





# Breast Diseases:

Tutorials are theoretical lectures, taken in small groups to ensure an interactive learning experience.

## Objectives

- The student is expected to describe and explain the pathogenesis and clinical features of the following conditions:
  - Lump and nodularity
  - Pain
  - Nipple discharges
  - Nipple changes
  - Breast enlargement
  - Breast skin changes and ulceration
- List the differential diagnosis of breast diseases

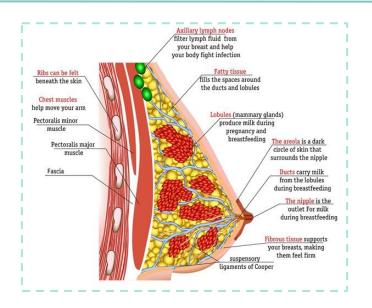
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- Main Text
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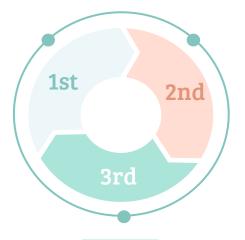
### **Overview**



### **Development of the breast:**

- Breast development and milk discharge might be seen in neonates (males & females) in first 2 weeks of life due to maternal hormones (oestrogens) crossing the placenta. This enlargement is normal and subsides within few weeks.
- The breast life cycle:

Development & Early reproductive life: Occurs at puberty and involves proliferation of ducts, ductules & fat associated with very rudimentary lobule formation, and regular changes in relation to the menstrual cycle.



#### Mature reproductive life: Occurs during pregnancy. The breast enlarges with proliferation of the ducts and lobules in preparation for the production of milk.

#### Involution:

By 30 years of age, involution is evident and continues to menopause and beyond. During involution, both the glandular and fibrous tissue atrophy and the shape of the breast changes.

### **Breast Symptoms:**

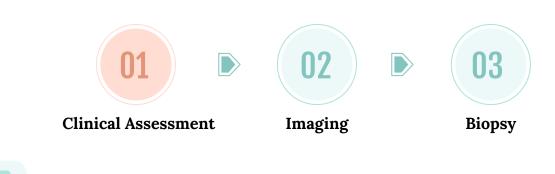
- More than a quarter of general surgical outpatient referrals are of females with breast symptoms.
- Less than 10% of general surgical operations are for breast disease.
- Breast symptoms include:
- Lump (most common symptom), Pain, breast tenderness, change in breast size or shape.



Nipple retraction, nipple discharge, scaling nipple or eczema, inflammation and ulceration of the overlying skin.

### **Breast Investigations (Triple Assessment):**

Triple assessment is the assessment of breast lump or other breast symptoms suspicious of carcinoma, where the diagnosis should be made by a combination of:



History:

Full & complete history should be taken, particular attention should be paid to:

- Breast development starting from childhood to present.
- Endocrine status of patient mainly menstruation and oral contraceptives.
- Premenopause vs perimenopause (menopausal transition) or postmenopause.
- For postmenopausal women: hormonal replacement therapy & date of menopause.
- Premenopause vs perimenopause (menopausal transition) or postmenopause.
- For postmenopausal women: hormonal replacement therapy & date of menopause.

- Size of lump in relation to menses.
- Pattern of pain in relation to menses.
  How regular the cycle is and quantity of blood.
- Changes in breast during previous pregnancies e.g. abscess, nipple discharge, retraction of nipple.
   Number of pregnancies.
- Breastfeeding.
   Abnormalities which took place during previous lactation period e.g. abscesses, nipple retraction, milk retention.

- Age at menarche.
- Age at 1st birth.
- Last menstrual period.
- Nipple discharge.
- Family history of breast diseases especially cancer & particularly in near relatives.



### Physical Exam:

- Disrobed from waist and above.
- Examine in sitting and supine position and 45° position.

• Always compare both breasts.

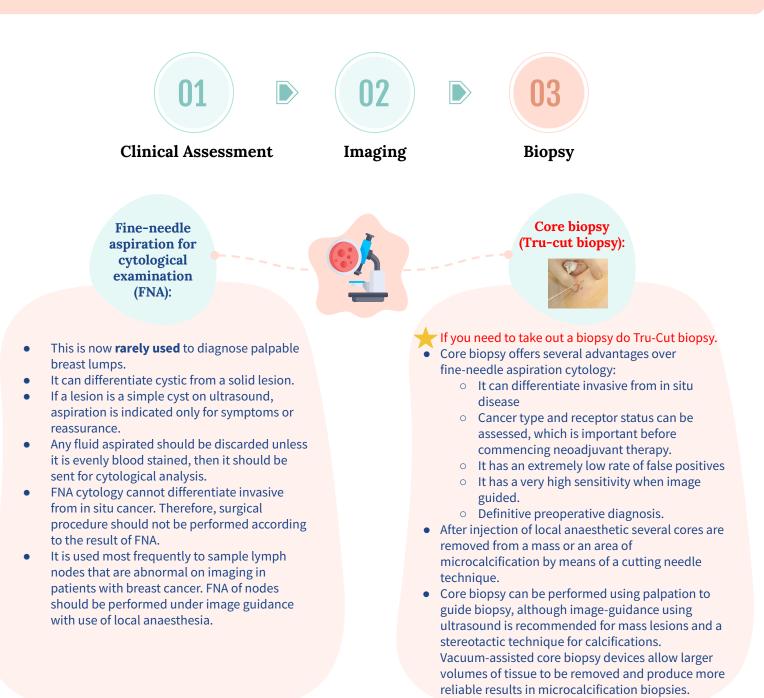
- Examine the normal side first.
- Before you comment on any changes on the appearance of nipples or chest, you must make sure that it's not congenital first.

- Inspection with arms by the side and above head: size, symmetry, skin changes, & nipple complex.
  - Examine axilla, arm, SCF.
  - If you find a mass in breast = Examine axillary lymph nodes and vice versa.
  - Examine abdomen.
  - Examine the back.

