

# Breast Disease

## Clinical presentation of breast disease

<b>Pain:</b>	-cyclic -noncyclic	diffuse, premenstrual edema and swelling. Localized, ruptured cyst or physical trauma, or infection	Almost all painful masses are <b>benign</b> except for 10% of cases that relates to cancers	
<b>Inflammation:</b>	-causes edematous and erythematous breast. -most often caused by infections ( <b>during lactation and breastfeeding</b> ). -An important <b>mimic of inflammatory breast cancer</b>			
<b>Nipple discharge:</b>	when small in quantity and bilateral.	Normal	•are associated with elevated prolactin levels (pituitary adenoma), hypothyroidism, or endocrine anovulatory syndromes, patients taking OCPs, tricyclic antidepressants, methyldopa, or phenothiazines.	#the risk of nipple discharge being due to cancer increases from 7% in women <60 years vs. 30% in women >60.
Milky discharges	(galactorrhea)	commonly due to large duct papillomas and cysts During pregnancy, result from the rapid growth and remodeling of the breast		
Bloody or serous discharges	<b>BUT spontaneous, unilateral, and bloody discharge increases concern for malignancy</b>			
<b>Palpable masses</b>	-95% are benign -all palpable masses require evaluation. <b>-The most common palpable lesions are cysts, fibroadenomas, and invasive carcinomas</b> -generally detected when they are 2 to 3 cm in size.		#only 10% of palpable masses in women <40 years are carcinomas vs. 60% in women >50.	
<b>Gynecomastia:</b>	-The only common breast symptom in <b>males</b> . -resulting from an imbalance between estrogens, which stimulate breast tissue, and androgens, which counteract these effects.			

## General Consideration in Breast disease

\*\*The underlying cause is **benign** in >90% of cases.

#The likelihood of malignancy increases with age:

## زي نقاط يلي فوق

\*\*Of women with cancer:

\*about 45% have symptoms

\*Palpable mass>>>> pain> nipple discharge > inflammatory changes

\*the remainder come to attention through screening tests

## Mammographic Screening

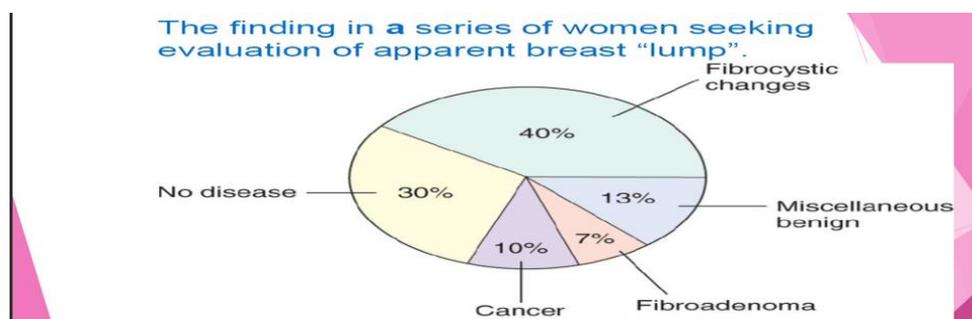
هو عبارة عن جهاز مخصص لحتى يصور microcalcification

\*\*detects early, non palpable asymptomatic breast carcinomas before metastasis.

\*\*the average size of invasive carcinomas detected by mammography is about 1 cm, at this stage only 15% will have metastasized to regional lymph nodes.

\*\*The sensitivity and specificity of mammography increase with age  
>> due to replacement of the (**fibrous, radiodense tissue**) of young women with the (**fatty, radiolucent tissue**) of older women

