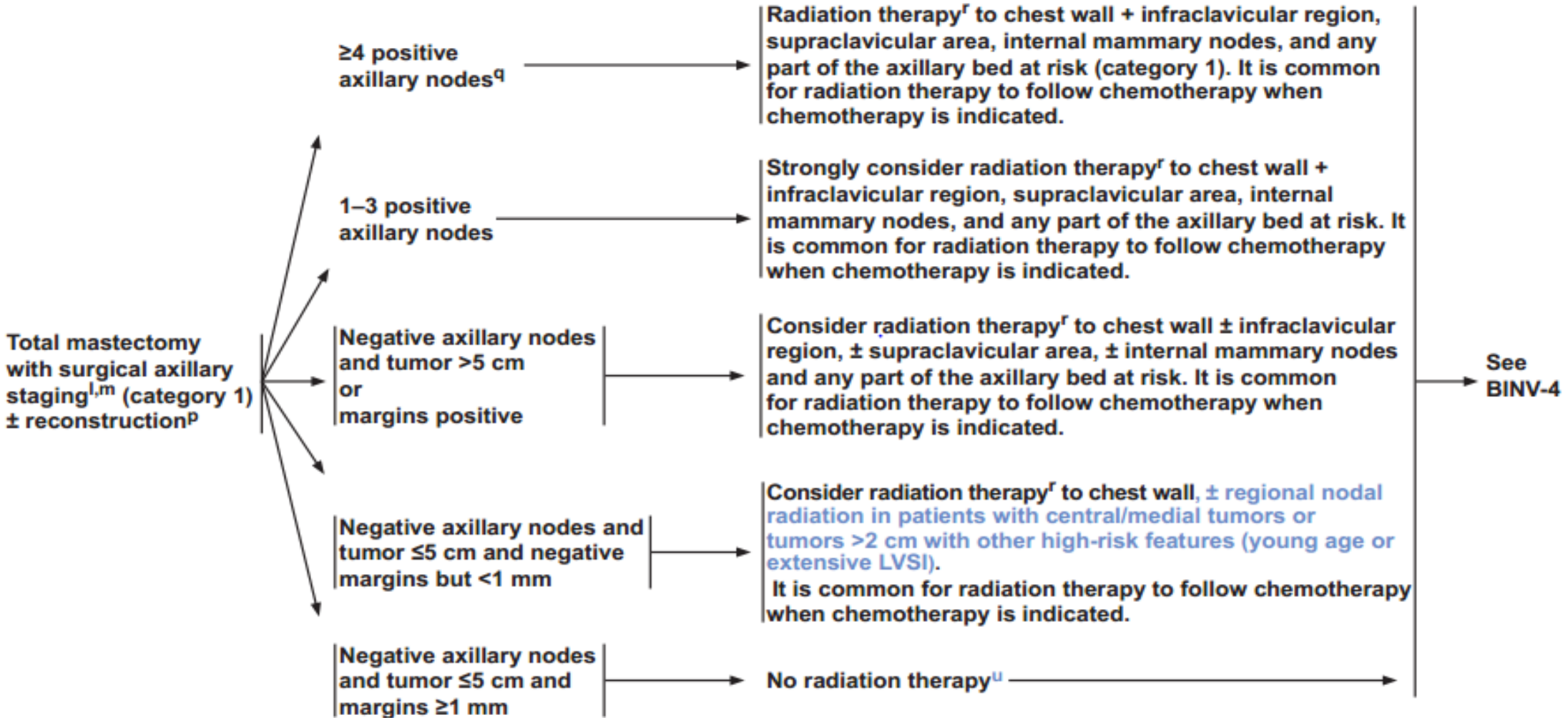
Nottingham prognostic Index

- Perineural and lymphovascular invasion
- Estrogen, Progesterone, HER 2 neu status

