

# **Breast 2**

*( Pathology )*

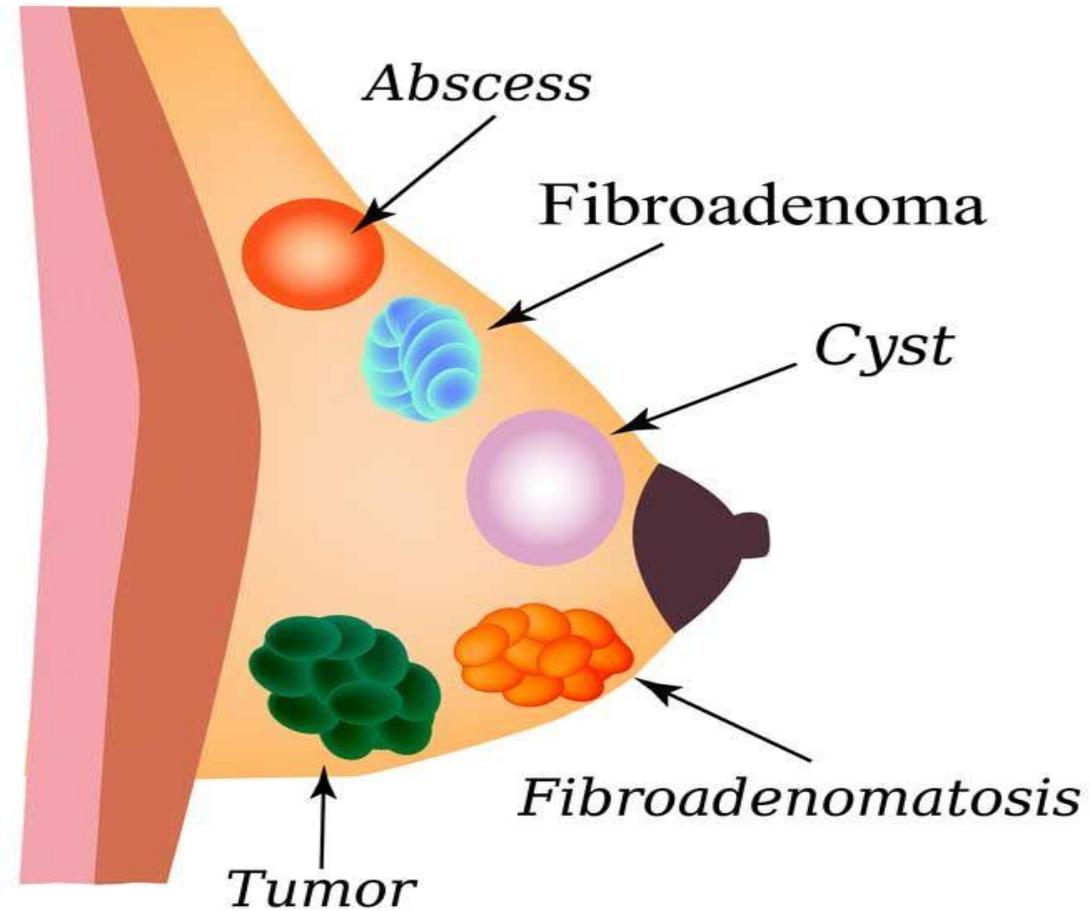
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# Breast Pathology

( Non-Neoplastic & Neoplastic Diseases )

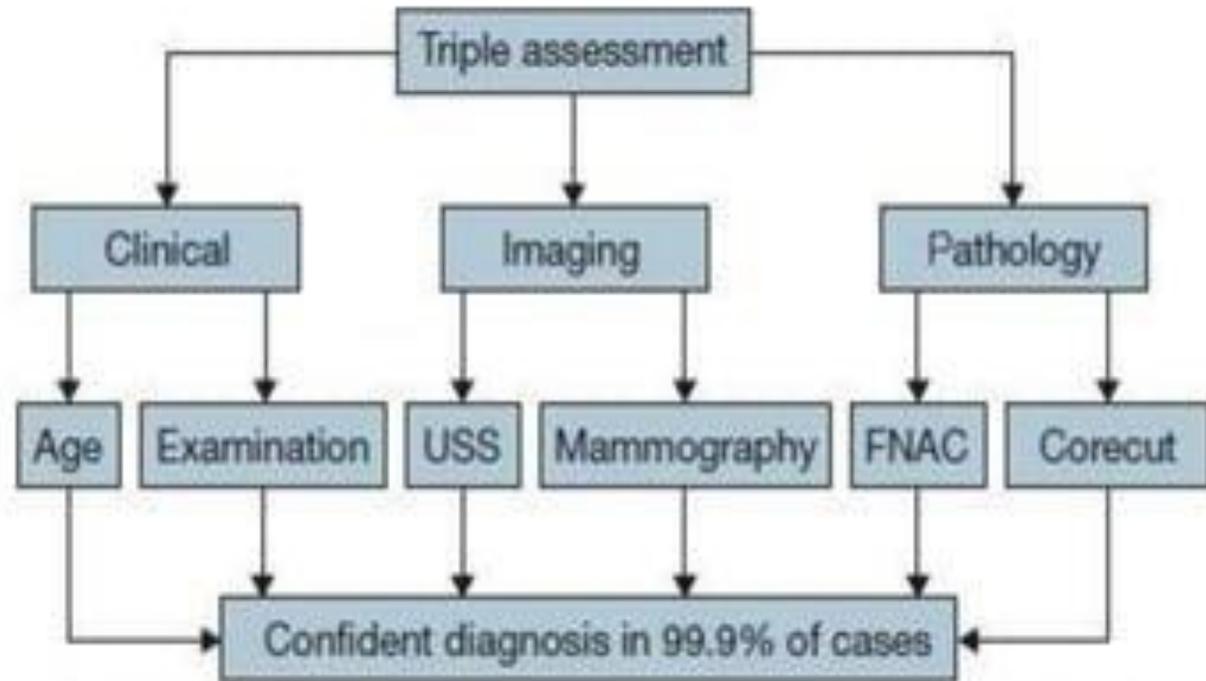


# Outlines:

- \* How to deal with Breast Symptoms .*
- \* Investigations In Breast Diseases.*
- \* Specific Benign and Malignant Breast Diseases.*

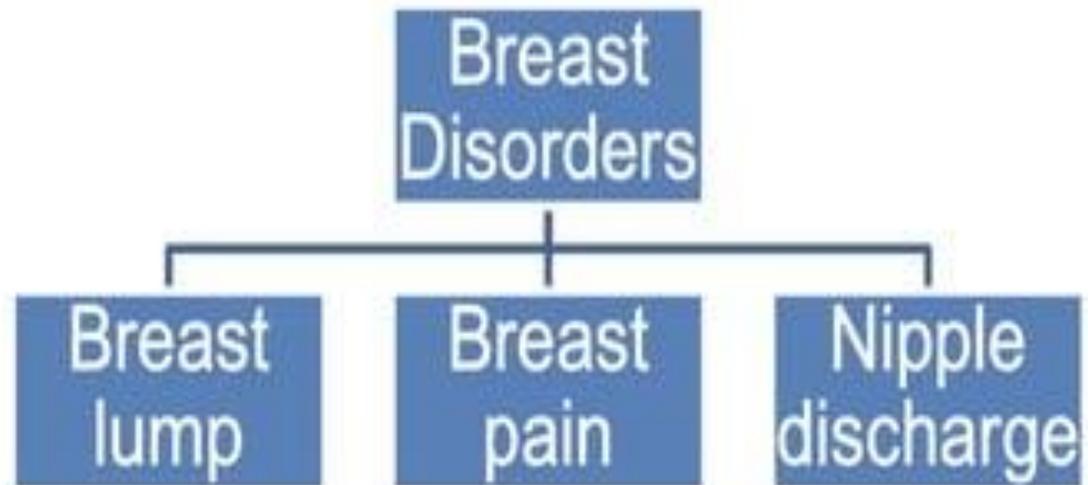
# Investigations of Breast Symptoms:

