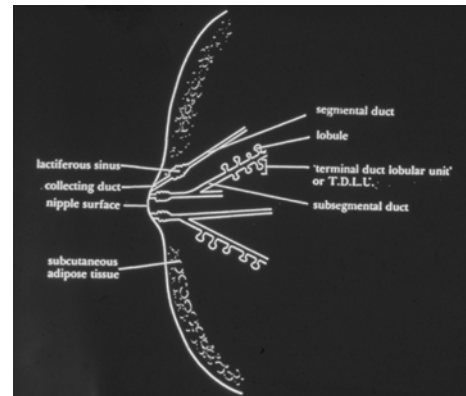


## Breast Pathology

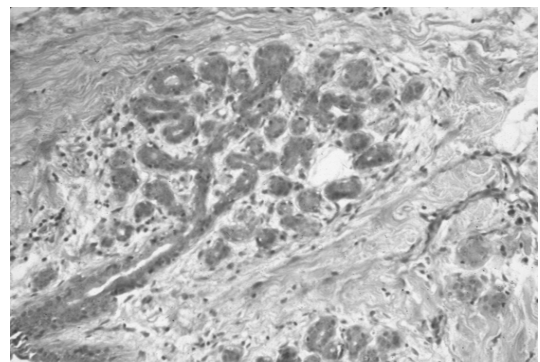
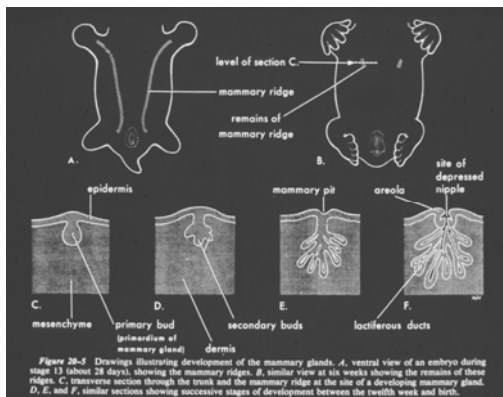
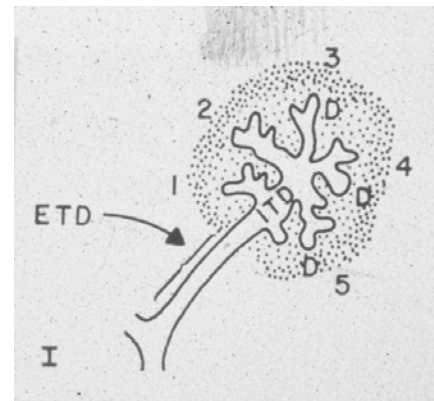
Lecturer: Hanina Hibshoosh, M.D.

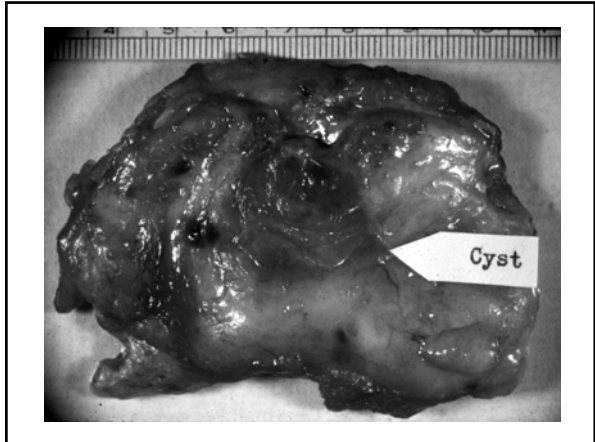
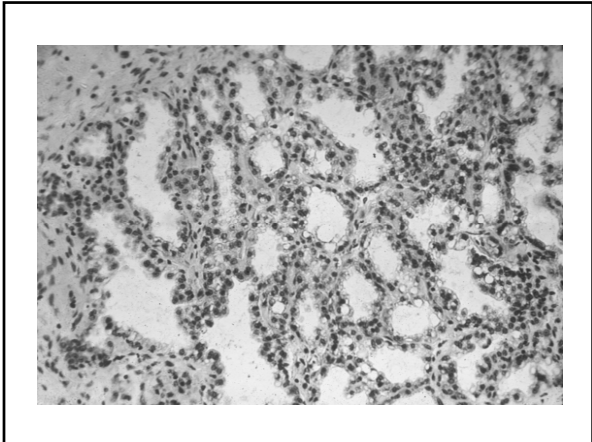
Reading: Kumar, Cotran, Robbins, Basic Pathology, 6th Edition, pages 623 - 635



## Breast Development

- 5th week - thickening of the epidermis - milk line formation
- Mammary ridges form from axilla to groin region
- Involution of mammary ridges except in chest region, persistence yield supernumerary breast (polythelia)
- 15th week - downward growth into stroma
- Last two months of gestation canalization of epithelial cords with formation of branching and lobuloalveolar structures