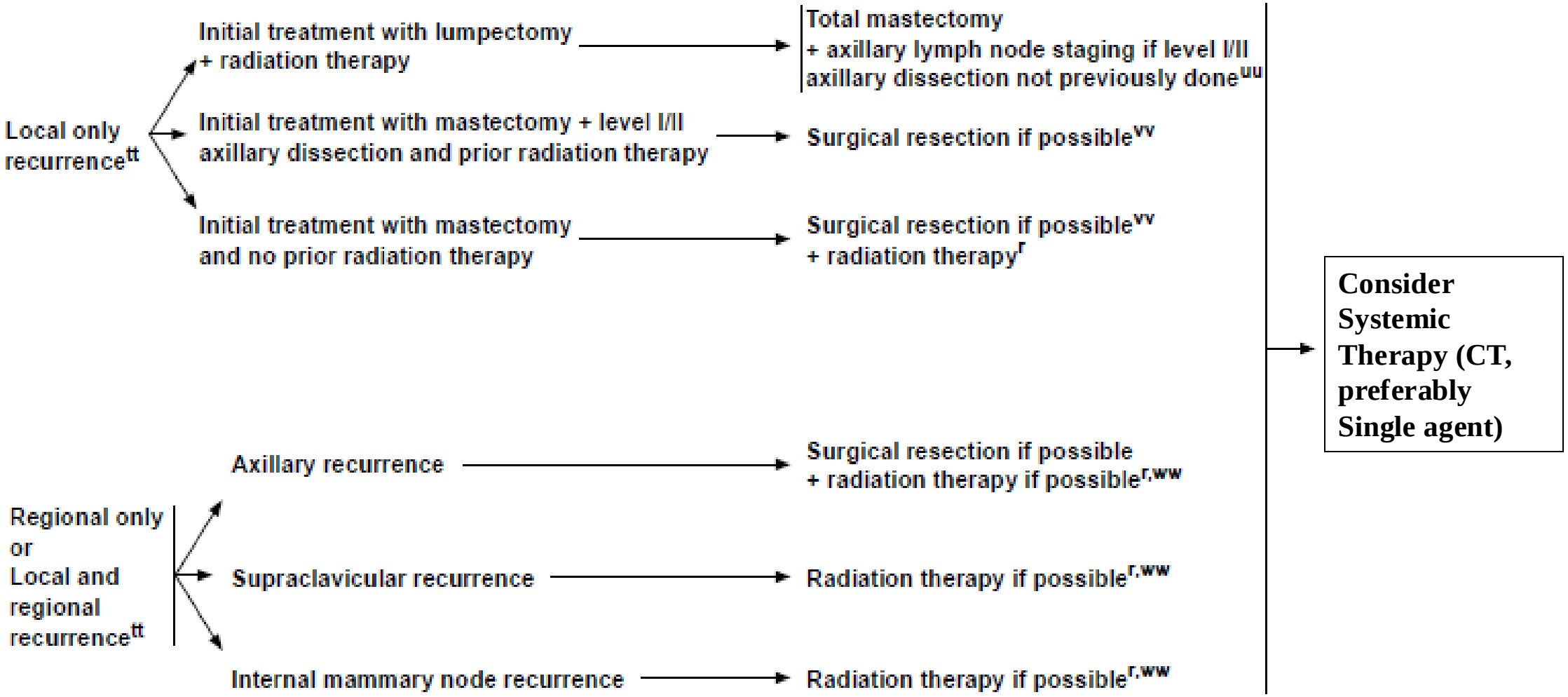
Breast Cancer, Version 1.2017



LOCOREGIONAL TREATMENT OF CLINICAL STAGE I, IIA, OR IIB DISEASE OR T3, N1, M0[k]



Recurrence of breast cancer:



Follow-Up of Patients Treated with BCS & RT:

	NCCN	ASCO
History & Physical examination	Year 1, every 3-4 mo Year 2, every 4 mo Year 3-5, every 6 mo Year 6+, annually	Year 1-3, every 3-6 mo Year 4-5, every 6-12 mo Year 6+, annually
Breast self-examination	No recommendation	Counseled to perform monthly breast self-examination
Mammography	6 mo after post-BCS RT Annually thereafter	6 mo after definitive RT Every 6-12 mo for surveillance of abnormalities Annually if stability of abnormalities is achieved
Pelvic examination	Annually, for women on tamoxifen Annual exam if uterus present	Regular gynecologic follow-up Patients on tamoxifen should be advised to report any vaginal bleeding
Routine blood tests	Not recommended	Not recommended
Imaging studies	Not recommended	Not recommended
Tumor marker testing	Not recommended	Not recommended

Challenges of breast cancer treatment in Jordan :

- ✓ low public awareness that breast cancer is treatable.
- ✓inadequate pathology services for diagnosis and staging.
- ✓Costly and poor treatment availability, especially for radiotherapy and drug treatments.
- ✓Most of the doctors who do breast surgeries are often general surgeons, and are not well trained in cancer diagnosis and treatment .
- ✓After surgery, patients fail to receive the critical drug therapies that can prevent metastatic disease from becoming established.
- ✓These factors combined are the reason that breast cancer morbidity and mortality rates are high.

References :

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- Bailey & Love's Short Practice of Surgery 27th edition
- Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice 20th edition
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God bless all Mothers
& Babies.
Thank you