Benign and Malignant Breast Diseases

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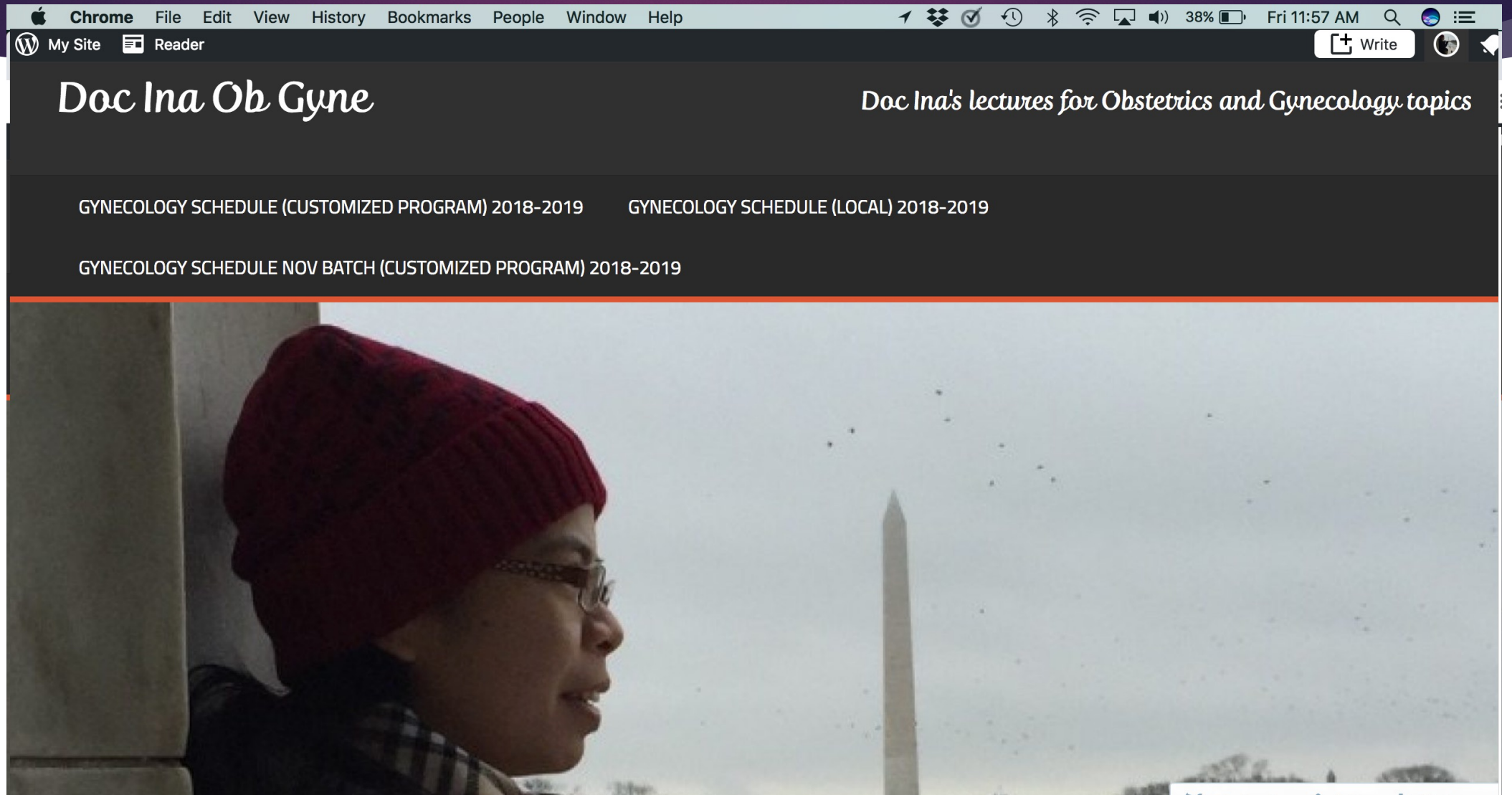

Outline

- 1. Benign Breast disorders
- 2. Breast carcinoma
  - Detection and diagnosis
  - classification
  - management

Reference

- Gershenson DM, Lentz GM, Valea F, Lobo RA (eds). Comprehensive Gynecology 8th edition, 2022. Chapter 15.

Benign Breast Disorders (BBDs)

- Benign breast disorders (BBDs) represent 90% of breast-related complaints and abnormalities; may be detected incidentally or may be detected clinically or radiographically.
- BBDs can be classified as follows:

1. Aberrations of normal development and involution (ANDI)
2. Pathologic classification
3. Clinical classification
4. Classification based on the risk for malignancy

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BBD: ANDI Classification

- Classifies BBD in relation to the normal processes of reproductive life and involution through a spectrum of breast conditions that range from "normal" to "disorder" to "disease"
- suggests that BBDs are a result of minor aberrations in the normal development process, hormonal response, and involution of the breast
- subdivided histologically by their potential future cancer risk
  - Non-proliferative disorders: no increased risk
  - Proliferative disorders without atypia: mild to moderate increase in risk
  - Atypical hyperplasia: substantial increase in risk

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TABLE 15.2 Breast Lesions and Breast Cancer Risk

Lesion Type	Lesion Subtype*	Aggregate Relative Risk of Future Breast Cancer (95% CI)
Nonproliferative	Simple cysts Mild hyperplasia (usual type) Papillary apocrine change	1.17 (0.94-1.47)†
Proliferative without atypia	Fibroadenoma Giant fibroadenoma Intraductal papilloma Moderate/florid hyperplasia (usual type) Sclerosing adenosis Radial scar	1.76 (1.58-1.95)†
Atypical hyperplasia	Atypical ductal hyperplasia Atypical lobular hyperplasia	3.93 (3.24-4.76)†
Lobular carcinoma in situ		6.9-11‡

*Dupont WD, Page DL. Risk factors for breast cancer in women with

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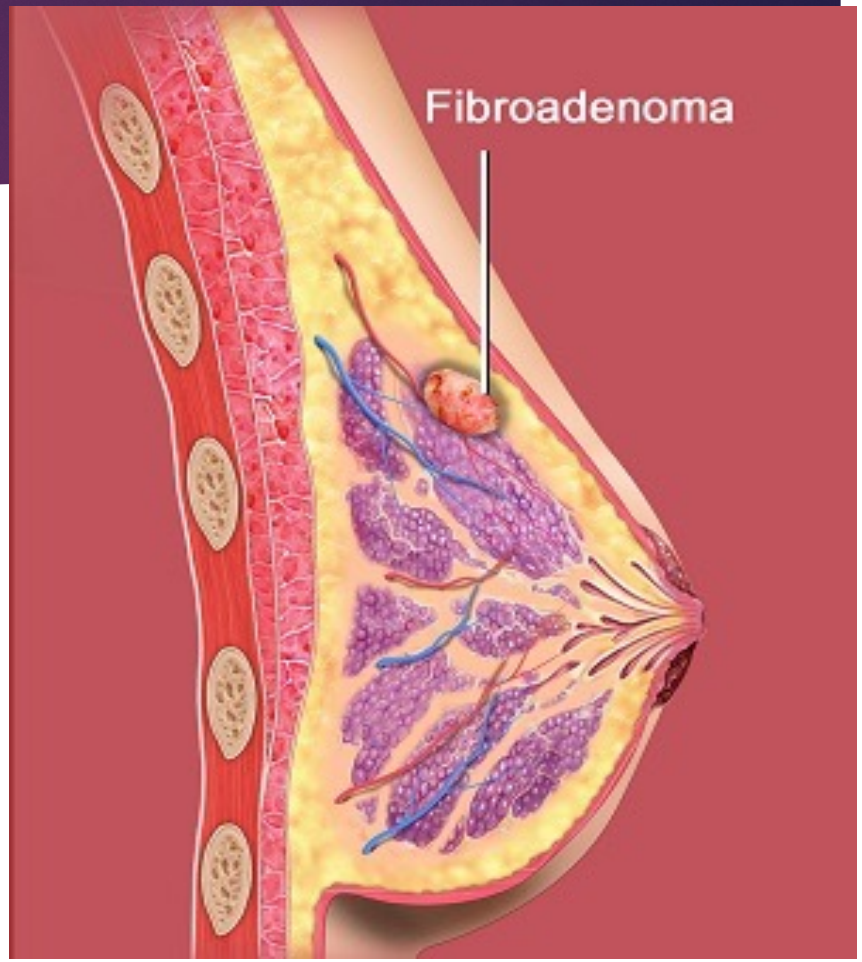
FIBROADENOMAS

- composed of fibrous and epithelial elements
- the most common benign solid breast neoplasms (15% to 20%) and are often noticed accidentally while bathing.
- most often occur in adolescents and young women (peak incidence at age 20 to 24)
- hormonally dependent, lactate during pregnancy, and involute (replaced by hyaline connective tissue during perimenopause)



https://www.breastsurgeryireland.com/fibroadenoma-general-reconstructive-aesthetic-breast-surgery-dublin.html

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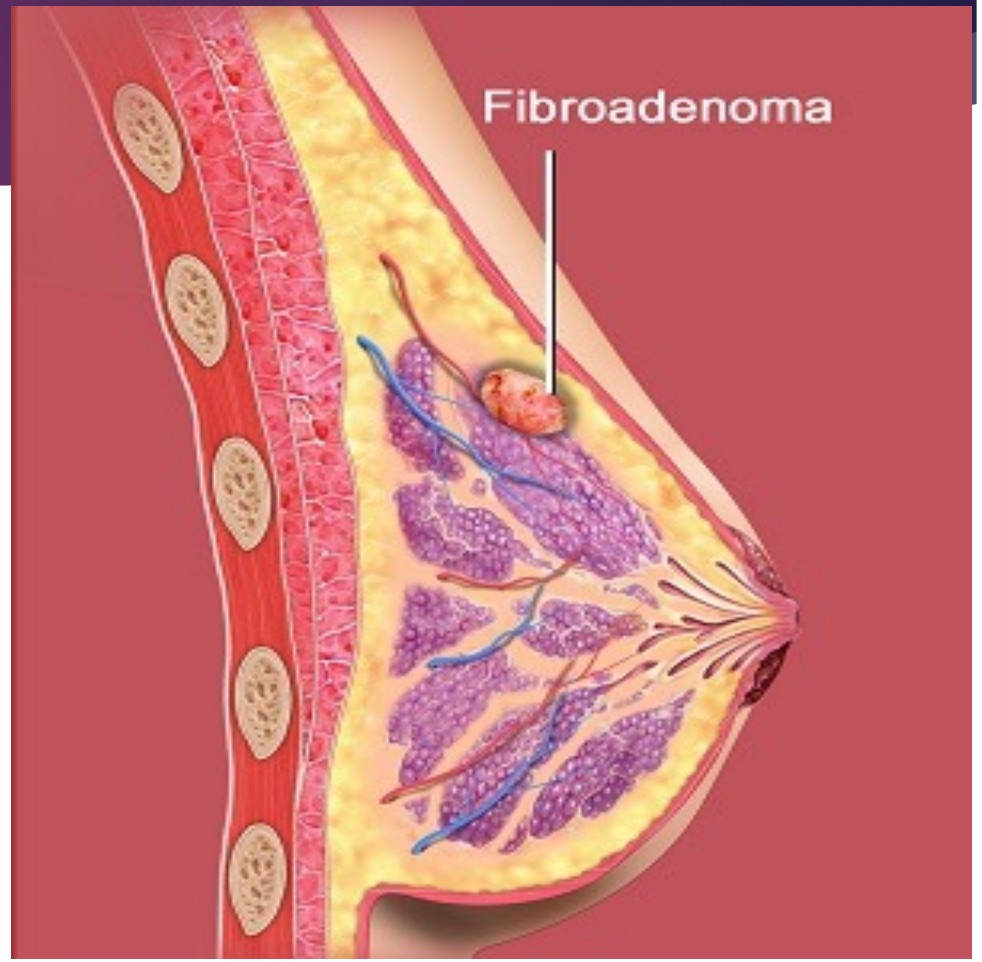
FIBROADENOMAS