## BREAST

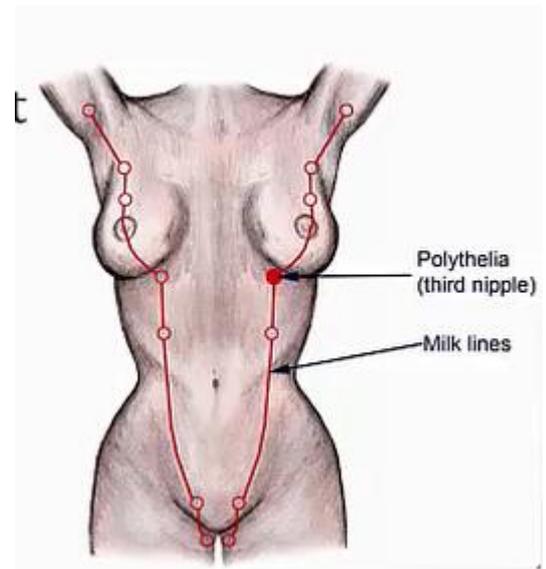


## Congenital anomalies

\*\*Some women have sufficient irregularity of the normal breast tissue to cause them to seek clinical attention.

<b>**Supernumerary nipples or breasts</b>	may be found along the embryonic ridge ( <b>milk line, especially the axilla</b> ) & are subject to the same diseases that affect the definitive breasts.
<b>Congenital inversion of the nipple</b>	is significant because similar changes may be produced by breast <b>ca</b> .
<b>Galactocele</b>	is painful cystic dilation of an obstructed duct that arises during lactation, which may rupture, inciting a local inflammatory reaction & fibrosis that may arouse suspicion of breast <b>ca</b> .

هادي صورة اضافية لتوضيح المقصود بالحالة الاولى



## Inflammatory lesions of the breast

\*rare

Note: Because inflammatory diseases are rare, the possibility that the symptoms are caused by inflammatory carcinoma **should always be considered**.

\***none** of which are associated with increased risk of ca >> benign .

\*All three are uncommon & during the acute stages usually cause **pain & tenderness** in the involved areas

	Cause	Presentation	Grossly	Histopath	Notes
<b>Acute mastitis</b>	<p>*rare *caused by infections, autoimmune disease, or foreign body–type reactions.</p> <p>*The only infectious agent is <b><i>Staphylococcus aureus</i></b> *Enters via fissures in nipple skin during the first weeks of breast feeding&gt; lactational abscesses.</p> <p>Develops when <b><u>bacteria gain access</u></b> to the breast tissue through the ducts; when <b><u>there is inspissation of secretions;</u></b> through fissures in the nipples,</p>	<p>which usually develop <b><u>during the early weeks of nursing (lactation)</u></b> or from various <b><u>forms of dermatitis involving the nipple.</u></b></p>	<p>*<b><u>staphylococcal infections</u></b> <b>induce single or multiple abscesses</b> accompanied by its typical clinical features. *They are usually small, when large they may heal with residual foci of <b><u>scarring</u></b> that are palpable as localized areas of induration <b><u>(that mimic ca).</u></b></p>		<p>**Streptococcal infections generally spread throughout the entire breast, <b><u>*causing pain,</u></b> *marked <b><u>swelling,</u></b> &amp; *breast erythema, edema and focal <b><u>tenderness,</u></b> usually heal by resolution *If untreated, tissue necrosis fistula tracks opening onto the skin <b>**Treatment:</b> antibiotics and continued <b><u>expression of milk.</u></b> *Rarely, <b><u>surgical incision and drainage is required.</u></b></p>

	Cause	Presentation	Grossly	Histopath	Notes
<b>Mammary duct ectasia (Periductal Plasma Cell Mastitis)</b>	Is a <b>nonbacterial</b> chronic inflammation of the breast associated with: (1) <b>inspissation of breast secretions in the main excretory ducts</b> (2) <b>ductal dilation &amp; rupture</b> leading to reactive inflammatory changes in the surrounding tissue.	It is an <b>uncommon condition</b> , usually encountered in <b>women in their 40s &amp; 50s who have borne children.</b> (multiparous)	usually the inflammatory changes are <b>confined to an area drained by one or several major excretory ducts of the nipple</b> with increase firmness of the tissue. <b>O/S dilated rope like ducts</b> are seen from which thick, cheesy secretions can be extruded.	<b>(1)dilated ducts are filled by granular debris, WBCs, mainly lipid-laden macrophages,</b> <b>(2)the duct epithelium lining is generally destroyed, &amp;</b> <b>(3)the most distinguishing features is the prominence of a lymphocytic &amp; plasma cell infiltration around the duct</b>	is of principal importance because it leads to induration of the breast substance & more significantly, to retraction of the skin or nipple, <b>mimicking the changes caused by ca.</b>
<b>Traumatic fat necrosis</b>	Is an uncommon lesion, Trauma from Biopsy – surgery – sports injury – seatbelt injury	<b>Most (but not all)</b> women with this condition report some antecedent trauma to the breast	, the early lesion is sharply localized, small, often tender, less than 2 cm in Ø.	*central focus of necrotic fat cells surrounded by neutrophils & lipid-filled macrophages, later enclosed by fibrous tissue & mononuclear leukocytes. *Eventually, the focus is replaced by scar tissue, or the debris becomes cystic, surrounded by a scar.	<b>*significant only because it produces a mass, mimicking ca.</b> *Calcifications on mammogram