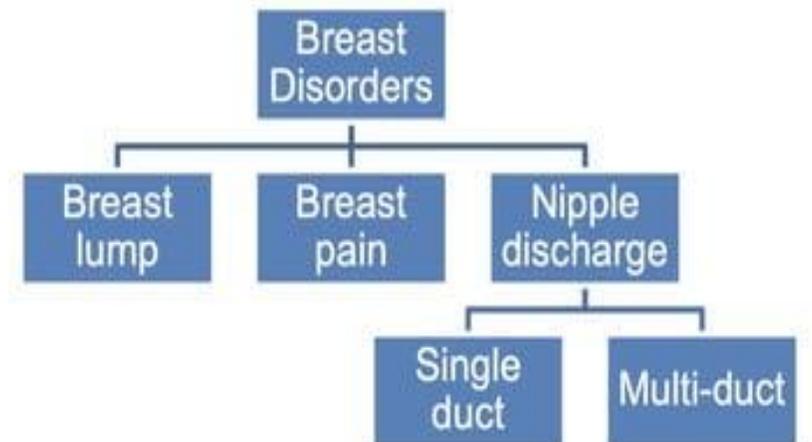
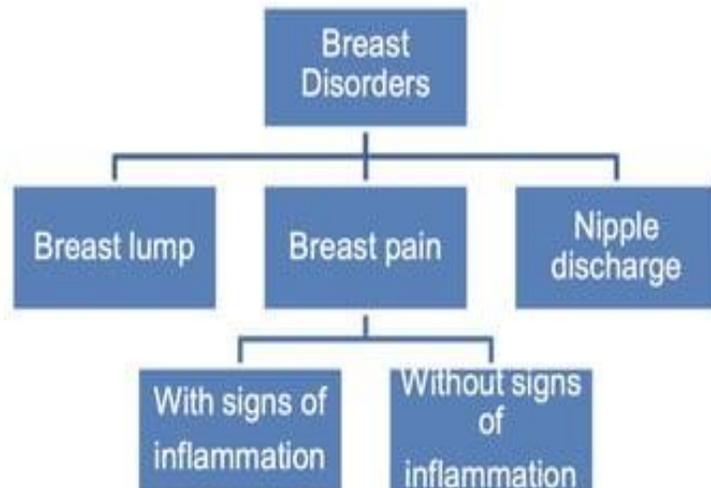
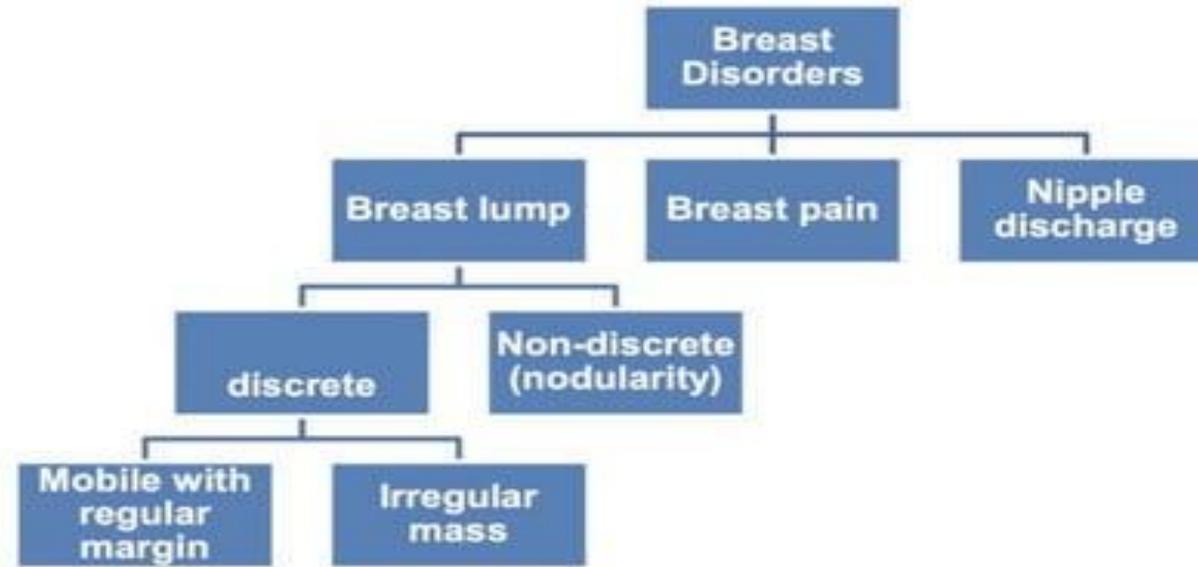
- **Clinical assesment**
- **Imaging**
  - Ultrasonography
  - Mammography
  - MRI
- **Tissue sampling:**
  - FNAC
  - Biopsy
    - Core
    - Incisional
    - Excisional



**Figure 53.8** Triple assessment of breast symptoms. FNAC, fine-needle aspiration cytology; USS, ultrasound scan.

# Clinical Assessment: ( History and Examination)

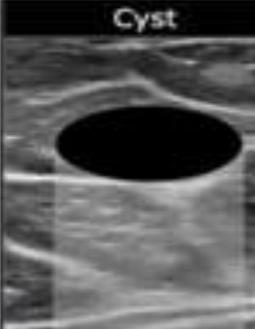
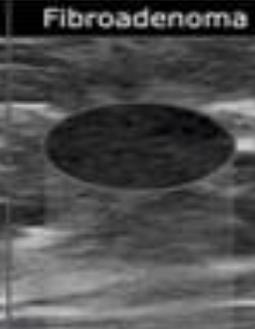
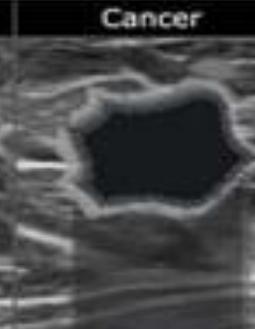
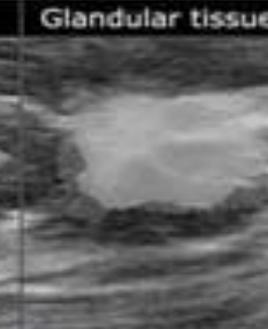




# Imaging:

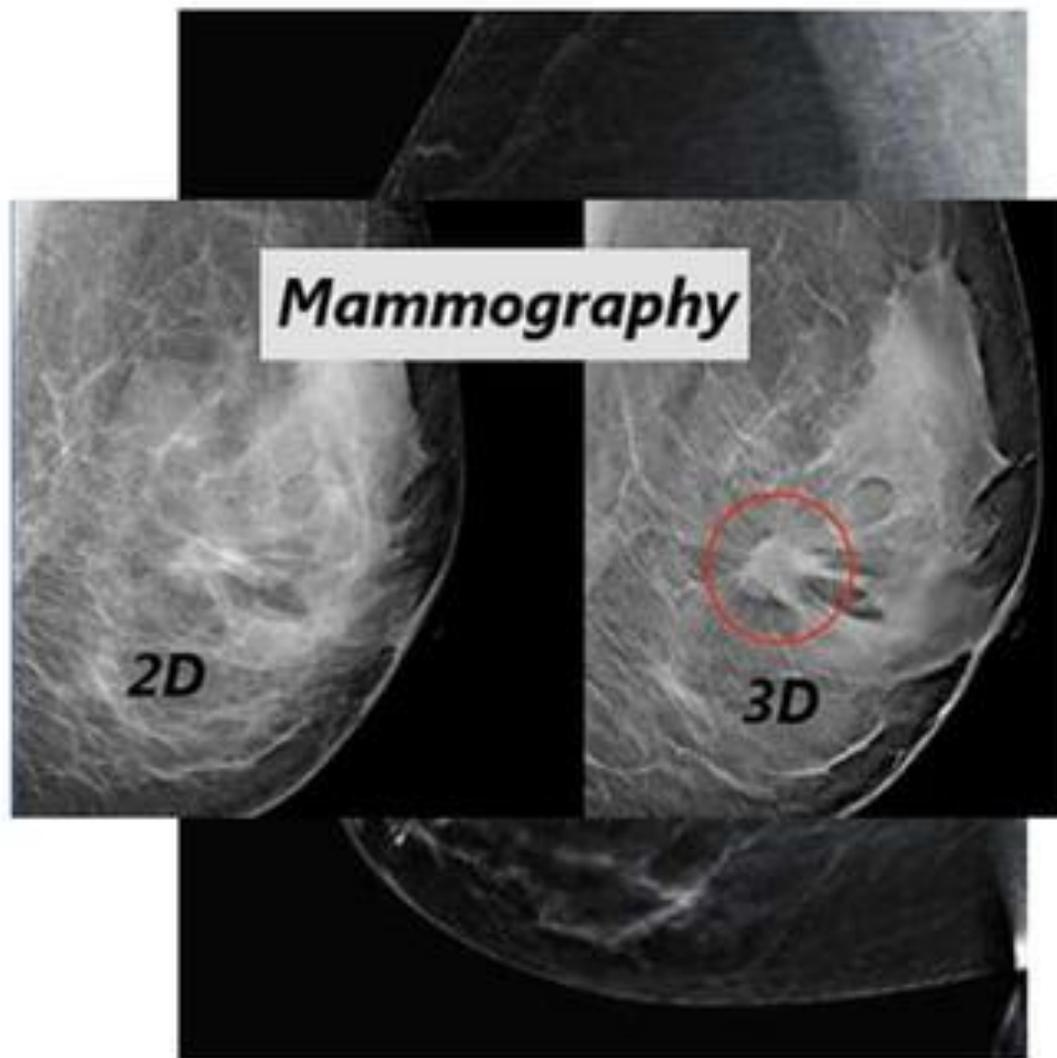
## Ultrasonography

- 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.



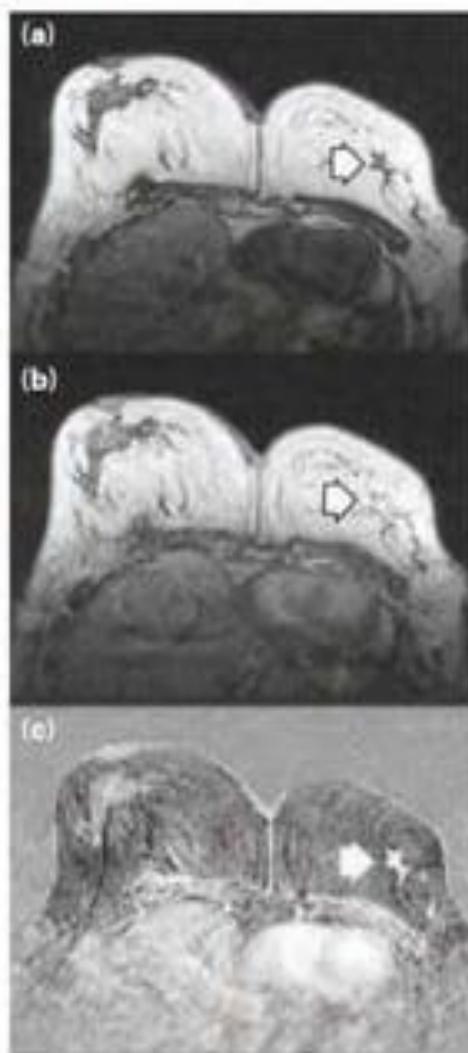
# BI-RADS classification

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



## MRI breast

- Distinguish – *scar / recurrence* – who have had previous breast conservation therapy for cancer (although it is less accurate within 9 months of radiotherapy because of abnormal enhancement);
- Assess – *multifocality and multicentricity* in lobular cancer; *extent* of high-grade DCIS.
- *Best* imaging modality for the breasts of women with *implants*.
- *Screening* tool in *high-risk* women (because of *family history*).



**Figure 53.5** Magnetic resonance imaging scan of the breasts showing carcinoma of the left breast (arrows). (a) Precontrast; (b) post-gadolinium contrast; (c) subtraction image.

