



# Lecture 8: Benign Breast Diseases

## Objectives:

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



MED437  
KING SAUD UNIVERSITY

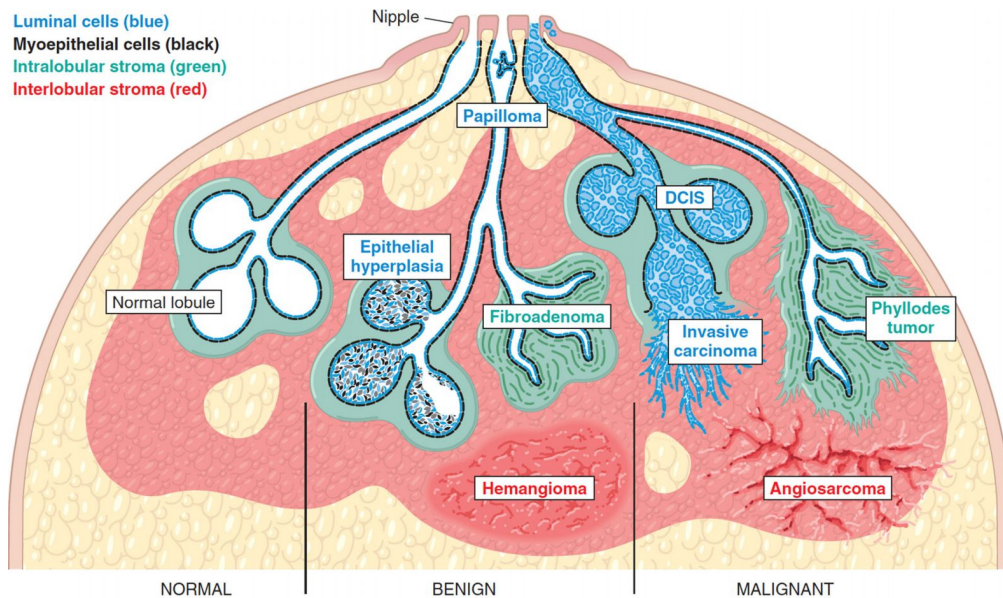


TEAM 437

**Important**  
**Terminology**  
**Doctor's Notes**  
Extra Information

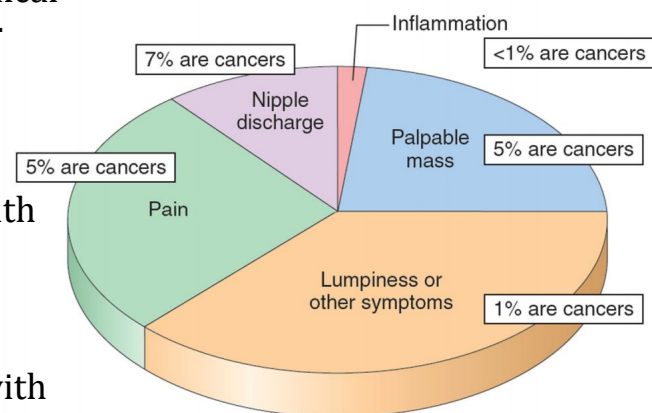
# Introduction

- The functional unit of the breast is the lobule, which is supported by a specialized intralobular stroma.
- 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 of Breast Diseases

- Pain (mastalgia): It is the most common breast symptom. May be cyclical (with menses) or non cyclical. Diffuse cyclical pain has no pathologic significance. Non-cyclical pain can be caused by ruptured cysts or areas of prior injury or infection, or no specific cause. Although the great majority of painful masses are benign, about 10% of breast cancers present with pain.
- Palpable mass
- Nipple discharge:
  1. Milky discharge: not associated with malignancy.
  2. Bloody or serous discharges: commonly associated with benign lesions but can rarely be due to a malignancy.



## Mammographic Screening

- Mammographic screening was introduced in the 1980s as a means to detect small, non-palpable, asymptomatic breast carcinomas.
- The principal mammographic findings of breast carcinoma are densities/masses and calcifications:
  - **Densities (mass):** Most tumors appear radiologically denser than the normal breast. Fibroadenomas and cysts can also present as densities.
  - **Calcifications:** Calcium gets deposited in secretions, necrotic debris, or hyalinized stroma. It can be seen in benign and malignant conditions
    - a. Calcifications **in malignancy are usually small, irregular, numerous, and clustered.**
    - b. Mammographic screening has increased the diagnosis of DCIS which usually present as mammographic calcifications.
- It is recommended to start mammographic screening at the age of 40 years.