- present as solitary, slow-growing, painless, freely mobile, firm, solid breast masses.
- They have a "rubbery" consistency, are usually well circumscribed, and are easily delineated from surrounding breast
- The average size is 2.5 cm, and they usually remain fairly constant in size.



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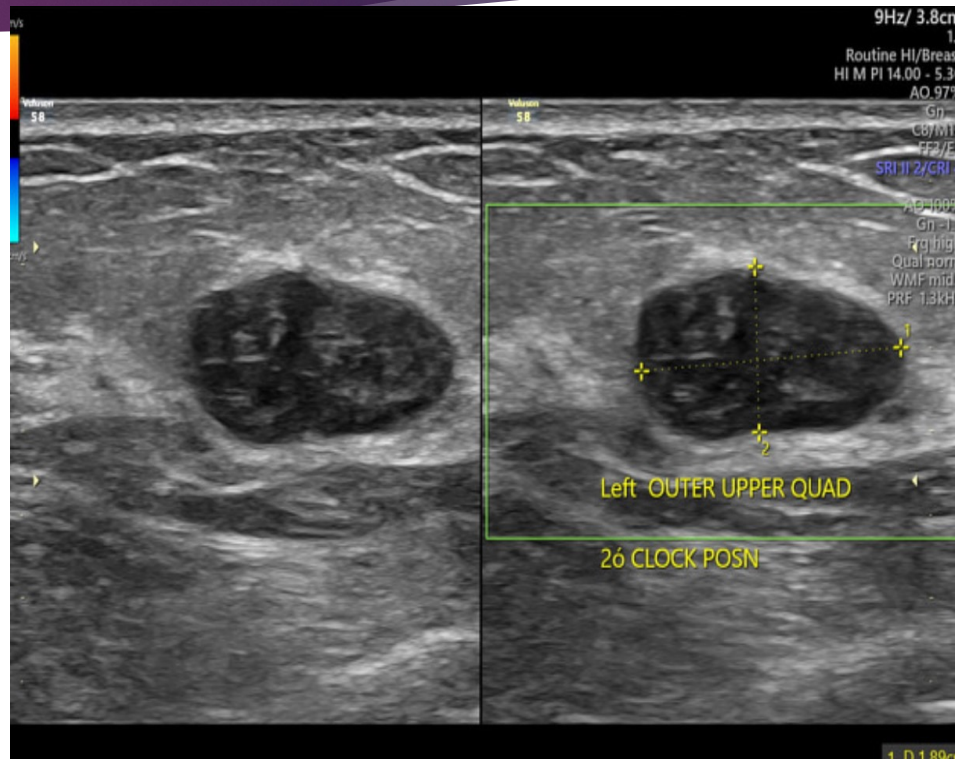
https://www.breastsurgeryireland.com/fibroadenoma-general-reconstructive-aesthetic-breast-surgery-dublin.html

FIBROADENOMAS

- Ultrasound is the initial noninvasive study to differentiate a solid versus a cystic mass
- **Core needle biopsy** is indicated when the cause of a palpable mass cannot be established.
- **Surgical evaluation** is appropriate for any mass (at any age) that exhibits a ***rapid increase in size, with complex cysts or solid areas***
- Fibroadenomas can be managed conservatively: continued surveillance at 6-month intervals for at least 2 years.



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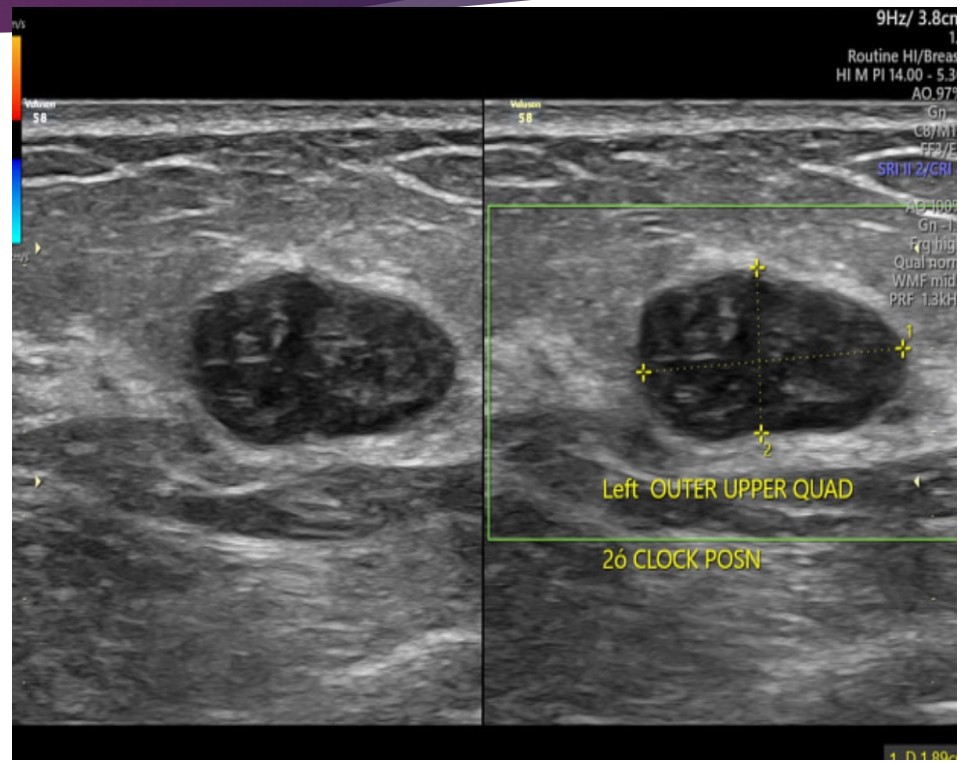
https://radiopaedia.org/cases/fibroadenoma-of-the-breast-2

FIBROADENOMAS

- Nonoperative management can be considered for small, asymptomatic fibroadenomas in women younger than 35 or if clinical examination, imaging evaluation (either mammogram or ultrasound), and biopsy (usually core needle) results are 100% concordant.
- Surgical excision of fibroadenomas should be considered if they are symptomatic or to relieve anxiety related to the palpable mass.



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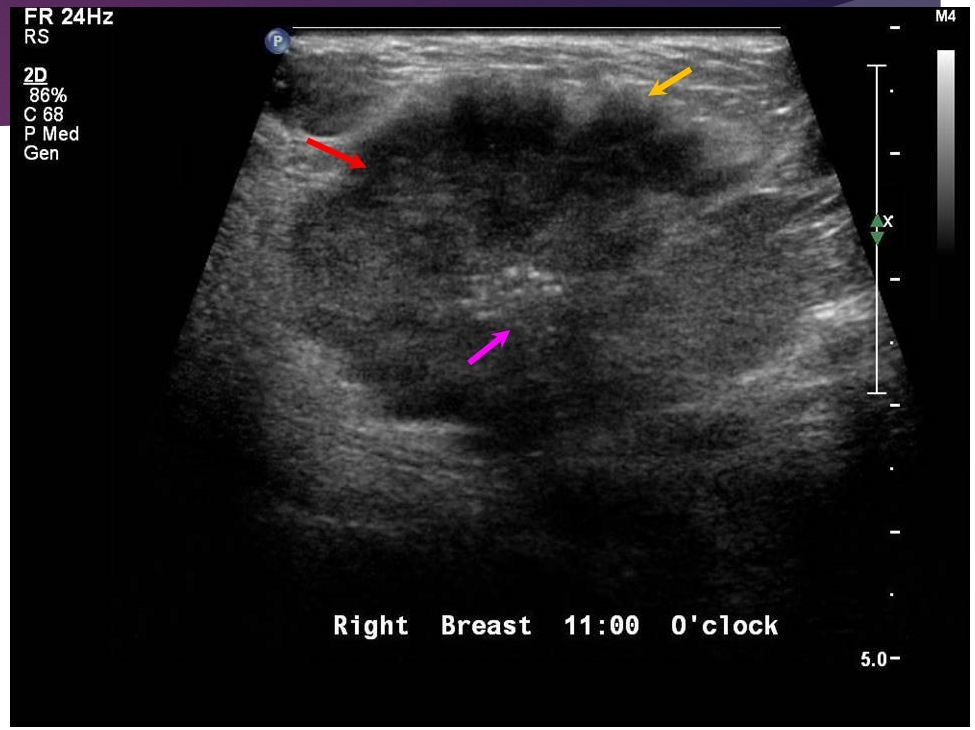
https://radiopaedia.org/cases/fibroadenoma-of-the-breast-2

FIBROADENOMAS

- when accompanied by *complex cysts larger than 3 mm in diameter, sclerosing adenosis, epithelial calcification, or papillary changes*

