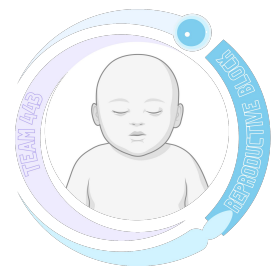
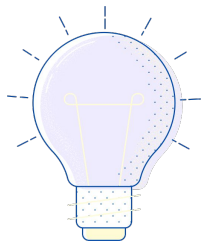




Benign Breast Diseases And Cancer





Objectives



Benign Breast Disease:

- Know the ways that benign breast conditions can clinically present.
- Know the common inflammatory conditions of breast (**mastitis and abscesses**).
- Understand the pathology of fibrocystic change.
- Know the common benign breast tumours with special emphasis on fibroadenoma and phyllodes tumour.
- Know the risk of subsequent breast cancer in women with diagnosed benign breast tissue.



Breast Cancer:

- Know the risk factors, classification, behavior and spread of breast cancer
- Know the prognostic indicators of breast carcinoma.

THIS LECTURE WAS PRESENTED BY DR.AMANY FATHADDIN & DR.HAMAD AL JAEDI



Pathology Alien Note :

Before you panic 10 pages out of this lecture is for Keywords , MCQ, And many many cases , since there is many types in this lecture practice makes perfect
Best Wishes



IF YOU WANT TO READ THE LECTURE FROM [ROBBINS](#)



IF YOU WANT TO READ THE LECTURE FROM [FIRST AID](#)



IF YOU WANT TO READ [OSMOSIS SUMMARY](#)



IF YOU WANT TO WATCH [OSMOSIS VIDEO](#) ON BENIGN TUMORS



IF YOU WANT TO WATCH [OSMOSIS VIDEO](#) ON MALIGNANT TUMORS

Editing File

Color index :

- Main text (black)
- Female Slides (Pink)
- Male Slides (Blue)
- Important (Red)
- Dr's note (Green)
- Extra Info (Grey)

Breast Inflammatory Diseases

Introduction

The functional unit of the breast is the lobule, which is supported by a specialized intralobular stroma. **Lined by myoepithelial and luminal cells.**

The inner luminal epithelial cells produce milk during lactation.

The basally located myoepithelial cells have contractile function to aid in milk ejection and also help support the basement membrane.

The ducts are conduits for milk to reach the nipple.

The size of the breast is determined primarily by interlobular stroma, which increases during puberty and involutes with age.

Each normal constituent is a source of both benign and malignant lesions

Clinical presentation

PAIN (MASTALGIA OR MASTODYNIA)

- 1- is a common symptom often related to menses, possibly due to cyclic edema and swelling.
- 2- Pain (**Non-cyclical**) **localized in a specific area is usually caused by a ruptured cyst or trauma to adipose tissue (fat necrosis) or areas of prior injury or infection, or no specific cause.**
- 3- **Almost all painful masses are benign, but for unknown reasons a small fraction of cancers (about 10%) cause pain.**

Females Slides

INFLAMMATION

- 1- causes an edematous and erythematous breast
- 2- It is rare and is most often caused by infections, which only occur with any frequency during lactation and breastfeeding.
- 3- **An important mimic of inflammation is "inflammatory" breast carcinoma**

Most common cause is HPV

NIPPLE DISCHARGE

- 1- may be normal when small in quantity and bilateral.
- 2- **The most common benign lesion producing a nipple discharge is a papilloma arising in the large ducts below the nipple.**
- 3- Discharges that are spontaneous, unilateral, and bloody are of greatest concern for malignancy.
- 4- **Milky discharge: not associated with malignancy. & Bloody or serous discharges: commonly associated with benign lesions but can rarely be due to a malignancy.**

LUMPINESS, OR A DIFFUSE NODULARITY

Females Slides

- 1- throughout the breast, is usually a result of normal glandular tissue.
- 2- When pronounced, imaging studies may help to determine whether a discrete mass is present.

PALPABLE MASSES

- 1- can arise from proliferations of stromal cells or epithelial cells and are generally detected when they are 2 to 3 cm in size.
- 2- Most (~95%) are benign; these tend to be round to oval and to have circumscribed borders. In contrast, malignant tumors usually invade across tissue planes and have irregular borders. However, because some cancers grow deceptively as circumscribed masses, all palpable masses require evaluation.

GYNECOMASTIA

Females Slides

- 1- is the only common breast symptom in males.
- 2- There is an increase in both stroma and epithelial cells resulting from an imbalance between estrogens, which stimulate breast tissue, and androgens, which counteract these effects.

Benign Breast Lesions

Mammographic screening

- Mammographic screening was introduced in the 1980s as a means to detect small/early, non-palpable, asymptomatic breast carcinomas **before metastatic spread has occurred.**
 - **Mammography has met this promise, as the average size of invasive carcinomas detected by mammography is about 1 cm (significantly smaller than cancers identified by palpation), and only 15% will have metastasized to regional lymph nodes at the time of diagnosis**
- Mammographic screening Generally recommended to start after age 40.
- **The principal mammographic findings of breast carcinoma are densities/masses and calcifications.**

DENSITIES (MASS)

- Most tumors appear radiologically denser than the normal breast.
- Fibroadenomas, cysts etc. can also present as densities.

CALCIFICATIONS

- 1-Calcium gets deposited in secretions, necrotic debris, or hyalinized stroma.
- 2-It can be seen in benign and malignant conditions.
- 3-**Calcifications in malignancy are usually small, irregular, numerous, and clustered.**
- 4- **Ductal carcinoma in situ (DCIS) is most commonly detected as mammographic calcifications. Mammographic screening has increased the diagnosis of DCIS. So whenever there is classification we should be evaluated by biopsy to exclude DCIS and invasive carcinoma.**

Benign Breast lesions

<p>Inflammatory lesions</p>	<ul style="list-style-type: none"> • Acute mastitis: Staphylococcus aureus infection is the most common organism • Periductal mastitis • Mammary duct ectasia → dilated ducts disease ★ Fat necrosis: It is usually due to a mechanical or surgical trauma. • Lymphocytic mastopathy (sclerosing lymphocytic lobulitis): It is seen in diabetic women. • Granulomatous mastitis: It can be idiopathic, due to sarcoidosis or TB.
<p>Benign epithelial lesions</p>	<ul style="list-style-type: none"> - Non proliferative breast changes (fibrocystic changes) - Proliferative breast disease without atypia - Proliferative breast disease with atypia / Atypical hyperplasia
<p>Benign stromal lesions</p>	<ul style="list-style-type: none"> - Fibroadenoma - Benign phyllodes tumors

Breast Inflammatory diseases

Acute Mastitis

Definition

- Inflammatory diseases of the breast are rare and may be caused by infections, autoimmune disease, or foreign body-type reactions .
- The only infectious agent to cause breast disease with any frequency is **Staphylococcus aureus**
- Almost all cases of acute mastitis occur during the first month of breastfeeding.

Pathogenesis:

Females Slides

01

Entry

typically Staph aureus gains entry via fissures in nipple skin during the first weeks of breastfeeding.

02

Abscesses

The invading organisms may lead to the formation of "lactational abscesses," collections of neutrophils and associated bacteria in fibroadipose tissue.

03

Complication

If untreated, tissue necrosis may lead to the appearance of fistula /first month of associated bacteria in tracks opening onto breastfeeding. fibroadipose tissue. the skin.

Symptoms include:

erythema and edema, often accompanied by pain and focal tenderness.

Fever is often present.

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

Most cases are treated adequately with antibiotics and continued expression of milk. Rarely, surgical incision and drainage is required.

Periductal Mastitis

This condition is not associated with lactation.

However, there is a strong association with cigarette smoking.

Benign epithelial lesions

Females Slides

Benign epithelial lesions of breast are divided into 3 basic types :

Benign changes are divided into three groups each associated with a different degree of breast cancer risk:

NON-PROLIFERATIVE DISEASE

is not associated with an increased risk of breast cancer.

PROLIFERATIVE DISEASE WITHOUT ATYPIA

encompasses polyclonal hyperplasias that are associated with a slightly increased risk of breast cancer.

PROLIFERATIVE DISEASE WITH ATYPIA

includes monoclonal "precancers" that are associated with a modest increase in the risk of breast cancer in both breasts; overall, 13% to 17% of women with these lesions develop breast carcinoma.

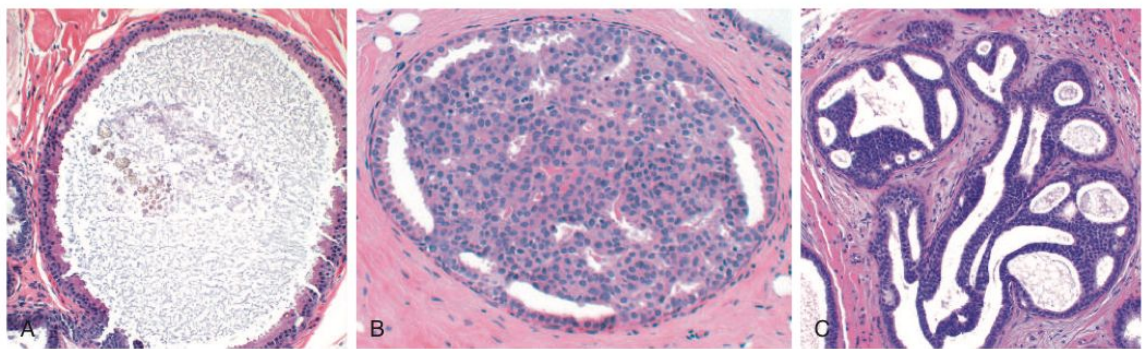


Fig. 19.25 Benign epithelial breast disease. (A) Nonproliferative disease. An apocrine cyst is shown that is a common feature of nonproliferative breast disease. (B) Proliferative breast disease is characterized by increased numbers of epithelial cells, as in this example of epithelial hyperplasia. (C) Proliferative breast disease with atypia. The proliferating epithelial cells are monomorphic in appearance and pile up to form abnormal architectural structures.

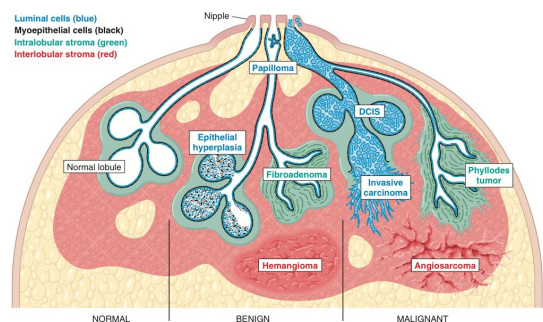
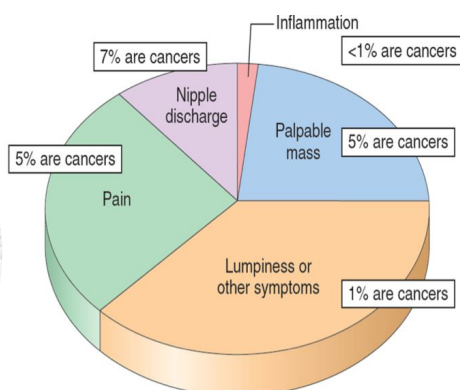


Fig. 19.22 Origins of breast disorders. Benign epithelial lesions include intraductal papillomas that grow in sinuses below the nipple and epithelial hyperplasia that arises in lobules. Malignant epithelial lesions are mainly breast carcinomas, which may remain in situ or invade into the breast and spread by metastasis. Specialized intralobular stroma (green) cells may give rise to fibroadenomas and phyllodes tumors, whereas interlobular stroma (green) may give rise to a variety of rare benign and malignant tumors.

Non proliferative Breast Changes (Fibrocystic changes/disease)

Definition

- Most common disorder of the breast.
- **No increased risk for cancer.**
- Produce palpable masses, mammographic densities, nipple discharge. It may also present with cyclical pain.
- Age: 20–55 years, decreases progressively after menopause.
- The cause is not known. Thought to be due to caused by hormonal imbalances. (increase estrogen to progesterone ratio) , Cyst have blue-domed appearance on gross

Histology

IMPORTANT

consists of three major morphologic changes

It is termed "non-proliferative" because the lesions contain single layers of epithelial cells.

Cysts with apocrine metaplasia

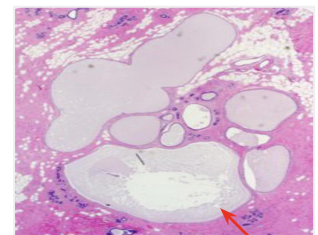
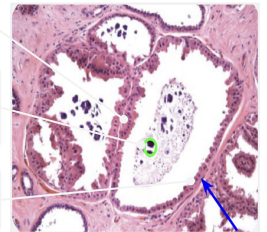
- Simple Cysts are lined by a layer of luminal benign flattened to columnar epithelium cells, that often undergo apocrine metaplasia.
- With focal apocrine metaplasia: cells become large and have abundant eosinophilic cytoplasm.
- Apocrine secretions may calcify within cyst and be detected by mammography.

Bulging

Calcifications
You have to take biopsy

Apocrine metaplasia

Diagnosis : fibrocystic changes



Fibrosis (fibrocystic changes)

- The cysts can rupture and cause chronic inflammation and fibrosis in response to the spilled debris, may produce palpable nodularity of the breast (so-called "fibrocystic changes").
- Fibrosis contribute to the palpable firmness of the breast.