## Benign Breast Lesions

- **Inflammatory lesions:**
  1. Acute mastitis: Staphylococcus aureus infection is the most common organism.
  2. Periductal mastitis
  3. Mammary duct ectasia, dilated ducts disease
  4. Fat necrosis: It is usually due to a mechanical or surgical **trauma. (can feel like a tumor)**
  5. Lymphocytic mastopathy (sclerosing lymphocytic lobulitis): It is seen in diabetic women.
  6. Granulomatous mastitis: It can be idiopathic, due to sarcoidosis or **TB (TB causes caseous necrosis)**
- **Benign epithelial lesions:**
  1. Non proliferative breast changes (fibrocystic changes)
  2. Proliferative breast disease without atypia
  3. Proliferative breast disease with atypia /Atypical hyperplasia
- **Benign stromal lesions:**
  1. Fibroadenoma
  2. Benign phyllodes tumors
- **The presence of a myoepithelial layer/basement membrane indicates that the lesion is benign.**

# Inflammatory Lesions

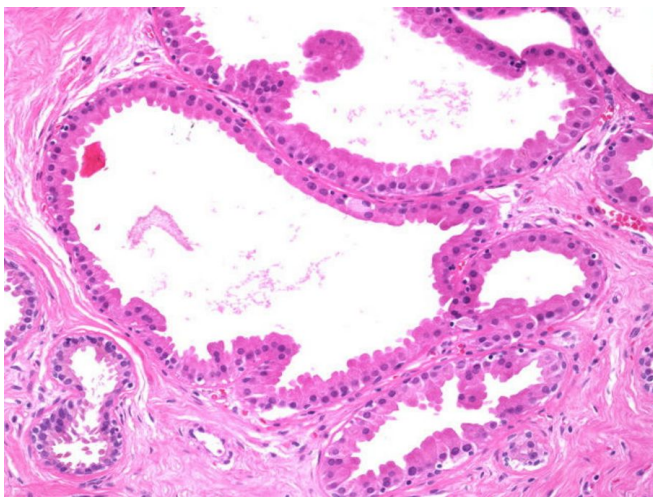
## Mastitis:

- **Acute mastitis:** Almost all cases of acute mastitis occur during the first month of breastfeeding. Staphylococcus aureus is the most common causative organism. The breast is erythematous and painful. Fever is often present.
- **Periductal mastitis:** This condition is not associated with lactation. However, there is a strong association with cigarette smoking.

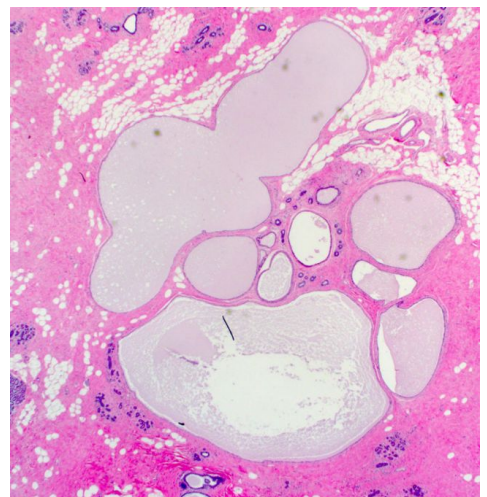
# Benign Epithelial Lesions

## Non Proliferative Breast Changes (Fibrocystic Changes)

- It is the **most common disorder of the breast**.
- Age: 20 - 55 years, decreases progressively after menopause (due to decrease of hormones)
- The cause is not known but it is thought to be hormonal imbalances.
- It can produce **palpable breast masses**, mammographic densities or calcifications, or nipple discharge. It may also present with cyclical pain.
- It carries **no increased risk for cancer**.
- Three histological patterns are seen:
  1. Cysts with apocrine metaplasia: cysts are lined by benign flattened to columnar epithelium with focal apocrine metaplasia. In apocrine metaplasia the cells become large and have abundant eosinophilic cytoplasm. The cysts can rupture and cause inflammation.
  2. Fibrosis: contribute to the palpable firmness of the breast.
  3. Adenosis: It is defined as an increase in the number of acini per lobule (adenosis can also be seen in pregnancy).



