Breast Cancer

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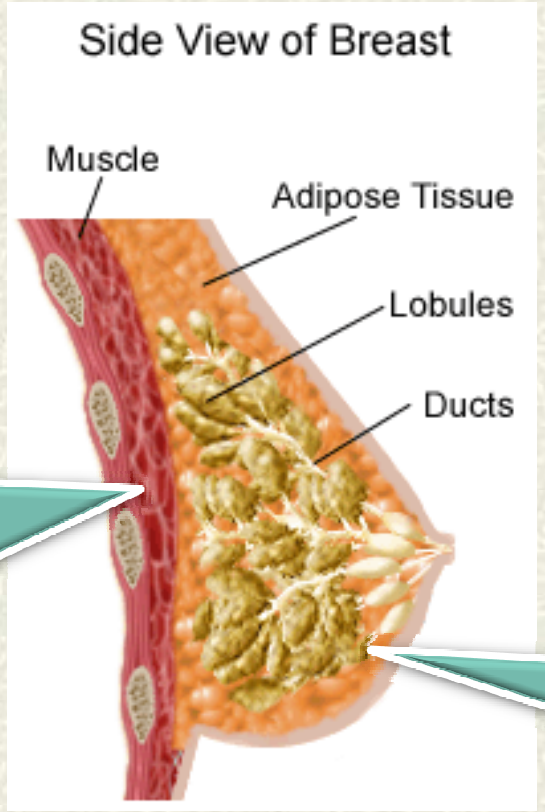
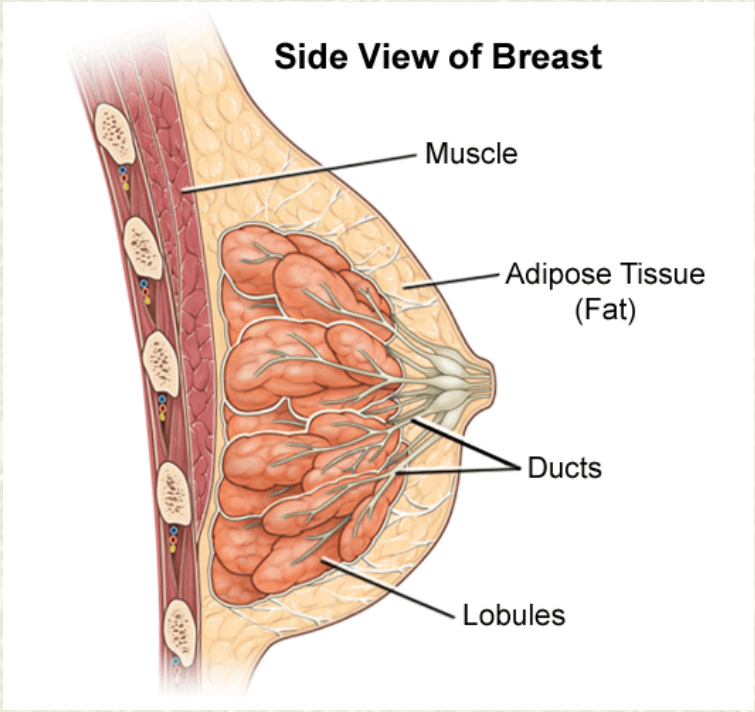
Muscles

Muscles underneath the breasts separating them from the ribs



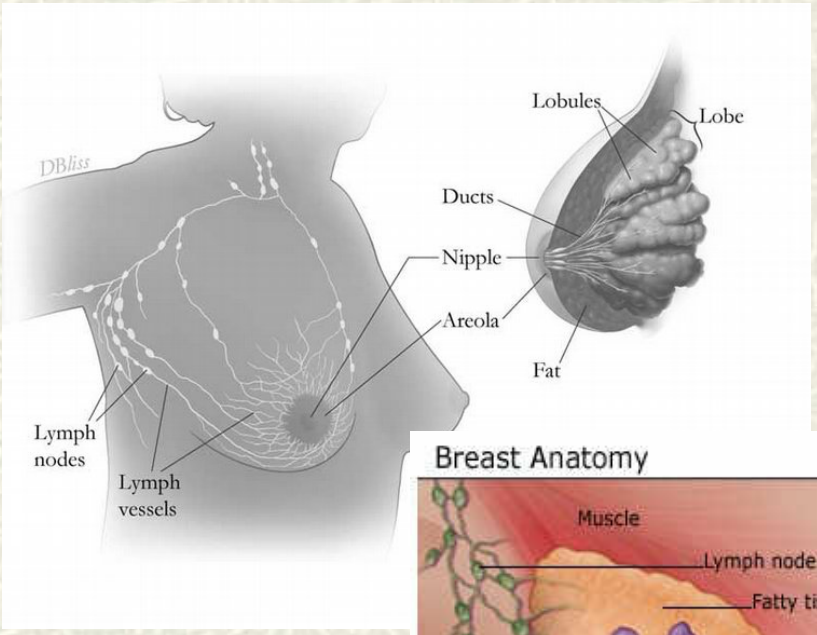
Breast has no muscle tissue

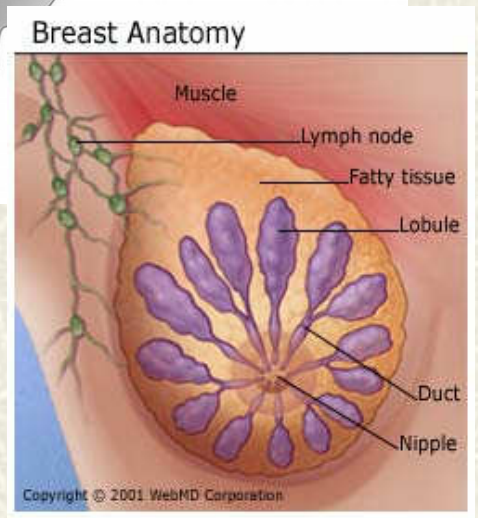
Female Breast Anatomy



- Breasts consist mainly of fatty tissue interspersed with connective tissue
- There are also less conspicuous parts
  - lobes
  - ducts
  - lymph nodes

Breast Gland





- Each breast has 15 to 20 sections (lobes) arranged like the petals of daisy
- Inside each lobe are many smaller structures called lobules
- At the end of each lobule are tiny sacs (bulbs) that can produce milk

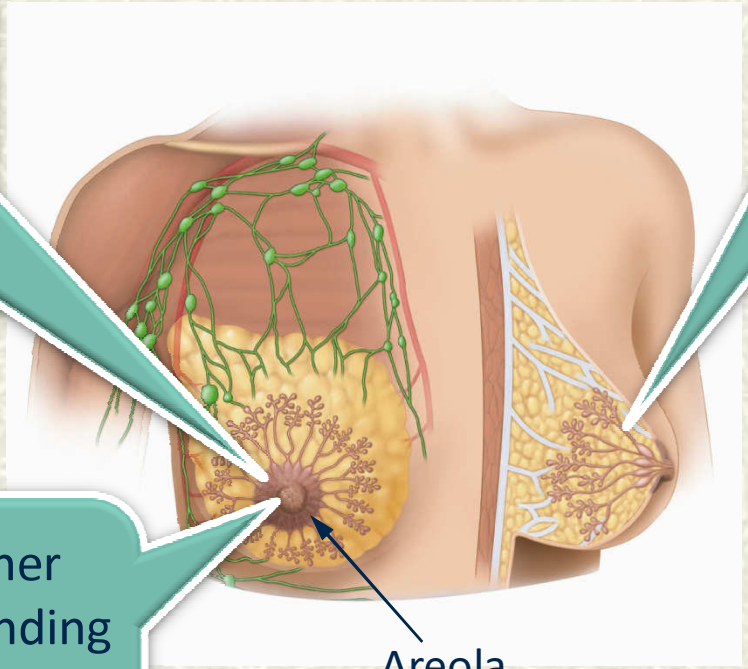
Ducts

2

Ducts carry milk from bulbs toward dark area of skin in the center of the breast (areola)

1

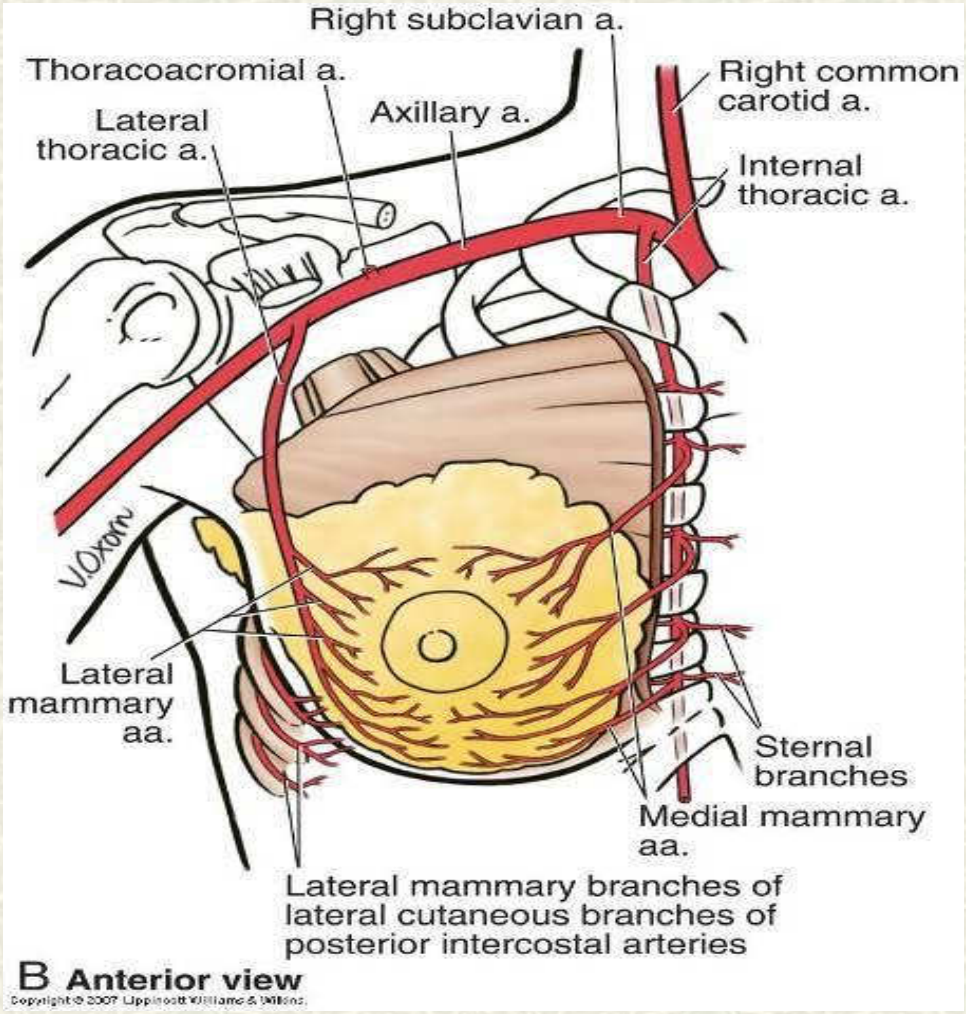
Lobes, lobules, and bulbs are Linked by a network of thin tubes (ducts)