# 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.

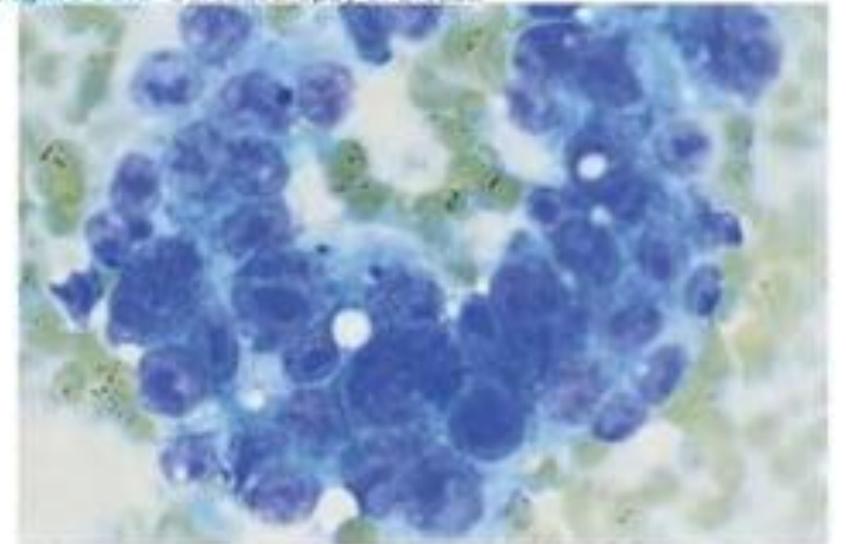


Figure 53.7 Fine-needle aspiration cytology showing grade III ductal carcinoma cells.

# Common Benign Breast Diseases:

## Classification of benign breast disorders

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### **Nonproliferative disorders of the breast**

- Cysts and apocrine metaplasia
- Duct ectasia
- Mild ductal epithelial hyperplasia
- Calcifications
- Fibroadenoma and related lesions

### **Proliferative breast disorders without atypia**

- Sclerosing adenosis
- Radial and complex sclerosing lesions
- Ductal epithelial hyperplasia
- Intraductal papillomas

### **Atypical proliferative lesions**

- Atypical lobular hyperplasia
- Atypical ductal hyperplasia

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Data from Godfrey SE: Is fibrocystic disease of the breast precancerous?  
*Arch Pathol Lab Med.* 1986 Nov;110(11):991.

# Benign Breast Disease :

- Most common breast problems.
- ~30% of women suffer at some point in their life.
- The most common symptoms are pain and lump.
- Aim :
  - Exclude Carcinoma.
  - Alleviate the symptoms.

# 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 3<sup>rd</sup> week.
  - Caused by stimulation of the fetal breasts by prolactin in response to drop in maternal estrogen.



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# 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.



# Injuries to breast

## 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



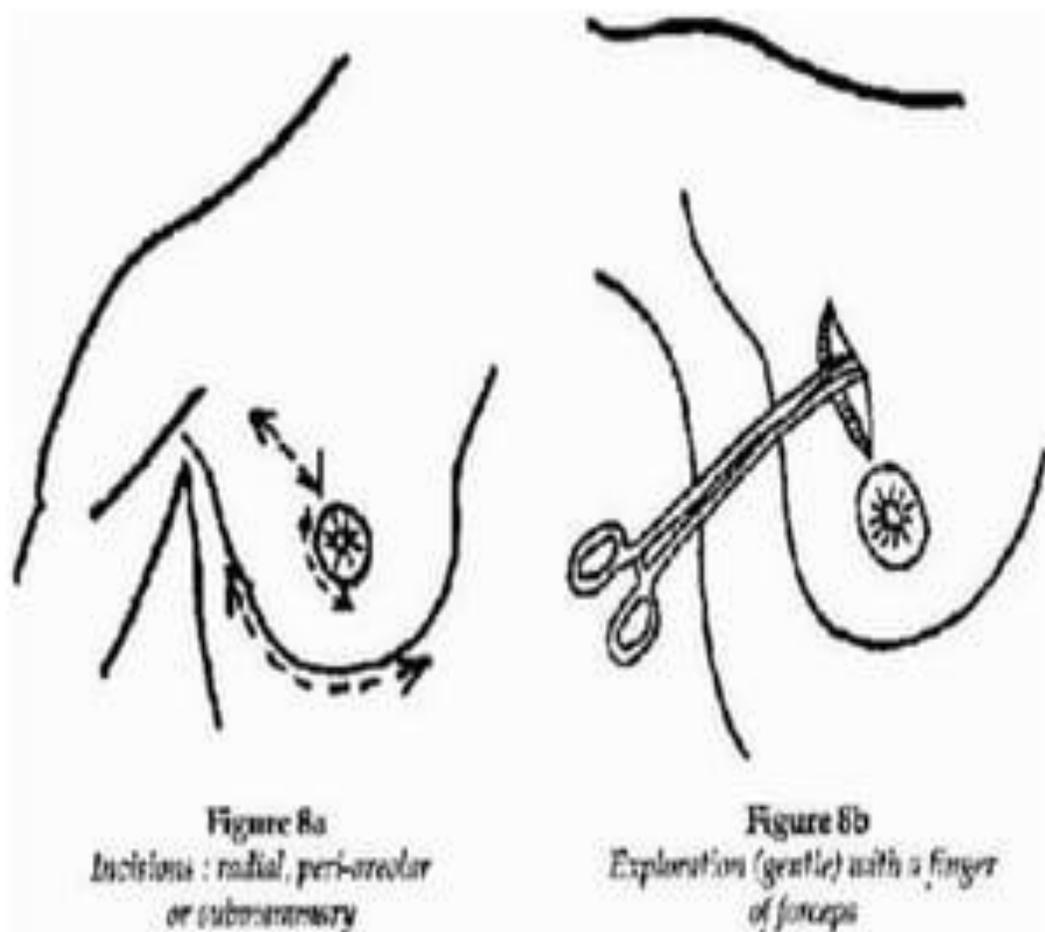
## Breast abscess

- 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).



## Chronic intramammary abscess

- May follow inadequate drainage or injudicious antibiotic therapy.
- Cultures and microbiological examinations are performed to identify acid-fast bacilli, anaerobic and aerobic bacteria, and fungi.
- Biopsy of the abscess cavity wall – considered at the time of incision and drainage:
  - To rule out inflammatory breast cancer in patients in whom previous treatments were ineffective.

# Mycotic infections of breast

- Rare and usually involve blastomycosis or sporotrichosis.
- Suckling infant inoculate.
- Mammary abscesses: close proximity to the nipple-areola complex.
- Pus mixed with blood may be expressed in lactiferous ducts.
- Systemic antifungal agents generally eliminates the necessity of surgical intervention.
- Occasionally – drainage, or even partial mastectomy to eradicate a persistent fungal infection.



Blastomycosis of breast

## 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.



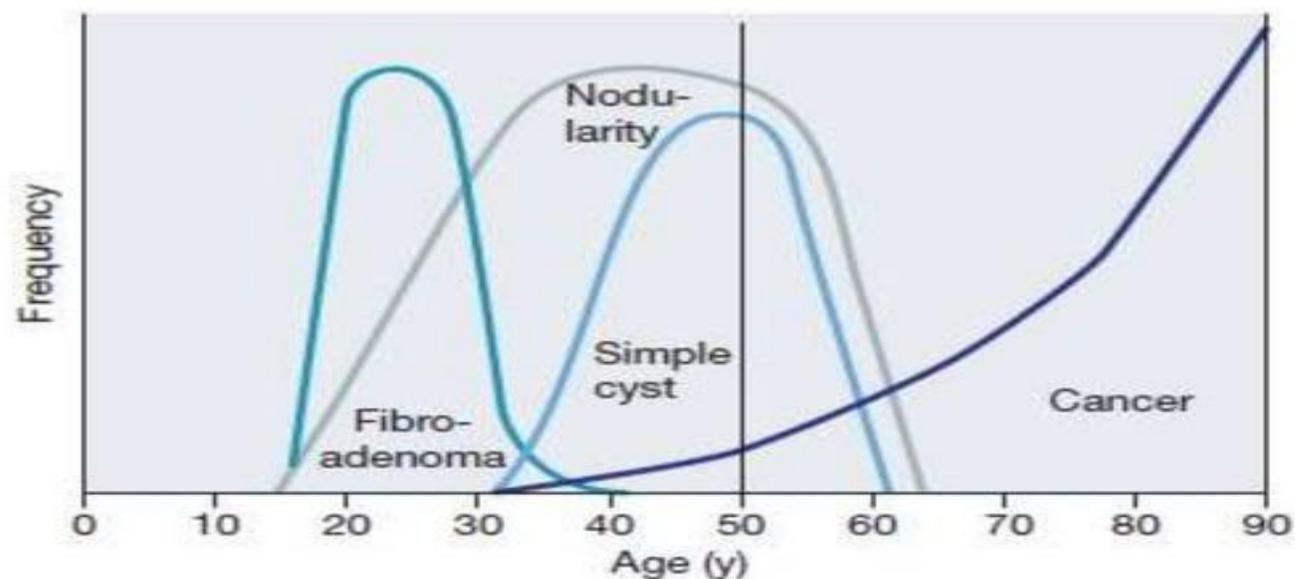
## Aberrations of Normal Development and Involution (ANDI)

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



## Typical USG picture: Fibroadenoma

- Hypoechoic
- Oval shaped
- Circumscribed margin
- Orientation parallel to the skin  
(Wider than taller).
- May have gross calcification



- 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.

## 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.

## Treatment

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

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

A Srivastava <sup>1</sup>, 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.