Cystic apocrine metaplasia



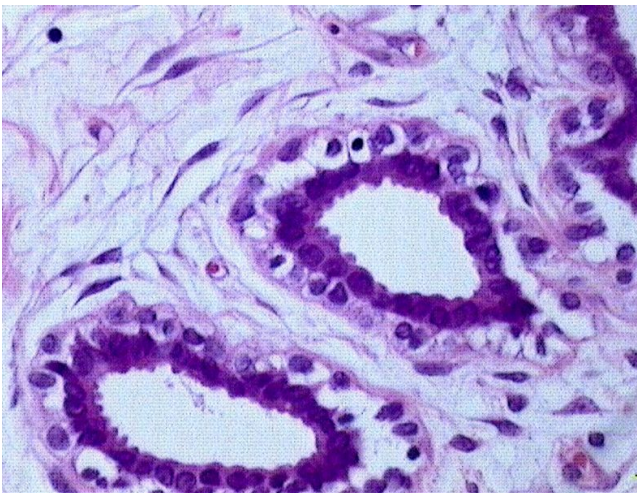
Cysts

## Proliferative Disease Without Atypia

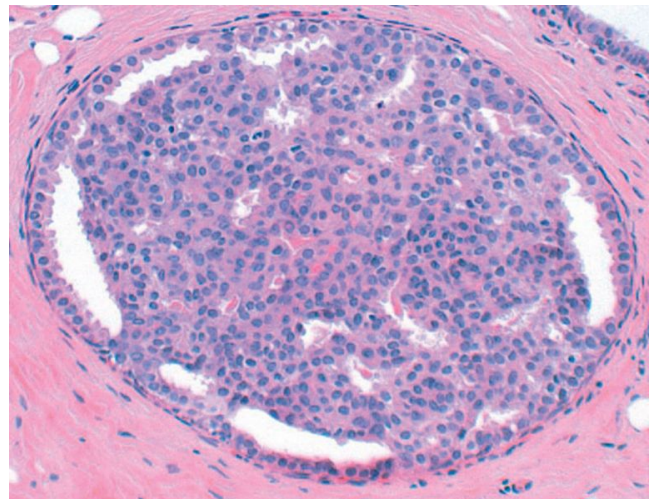
- They are incidental findings and rarely form palpable masses.
- They are detected as small mammographic densities.
- Risk for cancer is **1.5 – 2 times normal**. Risk elevated due to proliferation but is a relatively low elevation.
- The following entities are included in this category:
  1. Epithelial hyperplasia
  2. Sclerosing adenosis
  3. Complex sclerosing lesions/radial scar
  4. Papillomas
  5. Proliferative variant of fibrocystic disease.

## Epithelial Hyperplasia (usual ductal hyperplasia)

- The normal breast has a 2 layers of cells (epithelial and myoepithelial cells). Thus, epithelial hyperplasia is defined as the presence of more than 2 layers.
- Hyperplasia can range from mild, moderate and severe/florid.
- Both epithelial and myoepithelial cells proliferate.
- It can be seen in the ducts and the lobules.
- When it is seen in fibrocystic disease: it is called as proliferative type/variant of fibrocystic disease.



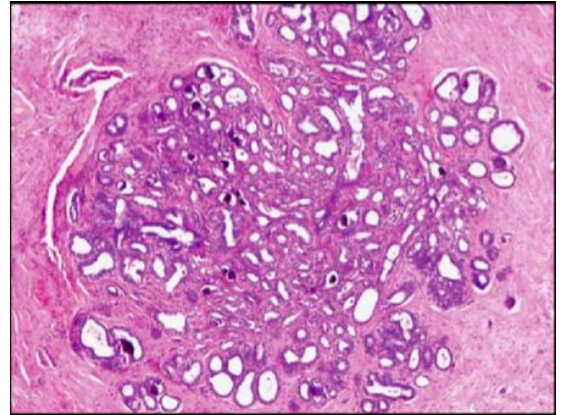
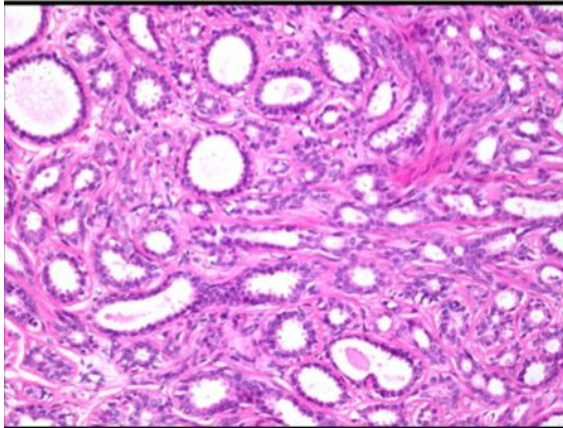
Normal acinus  
Two layer of cells (myoepithelial and outer epithelial)



Usual ductal hyperplasia  
Previously empty duct now full which could increase the size of the duct. All cells filling the duct are **benign**.  
**Slit like spaces not round**

