Epidemiology:

•The most common non-skin malignancy of women
•2nd most common cause of cancer deaths in women, following carcinoma of the lung.
•the incidence and mortality are improving with the increased screening and decreased use of hormone replacement therapy.

Risk factors:

1-Age:
•incidence increases rapidly after age 30
•75% of women with breast cancer are >50 yrs
2-Gender:
•The incidence in men is only 1% of that in women.
3-Family History of Breast Cancer:
•multiple affected first-degree relatives with early-onset breast cancer.
4-Geographic Factors:
•higher in the Americas and Europe than in Asia and Africa
•migrants from low incidence to high-incidence areas tend to acquire the rates of their new home countries due to change in diet, reproductive patterns, breastfeeding practices and adoption of Western habits.
5-Reproductive History:
•Early age of menarche<12, nulliparity (never pregnant), absence of breastfeeding, and older age at first pregnancy>35 are all associated with increased risk -->due to increased the exposure to estrogenic stimulation.
6-Ionizing Radiation (Chest Radiation)
7-Other Risk Factors:
•Postmenopausal obesity •postmenopausal hormone replacement
• mammographic density •alcohol consumption

Pathogenesis:

▪ Factors that contribute directly to the development of breast cancer can be grouped into:
1- genetic: BRCA1 and BRCA2 / HER2 amplification /TP53; PTEN
2-Hormonal: Estrogen related
3-environmental

Morphology:

- Location:
  - upper outer quadrant (50%) – central portion- subareolar (20%).
  - Lower outer quadrant 10% – Upper inner quadrant 10% – Lower inner quadrant 10%

- 4% have bilateral primary tumors or sequential lesions in the same breast.

Breast carcinoma:

A. Noninvasive:(confined by a basement membrane and do not invade into stroma or lymphovascular channels), include:

1. Ductal carcinoma in situ (DCIS) 2. Lobular carcinoma in situ (LCIS)

B. Invasive (infiltrating):

1. Invasive ductal carcinoma-NOS --> 70% to 80%
2. Invasive lobular carcinoma –>10% to 15%
3. Carcinoma with medullary features-->5%
4. Mucinous carcinoma (colloid carcinoma) –>5%
5. Tubular carcinoma–>5%
6. Other types

A-Noninvasive (in situ) carcinoma :

- include: 1. Ductal carcinoma in situ, DCIS 2. Lobular carcinoma in situ, LCIS
- By definition both confined by a basement membrane and do not invade into stroma or lymphovascular channels

LOBULAR carcinoma in-situ (LCIS)	Ductal carcinoma in-situ (DCIS)
■ Malignant clonal proliferation of cells within lobules and ducts ■ Cells grow in a discohesive fashion –> an acquired loss of the tumor suppressive adhesion protein Ecadherin. ■ The term "lobular" was used to describe this lesion because the proliferation takes an appearance resembling lobules	■ malignant clonal proliferation of epithelial cells within ducts and lobules. ■ DCIS has a wide variety of histologic appearances including: – solid – comedo –cribriform – papillary, and micropapillary

B- INVASIVE (INFILTRATING) BREAST CARCINOMA: Classification Systems

•Classification Systems

• In all cases of breast cancer, we examine the following Receptors:

- Estrogen receptor (ER);
-progesterone receptor (PR);
-human epidermal growth factor receptor 2 (HER2/neu)

• Cancer can be classified according to expression of hormone receptors into three major groups:

-ER positive (HER2 negative; ≈ 60%)
-HER2 positive (ER positive or negative; 20%)
-Triple negative (ER, PR, and HER2 negative; 1

Types:	Charactaristic	Receptor file
1- Invasive ductal carcinoma	■ 70% to 80% ■ Also called Carcinomas "not otherwise specified" ■ **Precancerous lesion**: usually DCIS ■ **Clinical presentation**: mammographic density or hard, palpable irregular mass.	Usually: ER, PR (+), HER2 (-)
2-Invasive lobular carcinoma	■ 10-15% of all breast carcinomas. ■ **Precancerous lesion**. 2/3 associated with LCIS. ■ multicentric and bilateral (10% to 20%). ■ **Clinical presentation**. Most present as palpable masses or mammographic densities ■ Histologically, cells invade stroma **individually** and often are aligned in **"single-file"**	■ receptor profile: Usually express ER & PR while HER2 overexpression is rare or absent.
3-carcinoma with Medullary features:	■5% ■ **Microscopically**: large anaplastic cells with pushing, well- circumscribed borders. With a pronounced lymphocytic infiltrate. ■ **Precancerous lesions.** usually absent ■ increased frequency in women with BRCA1 mutations.	■ receptor profile: Triple negative (ER, PR, and HER2 all negative).
4-Colloid (mucinous) carcinoma	■ a rare subtype. ■ **Grossly** the tumors are usually soft and gelatinous. ■ **Microscopic picture**. The tumor cells produce abundant quantities of extracellular **mucin** that dissects into the surrounding stroma.	■ receptor profile: ER-positive, HER2-negative

5-Tubular carcinomas	■<5% ■ **Clinical presentation**. Almost always detected as irregular mammographic densities. ■ **Microscopically**, well-formed tubules with low-grade nuclei. ■ **Lymph node metastases**: rare ■ **Prognosis: excellent.**	■ Receptor profile: ER-positive, HER2-negative

Features Common to All Invasive Cancers

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

Spread of Breast Cancer

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

Prognosis:

1. Tumor stage:
   - A-Invasive carcinoma versus carcinoma in situ
   - B- tumor size.
   - C-Lymph node involvement and the number of lymph nodes involved by metastases.
   - D- Distant metastases.
2. Histologic grade
3. histologic type of carcinoma
4. Lymphovascular invasion
5. estrogen or progesterone receptors expression
6. Overexpression of HER2
   - ■ the importance of evaluating HER2 s to predict response to a monoclonal antibody ("Herceptin") against the gene product.

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