PATHOLOGY

○ Sheet ✓ Slide ○ Handout

Number

11

Subject

Pathology of The Breast

Doctor

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Price:

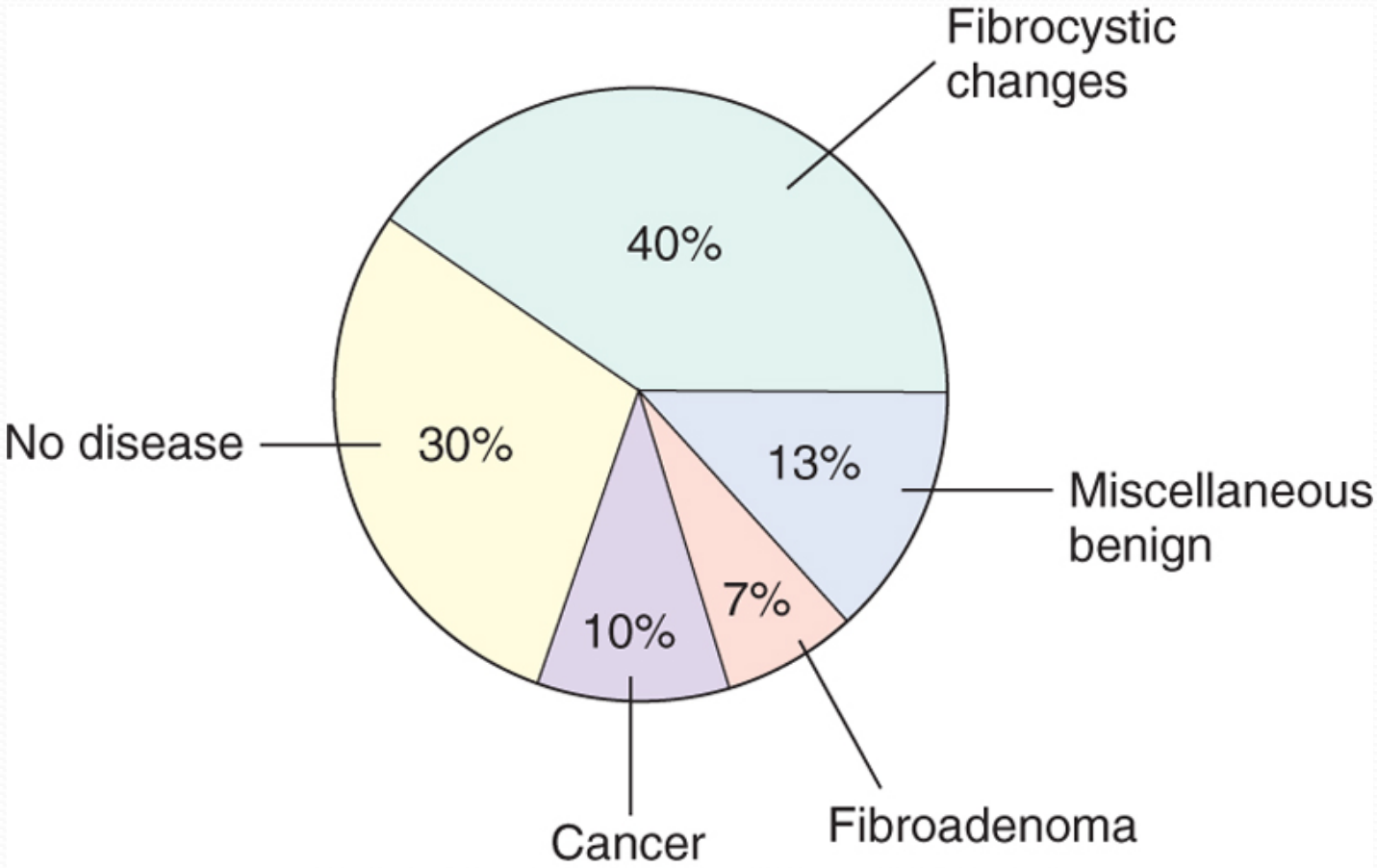
Pathology of The Breast

- Lesions of female breast are much more common than lesions of male breast
- Most of these lesions are benign
- **Breast cancer is 1st most common cancer; and 2nd most common cause of cancer deaths in women, following** carcinoma of the lung.
- clinical significance of **benign** conditions:

1- possible clinical confusion with malignancy

2- association of certain variants with breast carcinoma.