# Sclerosing Adenosis

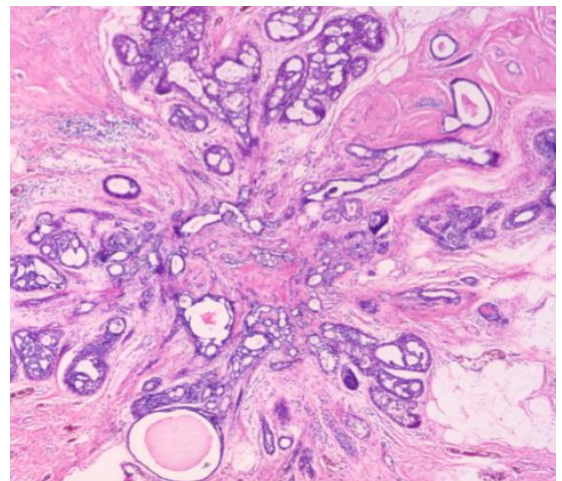
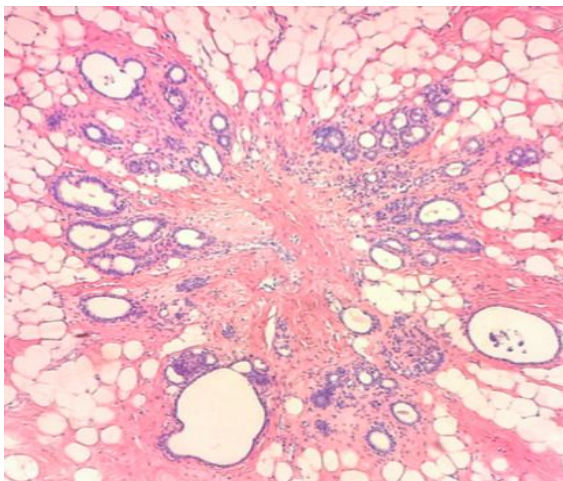
- It is commonly seen as an incidental microscopic finding but may occasionally present as a palpable mass that is mistaken clinically for cancer.
- **Calcifications** are commonly seen in the lesion, so even on mammography it can mimic cancer.
- **It is almost always associated with other forms of fibrocystic change.**
- Microscopically: **adenosis** and **stromal fibrosis** in the lobule which leads to **compression** and **distortion of the lobule**.



Adenosis refers to an increase in glands. Stronger stroma (sclerosis) to hold the glands together

## Complex Sclerosing Lesion (Radial Scar)

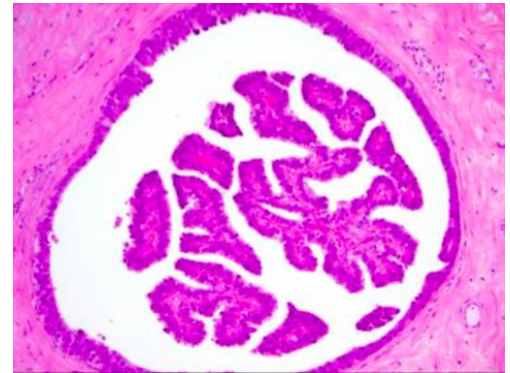
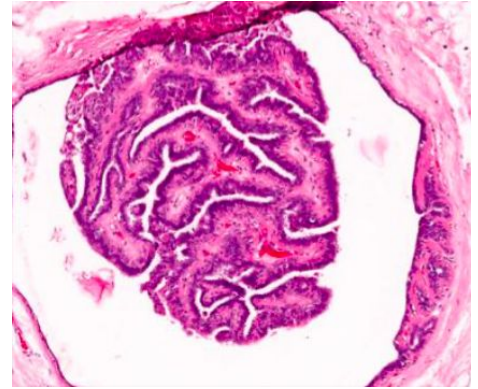
- Radial scars are stellate lesions characterized by a **central nidus** of entrapped glands in a **dense fibrotic** or **hyalinized stroma**. The nidus is surrounded by **radiating arms of epithelium with varying degrees of cyst formation and hyperplasia**.
- They typically present as an **irregular mammographic density** and closely mimic an invasive carcinoma both mammographically and clinically.
- The word "**scar**" refers to the morphologic appearance, and **not** a prior inflammation, trauma or surgery.



Star shape. This is a benign lesion.

# Intraductal Papillomas

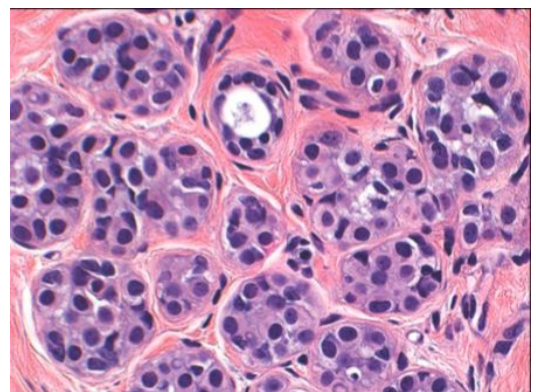
- It is a papillary tumor that arises from the **ductal epithelium**. It is more common in the **large lactiferous ducts** (present in the central part of the breast at the nipple) but can **also occur** in the **small ducts** in any quadrant of the breast.
  - **Large duct papillomas (central papillomas)**: 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 papillomas**: commonly **multiple** and located **deeper** within the ductal system. Small duct papillomas have been shown to **increase the risk of subsequent carcinoma**.



