Diseases of the Breast

- Congenital
  - Aplasia Turners
  - Juvenile Hypertrophy

- Inflammatory
  - Chronic/ Acute Infections
  - Duct Ectasia
  - Fat Necrosis

- Fibrocystic Changes
  - Non-Proliferative Changes
  - Duct Ectasia
  - Cysts and Fibrosis
  - Epithelial Hyperplasia
  - Sclerosing Fibrosis

- Neoplastic
  - Benign
    - Fibroadenoma, Duct Pappiloma, Adenoma, Connective Tissue Tumor
  - Malignant
    - Ductal
      - Ductal Carcinoma In Situ (15%)
      - Invasive Ductal Carcinoma (75%)
    - Lobular
      - Lobular Carcinoma In Situ (5%)
      - Invasive Lobular Carcinoma (5%)
<table>
<thead>
<tr>
<th>Diseases</th>
<th>Epidemiology/ Clinical Features</th>
<th>Morphology</th>
<th>Microscopic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Mastitis</strong></td>
<td>• Acute bacterial inflammation of the breast</td>
<td>• Single or multiple abscesses</td>
<td>• All acute inflammatory changes</td>
</tr>
<tr>
<td></td>
<td>• Due to bacterial infection usually Staph aureus</td>
<td>• Usually small</td>
<td></td>
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<tr>
<td></td>
<td>○ Gain access through</td>
<td>• When it is large, will undergo fibrosis leading to scar that can be</td>
<td></td>
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<tr>
<td></td>
<td>▪ Aspiration of secretions</td>
<td>palpatate as induration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>▪ Fissures at the nipple that developed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>● During early weeks of nursing</td>
<td>• Typical inflammatory changes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>● Due to pre-existing Dermatitis in the nipple</td>
<td>○ Breast swelling</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Painful</td>
<td>○ Breast tenderness</td>
<td></td>
</tr>
<tr>
<td><strong>Mammary Duct Ectasia/ Periductal/ Plasma Cell Mastitis</strong></td>
<td>• Chronic non-bacterial inflammation of the breast</td>
<td>• Affect the corresponding lobule in response to plugged ducts</td>
<td>• Granular debris</td>
</tr>
<tr>
<td></td>
<td>• Due to plugging of the breast main excretory duct</td>
<td>• Increased firmness of tissues</td>
<td>• Lipid-laden macrophages</td>
</tr>
<tr>
<td></td>
<td>• Happen in 40-50 years old women who have children</td>
<td>• Cut surface</td>
<td>• Periductal appearance of</td>
</tr>
<tr>
<td></td>
<td>• Clinical feature</td>
<td>○ Dilated rope-like duct</td>
<td>○ Lymphocytic and plasma cells infiltration</td>
</tr>
<tr>
<td></td>
<td>○ Induration of breast substance</td>
<td>○ Thick and cheesy secretion can be found</td>
<td>○ Granuloma</td>
</tr>
<tr>
<td></td>
<td>○ Retraction of the nipple and skin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>○ Mimicking the Breast Carcinoma</td>
<td></td>
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</tr>
<tr>
<td><strong>Traumatic Fat Necrosis</strong></td>
<td>• Uncommon lesion</td>
<td>• At the earlier stages, lesions appear</td>
<td>• Central focus of Touton giant cells</td>
</tr>
<tr>
<td></td>
<td>• Have history of</td>
<td>○ Small</td>
<td>• Surrounded by</td>
</tr>
<tr>
<td></td>
<td>○ Trauma</td>
<td>○ Often tender</td>
<td>○ Neutrophils</td>
</tr>
<tr>
<td></td>
<td>○ Prior surgical intervention</td>
<td>○ Sharply localized</td>
<td>○ Lipid-laden Macrophages</td>
</tr>
<tr>
<td></td>
<td>○ Radiation therapy</td>
<td></td>
<td>• Later enclosed by</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Fibrose tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>○ Mononuclear cells</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• The focus replaced by scar/ cysts</td>
</tr>
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<td></td>
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<td></td>
<td>○ Calcification can develop within the Cysts or Cyst wall</td>
</tr>
</tbody>
</table>
# Fibrocytic Changes of the Breast