Breast diseases



Fibrocystic changes

- **most common cause of breast "lumps"**
- ***exaggeration of cyclic breast changes that occur normally in the menstrual cycle***.
- HRT and OCPs do **not** increase incidence; (OCPs may ***decrease*** the risk).
- arise during reproductive period of life
- Very common (at autopsy 60%-80% of women)
- A spectrum of changes (fibrosis and cysts formation, to proliferative types)

TUMORS OF THE BREAST

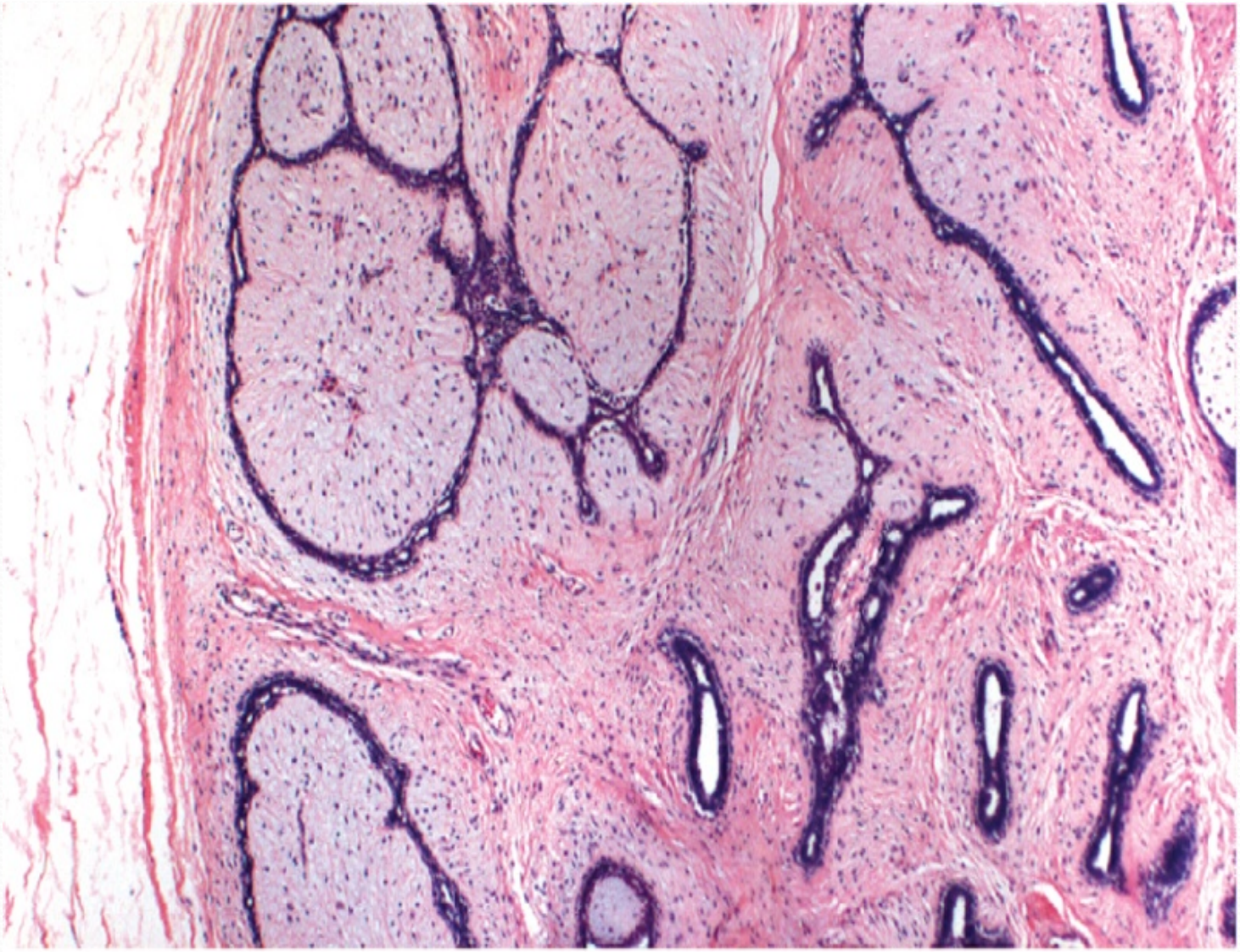
1- Fibroadenoma

- most common benign neoplasm of female breast.
- increase in estrogen activity
- Most in third decade of life.
- a discrete, solitary, freely movable nodule, (1 to 10 cm). Usually easily "shelled out“ surgically.
- enlarge late in menstrual cycle and during pregnancy.
- After menopause regress and calcify.