Adenosis

- An increase in the number of acini per lobule.
- can also be seen in pregnancy.

Proliferative Disease Without Atypia

Definition

- Rarely form palpable masses.
- Incidental finding; detected as small mammographic densities.
- ★ Risk for cancer is 1.5 – 2 times normal.
- Include the following entities:

Epithelial hyperplasia

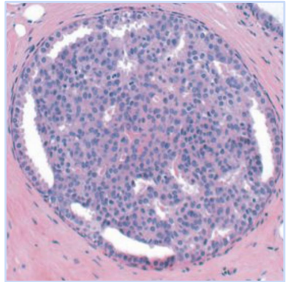
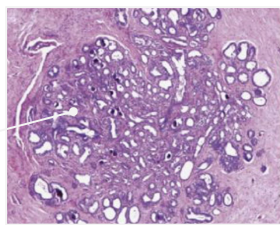
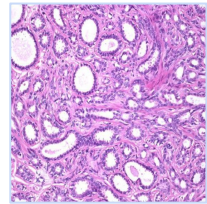
Sclerosing adenosis

Complex sclerosing lesions/radial scar

Proliferative variant of fibrocystic disease.

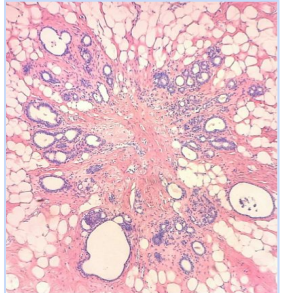
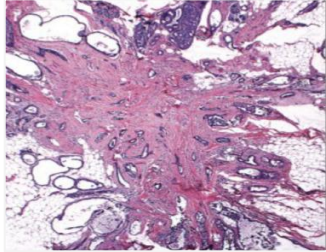
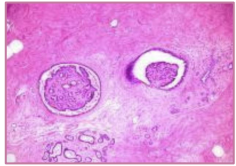
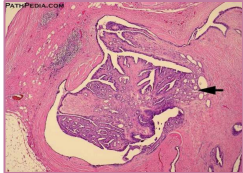
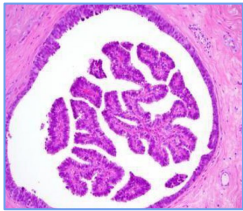
Papillomas

Types

Type	Definition	Microscopy
<p>IMPORTANT</p> <p>Epithelial Hyperplasia (usual ductal hyperplasia)</p>	<ul style="list-style-type: none"> • The normal breast has a 2 layers of cells: <ul style="list-style-type: none"> ○ Epithelial cells ○ Myoepithelial cells • Thus, epithelial hyperplasia is defined as the presence of more than 2 layers. • Hyperplasia can range from mild, moderate to severe/florid (fully developed). • When it is seen in fibrocystic disease: it is called as proliferative type/variant of fibrocystic disease. 	<ul style="list-style-type: none"> • Both epithelial and myoepithelial cells proliferate. • It can be seen in the ducts and the lobules. 
<p>IMPORTANT</p> <p>Sclerosing Adenosis</p>	<ul style="list-style-type: none"> • It is commonly seen as an incidental microscopic finding but may occasionally present as a palpable mass that is mistaken clinically for cancer. • Calcifications are commonly seen in the lesion, so even on mammography it can mimic cancer. • It is almost always associated with other forms of fibrocystic change. 	<ul style="list-style-type: none"> • Adenosis and stromal fibrosis (sclerosing) in the lobule which leads to compression and distortion of the lobule. <p>Increased numbers of glands with fibrous tissue</p>  

Proliferative Disease Without Atypia

Types

Type	Definition	Microscopy
<p>IMPORTANT</p> <p>Complex Sclerosing Lesion (Radial Scar)</p>	<ul style="list-style-type: none"> • Radial scars are stellate lesions characterized by a central Nidus of entrapped glands in a dense fibrotic or hyalinized stroma. • The nidus is surrounded by radiating arms of epithelium with varying degrees of cyst formation and hyperplasia. • The word "scar" refers to the morphologic appearance, and not a prior inflammation, trauma or surgery. • They typically present as an irregular mammograms density closely mimic an invasive carcinoma both mammographically and grossly (clinically). 	 
<p>IMPORTANT</p> <p>Intraductal Papillomas</p>	<ul style="list-style-type: none"> • It is a papillary tumor that arises from the ductal epithelium. • It is more common in the large lactiferous ducts (present in the central part of the breast at the nipple) but can also occur in the small ducts in any quadrant of the breast. 	  
Large Duct Papillomas (central papillomas)		
<ul style="list-style-type: none"> • usually solitary and situated in the lactiferous duct at the nipple. • Patients present with bloody nipple discharge and sometimes a subareolar palpable mass. 		
Small Duct Papilloma		
<ul style="list-style-type: none"> • commonly multiple and located deeper within the ductal system. • have been shown to increase the risk of subsequent carcinoma. 		

Proliferative Breast Disease With Atypia (Atypical hyperplasia)

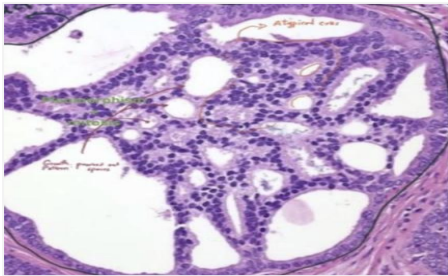
Definition

★ Risk for cancer is 4-5 times normal.

- Atypical hyperplasia is a cellular proliferation resembling ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) but lacking sufficient qualitative or quantitative features for a diagnosis of carcinoma in situ.
- Atypical hyperplasia has some of the architectural and cytologic features of carcinoma in situ but lack the complete criteria for that diagnosis and is categorized as ductal or lobular in type

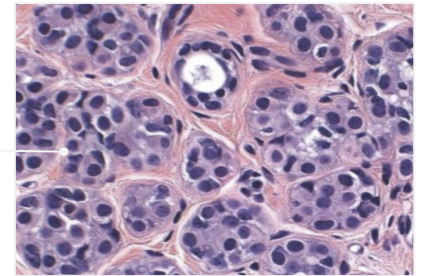
Include two entities

Atypical ductal hyperplasia



Atypical Lobular Hyperplasia

Proliferation within lobules



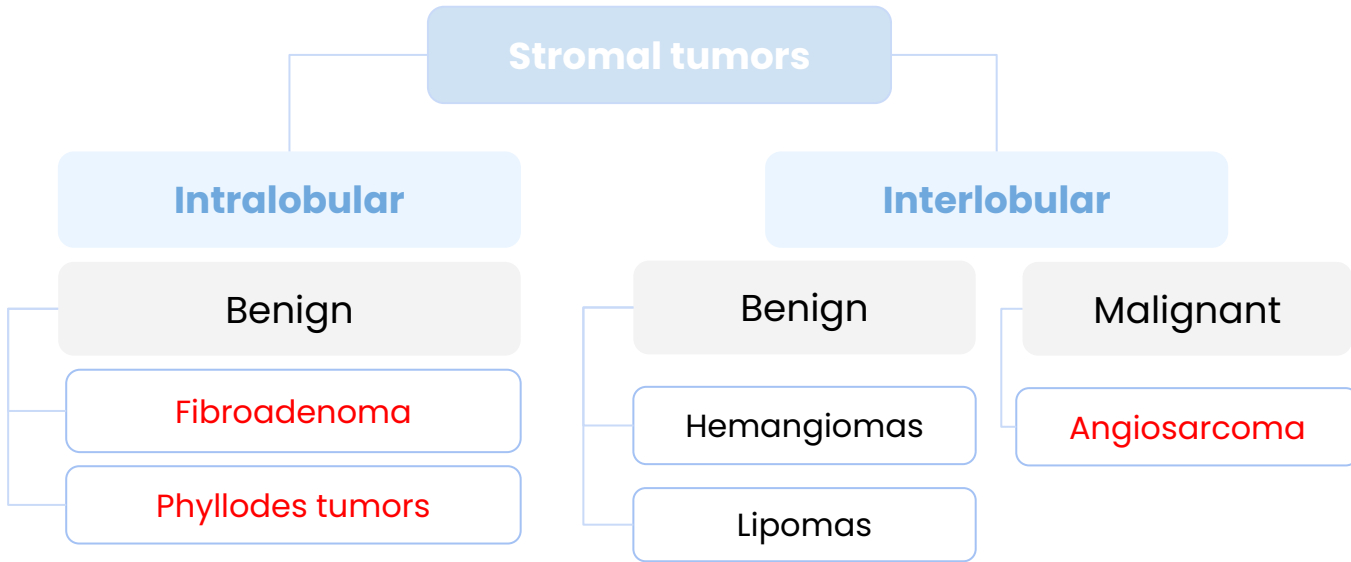
Pathologic lesion	Relative risk of development of invasive carcinoma	comments
Non-proliferative breast changes (Fibrocystic changes)	do not have an increased risk.	Fibrocystic disease
Proliferative disease without atypia	1.5 to 2 times normal	a) Epithelial hyperplasia b) Sclerosing adenosis c) Complex sclerosing lesions/radial scar d) Papillomas e) Proliferative fibrocystic disease.
Proliferative disease with atypia	4.0 to 5.0 times normal	a) ADH b) ALH/ ALD
Carcinoma in situ	8.0 to 10.0 times normal	a) DCIS b) LCIS

Introduction

Females Slides

BENIGN STROMAL LESIONS

Types	Morphology	Malignancy
<p>Tumors derived from intralobular stroma are comprised of both stromal cells and epithelial cells (i.e., they are "biphasic"), as the neoplastic proliferation of specialized lobular fibroblasts also stimulates reactive proliferation of lobular epithelial cells, Two types:</p> <ol style="list-style-type: none"> fibroadenoma phyllodes tumors. 	<p>Lesions of interlobular stroma are monophasic (only comprised of mesenchymal cells) and include benign soft tissue tumors found elsewhere in the body, such as hemangiomas and lipomas.</p>	<p>The only malignancy derived from interlobular stromal cells of note is angiosarcoma, which may arise in the breast after local radiotherapy.</p>



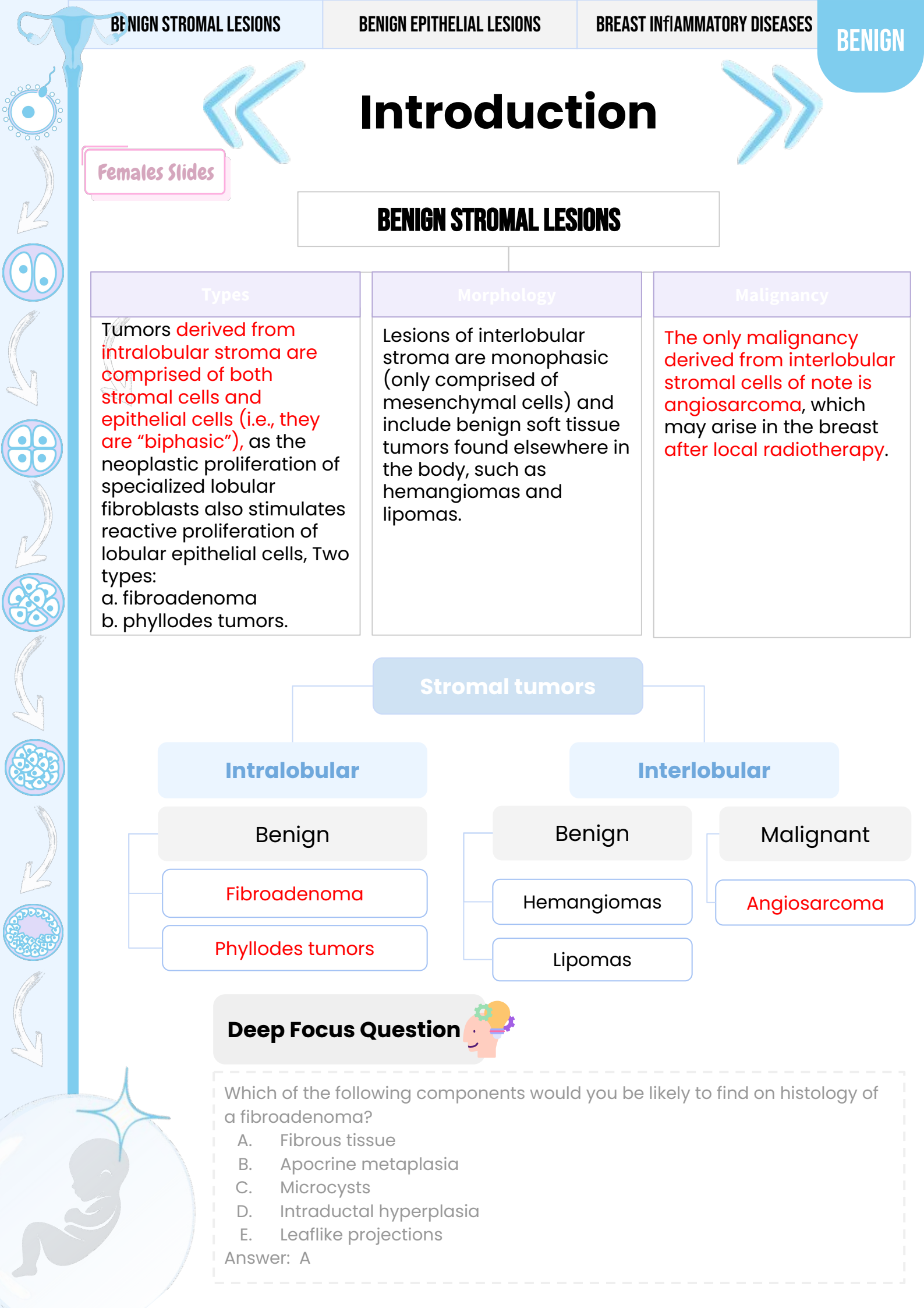
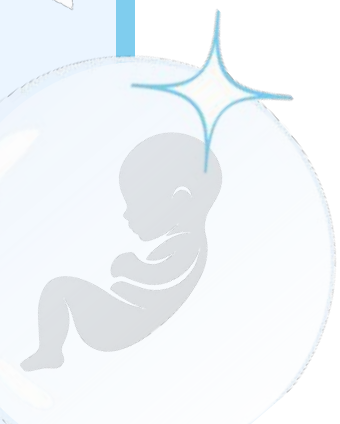
Deep Focus Question