## Non-Proliferative Changes

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Epidemiology/ Clinical Features</th>
<th>Gross</th>
<th>Morphology</th>
</tr>
</thead>
</table>
| **Cysts and Fibrosis**  | • Most common breast disorder in women  
|                         | • Diagnosed at the age of 20-40 years old  
|                         | • Not associated to progression to cancer  
|                         | • Might be due to hormonal imbalances    | • Often bilateral  
|                         |                                   | • Single of multifocal cysts  
|                         |                                   | • Appeared to be brown to blue (so called Blue Dome Cysts)  
|                         |                                   | • The content can be  
|                         |                                   | ▪ Turbid  
|                         |                                   | ▪ Serous  
|                         |                                   | ▪ May calcify and appear as microcalcification on the Mammogram  
|                         |                                   | • Smaller cysts  
|                         |                                   | ▪ Epithelium more Cuboidal/ Columnar polygonal cells  
|                         |                                   | ▪ Abundant Eosinophilic cytoplasm  
|                         |                                   | ▪ Hyperchromatic nuclei  
|                         |                                   | ▪ So called the Apocrine Metaplasia  
|                         |                                   | • Sometimes multi-layered in focal area  
|                         |                                   | • Larger cysts  
|                         |                                   | ▪ Epithelium often flattened and sometimes Atrophic  
| **Proliferative Changes** | • Premalignant lesion  
| **Epithelial Hyperplasia** | • Irregular palpable lumps mimicking Breast Ca  
|                         | • Increase the number of layers of cells lining the ducts and acini  
|                         | • Involved ducts and acini are filled with overlapping proliferating cells  
|                         | • Atypical Hyperplasia  
|                         | ▪ Atypical cytologic features  
|                         | ▪ Can be either  
|                         | ▪ Atypical Ductal Hyperplasia – Ducts  
|                         | ▪ Atypical Lobular Hyperplasia – Lobule  
|                         | ▪ It almost resemble Carcinoma In Situ but not enough evidential to be called one  
| **Sclerosing Adenosis** | • Less common compared to Cysts  
|                         | ▪ Hyperplasia  
|                         | ▪ Premalignant lesion  
|                         | • Lesions are  
|                         | ▪ Hard  
|                         | ▪ Rubbery consistency  
|                         | ▪ Breast cancer-like lesion  
|                         | • Proliferations of  
|                         | ▪ Epithelium  
|                         | ▪ Myoepithelium  
|                         | • Affecting the small duct and ductules  
|                         | ▪ Yielding small gland patterns  
|                         | ▪ Fibrous stroma  
|                         | • The glandular cells are interconnecting with each other forming aggregated glands (Adenosis)  
|                         | • Marked stromal fibrosis  
|                         | ▪ This fibrous tissue may compress the lumen of the ducts  
|                         | ▪ May appear as solid cords of cells  

## Neoplastic Diseases of the Breast
### Benign Tumor of the Breast

<table>
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<tr>
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<th>Morphology</th>
<th>Microscopic</th>
</tr>
</thead>
</table>
| **Fibroadenoma**  | • Most common benign tumor of the breast  
• Happen at the age of <30 years old                                                            | • Breast mouse  
  o Firm  
  o Mobile lump  
• Cut surface  
  o Uniform tan-white color  
  o Softer yellow-pink spot representing glandular areas  
• Giant lumps may appear in younger women  
• Very well circumscribed  
  o Loose fibroclastic stroma containing  
  o Duct-like  
  o Epithelium line spaces  
• These cells are regular in shape with intact basement membrane  
• Proliferating intralobular stroma may distort associated Epithelium  
• Can be sharply distinguish from the normal surrounding tissue |                                                                                               |
| **Intraductal Papilloma** | • Neoplastic growth within the duct  
• They presented as  
  o Serous/ bloody nipple discharge  
  o Presence of small subareolar tumor  
  o Nipple retraction  
• Lesions often  
  o Solitary  
  o Found in the Lactiferous Duct/ Sinuses  
  o Branching growth |                                                                                               | Multiples papillae  
  o With CT axis  
  o Covered by double-layered cuboidal epithelium  
  ▪ Inner layer Myoepithelium  
  ▪ Outer layer Epithelium |
| **Phyllodes Tumor** | • Less common compared to Fibroadenoma  
• Arise from  
  o Periductal stroma  
  o Intralobular stroma  
• Usually benign  
  o Transformation into  
    Malignancy is common  
• Recurrence in malignant is common after removal  
• 15% of cases may disseminated into various organs  
• The first lesion might be small but can grow massively; distending the breast  
• The lesion can become lobulated and cystic  
• Grossly appeared as Leaf-like clefts and slits (Phyllodes)  
• Localized  
• Increase stromal cellularity with  
  o Anaplasia  
  o Increased mitotic activity  
  o Rapidly increasing the size of lesion |                                                                                               |
# Neoplastic Diseases of the Breast