Fibroadenoma

- **Cytogenetic studies ➔ stromal cells are monoclonal and so represent the neoplastic element of these tumors (**the neoplastic stromal cells secrete growth factors that induce proliferation of epithelial cells**).**
- **Fibroadenomas almost never become malignant.**

Fibroadenoma



Carcinoma of the Breast

- **the most common cancer in females**
- **ranking second** only to lung cancer as a cause of **cancer death** in women.
- 75% are **older than age 50**.
- Only 5% are < 40.

Pathogenesis

(1)Genetic Changes

- familial syndromes (BRCA genes)
- sporadic breast cancer: e.g. overexpression of the ***HER2/NEU*** **proto-oncogene** (30% of cases)

(2)Hormonal Influences

- increased exposure to **<u>estrogen</u>**

(3)Environmental Variables

Factor	Relative Risk
Well-Established Influences	
Geographic factors	Varies in different areas
Age	Increases after age 30yr
Family history	
First-degree relative with breast cancer	3.0-1.2
Premenopausal	3.1
Premenopausal and bilateral	9.0-8.5
Postmenopausal	1.5
Postmenopausal and bilateral	5.4-4.0
Menstrual history	
Age at menarche <12yr	1.3
Age at menopause >55yr	2.0-1.5
Pregnancy	
First live birth from ages 25 to 29yr	1.5
First live birth after age 30yr	1.9
First live birth after age 35yr	3.0-2.0
Nulliparous	3.0
Benign breast disease	
Proliferative disease without atypia	1.6
Proliferative disease with atypical hyperplasia	2.0<
Lobular carcinoma in situ	12.0-6.9
Less Well-Established Influences	
Exogenous estrogens	
Oral contraceptives	
Obesity	
High-fat diet	
Alcohol consumption	
Cigarette smoking	

Major Risk Factors

- **Age.**
- **Genetics and Family History:**

- **50% of hereditary breast cancer → mutations in *BRCA1*; *30%* in *BRCA2* .**

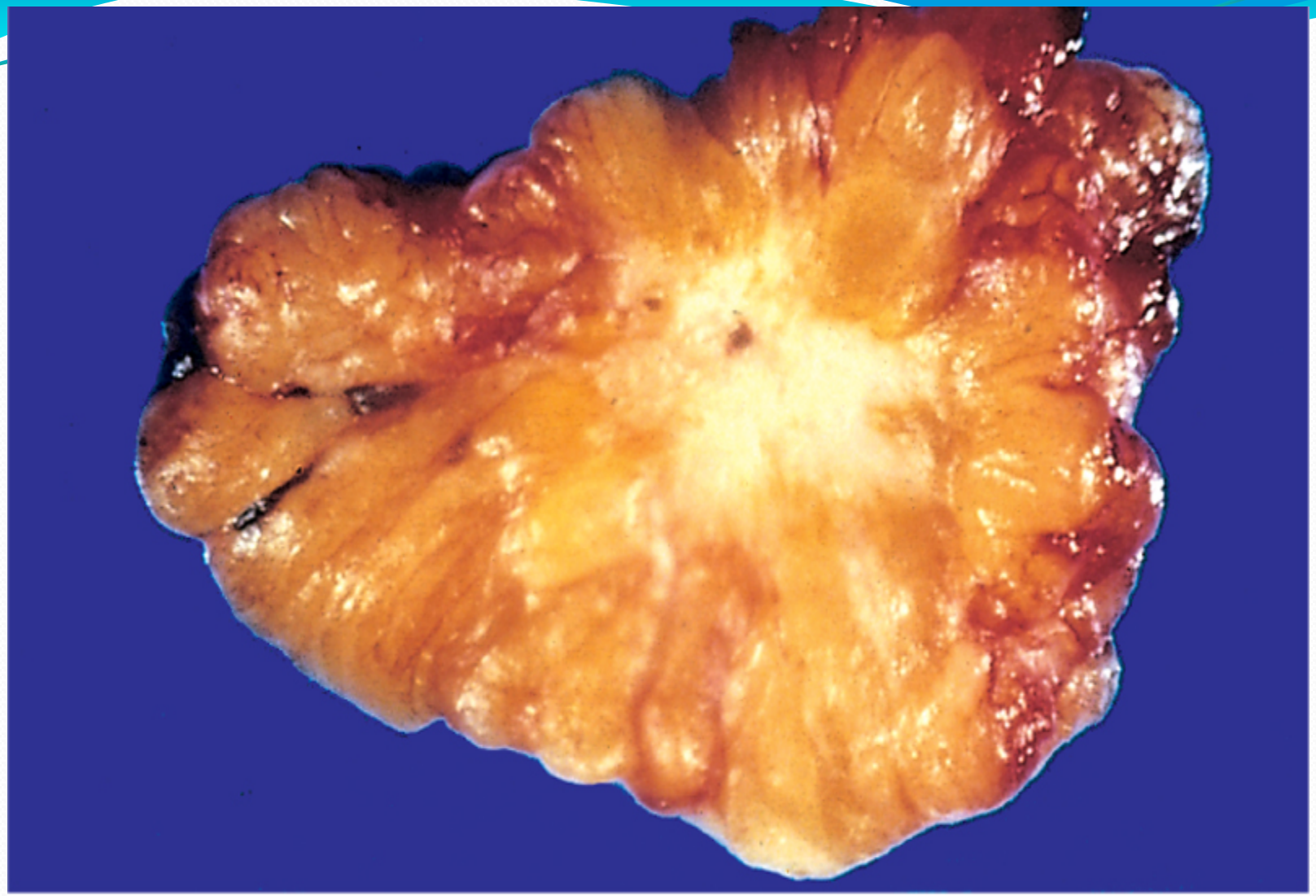
- **Prolonged exposure to exogenous estrogens postmenopausally (HRT)**
- **Ionizing radiation, in early life years**