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Ultrasound	<ul> <li>Useful for diagnosis of breast cancer, especially in young patients under the age of 40 (mammogram is difficult to interpret in young patients due to the dense breast tissue).</li> <li>Distinguishes cyst from a solid lesion (cysts show up as transparent objects while benign lesions tend to have well-demarcated edges and cancers usually have an irregular indistinct outline).</li> <li>Localizes an impalpable breast pathology.</li> <li>Guides percutaneous biopsy.</li> <li>Guides percutaneous biopsy for any suspicious axillary lymph node.</li> <li>Not useful screening tool for breast cancer.</li> </ul>
Mammography	<ul> <li>Useful for diagnosis of breast cancer.</li> <li>Safe (dose of radiation is low) but uncomfortable.</li> <li>Sensitivity increases with age as the breast become less dense.</li> <li>Normal mammogram doesn't exclude the presence of carcinoma.</li> <li>Rarely of value in the age below 30, because the breasts are relatively radiodense.</li> </ul>
MRI	<ul> <li>Distinguishes scar from recurrent cancer after conservative breast surgery.</li> <li>Assesses multicentricity and multifocality in lobular breast cancer.</li> <li>Assesses the extent of ductal carcinoma in situ (DCIS).</li> <li>Identifies a breast cancer in women with a malignant axillary node where there's no obvious primary cancer seen on mammography and ultrasound.</li> <li>Assesses young women with dense breasts who have a lump or a cancer that is not well visualised on other imaging.</li> <li>Assesses response to chemotherapy or endocrine therapy.</li> <li>Best imaging for the women with breast implants, to detect leak or rupture.</li> <li>Best screening tool when combined with mammogram, more effective than using mammogram alone in high-risk women between the age of 35-50 years (family history of breast cancer or BRCA1 or BRCA2).</li> </ul>

### To communicate with a radiologist use: BI-RADS (Breast Imaging-Reporting and Data System):

Final Assessment Categories						
	Category	Management	Likelihood of cancer			
ο	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	n/a			
1	Negative	Routine screening	Essentially 0%			
2 Benign		Routine screening	Essentially 0%			
3	Probably Benign	Short interval-follow-up (6 month) or continued	>0 % but ≤ 2%			
4	Suspicious	Tissue diagnosis	<ul> <li>4a. low suspicion for malignancy (&gt;2% to ≤ 10%)</li> <li>4b. moderate suspicion for malignancy (&gt;10% to ≤ 50%)</li> <li>4c. high suspicion for malignancy (&gt;50% to &lt;95%)</li> </ul>			
5	Highly suggestive of malignancy	Tissue diagnosis	≥95%			
6	Known biopsy- proven	Surgical excision when clinical appropriate	n/a			



#### Sensitivity of investigations in the diagnosis of symptomatic breast disease:

Test:	Clinical examination	Mammography	Ultrasonography	Core biopsy	Fine-needle aspiration cytology
Sensitivity for cancers	86%	86%	90%	98%	95%

### **Breast pain**

#### Cyclical breast pain (related to the menstrual cycle):

- Cyclical breast pain is very common.
- Almost all females go through this pain with variable degrees of pain.
- Hormonal in origin.
- During the second half of the cycle.
- Unilateral mostly (but can be bilateral), Upper outer quadrant.
- The pain is usually reduced by the use of oral contraceptives
- On Examination:
  - No discrete lump.
  - There may be **tenderness**
  - **Diffuse** nodularity is common.

#### Non-cyclical breast pain:

- Less common.
- Pathological, especially if it's associated with a mass, nipple discharge or skin changes.
- Usually resolves spontaneously.
- In elderly female careful examination is essential to exclude cancer (especially when the pain is described as 'prickling'.) and to make sure it's not musculoskeletal pain.
- Requires investigations after clinical examination:
  - Breast ultrasound.
  - Mammogram if the patient's age is >40.
  - MRI if patients is <40 y/o with strong family history of breast cancer.

### Lumps and nodularity

	0			—0			
				Revision pane A simplified p	el 12.7 plan for the diagnosis	of the common b	reast lumps
Туре	of Lump:				rface and shape and th and indistinct Rubbery V Nodularity	Smooth an   Hard	Rubbery Fibroadenoma
			<b>a b</b>				

	Age (years)	Pain	Surface	Consistency	Axilla
Solitary Cyst	40-55	Occasional	Smooth	Soft to hard	Normal
Nodularity	<b>20-55</b> (the years of ovarian activity)	Often	Indistinct	Mixed	Normal
Fibroadenoma	15-55	No	Smooth and bosselated	Rubbery	Normal
Carcinoma	35+	Uncommon	Irregular	Hard	Nodes may be <b>palpable</b>

### History



- The symptoms occur during the years of ovarian activity due to hormonal changes.
- One or more tender lumps with variable size and clearly related to menses (during the second half -second 2 weeks- of the cycle).

### Examination



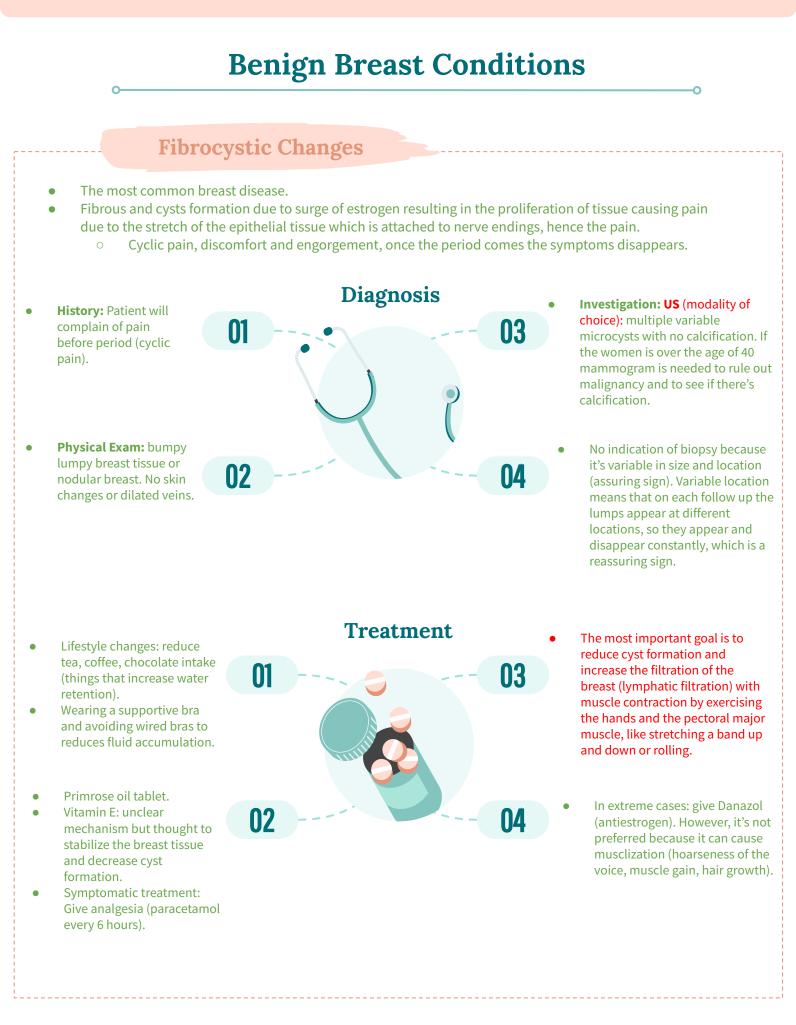
- Vary from a **diffuse** nodularity to quite **discrete** lesions.
- Most common site is **Upper outer quadrants** because this part has more breast tissue.
- Begin by assessing the asymptomatic breast to get an idea of its consistency
- Not fixed or tethered to the skin or the muscle. Unlike cancerous lumps which are <u>fixed</u> and associated with <u>skin</u> <u>changes</u> and tethering.
- NO lymph node enlargement