  → increased risk of breast cancer

- Women with fibroadenomas should be made aware of this risk and encouraged to maintain continued close surveillance.
- The postoperative risk of recurrent fibroadenoma is approximately **20%.**



https://screening.iarc.fr/atlasbreastdetail.php?Index=083

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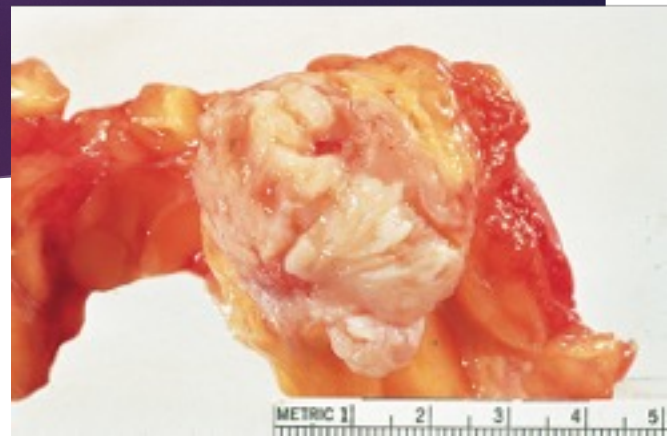
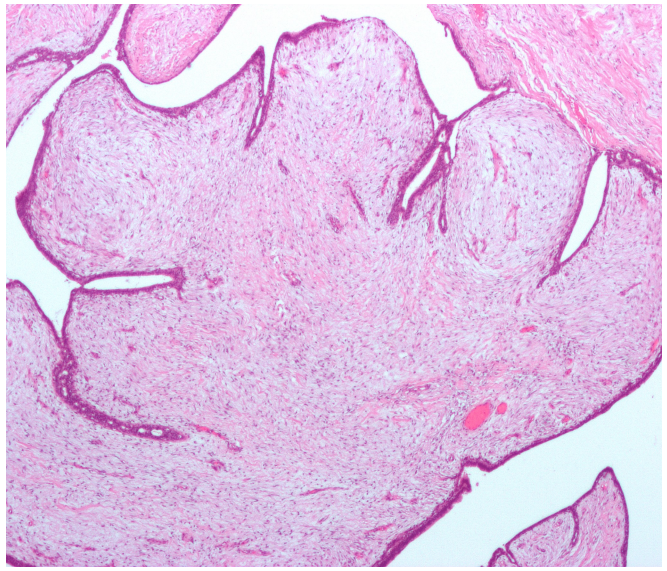
Phyllodes tumors

- previously termed *Cystosarcoma phyllodes*
- Rare (2.5% of fibroepithelial tumors and < 1% of breast malignancies)
- The typical age of onset: fourth and fifth decades of life
- may be benign, borderline, or malignant.
- often grow rapidly
- Histologically, stromal elements dominate and will invade the ducts in a "leafy" projection





https://en.m.wikipedia.org/wiki/File:Phyllodes_tum

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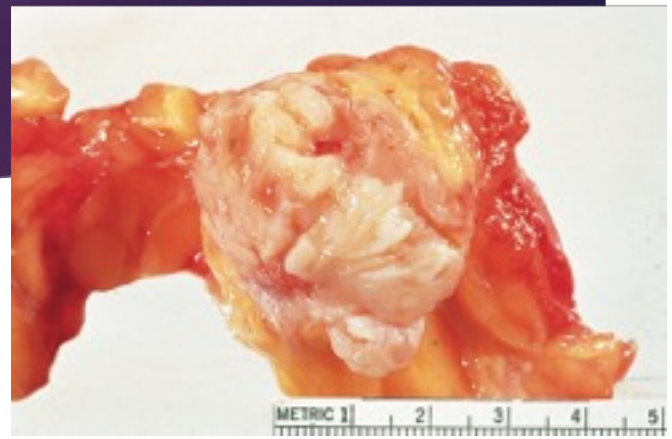
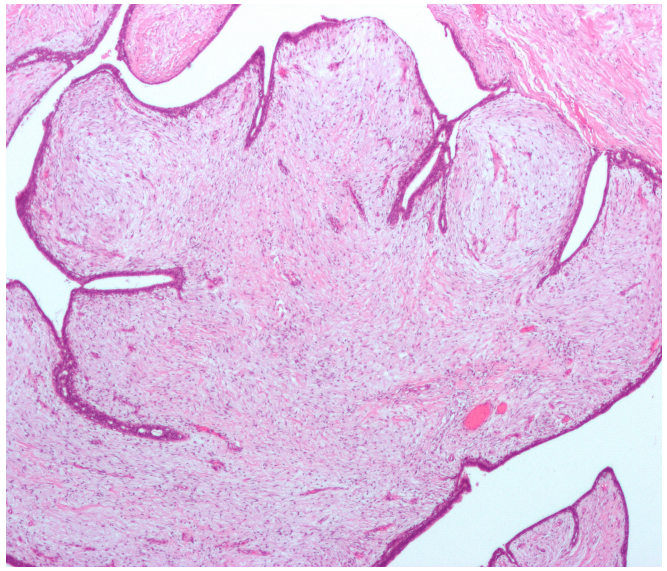
Phyllodes tumors

- mammographic appearance as a rounded density with smooth borders is similar to that of fibroadenomas → Mammography and ultrasonography are therefore unreliable
- Locally aggressive, and require wide local excision with 1-cm margins.
- Malignant tumors metastasize hematogenously, and the risk of metastases is **25%**; local recurrence is common (0.20%), even with benign and borderline tumors.





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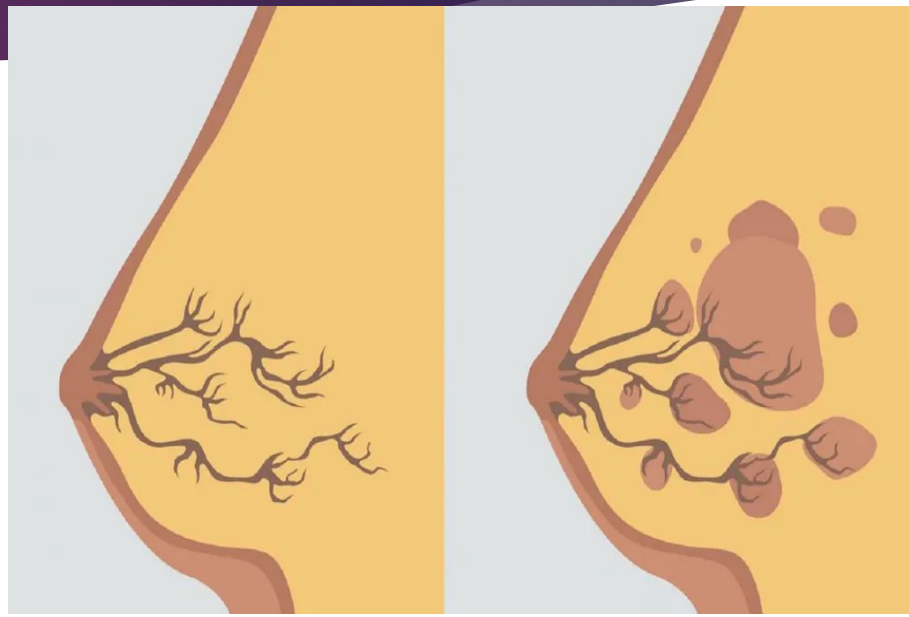
Fibrocystic change

- previously designated fibrocystic *disease,* which is a common and natural maturation of breast tissue over time.
- most common of all benign breast conditions
- presents as a spectrum of changes throughout a woman's reproductive age, with significant patient variation.
- The ICD-10 calls this ***diffuse cystic mastopathy.***
- represent an exaggeration of the normal physiologic response of breast tissue to the cyclic levels or ovarian hormones.
- most common in women of reproductive age (20 to 50 years)



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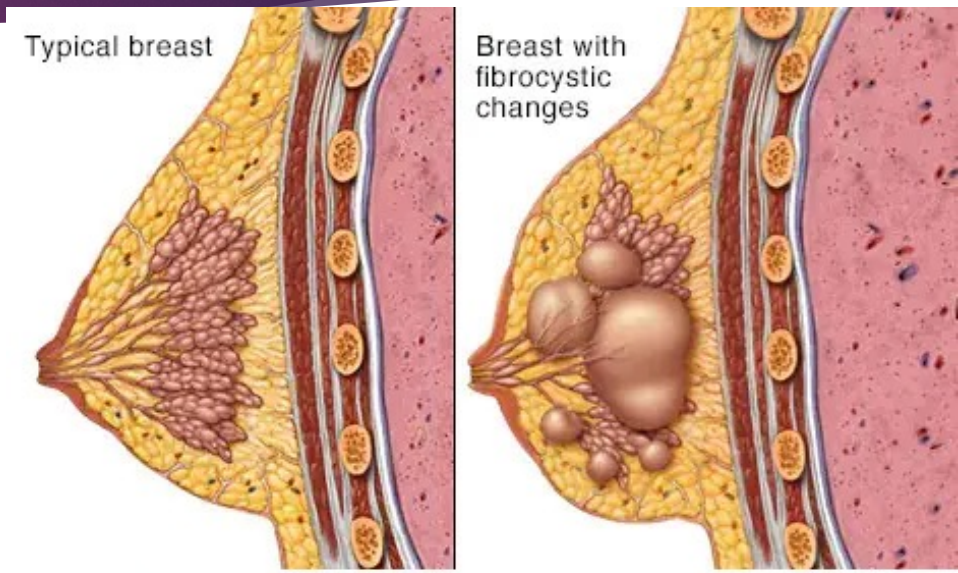
Fibrocystic change

- Clinical signs include increased breast engorgement and density, excessive breast nodularity, fluctuation in the size of cystic areas, increased tenderness, and, rarely, spontaneous nipple discharge.
- Signs and symptoms are typically more prevalent during the premenstrual state.
- Associated mastalgia is bilateral, often difficult to localize, and most common in the upper, outer breast quadrants. Pain may radiate to the shoulders and upper arms.
- The physical findings of excessive nodularity as a result of fibrocystic changes have been described as similar to palpating the **"surface of multiple peas" or "grapelike structures".**



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Fibrocystic change

- There are three general clinical stages of fibrocystic change
  - **mazoplasia (mastoplasia),** is associated with intense stromal proliferation and occurs in the early reproductive years (20s).
    - Breast pain is noted primarily in the upper, outer breast quad- rants, with most tenderness in the axillary tail.
  - adenosis is characterized by marked proliferation and hyperplasia of ducts, ductules, and alveolar cells
    - Premenstrual breast pain and tenderness is less severe.