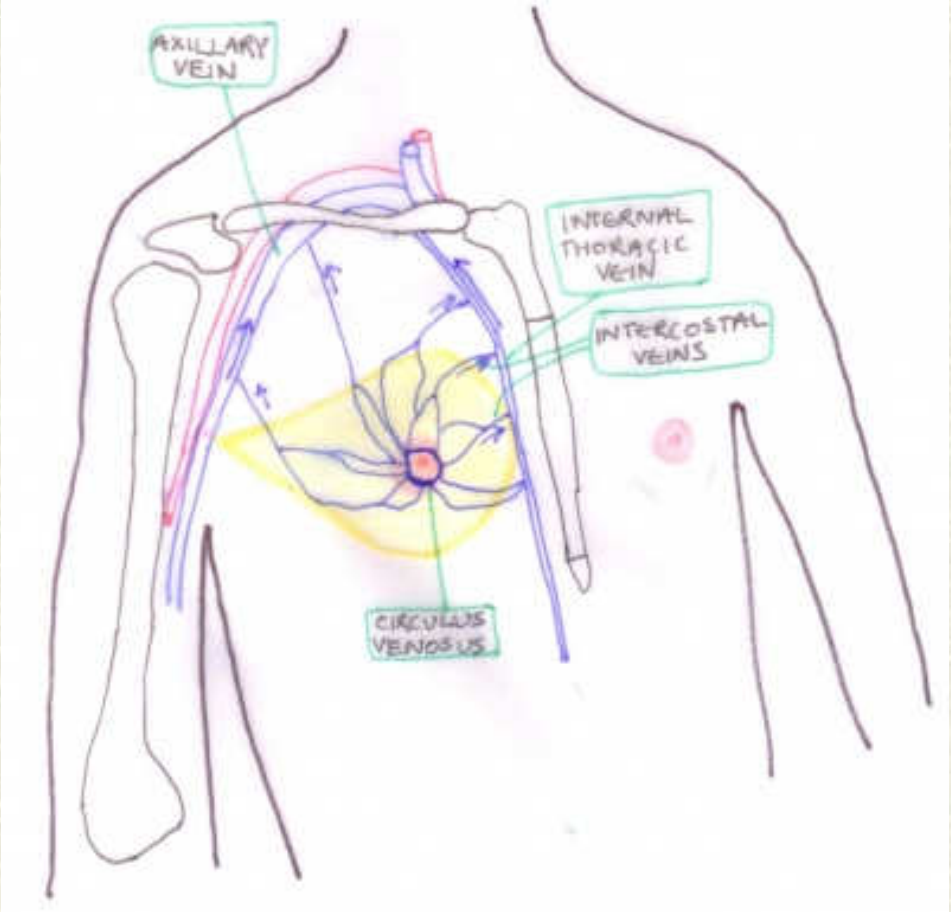
Ducts join together into larger ducts ending at the nipple, where milk is delivered

3

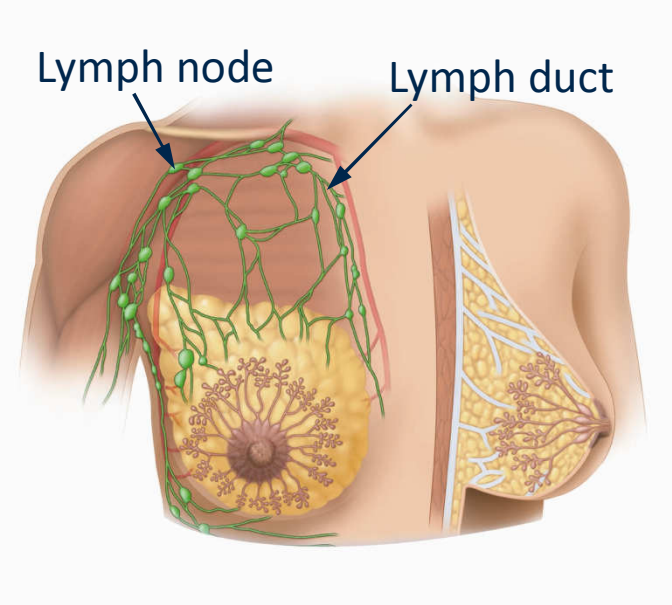
Blood Supply



Venous Drainage



Lymphatic System



A network of vessels

- **Lymph ducts**: Drain fluid that carries white blood cells (that fight disease) from the breast tissues into lymph nodes under the armpit and behind the breastbone
- **Lymph nodes**: Filter harmful bacteria and play a key role in fighting off infection

Lymphatic Drainage

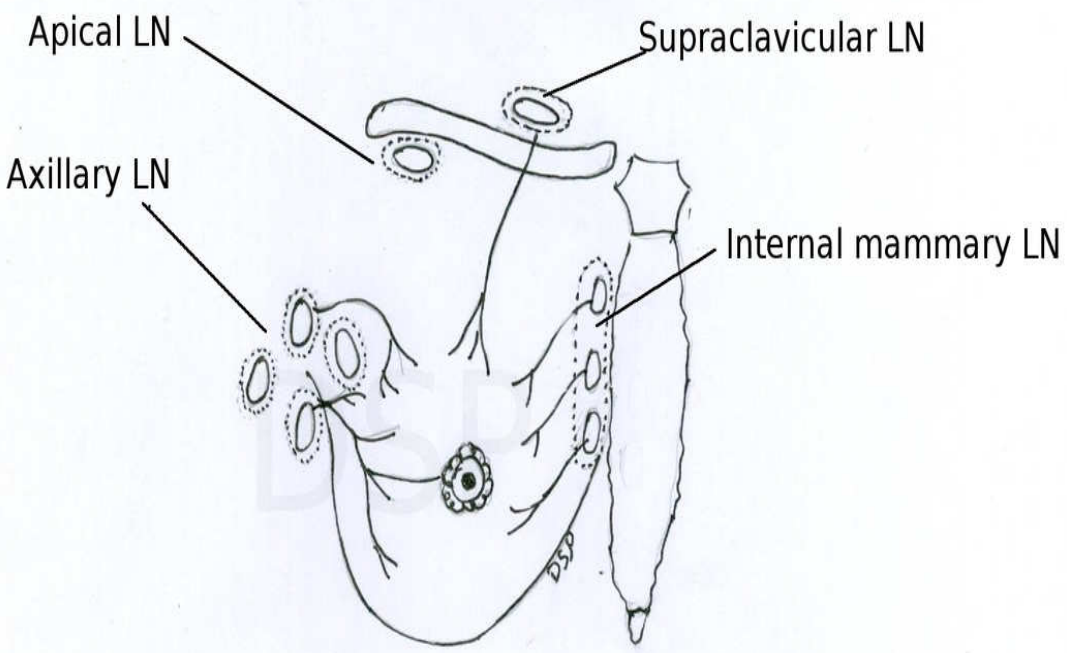


Fig.2.4 Lymphatic drainage of Breast

Three Types of Vessels

Lobules → 1 Ducts → Nipple → Milk

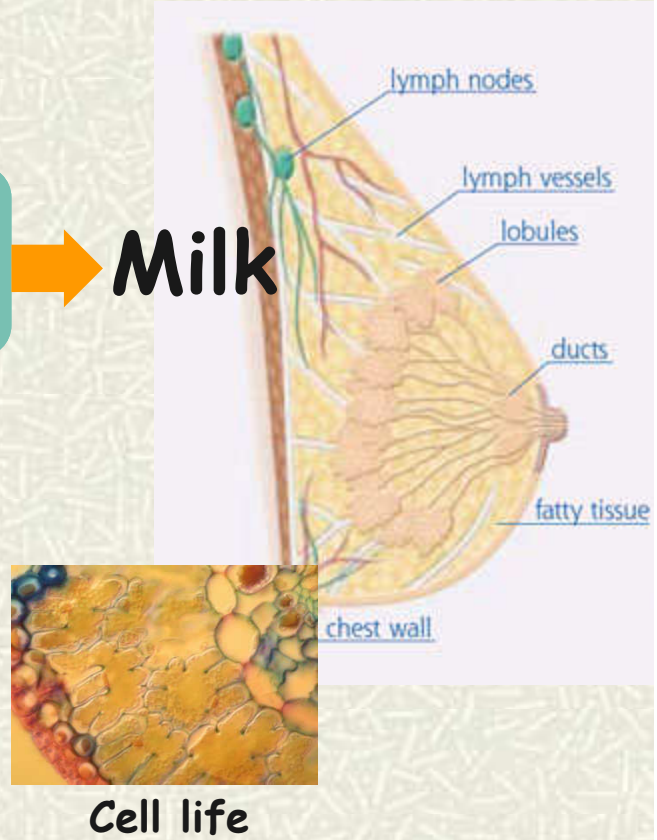
3 Lymph Vessels → Lymph Nodes

Bacteria

2 Blood Vessels

Waste products

Nourishment



Cell life

Normal Breast

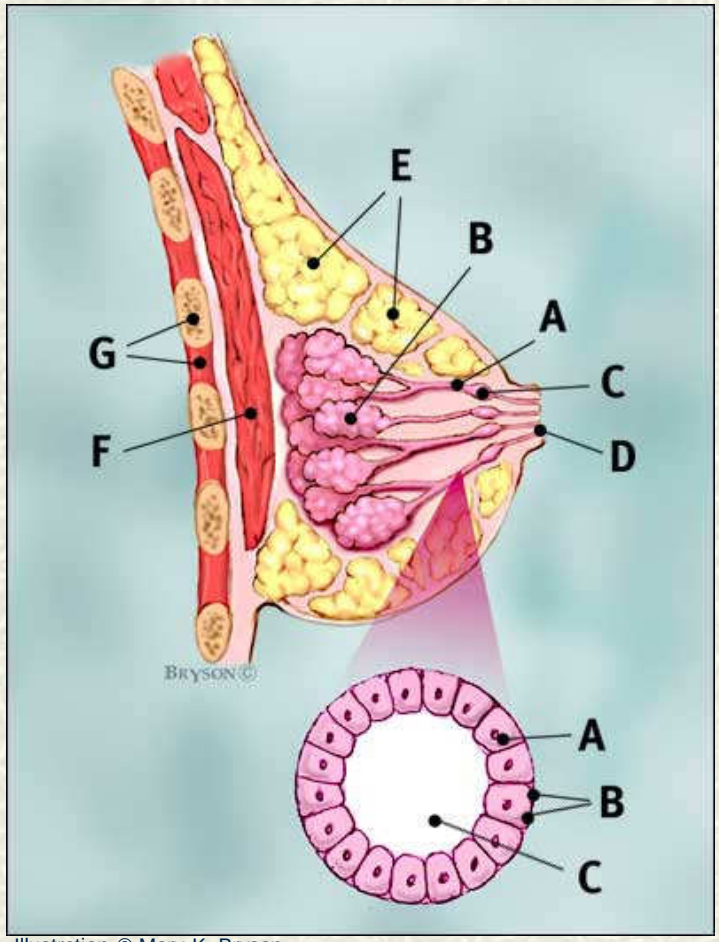
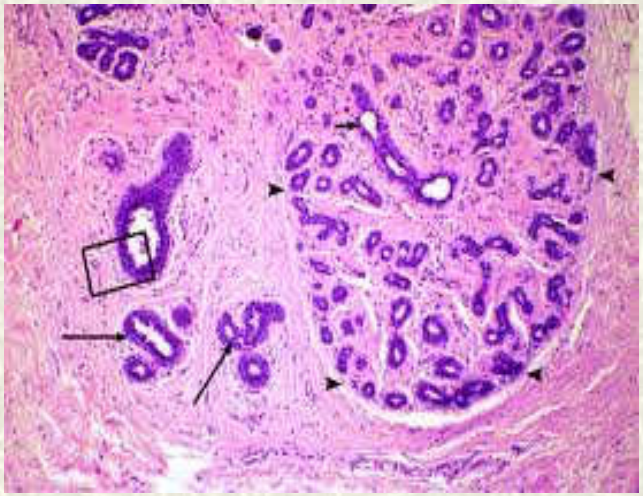