Morphology of breast cancer

- The locations of the tumors within breast are:

- Upper outer quadrant 50% (most common)
- Central portion (sub-areola) 20%
- Lower outer quadrant 10%
- Upper inner quadrant 10%
- Lower inner quadrant 10%

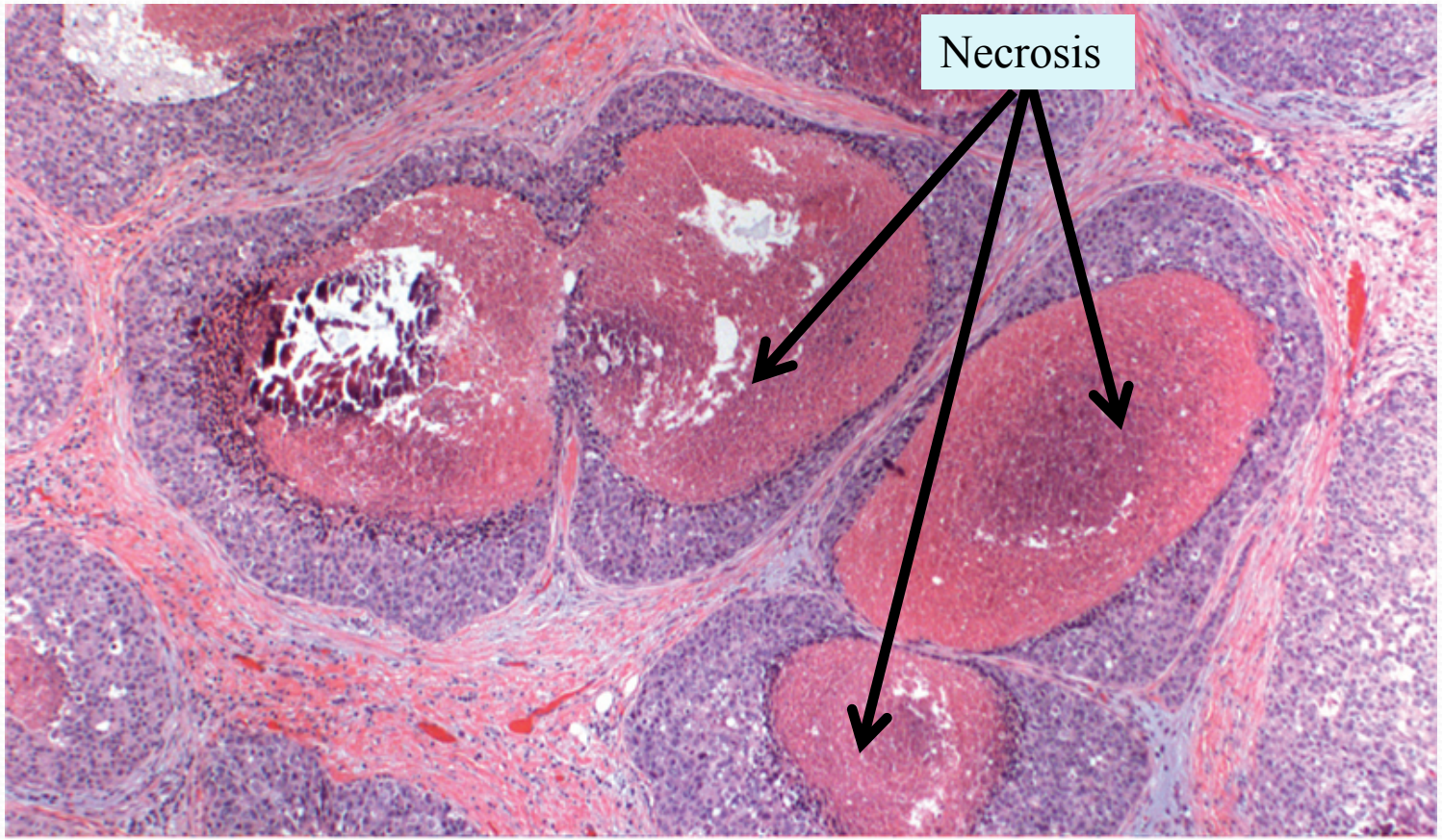
- **Breast cancers are classified into:**
- **Noninvasive** (*confined by a basement membrane and do not invade* into stroma or lymphovascular channels), include:
  - Ductal carcinoma in situ (DCIS)
  - Lobular carcinoma in situ (LCIS)
- **Invasive (infiltrating)**
  - Invasive ductal carcinoma – NOS (**most common** type)
  - Invasive lobular carcinoma
  - Medullary carcinoma
  - Colloid (mucinous) carcinoma
  - Tubular carcinoma
  - Other types