## **FIBROCYSTIC CHANGES (disease)**

\*\***Very common condition**, in which changes in the female B range from innocuous, to patterns associated with an ↑ risk of ca.

\*\*These changes have been called **fibrocystic disease**.

\*\***Most** of these changes have little clinical significance except that **some**(stromal fibrosis & microcysts or macrocysts) **produce palpable "lumps"**, which must be **distinguished from cancer by** examination of fine needle aspiration (**FNA**) material or, **more definitively by biopsy & histologic evaluation.**

\*\*A **small minority** represents forms of epithelial hyperplasia that are clinically important.

\*\*This range of changes is the **consequence of an** exaggeration & distortion of the cyclic breast changes that occur normally in the menstrual cycle.

\*\*Estrogenic therapy & oral contraceptives do not seem to increase the incidence of these alterations; indeed, oral contraceptives may decrease the risk

### **The Relationship of Fibrocystic Changes to Breast Ca**

The following statements represent opinion of the relationship:

\*\*Minimal or no increase risk of breast ca: fibrosis, microscopic or macroscopic cysts, apocrine metaplasia, mild hyperplasia, fibroadenoma.

\*\*Slightly increase risk(X1.5-2 times):hyperplasia without atypia, ductal papillomatosis & sclerosing adenosis.

\*\*Significantly increase risk (X5 times): ductular or lobular **atypical hyperplasia**(seen in 15% of biopsies). Proliferative lesions may be multifocal, & the risk of subsequent ca extends to both breasts.

\*\*A family history of breast ca may increase the risk in all categories(e.g., to X10-fold with atypical hyperplasia).

\*\*Fortunately,most women who have lumps related to fibrocystic change can be reassured that there is little or no increase predisposition to ca.

## Benign Epithelial lesions

\*The majority are incidental findings detected by mammography.

\*A stromal **lymphocytic infiltrate is common** in all variants of fibrocystic change (proliferative & non proliferative)

<p><b>Non proliferative changes</b></p>	<p>Common is <b>not associated with an increased risk of breast cancer</b></p>	<p>(1) cystic change, often with <b>apocrine metaplasia</b> (most common)</p>	<p>*Although it may present as a single large cyst within one breast ,the disorder is usually multifocal&amp; often <b>bilateral</b>, *H/P:</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 5px;">The smaller cysts</td> <td style="padding: 5px;">In larger cysts</td> </tr> <tr> <td style="padding: 5px;">epithelium is cuboidal to columnar &amp; is sometimes multilayered in focal areas.</td> <td style="padding: 5px;">it may be flattened or even totally atrophic .</td> </tr> </table> <p>*The stroma surrounding the cysts consist of compressed <b>fibrous tissue</b>.</p> <p>*Frequently, cysts are lined by large <b>polygonal cells</b>, with abundant <b>granular eosinophilic cytoplasm_ &amp; small, round, deeply chromatic nuclei</b>, called <b>apocrine metaplasia</b> ;this is <b>virtually always benign</b>.</p> <p style="text-align: right;">هي مفروض خلايا ال ducts تفرز ولا توصل؟؟ لا بس المفروض توصل بس هون صارت + granular eosinophilic معناها secretory</p>	The smaller cysts	In larger cysts	epithelium is cuboidal to columnar & is sometimes multilayered in focal areas.	it may be flattened or even totally atrophic .
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<p><b>(2) Fibrosis.</b></p>	<p>Cyst rupture &gt; inflammation &gt; fibrosis</p>						
<p><b>(3) Adenosis</b></p>	<p>Increase # of acini (glands )</p>						