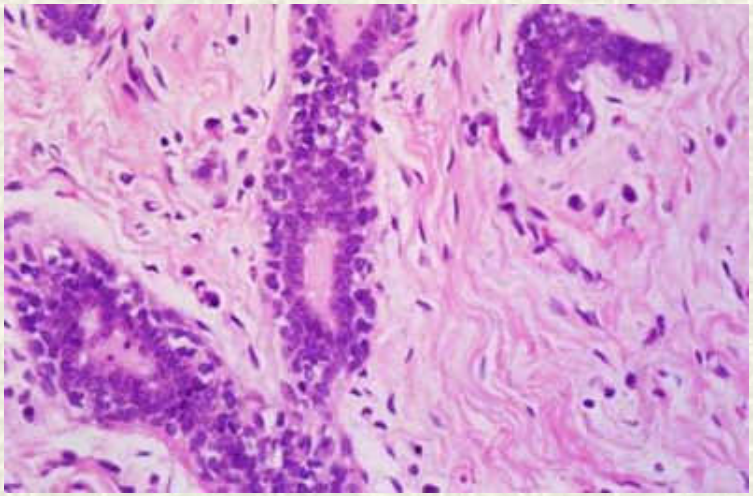
Illustration © Mary K. Bryson

Breast profile	
A	ducts
B	lobules
C	dilated section of duct to hold milk
D	nipple
E	fat
F	pectoralis major muscle
G	chest wall/rib cage

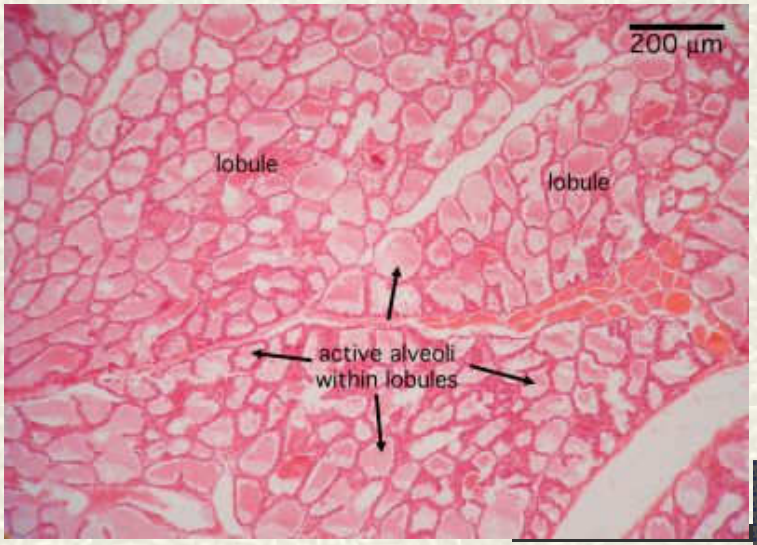
Enlargement	
A	normal duct cells
B	basement membrane (duct wall)
C	lumen (center of duct)

Normal Histology

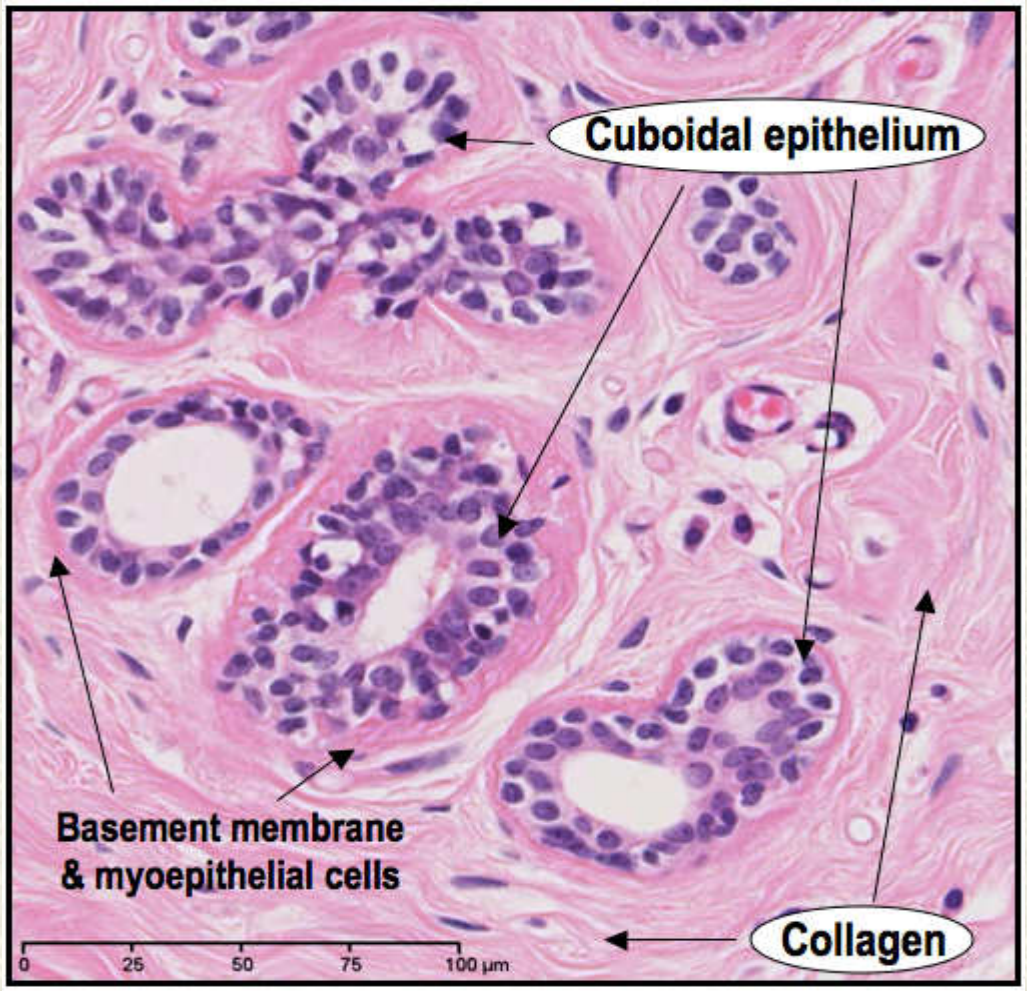




High power show inner cuboidal epithelia or low columbal layer & outer myoepithelial cell layer (contractile)



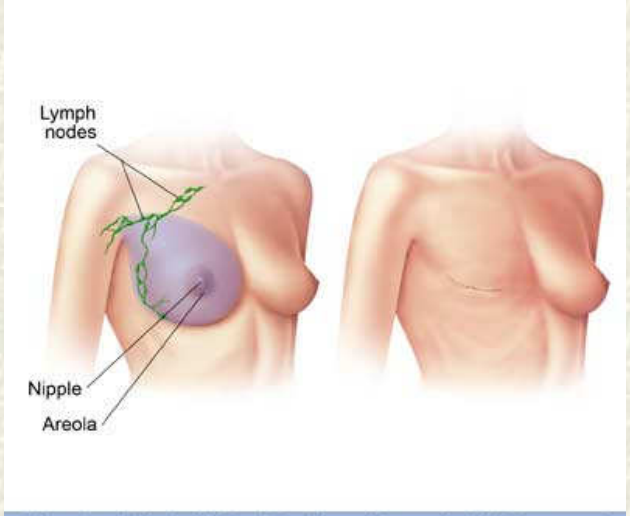
Normal Histology - Ducts



Intralobular excretory ducts & alveoli lined by luminal epithelium & myoepithelial cells

Breast Cancer

- Breast cancer is second only to lung cancer as a cause of cancer deaths in American women
- 2/3 or all breast cancer in PNG is premenopausal (Walters et al 2001)
- PNG incidence is 6.9 per 100 000 & has been rising in the last 40 years (Halder et al 2001).



Epidemiology in PNG

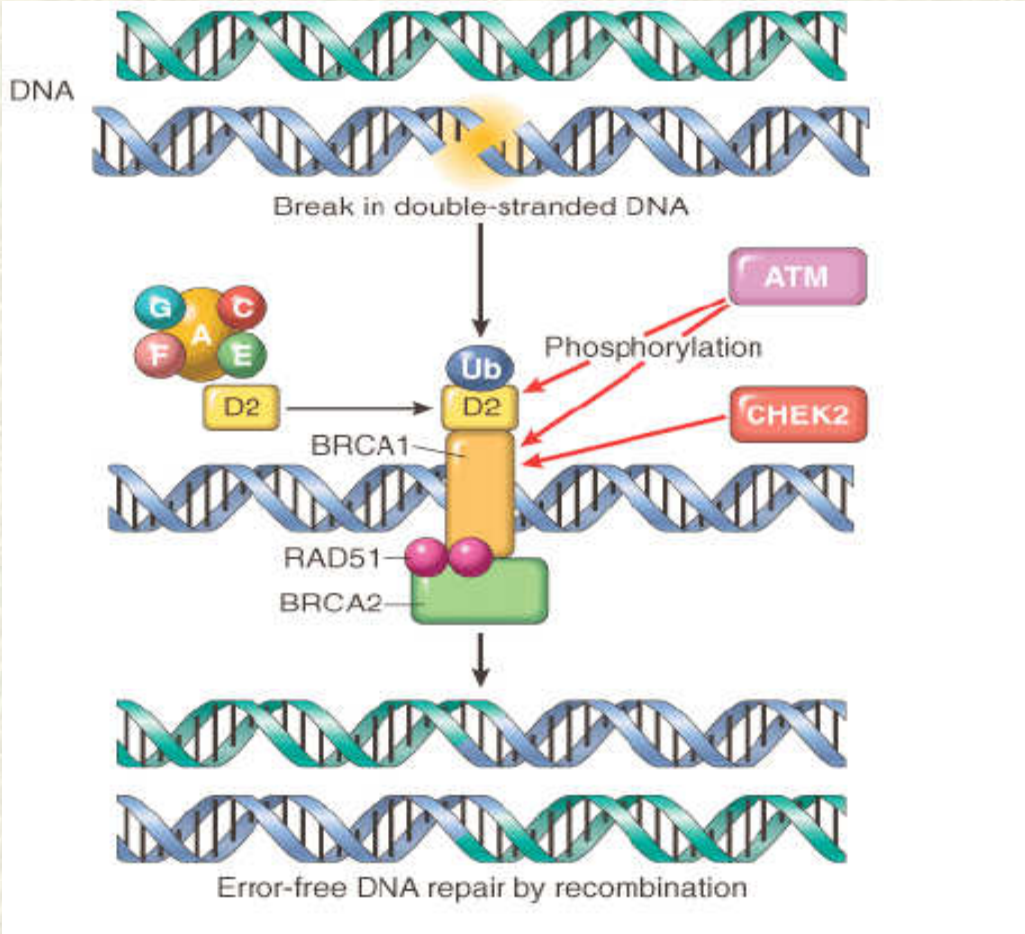
- Peak incidence: 45-54 age groups. But younger pts has been seen.
- Highest incidence is 35-54 age groups.
- 15% of all breast cancers <35 years of age.
- Most cases present late:
- Common clinical signs on presentation:
  - Ulceration of skin
  - Peu d' Orange
  - Nipple retraction
  - lymphoedema

Halder et al 2001 ANZ J Surg. 2001 Oct;71(10):590-3.