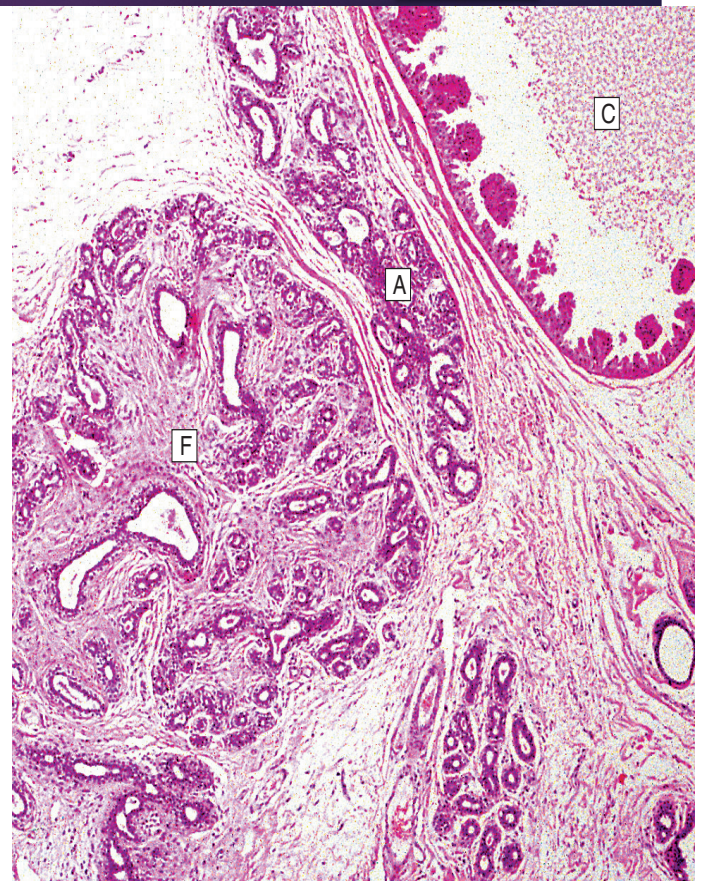

Fig. 15.9 Fibrocystic changes from histologic section. Note fibrosis *(F)*, adenomatous changes with increased ductal tissue *(A)*, and cysts *(C)*. (From Stevens A, Lowe J. *Human Histology.* 3rd ed. Philadelphia: Mosby; 2005:392.)

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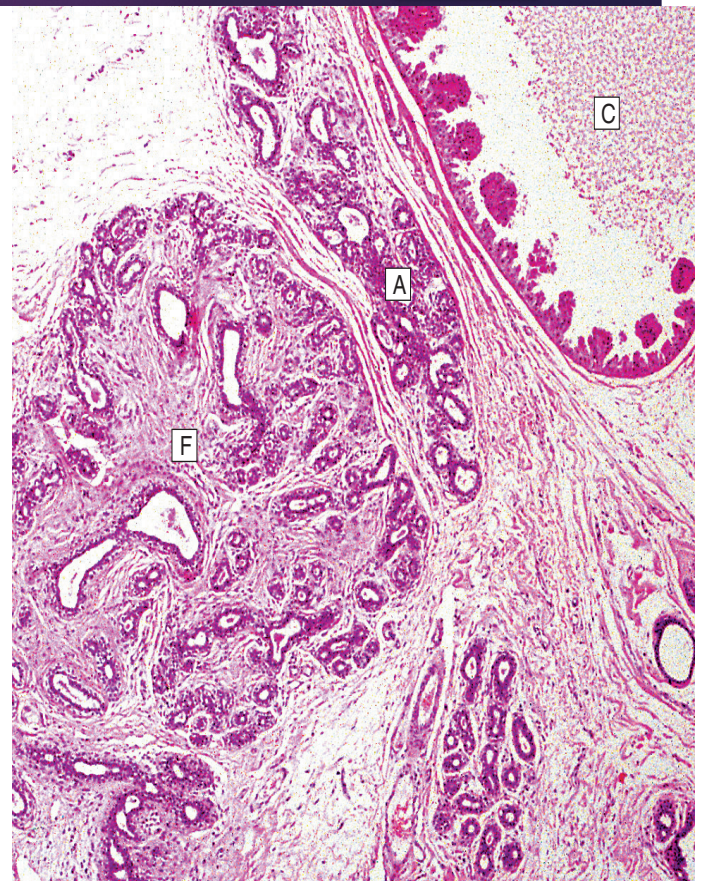
Fibrocystic change

- The **cystic phase** typically occurs another decade later, in women in their 40s.
  - Typically there is no breast pain unless a cyst increases rapidly in size, with associated sudden pain, point tenderness, and a lump.
  - Cysts are tender to palpation and vary from microscopic to 5 cm in diameter.
  - Complex cysts have internal septations, debris, or solid components and may require core needle biopsy if stability cannot be documented. The fluid aspirated from a large cyst is typically straw colored, dark brown, or green, depending on the chronicity of the cyst.



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Fibrocystic change: treatment

- Initial therapy for fibrocystic change involves mechanical support using a firm support or sports bra.
- Dietary changes to reduce methylxanthines, saturated fat intake, alcoholic beverages or caffeine exposure
- Diuretics are sometimes prescribed during the premenstrual phase and may lessen symptoms of breast discomfort and engorgement.
- Oral contraceptives or supplemental progestins during the secretory phase
- Danazol, 100, 200, and 400 mg daily for 4 to 6 months
- Tamoxifen, 10-20 mg daily, during luteal phase
- Selective estrogen receptor modulator (SERM) (Ormeloxifene; 30 mg twice weekly)
- gonadotropin-releasing hormone (GnRH) agonists

https://www.bodyandsoul.com.au/diet/lose-weight/how-to-lose-weight-by-drinking-alcohol-and-coffee/news-story/d42c198a4fb85ec7034789c8979ab3b1

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Mastalgia (breast pain)

- **90%** of conditions are benign.
- Breast pain is typically divided into **cyclic pain**, related to the menstrual cycle, and noncyclic pain.
  - Cyclic pain is diffuse and bilateral and most commonly associated with fibrocystic changes.
  - Noncyclic breast pain is commonly localized and related to a cyst.
  - Noncyclic breast pain should be evaluated, particularly in older women, because there is a small association with malignancy.
- differential diagnosis: cyst, chest wall pain, radicular pain, costochondritis, mastitis, pregnancy-related pain, prolactinomas, and medication exposure

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BOX 15.1 Medications Associated with Mastalgia

Antihypertensives
Atenolol and other beta-blockers
Hydrochlorothiazide
Methyldopa
Minoxidil
Spironolactone
Antidepressants and antipsychotic agents
Amitriptyline and other tricyclic antidepressants
Chlorpromazine/promethazine
Fluoxetine
Haloperidol
Hormonal agents
Estrogens
Progestins
Androgens
Ginseng
Clomiphene citrate
Digoxin
Chlorpropamide

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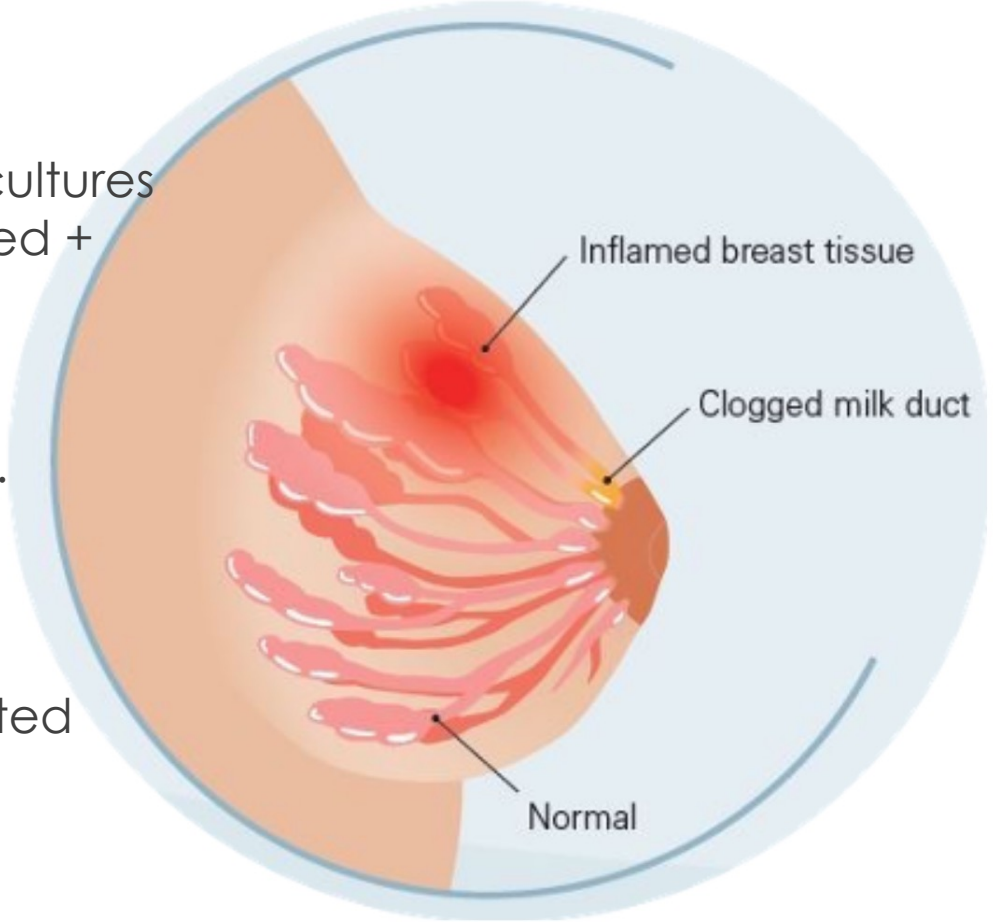
Mastitis and Inflammatory disease

- most commonly related to *Staphylococcus aureus.*
- If there is poor response to the initial course of antibiotics, cultures for methicillin-resistant *S. aureus* (MRSA) should be performed + doxycycline or sulfamethoxazole/trimethoprim
- **Lactational mastitis**
- commonly occurs during the first 6 weeks of breastfeeding.
- first-line antibiotics: cephalosporin, or cloxacillin
- may progress to a breast abscess in 5% to 11% of patients.
- Continued breastfeeding or manual pumping of the affected breast is recommended to decrease engorgement.