Ductal carcinoma in-situ DCIS

- ranges from low to high nuclear grade.
- **comedo** subtype: high-grade nuclei with *extensive central necrosis*. (The name derives from the toothpaste-like necrotic tissue).
- **Calcifications** are common→ screening by mammography
- Prognosis : excellent (97% survival post mastectomy)
- Treatment strategies: surgery, radiation, tamoxifen
- Significance: adjacent invasive CA; become invasive if untreated

Comedo DCIS

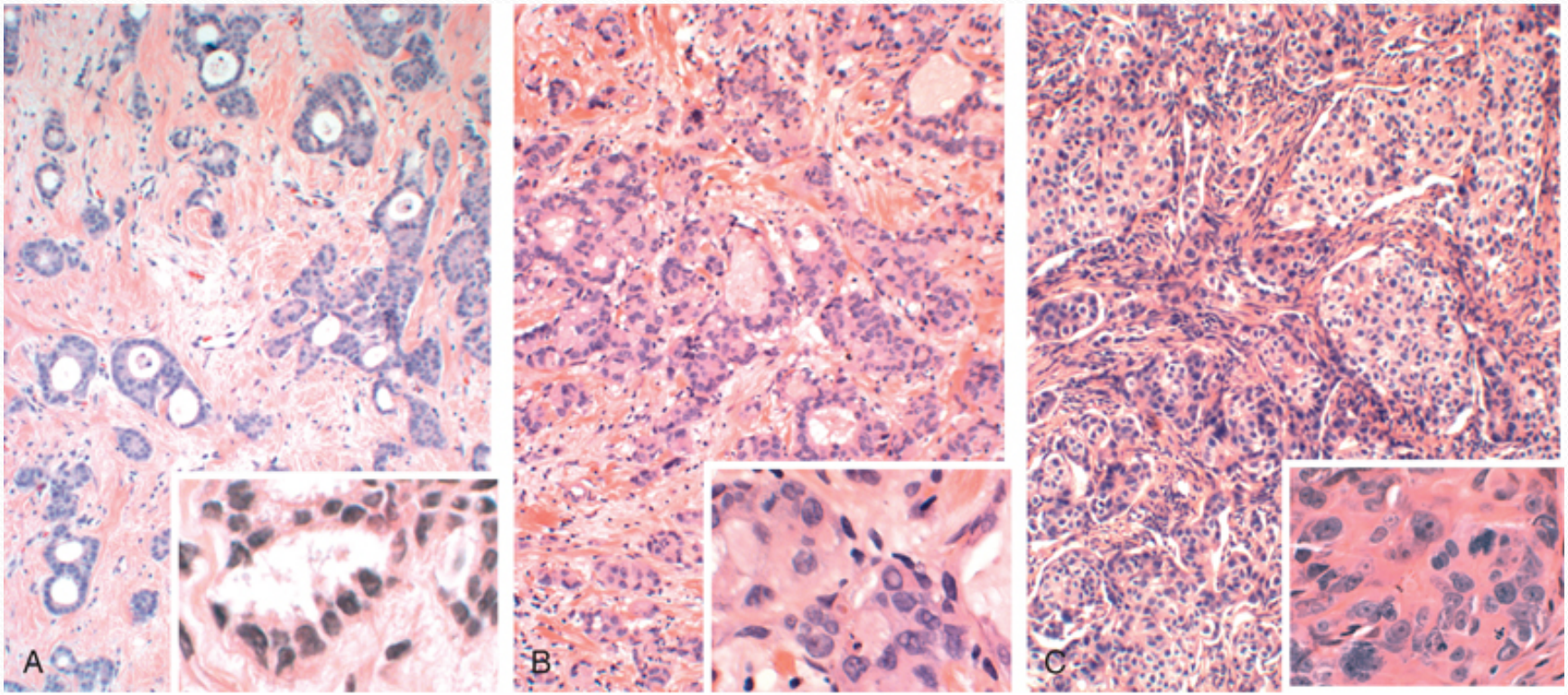


Kumar et al: Robbins Basic Pathology, 9e.

Invasive ductal carcinoma

- **"not otherwise specified“= NOS**
- 70% to 80%
- **Precancerous lesion**: DCIS
- **Clinical presentation:** a mammographic density; a hard mass. Advanced cancers may cause retraction of nipple, or fixation to chest wall.
- **Receptor profile**: 2/3 express ER or PR; 1/3 overexpresses HER2/NEU.

Invasive ductal carcinoma



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Invasive lobular carcinoma

- **< 20%** of all breast carcinomas.
- **Precancerous lesion**. LCIS (2/3) .
- multicentric and bilateral (10% to 20%).
- **Clinical presentation**. palpable masses or mammographic densities
- Almost all of these carcinomas express ER and PR, but HER2/NEU overexpression is usually absent.

Physical Features Common to All Invasive Cancers

- **Fixation: tumor** adherence to pectoral muscles or deep fascia of chest wall
- **retraction** or **dimpling** of skin or nipple: tumor adherence to overlying skin