Risk Factors for Breast Cancer

- Increasing age
- Proliferative breast diseases
- Carcinoma of the contralateral breast or endometrium
- Radiation exposure
- Geographical influences
- Length of reproductive life – increases with early menarche and late menopause
- Parity – increased risk in nulliparous
- Exogenous Estrogens – small
- Genetic factors – germ line mutations in BRAC1, BRAC2.
- Hormonal influences
- Environmental factors
- Age at first child – increased in older primip
- Obesity

BRAC 1 & BRAC 2



BRAC gene products involved in DNA repair

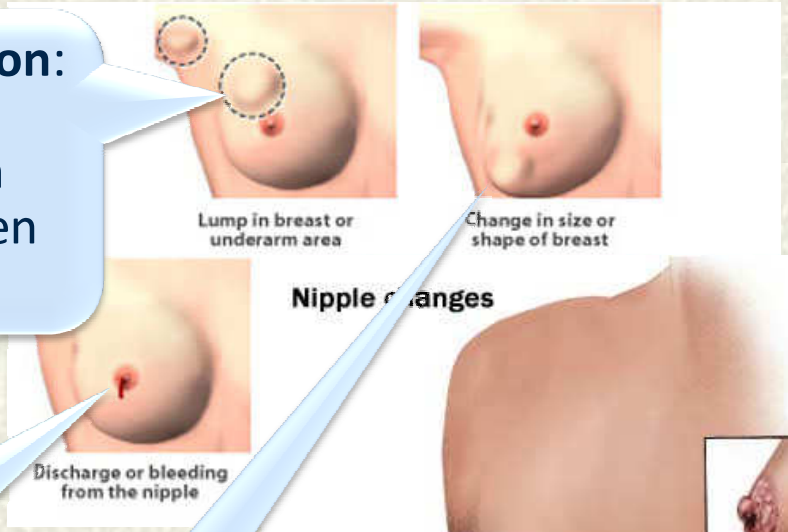
Classification

- **Invasive** – 70-85%
  - Ductal carcinoma – 79%
  - Lobular carcinoma – 10%
  - Tubular/Cribriform carcinoma – 6%
  - Colloid (mucinous) carcinoma – 2%
  - Medullary carcinoma – 2%
  - Papillary carcinoma – 1%
- **Non-invasive** (In Situ Carcinoma) – 15-30%
  - Ducal carcinoma in situ – 80%
  - Lobular carcinoma in situ – 20%

Robins Pathological Basis of Diseases, 6th Ed

Signs and Symptoms

Most common: lump or thickening in breast. Often painless



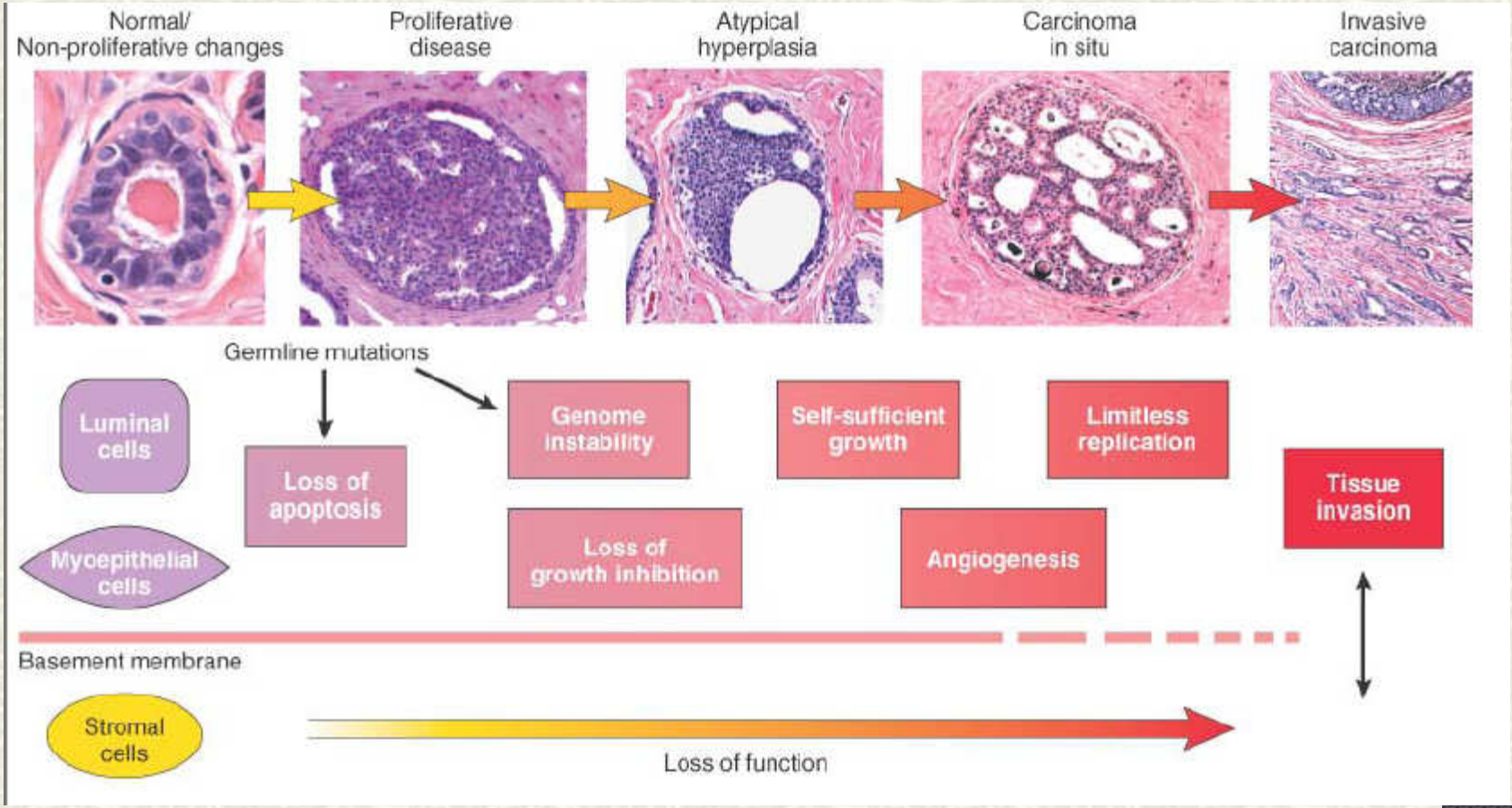
Discharge or bleeding

Change in size or contours of breast

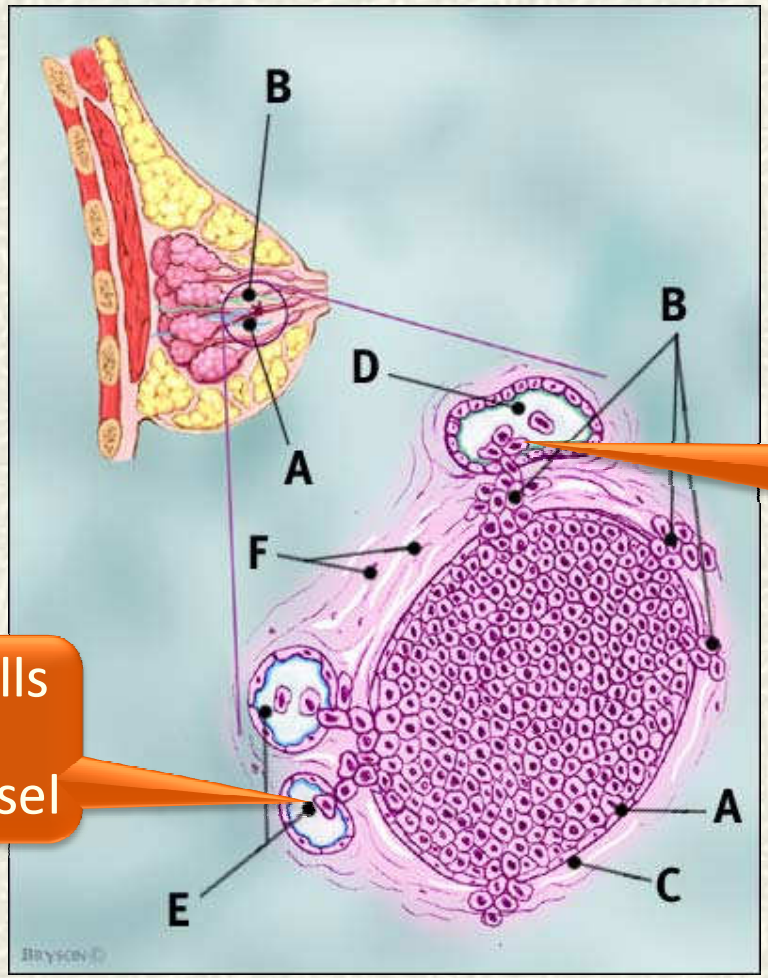
Redness or pitting of skin over the breast, like the skin of an orange

Change in color or appearance of areola

Breast Cancer



Cancer Can also Invade Lymph or Blood Vessels



Cancer cells invade lymph duct

Cancer cells invade blood vessel

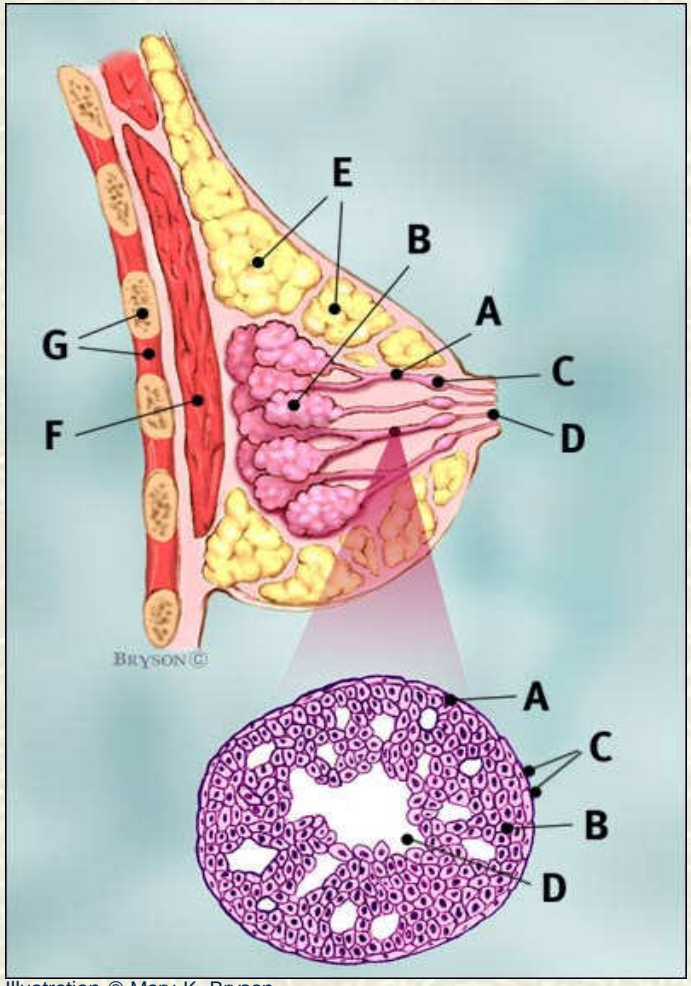
Illustration © Mary K. Bryson

NON-INVASIVE BREAST CARCINOMA

In Situ Carcinoma

- Ductal carcinoma in situ (including Paget's disease) most common
- Lesions contain malignant cells that lack capacity to invade BM
- However can spread throughout a ductal system
- Divided into 4 types based on microscopic features
  - Comedocarcinoma
  - Noncomedocarcinoma DCIS
  - Paget's disease of the nipple
  - DCIS with microinvasion

Ductal Carcinoma in situ (DCIS)