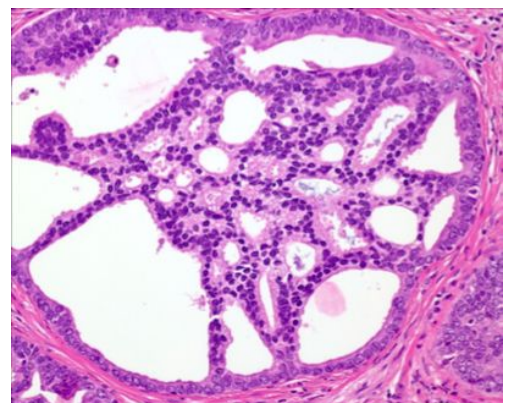
# Proliferative breast disease with atypia (Atypical hyperplasia)

- 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.
- Include two entities:
  - Atypical ductal hyperplasia
  - Atypical lobular hyperplasia
- 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.
- This lesion is between benign and DCIS/LCIS

ALH



ADH



# Pathological lesions (Nice table)

Pathologic lesions	Relative risk of development of invasive carcinoma	Comments
<b>Non-proliferative breast diseases (fibrocystic changes)</b>	No risk increased.	Fibrocystic disease.
<b>Proliferative disease without atypia</b>	1.5 to 2 times normal.	<ul style="list-style-type: none"> <li>● Epithelial hyperplasia.</li> <li>● Sclerosing adenosis.</li> <li>● Complex sclerosing.</li> <li>● Lesions/radial scars</li> <li>● Papillomas.</li> <li>● Proliferative fibrocystic disease.</li> </ul>
<b>Proliferative disease with atypia</b>	4 to 5 times normal	<ul style="list-style-type: none"> <li>● ADH (atypical ductal hyperplasia)</li> <li>● ALH (atypical lobular hyperplasia)</li> </ul>
<b>Carcinoma-in-situ</b>	8 to 10 times normal.	<ul style="list-style-type: none"> <li>● DCIS (ductal carcinoma in situ)</li> <li>● LCIS (lobular carcinoma in situ)</li> </ul>

## Stromal lesions

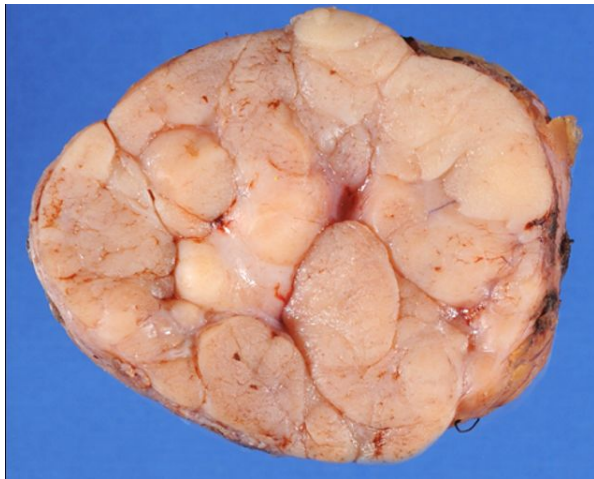
### Fibroadenoma:

- **Most common benign tumor of female breast.**
- Composed of benign proliferation of both **Epithelial** and **stromal** element.
- It occurs at any age, most common before 30 YO.
- Clinical presentation: Firm, mobile lump (**'breast mouse'**)
- It may increase in size during pregnancy. It may also stop growing and regress after menopause.
- Usually tumor is solitary, but may be multiple and involve both breasts.
- Tumor is completely benign. Almost never malignant.
- Treatment: lumpectomy (**only lump is removed**).