## Malignant Tumor of the Breast
- The first most common malignancy in women worldwide
- The second most common (after lung ca) causes of death by malignant tumor in women
- Very rarely happens before the age of 25

### Etiology
- Unknown, multifactorial
  - Genetic
  - Hormonal
  - Environmental factors

### Risk factors
- Female sex
- Age
- Obesity
- High fat diet
- Longer reproductive age
- Nulliparity
- Oral contraceptive
- Longer age of pregnancy
- Presence of previous
  - Atypical Hyperplasia
  - Breast Ca
  - Endometrial Ca
- Genes
  - BRCA1
  - BRCA2

## Locations of Tumors

<table>
<thead>
<tr>
<th>Upper Outer Quadrant</th>
<th>Lower Outer Quadrant</th>
<th>Central Portion</th>
<th>Lower Inner Quadrant</th>
<th>Most Left Breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>50%</td>
<td>20%</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

### Prognostic Factors

#### 1. The size of primary Carcinoma
   - Smaller invasive tumor (<1cm) without lymph node involvement has the best prognosis

#### 2. Lymph nodes involvement and number of lymph nodes involved
   - Absence of Axillary Nodes involvement – 90% 5 years survival rate
   - Involvement of Axillary Nodes – 50% 5 years survival rate

#### 3. Distant metastasize
   - Hematogenous spread patient rarely survive
   - Even if aggressive chemo conducted, it will only prolong the survival rate

#### 4. The grade of Carcinoma
   - Well-differentiated Carcinoma – the best prognosis
   - Moderately differentiated Carcinoma – better prognosis
   - Poorly differentiated Carcinoma – worst prognosis

#### 5. The Histological type of Carcinoma
   - Specialized type of Breast Carcinoma – better prognosis
     - Tubular
     - Medullary
     - Cribriform
     - Adenoid cystic
     - Mucinous
   - Unspecialized type – poor prognosis
     - Ductal Carcinoma

#### 6. The presence/absence of Estrogen/Progesterone receptors
   - Presence of receptors – slightly better prognosis
   - Absence of receptors – poor prognosis

#### 7. The proliferative rate of Carcinoma
   - Higher proliferative rates has the poorest prognosis
   - Proliferative rate can be determined by
     - Mitotic bodies counts
     - Flow cytometry
     - Immunohistochemical staining for proteins in different stages of cellular cycle

#### 8. Aneuploidy
   - Carcinoma cells with abnormal DNA count (Aneuploidy) has the poorest prognosis

#### 9. Overexpression of HER2/NEU
   - Overexpression of this gene will lead to massive replication of gene
   - Associated with poorer prognosis
Carcinomas of the Breast

Non-Invasive Carcinoma In Situ
- Ductal Carcinoma In Situ (DCIS)
- Lobular Carcinoma In Situ (LCIS)
- Invasive Ductal Carcinoma / Scirrhous Carcinoma (no special type) (IDC)

Invasive Carcinoma
- Invasive Lobular Carcinoma (ILC)
- Medullary Carcinoma
- Mucinous Carcinoma
- Tubular Carcinoma
- Inflammatory Carcinoma

Diagnosis of Breast Cancer
1. Mammography
2. Ultrasound
3. Fine Needle Aspiration Biopsy
4. Core Biopsy
5. Excision Biopsy
6. Frozen Section
7. Immunoperoxidase
8. Molecular Technique
   a. Gene detection
### Neoplastic Diseases of the Breast