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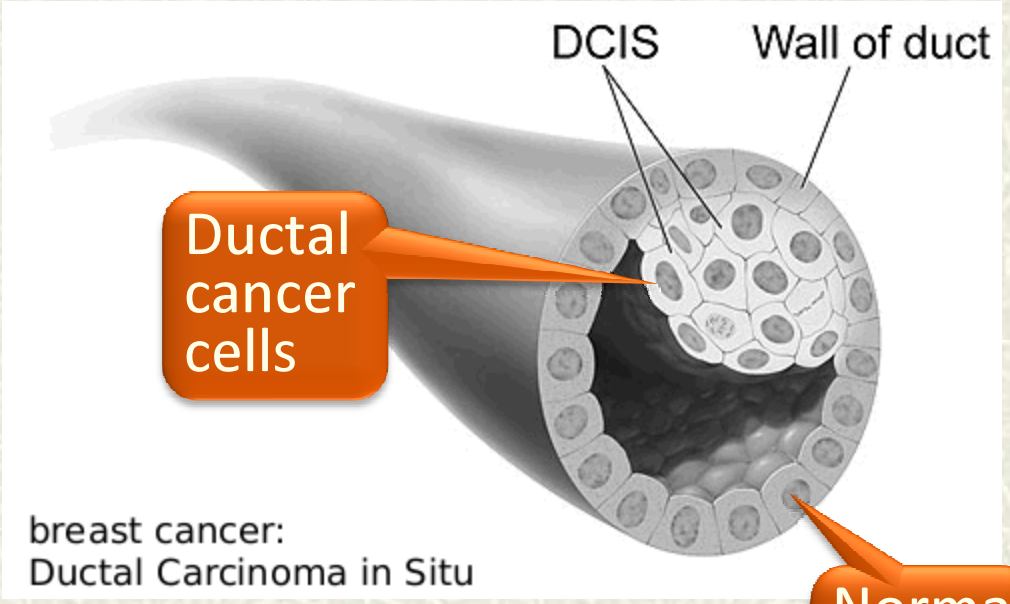
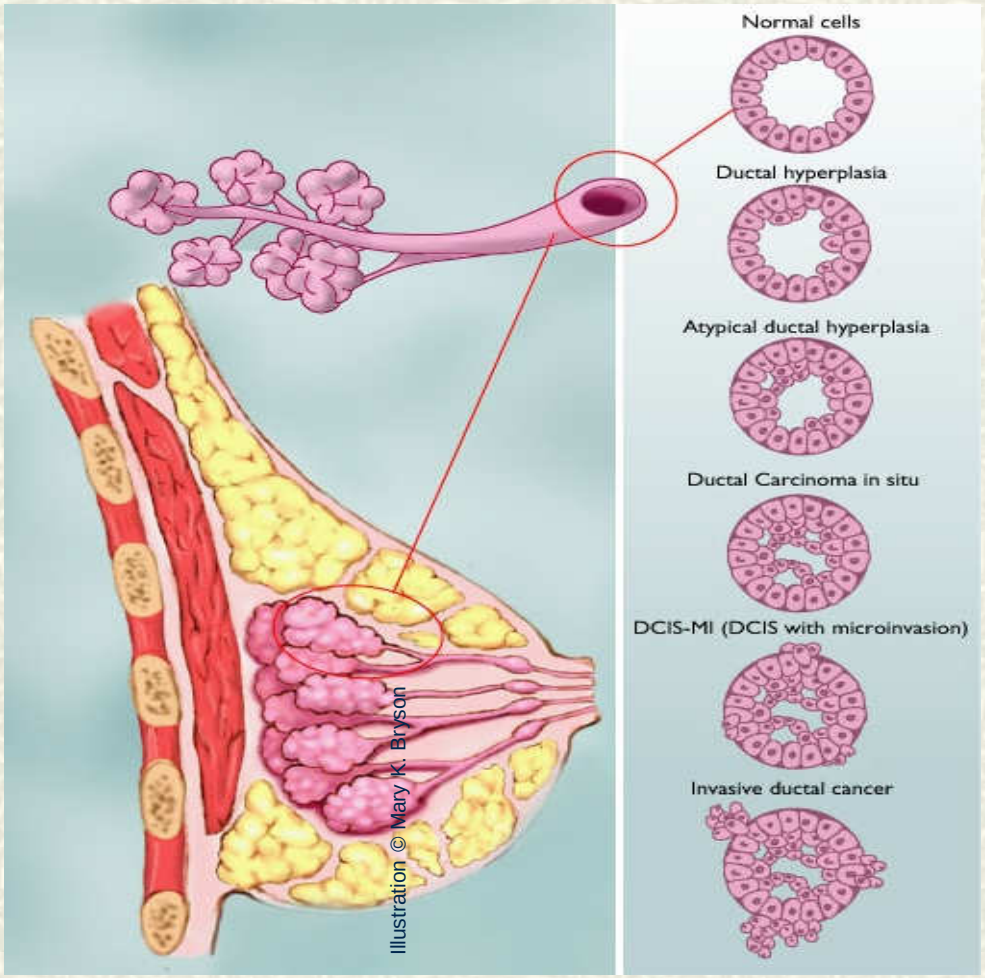


Carcinoma refers to any cancer that begins in the skin or other tissues that cover internal organs

Range of Ductal Carcinoma in situ

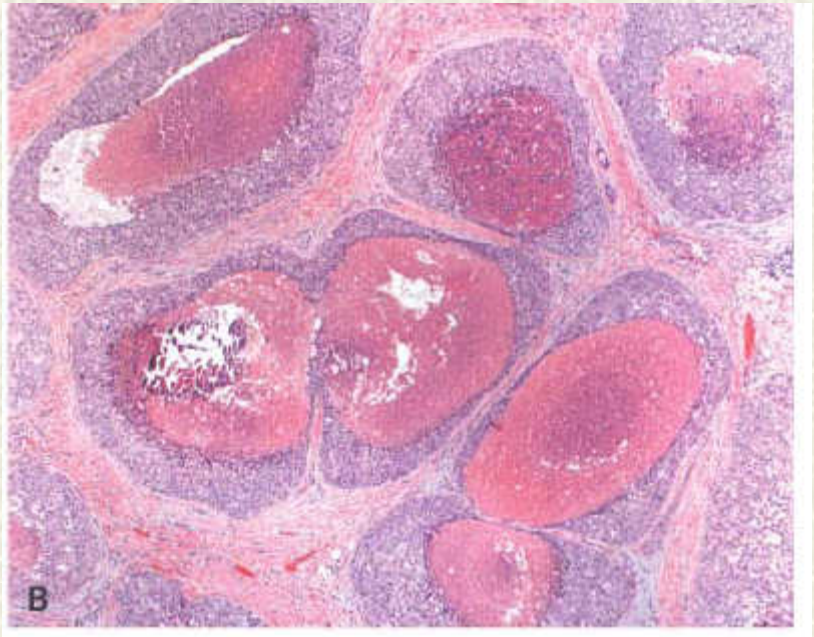


Microinvasion: invasive of carcinoma of the breast with no invasive focus measuring >1mm

Microinvasion

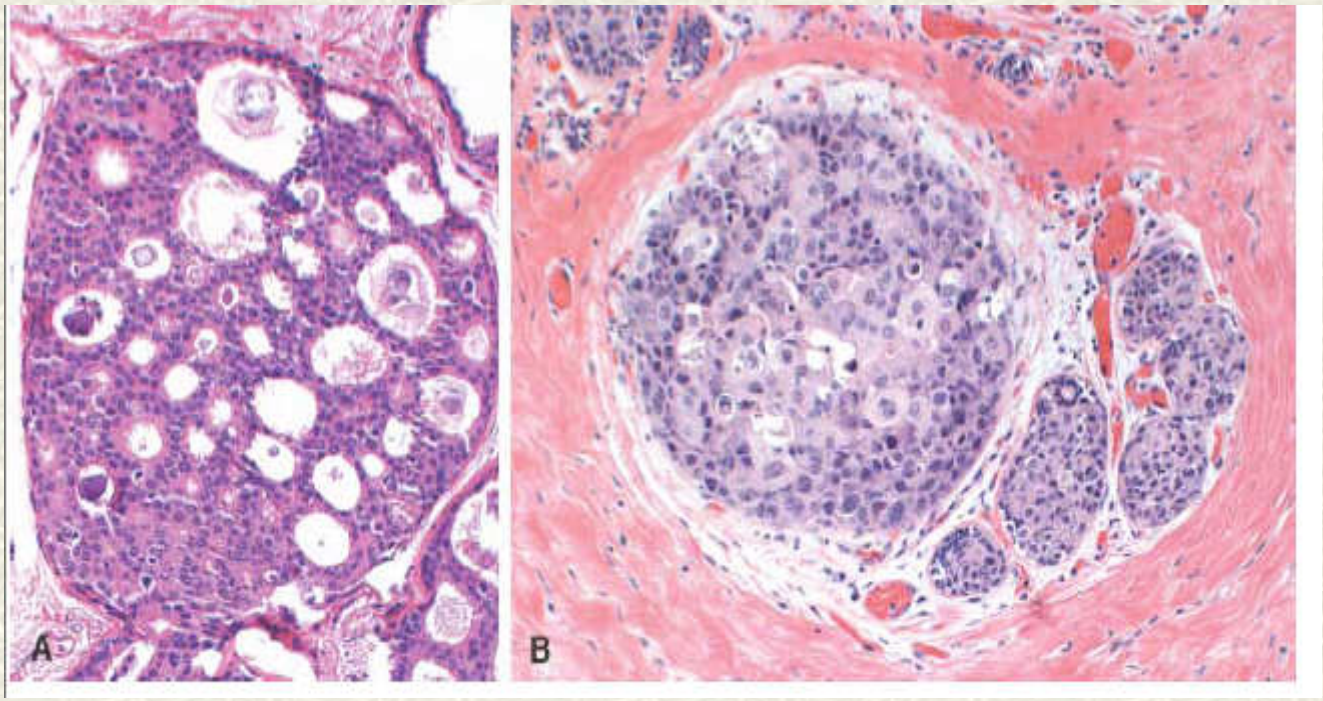
Comedocarcinoma

- Characterised by solid sheets of high-grade malignant cells and central necrosis.



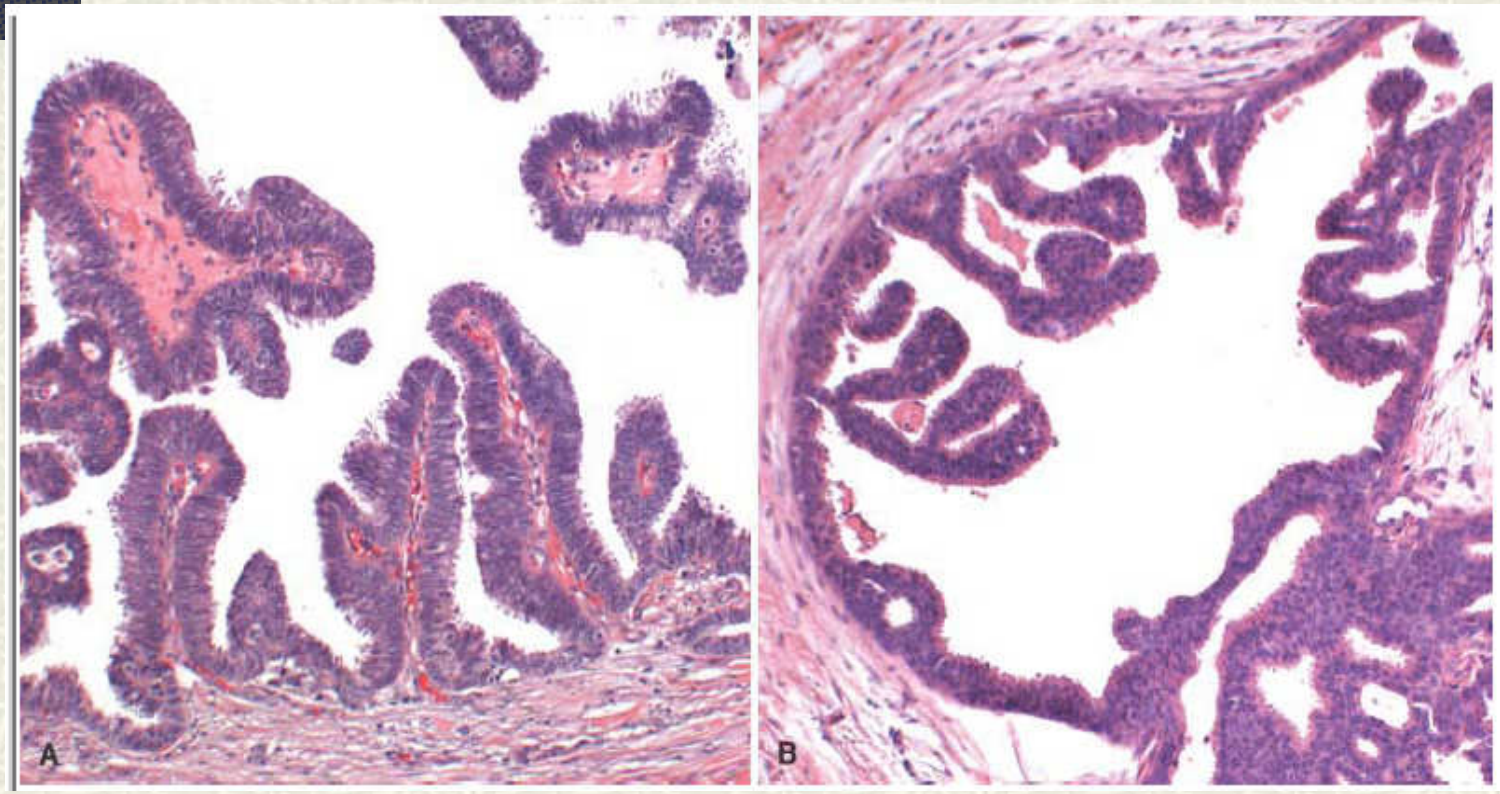
Noncomedo DCIS

- Very similar to comedocarcinoma
- Cells appear monomorphic
- 3 variants – cribriform, papillary and micropapillary DCIS