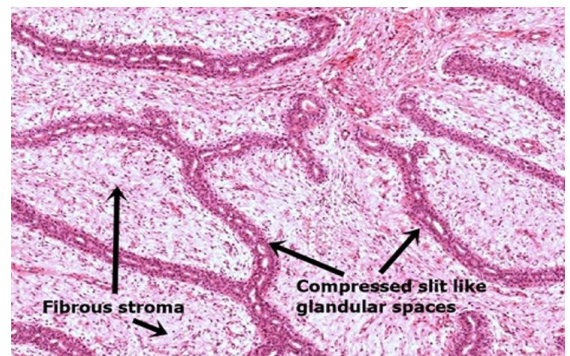
## Fibroadenoma grossly:

- Spherical nodules
- Sharply demarcated, **circumscribed** from the surrounding breast tissue
- **Freely movable. Can be shelled out.**
- Size between 1 to 10 cm in diameter.
- Cut surface appear pearl-white and whorled.
- **No breast tissue**

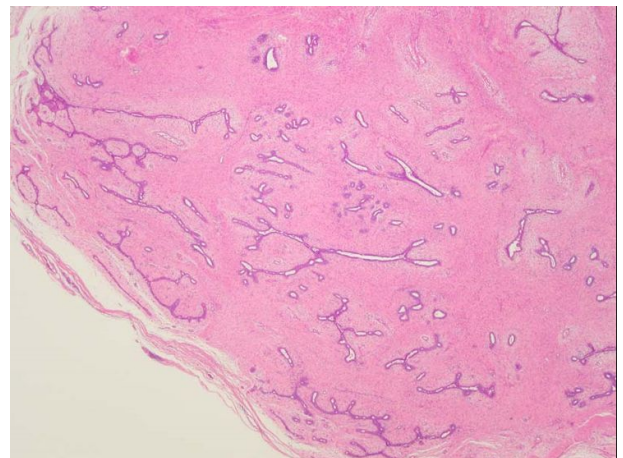


## Fibroadenoma histology :

- Composed of mixture of ducts and fibrous connective tissue/**fibromyxoid stroma**
- Proliferation of Interlobular stroma surroundings.
- Pushing and distorting associated epithelium **into elongated ducts.**
- Borders are sharply delimited.



Two layers of cells, **BENIGN.**

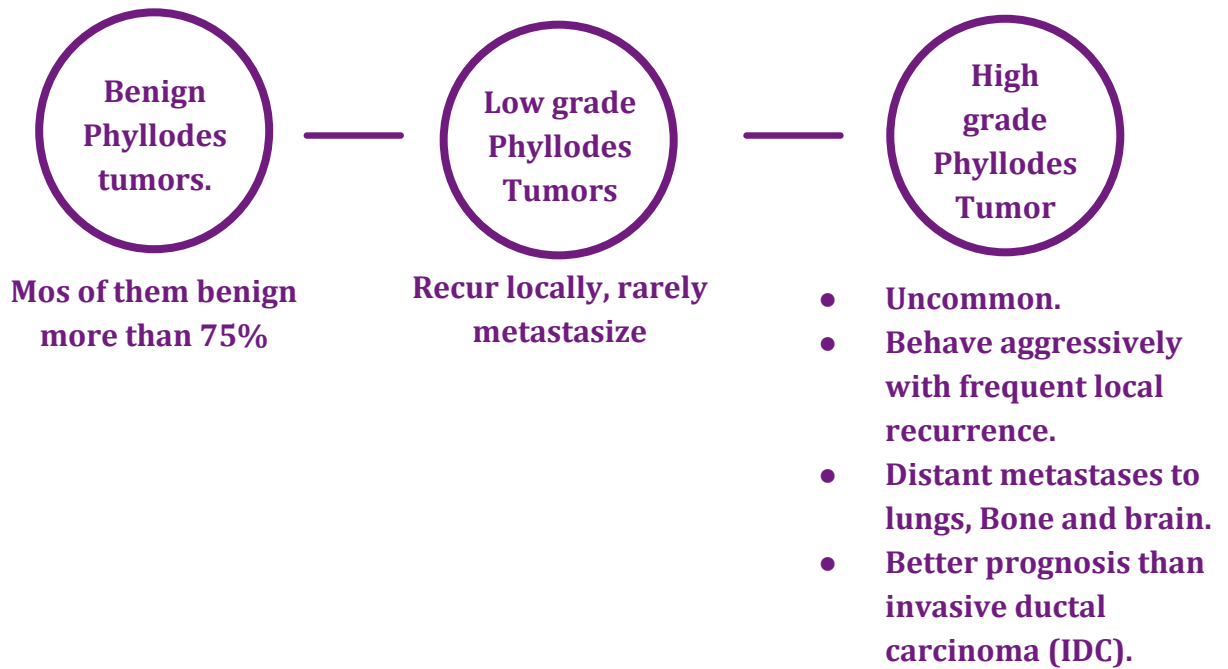


Fibrous tissue, glands are slit like due to compression.