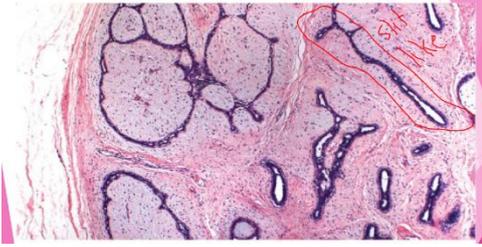
<b>Proliferative disease without atypia</b>	<p>*polyclonal hyperplasia          *associated with varying degrees of epithelial cell proliferation.          *not clonal and are not commonly found to have genetic changes          *associated with 1.5-2 (small) folds increase risk of breast cancer          *are predictors of risk but unlikely to be true precursors of carcinoma.</p>	<b>epithelial hyperplasia</b>	<p>,the epithelial cells are <b>multilayered</b> (luminal + myoepithelial )filling the duct and the acini, <b>myoepithelial cells are increased</b> , no epithelial atypia          .The duct lumen <b>is filled</b> with a heterogeneous <b>population of cells</b> of different morphologies.</p>
		<b>sclerosing adenosis</b>	<p>*Aggregated glands or <b>proliferating ductules</b> may be virtually back to back, with single or multiple layers of cells in contact with one another (<b>adenosis</b>).          *<b>Marked stromal (sclerosing fibrosis) compress &amp; distort the proliferating epithelium</b>, is always associated with the adenosis; hence, the designation <b>sclerosing adenosis</b>.          *This <b>overgrowth of fibrous tissue</b> may <b>completely compress the lumina of the acini &amp; ducts</b>, so that they appear as <b>solid cords of cells</b>, a pattern may be <b>difficult to distinguish histologically from an invasive scirrhous ca.</b>          باختصار رح يصير زيادة بعدد ال acini بس هدول ال          central portion رح يكون تبعمهم          compressed + distorted طب ليه ؟ بسبب stromal          fibrosis يلي حواليههم</p> <p>**The presence of <b>double layers</b> of epithelium &amp; the identification of <b>myoepithelial elements</b> are helpful in <b>suggesting a benign diagnosis</b>.          وجودها ينفي وجود السرطان مهم جدا لان الكانسر          مستحيل يكون اكثر من نوع من الخلايا</p> <p>**Although sclerosing adenosis is sometimes difficult to differentiate clinically &amp; histologically from ca, it is associated with only a minimally increase risk of progression to ca.          CP :result in calcification</p>
		<b>complex sclerosing lesion</b>	<p>Means sclerosing adenosis +papilloma + Epithelial hyperplasia present          كل هدول موجودين</p>
		<b>Ductal papillomatosis</b>	<p>*with proliferating epithelium projecting in multiple small <b>papillary projections</b> into the <b>ductal lumen</b>.          *The <u>degree of hyperplasia</u>, manifested in part by the <u>number of layers</u> of intraductal <b>epithelial proliferation</b>, can be mild, moderate, or severe          CP : bloody serous discharge +mass near the nipple (ductal)</p>

<b>Proliferative disease with atypia:</b> Atypical = nuclear changes	<b>**monoclonal</b> **are clonal proliferations having some, but not all, histologic features that are required for the diagnosis of carcinoma in situ.	<b>atypical lobular hyperplasia (ALH)</b>	resembles lobular carcinoma in situ (LCIS).
	- <b>**“precancers”</b> & associated with <b>4-5 folds (moderately) increase risk of breast cancer in both breast</b>	<b>atypical ductal hyperplasia (ADH)</b>	resembles ductal carcinoma in situ (DCIS)