Cribriform DCIS: Lumen fills with secretions. Evenly spaced intraepithelial space

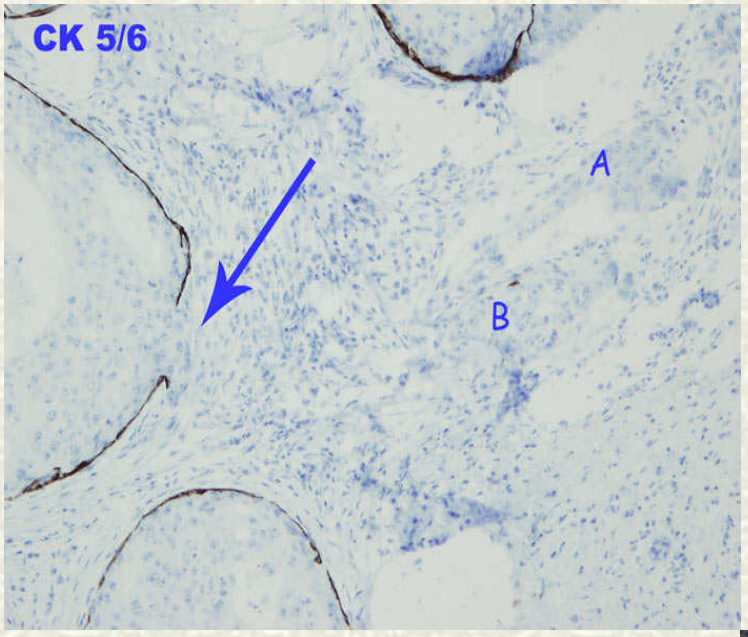
Papillary & Micropapillary DCIS



- Fibrovascular core lined by monomorphic cells. No myoepithelial cells

DCIS with Microinvasion

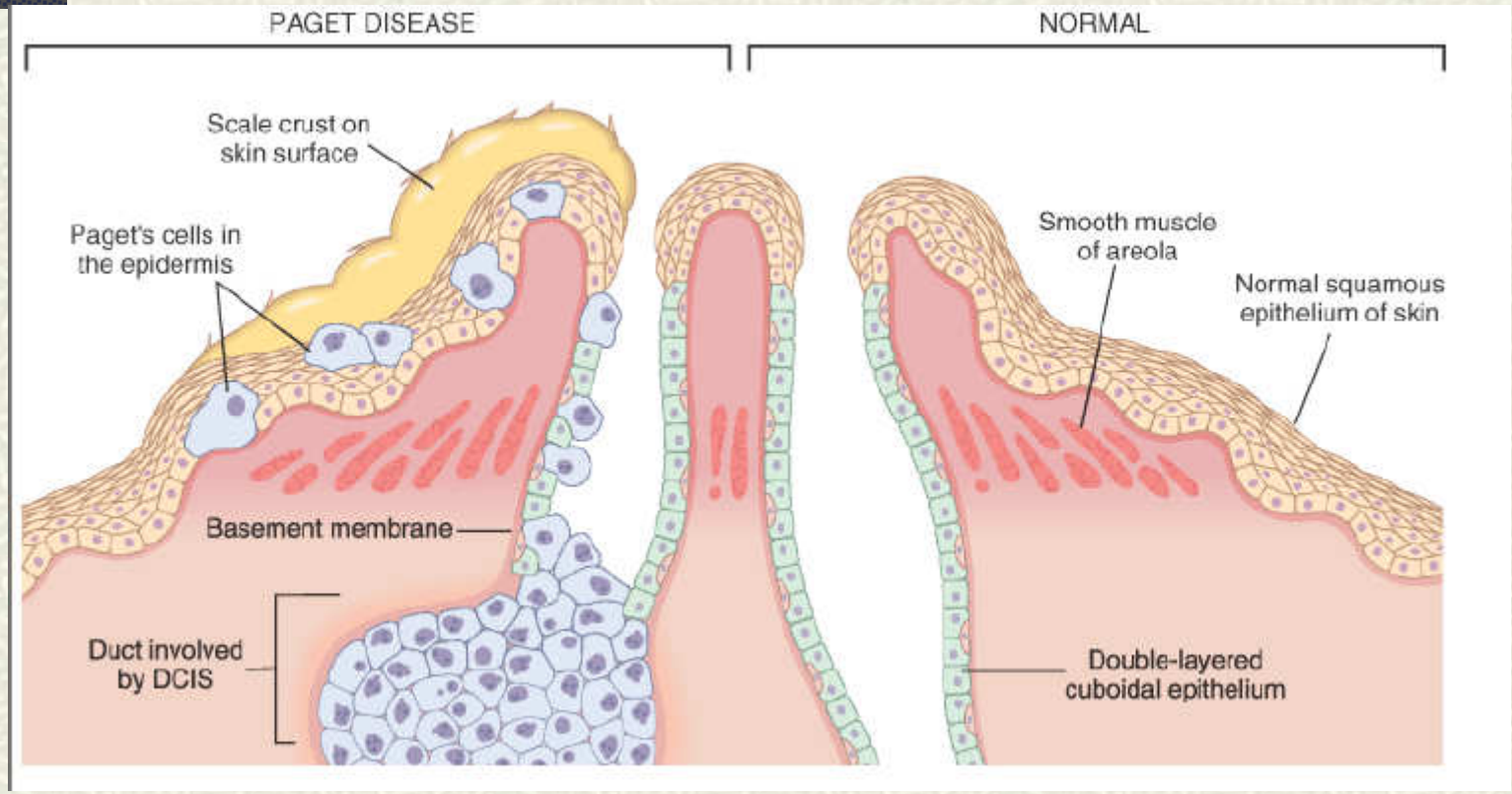
- Invasive foci of tumor cells measuring <1.0mm invading stroma.



Paget's Disease of Nipple

- Form of DCIS extending from nipple ducts into nipple skin and areola
- Skin is fissured, ulcerated and oozing. Surrounding inflammatory hyperemia & edema. Resembles eczema.
- Involvement of epidermis by malignant cells (Paget cells)

Paget's Disease of Nipple

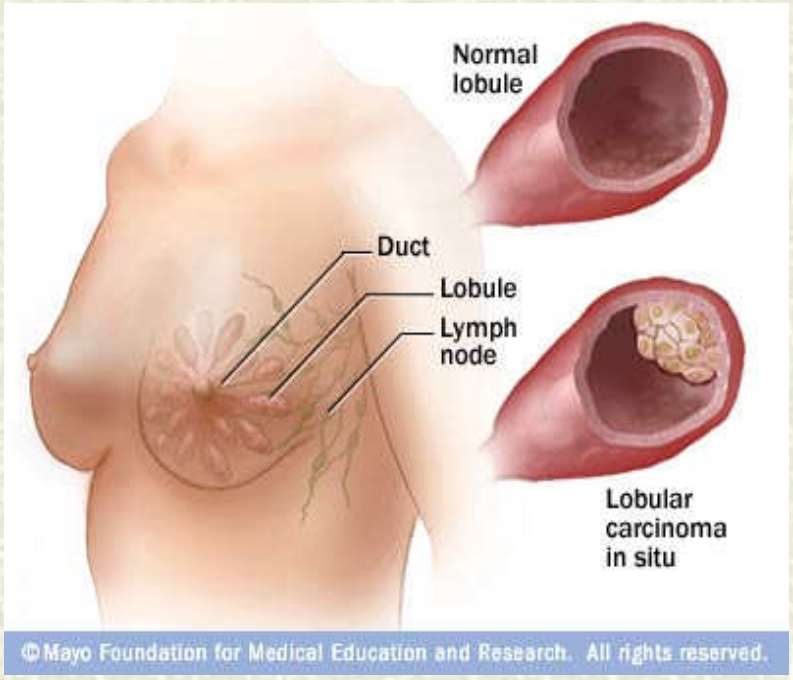


Involvement of epidermis by malignant cells

Lobular Carcinoma In Situ

- Proliferation in one or more terminal ducts or ductules (acini)
- Monomorphic population of cells, loosely cohesive and larger than normal.
- Oval to round nuclei with small nucleoli
- Signet-ring cells containing mucin commonly present

Lobular Carcinoma In Situ



Commonly incidental finding on biopsies. Rarely forms mass

INVASIVE BREAST CARCINOMA

Invasive Ductal Carcinoma (IDC – 80% of breast cancer)

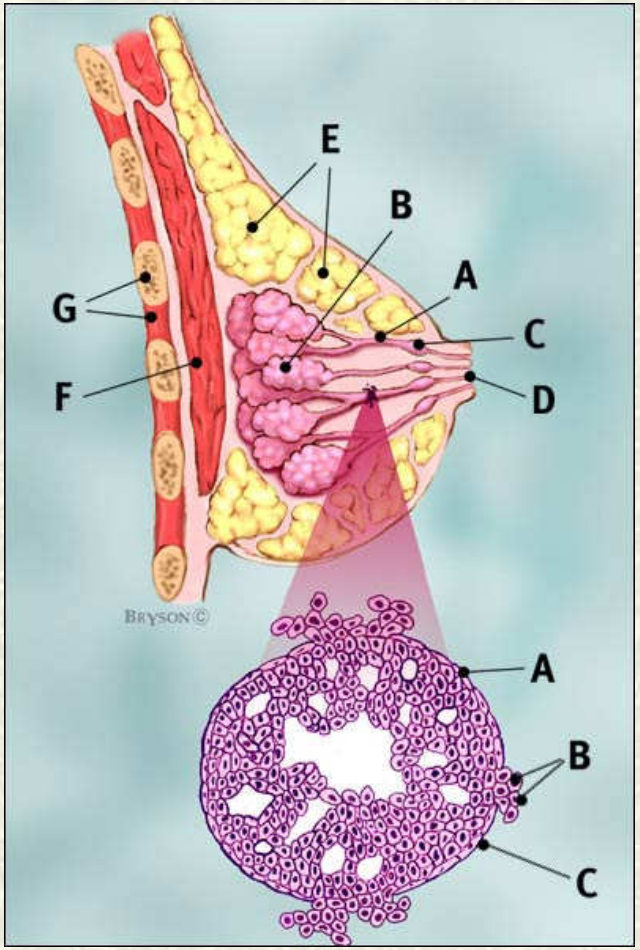
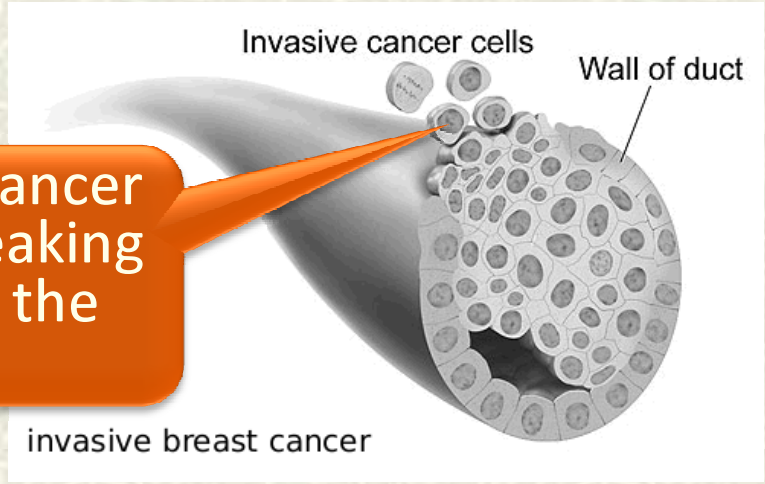