- Breast masses must be investigated: most of the time is benign.
- Radiologically by breast ultrasound or mammogram as age indicates.
- Pathologically by ultrasound guided trucut biopsy.



### Fibroadenomas

- Common in young age group (puberty to late 20s or early 30s).
- Fibroadenomas develop from a **whole lobule** rather than from a single cell, and show hormonal dependence similar to that of normal breast tissue, lactating during pregnancy and involuting in the perimenopausal period.
- Presentation: mass and occasional pain. No discharge or skin changes.
- Diagnosis:



 Hx: young females
 Examination: well localized, mobile and non tender mass. Could be multiple.

- US: solid well encapsulated mass,
- variable in size, single or multiple.
  Ultrasound is used to differentiate between fibroadenoma and cysts.
- Biopsy is needed, ultrasound guided trucut (core) biopsy to differentiate between fibroadenoma and phyllodes.

**Fate of fibroadenoma:** 50% disappear spontaneously, the other 50% either gets smaller or bigger or the stays the same. **Transformation to malignancy = 0%** 

Once a diagnosis of fibroadenoma has been established, options for management are **reassurance** with **no follow-up** or **surgical excision.** 

#### **Criteria for surgery:**

Any **fibroadenoma >4cm** (to ensure that a phyllodes tumor is not missed). **Painful** and **rapidly growing** fibroadenoma.

**Family Hx** of malignancy (however there's no chance for fibroadenomas to be malignant, it's just to relieve the patient from stress).



- **Unusual age group** (40-50 yo), First you're gonna perform US then Mammogram then eventually a biopsy to confirm your diagnosis, then remove it.
- **Unclear pathology** (e.g. the pathology report says fibroadenoma with hypercellularity, or phyllodes atypia).

### **Phyllodes Tumor**

- It differs from fibroadenoma in that it has:
  - More fibrous tissue component
  - Malignant potential of <1%
  - If not excised completely there is a high chance of recurrence.
- Getting another phyllodes tumor somewhere else in the body is different from recurrence in the same location. Why? Because of the hormonal stimulation.
- Phyllodes tumor can be graded to benign, mild and malignant (Sarcoma, which is a very nasty cancer, that rapidly grows and spreads via blood. Almost ¼ of malignant cases metastasise, most commonly to the lungs).



Female >30 y/o



Similar presentation to fibroadenoma but single large (>4 cm) fibroepithelial mass, well localized, mobile and non tender mass. Skin changes and discharge when malignant.



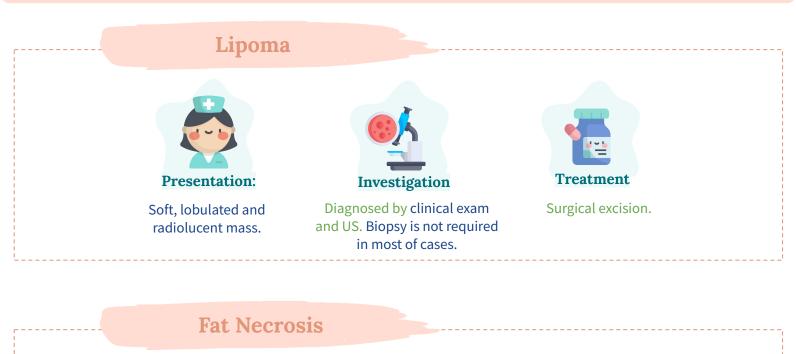
Investigation Biopsy is a must, after the US



#### Treatment

surgical excision for both malignant or benign. While for larger lesions, mastectectomy may be needed. (the chance of malignancy increases with size).







Occurs due to trauma (impaction and disimpaction)



Present later after 3-4 months from the injury as irregular, hard, non tender mass of dead or damaged breast tissue.



Trucut biopsy



Reassurance (resolves with time).

### **Breast Cysts**

#### Simple

- Cyst filled with **clear fluid.**
- Presentation: localized painful single mass.
- Diagnosis:
  - $\circ$  US  $\rightarrow$  well circumscribed simple cyst filled
  - with fluid lined with single layer of epithelium. Aspiration (diagnostic and therapeutic) then send it for **cytology**. Blood could be malignant of traumatic.
  - $\circ \qquad \mbox{Repeat US after 6 weeks: if the cyst refilled,} \\ \mbox{aspirate it for the second time and send it for} \\ \mbox{cytology (if it's benign} \rightarrow \mbox{follow up in 6 weeks)} \\ \end{aligned}$
  - If it refills for the third time it needs to be excised, because the epithelial lining can have malignant potential.

#### **Complicated / Complex**

- Complicated cyst: cyst with turbid fluid
- Complex cyst: cyst with **solid component or septation**

#### Diagnosis:

- Trucut biopsy is needed from inside the cyst if it's benign just asprate it.
- If there is atypia then excise it.

### Galactocele

Galactic lump is a cystic lump which contains milk, develops in lactating women and usually resolves upon the cessation of breastfeeding but large ones may require repeated aspiration. How to differentiate between galactocele and abscess?