## Benign tumors of the breast

<b>Stromal tumor</b>	<b>Fibroadenoma (FA)</b>	<p>*Most common benign tumor of the female breast.</p> <p>*An absolute or relative <b>increase in estrogen</b> activity is thought to contribute to its development.</p> <p>*It may <b>enlarge late in the menstrual cycle &amp; during pregnancy</b>; while it may <b>regress</b> &amp; calcify after <b>menopause</b>.</p> <p>*Usually appear in <b>young women</b>; the peak incidence is <b>in the 3<sup>rd</sup> decade (21 to 30 years) of life</b>.</p> <p>*<b>Clinically</b> as solitary, discrete, <b>freely ( not attached to breast tissue )</b> <b>movable nodule</b> (so-called <b>Breast mouse</b>), 1-10 cm in Ø.</p> <p>*<b>On mammogram</b> appears <b>denser (darker )</b> than the surrounding tissue because it does not contain adipose tissue ( <b>remember that it develops in lobule</b> ) .</p> <p>*Rarely, multiple fibroadenomas are encountered &amp;, *Rarely, they exceed 10 cm in Ø(<b>giant fibroadenoma</b>).</p> <p>*Whatever their size, they are usually easily "shelled out."</p> <p>*Grossly, all FA are firm, with a uniform white cut section</p> <p>*H/P, there is</p> <p>(I) a loose intralobular fibroblastic stroma containing</p> <p>☐(II) duct-like, epithelium-lined spaces of various forms &amp; sizes, lined with single or multiple layers of cells that are regular &amp; have a <b>well-defined, intact basement membrane</b> .Also it is encapsulated</p> <p>*The ductal lumens or spaces are either:</p> <table border="1" style="width: 100%; border-collapse: collapse; margin: 10px 0;"> <tr> <td style="width: 50%; padding: 5px; text-align: center;"><b>(pericanalicular FA)</b></td> <td style="width: 50%; padding: 5px; text-align: center;"><b>(intracanalicular FA)</b></td> </tr> <tr> <td style="padding: 5px;"> <ul style="list-style-type: none"> <li>•open, round to oval, &amp; fairly regular</li> </ul> </td> <td style="padding: 5px;"> <ul style="list-style-type: none"> <li>•the lumens (ducts ) are compressed by extensive proliferation of the surrounding stroma so they appear as slits or irregular star-shaped structures</li> </ul> </td> </tr> </table> <p>**Fibroadenomas almost never become malignant</p>	<b>(pericanalicular FA)</b>	<b>(intracanalicular FA)</b>	<ul style="list-style-type: none"> <li>•open, round to oval, &amp; fairly regular</li> </ul>	<ul style="list-style-type: none"> <li>•the lumens (ducts ) are compressed by extensive proliferation of the surrounding stroma so they appear as slits or irregular star-shaped structures</li> </ul>
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<b>PhyllodesTumor (T)</b>	<p>** are much <b>less common</b> than fibroadenomas &amp; are thought to arise from the <b>periductal stroma</b> &amp; not from preexisting fibroadenomas.</p> <p>*<b>Types:</b></p> <p><b>1- Most</b> of these phyllodes T are <b>benign</b>, may be small (3-4 cm in Ø, <b>but most grow to large, possibly massive size</b>, distending the breast.</p> <p>*<b>Some</b> become lobulated &amp; cystic (because their section grossly exhibit leaf like clefts &amp; slits, they have been designated <b>phyllodes, from Greek, for "leaflike" T</b></p> <p>**Some of the phyllodesT show</p> <ul style="list-style-type: none"> <li>*increase stromal cellularity, anaplasia &amp; high mitotic activity,</li> <li>*accompanied by rapid increase in size,</li> </ul> <p style="text-align: right; margin-right: 50px;">بكون كبير كثير ال breast</p> <p>*usually with <b>invasion</b> of adjacent breast tissue.</p> <p>**Most of these T remain localized &amp; are cured by excision;</p> <p><b>2- Malignant ( high grade ) phyllodes T</b> (cystosarcoma phyllodes, may recur, but they tend to remain localized. Only the most malignant, (15% of cases), <b>metastasize</b> to distant sites</p> <p>CP : occur in women older than 60 + on mammogram appear as mixture gray + black</p>					

**Fibroadenoma**, consisting of a proliferating intralobular stroma surrounding, pushing & distorting the associated epithelium. The border is sharply delimited, by a capsule from the surrounding tissue.