Illustration © Mary K. Bryson



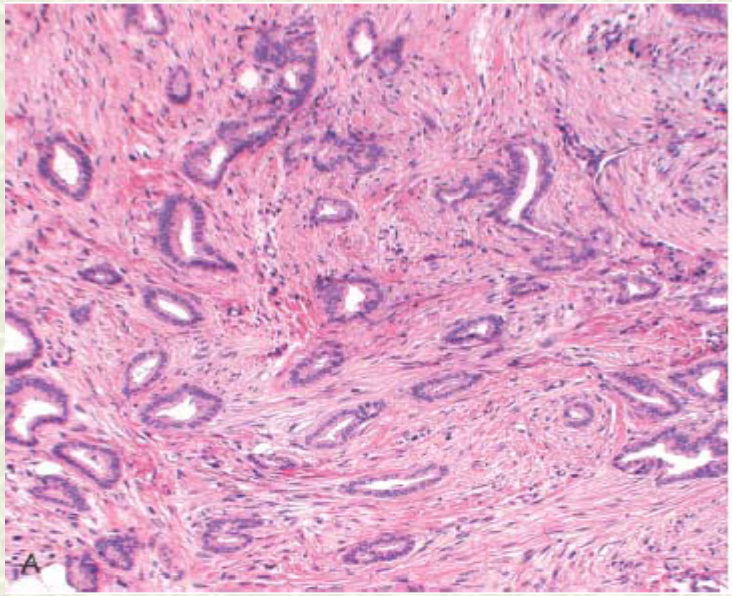
- The cancer has spread to the surrounding tissues

Invasive Breast Cancer

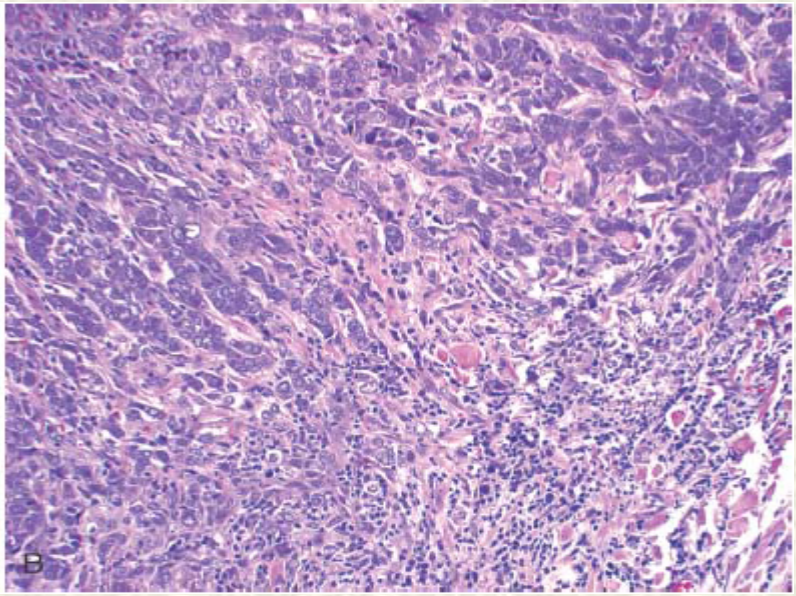
- Invasive ductal carcinoma accounts for 70-80% of invasive breast carcinoma.
- Sharply demarcated nodules (1-2cm)
- May attach to underlying structures
- Macroscopic: Lesion is retracted below cut section and infiltrates surrounding tissue.

Invasive Ductal Carcinoma

- Cells in cords, solid cell nests, tubules, anastomosing massess invading stroma.
- Small to moderately hyperchromatic regular nuclei
- Huge cells with large irregular hyperchromatic nuclei.

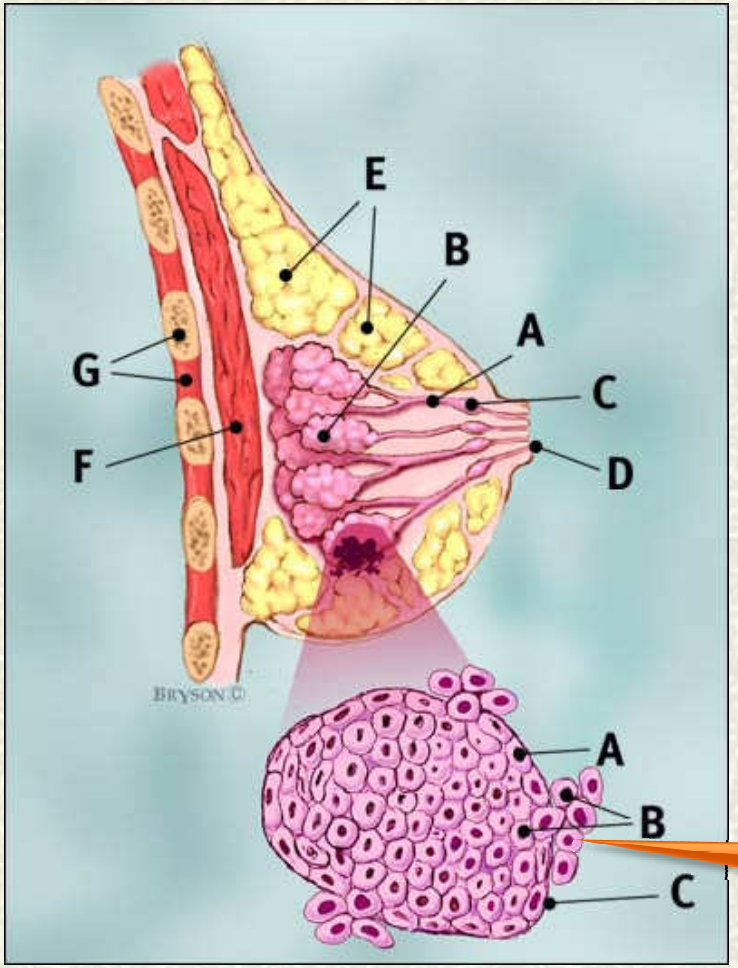


Well differentiated



Poorly differentiated

Invasive Lobular Carcinoma (ILC)



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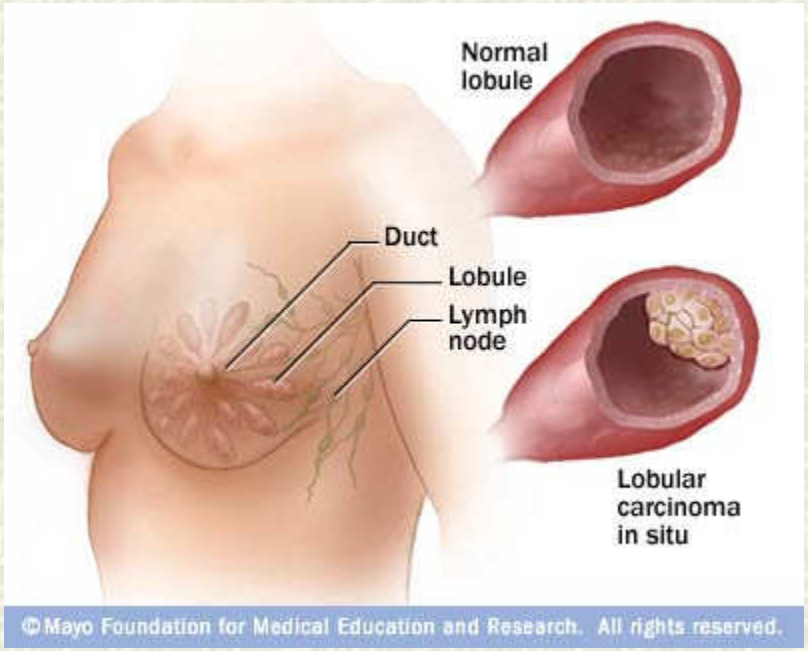
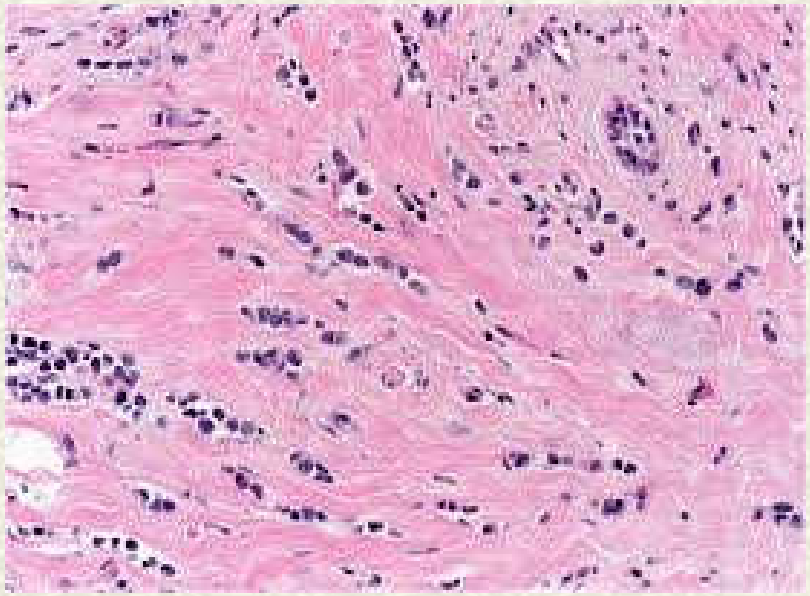


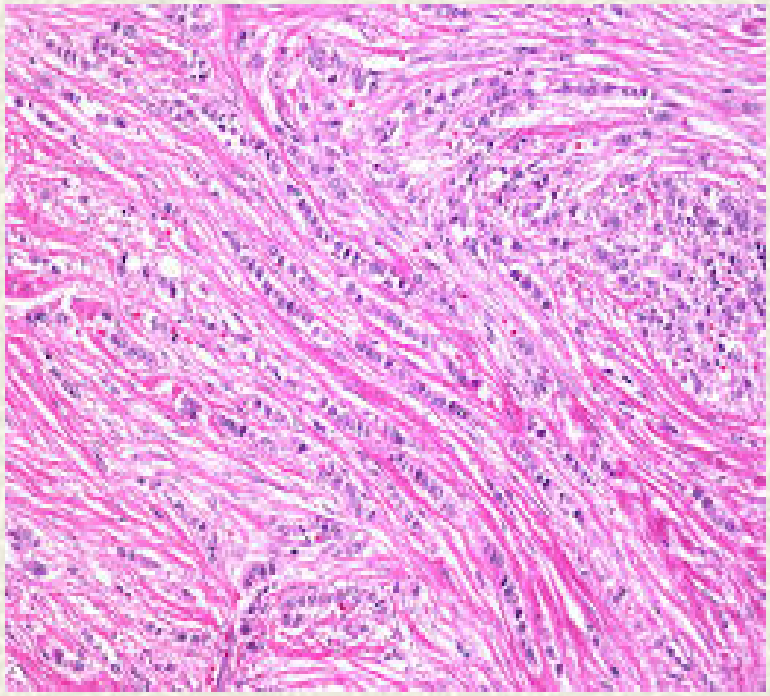
Lobular cancer cells breaking through the wall

Invasive Lobular Carcinoma

- Makes up 5-10% of cases
- Bilateral (20% risk in contralateral breast) & multicentric within same breast
- Frequent metastasis
- Microscopy:
  - Strands of infiltrating tumor cells with no formation of tubules or papillae