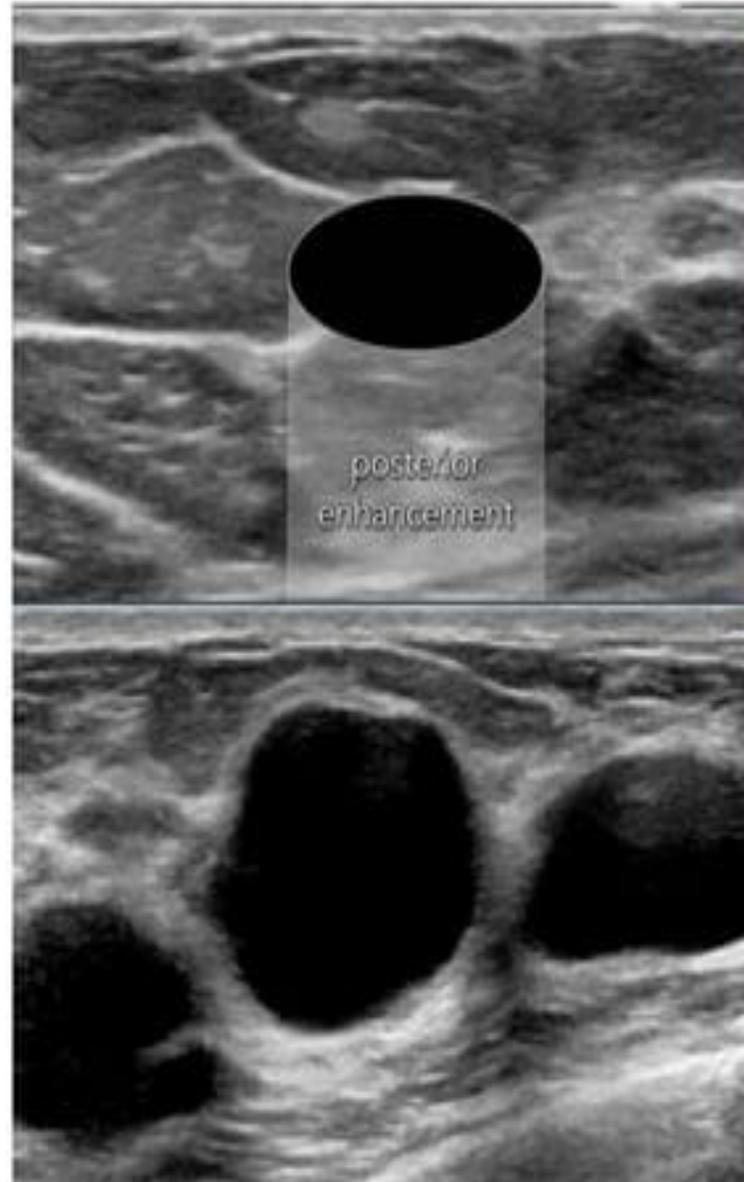


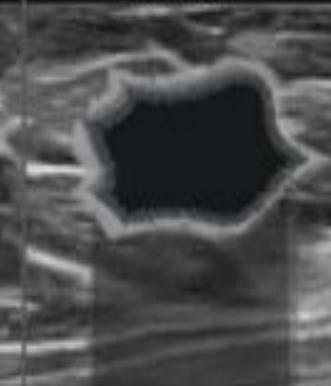
## Pathogenesis

- Involution of lobular epithelium dependent on specialized stroma around it.
- Integrated involution of breast stroma and epithelium is not always seen.
- If stroma involutes too quickly, alveoli remain and form microcysts.

## Typical USG picture: Cyst

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



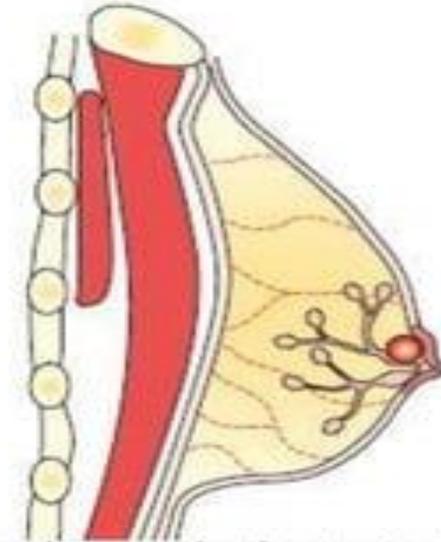
Cyst	Fibroadenoma	Cancer
		
Anechoic pattern	Hypoechoic	Hypoechoic
Oval or round shape	Most common: • oval or round  Less frequent: • lobulated	Most common: • irregular shape  Less frequent: • round or oval
Circumscribed margin	Circumscribed margin	Margin is not circumscribed: • Indistinct • angular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

# Also, Breast Cysts....

- 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.

## 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: 1<sup>st</sup> 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

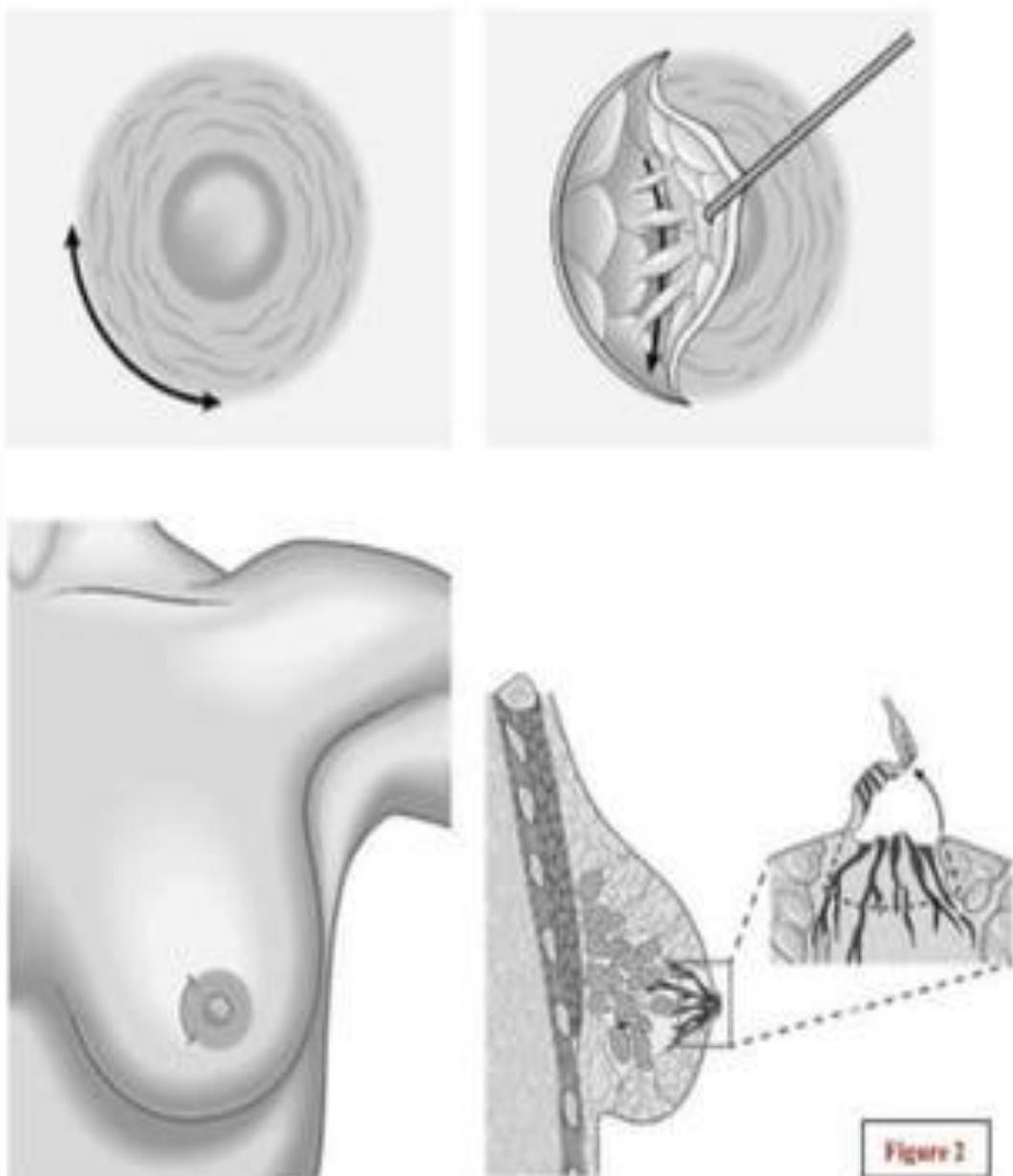


Figure 2

## 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.

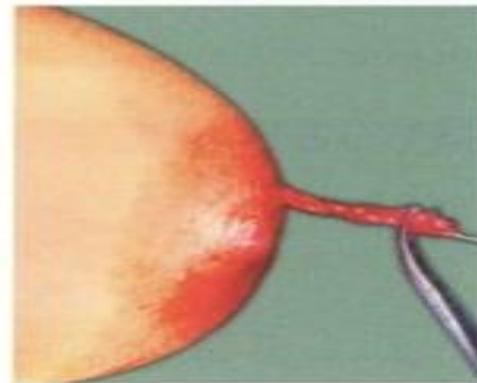


Fig. 21.33: Papilloma excision

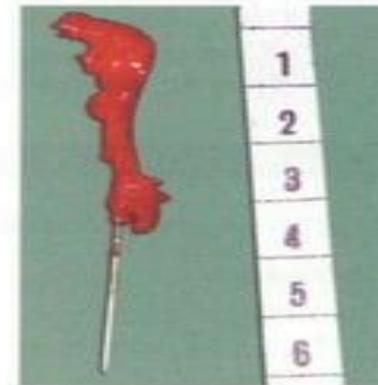


Fig. 21.34: Specimen of papilloma

# Papillomatosis

- Commonly occurs in younger women.
- Refers to epithelial hyperplasia and a/w with fibrocystic change.
- Not composed of true papillomas but rather consists of hyperplastic epithelium that may fill individual ducts similar to a true polyp but has no stalk of fibrovascular tissue.

## f. Sclerosing adenosis

- **Adenosis** : increased number of small terminal ductules or acini.
- Deposition of calcium seen on a mammogram in a pattern indistinguishable from the microcalcifications of intraductal carcinoma.
- Most common pathologic diagnosis in patients undergoing needle biopsy of microcalcifications.
- Frequently listed as one of the component lesions of fibrocystic disease; not believed to have significant malignant potential.