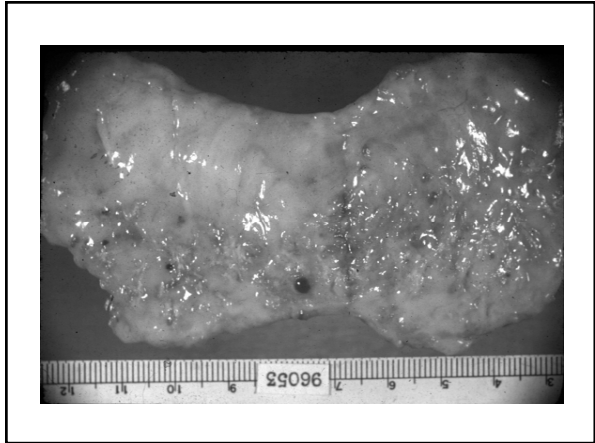




**Fibrocystic Changes**

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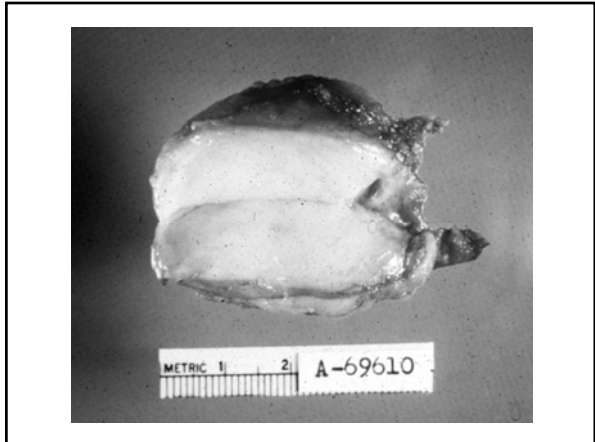
- Miscellaneous changes of breast involving ducts, lobules, and stroma
- Clinical incidence approximately 40 to 50% of patients, "lumps"
- Pathological incidence greater than 60 to 80%
- Terminology - fibrocystic change favored over disease
- Pathogenesis - reflects exaggerated changes occurring normally in the menstrual cycle

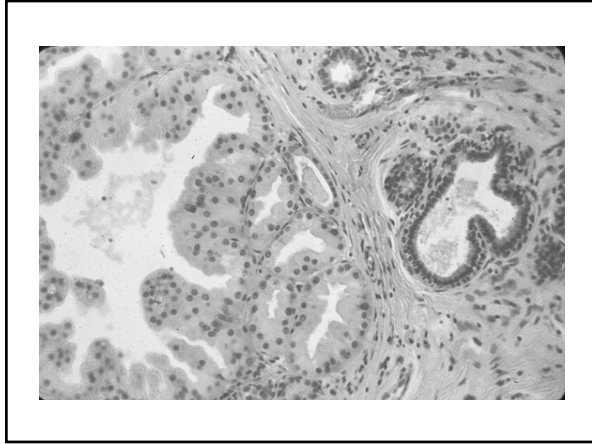
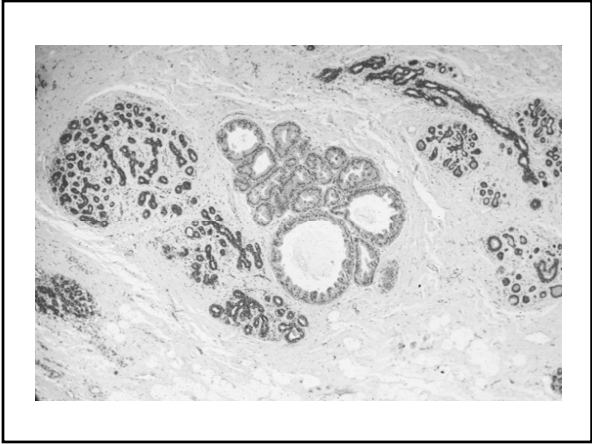
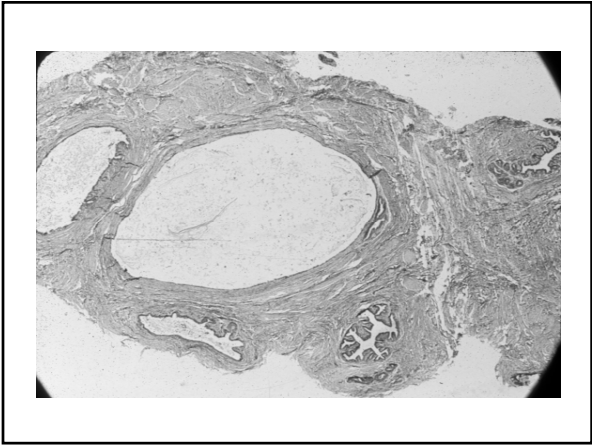
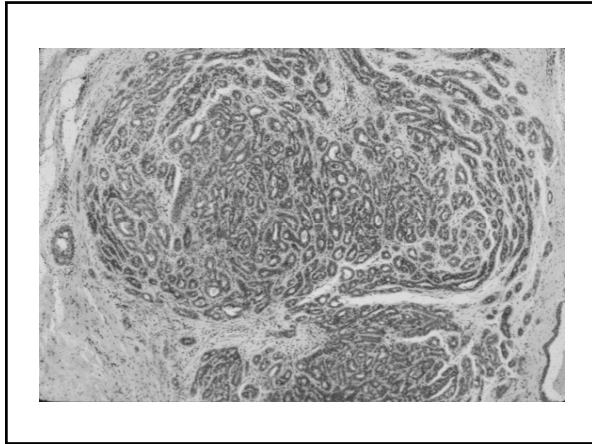
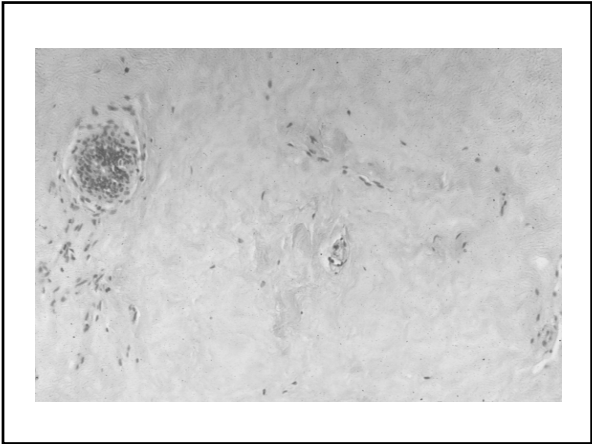