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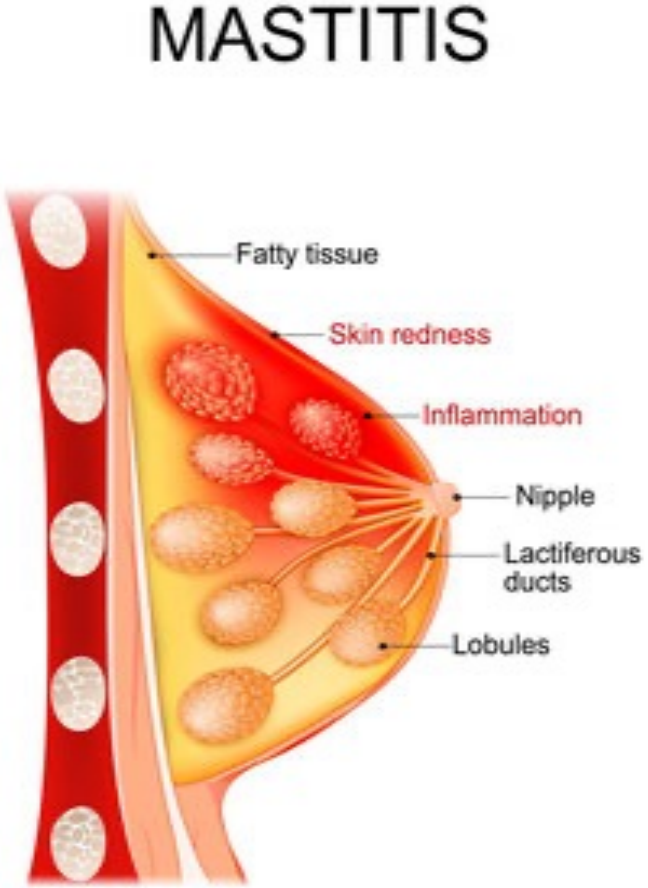
Mastitis and Inflammatory disease

2. Nonpuerperal mastitis

- associated with breast cysts and cyst rupture.
- Ultrasonography assists in excluding an abscess.
- Exclude the presence of malignant breast disease, particularly inflammatory cancer.
- Additional test for diabetes and human immunodeficiency virus (HIV) may be indicated, particularly if yeast is the offending organism.
- In patients with recurrent mastitis, choose an antibiotic to cover MRSA, such as clindamycin, sulfamethoxazole/trimethoprim, doxycycline, or vancomycin.



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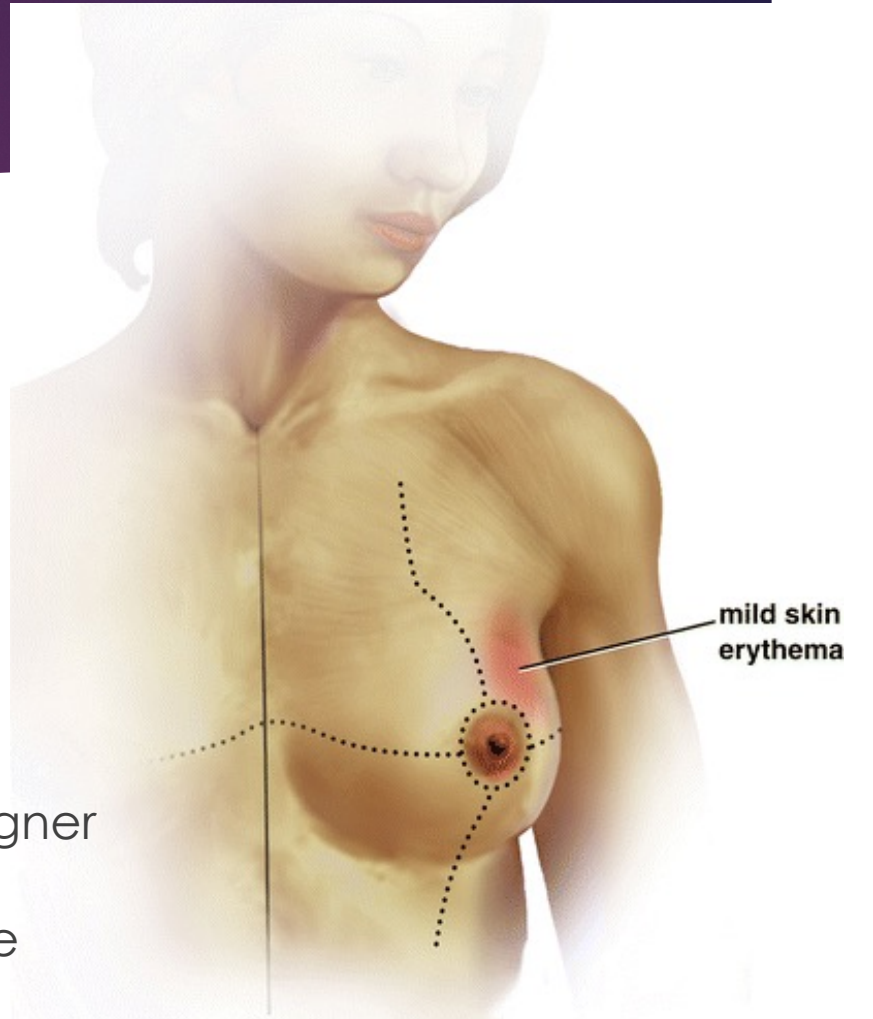
Mastitis and Inflammatory disease

3. Idiopathic granulomatous mastitis (IGM),

- also called **idiopathic granulomatous lobular mastitis (IGLM)**
- may present with a mass, abscess, inflammation, or granuloma formation.
- Steroid treatment has been reported to be effective
- usually self-limited, resolving within months.
- Skin scarring and residual small abscesses may remain, often necessitating surgical treatment. C
- chronic inflammatory diseases, such as lupus, sarcoidosis, and Wegner granulomatosis, are rare causes of noninfectious mastitis, and evaluation for these diseases should be performed if antibiotics are not effective.



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Code=radiographics

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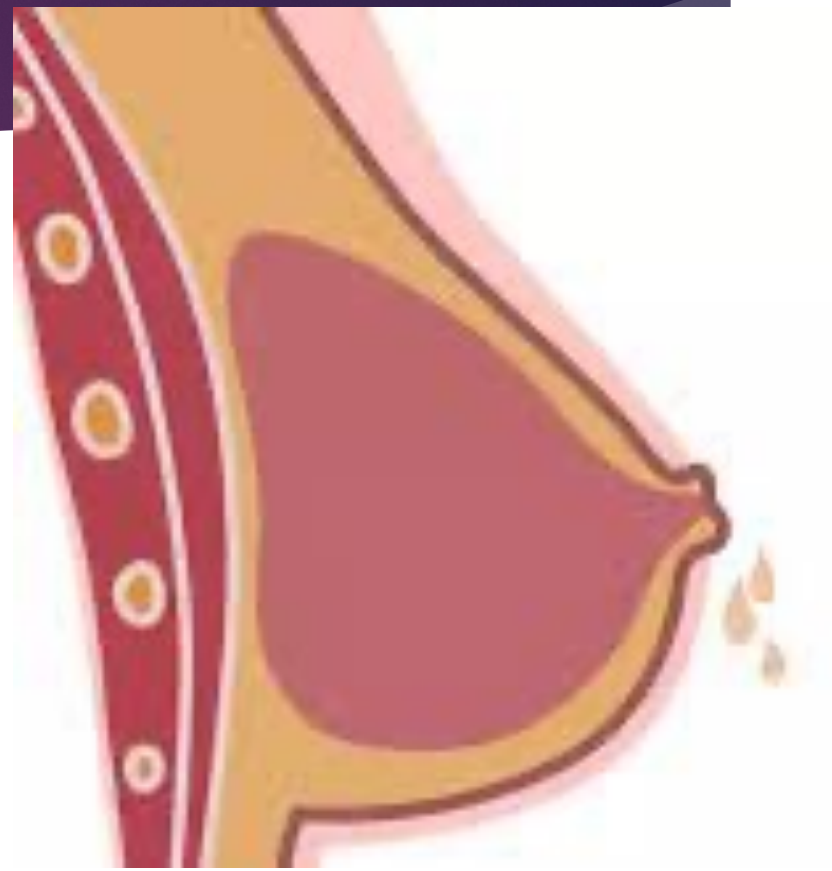
Nipple discharge

- majority have a benign cause;
- An underlying malignancy is more likely when:
  - ✓ the discharge is spontaneous (vs. induced with nipple pressure)
  - ✓ arises from a single duct
  - ✓ blood stained
  - ✓ unilateral and persistent (occurring more than twice weekly).
- Age is important because an underlying malignancy is present in:
  - 3% of women younger than 40
  - 10% of women between 40 and 60
  - 32% of women older than 60
- **Intraductal papilloma** and **fibrocystic changes** are the two most common causes of spontaneous non-milky discharge.



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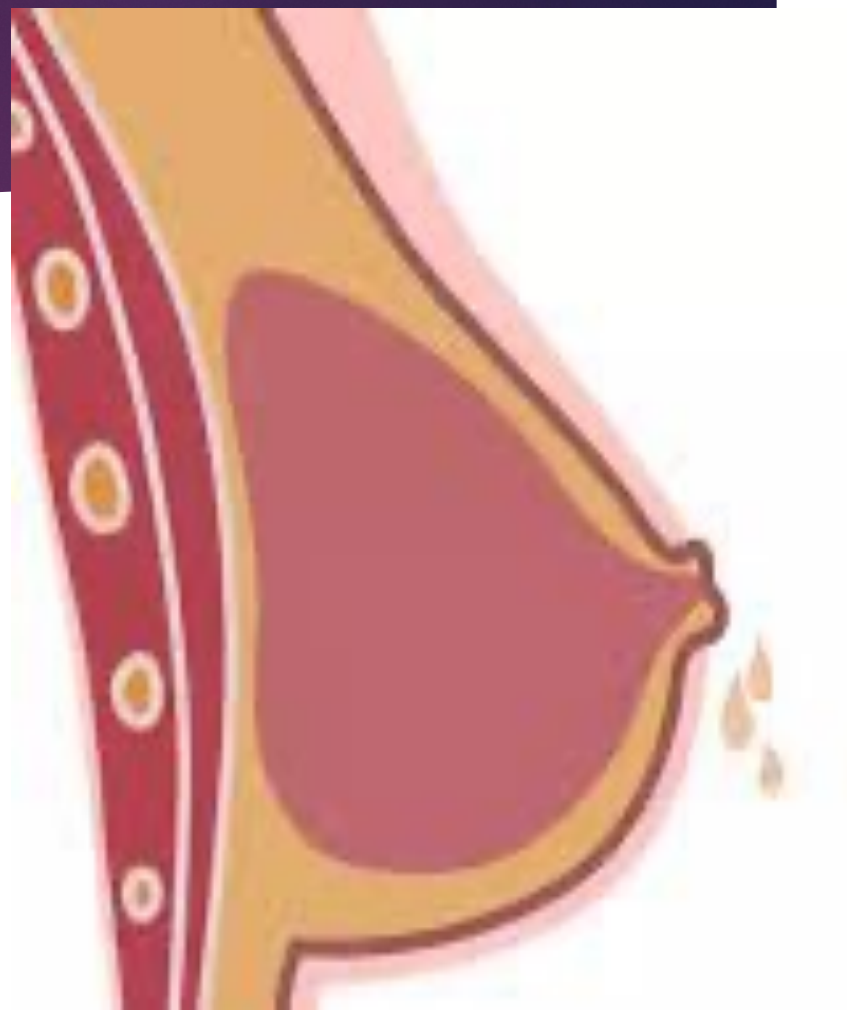
Nipple discharge

- Galactorrhea is likely when breast discharge is bilateral, copious, milky pale in color, and occurs from multiple ducts.
- Numerous medications and conditions can affect the hypothalamic-pituitary axis and lead to prolactin secretion and galactorrhea.
- As many as 65% of premenopausal women may have a normal benign physiologic discharge with gentle squeezing of the nipple.
- Evaluation includes physical examination, mammography, and sonography.