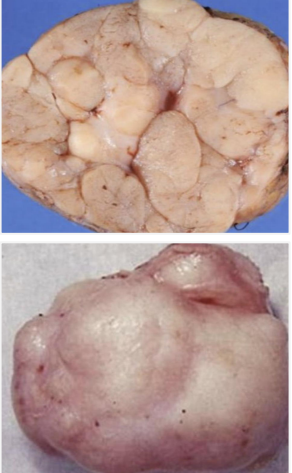
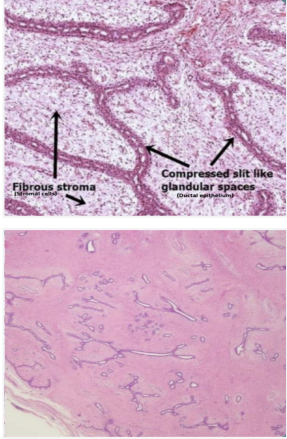
Which of the following components would you be likely to find on histology of a fibroadenoma?

- A. Fibrous tissue
- B. Apocrine metaplasia
- C. Microcysts
- D. Intraductal hyperplasia
- E. Leaflike projections


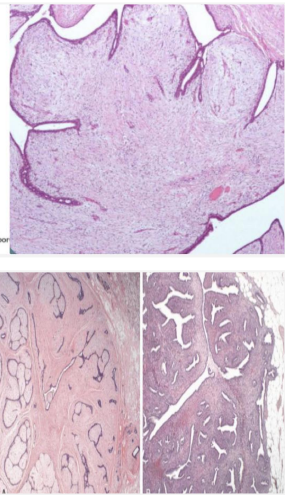
Answer: A



Fibroadenoma (FA)

Overview	<ul style="list-style-type: none"> The most common benign tumor of the female breast. It is composed of benign proliferation of both epithelial and stromal elements. Any age, most common before age 30. 		
Clinical Presentation	<ul style="list-style-type: none"> Firm, mobile lump ("breast mouse"). It may increase in size during pregnancy. It may stop growing and regress after menopause. "Estrogen sensitive" The tumor is usually solitary but may be multiple and involve both breasts. The tumor is completely benign and almost never malignant. 		
Treatment	lumpectomy (only the lump is removed).		
<div style="border: 2px solid red; padding: 5px; display: inline-block; transform: rotate(-2deg); color: white; font-weight: bold;">IMPORTANT</div>	Grossly	<ul style="list-style-type: none"> spherical nodules, sharply demarcated and circumscribed from the surrounding breast tissue and freely movable so it can be shelled out. The size varies between 1 cm to 10 cm in diameter. The cut surface is pearl-white and whorled. 	
Morphology	Histology	<ul style="list-style-type: none"> tumor is composed of a mixture of ducts and fibrous connective tissue (fibromyxoid) The lesion consists of a proliferation of intralobular stroma surrounding and often pushing and distorting the associated epithelium. The border is sharply delimited. (non invasive). 	

Benign Phyllodes Tumor

Overview	<ul style="list-style-type: none"> Phyllodes tumors can occur at any age, but most present in the 40s and 50s, that is 10 to 20 years later than the average presentation of a fibroadenoma. These tumors are much less common than fibroadenomas 		
Clinical Presentation	<ul style="list-style-type: none"> Most present as large palpable masses (usually 3 to 4 cm in diameter). sometimes 10-20 cm(1) "may reach 25 cm" 		
Classifications	HIGH GRADE (MALIGNANT) PHYLLODES TUMOR	LOW-GRADE (BORDERLINE) PHYLLODES TUMORS	BENIGN PHYLLODES TUMORS
	<p>they are uncommon and they behave aggressively with frequent local recurrences and can have distant metastases to lung, bone and brain (CNS). They have better prognosis than invasive ductal carcinoma</p>	<p>they tend to recur locally and a rarely metastasize</p>	<p>most (75%) phyllodes tumors are benign</p>
 Morphology	Histology	<ul style="list-style-type: none"> ★ They are fibro-epithelial tumors, have a leaf like pattern and a cellular stroma "phyllodes" Greek for "leaf-like" 	

Introduction to Breast Carcinoma

Introduction

- The most common malignancy (excluding non melanoma skin cancer) and causes the majority of cancer deaths of women.
- Carcinoma of the breast is one of the most common cancer in women
- Women by the age of 90, have a 1 in 8 chance of developing breast cancer in US.
- Since the mid-1980's the mortality rate has dropped from 30% to less than 20%. The decrease is attributed to both improved screening, which detects some cancers before they have metastasized, and more effective systemic treatment.
- Mammographic screening has dramatically increased the detection of small invasive cancers.
- DCIS by itself is almost exclusively detected by mammography, so the incidence of DCIS is increased with the use of mammography. Therefore number of women with invasive/advanced cancer is markedly decreased
- The mortality rate have started to decline. Currently only 20% of women with breast cancer are expected to die of the disease.
- The most common location is in the upper outer quadrant (50%), followed by the central portion (20%). About 4% of women have bilateral primary tumors or sequential lesions in the same breast.

Table 19.6 Factors Associated With Development of Invasive Carcinoma

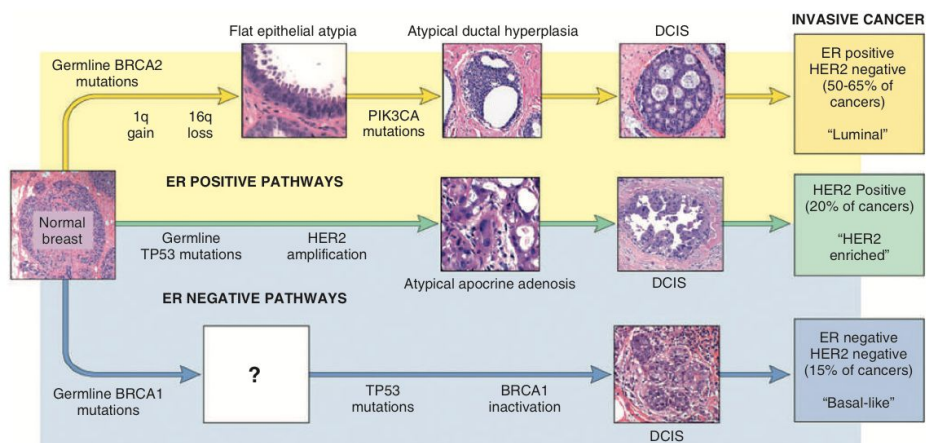
Factor	Relative Risk ^a	Absolute Lifetime Risk ^b
Women with no risk factors	1.0	3%
First-degree relative(s) with breast cancer ^c	1.2-9.0	4%-30%
Germline tumor suppressor gene mutation (e.g., BRCA1 mutation)	2.0-45.0	6% to >90%
Menstrual History		
Age at menarche <12 years	1.3	4%
Age at menopause >55 years	1.5-2.0	5%-6%
Pregnancy		
First live birth <20 years (protective)	0.5	1.6%
First live birth 20-35 years	1.5-2.0	5%-6%
First live birth >35 years	2.0-3.0	6%-10%
Never pregnant (nulliparous)	3.0	10%
Breast-feeding (slightly protective)	0.8	2.6%
Benign Breast Disease		
Proliferative disease without atypia	1.5-2.0	5%-6%
Proliferative disease with atypia (ALH and ADH)	4.0-5.0	13%-17%
Carcinoma in situ (ductal or lobular)	8.0-10.0	25%-30%
Ionizing radiation	1.1-1.4	3.6%-4.6%
Mammographic density	3.0-7.0	10%-23%
Postmenopausal obesity and weight gain	1.1-3.0	3.6%-10%
Postmenopausal hormone replacement	1.1-3.0	3.6%-10%
Alcohol consumption	1.1-1.4	3.6%-4.6%
Alcohol consumption	1.1-1.4	3.6%-4.6%

^aRelative risk is the likelihood of developing cancer compared to a woman with no risk factors—whose relative risk is 1.0. Absolute lifetime risk is the fraction of women expected to develop invasive carcinoma without a risk-reducing intervention. For women with no risk factors, there is about a 3% chance of developing invasive breast cancer. ^bThe most common family history is a mother who developed cancer after menopause. This history does not increase the risk of her daughters.

Table 19.7 Summary of the Major Biologic Types of Breast Cancer

Feature	ER Positive/HER2 Negative	HER2 Positive (ER Positive or Negative)	Triple Negative (ER, PR, and HER2 Negative)
Overall frequency	50%-65%	20%	15%
Typical patient groups	Older women; men; cancers detected by screening; germline BRCA2 mutation carriers	Young women; germline TP53 mutation carriers	Young women; germline BRCA1 mutation carriers
Ethnicity			
European/American	70%	18%	12%
African/American	57%	27%	16%
Hispanic	60%	24%	16%
Asian/Pacific Islander	63%	26%	11%
Grade	Mainly grade 1 and 2	Mainly grade 2 and 3	Mainly grade 3
Complete response to chemotherapy (10%)	Low grade (<10%), higher grade (>30%)	ER positive (15%), ER negative (>30%)	30%
Timing of relapse	May be late (>10 years after diagnosis)	Usually short (<10 years after diagnosis)	Usually short (<8 years after diagnosis)
Metastatic sites	Bone (70%), viscera (25%), brain (<10%)	Bone (40%), viscera (45%), brain (30%)	Bone (40%), viscera (35%), brain (25%)
Similar group defined by mRNA profiling	Luminal A (low grade), luminal B (high grade)	Luminal B (ER positive), HER2-enriched (ER negative)	Basal-like
Common special histologic types	Lobular, tubular, mucinous, papillary	Apocrine, micropapillary	Carcinoma with medullary features
Common somatic mutations	PIK3CA (40%), TP53 (26%)	TP53 (75%), PIK3CA (40%)	TP53 (85%)

PIK3CA encodes phosphoinositide 3-kinase (PI3K).



Extra Pic from Robbins

Introduction to Breast Carcinoma

Classification

IMPORTANT

Females Slides

First system

- Almost all breast malignancies are adenocarcinomas (>95%). In the most clinically useful classification system, breast cancers are divided based on the expression of:
 - hormone receptors: estrogen receptor (ER) and progesterone receptor (PR)
 - human epidermal growth factor receptor 2 (HER2, also known as ERBB2)
- into three major groups:

	ER positive	HER2 positive	Triple negative
ER	+	+/-	- (Also PR negative)
HER2	-	+	-
Prevalence	50%–65% of cancers	10%–20% of cancers	10%–20% of cancers / poor prognosis

These three groups show striking differences in patient characteristics, pathologic features, treatment response, metastatic patterns, time to relapse, and outcome .
Within each group are additional histologic subtypes

Second system

An alternative classification system with substantial overlap relies on gene expression profiling. This system, which is currently used mainly in the context of clinical research, divides breast cancers into four major types:

Luminal A	Luminal B
The majority are <ul style="list-style-type: none"> • lower-grade • ER-positive • HER2 negative 	The majority are <ul style="list-style-type: none"> • higher-grade • ER-positive • may be HER2 positive
HER2-enriched	Basal-like
The majority <ul style="list-style-type: none"> • overexpress HER2 • do not express ER 	The majority by gene expression profiling resemble basally located myoepithelial cells and are ER-negative, HER2-negative

IMPORTANT

Introduction to Breast Carcinoma

Risk factors

- The etiology of breast cancer in most women is unknown but most likely is due to a combination of genetic, hormonal and environmental risk factors.
- The major risk factors are hormones and genetics i.e. family history.
- Breast carcinomas can, therefore, be divided into sporadic cases, possibly related to hormonal exposure, and hereditary cases, associated with a family history or germ-line mutations.

Hereditary breast cancer

males Slides

Sporadic breast cancer

- A family history of breast cancer in a first-degree relative.
- About 25% of familial cancers (or around 3% of all breast cancers) can be attributed to two autosomal-dominant genes: BRCA1 and BRCA2.

- The major risk factors for sporadic breast cancer are related to exposure to hormones, gender, age at menarche and menopause, reproductive history, breast-feeding, and exogenous estrogens.
- The majority of these cancers occur in postmenopausal women and in cases of overexpression to estrogen.