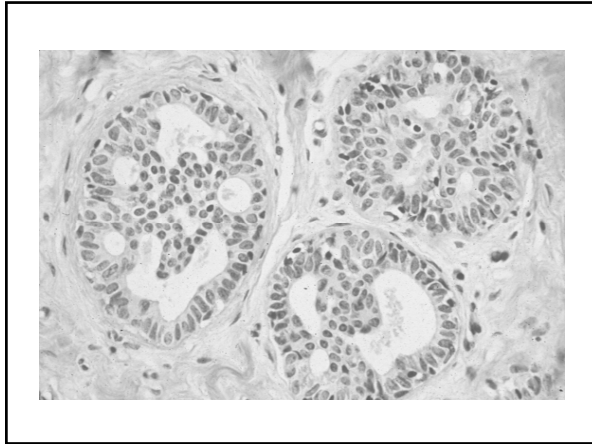
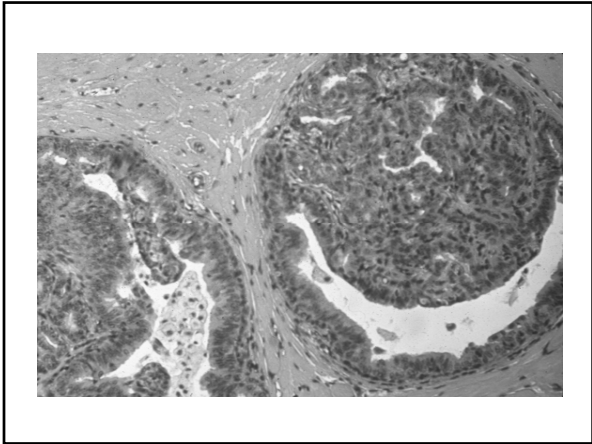
**Fibrocystic Disease of Breast**

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1. Fibrosis
2. Cysts
3. Apocrine Metaplasia
4. Sclerosing Adenosis
5. Papillomatosis (epithelial hyperplasia)







**Consensus Statement Cancer Committee of the  
College of American Pathologists**

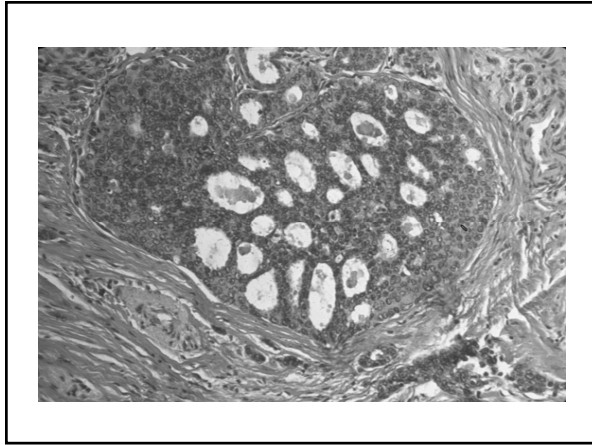
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Relative Risk for Invasive Breast Cancer Following Pathological  
Diagnosis of Benign Breast Disease

<p><u>No increased risk</u></p> <p>Hyperplasia, mild (2-4 cells)</p> <p>Apocrine metaplasia</p> <p>Cysts (macro and micro)</p> <p>Duct ectasia</p> <p>Fibroadenoma</p>	<p><u>Slightly increased risk (1.5-2x)</u></p> <p>Hyperplasia, moderate or florid (ductal and lobular)</p> <p>Papilloma with fibrovascular core</p> <p>Adenosis (sclerosing or florid)</p>
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Moderately increased risk (5x)

Atypical Ductal and Lobular Hyperplasia-Borderline Lesions



**Atypical Ductal Hyperplasia (ADH)**

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Borderline lesion is defined by some as a proliferative lesion in which some of the cytologic and architectural criteria of carcinoma in situ are met but are not fully satisfied. Page and Rogers have more recently published criteria including qualitative and quantitative features in the classification of ductal and lobular proliferative lesions.