#### Non-Invasive (In Situ) Carcinoma of the Breast
- Both DCIS and LCIS arise from Terminal Duct of Lobular Unit
- Both

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</table>
| Ductal Carcinoma In Situ (DCIS) | • Increased incidence in population with reduced screening  
  o 50% patient detected through early screening  
  • Detection can be made through finding of Calcifications in the Mammogram  
  • Women with DCIS are at risk for  
  o Recurrent of DCIS after treatment  
  o Undergoing invasive attitude at the same breast  
  • Grading  
  o Low grade DCIS  
  o Intermediate grade DCIS  
  o High grade DCIS  
  • Prognosis  
  o Excellent prognosis after Mastectomy  
  o May metastasize to distant tissue in extensive high grade nuclei  
  o Without treatment may become Invasive tumors  | • Palpable mass  
  • Often multifocal lesion  
  • Nipple discharge  
  • Histological variant (architectural patterns often mixed)  
  o Solid  
  o Comedo  
  • Cell with high grade nuclei  
  • Distending spaces  
  • Central toothpaste-like necrotic tissue  
  • Extruded from the transacted ducts  
  o Cribriform  
  o Papillary  
  o Micropapillary  
  o Clinging  
  • Necrosis and calcification is common in all patterns  
  • Nuclear appearance  
  o Bland and monotonous (low grade nuclei)  
  o Pleomorphic (high grade nuclei)  
  • Basement membrane remain intact  |
| Lobular Carcinoma In Situ (LCIS) | • Relatively uncommon  
  • 1/3 may develop into Invasive Carcinoma  
  o Develop in both Breasts upon recurrence compared to DCIS which is unilaterally  
  o Usually patient will undergo bilateral Mastectomy for Prophylaxis treatment  | • Less commonly produce palpable mass  
  • Rarely associated with calcification  
  • Therefore, often misdiagnosed during Mammogram  
  • Uniform like low grade DCIS  
  • Cells are  
  o Monomorphic  
  o Bland, round nuclei  
  • Lesions happen in loosely cohesive clusters at  
  o Ducts  
  o Lobules  
  • Intracellular mucin vacuoles are common (Signet Ring Cells)  
  • The basement membrane remain intact  |
## Neoplastic Diseases of the Breast

### Invasive Carcinoma of the Breast

- **Common features**
  - Tendency to adhere to
    - Pectoralis Major muscle
    - Deep Fascia of the Abdominal wall
    - Underlying skin (dimpling of the skin)
  - Retraction of nipple
  - Localized Lymphedema (Peau d’orange/Orange peel)
    - Thickened skin
    - Exaggerated hair follicles

#### Diseases

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</thead>
<tbody>
<tr>
<td><strong>Invasive Ductal Carcinoma (IDC)</strong></td>
<td>• The most common form of Breast Ca in poorer population</td>
<td>• Mass that is</td>
<td>• Desmoplastic changes; replacing Breast fatty tissue with Collagen</td>
</tr>
<tr>
<td></td>
<td>• Clinical features</td>
<td>- Stony hard upon palpation</td>
<td>• Tumor margins are irregular</td>
</tr>
<tr>
<td></td>
<td>- Tethering of the skin</td>
<td>- Irregular</td>
<td>• Various appearance</td>
</tr>
<tr>
<td></td>
<td>- Axillary mass</td>
<td>- Retracted</td>
<td>- Well-developed tubule formation with low-grade nuclei</td>
</tr>
<tr>
<td></td>
<td>- Retraction of the skin</td>
<td>- Infiltrating surrounding tissue</td>
<td>- Tumors with sheath of Anaplastic cells</td>
</tr>
<tr>
<td></td>
<td>- Peau d’orange</td>
<td>• Paget’s disease of the nipple</td>
<td>• Fibrous stroma</td>
</tr>
<tr>
<td></td>
<td>- Palpable mass</td>
<td>- Ulceration</td>
<td>• Infiltrating malignant cells</td>
</tr>
<tr>
<td></td>
<td>• The commonest sites of metastasize</td>
<td>- Invasion to the nipple</td>
<td>• Obliterated basement membrane</td>
</tr>
<tr>
<td></td>
<td>- Lungs</td>
<td>• Massive fibrotic tissue, often called Scirrhous Carcinoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Brain</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Regional lymph nodes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Less common compared to IDC</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Invasive Lobular Carcinoma (ILC)</strong></td>
<td>• Clinical features are almost the same to that of IDC</td>
<td>• Commonly bilateral Breasts</td>
<td>• Small, uniform cells arranged as</td>
</tr>
<tr>
<td></td>
<td>• Often as a result of recurrence previous LCIS</td>
<td>• Multiple lesions</td>
<td>- Around uninvolved ducts – Bull’s eyes pattern</td>
</tr>
<tr>
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<td>- Commonly involved both breasts</td>
<td></td>
<td>- Columns within fibrous stroma – Indian-file</td>
</tr>
<tr>
<td></td>
<td>• Metastasize commonly to</td>
<td></td>
<td>• Almost all cells expressed HER/NEU receptors</td>
</tr>
<tr>
<td></td>
<td>- CSF</td>
<td></td>
<td>• Obliterated basement membrane</td>
</tr>
<tr>
<td></td>
<td>- Serousal surface</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Pelvic organs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>