## g. Phyllodes' tumor

- Fibroepithelial tumors composed of epithelial and stromal component.
- > Predilection 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

## 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.

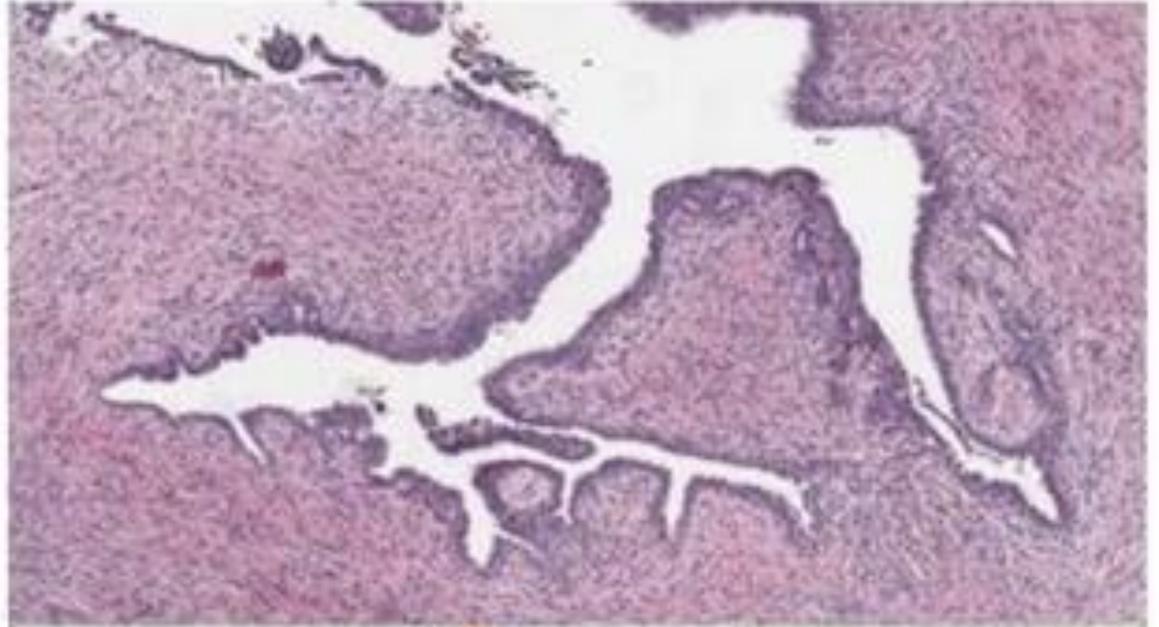


Figure 53.18 Phyllodes tumour (courtesy of Professor Mike Dixon).



# Diagnosis

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



## 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

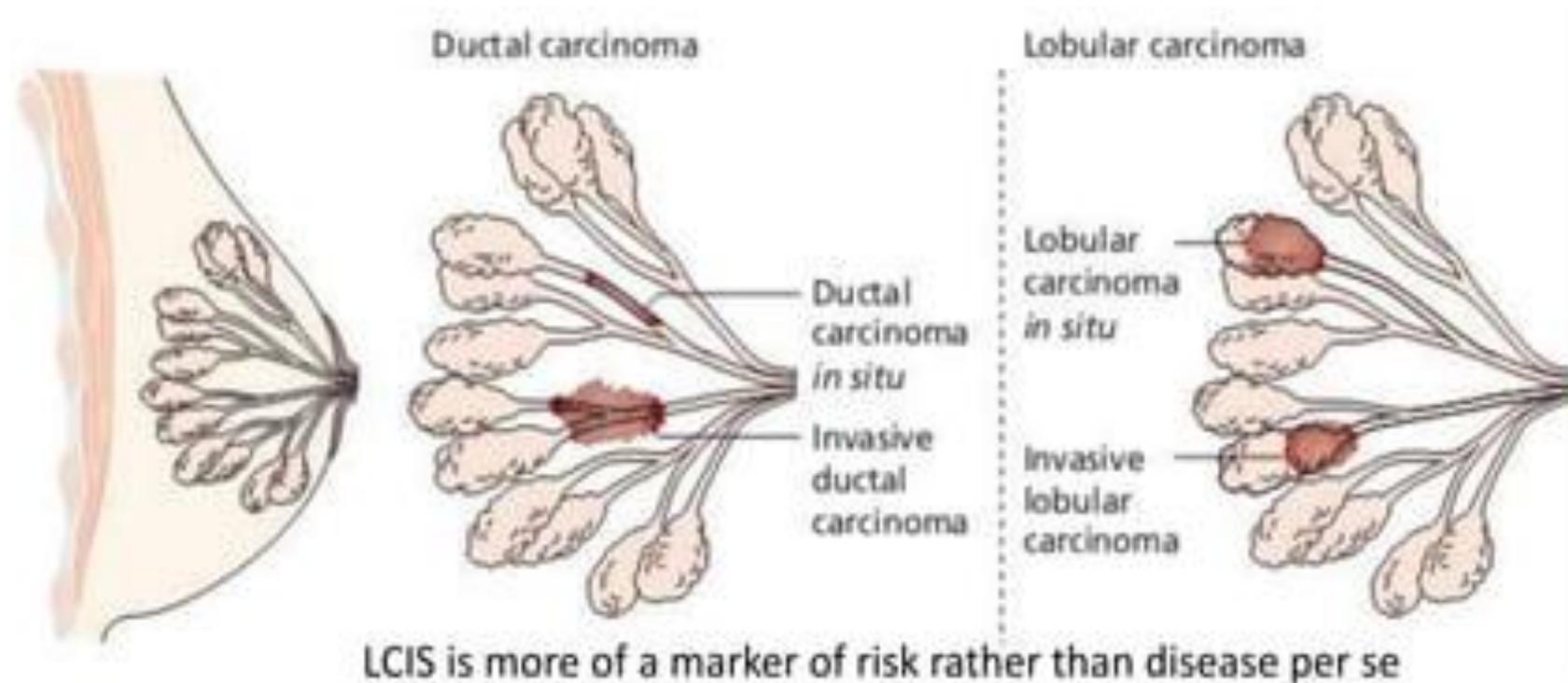


## Differentiation from carcinoma

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

# Breast Cancer :

- Preceded by carcinoma in situ = DCIS\*
- Breach of basement membrane = invasive disease
- Can be ductal or lobular carcinoma



# Risk factors

## **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.

## **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**

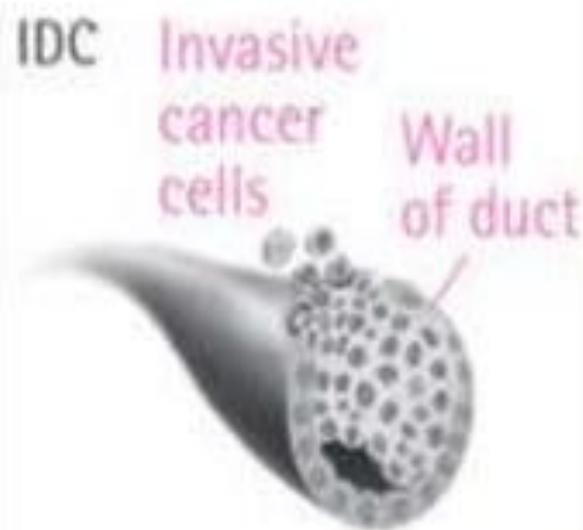
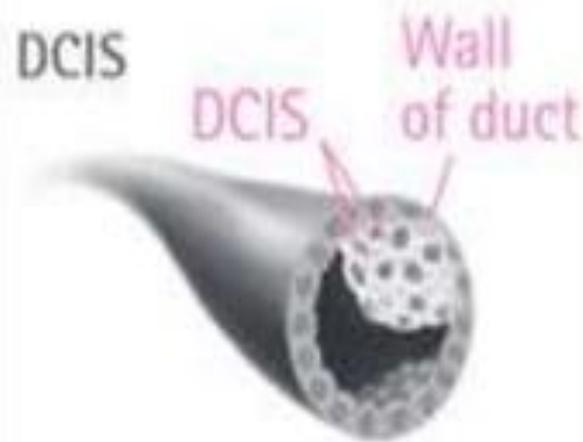
- Age – the older the woman, the higher the risk. 80% of new breast cancer cases occur in women >50 years.
- Increased body weight
- Lack of physical activity
- Excess alcohol consumption
- Caucasian race.

## *Gail model :*

- Age
- Race
- Age at first live birth or nulliparity
- Number of first-degree relatives with a history of BC
- Age at menarche
- # of previous breast biopsies
- Atypical hyperplasia

# Pathology

- In situ carcinoma – no breach of basement membrane (LCIS, DCIS)
- Ductal carcinoma – arises from the epithelium of the ducts
- Lobular carcinoma – epithelium of the lobules
- Inflammatory carcinoma – blockage of lymphatics with malignant cells causing swelling



# Spread

- Local
  - Skin
  - Chest wall
- Nodal
  - Axillary
    - Lateral, anterior, posterior, central, apical
  - Internal mammary
  - Subclavian
- Distant
  - Bones: vertebrae, ribs, femur, skull
  - Liver
  - Lung
  - Brain

# Presentation

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

# TNM stage

## **Primary tumour (T)**

- Tis: in situ carcinoma
- T1: tumour  $\leq 20$  mm
  - T1mic: microinvasion 1 mm but  $\leq 5$  mm
  - T1b: tumour  $> 5$  mm but  $\leq 10$  mm
  - T1c: tumour  $> 10$  mm but  $\leq 20$  mm
- T2: tumour  $> 20$  mm but  $\leq 50$  mm
- T3: tumour  $> 50$  mm
- T4: tumour of any size with direct extension to chest wall  $\pm$  skin
  - T4a: extension to chest wall, not including only pectoralis muscle adherence/invasion
  - T4b: ulceration  $\pm$  ipsilateral satellite nodules  $\pm$  oedema (including peau d'orange) of skin
  - T4c: both T4a and T4b
  - T4d: inflammatory carcinoma.

## **Regional lymph nodes (N)**

- N0: no regional lymph node metastases
- N1: mobile ipsilateral level I, II axillary lymph node(s)
- N2a: ipsilateral level I, II axillary lymph nodes fixed to one another or other structures
- N2b: clinically detected (including on imaging) ipsilateral internal mammary nodes without level I, II axillary lymph node metastases
- N3a: ipsilateral infraclavicular lymph node(s)
- N3b: ipsilateral internal mammary lymph node(s) and axillary lymph node(s)
- N3c: ipsilateral supraclavicular lymph node(s).