- a) **Cytologic criteria** - This guideline emphasizes the need for a population of cells bearing similarity to neoplastic cells.
- b) **Histologic or architectural criteria** - the ductal epithelial proliferation predominant pattern is cribriform with secondary spaces having both punched-out regular (typical of non-comedo carcinoma in situ) and irregular borders (typical of florid hyperplasia without atypia).
- c) **Quantitative criteria - anatomic extent of lesion.** At least two basement membrane-bound spaces need to be completely involved by a cell population with the cytologic and histologic features of ductal carcinoma in situ (DCIS) for a diagnosis of DCIS. Therefore, a lesion with a single space with diagnostic features of DCIS is diagnosed as atypical ductal hyperplasia. In addition, support for an overall size criterion such as advocated by Tavassoli (2mm cumulative changes) is expressed.

**Atypical Ductal Hyperplasia (ADH)**

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- Incidence approximately 5%
- Risk for developing invasive cancer 4-5x general population
- Approximately 10% of patients will develop cancer
- Risk for cancer is bilateral
- Risk greatest in first decade following diagnosis
- Patients with atypical ductal hyperplasia with family history have same risk as in-situ cancer group for the development of invasive cancer, 8-10x.
- Prognosis of atypical ductal hyperplasia associated cancer same as cancer lacking atypical ductal hyperplasia
- ~30% of patients with ADH on needle biopsy have cancer on excision

## Benign Neoplasma

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- Fibroadenoma
- Intraductal papilloma

### Tumor of variable malignant potential

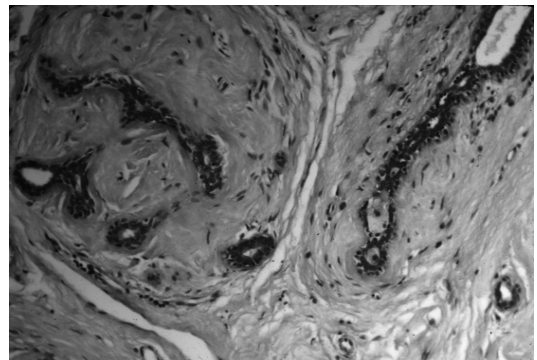
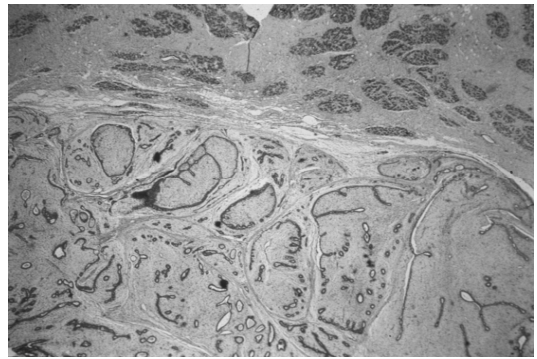
- Cystosarcoma phyllodes



## Fibroadenoma

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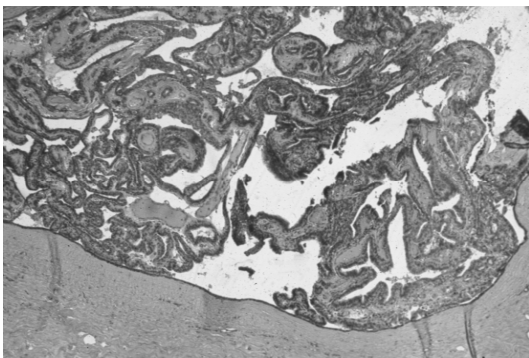
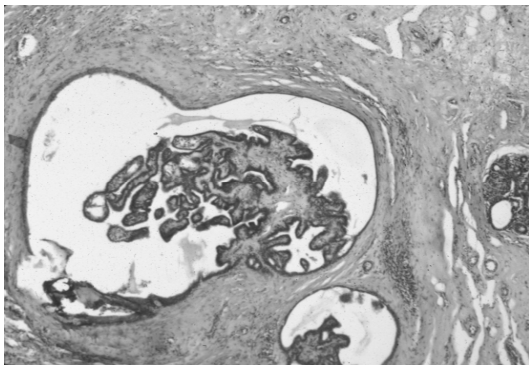
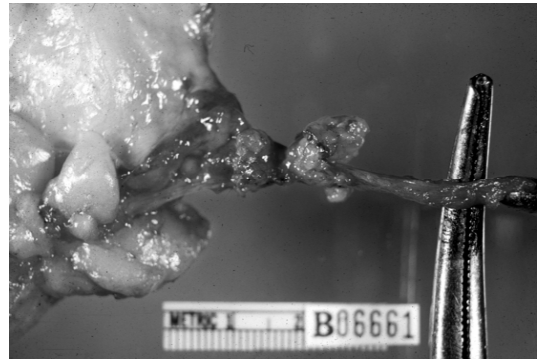
- Most common benign tumor of the female breast
- Usually appears in young women
- Peak incidence in the third decade of life
- A benign fibroepithelial tumor usually solitary may be multiple
- Rarely associated with carcinoma