## Phyllodes Tumors

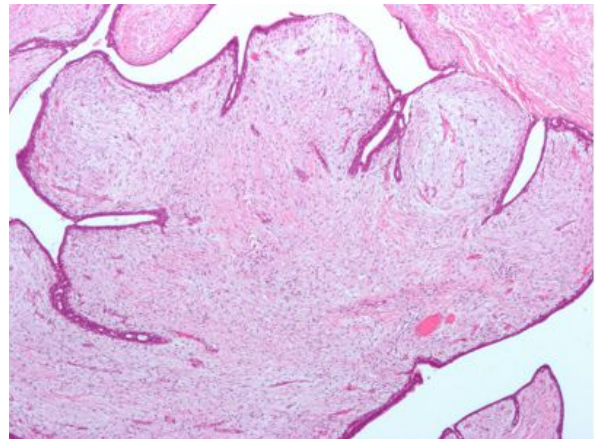
- Occur at any age. **More between 40s and 50s**, which is 10 to 20 years later than average age of fibroadenoma presentation.
- Less common than fibroadenoma.
- Most common presentation: large palpable masses (3 to 4 cm in diameter).
- **Rare tumor**

# Types of Phyllodes tumors



## Benign Phyllodes Tumors:

- Fibro-epithelial Tumors.
- Have a **leaf-like** pattern and a cellular stroma



# Pathoma Overview

## INTRODUCTION

### 1. BREAST

- a. Modified sweat gland embryologically derived from the skin
  - i. Breast tissue can develop anywhere along the milk line, which runs from the axilla to the vulva (e.g., supernumerary nipples).
- b. The terminal duct lobular unit is the functional unit of the breast; lobules make milk that drains via ducts to the nipple.
- c. Lobules and ducts are lined by two layers of epithelium.
  - i. Luminal cell layer-inner cell layer lining the ducts and lobules; responsible for milk production in the lobules
  - ii. Myoepithelial cell layer-outer cell layer lining ducts and lobules; contractile function propels milk towards the nipple.
- d. Breast tissue is hormone sensitive.
  - i. Before puberty, male and female breast tissue primarily consists of large ducts under the nipple.
  - ii. Development after menarche is primarily driven by estrogen and progesterone; lobules and small ducts form and are present in highest density in the upper outer quadrant.
  - iii. Breast tenderness during the menstrual cycle is a common complaint, especially prior to menstruation.
  - iv. During pregnancy, breast lobules undergo hyperplasia. i. Hyperplasia is driven by estrogen and progesterone produced by the corpus luteum (early first trimester), fetus, and placenta (later in pregnancy) 5. After menopause, breast tissue undergoes atrophy.
- e. Galactorrhea refers to milk production outside of lactation.
  - i. It is not a symptom of breast cancer.
  - ii. Causes include nipple stimulation (common physiologic cause), prolactinoma of the anterior pituitary (common pathologic cause), and drugs.

## INFLAMMATORY CONDITIONS

### 1. ACUTE MASTITIS

- a. Bacterial infection of the breast, usually due to *Staphylococcus aureus*
- b. Associated with breast-feeding; fissures develop in the nipple providing a route of entry for microbes.
- c. Presents as an erythematous breast with purulent nipple discharge; may progress to abscess formation
- d. Treatment involves continued drainage (e.g., feeding) and antibiotics (e.g., dicloxacillin).

### 2. PERIDUCTAL MASTITIS

- a. Inflammation of the subareolar ducts
- b. Usually seen in smokers
  - i. Relative vitamin A deficiency results in squamous metaplasia of lactiferous ducts, producing duct blockage and inflammation.

C. Clinically presents as a subareolar mass with nipple retraction

# Pathoma Overview

## INFLAMMATORY CONDITIONS

### 1. MAMMARY DUCT ECTASIA

- a. Inflammation with dilation (ectasia) of the subareolar ducts
  - i. Rare; classically arises in multiparous postmenopausal women
- b. Presents as a periareolar mass with green-brown nipple discharge (inflammatory debris)
  - i. Chronic inflammation with plasma cells is seen on biopsy.

### 2. FAT NECROSIS

- a. Necrosis of breast fat
- b. Usually related to trauma; however, a history of trauma may not always be evident.
- c. Presents as a mass on physical exam or abnormal calcification on mammography (due to saponification)
- d. Biopsy shows necrotic fat with associated calcifications and giant cells.

## BENIGN TUMORS AND FIBROCYSTIC CHANGES

### 1. FIBROCYSTIC CHANGE

- a. Development of fibrosis and cysts in the breast
  - i. Most common change in the premenopausal breast; thought to be hormone mediated
- b. Presents as vague irregularity of the breast tissue ('lumpy breast'), usually in the upper outer quadrant
- c. Cysts have a blue-dome appearance on gross exam.
- d. Benign, but some fibrocystic-related changes are associated with an increased risk for invasive carcinoma (increased risk applies to both breasts)
  - i. Fibrosis, cysts, and apocrine metaplasia -no increased risk
  - ii. Ductal hyperplasia and sclerosing adenosis -2x increased risk
  - iii. Atypical hyperplasia -5x increased risk

### 2. INTRADUCTAL PAPILLOMA

- a. Papillary growth, usually into a large duct
- b. Characterized by fibrovascular projections lined by epithelial (luminal) and myoepithelial cells
- c. Classically presents as bloody nipple discharge in a premenopausal woman
- d. Must be distinguished from papillary carcinoma, which also presents as bloody nipple discharge
  - i. Papillary carcinoma is characterized by fibrovascular projections lined by epithelial cells without underlying myoepithelial cells.
  - ii. Risk of papillary carcinoma increases with age; thus, it is more commonly seen in postmenopausal women.