Phyllodes Tumor



## Intraductal Papilloma

\*\*A benign papillary tumor growth within a duct.

\*\*Most are solitary, found within the main lactiferous ducts or sinuses.

\*\*They **present clinically** as a result of:

(1)the appearance of **serous or bloody nipple discharge**,

(2)the presence of a small **subareolar mass** a few mm inØ,

(3)**nipple retraction**.

\*\***Grossly, T** usually **solitary**, less than 1 cm in Ø, consisting of delicate, branching papillae within a dilated duct or cyst.

\*\*H/P:the multiple papillae have connective tissue stromal axis covered by cuboidal epithelial cells that are frequently **double layered** (epithelial layer overlying a myoepithelial layer).

\*\***Solitary papilloma** almost always remains **benign**, but if **multiple papillomas**, (intraductal papillomatosis), they sometimes become malignant.

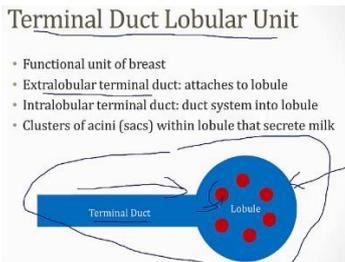
\*\***Papillary carcinoma** must be excluded; **it often lacks a myoepithelial component** & shows either **monotonous ductal epithelium or severe cytologic atypia**

## Non-Invasive In-situ Carcinoma

include:

1. Ductal carcinoma in situ, DCIS
2. Lobular carcinoma in situ, LCIS

**\*\*both types arise from cells in the terminal duct that give rise to lobules.**



\*LCIS usually expands involved lobules, whereas DCIS distorts lobules into duct like spaces

**\*\*By definition both confined by a basement membrane and do not invade into stroma or lymphovascular channels**

هون الوحدة من المستحيل تكتشف انه معها كanser لانه جوا duct بتكتشفه ب  
mammogram

## Lobular carcinoma in Situ

\*Malignant clonal proliferation of cells within ducts and lobules.

\*Cells grow in a discohesive fashion and an **acquired loss of the tumor suppressive adhesion protein E-cadherin.**

\*The term “lobular” was used to describe this lesion because the cells expand but do not distort involved spaces and, thus, the underlying lobular architecture is preserved.

## Ductal Carcinoma in Situ

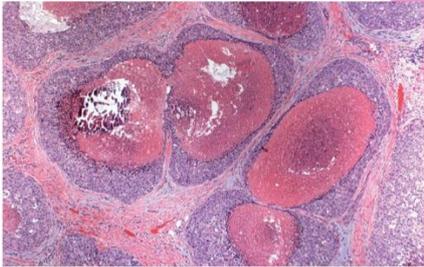
\*malignant clonal proliferation of epithelial cells within ducts and lobules.

☒DCIS has a wide variety of histologic appearances including:

1- solid

2- comedo

COMEDO DCIS , High Grade Proliferation associated with central zone of necrosis and calcification



بنتكون الخلايا السرطانية بس على الاطراف والمركز بكون necrotic

طب شو يعني كلمة comedo بالاصل؟؟

هاي دكاترة الجلدية بحكوها على الحبة يلي فيها صديد طب شو وجه الشبه؟؟

انه برضه هاي ال ducts بس تيجي تعصرها بتطلع مادة صفرا شبه الصديد

وهي عبارة necrotic tissue

>>extensive central necrosis. (The name derives from the **toothpaste-like necrotic tissue**).

>>**Frequently associated with Calcifications** detected by mammograph

3- Cribriform:

يعني في anaplastic cells بس فيها بينها مناطق فارغة وكأنها مخرمة

4- Papillary

5- and micropapillary

\*\*Ranges from low to high nuclear grade (pleomorphic).

\*\***Management DCIS**

\*The prognosis : **excellent** (97% long-term survival **after simple** mastectomy).

يعني بس بشيلوا الجزء المصاب مو كل ال breast

\*Current treatment strategies: surgery and irradiation, tamoxifen

\*Significance: adjacent invasive CA; become invasive if untreated (1/3 of cases)