• Galactocele mass is associated with slight tenderness with **no fever or rigors.** 

### **Accessory Breast Tissue**

- Located under the arm or breast, as extension of the axillary fat.
- Occurs during puberty, lactation or pregnancy.
- Examination: If you find a mass in the axilla, does the size of the mass changes with period? If yes, accessory breast tissue. Is the mass mobile & hard? If yes and does not change with period, then it's lymph node.
- Diagnosis: US and biopsy if needed.
- Surgical indication: if it's big enough to limit the movement of the patient arm or for cosmetic reasons.

### **Accessory Nipple**

- Accessory nipples are usually found along the line of nipple development.
- looks like a nevus, might be unnoticeable.
- Some patients will have swelling and discharges during their period.
- Treatment is not needed unless for cosmetic reasons.

### **Mondor's disease**

- A thrombophlebitis of the lateral thoracic vein
- Produces a cord-like, linear skin puckering that can alarm patient and clinician
- causes pain at an early stage and subsequently becomes a painless fibrous band
- It Resolve spontaneously

### The Nipple

The symptoms associated with the nipple are:









### Nipple discharge:

- It occurs in any age group , commonly during reproductive life.
- It could be thick or thin, cloudy or clear, or bloodstained. Unilateral or bilateral, spontaneous or induced, single duct or multiple ducts.
- Will be considered pathological if it's unilateral & spontaneous (coming out by itself without squeezing the nipple) from a single duct or associated with pain or mass.
- If the discharge is:
  - **Milk** → usually benign, and if it's related to pregnancy or lactation it's considered normal. If not then investigations are needed.
  - $\circ$  Serous or bloody  $\rightarrow$  always requires investigating.
  - Investigations include:



- Radiology by breast ultrasound or mammogram or MRI depending on the patient's age.
- If it's associated with mass then biopsy is needed.

	Pathology	Discharge Characteristics	Management	
<b>Duct Ectasia</b> (Explained in details in the next slide.)	<ul> <li>Most common cause of nipple discharge.</li> <li>Inflammatory condition that causes dilatation of the duct beneath the nipple.</li> </ul>	<ul> <li>Variable color and consistency.</li> <li>Multiple ducts discharging.</li> </ul>	<ul><li> Reassurance</li><li> Excision of the ducts</li></ul>	
Duct Papilloma	<ul> <li>Intraductal papilloma is the most common cause of blood-stained discharge.</li> <li>Benign neoplasm arise from the ducts under the nipple and can be single or multiple.</li> <li>May show minimal malignant potential.</li> </ul>	<ul> <li>Copious serous, bloody.</li> <li>Single duct.</li> </ul>	Most of the time it's self limiting. If persistent: <b>Microdochectomy</b> to make sure that the papilloma doesn't harbor DCIS.	
Carcinoma in situ (DCIS)	• Least common cause of nipple discharge.	<ul> <li>Bloodstained, spontaneous persistent, serous discharge.</li> <li>Single duct.</li> </ul>	Image-guided biopsy, or Microdochectomy.	
Prolactinoma	<ul> <li>Benign hormone-secreting pituitary tumor that produces the hormone prolactin.</li> </ul>	<ul><li>Milky, bilateral.</li><li>Multiple ducts.</li></ul>	Reassurance & Endocrine evaluation. No need of surgical intervention for the breast.	

### Nipple inversion:

Usually associated with significant disease and always merits full assessment. When is nipple inversion worrisome? If the onset is **recent**, if the inversion is **unilateral** and if upon examination you **can't evert** the nipple.

Paget's Disease



#### Pathology of Paget's Disease:

- Paget's disease of the nipple is caused by cancer cells migrating or spreading along the duct system & the subdermal layer of the areola, from an underlying breast carcinoma situated deeply in the breast, which in the early stages is usually confined to the epithelium (DCIS).
- Patches of skin first become red and then encrusted and oozy.
- Any patient coming to the clinic complaining of nipple inversion and skin changes around the nipple, **always** assume that it's paget's disease until proven otherwise. Because if the diagnosis of paget's disease is missed, the cancer will progress.

#### Investigations & Treatment:

- Investigations: Skin biopsy.
- **Treatment:** mastectomy.
- Patients may present with symptoms mimicking Eczema:

#### Eczema

- Bilateral
- Sometimes
- lactatingltches
- Vesicles
- Nipple intact
- Nolumps

#### Paget's Disease

- Unilateral
- Older females
- Does not itch
- No vesicles
- Nipple may be destroyed
- May be an underlying lump. If you can't feel a lump that doesn't rule out cancer!

Duct Ectasia



#### Investigations & Treatment:

#### Investigation:

- **US:** is diagnostic.
  - Over the age of 40 mammogram is needed to exclude malignancy.
- Treatment:
  - **Reassurance**, local cleaning externally and avoid squeezing the nipple as it will only increase the chance of trauma and retraction.
  - If there's fever, pain and tenderness, excise the dilated ducts surgically to avoid the risk of developing periductal mastitis and abscess.
  - Diabitic patient with duct ectasia are at increased risk for periductal abscess.

Pathology of Duct Ectasia:

- Common inflammatory condition of **unknown aetiology**.
- Dilatation of the mammary ducts for more than 4 cm.
- Presenting features:
  - Nipple inversion, transverse slit appearance.
  - Difficulty in breastfeeding.
  - Nipple discharge.
- Anyone can get duct ectasia. However the **complications** are seen in **smokers**.
- Complications:
  - Chronic low-grade infection of the periareolar area.
  - Periductal abscess
  - Mammillary fistula between the skin and the ducts.<sup>1</sup>

1. Extra: fistula is an opening between two epithelial surfaces. While sinus is a blind-ended tract that extends from the surface of an organ to an underlying area or abscess cavity.

### **Breast Infection**

- Can be divided into lactational and non-lactational.
- The principles of treatment:



Give appropriate antibiotics early to **prevent** abscess formation.

Lactating infection:

Non-lactating

infection:

Confirm Abscess by ultrasound then aspirate if small or surgically drain.

**Exclude** breast cancer by taking a biopsy from the walls of the abscess. Because some types of breast cancers present with abscess formation.



After it resolves **reassess** the patient to make sure there's **no residual mass** that was hidden by the abscess.

