BREAST PATHOLOGY

- Lesions of the breast are very common, and they present as palpable, sometimes painful, nodules or masses.
- Most of these lesions are benign.
- **Breast cancer is the 2nd most common cause of cancer deaths in women, following** carcinoma of the lung.
- If a women presents with a mass:
  - Most commonly, the change is a fibrocystic change → 40%
  - There will be no disease in 30% of cases
  - Only in 10% there will be cancer
  - Fibroadenoma in 7%
  - Others 13%

We don't need to know the numbers, just know that the most common change is fibrocystic and that there is a good percentage of women that feel a mass but there is in fact no disease.

❖ Fibrocystic Changes

- Previously called *fibrocystic* ***disease*** which is misleading to physicians, the term *fibrocystic* ***changes*** is preferred.
- Very common → **75%** of women are found to have it on autopsy.
- It is a normal change due to cyclic hormonal changes. Oral contraceptives and hormonal replacement therapy do NOT increase the risk of fibrocystic changes.
- ***Asymptomatic*** in most cases.
- Certain changes will occur at the affected location in the breast, which range from very benign changes that do not go into malignancy to more dangerous changes, and these changes are divided into two types:

1. Proliferative:

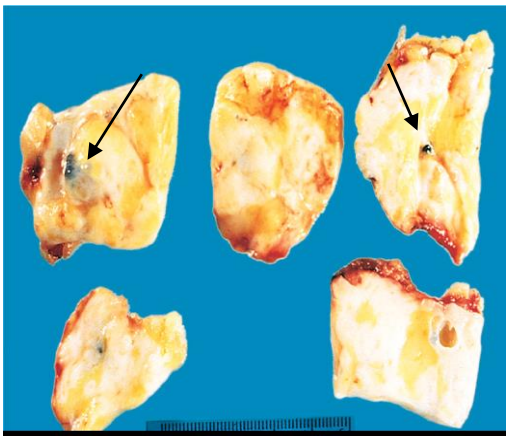
- A continuum of changes which start out as **hyperplasia** and progress into atypical hyperplasia (atypical nuclear changes: irregularity in membrane, increased mitoses, etc)
- As atypia increases, there is an increased risk of malignancy (still, not a huge risk)
- Clinical findings of Hyperplasia:
  - Alone: does not produce symptoms
  - Hyperplasia is associated with ***microcalcifications***, which are common and can be detected in a mammogram. Early detection by mammography can help prevent progression into carcinoma.

It does NOT produce a mass, and this is NOT what we detect in mammograophy.

- Lesions can be **multifocal**, therefore the risk of malignant transformation increases in both breasts. A patient could present with microcalcification in the right breast then develop carcinoma in the left one a few years later. This is since lesions are commonly **bilateral** and there might have been an unnoticed lesion in her left breast.
- The presence of **family history** increases the risk of malignancy **2x** more, and **Atypical** hyperplasia increases the risk **5x**, therefore if both are found the risk is increased 10x.

2. **<u>Non-Proliferative</u>**:

- Fibrotic and Cystic changes that are completely benign (increase in fibrous stroma and formation of cysts).
- The cystic epithelial cells may undergo ***apocrine metaplasia***: the cell becomes larger, contains a larger nucleus, with abundant granular, eosinophilic cytoplasm → contains lots of **mitochondria.**
- Grossly: we see tiny cysts, the white color seen refers to the fibrosis (normally, breast tissue is yellow as it is adipose tissue).



- **<u>Fibrocystic changes & their relation with cancer:</u>**

***1*- Minimal or no increased risk (Negligible):**
Fibrosis, Cysts (microscopic or macroscopic), Apocrine metaplasia, Mild hyperplasia.
***2*- Slightly increased risk (1.5-2 times normal):**
Moderate to florid (severe) hyperplasia: <u>without atypia.</u>
***3*- Significantly increased risk (<u>5 times</u>):**
<u>Atypical</u> hyperplasia.

❖ Inflammation of The Breast

- Common, especially in *lactating* women and is mostly an abscess. HOWEVER, you should never neglect a mass in the breast as a doctor and send a lactating woman home, telling her that this is caused by lactation.

EVERY MASS IN THE BREAST SHOULD BE CONSIDERED AS A MALIGNANT MASS UNLESS PROVEN OTHERWISE. The masses should always be investigated through fine needle aspiration and biopsy to confirm if the lesion is malignant or benign.

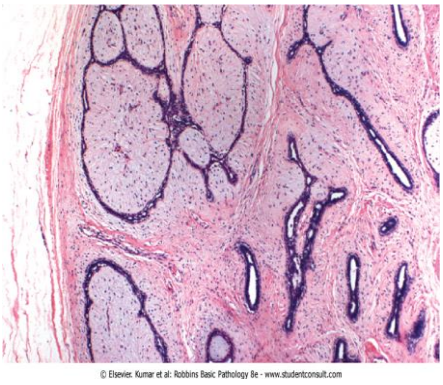
- **Not** associated with an increased risk of carcinoma.
- Could be due to infectious or non-infectious causes.
- The most common causes of bacterial inflammation: Strept. + Staph., to treat this we give antibiotics and drain the abscess.