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Nipple discharge

- Evaluation and diagnosis include clinically separating the discharges into those that are spontaneous and those that only are expressed by pinching or squeezing the nipple
- Malignancy should be excluded in any woman with:
  - ✓ a bloody discharge
  - ✓ any discharge associated with a mass
  - ✓ if the discharge originates from only one or two adjacent ducts.
- Assessment of *pathologic* nipple discharge involves a careful breast examination to identify the presence or absence of a breast mass.
- Firm areola pressure can assist in identifying the site of any dilated duct (pressure over a dilated duct will produce the discharge)
  - ✓ this finding helps to define where an incision should be made for any subsequent surgery.
  - ✓ The nipple is squeezed with firm, gentle digital pressure, and if fluid is expressed, the site and character of the discharge are recorded.

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Nipple discharge

- Management of a suspicious discharge:
  - ✓ physical examination with imaging (mammography/ultrasound)
  - ✓ magnetic resonance imaging (MRI).
- Any mass associated with discharge requires appropriate biopsy.
- A number of techniques have been evaluated to determine the cause and avoid unnecessary extirpative surgery:
  - **Ductoscopy** (using a microendoscope passed into the offending duct) allows direct visualization.
  - **Ductal lavage** involves duct canalization, and collection of fluid for cytologic evaluation.
  - **Ductography** (imaging of the ductal system by injecting contrast into the symptomatic duct), also called a **galactogram**,
  - **Surgical excision of the duct and its associated lobular unit** is both diagnostic and therapeutic.

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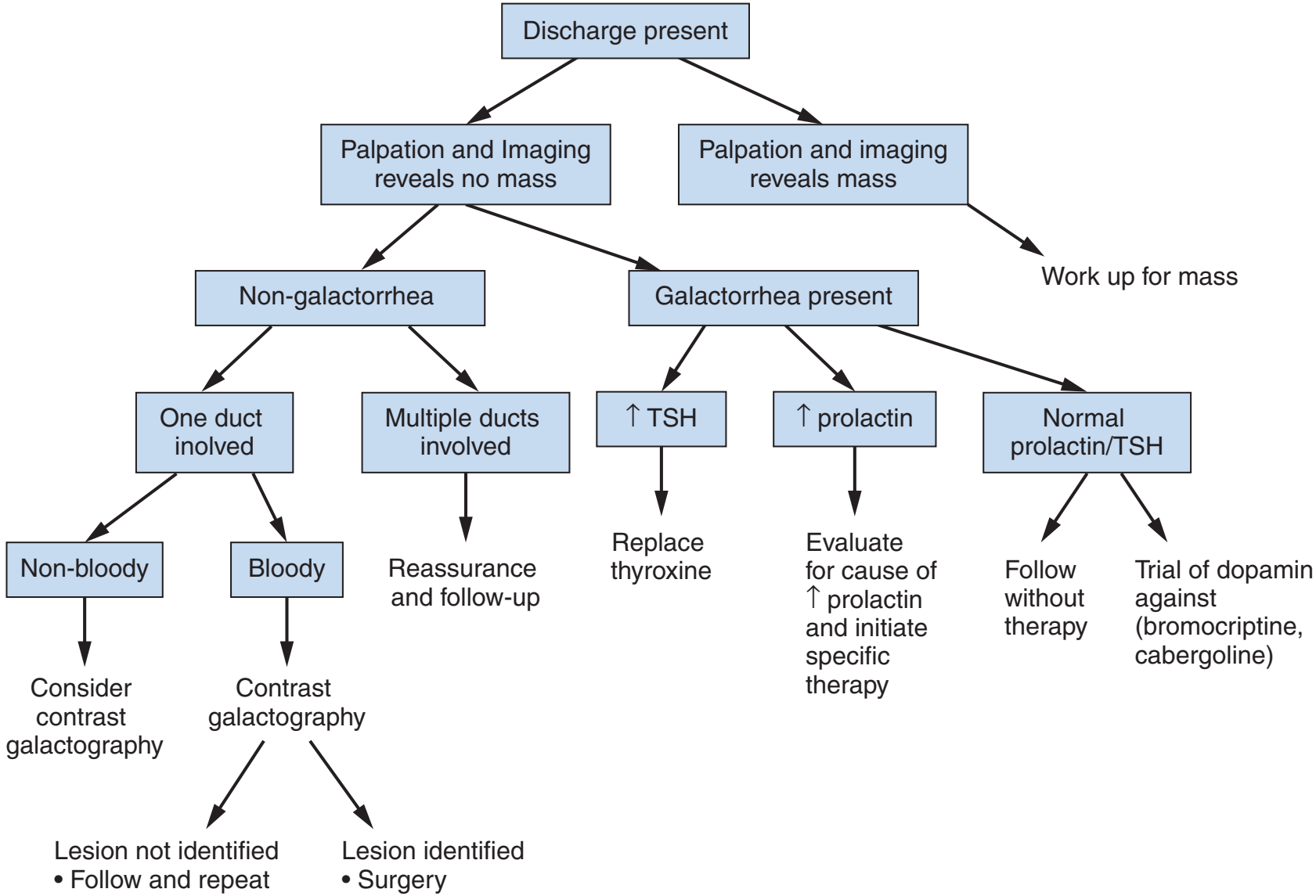
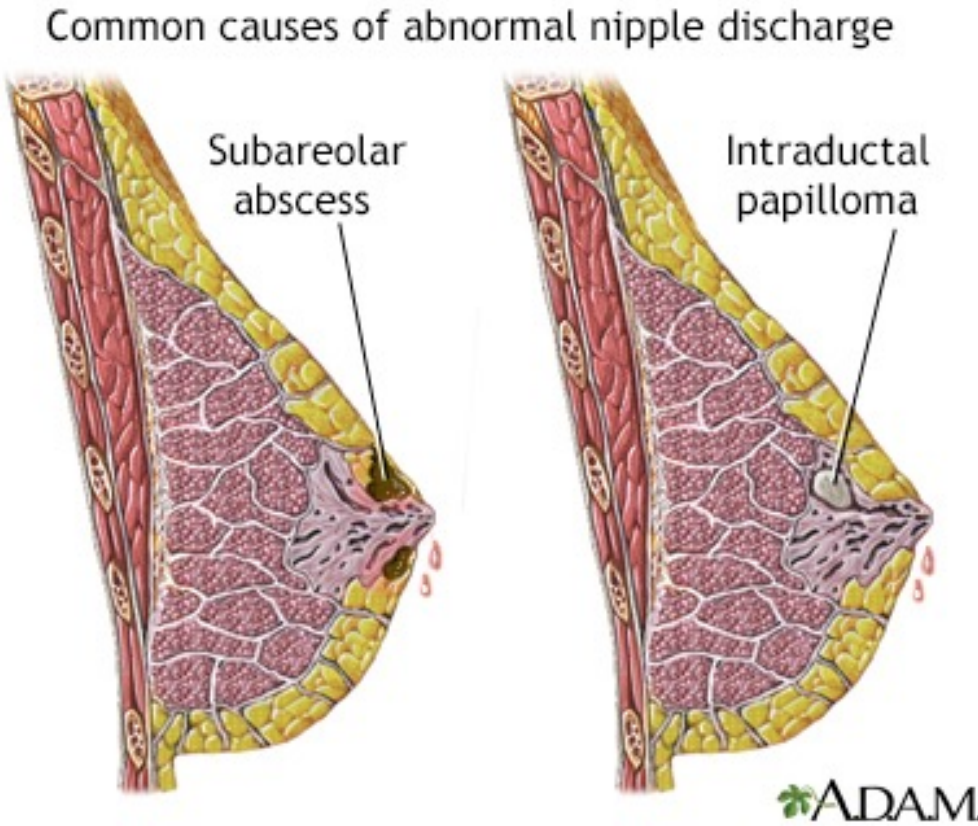


Fig. 15.10 Algorithm for Evaluation of Nipple Discharge. (From Santen RJ. Benign breast disease in women. [Updated May 25, 2018.] In: Feingold KR, Anawalt B, Boyce A, et al., eds. *Endotext.* South Dartmouth, MA: MDText.com, Inc.; 2000.)

Intraductal papilloma

- broad-based or pedunculated polypoid epithelial lesions that may obstruct and distend the involved duct.
- most commonly diagnosed in perimenopausal women.
- Intermittent, spontaneous discharge from one nipple involving one or two ducts.
- discharge can be watery, serous, or bloody,
- 75% of intraductal papillomas are located beneath the areola, are small and soft, and are often difficult to palpate, typically measuring 1 to 3 mm in diameter.



https://www.mountsinai.org/health-library/diseases-conditions/intraductal-papilloma

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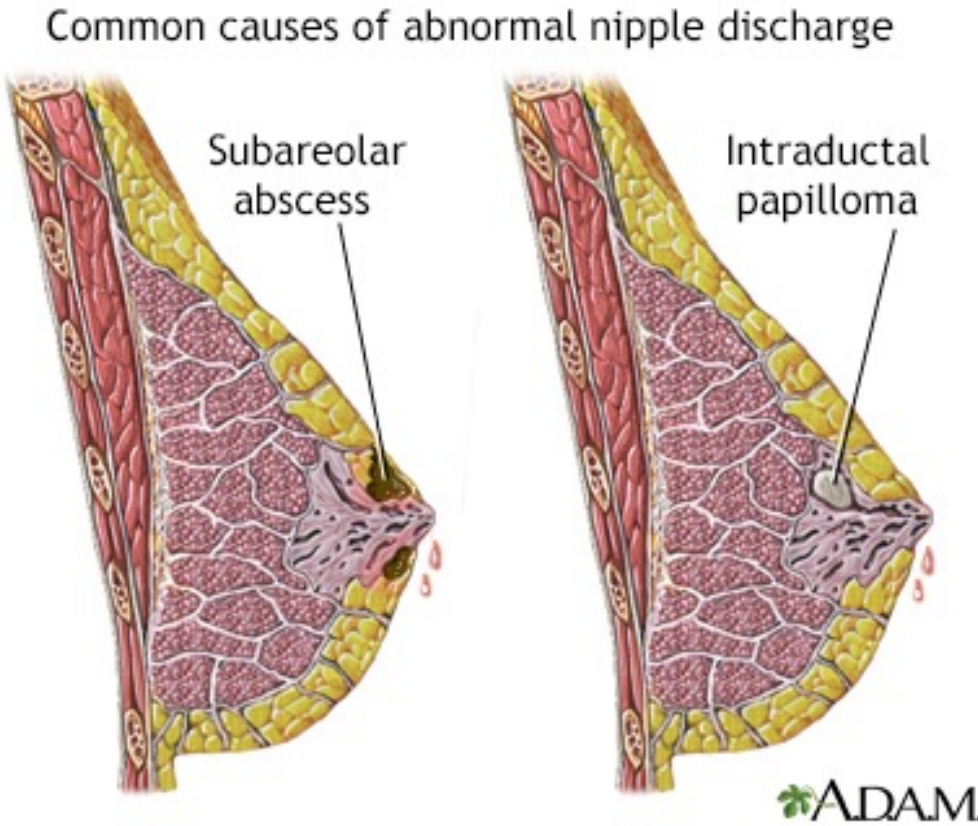
Intraductal papilloma

- During examination of the breast it is important to circumferentially put radial pressure on different areas of the areola.
  - helps to identify whether the discharge emanates from a single duct or multiple openings.
  - When the discharge comes from a single duct, the differential diagnosis includes both intraductal papilloma and carcinoma.
- Treatment of intraductal papilloma involves **excisional biopsy** of the involved duct and a small amount of surrounding tissue.
- Careful surveillance at 3- to 4-month intervals is necessary if the papilloma is not surgically excised.
- Women with a solitary papilloma have a twofold increase in subsequent development of breast carcinoma.