- Usually develops within the first 6 weeks of breastfeeding secondary to bacterial infection contracted from the baby's mouth which is colonized by staph aureus that can enter through nipple cracks and skin abrasions on the mother's breast.
- Present with pain, swelling, tenderness and a cracked nipple or skin abrasion.
- Most common pathogen: Staphylococcus aureus.
- Women should be **encouraged to breastfeed** because the milk comes from the lactocytes which's nowhere near the infection. Stop breastfeeding **only** if the baby is quiet, or having diarrhea because the antibiotic can be excreted in the milk. But she has to pump her breast and discard it so that the breast won't become engorged and tender and milk production won't stop.
- **Treatment:** as mentioned above. First give antibiotics (IV antibiotic against staph aureus: floxacillin, cloxacillin, augmentin for 24 hrs then continued orally) and if at any point they develop an abscess you have to confirm it by US then drain it.
- If left untreated the body will try to fight it off and an abscess will be formed (filled with necrotic debris and inflammatory cells walled by fibrous tissue)
  - Abscess presentation is more acute, with **way more tender breasts**, **sky high fever and rigors**.

#### Types of non-lactating infections:

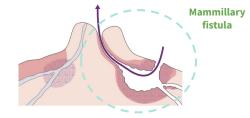
- Central (periareolar) infection.
- Peripheral non-lactating abscesses.
- Tubercular mastitis.
- Skin-associated infection.

### **Central (periareolar) infection:**

- A complication of duct ectasia.
- Commonly seen in young women, with periductal mastitis (inflammation and infection of the ducts).
- **Smoking** is an important **etiological factor**<sup>1</sup>.
- **Presentation:** Breast pain, erythema, swelling and tenderness.
- **Treatment:** Antibiotics, aspiration or incision and drainage.

### Mammary duct fistula:

- Occurs when a periductal abscess -formed due to periductal mastitis- ruptures (or is drained externally) and stays in communication with the duct system.
- **Treatment:** excision and antibiotic.



1. Remember: the **etiological factor of duct ectasia** is **unknown**. However the **complications** of duct ectasia are caused by **smoking**.

### Peripheral non-lactating abscesses:

- A general infection similar to any other skin infection.
- Some are associated with an **underlying condition**, such as diabetes, Rheumatoid arthritis, steroid treatment or trauma.

### **Tubercular mastitis:**

- Reproductive age group with **painless lump**.
- They don't have open TB but they have history of TB themselves or history of contact with TB patients.
- Confirm TB with FNA or needle Biopsy.
- A prolonged course of antitubercular treatment is preferred. No need for surgical intervention unless they develop an abscess.

### **Skin-associated infection**

- Anyone can get this infection regardless if they have underlying conditions or not.
- Commonly affects the lower half of the breast (inframammary area) and can be recurrent.
- Intertrigo: present with redness itching and pain. Advice the patient to keep the area clean and dry.
- Epidermoid (sebaceous cysts): often forms within sebaceous glands.
- **Hidradenitis suppurativa:** seen in the axilla, groin and inframammary area. Patients need antibiotics and surgical excision of the skin involved.

### Gynaecomastia

- Abnormal development of both the ductal and stromal elements of the breast in males.
- Presentation:



Breast development in adolescents: is due to hormonal changes during puberty, and it is Bilateral

### $\longrightarrow$

Breast enlargement in **middle-aged** adults: is usually associated with bilateral **trauma** to the breast. Not caused by hormones!  $\rightarrow$  04

Breast enlargement in **elderly males**: is usually caused by **medications** as a side effect. 05 Inappropriate hormone secretion: with liver diseases or cancers that secrete hormones such as testicular tumors or adrenal gland tumors.

#### **History**:



- **Painless**, enlargement of one or both breasts.
- Taking a drug history is essential.
- Rule out taking steroids, endocrine hormones, obesity.



02



- In young patients: Palpable rounded hard disc of breast tissue. In elderly patients: More diffuse,
- with fatty elements.
- Axillary lymph glands will **not** be enlarged. If enlarged, suspect cancer.
- General examination, especially of the abdomen scrotum and testes.

#### **Investigation**:

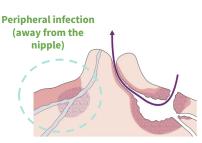


 Ultrasound (mainly)
 Mammogram, and biopsy if there is a mass.

#### Treatment:



Liposuction



### **Breast Cancer**





Male represent <1% of patients with breast cancer





The most common malignancy in women, comprising 18% of all female cancers.



### **Risk factors:**

#### Age:

The risk is higher in young age groups, but the incidence increases with age until menopause. It's extremely rare below the age of 20 years.

#### **Geographical variations:**

Higher in developed countries (Caucasian, Western Europe and Australia).

#### Menstrual and pregnancy factors:

Early menstruation, late menopause, nulliparous women, late first childbirth after the age of 30 are at higher risk.

The highest risk is in women having a first pregnancy over the age of 40.

Early first delivery and breastfeeding may protect against breast cancer.

#### **Radiation:**

Women treated by mantle radiotherapy for Hodgkin's or non-Hodgkin's lymphoma during adolescence and teenage are at significant risk of developing early-onset breast cancer.

#### **Benign disease:**

Severe atypical hyperplasia is associated with increased risk of breast cancer.



High alcohol intake and saturated fat increases breast cancer risk.

#### Horn Cont

#### **Exogenous hormones:**

Hormonal Replacement Therapy and Oral Contraceptive Pills increase the risk, but combined Progesterone and estrogen HRT is associated with a greater risk than preparations containing estrogen alone.



#### Physical activity, weight and height:

Moderate physical activity reduces the risk, obesity increases the risk in postmenopausal women while may reduce the risk in premenopausal women, and taller women have higher risk.

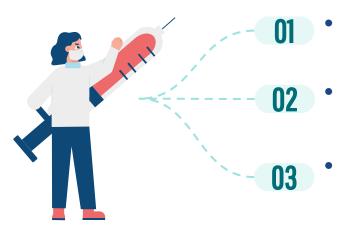
#### **Genetics:**

Many genes involved in breast and ovarian cancers are DNA repair genes (Mutations, insertions or deletions).

High Risk Genes: The vast majority of families having members with breast and ovarian cancers are linked to **BRCA1** & **BRCA2** genes.

Mutations in the p53 gene and mutation of PTEN can also lead to breast cancer.

### Management for high risk women:



- Bilateral risk reducing surgery by removing as much of the breast and the nipples if required.
- Regular screening involving MRI and Mammography.