Invasive Lobular Carcinoma

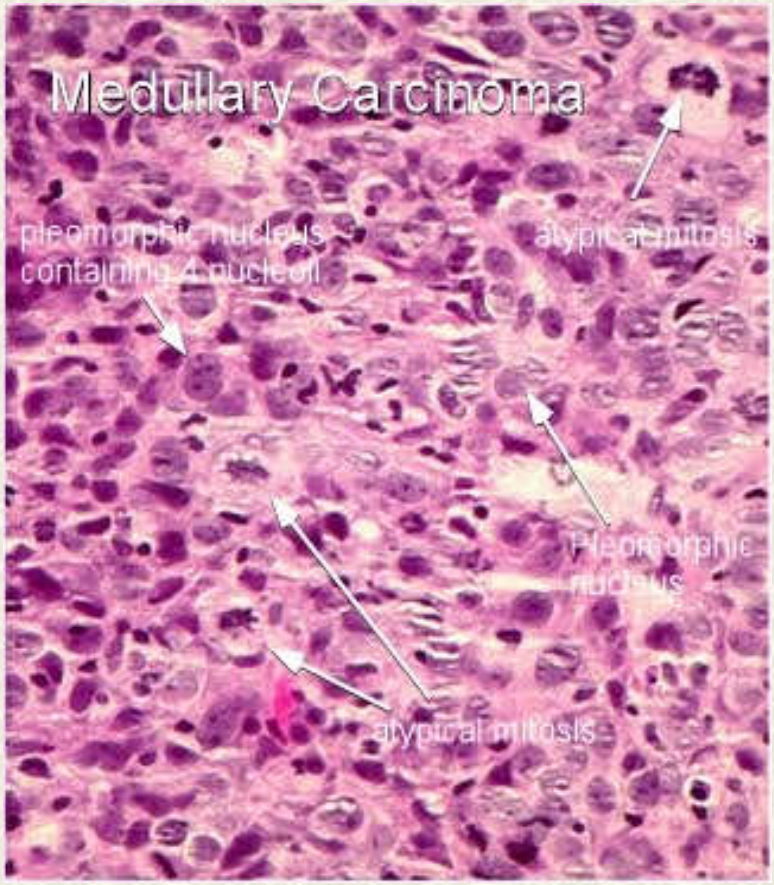


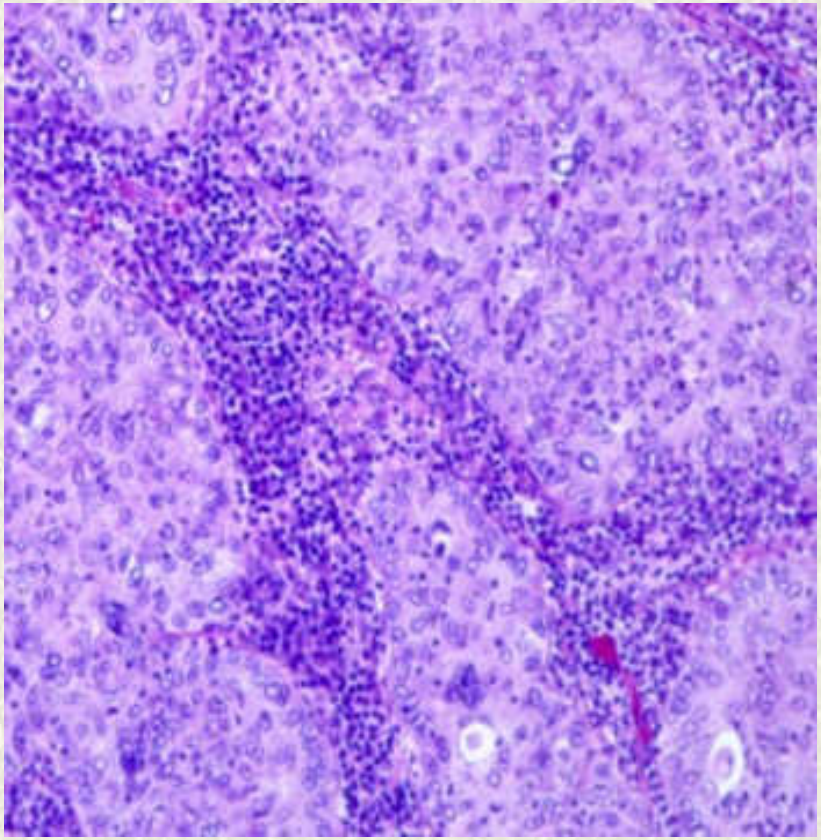


Medullary Carcinoma

- 1-5% of invasive breast carcinoma
- Large fleshy tumor (2-3cm)
- Soft, fleshy consistency and well circumscribed.
- Microscopy:
  - Solid, syncytium-like sheets of large cells with pleomorphic nuclei.
  - Moderate to marked lymphoplasmacytic infiltrate
  - Noninfiltrating border (pushing border)

Medullary Carcinoma



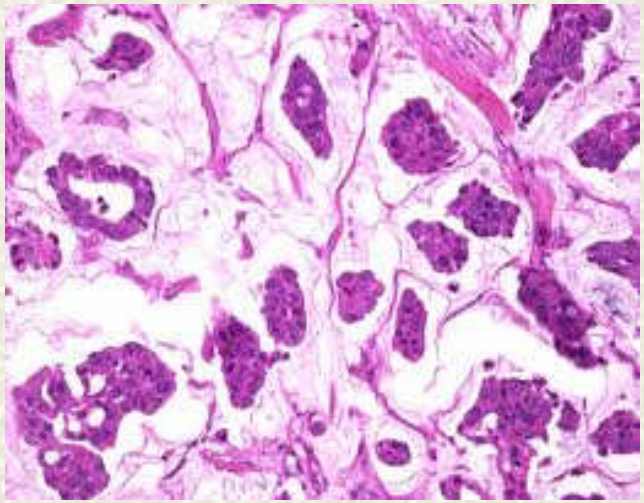


Colloid (Mucinous) Carcinoma

- Occurs in older women and grows slowly
- 1-6% of cases
- Soft tumors and may mimic benign tumors
- Microscopy shows large lakes of light staining mucin dissecting tissue spaces.
- Floating within this mucin are small islands and isolated neoplastic cells

Colloid (Mucinous) Carcinoma

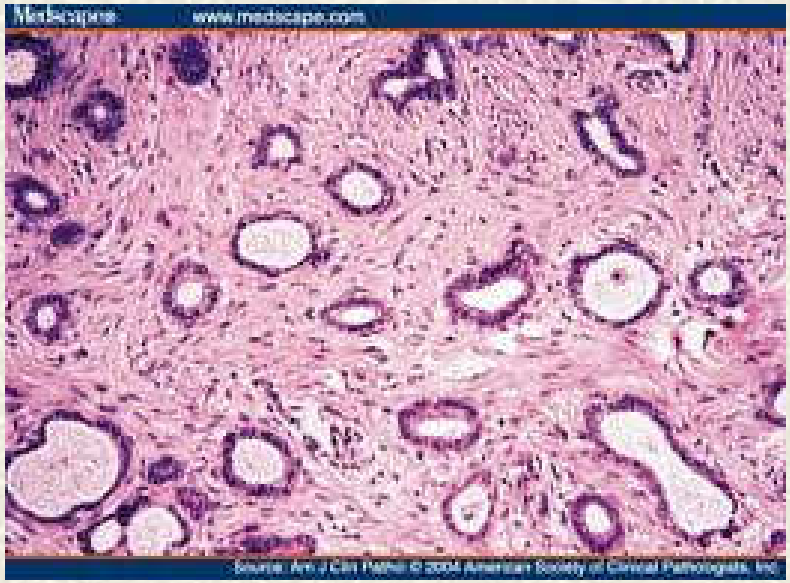
Balls of tumor cells floating in mucin

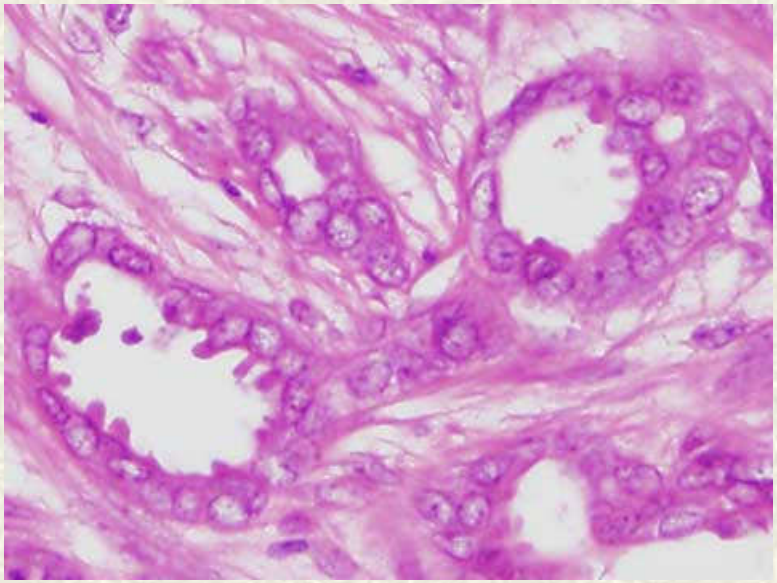


Tubular Carcinoma

- 2-10% of carcinomas less than 1cm on mammography.
- Commonly picked up on mammogram
- Present in late 35-40s.
- Multifocal within one breast or can be bilateral.
- Microscopy shows well formed tubules but no myoepithelial cells. Tumor cells in direct contact with stroma. Can be mistaken for a benign lesion.
- DCIS (40%) & LCIS (10%) present

Tubular Carcinoma





Tubular arrangement of cells. Single layer of infiltrating tumor cells. No myoepithelial cells

Features Common to Invasive Cancers

- Adherent to underlying structures
- Extension to skin show retraction & dimpling
- Lymphedema
- Nodal involvement
- Distant sites: lung, bone, liver, adrenals, brain & meninges.

Staging & Clinical Course: AJCCS

- Stage 0: DCIS or LCIS. 5 year rate of 92%.
- Stage I: invasive carcinoma <2cm including carcinoma in situ with microinvasion. No node. No distant metastasis. 5 year rate of 87%.
- Stage II: Invasive carcinoma 5cm or less. Node involved but moveable. No distant site involved OR tumor >5cm but no nodal involvement or distant metastasis. 5 year rate of 75%

American Joint Committee on Cancer Staging,1997

Staging & Clinical Course: AJCCS

- Stage III: >5cm with nodal involvement OR cancer fixed to axillary node. OR any breast cancer with involvement of ipsilateral internal mammary lymph nodes. OR Any breast cancer with skin involvement, pectoral or chest wall fixation, edema, clinical inflammatory carcinoma. No distant metastasis. 5 year rate of 46%

American Joint Committee on Cancer Staging,1997

Staging & Clinical Course: AJCCS

- Stage IV: any form of breast cancer with distant metastasis, including ipsilateral supraclavicular lymph node. 5 year rate of 13%.
- Stage II & III are also subdivided according to number of axillary lymph node involvement.

American Joint Committee on Cancer Staging,1997

Prognostic Indicators

- Lymph node metastasis
- Locally advanced disease
- Tumor size
- Histological subtypes
- Tumor grade
- Oestrogen & progesterone receptor +ve or –ve.
  - 54% of PNG tumors lack oestrogen or progesteron receptors (Walters et al 1998)
  - 4% positive for oesterogen & progesterone receptors (Walters et al 1998)
- Lymphvascular invasion
- DNA content
- Expression of oncogenes or loss of expression of tumor-supressor genes
- Angiogenesis
- Presence of proteases
- Proliferative rate

Diagnosis

- History
- Triple Test for breast lumps Inx: Clinical Exam, FNA, Imaging (ultrasound or mammogram)
  - Ultrasound - <35 y.o
  - Mammography - >50 y.o
  - 35-49 both can be used.
- True cut biopsy

Management

- Surgery
- Chemotherapy
- Radiotherapy
- Monitoring

References Robins Pathological Basis of Diseases 6th Ed.

Various sources via Google images for images.

Download seminar notes at www.pathologyatsmhs.com

END