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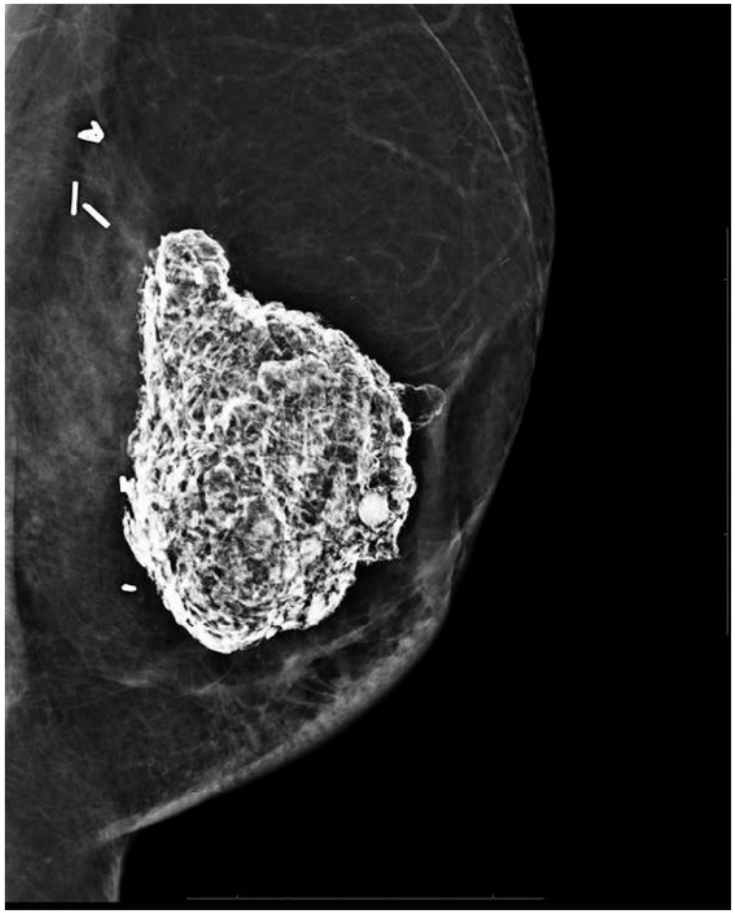
Fat Necrosis

- benign nonsuppurative inflammatory process of adipose tissue
- The incidence of fat necrosis of the breast is estimated to be 0.6%, representing 2.75% of all breast lesions.
- most commonly the result of trauma to the breast, or associated with radiotherapy, anticoagulation (warfarin), infection, or breast procedures (breast aspiration or biopsy, lumpectomy, reduction mammoplasty, implant removal, and breast reconstruction)
- Other rare causes include polyarteritis nodosa, Weber-Christian disease, and granulomatous angiopanniculitis.
- firm, tender, indurated, ill- defined mass that may have coexisting ecchymosis, erythema, inflammation, pain, skin retraction or thickening, nipple retraction, and occasionally lymphadenopathy.
- Treatment of fat necrosis is **excisional biopsy.**
- There is no relationship between fat necrosis and the development of cancer



https://www.hindawi.com/journals/rrp/2015/61313

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Breast Carcinoma

- most common malignancy of women
- Earlier detection, combined with improvements in therapy, has resulted in improved survival rates.
- With the advent of chemoprevention in high-risk women, there is an opportunity to alter the natural course of the disease.
- **Breast carcinoma** generally presents in one of two ways: either with clinical symptoms or found on screening evaluation.
- Screening includes examination by a health provider (referred to as *clinical breast examination*) and imaging.
- If no risk factors are noted, woman is said to be at **average or normal risk**, corresponding to the **12% (or 1 in 8) risk** for a woman of developing breast malignancy during her lifetime.

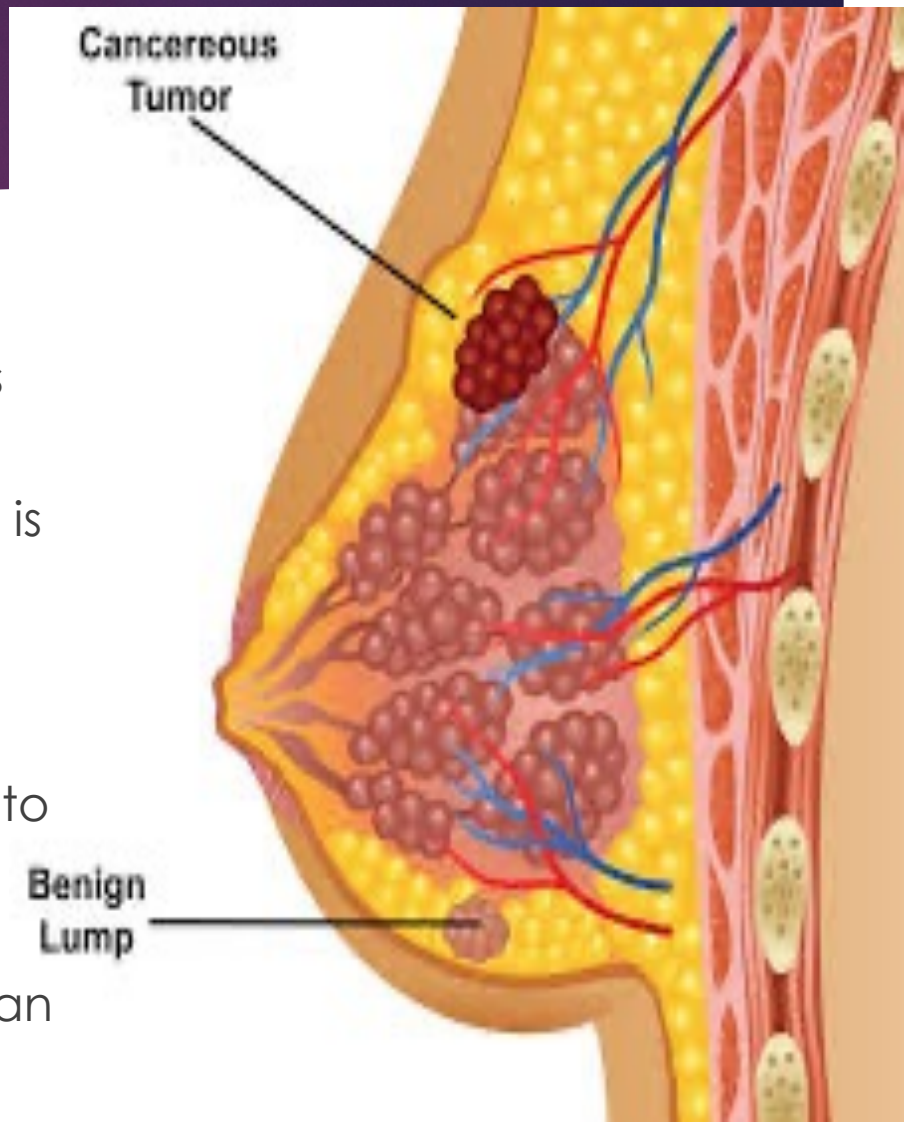

TABLE 15.3 Risk Factors for Breast Cancer

Risk Factor	Qualification	Relative Risk
Age	≤49 y 50-59 y Age 60-69 y ≥70 y	2.0 2.3 3.5 6.7
Geographic	Common in Western countries	
Age at menarche	>14 y (low risk) vs. <12 y	1.5
Age at first full-term pregnancy	<20 y (low risk) vs. >30 y	1.9-3.5
Late menopause	<45 y (low risk) vs. >55 y (high risk)	2.0
Hormone replacement therapy	No use vs. current	1.2
Contraceptive pill use	None vs. past or current use	1.07-1.2
Alcohol use	None vs. 2-5 drinks/day	1.4
Postmenopausal weight gain	Women with a higher BMI	1.1 per 5 BMI units
Bone density	Lowest vs. highest quartile	2.7-3.5
Nightshift work	Exposed to nightshift work	1.48
Smoking	History of smoking	1.10*
Benign breast disease	None vs. positive biopsy result	1.7
Breast density (as measured by mammography)	0% vs. ≥75%	1.8-6.0
Hyperplasia with atypia	None vs. positive biopsy result	3.7
Multiple relatives, not first degree, with breast cancer		
One first-degree relative with breast cancer (mother or sister)	None vs. yes	2.6
Two or more first-degree relatives	Increased risk if the cancers are pre-menopausal	
Deleterious *BRCA1/BRCA2* genes	Negative vs. positive	2.0-7.0
Mantle radiation for treatment of malignancy	Very high risk, which increases with age	

