COMMON BENIGN DISORDERS AND DISEASES OF THE BREAST

• Aberrations of Normal Development and Involution (ANDI).
• The basic principles underlying the aberrations of normal development and involution (ANDI) classification of benign breast conditions are the following:
  (a) benign breast disorders and diseases are related to the normal processes of reproductive life and to involution;
  (b) there is a spectrum of breast conditions that ranges from normal to disorder to disease; and
  (c) the ANDI classification encompasses all aspects of the breast condition, including pathogenesis and the degree of abnormality.

• a spectrum from normal, to mild abnormality (disorder), to severe abnormality (disease).
Aberrations of Normal Development and Involution

Early Reproductive Years.

• Fibroadenomas:
  - women aged 15 to 25 years
  - Small fibroadenomas (≤1 cm in size) are considered normal, whereas larger fibroadenomas (≤3 cm) are disorders and giant fibroadenomas (>3 cm) are disease.
  - Similarly, multiple fibroadenomas (more than five lesions in one breast) are very uncommon and are considered disease.

• A spectrum of changes from limited to massive stromal hyperplasia (gigantomastia) is seen.
• Nipple inversion is a disorder of development of the major ducts.
• Mammary duct fistulas arise when nipple inversion predisposes to major duct obstruction, leading to recurrent subareolar abscess and mammary duct fistula.
Later Reproductive Years.

- Cyclical mastalgia and nodularity usually are associated with premenstrual enlargement of the breast and are regarded as normal.
- Painful nodularity that persists for >1 week of the menstrual cycle is considered a disorder.
- Papillary projections
- Sometimes give rise to bilateral bloody nipple discharge.
Involution.

- Involution of lobular epithelium is dependent on the specialized stroma around it.
- When the stroma involutes too quickly, alveoli remain and form microcysts, which are precursors of macrocysts. The macrocysts are common, often subclinical, and do not require specific treatment.
- Sclerosing adenosis is considered a disorder of both the proliferative and the involutional phases of the breast cycle.
- Duct
- Ectasia (dilated ducts) and periductal mastitis are other important components of the ANDI classification
- About 60% of women ≥70 years of age exhibit some degree of epithelial hyperplasia
- Atypical proliferative diseases include ductal and lobular hyperplasia, both of which display some features of carcinoma in situ.
<table>
<thead>
<tr>
<th>ANDI classification of benign breast disorders</th>
<th>Normal</th>
<th>Disorder</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early reproductive years</strong> (age 15–25 y)</td>
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<td></td>
<td></td>
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<tr>
<td>Lobular development</td>
<td></td>
<td>Fibroadenoma</td>
<td>Giant fibroadenoma</td>
</tr>
<tr>
<td>Stromal development</td>
<td></td>
<td>Adolescent hypertrophy</td>
<td>Gigantomastia</td>
</tr>
<tr>
<td>Gigantomastia</td>
<td></td>
<td>Nipple inversion</td>
<td>Subareolar abscess</td>
</tr>
<tr>
<td><strong>Later reproductive years</strong> (age 25–40 y)</td>
<td>Cyclical changes of menstruation</td>
<td>Cyclical mastalgia</td>
<td>Incapacitating mastalgia</td>
</tr>
<tr>
<td>Nodularity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epithelial hyperplasia of pregnancy</td>
<td></td>
<td>Bloody nipple discharge</td>
<td></td>
</tr>
<tr>
<td><strong>Involution</strong> (age 35–55 y)</td>
<td>Lobular involution</td>
<td>Macrocysts</td>
<td></td>
</tr>
<tr>
<td>Sclerosing lesions</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Duct involution</td>
<td></td>
<td></td>
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<tr>
<td>Dilatation</td>
<td></td>
<td>Duct ectasia</td>
<td>Periductal mastitis</td>
</tr>
<tr>
<td>Sclerosis</td>
<td></td>
<td>Nipple retraction</td>
<td></td>
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<tr>
<td>Epithelial turnover</td>
<td></td>
<td>Epithelial hyperplasia</td>
<td></td>
</tr>
</tbody>
</table>

ANDI = aberrations of normal development and involution.
• Table 17-4
• Classification of benign breast disorders
• Nonproliferative disorders of the breast
  • Cysts and apocrine metaplasia
  • Duct ectasia
  • Mild ductal epithelial hyperplasia
  • Calcifications
  • Fibroadenoma and related lesions
• Proliferative breast disorders without atypia
  • Sclerosing adenosis
  • Radial and complex sclerosing lesions
  • Ductal epithelial hyperplasia
  • Intraductal papillomas
• Atypical proliferative lesions
  • Atypical lobular hyperplasia
  • Atypical ductal hyperplasia
• Fibrocystic Disease.
Table 17-3
Cancer risk associated with benign breast disorders and in situ carcinoma of the breast