- **<u>Traumatic Fat Necrosis</u>**:

- An inflammatory condition that is significant due to the fact that it ***clinically resembles carcinoma***
- Common in women due to "Seat-Belt Trauma", or any minor trauma of the breast → leads to fatty necrosis, and eventually this solidifies into a non-mobile mass that is clinically similar to breast carcinoma.
- It is easily differentiated thorough a histological exam.

❖ Tumors of The Breast

1. ***Fibroadenoma:***



- The most common benign tumor of the breast
- Presents as a mobile, rubbery, soft mass that is encapsulated
- It does NOT undergo malignant transformation
- Histologically: There is proliferation of the ducts (glands) and stroma.

Note that:

- Proliferation of the glands without the stroma → hyperplasia.
- 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).

- Increased **Estrogen** activity causes it

- Therefore, they may enlarge late in the menstrual cycle and during pregnancy.
- After menopause they usually regress and calcify.

2. ***Phyllodes Tumor:***

- Could be benign, borderline or malignant. This depends on the cellularity, the mitotic activity, and behavior (infiltrative or not).
- In most of the cases it is a benign tumor.
- Comparison to Fibroadenoma:
  - ***Prominent Stroma***: Stromal Proliferation much more significant than that seen in Fibroadenoma. The stroma is also *extremely cellular* and their *mitotic activity is very high.*
  - ***Glands***: proliferate much less than Fibroadenoma. They have a **leaf-like** pattern.
- Only 15% are frankly malignant and undergo distant metastasis.

3. *Carcinoma of The Breast:*

- It is the **most common cancer** in females and the **second most common cause of death**.
- Occurrence is usually after the **age of 50**, but nowadays we see it at much younger ages.
- Recurrences are very common, can occur even after 15 years after treatment, while in colon cancer, if the patient survived for 5 years after the cancer, he is normal again. So, in breast cancer, your patient will have to checkup with you forever.

- **Pathogenesis of breast cance**r:
  - *Genetic Changes*

Familial cases are associated with mutations in these genes BRCA1, BRCA2, Her-2 (treated with Herceptin).

  - *Hormonal Influences*

Caused by Estrogen (any unopposed "high" estrogen is dangerous), so it is accepted nowadays that oral contraceptives do not increase the risk for breast cancer because they balance estrogen and progesterone.

  - *Environmental Variables*

Pregnancies, younger age of first childbirth, and lactation are protective.

- **Risk Factors:**
  - *Menstrual age and Age of onset of Menopause*: as reproductive age increases, the time that a woman is exposed to estrogen increases, and this increases the risk.
  - Pregnancy: as age of the first babe increases (25-30) "being nullipara", risk increases.
  - Breast feeding: it is protective, so who does not breast feed will have an increased risk.
  - Family history of breast cancer *significantly* increases the risk:

▪ If a first degree relative has a history of breast cancer, this increases the risk up to 2-3x. If this first degree relative had the tumor at a young age (<50) and her cancer is bilateral, the risk increases 8.5-9x.

  - Proliferative lesions: as atypia and severity of proliferation increases the risk increases.
  - Exogenous Estrogen.
  - Obesity increases the risk since it is related to estrogen.
  - Oral contraceptives most likely carry no increased risk.

Note: the most important ones to know are the family history and which proliferative lesions increase the risk.

- **Morphology of breast cance**r:
- The **most common location** of breast carcinoma is the **<u>UPPER OUTER quadrant</u>** and this is in 50% of tumors. 20% are centrally located, and 10% for other three quadrants.

- **Breast Cancer Spreads Through: lymphatic and hematogenous (blood) channels.**

The spread is commonly through the axillary lymph nodes and they must be examined when breast cancer is suspected**.**

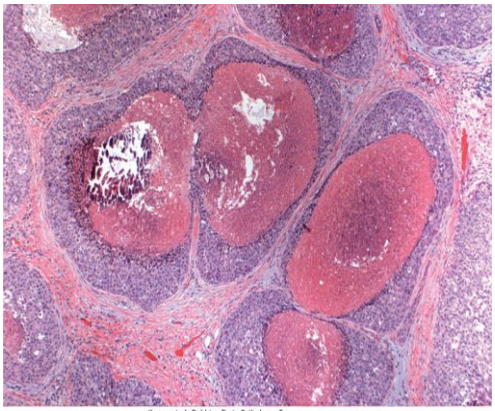
- **Sites of Metastasis: Lungs, Liver, Bone (breast cancers commonly go to the bone.)**
- **Prognosis:** depends on many factors but most commonly **the Stage of the cancer (spread)**

- **Breast cancers are classified as:**

• Non-invasive "In Situ"