### Intraductal Papilloma

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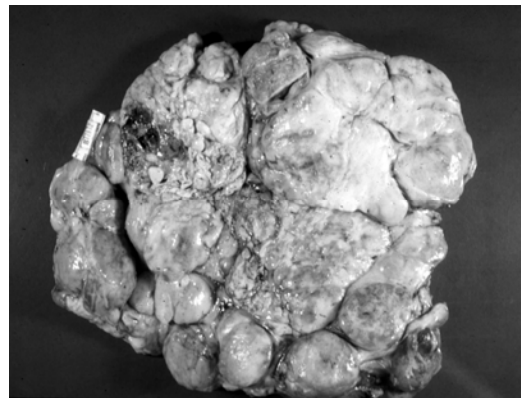
- A benign papillary neoplasm within a duct
- Identified peripherally or centrally (nipple duct) in which case it may be associated with bloody nipple discharge
- Mild increased risk (1.5 - 2x) of development of invasive cancer in patients with multiple peripheral intraductal papillomas

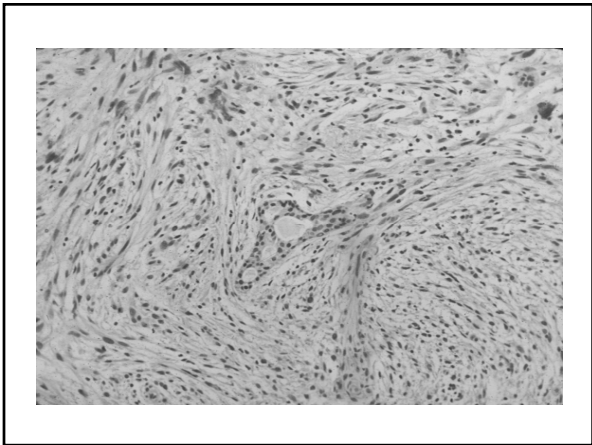
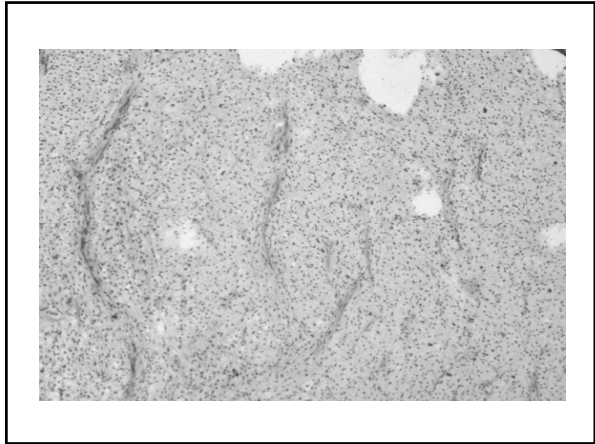
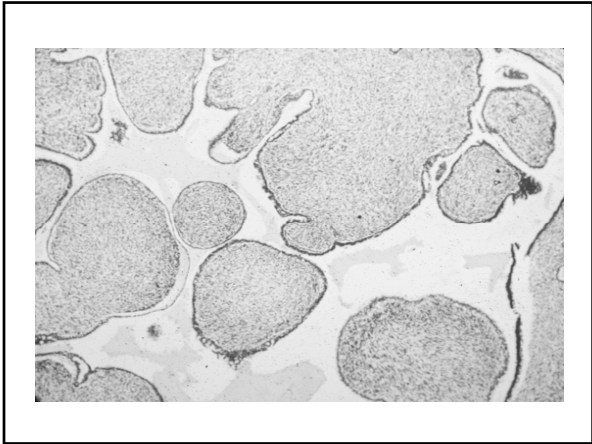


### Cystosarcoma Phyllodes

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- A fibroepithelial neoplasm of variable malignant potential
- Neoplastic component is the stroma
- Degenerates into a frank sarcoma with metastasis to lung and distant organs
- The majority can be cured by complete excision
- Peak incidence at 50 years of age

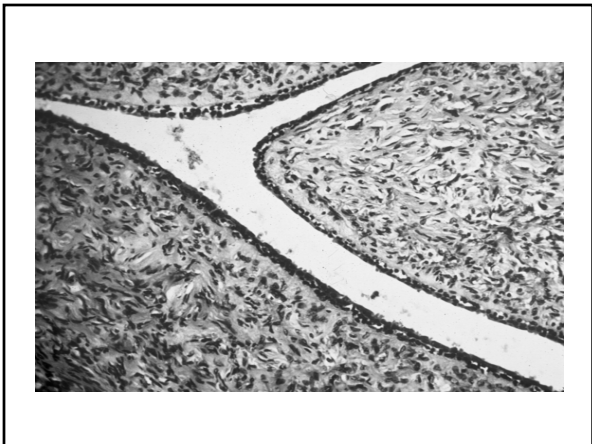




**Malignant Breast Lesions**

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- Epithelial derived tumors
  - Intraductal and invasive ductal carcinoma
  - In situ and invasive lobular carcinoma
- Mesenchymal neoplasm (sarcoma)
  - Cystosarcoma phyllodes
  - Angiosarcoma
  - Others