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonproliferative lesions of the breast</td>
<td>No increased risk</td>
</tr>
<tr>
<td>Sclerosing adenosis</td>
<td>No increased risk</td>
</tr>
<tr>
<td>Intraductal papilloma</td>
<td>No increased risk</td>
</tr>
<tr>
<td>Florid hyperplasia</td>
<td>1.5 to 2-fold</td>
</tr>
<tr>
<td>Atypical lobular hyperplasia</td>
<td>4-fold</td>
</tr>
<tr>
<td>Atypical ductal hyperplasia</td>
<td>4-fold</td>
</tr>
<tr>
<td>Ductal involvement by cells of atypical ductal hyperplasia</td>
<td>7-fold</td>
</tr>
<tr>
<td>Lobular carcinoma in situ</td>
<td>10-fold</td>
</tr>
<tr>
<td>Ductal carcinoma in situ</td>
<td>10-fold</td>
</tr>
</tbody>
</table>
Pathology of Nonproliferative Disorders

• Of paramount importance for the optimal management of benign breast disorders and diseases is the histologic differentiation of benign, atypical, and malignant changes. Determining the clinical significance of these changes is a problem that is compounded by inconsistent nomenclature.

• The classification system originally developed by Page separates the various types of benign breast disorders and diseases into three clinically relevant groups:
  - nonproliferative disorders,
  - proliferative disorders without atypia, and
  - proliferative disorders with atypia

• This category includes:
  - cysts, duct ectasia, periductal mastitis, calcifications, fibroadenomas, and related disorders. Adenomas, Hamartomas, Adenolipomas, *Fibrocystic Disease*. The term *fibrocystic disease* is nonspecific.
  - and carry no increased risk for the development of breast cancer.
Pathology of Proliferative Disorders Without Atypia:

- include sclerosing, adenosis, radial scars, complex sclerosing lesions, ductal epithelial hyperplasia, and intraductal papillomas.
Pathology of Atypical Proliferative Diseases:

- The atypical proliferative diseases have some of the features of carcinoma in situ but either lack a major defining feature of carcinoma in situ or have the features in less than fully developed form.

- Atypical ductal hyperplasia (ADH) appears similar to low grade ductal carcinoma in situ (DCIS) histologically and is composed of monotonous round, cuboidal, or polygonal cells enclosed by basement membrane with rare mitoses.

- A lesion will be considered to be ADH if it is up to 2 or 3 mm in size but would be called DCIS if it is larger than 3 mm. The diagnosis can be difficult to establish with core needle biopsy specimen alone and most cases will require excisional biopsy specimen for classification.

- Atypical lobular hyperplasia (ALH) results in minimal distention of lobular units with cells that are similar to those seen in lobular carcinoma in situ (LCIS).
Treatment of Selected Benign Breast Disorders and Diseases

Cysts.

- Because needle biopsy of breast masses may produce artifacts that make mammography assessment more difficult, many multidisciplinary teams prefer to image breast masses before performing either fine needle aspiration or core needle biopsy. In practice, however, the first investigation of palpable breast.

- In practice, however, the first investigation of palpable breast masses may be a needle biopsy, which allows for the early diagnosis of cysts.

- A 21-gauge needle attached to a 10-mL syringe is placed directly into the mass, which is fixed by fingers of the nondominant hand. The volume of a typical cyst is 5 to 10 mL, but it may be 75 mL or more.

- If a mass was noted on initial ultrasound or there is a residual mass post-aspiration then a tissue specimen is obtained usually by core biopsy.

- When cystic fluid is bloodstained, fluid can be sent for cytologic examination.
Fibroadenomas.

- Most fibroadenomas are self-limiting and many go undiagnosed, so a more conservative approach is reasonable.
- Careful ultrasound examination with core-needle biopsy will provide for an accurate diagnosis.
- Ultrasonography may reveal specific features that are pathognomonic for fibroadenoma and in a young woman (e.g., under 25 years) where the risk of breast cancer is already very low a core-needle biopsy may not be necessary.
- Cryoablation and ultrasound-guided vacuum assisted biopsy are approved treatments for fibroadenomas of the breast, especially lesions <3 cm. Larger lesions are often still best removed by excision.
- Larger lesions are often still best removed by excision.
- With short-term follow-up a significant percentage of fibroadenomas will decrease in size and will no longer be palpable.
- However, many will remain palpable, especially those larger than 2 cm.
- Women should be counseled that the options for treatment include surgical removal, cryoablation, vacuum assisted biopsy, or observation.
Sclerosing Disorders:
• The clinical significance of sclerosing adenosis lies in its imitation of cancer.
• Excisional biopsy and histologic examination are frequently necessary.
• The diagnostic work-up for radial scars and complex sclerosing lesions frequently involves stereotactic biopsy.
• It usually is not possible to differentiate these lesions with certainty from cancer by mammographic features, so a larger tissue biopsy is recommended either by way of vacuum assisted biopsy or an open surgical excisional biopsy.
Periductal Mastitis:

- Painful and tender masses behind the nipple-areola complex are aspirated with a 21-gauge needle attached to a 10-mL syringe. Any fluid obtained is submitted for culture using a transport medium appropriate for the detection of anaerobic organisms.
- In the absence of pus, women are started on a combination of metronidazole and dicloxacillin while awaiting the results of culture. Antibiotics are then continued based on sensitivity tests. Then continued based on sensitivity tests.
- When considerable purulent material is present, repeated ultrasound guided aspiration is performed and ultimately in a proportion of cases surgical treatment is required.
- In a woman of childbearing age, simple drainage is preferred, but if there is an anaerobic infection, recurrent infection frequently develops. Recurrent abscess with fistula is a difficult problem.
- Treatment of periductal fistula was initially recommended to be opening up of the fistulous track and allowing it to granulate.
- However, nowadays the preferred initial surgical treatment is by fistulectomy and primary closure with antibiotic coverage.
- Excision of all the major ducts is an alternative option depending on the circumstances.
- However, when subareolar sepsis is diffuse rather than localized to one segment or when more than one fistula is present, total duct excision is the most expeditious
Nipple Inversion:

- More women request correction of congenital nipple inversion than request correction for the nipple inversion that occurs secondary to duct ectasia.
- Although the results are usually satisfactory, women seeking correction for cosmetic reasons should always be made aware of the surgical complications of altered nipple sensation, nipple necrosis, and postoperative fibrosis with nipple retraction.
- Because nipple inversion is a result of shortening of the subareolar ducts, a complete division of these ducts is necessary for permanent correction of the disorder.
• **Gynecomastia:**
  • Gynecomastia refers to an enlarged breast in the male.
  • Physiologic gynecomastia usually occurs during three phases of life: the neonatal period, adolescence, and senescence.
  • However, the hypoandrogenic state of Klinefelter’s syndrome (XXY), in which gynecomastia is usually evident, is associated with an increased risk of breast cancer.
  • Neonatal gynecomastia is caused by the action of placental estrogens on neonatal breast tissues, whereas in adolescence, there is an excess of estradiol relative to testosterone, and with senescence, the circulating testosterone level falls, which results in relative hyperestrinism.
  • Treatment: medical or surgical.
INFECTIOUS AND INFLAMMATORY DISORDERS OF THE BREAST:

- **Bacterial Infection**

- **Mycotic Infections:** Fungal infections of the breast are rare.

- **Hidradenitis Suppurativa:** Hidradenitis suppurativa of the nipple-areola complex or axilla is a chronic inflammatory condition that originates within the accessory areolar glands of Montgomery or within the axillary sebaceous glands.
  
  When located in and about the nipple-areola complex, this disease may mimic other chronic inflammatory states, Paget’s disease of the nipple, or invasive breast cancer.

- **Treatment:** Antibiotics, Surgery, Surgery with graft.
Mondor’s Disease:

- Mondor’s disease is a variant of thrombophlebitis that involves the superficial veins of the anterior chest wall and breast.
Embryology:

- In most mammals, paired breasts develop along these ridges, which extend from the base of the forelimb (future axilla) to the region of the hind limb (inguinal area).
- These ridges are not prominent in the human embryo and disappear after a short time.
- Accessory breasts (*polymastia*) or accessory nipples (*polythelia*) may occur along the milk line.
- Absence of the breast (*amastia*) is rare and results from an arrest in mammary ridge development that occurs during the sixth fetal week.
- Accessory axillary breast tissue is uncommon and usually is bilateral.
DIAGNOSIS OF BREAST CANCER

• History.
• Examination.
• Imaging Techniques:
  – Mammography.
  – Ductography. The primary indication for ductography is nipple discharge, particularly when the fluid contains blood. Radiopaque contrast media is injected into one or more of the major ducts and mammography is performed.
  – Ultrasonography.
  – Magnetic Resonance Imaging.
DIAGNOSIS OF BREAST CANCER (cont.)

• Breast Biopsy:
  - Nonpalpable Lesions. Image-guided breast biopsy: Ultrasound localization techniques. The combination of diagnostic mammography, ultrasound or stereotactic.
  
  fine-needle aspiration (FNA) biopsy achieves almost 100% accuracy in the preoperative diagnosis of breast cancer.
  
  core-needle permits the analysis of breast tissue architecture and allows the pathologist to determine whether invasive cancer is present.
  Core-needle biopsy is preferred over open biopsy for nonpalpable breast lesions because a single surgical procedure can be planned based on the results of the core biopsy.
    - Palpable Lesions.
  
  FNA or core biopsy of a palpable breast mass can usually be performed in an outpatient setting.

• A 1.5-in, 22-gauge needle attached to a 10-mL syringe or a 14 gauge core biopsy needle is used. Both air-dried and 95% ethanol–fixed microscopic sections are prepared for analysis.
  
  Core-needle biopsy of palpable breast masses is performed using a 14-gauge needle, such as the Tru-Cut needle. If the target lesion was microcalcifications, the specimen should be radiographed to confirm appropriate sampling.
  
  Tissue specimens are placed in formalin and then processed to paraffin blocks.