Chemoprophylaxis with tamoxifen, raloxifene and the aromatase inhibitors.

### Pathology of breast cancer:

- Breast cancers are derived from epithelial cells that line the terminal duct lobular unit.
  - Breast cancer is classified into:
    - In situ (noninvasive).
      - Invasive.
- Both in situ and invasive cancers have characteristic patterns by which they are classified.
- The most commonly used classification of **invasive** cancers divides them into **ductal** and **lobular** types and is based on the belief that ductal carcinomas arise in ducts and lobular carcinomas in lobules.
- This is now known to be incorrect, as almost all cancers arise in the terminal duct lobular unit. The two types behave differently, so the classification remains in use.

### Hormone and growth factor receptors:

#### ERs & PgRs

- Estrogen receptors (ERs) and progesterone receptors (PgRs) are expressed in breast tissue and expressed in much greater amount in breast cancer cells.
- Breast cancer positive for ERs or PgRs is associated with better prognosis.
- It'll be a target for the hormonal therapy.

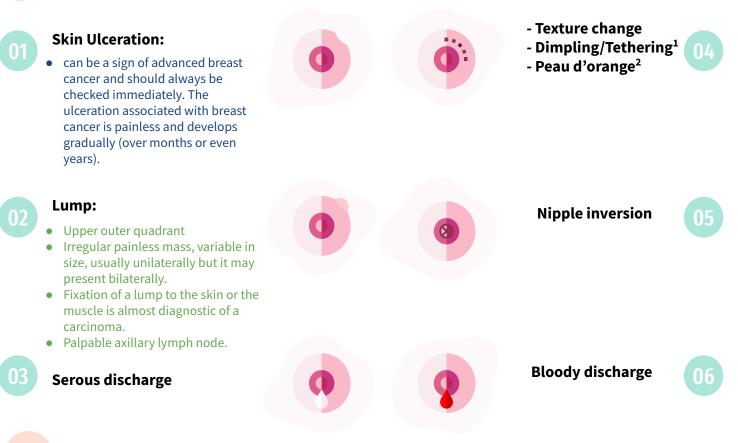
overexpression of HER2

The most important growth factor is human epidermal growth factor receptors (HER2). Breast cancer with overexpression of HER2 is associated with worse prognosis.

 It'll be a target for the monoclonal antibody therapy (trastuzumab). Triple negative

- Triple negative cancer (ERs, PgRs, HER2) is associated with the worst prognosis.
- Triple negative cancers are more common in BRCA1 gene mutation carriers.
- Chemotherapy.

### **Presentation:**



### **Diagnosis**:

- US: solid mass with irregular border.
- Mammogram: solid mass with or without stellate features, irregular borders of the mass, asymmetric thickening of breast tissue, clustered microcalcification (presence of fine, stippled calcium in and around a suspicious lesion is suggestive of breast cancer).
- Trucut biopsy is a must.

### Staging:



Stage 01 less than 2 cm with no lymph nodes involvement.



Stage 02 2-5 cm with presence of one mobile lymph node in the axilla



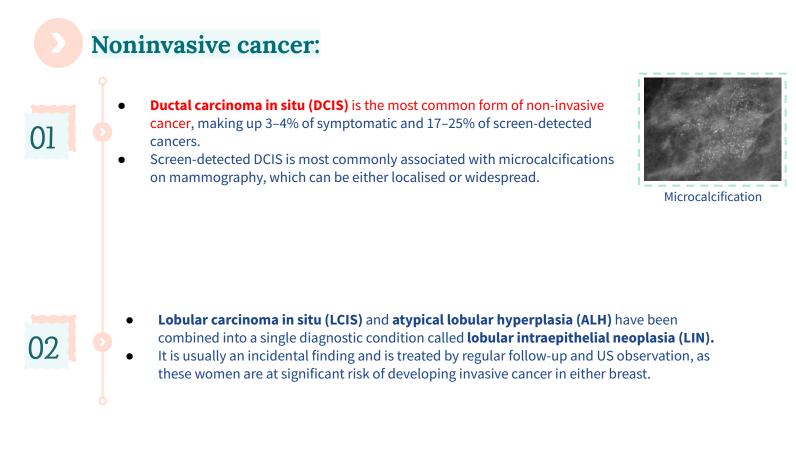
Stage 03 >5 cm, skin involvement, nipple retraction, fixed lymph node.



**Stage 04** anything with metastasis (CT scan chest, abdomen, pelvic, bone scan).

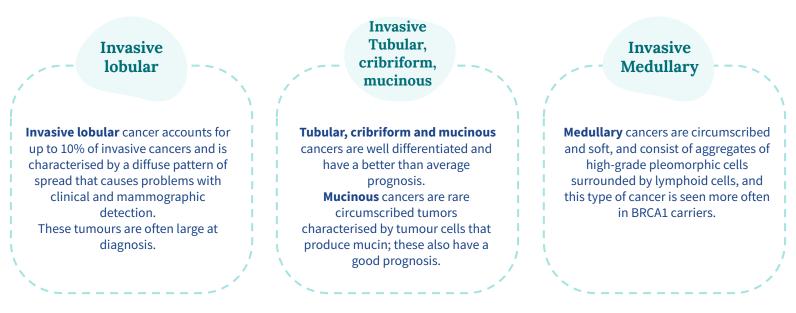
### Prognostic Factors: ★

- Stage of the tumour at diagnosis: its size and involvement of the axillary lymph nodes or the presence of any metastases.
- Biological factors: histological grade, histological type, presence of lymphatic and/or vascular invasion, hormone receptor and HER2 status.
- Genomic
- -----
- Tethering is a feature of cancerous lumps and it's pulling of the overlying skin inward causing a visible dimple.
   Peau d'orange (orange peel appearance): characterized by edema and pitting and results from blockage of lymple
  - Peau d'orange (orange peel appearance): characterized by edema and pitting and results from blockage of lymphatic drainage. The infiltrated skin is tethered by the sweat gland ducts where it cannot swell, leading to an orange skin like appearance.



### **Invasive cancer:**

- The majority of invasive cancers are of no special type and are often referred to as ductal cancers.
- Certain invasive carcinomas show distinct patterns of growth and are classified as tumors of 'special type'; this includes
  - lobular, tubular, cribriform, papillary, mucinous, medullary and inflammatory cancers.
- The presence of tumour cells in lymphatics or blood vessels is associated with an increased risk of both local and systemic recurrence.
- Breast cancers can be graded.
  - Grade I have the best prognosis.
  - Grade II have an intermediate prognosis.
  - Grade III or high-grade cancers have a poorer prognosis than Grade 1 or 2 cancers.