AGE & GENDER

- ❖ Rare in women < age 25, except in familial forms.
- ❖ **The majority 75%** of women with breast cancer are > age 50
- ❖ Increases in incidence rapidly after age 30
- ❖ Incidence in men is only 1% of that in women.
- ❖ it increases the incidence in women.

ESTROGEN EXPOSURE / REPRODUCTIVE HISTORY

- ❖ Factors associated with exposure to increased levels of estrogen have been shown to increase a woman's risk for breast cancer. These factors include:
 - Early age at menarche: **the younger the age at menarche, the higher her risk of breast cancer.**
 - Late age at menopause.**
 - Nulliparity & **absence of breastfeeding**
 - Late age at first childbirth / older age at first pregnancy: the earlier a woman has her first birth, the lower her lifetime risk for breast cancer. A woman who has her first birth after 30 years has an increased risk.**
 - Also postmenopausal hormone replacement slightly increases the risk.**
- ❖ All are associated with increased risk, probably because each increases the exposure of "at-risk" breast epithelial cells to estrogenic stimulation.

IONIZING RADIATION

- ❖ Radiation to the chest increases the risk of breast cancer if exposure occurs while the breast is still developing.
- ❖ Higher rate of breast cancer.

Introduction to Breast Carcinoma

Risk factors

FAMILY HISTORY

First-degree relative with breast cancer:

- ❖ The greatest risk is for individuals with multiple affected first-degree relatives with early-onset breast cancer
- ❖ Women with history of cancer in first degree relative (mother, sister, aunt or daughter) are at higher risk of breast cancer. The risk increases with the number of affected first degree relatives.
- ❖ At least two genes that predispose to breast cancer have been identified—BRCA 1 and 2
- ❖ Majority of cancers occur in women without such history.

RACE / ETHNICITY & GEOGRAPHIC FACTORS

- ❖ incidence of breast cancer is lower in African American women.
- ❖ Generally Caucasians have the highest rate of breast cancers.
- ❖ The highest rate of breast cancer is in women of European descent, largely because of a higher incidence of ER-positive cancers
- ❖ Breast cancer is more common in Western industrialized countries than in developing countries.
- ❖ Significant differences in the incidence and mortality rates of breast cancer have been reported in various countries.
- ❖ The risk is significantly higher in the Americas and Europe than in Asia and Africa. Diet, reproductive patterns, and breastfeeding practices are thought to be involved.

OTHERS

- ❖ History of breast cancer: Women who have had a breast cancer or have cancer in one breast are at increased risk of developing a second primary breast cancer.
- ❖ History of other cancers: women who have a history of ovarian or endometrial cancer are at high risk.
- ❖ Certain breast diseases: As noted previously women with certain types of benign breast diseases are at risk.
- ❖ Dietary factors e.g. high fat intake and excessive alcohol consumption also have been implicated as risk factors.
- ❖ Postmenopausal obesity may play a role
- ❖ mammographic density
- ❖ postmenopausal hormone replacement
- ❖ Exercise: some studies showed decreased risk with exercise.
- ❖ Breastfeeding: the longer the women breast fed, the lower the risk.
- ❖ Environmental toxins: pesticides.
- ❖ Tobacco: Not associated with breast cancer, but associated with the development of periductal mastitis or subareolar abscesses.

Introduction to Breast Carcinoma

Morphological classification

Breast cancers are classified morphologically according to whether they have penetrated the basement membrane. Those that remain within this boundary are termed **in situ carcinomas**, and those that have spread beyond it are designated invasive carcinomas. Almost all (majority) are adenocarcinoma

Morphological classification

Carcinoma in Situ

This is an epithelial proliferation that is **still confined to the TDLU** and has not invaded beyond the basement membrane. It does not invade into stroma or lymphovascular channels, and is therefore incapable of metastasis

Ductal carcinoma in situ (DCIS) or intraductal carcinoma (80%).

Lobular carcinoma in situ (20%).

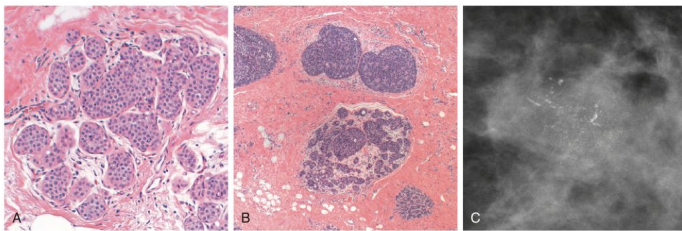


Fig. 19.28 Carcinoma in situ. (A) Lobular carcinoma in situ (LCIS). (B) Ductal carcinoma in situ (DCIS). DCIS partially involves the lobule in the lower half of this photo and has completely effaced the upper lobules, producing a ductlike appearance. (C) Mammographic detection of calcifications associated with DCIS.



Invasive Breast Carcinoma

Invasive breast carcinoma is a tumor that has **extended across the basement membrane**. This permits access to lymphatics and vessels therefore the potential to metastasize.

Invasive ductal carcinoma: 70% to 80%. (NOS; not otherwise specified, include all carcinoma that are not of special type)

Invasive lobular carcinoma: ~10% to 15%.

Carcinoma with medullary features: ~5%, 2%

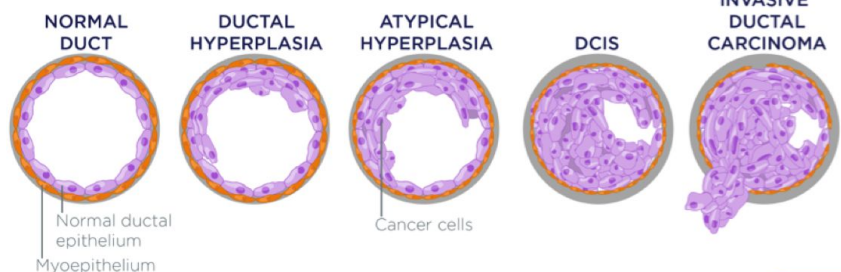
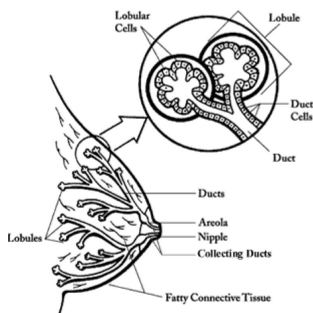
Mucinous carcinoma (colloid carcinoma): ~5%, 2%

Tubular carcinoma: ~5%. ~6%

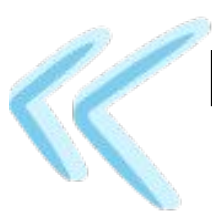
Other types

Papillary 1%

Metaplastic Carcinoma 1%



Ductal carcinoma in situ (DCIS)



Overview

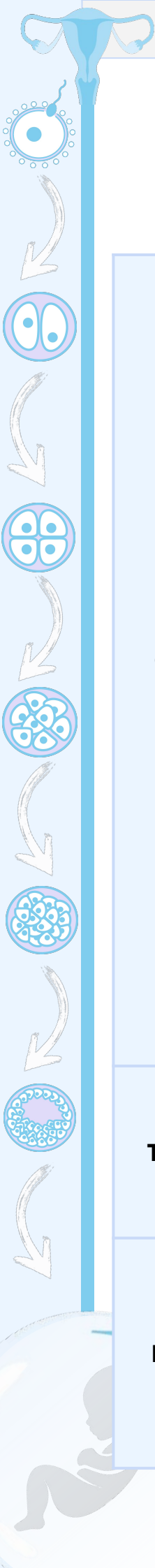
- ❖ Non-invasive proliferation of malignant cells within the duct system without breaching the underlying basement membrane
- ❖ DCIS constitutes only 5% of breast cancers in unscreened populations but up to 30% in screened populations.
- ❖ Largely because of the ability of the mammography to detect calcifications
- ❖ They have a very high risk of developing a subsequent invasive carcinoma.
- ❖ The tumor distends and distorts the ducts.
- ❖ Age range: same age range of invasive breast carcinoma.
- ❖ Often multifocal: malignant cells can spread widely through the ductal system without breaching the basement membrane
- ❖ Women with DCIS are at risk of recurrent DCIS following treatment.
- ❖ DCIS frequently shows micro-calcifications on mammography. Mammography is a very sensitive diagnostic procedure for detecting DCIS since majority of DCIS are not palpable. Less frequently they can present as a mammographic density or a vaguely palpable mass or nipple discharge.
- ❖ Because of mammography there has been a marked increase in the detection and diagnosis of DCIS in the last two decades.

Treatment

- ❖ **Surgery (Wide local excision) and irradiation to eradicate the lesions**
- ❖ mastectomy
- ❖ anti-estrogenic such as tamoxifen which also reduces the risk of recurrence in ER-positive DCIS

Prognosis

- ❖ Very High risk of developing subsequent invasive carcinoma
- ❖ Excellent prognosis with greater than 97% long-term survival.
- ❖ If untreated, DCIS progresses to invasive cancer in roughly one-third of cases, usually in the same breast quadrant



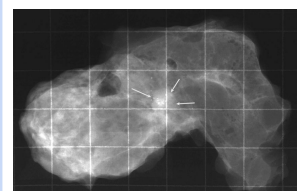
Ductal carcinoma in situ (DCIS)

IMPORTANT

Morphology

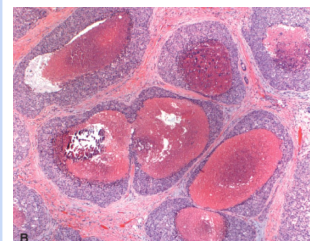
Grossly

- Calcifications frequently are associated with DCI

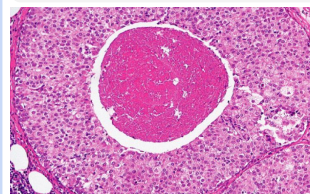


Histology

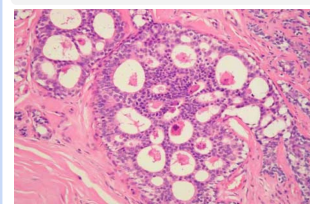
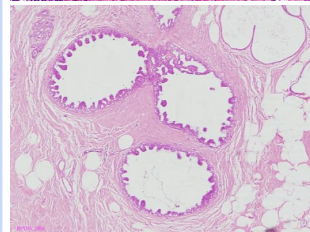
- ❖ Variety of histological patterns / subtypes:
 - A. Solid (cells fill spaces)
 - B. Comedo (central necrosis)
 - C. Cribriform (cells arranged around "punched-out" spaces)
 - D. Papillary
 - E. micropapillary
 - F. "clinging: types.
- ❖ Nuclear appearance ranges from bland to monotonous (low nuclear grade) to pleomorphic (high nuclear grade)
- ❖ The distinctive Comedo is characterised by; extensive large central necrosis, resulting in toothpaste-like necrotic tissue with calcified debris
- ❖ This type (Comedo) of DCIS is most frequently detected as radiologic calcifications. Less commonly, the surrounding desmoplastic response results in an ill-defined palpable mass or a mammographic density.
- ❖ Cribriform DCIS comprises cells forming round, regular "cookie cutter" spaces. The lumens are often filled with calcifying secretory material.



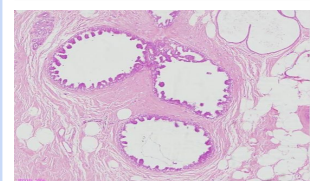
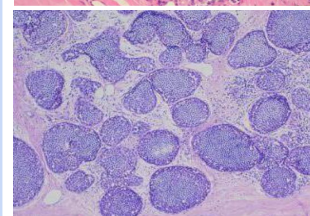
Comedo DCIS: is characterized by large central zones of necrosis with calcified debris



Micropapillary DCIS



Solid Pattern



Micropapillary Pattern

Clinical Behavior

males Slides

- ❖ may vary depending on the subtype and the grade
 - A. Comedocarcinoma has essentially a 100% chance of becoming invasive if left untreated.
 - B. Pure cribriform/micropapillary carries only a 30% chance of becoming invasive carcinoma.

Paget's disease

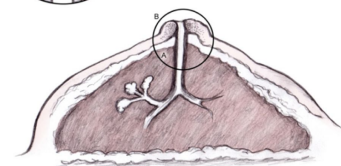
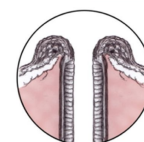
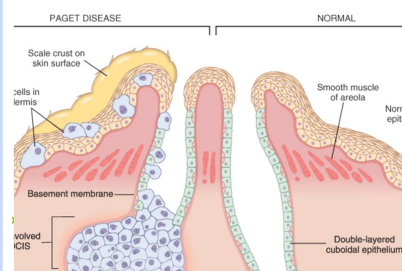
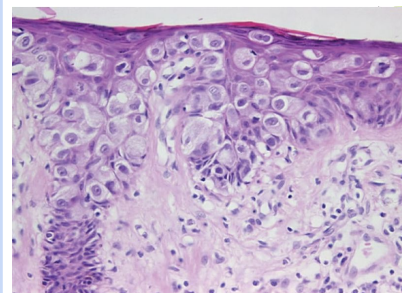
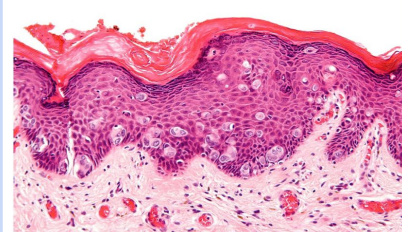
Overview

- ❖ A rare type of cancer of the breasts cancer
- ❖ Paget disease of the nipple is **caused by the extension of DCIS up the lactiferous ducts and into the contiguous skin of the nipple, producing a unilateral crusting exudate over the nipple and areolar skin.**
- ❖ Paget's disease of the nipple stems from in situ extension of an underlying carcinoma which **produces palpable mass that can be seen in 50% of women with Paget disease.**

IMPORTANT

Morphology

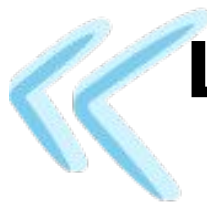
- ❖ **Red scaly eczematous lesion on the nipple and the surrounding areola**
- ❖ **The histological hallmark of the nipple is the infiltration of the epidermis by large neoplastic ductal cells with abundant cytoplasm, pleomorphic nuclei and prominent nucleoli.**
- ❖ **The cells usually stain positively for mucin.**
- ❖ It extends from DCIS within the ductal system into nipple skin **without crossing the basement membrane**
- ❖ Paget's disease may be subtle or appear as an eroded and weeping erythematous eruption. **Pruritus is common and it might be mistaken for eczema.**
- ❖ Malignant cells are called Paget cells and are found scattered in the epidermis.