- **peau d'orange** (orange peel): Involvement of lymphatic pathways cause localized lymphedema; the skin becomes thickened around exaggerated hair follicles

Spread of Breast Cancer

- **lymphatic** and **hematogenous** channels.
- Favored mets are the **lungs**, **skeleton**, **liver**, and **adrenals** and (less commonly) the brain, spleen, and pituitary.
- *Metastases may appear many years after apparent therapeutic control of the primary lesion*
- **SCREENING :**
- mammographic screening
- Magnetic resonance imaging MRI

Prognosis depends on:

1- **Tumor size**.

2- **Lymph node involvement (&number of lymph nodes involved) by metastases**.

3- **Distant metastases**.

4- Grade

5- Histologic type (invasive ductal NOS is the worst)

6- Presence or absence of estrogen or progesterone receptors.

7- **Proliferative rate of cancer**.

8- **Aneuploidy (**worse prognosis).

9- **Overexpression of HER2/NEU (**predict response to a monoclonal antibody ("Herceptin")).

Male breast pathology

Gynecomastia

- Enlargement of the male breast
- absolute or relative estrogen excesses.
- According to cause, divided into:

1- **pathologic gynecomastia:** cirrhosis of the liver; Klinefelter syndrome; estrogen-secreting tumors; estrogen therapy; digitalis therapy.

2- Physiologic gynecomastia: puberty and extreme old age.

Carcinoma of the male breast

- male: female breast cancer →1: 125.
- advanced age.
- Because of scant amount of breast substance in male, the tumor rapidly infiltrates overlying skin and underlying thoracic wall.
- Unfortunately, (½) have lymph nodes mets and more distant sites by time of diagnosis.