#### Inflammatory Breast Cancer:

- **Inflammatory breast cancer (IBC)** is a specific type of invasive breast cancers that's highly aggressive.
- IBC often does not produce a lump that can be felt within the breast. Instead, it presents as a painful, swollen, tender, warm, breast with with widespread peau d'orange, due to edema from obstruction of dermal lymphatics by tumour cells.
- It mimics infective mastitis or breast abscess.
- Biopsy confirms the diagnosis.
- Inflammatory carcinomas are uncommon but they're fast-growing and have the worst prognosis of all invasive cancers.
- It's a rapidly fatal breast cancer that needs aggressive chemo-radiotherapy followed by surgery.





Take a Break



### **Treatment:**



### **Operable Breast Cancer**

- All invasive and non-invasive cancer must be completely excised.
- There are two accepted methods of local therapy for operable breast cancer:

#### **Breast-conserving surgery:**

- Breast conserving surgery is done when there is **no evidence of metastasis beyond the axillary nodes**, and it includes **wide local excision to clear histological margins.**
- Should be combined with sentinel node biopsy or axillary clearance. Sentinel lymph node biopsy has reduced the complications that were seen after axillary clearance such as **lymphoedema** (A long-term swelling of the arm after axillary surgery or radiotherapy to the axilla).
- Wide excision should be followed by **radiotherapy** to reduce the local recurrence which is too high after treatment by local excision only.
- The aim of this procedure is to remove the breast cancer completely in as small volume of breast tissue as possible with the best cosmetic outcome.

#### Mastectomy:

- This is an alternative method for the local treatment of operable breast cancer.
- Mastectomy includes the **removal of all breast tissue** (usually including the nipple) but leaves the muscles of the chest wall intact.
- Should be combined with sentinel node biopsy or axillary clearance.
  - Indicated in the following situations:
    - Radiotherapy isn't available.
    - $\circ$   $\qquad$  The desire of the patient to avoid radiotherapy.
    - The desire of the patient to have mastectomy.
    - Incomplete excision after breast conserving surgery.
    - Large cancer (>4 cm) in comparison to the size of the breast.
    - Multifocal breast cancer.
    - Inflammatory breast cancer.
    - Localized invasive cancer with a large area of surrounding non-invasive disease.
    - Central breast cancer involving the nipple or directly underneath it.
    - Pregnancy.
- Women with high risk of local recurrence should get radiotherapy following mastectomy.
- Risk factors for local recurrence after mastectomy include:

### • Involvement of axillary lymph node (>3 nodes).

- Lymphatic invasion.
- Vascular invasion.

Grade III cancer.

0

0

- Tumor >5 cm (pathological measurement).
- The tumor involves the pectoral fascia or pectoral muscle.

### **Treatment Cont.:**



#### Adjuvant Systemic Therapy

- The aim of adjuvant systemic therapy is to delay recurrence and prolong survival in a patient with micrometastatic disease.
- Indications for adjuvant systemic therapy:
  - Lymph node-positive.
  - Higher risk node-negative women.
  - Women with hormone receptor-positive cancers.



#### Hormone Therapy:

- Tamoxifen:
  - reduces the rate of recurrence, reduces the risk of tumors in the contralateral breast, preventative agent.
  - It's effective in premenopausal and postmenopausal women.
  - Luteinizing hormone releasing hormone (LHRH) agonists (Goserelin):
    - induces a reversible ovarian suppression.
    - $\circ$   $\qquad$  Only of benefit in premenopausal women with receptor-positive cancer.
  - Aromatase inhibitors (Letrozole, Anastrozole).
    - $\circ$  For postmenopausal women.



#### Chemotherapy:

- Combination of chemotherapeutic drugs is more effective than a single drug.
- Chemotherapy regimen include:
  - First generation chemotherapy (cyclophosphamide, methotrexate, 5-Fluorouracil-CMF).
  - Modern regimens (anthracycline, doxorubicin or epirubicin)
  - Newer agents (taxanes)

Anti-H

#### Anti-HER2 Therapy:

• Monoclonal antibodies (trastuzumab - Herceptin).



### Neoadjuvant Therapy

- This's when chemotherapy, hormonal, or biological therapy is given before surgery to shrink the tumor.
- Must be preceded by core biopsy of the cancer and nodes (if involved).
- Should be considered in patients with large or locally advanced tumors that would otherwise require a mastectomy who may become suitable for breast-conserving surgery or in patients with inoperable cancer that may become operable.

### **Treatment Cont.:**

0



**Breast Reconstruction:** 

- Options include placement of an implant (silicon gel) at the time of mastectomy behind the pectoral muscle.
- Other options are myocutaneous flaps, and the most commonly used is latissimus dorsi myocutaneous flap with or without an implant, and the rectus abdominis myocutaneous flap alone. These are used if the skin at the mastectomy site is poor (e.g. following radiotherapy).

	Stage 1-2	Stage 3	Stage 4
Summary of management made by the doctor	Mastectomy or conservative breast surgery with radiation. Sentinel lymph node needs to be excised and assessed.	Neoadjuvant chemotherapy and surgical removal.	Chemotherapy and surgery and radiation and hormonal therapy (Tamoxifen).

### **Breast Self-Exam (Extra)**

01	A breast self-examination involves checking your breasts for lumps or changes. Many breast problems are first discovered by women themselves, often by chance.
02	The best time to examine your breasts is usually 1 week after your menstrual period starts, when your breasts are least likely to be swollen or tender.
03	Remove all your clothes above the waist. Lie down. Lying down spreads your breasts evenly over your chest and makes it easier to feel lumps or changes.
04	Use the pads of your three middle fingers—not your fingertips. Use the middle fingers of your left hand to check your right breast. Use the middle fingers of your right hand to check your left breast. Move your fingers slowly in small coin-sized circles. You can use an up-and-down pattern or a spiral pattern or circular pattern.