Prognosis

- ❖ The prognosis of the carcinoma of origin is affected by the presence of Paget's disease and is determined by other factors

Lobular carcinoma in situ (LCIS)



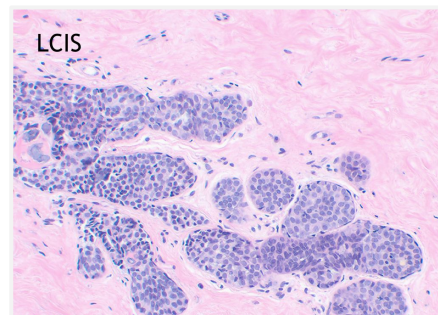
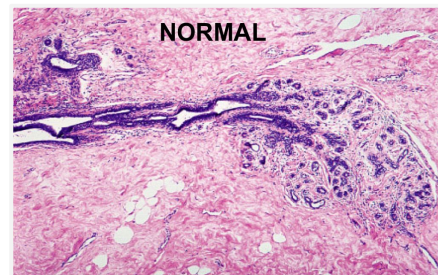
Overview

- ❖ Is virtually always an incidental finding in breast biopsies performed for another reason ,unlike DCIS, it is only rarely associated with calcifications.
- ❖ does not form a palpable mass and cannot be detected clinically on palpation or on gross pathological examination
- ❖ uncommon.
- ❖ tends to be multicentric and bilateral and therefore subsequent carcinomas can occur both breasts.
- ❖ Microcalcifications in LCIS are infrequent and so mammography is not useful for detection.

Microscopy



- ❖ Has a uniform appearance.
- ❖ The cells are monomorphic : With bland, round nuclei, and are found in loosely cohesive clusters within lobules
- ❖ Small rounded cells, the cells fill and expand the acini of lobules, but the underlying lobular architecture can still be recognized.



Prognosis

- Approximately one-half of women with LCIS eventually develop invasive carcinoma. within 20 years of diagnosis. The invasive cancer that develops is usually lobular (but can be ductal too):
 - A. Unlike DCIS, invasive carcinomas following diagnosis of LCIS may arise in either breast 2/3 in the same a breast and 1/3 in the contralateral breast.
 - B. LCIS is both a marker of an increased risk of carcinoma in both breasts and a direct precursor of some cancers.

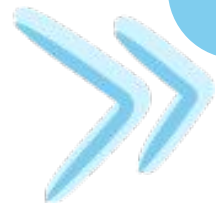
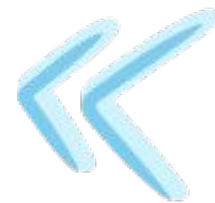
Treatment

- Current treatment options include close clinical and radiologic follow-up
- Chemoprevention with tamoxifen OR Less commonly, bilateral prophylactic mastectomy.

Females Slides



Invasive Ductal Carcinoma



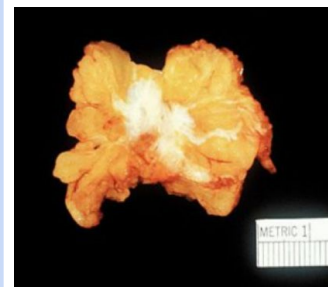
Overview

- ❖ Invasive ductal carcinoma (NOS) is term for all carcinomas that cannot be subclassified into one of the specialised types.
- ❖ A majority (70%-80%) of cancers fall into this group.
- ❖ This type of cancer usually is associated with DCIS.
- ❖ About 50%-65% of ductal carcinomas are ER-positive, 20% are HER2 positive, and 15% are negative for both ER and HER2.
- ❖ Carcinomas associated with a large amount of DCIS require large excisions with wide margins to reduce local recurrences.
- ❖ Most of these tumors induce a marked fibroblastic (desmoplastic) stromal reaction to the invading tumor cells producing a palpable mass with a hard consistency (scirrhous carcinoma). And therefore a palpable mass is the most common presentation.
- ❖ The tumor shows an infiltrative attachment to the surrounding structures and may cause dimpling of the skin (due to traction on suspensory ligaments) or nipple retraction.

Morphology

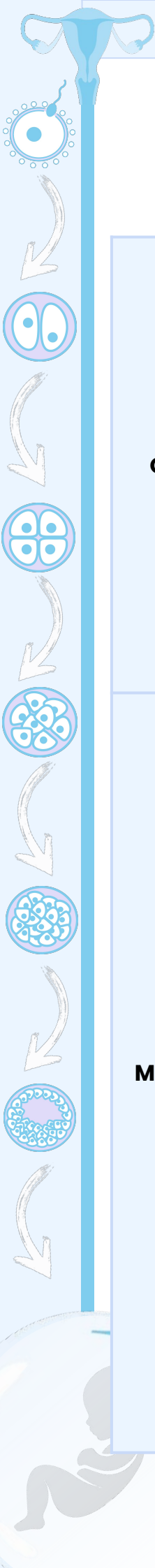
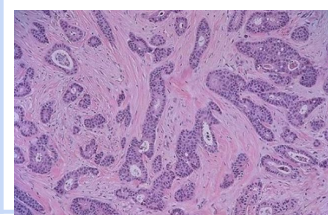
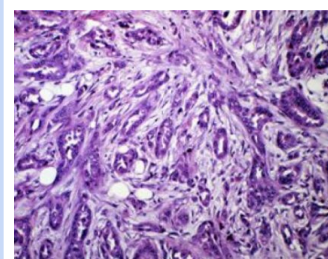
Grossly

- ❖ tumor is firm, hard with an irregular border.
- On cut surface:
- ❖ it's gritty and shows irregular margins with stellate infiltration (sometimes it can be soft and well demarcated)
 - ❖ in the center there are small foci of chalky white stroma
 - ❖ occasionally calcification which have characteristic grating sound when cut or scraped

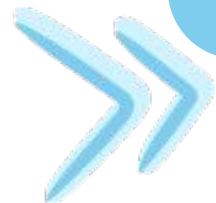


Histology

- ❖ the tumor cells are large and pleomorphic usually within a dense stroma. They are adenocarcinomas and so they show glandular formation but can also be arranged in cords or sheets of cells.
- ❖ Ranges from well differentiated to moderate or poorly differentiated.



Invasive Lobular Carcinoma



Overview

- ❖ It is the second most common invasive breast cancer.
- ❖ It may occur alone or in combination with ductal carcinoma.

Clinical Features

- ❖ Tend to be **bilateral** and **multicentric**.
- ❖ 2/3 of the cases are associated with LCIS.
- ❖ Almost all lobular carcinoma express one hormone receptors, whereas **HER2 overexpression is rare**.
- ❖ The pattern of metastasis is unique: they frequently spread to cerebrospinal fluid, serosal surfaces, gastrointestinal tract, ovary, uterus, and bone marrow.
- ❖ The amount of stromal reaction to the tumor varies: Marked fibroblastic (desmoplastic) response to little to no reaction therefore the presentation varies from a discrete mass to a subtle, diffuse indurated area.
- ❖ Although most manifest as palpable masses or monographic densities, a significant subgroup invade without producing desmoplastic response such tumors may be clinically occult and difficult to detect by imaging.

Morphologically similar to the tumor cells seen in LCIS.

Grossly

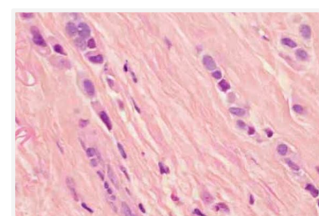
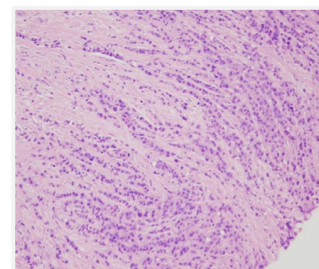
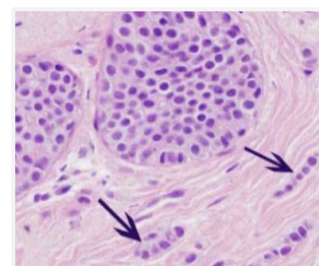
- ❖ Most are firm to hard with irregular margin.



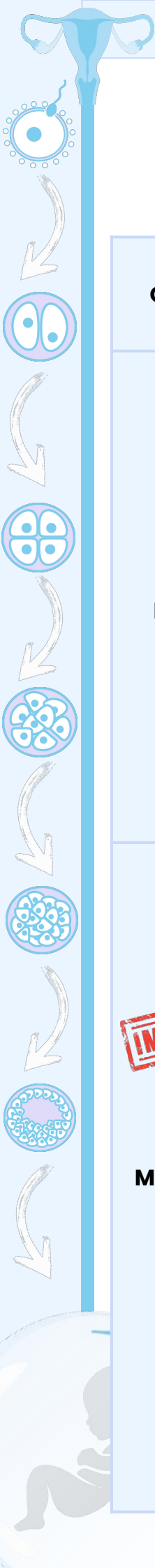
Morphology

Histology

- ❖ **Single infiltrating malignant cells, forming a line often one cell width (called as indian file pattern).**
- ❖ The cell invade stroma individually and often are aligned in a **"single file"** pattern
- ❖ No tubules or papillary formation.



Indian file pattern !



Medullary Carcinoma

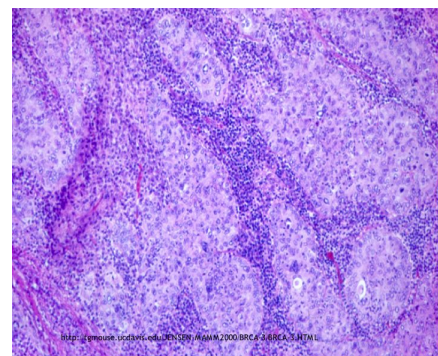
Medullary Carcinoma

Introduction

- ❖ Special type of **triple-negative** cancer comprising about 5% of all breast cancers.
- ❖ Typically grow as rounded well circumscribed masses **that can be difficult to distinguish from benign tumors on imaging.** (May be mistaken clinically and radiologically for a fibroadenoma.)
- ❖ It does not produce any fibroblastic (desmoplastic) reaction and therefore it is soft and fleshy.
- ❖ Seen frequently in women with germline BRCA1 mutations, but most women with these carcinomas are not carriers.

Morphology

- ❖ Solid Sheets of large anaplastic cells. **surrounded by many lymphocytes and plasma cells.** There is scant fibrous stroma.
- ❖ Pronounced lymphocytic infiltrates predominantly (T cells).
- ❖ The presence of lymphocytes lead to better response to chemotherapy compared to poorly differentiated carcinomas without lymphoid infiltrates



Colloid Carcinoma (mucinous)

Tubular Carc Females Slides

General

- ❖ Tends to occur in older women.
- ❖ ER-positive/HER2 negative
- ❖ produce abundant extracellular mucin
- ❖ may be pure, more mixed with other type

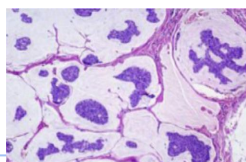
- ❖ ER-positive/HER2 negative cancer
- ❖ and is almost always detected on mammography as a small irregular mass.