## Distant metastases (M)

- M0: no distant metastases
- cM0(i+): no clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumour cells in circulating blood, bone marrow or other nonregional nodal tissue that are no larger than 0.2 mm in a patient without symptoms or signs of metastases.
- M1: distant detectable metastases as determined by classic clinical and radiographic means  $\pm$  histologically proven larger than 0.2 mm

# Staging

- Manchester clinical staging
- **Stage I.** Tumour confined to breast. Any skin involvement covers an area less than the size of the tumour.
- **Stage II.** Tumour confined to breast. Palpable, mobile axillary nodes.
- **Stage III.** Tumour extends beyond the breast tissue because of skin fixation in an area greater than the size of the tumour or because of ulceration. Tumour fixity underlying fascia.
- **Stage IV.** Fixed axillary nodes, supraclavicular nodal involvement, satellite nodules or distant metastases.

# TNM

- Tumor

- T1 - <2cm
- T2 - 2-5 cm
- T3 - >5 cm
- T4 - attaches to chest wall or ulcerates the skin

- Nodes

- N1
- N2

- Metastasis

- M0 - no mets
- M1 - distant mets

Tumor size	Tumor size < 2 cm	Tumor size 2-5 cm	Tumor size > 5 cm	Tumor extends to skin or chest wall
<b>T</b>	 T1	 T2	 T3	 T4
<b>Lymph Nodes</b>	<b>N0</b> No lymph node metastasis	<b>N1</b> Metastasis to ipsilateral, movable, axillary LNs	<b>N2</b> Metastasis to ipsilateral fixed axillary, or IM LNs	<b>N3</b> Metastasis to infraclavicular/supraclavicular LN, or to axillary and IM LNs
<b>Metastasis</b>	<b>M0</b> No distant metastasis	<b>M1</b> Distant metastasis	LN= Lymph Nodes; IM= Internal Mammary	
<b>M</b>				

## 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%)

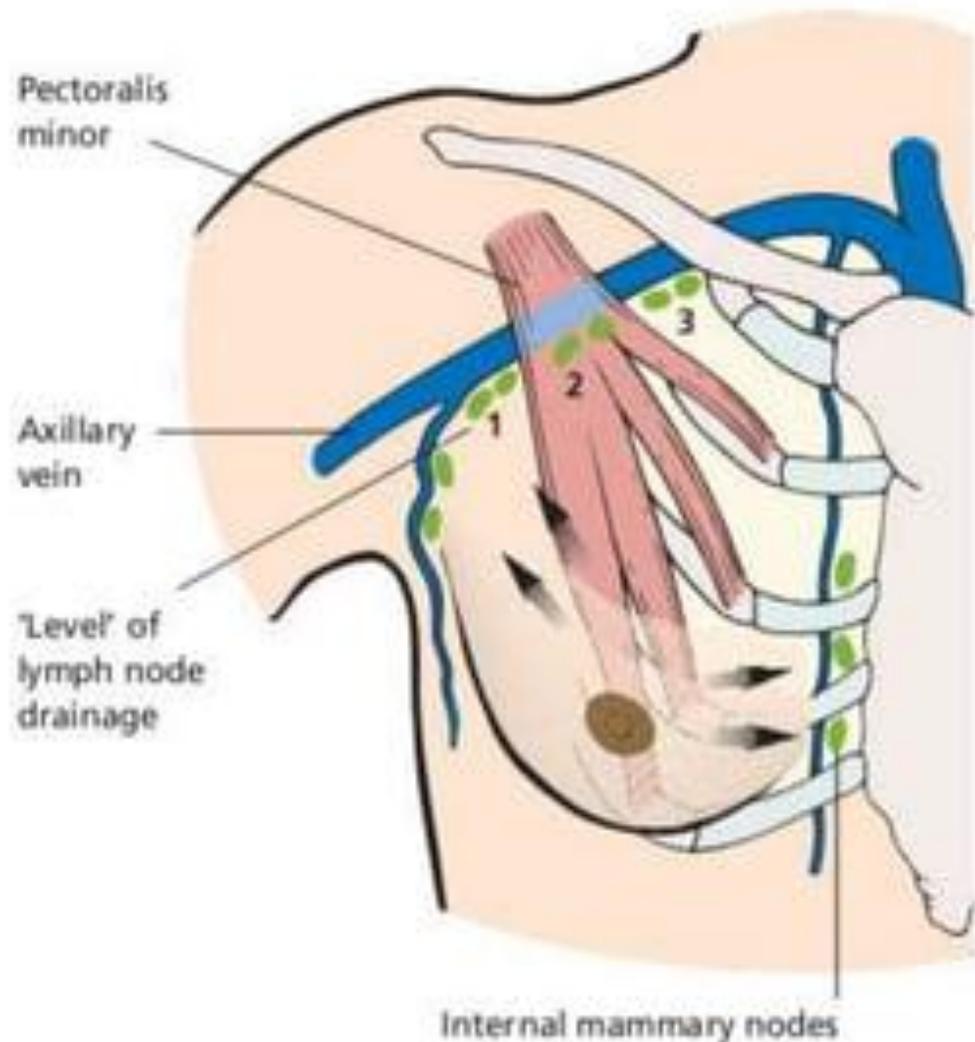
# Investigation

- 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 sandwich
  - CDF, CMF, second line: taxanes
- Radiotherapy
  - In combination with chemo – if  $<2\text{mm}$
  - Local vs axillary (extensive nodal disease)
- Endocrine therapy
- Targeted therapy



# Surgical treatment

## Primary tumours

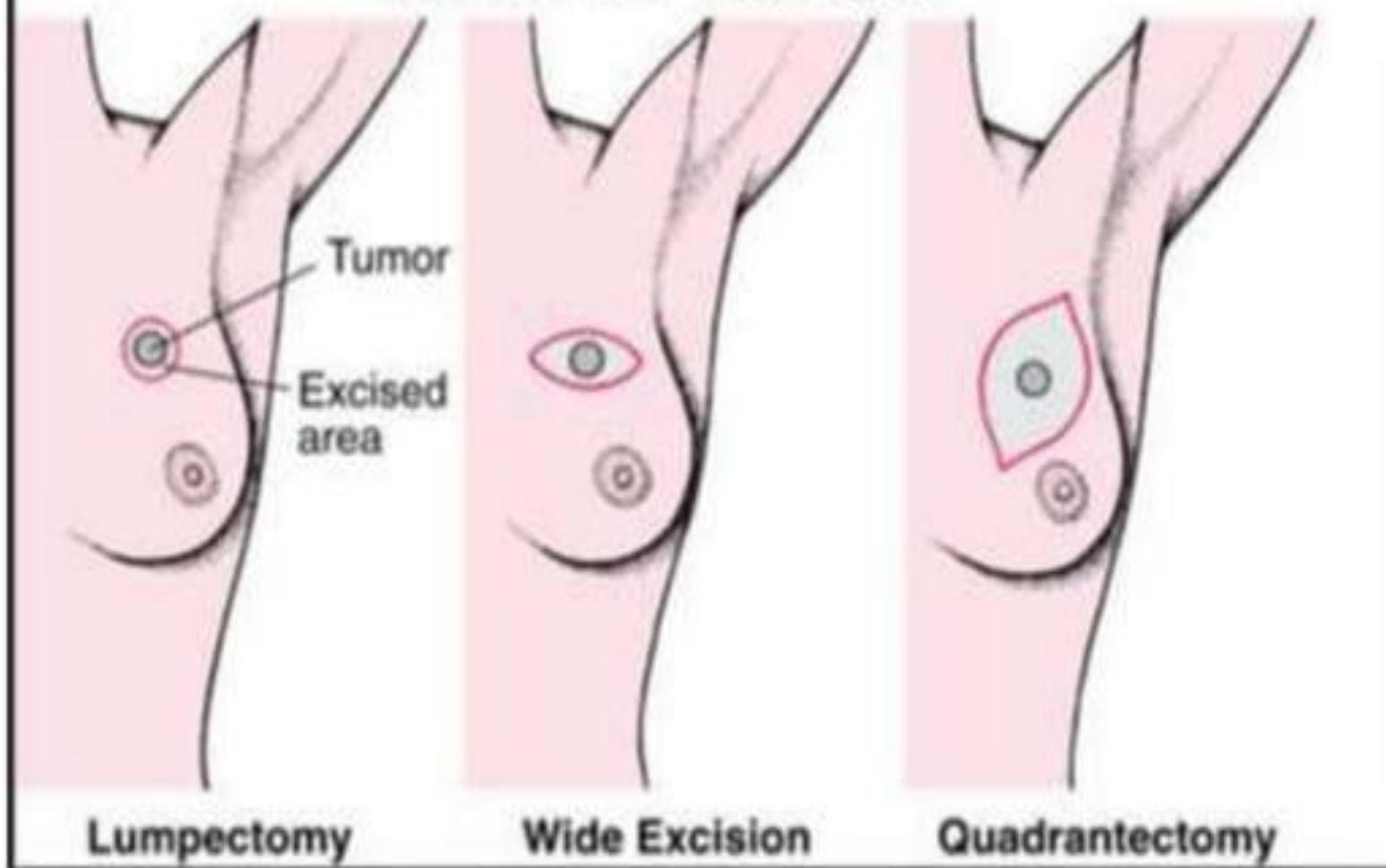
- **Breast conserving surgery**

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

- **Mastectomy**

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

### Breast-Conserving Surgery



## Wide local excision (WLE)

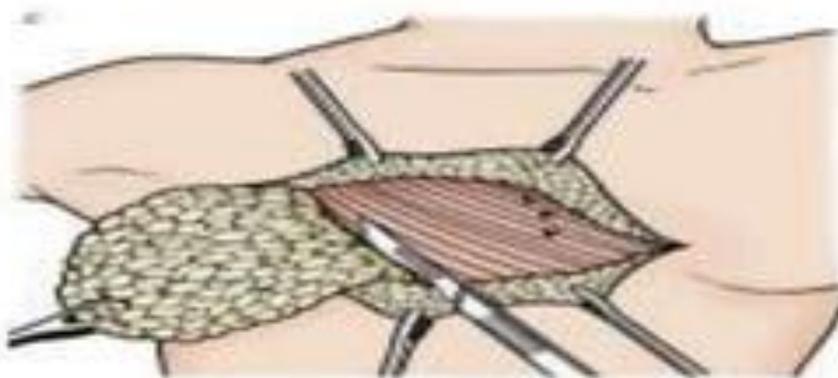
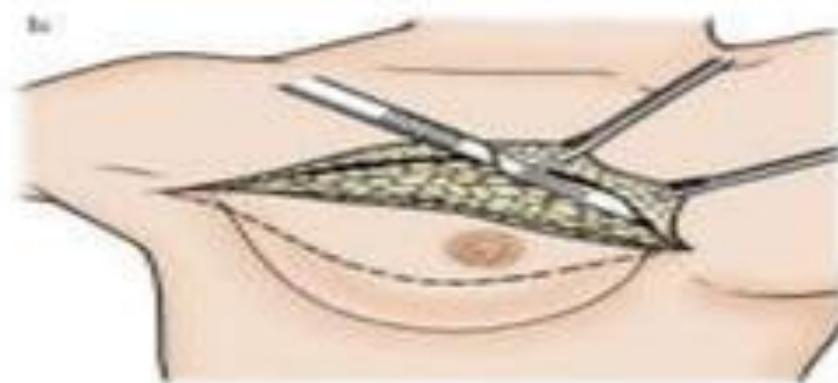
- Primarily indicated for selected patients with stage 1 or stage 2 disease.
- Not suitable for: Widespread disease , Patients with small breasts.
- Determining the extent of disease may require MRI in some cases, particularly for invasive lobular cancer or in dense breasts.