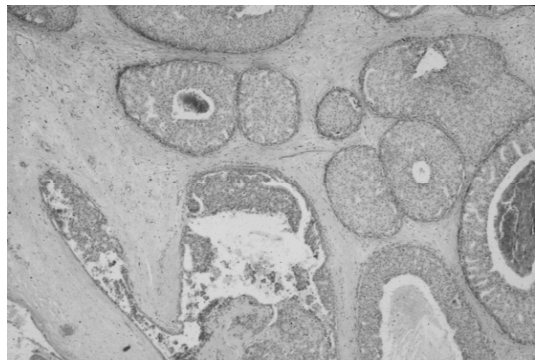
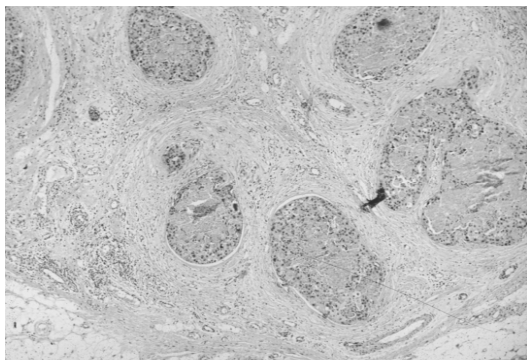
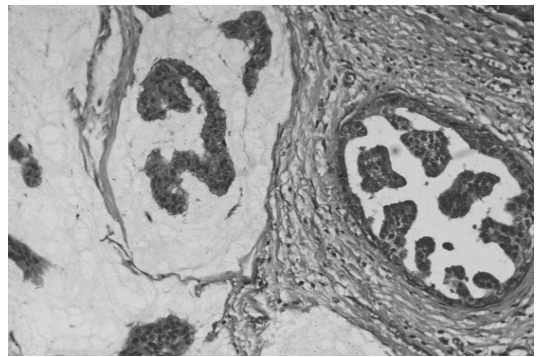
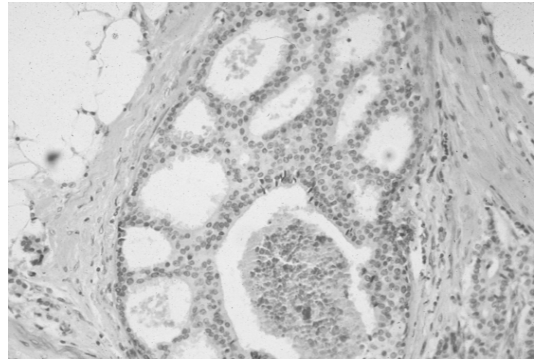
**Pathology of Breast Carcinoma**

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- Most cancers (90%) show ductal epithelium differentiation
- 10% referred to as lobular type
- In situ and invasive components

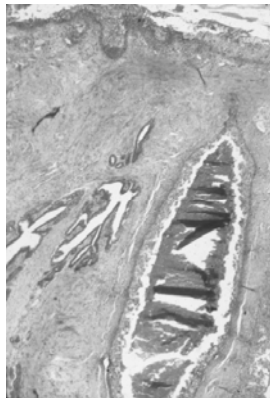
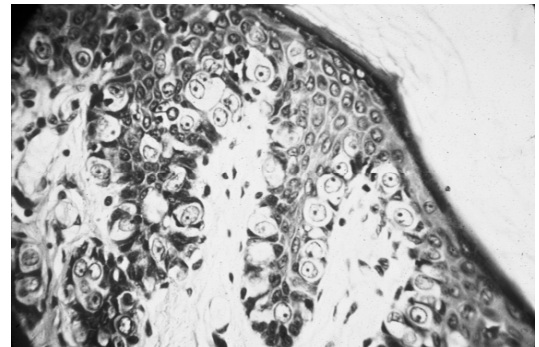
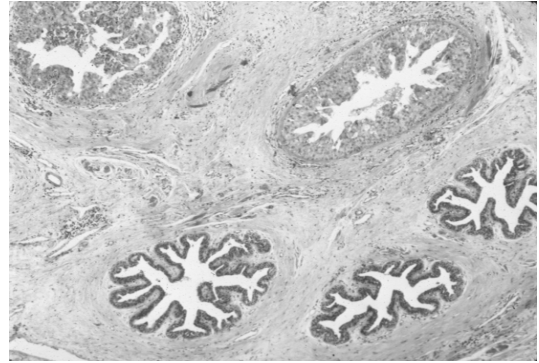
## Ductal Carcinomas In Situ

- Neoplastic transformation of ductal epithelium within ducts or lobules (intraductal) confined by basement membrane
- Various histologic patterns: comedo, solid, cribriform, clinging, and papillary type
- May be detected by its association with microcalcifications
- May represent up to 25% of breast carcinoma
- High grade and large size of the in situ carcinoma predicts multifocality and propensity for invasion
- Relative risk for the development of an invasive carcinoma 8-10 fold greater than the general population
- Risk is primarily ipsilateral