Gross

- ❖ The tumors usually are soft and gelatinous because of the presence of mucin pools that create an expansile circumscribed mass.
- ❖ Sharply circumscribed, Lack fibrous stroma slow growing

Microscopy

- ❖ **Small islands of tumor cells and single cells in a pool of mucin**



- ❖ Cells are arranged in well formed tubules
- ❖ have low grade nuclei

Prognosis

Wide local excision (Lumpectomy), mastectomy:
 – Simple, Modified radical, Radical

Lymph node metastases are rare and the prognosis is excellent

Inflammatory carcinoma

<p>Overview</p>	<ul style="list-style-type: none"> ❖ Defined by its clinical presentation of a carcinoma rather than a specific morphology extensively involving dermal lymphatics, resulting in an enlarged erythematous breast. ❖ Patients present with a swollen erythematous breast without a palpable mass. ❖ The diagnosis is made on clinical grounds and does not correlate with a specific histologic type of carcinoma 	
<p>Prognosis</p>	<ul style="list-style-type: none"> ❖ Many of these tumors metastasize to distant sites. ❖ The overall 5-year survival is less than 50%, and lower in those with metastatic disease at diagnosis. ❖ About half express ER. ❖ 40% to 60% overexpress HER2. 	
<p>Morphology</p>	<p>Grossly</p>	<ul style="list-style-type: none"> ❖ The underlying invasive carcinoma obstructs dermal lymphatic spaces, causing the "inflamed" appearance; true inflammation is absent.
	<p>Histology</p>	<ul style="list-style-type: none"> ❖ The underlying invasive carcinoma is poorly differentiated and diffusely infiltrates



Clinical Note

Breast Cancer Risk Assessment Tool (Gail model):
 The most commonly used risk model, indicated for patients with no personal or strong family history of breast cancer (including ductal or lobular carcinoma in situ), takes into account age, ethnicity, age at menarche, parity, and family history of breast cancer. Less precise for older women. Cannot be used in certain subgroups (such as patients with genetic mutations, e.g., BRCA1 or BRCA2 mutations) [Gail model calculator](#)

Deep Focus Question



Which statement regarding noninvasive breast cancer is true?

- A. LCIS is often multifocal with calcifications.
- B. LCIS and DCIS most often present with calcifications.
- C. LCIS and DCIS are most commonly multifocal.
- D. DCIS is typically unifocal, often with calcifications.
- E. DCIS is often unifocal without calcifications.

Answer: D



Breast Carcinoma

Clinical Presentations

UNSCREENED POPULATION

- ❖ Most breast cancers are detected as a palpable mass by the affected patient.
- ❖ Such carcinomas are almost all invasive and are typically at least 2 to 3 cm.
- ❖ At least ½ of these cancers will already have spread to regional (axillary) lymph nodes.
- ❖ Large carcinomas may be fixed to the chest wall, causing dimpling of the skin

OLDER SCREENED POPULATIONS

- ❖ Approximately 60% of breast cancers are discovered before symptoms are present.
- ❖ About 20% are in situ carcinomas.
- ❖ On mammography, invasive carcinomas commonly present as a density.
- ❖ Invasive carcinomas presenting as mammographic calcifications without an associated density are usually very small in size.
- ❖ Invasive carcinomas detected by screening in older women are 1 to 2 cm. Only 15% will have metastasized to lymph nodes.

PEAU D' ORANGE

- ❖ Lymphatics may become involved and the lymphatic drainage of that area and the overlying skin gets blocked causing lymphedema and thickening of the skin a change referred to as peau d'orange.
- ❖ When the tumor involves the central portion of the breast, retraction of the nipple may develop.

Invasive carcinoma grading

Females Slides

- All types of invasive breast carcinoma are assigned a grade from 1 (low grade) to 3 (high grade)
- Based on nuclear pleomorphism, tubule formation and proliferation :

Low grade nuclei

- Similar in appearance to the nuclei of normal cells.
- Most form well-defined tubules,
- Difficult to distinguish from benign lesions.

High grade nuclei

- nuclei are enlarged and have irregular nuclear contours
- lose the capacity and invade as solid sheets or single cells.
- Proliferation is evaluated by counting mitotic figures.

Breast Carcinoma

Factors influencing the outcome

IMPORTANT

The clinical outcome for a woman with breast cancer can be predicted based on the **molecular** and **morphologic** features of the cancer and its **stage** at the time of diagnosis.

Biological type

- The biological type of cancer is evaluated by a combination of **histological appearance, grade (including proliferative rate), expression of hormone receptors, and expression of HER2.**
 - **Proliferation** is evaluated by mitotic count and is closely tied to responsiveness to cytotoxic chemotherapy
 - **Expression of estrogen or progesterone receptors** predicts response to anti-estrogen therapy. The growth of hormone receptors- positive cancers can be inhibited for many years with therapy and it is possible for patients to survive for long periods with distant metastases. However, resistance often eventually develops- in some cancers because of mutations for ER. in contrast, there is no targeted therapy available for triple-negative cancers, which are treated with chemotherapy.
 - **Overexpression of HER2** is seen in about 20% of breast cancers. HER2 remains one of the best characterized examples of an effective therapy that is directed against tumor-specific molecular lesions (trastuzumab)

RNA expression

RNA expression profiling is a newer method of sub classifying cancers.

Tumor stage

- **Stage is a measure of the extent of tumor** at the time of diagnosis and is important for all biologic types of carcinoma.
- It is based on features of the primary tumor (T), involvement of regional lymph nodes (N), and the presence of distant metastases (M). The AJCC/UICC staging system, used in the United States and Europe, classifies tumors as
 - **Tumor size (T):** T1, T2, and T3 based on the tumor size, whereas **T4** tumors have ulceration of the skin, involvement of the deep muscles of the chest wall, or are clinically diagnosed as **inflammatory carcinoma.**
 - **Involvement of regional lymph nodes (N):** The majority of cancers first metastasize to regional nodes, and nodal involvement is a very strong prognostic factor. Lymphatic drainage goes to one or two sentinel lymph nodes in the axilla in most patients. If these nodes are not involved, the remaining axillary nodes are usually free of carcinoma. Sentinel node biopsy has become the standard for assessing nodal involvement, replacing more extensive lymph node dissections, which are associated with significant morbidity.
 - **The presence of distant metastases (M):** Distant metastases (M) are only detected in 5% of newly diagnosed women.

Deep Focus Question



Inflammatory breast cancer presents with which finding on physical examination?

- Localized discoloration without breast edema
- Absence of skin changes
- Salmon-colored patch
- Peau d'orange

Answer: D

Breast Carcinoma

Prognostic Factors

Major	
Invasive or In situ disease	Invasive carcinoma has poorer prognosis as it can metastasize. In-situ carcinoma is confined to the ductal/lobular system and cannot metastasize, so it has better prognosis.
Distant metastasis	Once distant metastases is present, cure is unlikely, although long-term remissions and palliation can be achieved. Favored sites for dissemination are the lungs, bones, liver, adrenals, brain, and meninges.
Lymph node metastasis	Axillary lymph node status is the most important prognostic factor for invasive carcinoma. The clinical assessment of nodal involvement is very inaccurate, therefore, biopsy is necessary for accurate assessment.
Tumor Size	The size of the carcinoma is the second most important prognostic factor. The risk of axillary lymph node metastases increases with the size of the carcinoma.
<p>all the above parameters are used to stage the tumor. Stage is a combination of size, lymph node status and distant metastasis. Tumor size less than 2 cm is associated with a favorable prognosis. The single most important prognostic indicator is the lymph node status. Negative lymph nodes have the best prognosis. Involvement of 1 to 3 lymph nodes has an intermediate prognosis and 4 or more positive nodes have the worse prognosis.</p>	
Locally advanced disease	Tumors invading into overlying skin or underlying skeletal muscle are frequently associated with concurrent or subsequent distant disease. With increased awareness of breast cancer detection, such cases have fortunately decreased in frequency and are now rare at initial presentation.
Inflammatory carcinoma	Women presenting with the clinical appearance of breast swelling and skin thickening have a poor prognosis.
Minor	
Histologic Subtype	Infiltrating ductal and lobular carcinomas have the worst prognosis. Medullary and mucinous have intermediate prognosis. And tubular and cribriform have the most favorable prognosis
Tumor Grade	It is calculated using a grading system called modified Scarff-Bloom-Richardson (SBR) grading system. There are three grades: 1, 2 and 3. Grade 1 has better prognosis and grade 3 has poorer prognosis. This SBR grading system is based on the estimation of the amount of well formed glands, the degree of nuclear pleomorphism, and the mitotic rate, on microscopic examination. It is calculated by the pathologist.
Tumor cells with estrogen and progesterone positive receptors	majority of breast carcinoma cells express estrogen and progesterone receptors. Such hormone positive cancers have better prognosis. They respond well to specific drugs e.g. Tamoxifen. Therefore it is mandatory to identify which tumors are ER/PR positive as they respond well to treatment and have better prognosis when compared to ER/PR negative tumors.
HER2 (human epidermal growth factor receptor 2)	is a glycoprotein overexpressed in about 30% of breast carcinomas. Many studies have shown that overexpression of HER2 is associated with a poor prognosis . In addition, ongoing studies have shown that HER2- overexpressing tumors respond very well to a chemotherapy drug named Trastuzumab (Herceptin). Therefore, it is mandatory to determine the HER2 status of the tumor when reporting breast cancer in order to help decide the chemotherapy plan.
Lymphovascular invasion	is strongly associated with the presence of lymph node metastases and is a poor prognostic factor.
Proliferative rates	ki67 index (the higher the ki67 proliferative index, the more aggressive the tumor is)

Summary

BENIGN BREAST TUMORS

- ❖ The majority of benign epithelial lesions are incidental findings detected by mammography. Their major clinical significance is their relationship to the subsequent risk of developing breast cancer.
- ❖ Benign changes are divided into three groups, nonproliferative disease, proliferative disease each associated with a different degree of breast cancer risk.
- ❖ Nonproliferative disease is not associated with an increased risk of breast cancer.
- ❖ Proliferative disease without atypia encompasses polyclonal hyperplasias that are associated with a slightly increased risk of breast cancer.
- ❖ Proliferative disease with atypia includes monoclonal "precancers" that are associated with a modest increase in the risk of breast cancer in both breasts.

MALIGNANT BREAST TUMORS

- ❖ The lifetime risk of developing breast cancer for an American woman is 1 in 8.
- ❖ A majority (75%) of breast cancers are diagnosed after the age of 50.
- ❖ The major risk factors for developing breast cancer are related to hormonal factors and inherited susceptibility.
- ❖ About 12% of all breast cancers are caused by identified germline mutations; BRCA1 and BRCA2 genes account for one-half of the cases associated with single-gene mutations.
- ❖ DCIS is a precursor to invasive ductal carcinoma and is most often found on mammographic screening as calcifications. When carcinoma develops in a woman with a previous diagnosis of untreated DCIS, it is usually is an invasive ductal carcinoma in the same breast.
- ❖ LCIS is both a marker of increased risk and a precursor lesion. When carcinoma develops in a woman with a previous diagnosis of LCIS, two-thirds are in the same breast and one-third is in the contralateral breast.
- ❖ Invasive carcinomas are classified according to histologic type and biologic type: ER-positive/HER2-negative, HER2-positive, and ER/PR/HER2-negative (triple-negative)
- ❖ The biologic types of cancer have important differences in patient characteristics, grade, mutation profile, metastatic pattern, response to therapy, time to recurrence, and prognosis.
- ❖ Prognosis is dependent on the biologic type of tumor, stage, and the availability of treatment modalities

Keywords

Benign Breast lesions

Inflammatory lesions	Mastitis	Acute	<ul style="list-style-type: none"> only infectious agent : Staphylococcus aureus lead to the formation of "lactational abscesses,"
		Periductal	<ul style="list-style-type: none"> association with cigarette smoking.
		Granulomatous	<ul style="list-style-type: none"> can be idiopathic, due to sarcoidosis or TB.
	Fat necrosis		<ul style="list-style-type: none"> mechanical or surgical trauma.
	Lymphocytic mastopathy		<ul style="list-style-type: none"> seen in diabetic women.
Benign epithelial lesions	Non proliferative Breast Changes (Fibrocystic)	<ul style="list-style-type: none"> Most common disorder of the breast. No increased risk for cancer. 	
		Cysts With Apocrine metaplasia	<ul style="list-style-type: none"> simple Cysts are lined by luminal columnar epithelium undergo apocrine metaplasia : have abundant eosinophilic cytoplasm.
		Fibrosis	<ul style="list-style-type: none"> The cysts can rupture and cause chronic inflammation
		Adenosis	<ul style="list-style-type: none"> An increase in the number of acini per lobule. can be seen in pregnancy
	Proliferative Disease Without Atypia	<ul style="list-style-type: none"> Rarely form palpable masses. Risk for cancer is 1.5 – 2 times normal. 	
		Epithelial Hyperplasia	<ul style="list-style-type: none"> presence of more than 2 layers. When it is seen in fibrocystic disease: it is called as proliferative type/variant of fibrocystic disease.
		Sclerosing Adenosis	<ul style="list-style-type: none"> incidental microscopic finding Calcifications : it can mimic cancer in mammography compression and distortion of the lobule.
		Complex Sclerosing Lesion (Radial Scar)	<ul style="list-style-type: none"> stellate lesions central Nidus of entrapped glands in a dense fibrotic or hyalinized stroma. nidus is surrounded by radiating arms of epithelium closely mimic an invasive carcinoma both mammographically and grossly
		Papillomas	<ul style="list-style-type: none"> papillary tumor that arises from the ductal epithelium. Large Duct Papillomas (central papillomas) : bloody nipple discharge and sometimes a subareolar palpable mass. Small Duct Papilloma : multiple & deeper · increase the risk of subsequent carcinoma.
		Proliferative Breast Disease With Atypia	<ul style="list-style-type: none"> Risk for cancer is 4-5 times normal. resembling ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) 2 types : Atypical ductal hyperplasia , Atypical Lobular Hyperplasia
Benign Stromal Lesions	<ul style="list-style-type: none"> derived from intralobular stroma are comprised of both stromal cells and epithelial cells (i.e., they are "biphasic") The only malignancy derived from interlobular stromal : angiosarcoma 		
	Fibroadenoma	<ul style="list-style-type: none"> most common benign tumor , most common benign tumor Firm, mobile lump ("breast mouse"). freely movable , pearl-white and whorled. mixture of ducts and fibrous connective tissue (fibromyxoid) 	
	Phyllodes	<ul style="list-style-type: none"> large palpable masses They are fibroepithelial tumors, have a leaf like pattern and a cellular stroma 	