## Quadrantectomy

- Removes an entire quadrant of the breast.
- Primarily used for T2 tumours.
- Significant deformity may result if the defect is not reconstructed.

## Simple (total) mastectomy

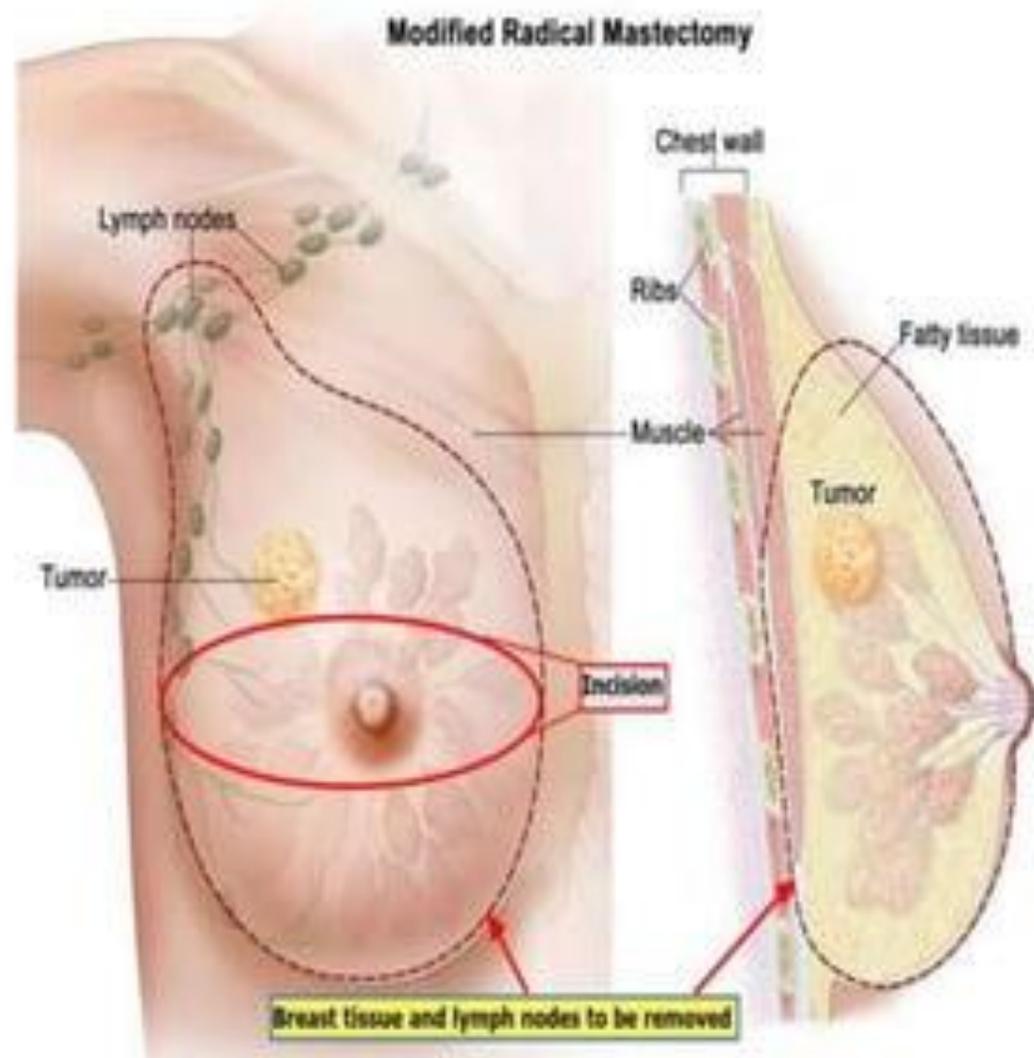
- Removes the entire breast without axillary nodes.
- Usually done for:
  1. T2 tumours in patients with small breasts
  2. Multicentric tumours
  3. Small invasive breast cancer but with widespread DCIS



## Modified radical mastectomy

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

- Pateys
- Scanlon
- Auchincloss



## Skin sparing (subcutaneous) mastectomy (SSM)

- Removes 90–95% of breast tissue but preserves most of the skin to facilitate reconstruction.
- Breast tissue is excised through a periareolar incision.
- Cancers involving skin are not suitable for SSM.
- In large breasts, a Wise pattern can help reduce the skin envelope. ◦ The de-epithelialised skin flap can be used to cover an implant.



# Nipple sparing mastectomy (NSM)

- Similar to SSM, but all the skin and NAC are preserved.

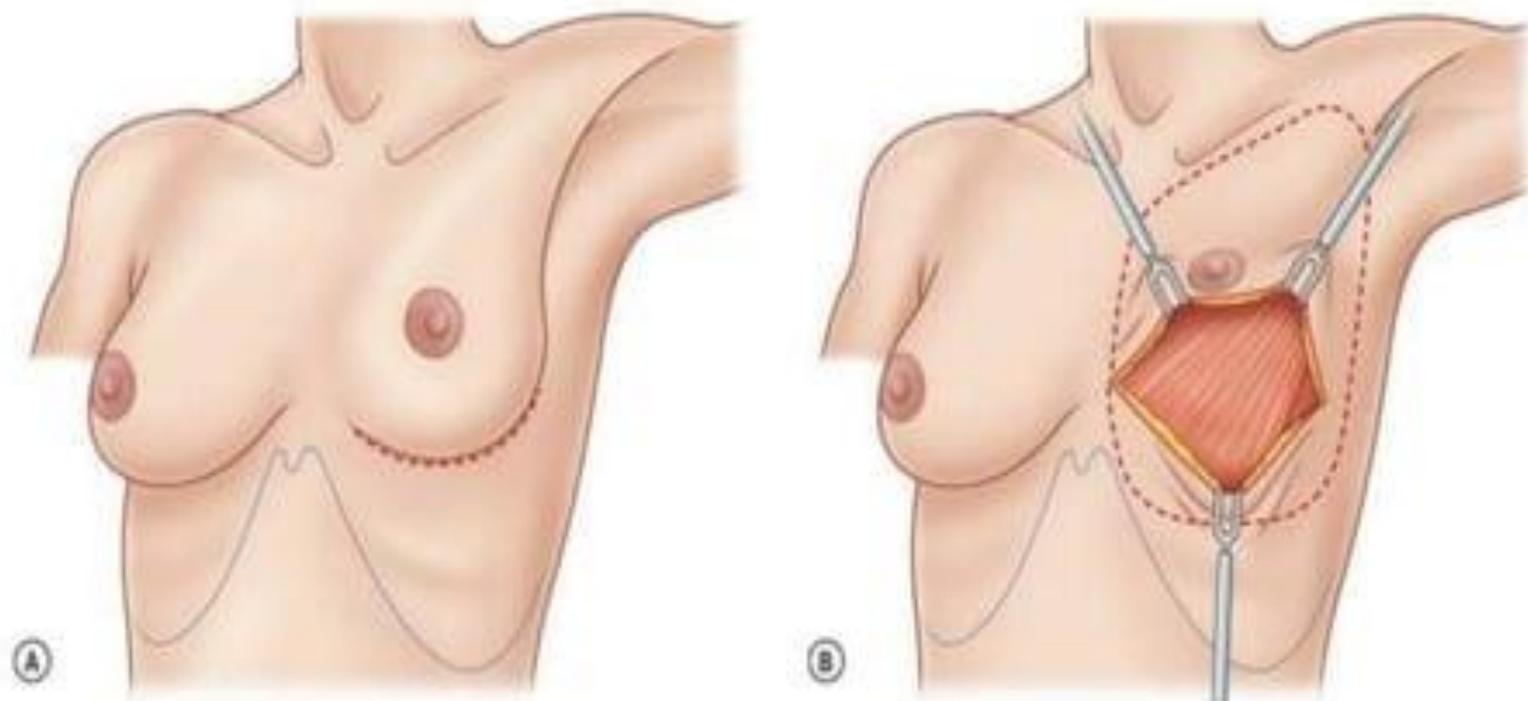
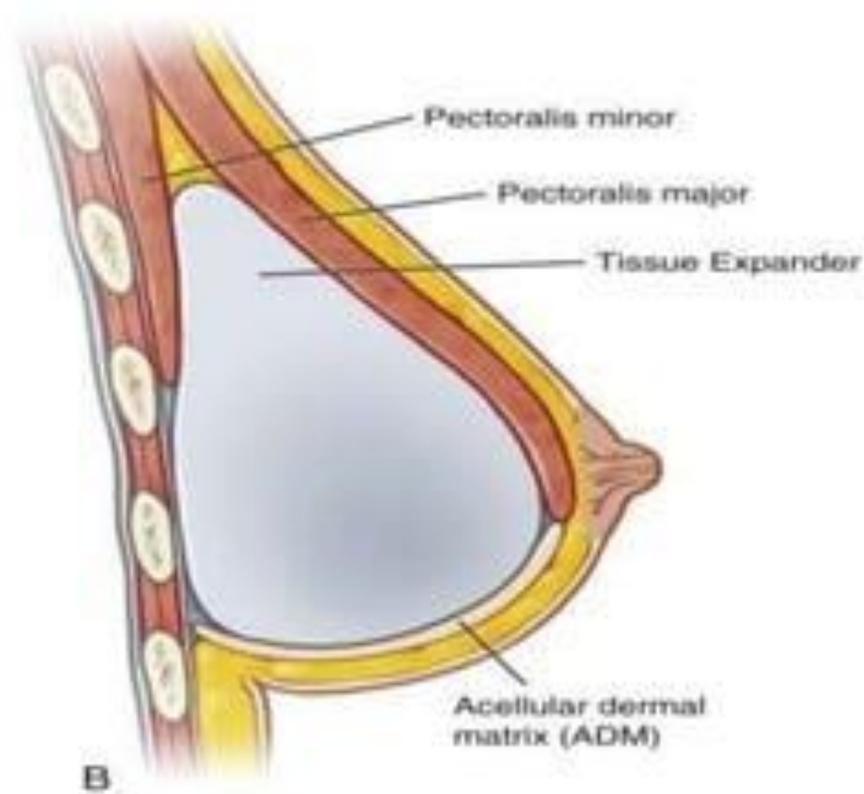