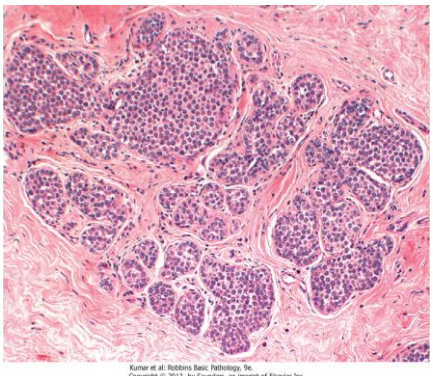
○ ***Ductal Carcinoma In Situ (DCIS):***

- Breast duct enlarged due to malignant growth but is confined to the duct by a basement membrane → in situ (dysplasia confined to the duct).
- Pre-malignant.
- More common than lobular.
- Can transform into *invasive ductal carcinoma.*
- One of its types is ***Comedo Necrosis*** → ducts with extensive central necrosis, it is a very aggressive type with a high risk of transformation into an invasive carcinoma.
- DCIS is detected by seeing the calcifications in a mammogram, but it CAN cause a mass (unlike fibrocystic hyperplasia), but it is most commonly detected due to the presence of microcalcifications.
- Neoplastic cells are usually positive for estrogen and progesterone receptors and therefore might be treatable hormonally.
- ***Histologically***: Stroma has no abnormal cells. The ducts are dilated and are filled with malignant cells, and in the Comedo type "only" there is necrosis in the middle.



○ ***Lobular Carcinoma In Situ (LCIS):***

- Can transform into *invasive lobular carcinoma* (usually) but might transform into *invasive ductal carcinoma* less commonly.
- Dysplasia inside the lobules with abnormal neoplastic cells which fill and distend the lobules, they are surrounded by a basement membrane.
- **Rarely** associated with calcification → can't be detected through mammography.
- Subsequent invasive carcinomas arise in **either breast** at significant frequency.
- Usually does not form a mass.
- Note: **Lobular:** more likely to go into the *CNS and the brain* than the ductal. And they are more likely to be *bilateral and multicentric*.



• Paget Disease Of The Nipple:

- Tumor cells migrate from the ducts or lobules, up to the lactiferous ducts and into the epithelium of the nipple.
- It could be associated with invasive as well as non-invasive types of breast cancer.
- Tumor cells pass within the duct system, therefore the cancer does not reach blood vessels or lymph nodes.

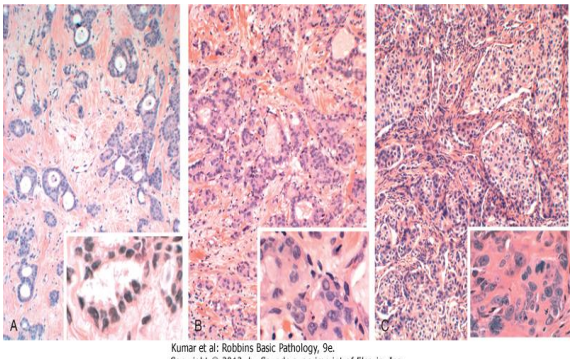
- **Invasive**
  - ***Ductal***:

- Much more common than lobular, not confined.
- Has many types:

Invasive Ductal Carcinoma NOS (not otherwise specified) is the most common type. It also has many variants, which are named accordingly:
Medullary, Colloid (Mucinous), Tubular.

Tubular Carcinoma is very well-differentiated and has a much better prognosis than the other variants.

- Its precursor lesions are commonly DCIS and rarely LCIS.
- Infiltrative, solid, hard masses which are fixed to the breast tissue.
- 2/3 express estrogen or progesterone and 1/3 over-express HER2/NEU.
- Ranges from well-differentiated tumors to poorly differentiated ones consisting of sheets of anaplastic cells.



  - ***Lobular***

- < 20% of all breast carcinomas. Each cell lines are often aligned in chains or strands (Indian/single filing pattern). They do NOT have a glandular pattern.
- Express hormone receptors (estrogen and progesterone), but HER2/NEU over expression is very rare or absent.
- More commonly goes to the brain and CNS than the ductal.
- More common to be bilateral and multi-centric. “this must be thought of while doing incision”.

❖ Male Breast Pathology

1. Gynecomastia

- Enlargement of the male breast due to increased estrogen levels.
- This increased estrogen could be due to different causes:
  - **Exogenous**: anabolic steroids, converted to estrogen in our body.
  - **Endogenous**: cirrhosis of liver, estrogen-secreting tumors.
- **Morphology**: similar to those of intraductal hyperplasia (increase in size as well as the number of cells).

2. Carcinoma of the male breast

- Very rare: frequency ratio to breast cancer in the female of **1: 125.**
- Both morphologically and biologically, resemble invasive carcinomas in the female.
- The problem here is that it easily penetrates and spreads due to the scant amount of breast substance in the male. Unfortunately, almost 1/2 have spread to regional lymph nodes and more distant sites by the time they are discovered.

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