Keywords

Malignant Breast lesions

Non-Invasive breast carcinoma (in situ)	Ductal carcinoma in situ (DCIS)	<ul style="list-style-type: none"> within the duct system without breaching the underlying basement membrane frequently shows micro-calcifications on mammography. Comedo isn subtype characterised by; Histology extensive central necrosis, resulting in toothpaste-like necrotic tissue with calcified debris Cribiform DCIS comprises cells forming round, regular "cookie cutter" spaces.
	Lobular carcinoma in situ (LCIS)	<ul style="list-style-type: none"> always an incidental finding in breast biopsies rarely associated with calcifications. uniform appearance , cells are monomorphic : With bland, round nuclei, and are found in loosely cohesive clusters within lobules
	Paget's disease	<ul style="list-style-type: none"> Paget's of the nipple is caused by the extension of DCIS up the lactiferous ducts and into the contiguous skin of the nipple unilateral crusting exudate over the nipple and areolar skin. Red scaly eczematous lesion on the nipple and the surrounding areola infiltration of the epidermis by large neoplastic ductal cells extends from DCIS within the ductal system into nipple skin without crossing the basement membrane
Invasive breast carcinoma	Invasive Ductal Carcinoma	<ul style="list-style-type: none"> associated with DCIS. induce a marked fibroblastic (desmoplastic) stromal reaction palpable mass : tumor is firm, hard with an irregular border. in the center there are small foci of chalky white stroma pleomorphic usually within a dense stroma. show glandular formation but can also be arranged in cords or sheets of cells.
	Invasive Lobular Carcinoma	<ul style="list-style-type: none"> Tend to be bilateral and multicentric. Almost all express hormone one receptors, whereas HER2 overexpression is rare. they frequently spread to cerebrospinal fluid Single infiltrating malignant cells, forming a line often one cell width (called as indian file pattern). No tubules or papillary formation.
	Medullary Carcinoma	<ul style="list-style-type: none"> triple-negative cancer rounded well circumscribed masses does not produce any fibroblastic (desmoplastic) reaction Sheets of large anaplastic cells surrounded by many lymphocytes and plasma cells. Pronounced lymphocytic infiltrates predominantly (T cells). Seen frequently in women with germline BRCA1 mutations, but most women with these carcinomas are not carriers.
	Colloid Carcinoma (mucinous)	<ul style="list-style-type: none"> ER-positive/HER2 negative produce abundant extracellular mucin soft and gelatinous
	Tubular Carcinoma	<ul style="list-style-type: none"> ER-positive/HER2 negative detected on mammography as a small irregular mass. Cells are arranged in well formed tubules Excellent prognosis
Classification	Luminal A	<ul style="list-style-type: none"> low grade , ER positive , HER 2 Negative
	Luminal B	<ul style="list-style-type: none"> high grade , ER positive , maybe HER2 Positive
	Luminal HER2-enriched	<ul style="list-style-type: none"> overexpress HER2 Don't express ER
	Basal-like	<ul style="list-style-type: none"> ER-negative, HER2-negative



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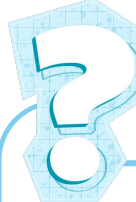
YOU VS MCQs



Question 1

A 26 years old female had a mobile lump on her breast while being pregnant. It diminished in size after delivery and she has no complications with breastfeeding. Which of the following is the most likely diagnosis ?

- Fibroadenoma
- Ductal carcinoma in situ
- Ductal carcinoma
- Fibrocystic disease of breast



Question 2

What gene mutation you should check for screening of breast cancer

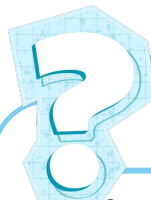
- N/MYC
- BRCA1
- PTEN
- P53



Question 3

A patient came to the clinic with a large breast mass approximately 18 cm , Histological examination showed a fibrocollagenous stroma with a leaf like pattern , what is the most likely diagnosis?

- Giant fibroadenoma
- Medullary carcinoma
- Phyllodes tumor
- Colloid carcinoma



Question 4

A 34 year old lady comes to ER and complains of bloody discharge , a radiological examination reveals a mass arising from sub-areolar region. What is the most likely diagnosis?

- Epithelial hyperplasia
- Sclerosing Adenosis
- Ectopic pregnancy
- Intraductal papilloma

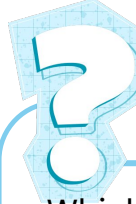
YOU VS MCQs



Question 5

Which of the following is considered a risk factor related to developing breast cancer?

- Increased estrogen levels
- Multiple pregnancies
- Early menopause
- Late age of menarche



Question 6

Which of the following tumors has a gelatinous surface and is composed of small islands of tumor cells and single tumor cells floating in pools of extracellular mucin?

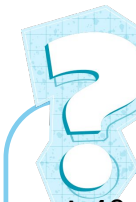
- Tubular
- Lobular
- Medullary
- Colloid



Question 7

A patient came to the clinic with a bilateral breast mass, in microscope there was no papillary or tubules formation and there was Single infiltrating malignant cells, forming a line often one cell width
What is the possible diagnosis

- Invasive Lobular Carcinoma
- Invasive ductal Carcinoma
- Ductal carcinoma in situ (DCIS)
- Pagets disease



Question 8

A 46 year old woman comes to ER with breast mastodynia and swelling in histopathology showed Comedo with calcified debris

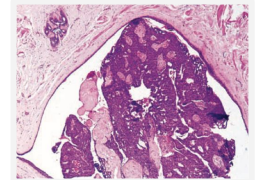
- Invasive Lobular Carcinoma
- Invasive ductal Carcinoma
- Ductal carcinoma in situ (DCIS)
- Pagets disease

Cases

1. A 30-year-old woman suffers traumatic injury to her breast while playing soccer. Physical examination reveals a 3-cm area of ecchymosis on the left breast. Two weeks later, the patient palpates a firm lump beneath the area where the bruise had been located. Which of the following is the most likely pathologic diagnosis?

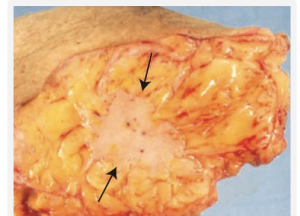
- A. Duct ectasia B. Fat necrosis C. Fibrocystic change D. Granulomatous mastitis

2. A 54-year-old woman complains of bloody discharge from her left nipple. Physical examination reveals a 0.5-cm nodule in the subareolar breast tissue, which is surgically excised. Histologic examination (shown in the image) reveals cuboidal and myoepithelial cell-lined vascular connective tissue cores, which project into the lumen of a major lactiferous duct. Which of the following is the appropriate diagnosis?



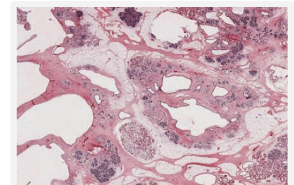
- A. Ductal carcinoma in situ B. Intraductal papilloma C. Lobular carcinoma in situ D. Paget disease

3. A 53-year-old woman discovers a lump in her breast and physical examination confirms a mass in the lower, outer quadrant of the left breast. Mammography demonstrates an ill-defined, stellate density measuring 1 cm. Needle aspiration reveals malignant ductal epithelial cells. A modified radical mastectomy is performed. The surgical specimen reveals a firm irregular mass (arrows). Which of the following cellular markers would be the most useful to evaluate before considering therapeutic options for this patient?



- A. Collagenase B. Estrogen receptors C. Galactosyltransferase D. Lysosomal acid hydrolases

4. A 35-year-old nulliparous woman complains that her breasts are swollen and nodular upon palpation. A mammogram discloses foci of calcification in both breasts. A breast biopsy reveals cystic duct dilation and ductal epithelial hyperplasia without atypia (shown in the image). What is the appropriate diagnosis?



- A. Ductal carcinoma in situ B. Fibroadenoma C. Fibrocystic change D. Intraductal papilloma

5. A 24-year-old woman delivers a 3.5-kg baby and begins breastfeeding her infant. The patient presents 2 weeks later with a fever of 38°C (101°F). Physical examination shows no abnormal vaginal discharge or evidence of pelvic pain but does reveal redness on the lower side of the left breast. The patient stops nursing the infant temporarily, but the symptoms persist, and the entire breast becomes swollen and painful. What is the most likely diagnosis?

- A. Acute mastitis B. Chronic mastitis C. Duct ectasia D. Granulomatous mastitis

6. A 35-year-old woman consults her family physician because of painful swelling of her breasts, particularly as she approaches the end of her menstrual cycle. On self-examination she recently felt a tender nodule in the right breast. Physical examination reveals an irregular nodularity of both breasts with diffuse tenderness. Examination of the axilla is negative. A mammogram demonstrates irregular areas of density in the lower, outer quadrants of both breasts. Which of the following histopathologic features is considered to be a risk factor for the development of carcinoma in this patient?

- A. Apocrine metaplasia B. Cystic change C. Duct ectasia D. Papillomatosis

1-B / 2-B / 3-B / 4-C / 5-A / 6-D

NEED EXPLANATION ? [CLICK HERE](#)

Cases

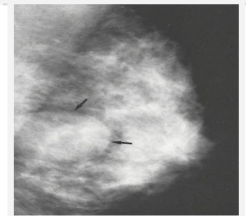
7. A woman consults her physician because of painful swelling of her breasts. Physical examination reveals nodularity of both breasts. Mammography shows irregular areas of increased density in the lower, outer quadrants of both breasts. A breast biopsy reveals increased fibrous stroma, cystic dilation of the terminal ducts, and varying degrees of apocrine metaplasia. This patient's condition is most commonly seen in which of the following groups?

- | | | | |
|---|-------------------------|-------------------|------------------------------|
| A. Patients with testicular feminization syndrome | B. Postmenopausal women | C. Pubertal girls | D. Women of reproductive age |
|---|-------------------------|-------------------|------------------------------|

8. A 20-year-old woman asks for your advice regarding her risk of developing breast cancer. Her mother, maternal aunt, and maternal grandmother all developed breast cancer. She would like to know if she has a genetic predisposition. Laboratory tests for mutations in which of the following genes would be most likely to answer your patient's question?

- | | | | |
|----------|----------|----------------------|-------------|
| A. BRCA1 | B. C-myc | C. Estrogen receptor | D. HER2/neu |
|----------|----------|----------------------|-------------|

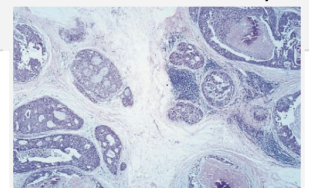
9. A 26-year-old woman presents with a breast mass that was detected on self-examination 1 week earlier. Mammography reveals a round, sharply demarcated 1-cm nodule in the right breast (shown in the image). Biopsy of the breast mass shows neoplastic epithelial ductal structures situated within a fibromyxoid stroma. The patient refuses further treatment and informs you that she wishes to become pregnant. Which of the following is the most likely effect of pregnancy on this breast lesion?



- | | | | |
|---|---------------------------------------|---------------------------------------|-----------------|
| A. Development of invasive ductal carcinoma within the lesion | B. Formation of intraductal papilloma | C. Metastasis to regional lymph nodes | D. Rapid growth |
|---|---------------------------------------|---------------------------------------|-----------------|

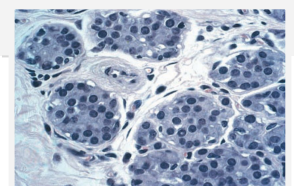
10. Upon self-examination, a 53-year-old woman discovers a lump in her left breast. Physical examination reveals a palpable lump about 1 cm in diameter in the outer quadrant of the left breast. No palpable lymph nodes are found in the axilla. Mammography reveals an ill-defined, stellate density measuring 1 cm in the left breast. Fine-needle aspiration of the mass discloses malignant epithelial cells. A partial mastectomy is performed and shows invasive ductal adenocarcinoma. Which of the following is the most important prognostic factor for this patient?

- | | | | |
|---|----------------------------------|----------------------------------|---------------------------|
| A. Estrogen receptor status of the tumor tissue | B. Histologic grade of the tumor | C. Inherited BRCA1 gene mutation | D. Status of the axillary |
|---|----------------------------------|----------------------------------|---------------------------|



11. A 45-year-old woman discovers a solitary, freely movable mass in her right breast on self examination, which is confirmed on physical examination. Mammography demonstrates focal calcification, with a linear configuration in the region of the breast mass. A breast biopsy (shown in the image) reveals large, pleomorphic epithelial cells confined to dilated ducts, with central zones of necrosis. What is the appropriate pathologic diagnosis?

- | | | | |
|----------------------|---|------------------------|--------------------|
| A. Colloid carcinoma | B. Ductal carcinoma in situ, comedocarcinoma type | C. Medullary carcinoma | D. Phyllodes tumor |
|----------------------|---|------------------------|--------------------|



12. A 58-year-old woman presents with an irregular nodularity that has developed in her right breast over the past 3 months. Mammography demonstrates irregular densities in both breasts. A needle biopsy of one breast lesion is shown. An excisional biopsy of the contralateral breast shows similar histology. Which of the following is the most likely pathologic diagnosis?