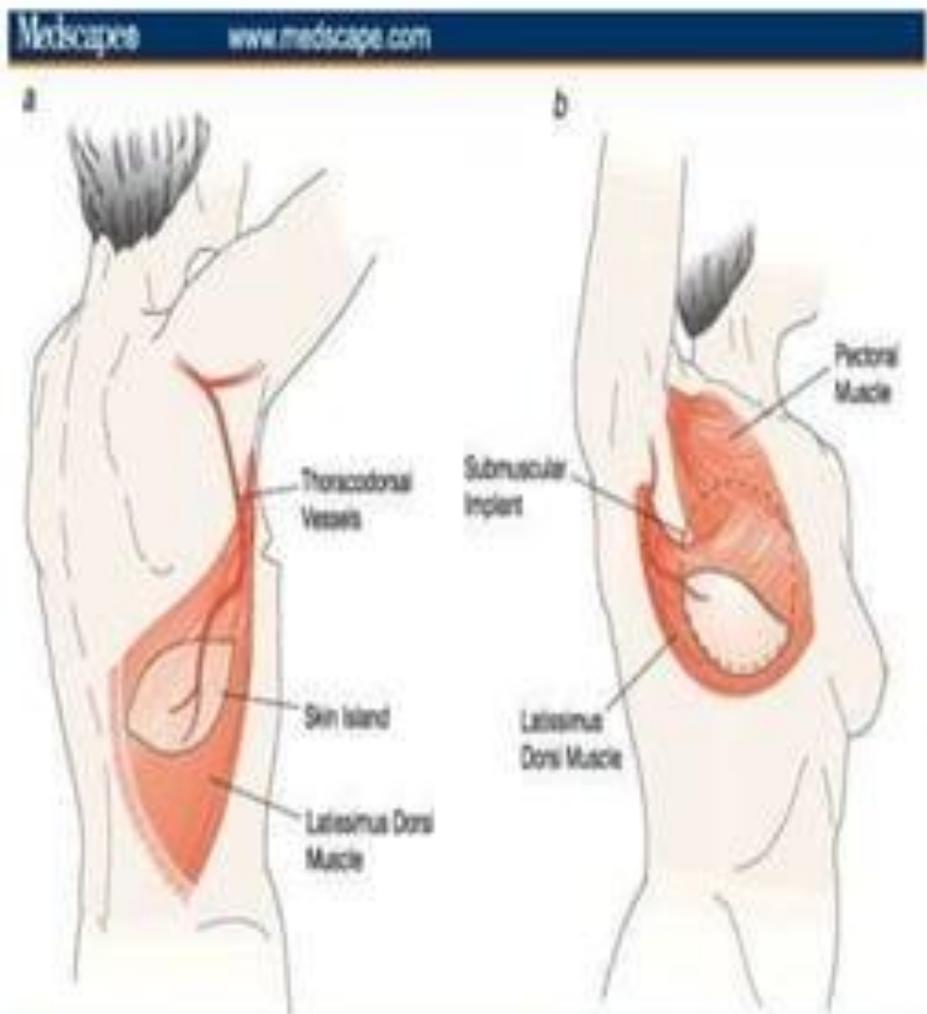
Fig. 10.31 Subcutaneous mastectomies incorporate a concentric incision, typically in the inframammary crease. This type of mastectomy is not considered oncologically sound given the propensity for thick mastectomy flaps.

- 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.

# Examples post nipple/skin sparing mastectomy

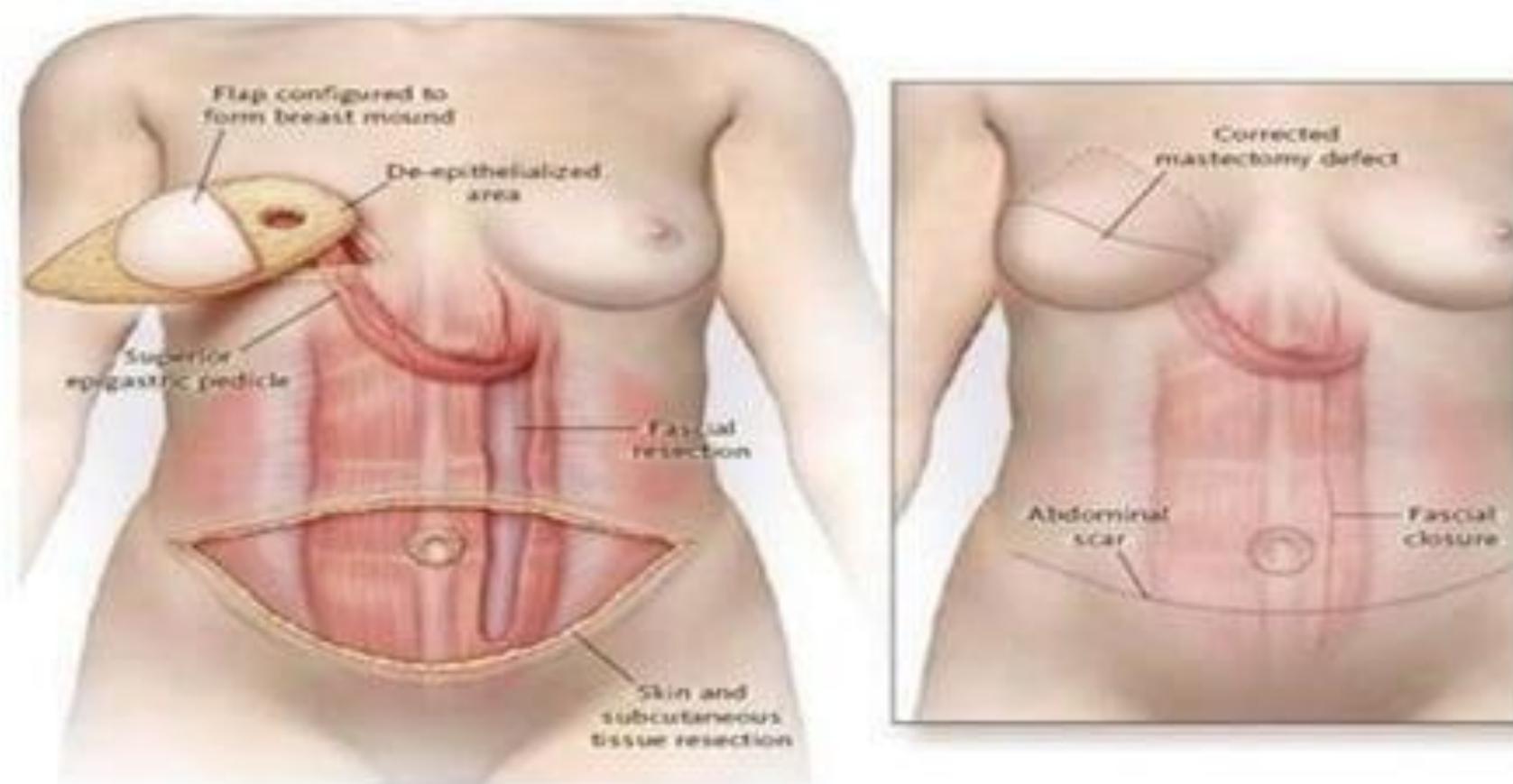


Subpectoral implant or expander, with inferior pole coverage using ADM placed between the inferior border of pectoralis major and IMF.



Implant or expander placed beneath a latissimus dorsi (LD) flap

## 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.  $\geq 4$  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
  - Perineural and lymphovascular invasion
  - Estrogen, Progesterone, HER 2 neu status
- 
- The diagram shows a vertical list of five prognostic factors. A bracket on the right side of the first three items (Axillary spread, Tumor size, and Tumor grade) points to a rectangular box containing the text "Nottingham prognostic Index".
- Nottingham prognostic Index

## Breast Cancer Follow-up

### Recommended for Routine Surveillance

History/physical examination	Every 3–6 mo for the first 3 y, every 6–12 mo for years 4 and 5, and annually thereafter
Mammography	Annually, beginning no earlier than 6 mo after radiation therapy
Breast self-examination	All women should be counseled to perform monthly.
Pelvic examination	Annually
Coordination of care	Continuity of care with breast cancer specialist and appropriate other health-care providers

### Not Recommended for Routine Surveillance

Routine blood tests	Complete blood cell count and liver function tests are not recommended
Imaging studies	Chest radiograph, bone scans, liver ultrasound, computed tomography scans, fluorodeoxyglucose–positron emission tomography scans, and breast magnetic resonance imaging are not recommended for routine breast cancer surveillance
Tumor markers	Cancer antigen 15-3, cancer antigen 27.29, and carcinoembryonic antigen are not recommended.

## *References :*

- Gray's Anatomy: The Anatomical Basis of Clinical Practice 41<sup>st</sup> edition
- Bailey & Love's Short Practice of Surgery 27<sup>th</sup> edition
- Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice 20th edition
- Schwartz's Principles of Surgery 11<sup>th</sup> edition.
- Manipal manual of surgery.

***God bless all Mothers  
& Babies.***

*Thank you*