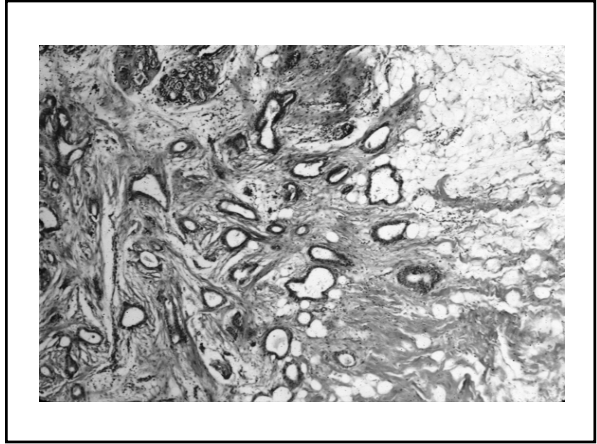
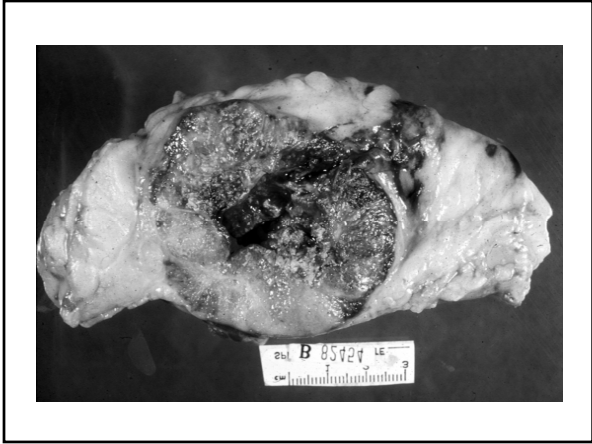
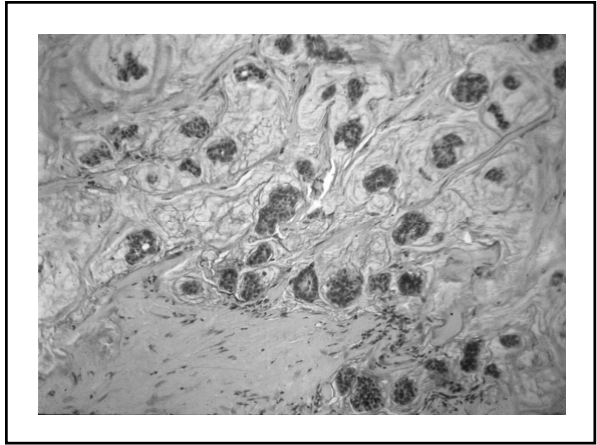
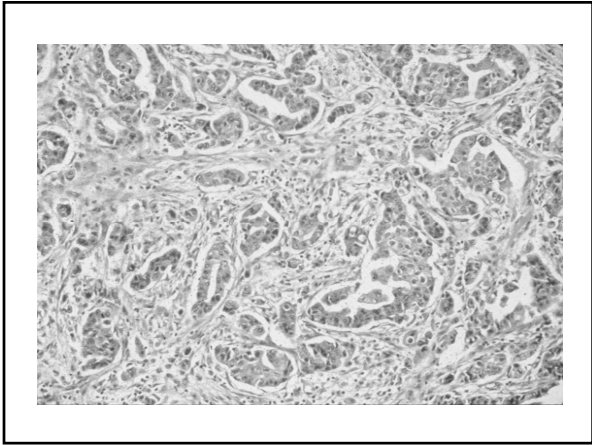
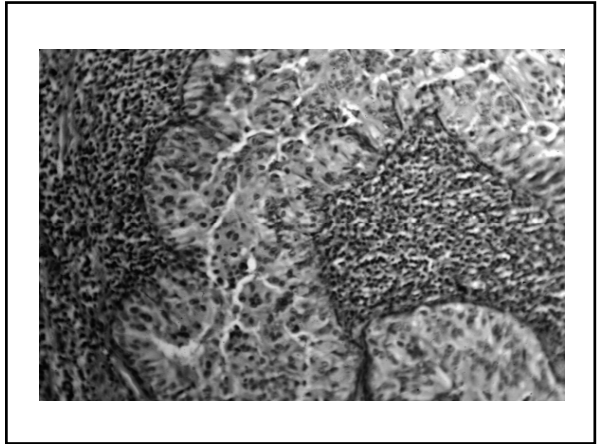
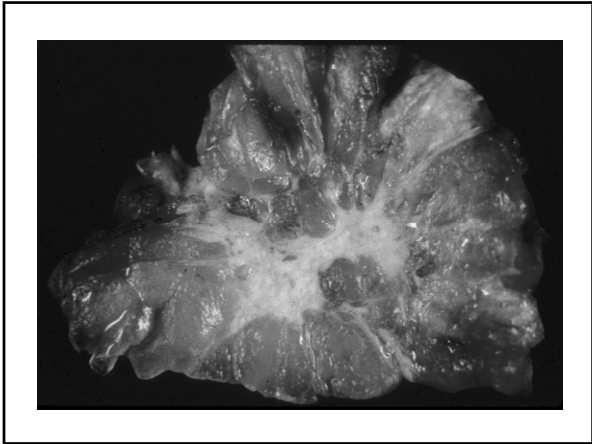
## Paget's Disease of the Breast

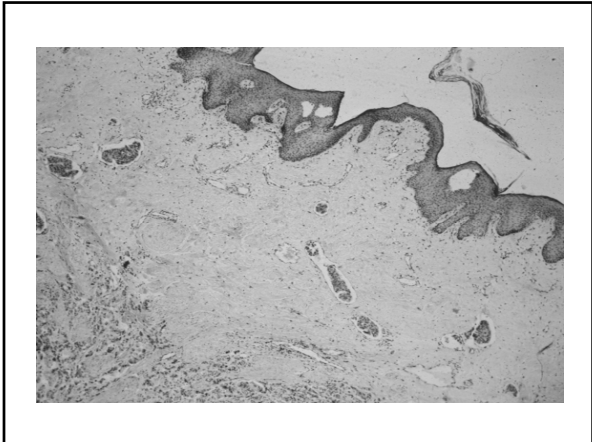
- In situ carcinoma of lactiferous ducts with extension to epidermis
- Involving the nipple and areola
- May present with nipple discharge, crusting, or excoriation of nipple surface