# Pathoma Overview

## BENIGN TUMORS AND FIBROCYSTIC CHANGES

### 1. FIBROADENOMA

- a. Tumor of fibrous tissue and glands
- b. Most common benign neoplasm of the breast; usually seen in premenopausal women
- c. Presents as a well-circumscribed, mobile marble-like mass
- d. Estrogen sensitive- grows during pregnancy and may be painful during the menstrual cycle
- e. Benign, with no increased risk of carcinoma

### 2. PHYLLODES TUMOR

- a. Fibroadenoma-like tumor with overgrowth of the fibrous component; characteristic 'leaf-like' projections are seen on biopsy
- b. Most commonly seen in postmenopausal women
- c. Can be malignant in some cases

# MCQ

- 1) Which of the following is correct about large duct papilloma?
  - a) Below the nipple
  - b) Arise from the interstitium
  - c) Solitary
  - d) Multiple
- 2) Which of the following is characterized by a central nidus?
  - a) Phyllodes tumors
  - b) Fibroadenoma
  - c) Simple sclerosing lesion
  - d) Complex sclerosing lesion
- 3) A 44-year-old woman feels painless lumps in her armpit, which were not present a month ago. On examination, right axillary lymphadenopathy is present. The nodes are painless but firm. Which of the following is the most likely lesion in her right breast?
  - a) Acute mastitis with abscess
  - b) Fibroadenoma
  - c) Infiltrating lobular carcinoma
  - d) Intraductal carcinoma
- 4) A 34-year-old woman has noticed a bloody discharge from the nipple of her left breast for the past 3 days. On physical examination, the skin of the breasts appears normal, and no masses are palpable. There is no axillary lymphadenopathy. She has regular menstrual cycles and is using oral contraceptives. Excisional biopsy is most likely to show which of the following lesions in her left breast?
  - a) Acute mastitis
  - b) Fibroadenoma
  - c) Intraductal papilloma
  - d) Phyllodes tumor
- 5) 31 years old woman came to clinic complaining of a lump she feels sometimes, and sometimes she doesn't. What are you going to tell the patient about her condition?
  - a) "Don't worry about it it's mostly a benign lesion."
  - b) "Oh my god, this serious you will die in 5 years."
  - c) "I don't know, I didn't pay attention in pathology lecture."
  - d) "It's probably a condense milk mass."
- 6) A biopsy is taken from a breast, showing a leaf like pattern. What's the most likely diagnosis?
  - a) Fibroadenoma
  - b) Ductal carcinoma in situ
  - c) Phyllode tumor
  - d) Intraductal papilloma

# Cases

1. A 24-year-old woman is breastfeeding 3 weeks after giving birth to a normal term infant. She notices fissures in the skin around her left nipple. Over the next 3 days, a 5-cm region near the nipple becomes erythematous and tender. Purulent exudate from a small abscess drains through a fissure.

Q1) What is the organism that is most likely to be cultured from the exudate?

Q2) What is the most likely diagnosis?

2. A 27-year-old woman feels a lump in her right breast. She has normal menstrual cycles, she is G3, P3, and her last child was born 5 years ago. On examination a 2-cm, irregular, firm area is palpated beneath the lateral edge of the areola. This lumpy area is not painful and is movable. There are no lesions of the overlying skin and no axillary lymphadenopathy. A biopsy specimen shows microscopic evidence of an increased number of dilated ducts surrounded by fibrous connective tissue. Fluid-filled ducts with apocrine metaplasia also are present.

Q3) What is the most likely diagnosis?

Q4) Does it carry a risk for cancer?

Answers:

Q1) Staph aureus

Q2) Acute Mastitis

Q3) Fibrocystic Changes

Q4) No it does not



## Team Members:

Fahad Alfaiz  
Abduljabbar Alyamani  
Abdullah Alomar  
Abdulaziz Aldrgam  
Abdulelah Aldossari  
Hassan Aloraini  
Mohammad Alasqah  
Dawood Ismail  
Khalid Almutairi  
Norah Alkadi

## References:



MED437  
KING SAUD UNIVERSITY