**Palpate** 



Circles



**Up-and-down** 

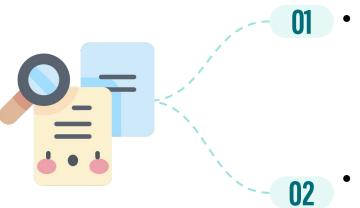


Spiral



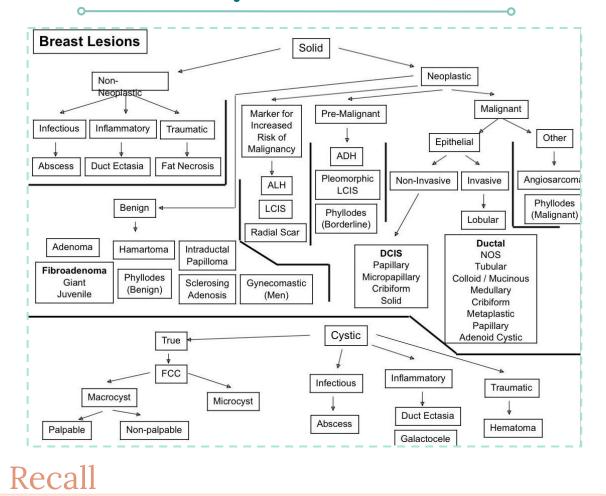
	DDx
A painless lump	<ul> <li>Carcinoma</li> <li>Cyst</li> <li>Fibroadenoma</li> <li>An area of fibroadenosis</li> </ul>
A painful lump	<ul> <li>An area of fibroadenosis</li> <li>Cyst</li> <li>Periductal mastitis</li> <li>Abscess (usually postpartum or lactational)</li> <li>Sometimes a carcinoma</li> </ul>
Pain and tenderness but no lump	<ul> <li>Cyclical breast pain</li> <li>Non-cyclical breast pain</li> <li>Very rarely, a carcinoma</li> </ul>
Nipple discharge	<ul> <li>Duct ectasia</li> <li>Intraductal papilloma</li> <li>Ductal carcinoma-in-situ</li> <li>Associated with a cyst</li> </ul>
Changes in the nipple and/or areola	<ul> <li>Duct ectasia</li> <li>Carcinoma</li> <li>Paget's disease</li> <li>Eczema</li> </ul>
Changes in breast size and shape	<ul> <li>Pregnancy</li> <li>Carcinoma</li> <li>Benign hypertrophy</li> <li>Rare large tumours</li> </ul>





- lactating female with breast mass and pain < mastitis ( if signs of infection are present ) or milk cyst ( no signs of infection ).
- Young female with cyclic breast pain, on PE you found a mass 2x2 in size < most likely fibroadenoma.

### **Summary From the Doctor**



### Q1: What option exists to decrease the risk of breast cancer in women with BRCA?

Prophylactic bilateral mastectomy.

#### Q2: What is the "TRIAD OF ERROR" for misdiagnosed breast cancer?

- 1. Age <45 years
- 2. Self-diagnosed mass
- 3. Negative mammogram

Note: >75% of cases of MISDIAGNOSED breast cancer have these 3 characteristics.

#### Q3: Why does skin retraction occur?

Tumor involvement of Cooper's ligaments and subsequent traction on ligaments pull skin inward.

#### Q4: What is the most common type of breast cancer?

Infiltrating ductal carcinoma.

#### Q5: What is the differential diagnosis?

- Fibrocystic disease of the breast
- Fibroadenoma
- Intraductal papilloma
- Duct ectasia
- Fat necrosis
- Abscess
- Radial scar
- Simple cyst

Q6: What follows a positive sentinel node biopsy? Removal of the rest of the axillary LNs.

Q7: Is the fluid from a breast cyst sent for cytology? Not routinely. However, bloody fluid should be sent for cytology.

# Quiz

### MCQ

Q1: Which of the following conditions have an increased risk of breast carcinoma? A) Atypical ductal or lobular hyperplasia B) Fibroadenoma C) Duct ectasia

Q2: A 29-year-old woman presents with a 6-month history of erythema and edema of the right breast with palpable axillary lymphadenopathy. A punch biopsy of the skin reveals neoplastic cells in the dermal lymphatics. Which of the following is the best next step in her management?

A) Mastectomy followed by adjuvant chemotherapy.

B) Mastectomy followed by hormonal therapy.

C) Combined modality therapy with chemotherapy, surgery, and radiation.

Q3: A 35-year-old woman presents with a lump in the left breast. Her family history is negative for breast cancer. On examination the mass is rubbery, mobile, and nontender to palpation. There are no overlying skin changes and the axilla is negative for lymphadenopathy. An ultrasound demonstrates a simple 1-cm cyst in the area of the palpable mass in the left breast. Which of the following represents the most appropriate management of this patient?

A) Reassurance and reexamination.

B) Mammography and reevaluation of options with new information.

C) Immediate excisional biopsy.

Q4: A 14-year-old black girl has her right breast removed because of a large mass. The tumor weighs 1400 g and has a bulging, very firm, lobulated surface with a whorl-like pattern, as illustrated here. Which of the following is the most likely diagnosis? A) Intraductal carcinoma



B) Fibroadenoma

C) Cystosarcoma phyllodes

Q5: A 33-year-old pregnant woman notices a persistent, painless lump in the left breast. On examination the left breast has a single mobile mass without evidence of skin changes or lymphadenopathy in the neck or axilla. An ultrasound demonstrates a solid, 1-cm mass in the upper outer quadrant of the breast. A core-needle biopsy shows invasive ductal carcinoma. The patient is in her first trimester of pregnancy. Which of the following is the most appropriate management of this patient?

A) Administration of radiation in the third trimester followed by modified radical mastectomy after delivery of the baby. B) Mastectomy

C) Immediate administration of chemotherapy followed by modified radical mastectomy after delivery of the baby.

Q6: A 33-year-old, non-smoking, breastfeeding woman is 10 days postpartum. She has a 4-day history of a slight crack on the surface of her left nipple. She presents with a 2-day history of severe continuous pain in the left breast, spiking pyrexia up to 38.8 with rigours which has prevented her from sleeping. On examination, you find the outer quadrants of the left breast to be red, warm and tender with a hard 3 cm lump at the edge of the left nipple. The most likely diagnosis is

A) Periductal mastitis

B) Breast cyst

C) Breast abscess

Answers Click here for explanation	Q1	A	Q4	
	Q2		Q5	
	Q3	А	Q6	



# Good Luck!



# Team leaders:

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