## Invasive Ductal Carcinoma

- An infiltrative malignant epithelial process resembling cells lining ducts--most common breast carcinoma
- Classified according to histologic appearance as:
  1. Carcinoma not otherwise specified -- majority
  2. Special good prognosis subtype including medullary carcinoma, colloid (mucinous) carcinoma, and tubular carcinoma . . .
  3. Poor prognosis -- inflammatory carcinoma



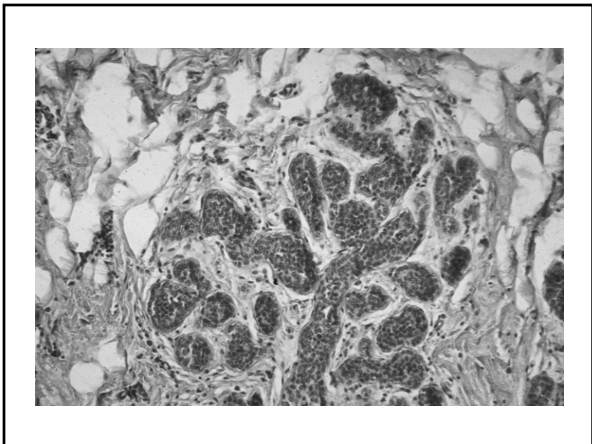
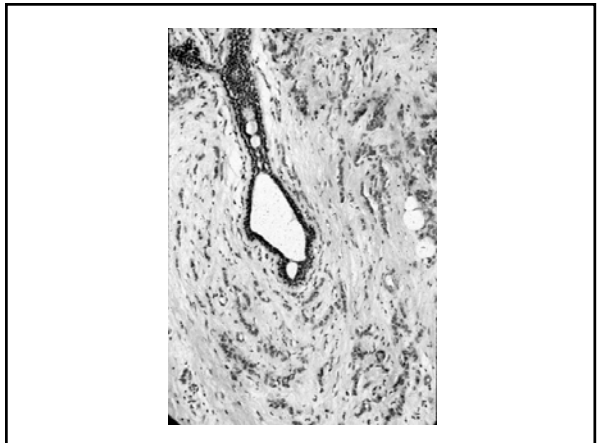


### Invasive Lobular Carcinoma

- An infiltrating carcinoma resembling cells lining the lobules (of LCIS)
- Histologically showing classical "Indian file" pattern and targetoid "bull's eye" pattern
- Composed of relatively small cells with scanty cytoplasm, sometimes vacuolated (E-cadherin negative)
- Represents approximately 10% of breast cancer with a higher than usual incidence of bilaterality (approximately 20%)

### Lobular Carcinoma In Situ (LCIS)

- Neoplastic transformation of epithelial cells lining terminal ducts and acini of small size – E-cadherin negative
- Typically multifocal and bilateral
- 6 - 9 fold increased risk for development of invasive cancer
- Bilateral risk for development of invasive cancer
- 3/4 of invasive cancer are of ductal type
- Considered primarily a marker for invasion

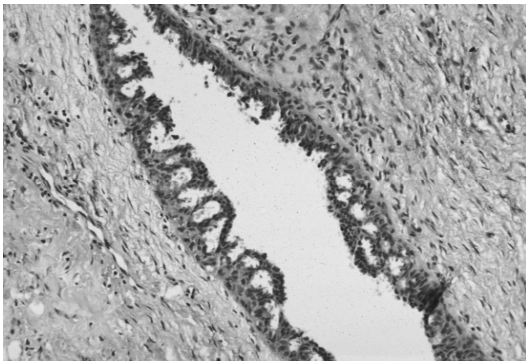
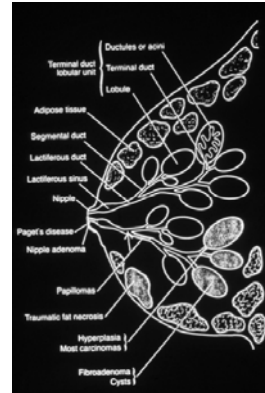


### Prognostic Factors of Breast Cancer

- Size of primary tumor
- Lymph node involvement and extent
- Grade
- Histologic type
- To a lesser extent, estrogen/progesterone receptors, S-phase fraction but not DNA content, C-Erb B2 and . . .

## Gynecomastia

- Button-like subareolar swelling, bilateral, histologically corresponding to intraductal epithelial hyperplasia and increased periductal stromal cellularity and edema
- Associated with relative estrogen excess, cirrhosis of liver, Klinefelter's, estrogen secreting tumor, estrogen therapy, and digitalis therapy
- Physiological gynecomastia most common in puberty and old age
- No clear cut association with development of carcinoma



## Male Breast Carcinoma

- Rare, ratio of male to female breast cancer 1:125
- Occurs in advanced age
- Identified in peri-nipple/areolar region
- Presents in advanced stage
- Resembles morphologically and biologically invasive carcinomas of the female breast