- | | | | |
|----------------------|------------------------------|------------------------------|------------------------|
| A. Colloid carcinoma | B. Lobular carcinoma in situ | C. Malignant phyllodes tumor | D. Medullary carcinoma |
|----------------------|------------------------------|------------------------------|------------------------|



7-D / 8-A / 9-D / 10-D / 11-B / 12-B



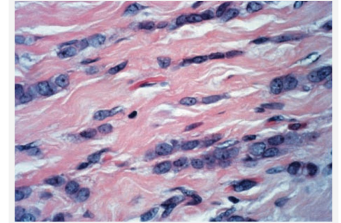
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Cases

13. A 22-year-old woman nursing her newborn develops a tender erythematous area around the nipple of her left breast. On physical examination, a purulent exudate is observed to drain from an open fissure. Culture of this exudate will most likely grow which of the following microorganisms?

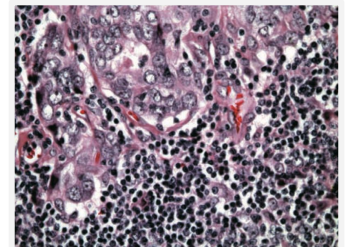
- A. *Escherichia coli* B. *Haemophilus influenzae* C. *Lactobacillus acidophilus* D. *Staphylococcus aureus*

14. A 52-year-old woman presents with a 3-month history of a palpable breast mass. Physical examination confirms a 1-cm nodule in the upper outer quadrant of the right breast. A biopsy reveals small cuboidal cells, with round nuclei and prominent nucleoli. The cells are arranged in single cell columns, between strands of connective tissue (shown in the image). Which of the following is the appropriate diagnosis?



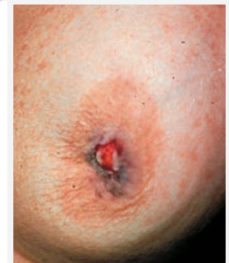
- A. Ductal carcinoma in situ B. Invasive ductal carcinoma, tubular type C. Invasive lobular carcinoma D. Lobular carcinoma in situ

15. A 58-year-old woman has a screening mammography and is found to have a 4-cm circumscribed mass, without calcifications, in her left breast. An excisional biopsy shows solid nests and sheets of highly pleomorphic cells, with many mitotic figures, surrounded by a dense infiltrate of lymphocytes. Which of the following is the most likely diagnosis?



- A. Invasive ductal carcinoma B. Invasive lobular carcinoma C. Medullary carcinoma D. Paget disease

16. A 45-year-old woman presents with an oozing, reddish patch on her left nipple (patient shown in the image). The patient has a history of skin rashes and food allergies and believes this condition is due to an allergic reaction to her bra. Cytologic examination of fluid oozing from the skin lesion reveals neoplastic cells. Excisional biopsy shows large clear malignant cells in the epidermis of the areola. Which of the following is the most likely diagnosis?

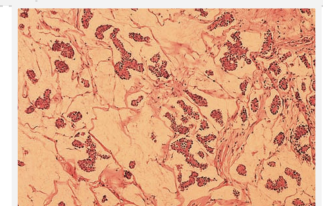


- A. Chronic dermatitis B. Colloid carcinoma C. Intraductal papilloma D. Paget disease

17. A 60-year-old woman presents with a large breast mass that she first detected 3 months ago. Mammography reveals a well-circumscribed mass measuring 8 cm in diameter. A breast biopsy shows loose fibroconnective tissue with a sarcomatous stroma, abundant mitoses, and nodules and ridges lined by cuboidal epithelial cells. Which of the following is the appropriate diagnosis?

- A. Fibroadenoma B. Medullary carcinoma C. Paget disease D. Phyllodes tumor

18. A 65-year-old woman presents with a palpable breast mass that she palpated 1 month earlier. Physical examination reveals an soft, jelly-like tumor measuring 5 cm in diameter. Histologic examination of a breast biopsy is shown in the image. What is the appropriate diagnosis?



- A. Colloid carcinoma B. Lobular carcinoma C. Medullary carcinoma D. Paget disease

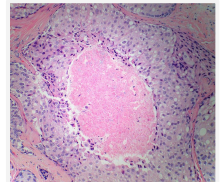
Cases

EXTRA CASES MAY REQUIRE EXTRA INFO

1. A 30-year-old woman presents with nipple discharge of 3 weeks in duration. Physical examination reveals a white discharge from both nipples. The patient has not menstruated for the past 4 months, and she is not pregnant. The breasts are firm and nontender. A cytologic smear of the discharge shows no evidence of acute or chronic inflammatory cells. Which of the following is the most likely cause of galactorrhea in this patient?

- | | | | |
|-------------------------------|-------------------------------------|----------------------|---------------------|
| A. Fibroadenoma of the breast | B. Fibrocystic change of the breast | C. Pituitary adenoma | D. Sheehan syndrome |
|-------------------------------|-------------------------------------|----------------------|---------------------|

2. A 66-year-old woman comes to the clinic due to an abnormal calcification that was observed on routine screening mammography. She is currently asymptomatic, and medical history is remarkable only for hypertension for which she takes hydrochlorothiazide. The patient does not smoke or use alcohol or illicit drugs. Vitals are within normal limits. On physical examination, a fixed, non-tender, palpable lump is noted in the left breast. There are no skin changes or nipple discharge. The biopsy results are shown:



- | | | | |
|------------------------|--------------------|--------------------------|------------------------------|
| A. Medullary carcinoma | B. Comedocarcinoma | C. Intraductal papilloma | D. Lobular carcinoma in situ |
|------------------------|--------------------|--------------------------|------------------------------|

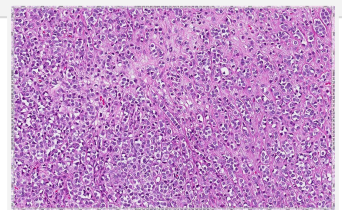
3. A 34-year-old woman comes to the clinic due to a breast lump. A suspicious mass is found on mammogram, which is followed by a core needle biopsy that confirms the diagnosis of invasive carcinoma. Medical history is unremarkable. The patient's mother died of breast cancer, and her sister was recently diagnosed with ovarian cancer; the doctor suspects a hereditary mutation. In healthy individuals, the involved gene has which of the following roles?

- | | | | |
|---------------|--------------------------|---|--------------------|
| A. DNA repair | B. Cell cycle regulation | C. Negative regulation of signal transduction | D. Mismatch repair |
|---------------|--------------------------|---|--------------------|

4. A 56-year-old woman comes to the office following abnormal results of screening mammography. The mammogram showed suspicious microcalcifications. The patient is in good health, and medical history is unremarkable. Family history is negative for cancer. Vital signs are within normal limits. On physical examination, there are no breast changes, palpable masses, or lymphadenopathy. There is no nipple discharge. She is scheduled for a biopsy. Based on these features alone, which of the following is the most likely diagnosis?

- | | | | |
|-----------------------------|------------------------------|-------------------------------|------------------------------|
| A. Ductal carcinoma in situ | B. Lobular carcinoma in situ | C. Invasive lobular carcinoma | D. Invasive ductal carcinoma |
|-----------------------------|------------------------------|-------------------------------|------------------------------|

5. A 62-year-old woman comes to the clinic due to a breast lump she felt while showering. Medical history is significant for hyperlipidemia and hypertension, which is managed with lovastatin and hydrochlorothiazide, respectively. Vitals are within normal limits. On physical examination, a lump in the right upper quadrant of the right breast and a palpable axillary lymph node are noted. She is sent for a mammography, which reveals no abnormalities. Ultrasound is obtained and shows a mass lesion. Core needle biopsy reveals the following image:



- | | | | |
|---------------------|-------------------------------|------------------------------|-----------------------------|
| A. Comedo carcinoma | B. Invasive lobular carcinoma | C. Invasive ductal carcinoma | D. Ductal carcinoma in situ |
|---------------------|-------------------------------|------------------------------|-----------------------------|

6. A 50-year-old woman comes to the clinic due to right breast erythema and tenderness that have progressed over the past 2 weeks. She is generally healthy and has not experienced any trauma in the area. Her only medication is a daily multivitamin. Family history is negative for cancer. Temperature is 37.0°C (98.6°F), pulse is 65/min, and blood pressure is 125/70 mmHg. On physical examination, the skin on the right breast is indurated and thickened with dimpling of the hair follicles. A palpable lymph node is present in the right axilla. The nipple appears normal. A core needle biopsy reveals an invasive carcinoma. Which of the following is most likely responsible for this patient's skin findings?

- | | | | |
|---------------------------------------|--|-----------------------|--------------------|
| A. Obstruction of the skin lymphatics | B. Shortening of the lactiferous ducts | C. Bacterial invasion | D. Trauma to chest |
|---------------------------------------|--|-----------------------|--------------------|

Cases

EXTRA CASES MAY REQUIRE EXTRA INFO

6. A 45-year-old woman comes to the clinic due to a breast mass she noticed while showering. The patient is healthy, and she has no significant medical history. She is concerned because she recently found out she is a carrier of BRCA1 mutation. Her mother was diagnosed with breast cancer at the age of 48 and her sister at 46 years. The patient does not smoke or use alcohol excessively. Vitals are within normal limits. On physical examination, a well-circumscribed, soft non-tender mass is palpated in the right breast. There are no nipple or skin changes, and no palpable lymph nodes. A core-needle biopsy is obtained and reveals sheets of large anaplastic cells with dense lymphocytic infiltrates. Which of the following is the most likely diagnosis?

- A. Comedocarcinoma B. Fibroadenoma C. Medullary carcinoma D. Medullary carcinoma

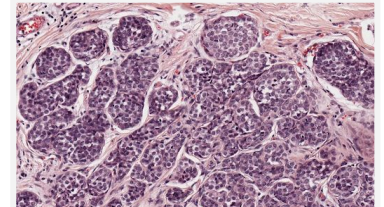
7. A 58-year-old woman comes to the clinic due to an itchy, oozing rash from the left nipple for the past few weeks. It first started as a small ulcer which then spread to the areola, with a copious clear yellowish exudative discharge. Medical history is significant for allergic rhinitis, for which she takes nasal corticosteroids and antihistamines as needed. She has tried some steroid cream, but she did not notice any improvement. Vitals are within normal limits. On physical examination, the left nipple is ulcerated and oozing yellowish fluid. There is no palpable mass, and the right nipple appears normal. Which of the following is most likely responsible for this patient's skin condition?

- A. Intertrigo B. Mastitis C. Paget disease D. Eczema

8. A 50-year-old woman comes for a follow-up meeting after she was diagnosed with invasive ductal carcinoma breast cancer. A 2-cm spiculated lesion was seen on mammography and confirmed with biopsy. She would like to know what the prognosis is for her condition. Which of the following findings is the worse prognostic factor for her conditions?

- A. High grade of cellular differentiation B. Large tumor size C. Progesterone receptor D. HER2 receptor underexpression

9. A 50-year-old woman comes to the clinic following an abnormal mammogram showing calcifications in the right breast. Medical history is remarkable for type 2 diabetes mellitus managed with metformin. She does not smoke or use alcohol excessively, and she has not experienced weight loss, fever, or trauma. She is referred for a biopsy, which confirms the diagnosis of benign fat necrosis. However, during the biopsy, another area suspected of malignancy is found. The results of the biopsy of this additional area are shown below: This type of cancer is associated with which of the following?



- A. Invasion to the overlying skin B. Aggressive behavior C. Bilateral disease D. Lymphatic and vascular invasion

10. A 55-year-old woman comes to the clinic for a follow-up appointment after a core-needle biopsy confirmed the diagnosis of breast cancer. The results are sent for further immunohistochemistry analysis. The patient would like to know the prognosis of her condition. Which of the following characteristics, if found, would confer the worst prognosis?

A	B	C	D
Estrogen receptor expression -	Estrogen receptor expression +	Estrogen receptor expression -	Estrogen receptor expression -
Progesterone receptor expression -	Progesterone receptor expression +	Progesterone receptor expression -	Progesterone receptor expression +
HER2 receptor overexpression -	HER2 receptor overexpression -	HER2 receptor overexpression +	HER2 receptor overexpression -

Pathology Team

Leader

لمى العتيبي



سديم اليحيى



الجوهرة الوهبي



عائشة إبراهيم



ريناد صالح الشهري



شادن الهزاني



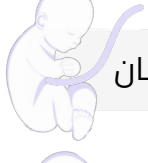
دانه المحيسن



ساره الدوسري



الدانه عبدالله



هدى الجدعان



ساره الشهراني



ليان الرويلي



أفنان الأحمري



ساره العجاي



هيا الزير



رغد الحامد



محمد معشي



مشعل الدخيل



يزيد المطيري



سلمى السعدون



ريما القرني

Leader

زياد العتيبي



رغد المصلح



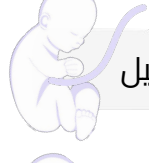
ألين الكلية



مريم الغنام



محمد العرفج



رند ابا الخيل



وجد المطيري



ريوف الأحمري



سلطان البقمي



شوق الخليفة



عروب المحمود



هياء العجمي



ريماس المحمود



لؤي الحديثي



فيصل الشوبعر



محمد السلامة



عبدالمحسن الدايل



أريج القريني



عبدالله الزامل



رزان السطحي