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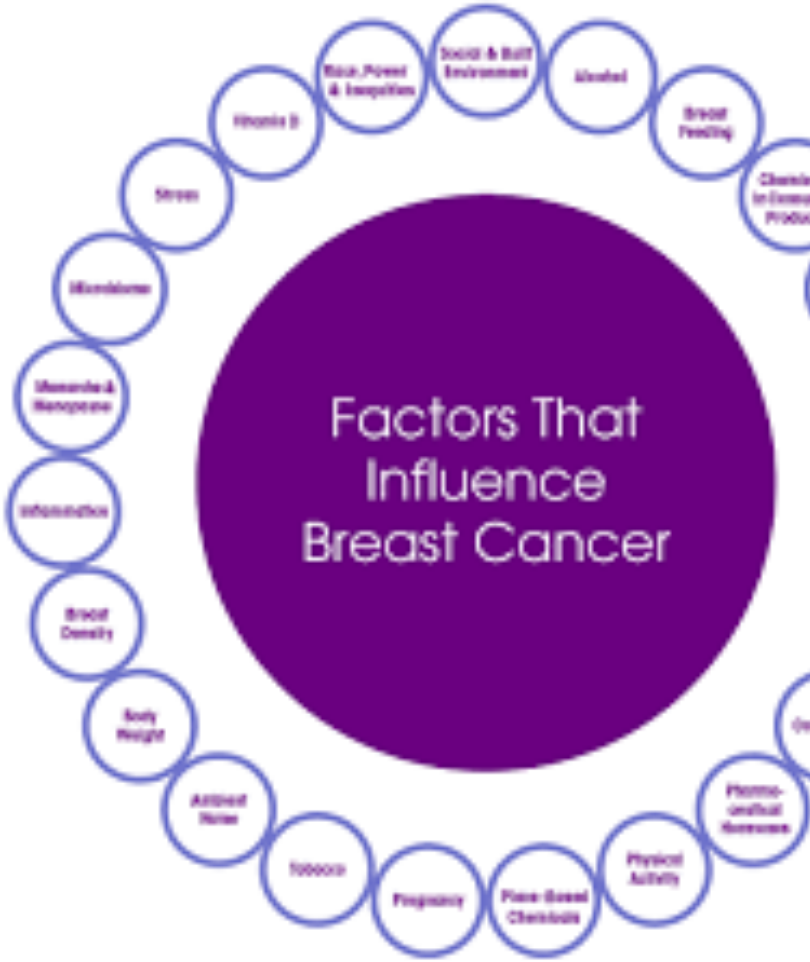
Breast cancer: risk factors

- Age remains the strongest risk factor for developing breast cancer.
- Estrogen-related exposures:
  - **Nulliparous women** are at an increased risk of breast cancer compared with parous women (but the protective effect of pregnancy is not noted until 10 years after delivery)
  - **Age at first pregnancy**: women who delivered their first child at age 20, 25, or 35 years had a cumulative incidence of breast cancer (up to age 70) that was 20% lower, 10% lower, and 5% higher, respectively
  - **Early age at menarche**: women with menarche at or after age 15 years of age are were less likely to develop ER-positive breast cancer compared with those with menarche before the age of 13 years.



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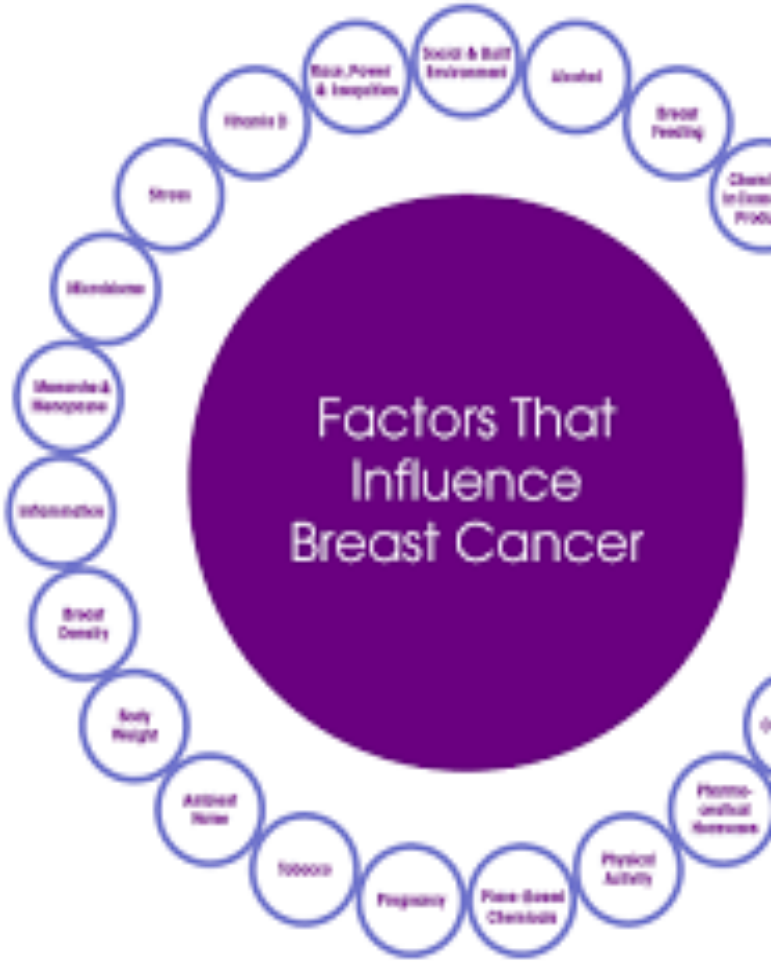
Breast cancer: risk factors

- **Breastfeeding:** relative risk of breast cancer decreases by 4.3% per 12 months of breastfeeding.
- **Hormone replacement**— use of combined estrogen and progesterone is an established risk factor for breast cancer.
  - Data from the Women's Health Initiative (WHI) showed that compared with the placebo group, combined hormone therapy increases the risk of breast cancer by **24%.**
- **Lifestyle and dietary factors:**
  - Obese women are at a higher risk
  - Alcohol consumption
  - low levels of vitamin D and calcium



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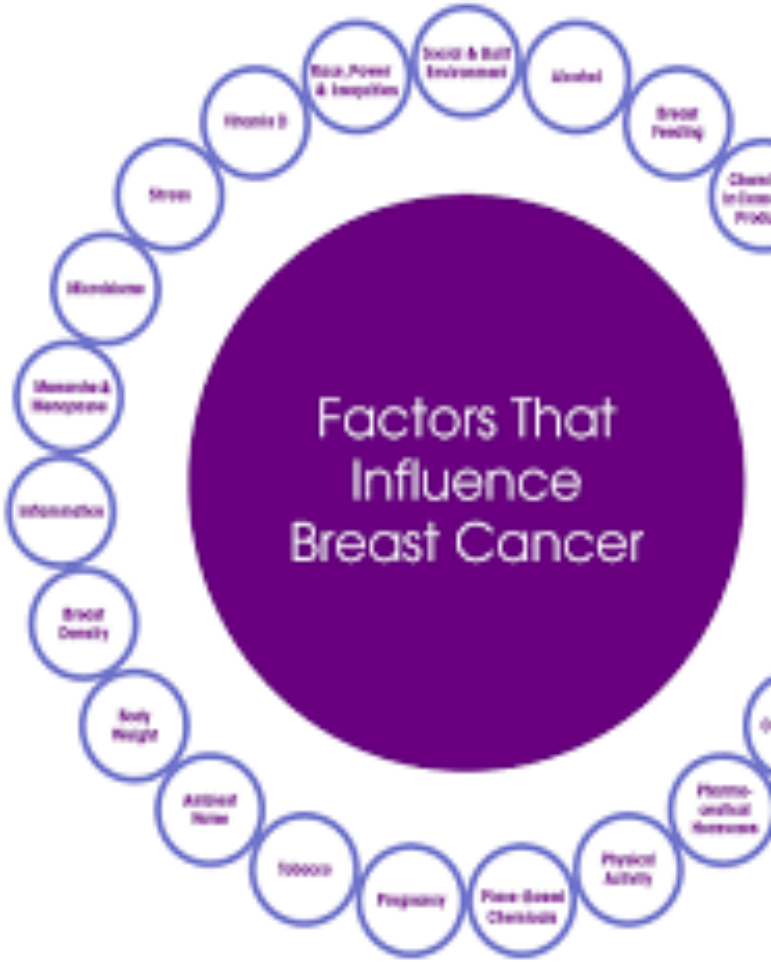
Breast cancer: risk factors

- **History of breast cancer/ hyperplasia:**
  - incidence of invasive contralateral breast cancer in women with a history of primary breast cancer was 4% during a 7.5-year follow-up period
  - hyperplasia with atypia increases the risk by 4 to 6x. The cumulative incidence of breast cancer among women with atypical hyperplasia approaches 30% at 25 years of follow-up.
- **Breast density:** women with dense breasts, as defined by more fibrous tissue, have a **relative risk of 4.7** (CI, 2 to 6.2) for breast cancer



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Breast cancer: inherited and familial risks

- There are at least four autosomal dominant breast cancer syndromes:
  - The most common are the mutations in the breast cancer susceptibility genes, ***BRCA1* and *BRCA2*.**
  - Less common are **Li-Fraumeni syndrome**, associated with ***P53* gene mutations**, and **Cowden syndrome**, associated with ***PTEN*** gene mutations
- Women with genetic syndromes tend to develop breast cancer at earlier ages and tend to have more aggressive tumors and higher prevalence of bilateral disease.
- **Hereditary breast and ovarian cancer (HBOC) syndrome** is the most common cause of hereditary breast and ovarian cancers.
  - This syndrome is associated with *BRCA1* and *BRCA2* mutations.
  - This genomic instability of women with *BRCA* mutations causes them to be more susceptible to further mutations of DNA, which subsequently leads to malignant transformation of breast and ovarian epithelial cells.

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TABLE 15.6 Major Inherited Gene Mutation Syndromes Associated with Breast Cancer

Syndrome	Gene	Incidence	Lifetime Breast Cancer Risk	Associated Cancer Risks
BRCA1	*BRCA1*	1/500-1/1000	85%	Ovary and pancreas
BRCA2	*BRCA2*	Unclear	85%	Ovary and pancreas
Cowden	*PTEN*	1/100,000-1/200,000	50%	Thyroid and endometrium
Li-Fraumeni	*TP53*	1/20,000	90%	Sarcoma, brain, and leukemia

Other syndromes, including Peutz-Jeghers syndrome, ataxia telangiectasia, *CHEK2* gene mutation, and Fanconi syndrome, have much smaller lifetime risks with poorer penetrance.

Breast cancer: inherited and familial risks

- ***BRCA1 gene:***
  - mapped at 17q21; involved in repair of double-strand DNA breaks and control of cell cycle checkpoints.
  - Women with a *BRCA1* mutation have a risk of breast cancer of approximately 55% to 70% to age 70 and an average lifetime risk of ovarian cancer approaching **40%**.
- ***BRCA2 gene***
  - mapped to chromosome 13q12
  - Women with a *BRCA2* gene mutation have a 45% to 70% risk of breast cancer to age 70 and a **15% to 20**% lifetime risk of ovarian cancer.
  - *BRCA2* mutations are also associated with male breast cancers, conferring a 5% to 10% risk for a man who has inherited the mutation.
- The risk of a contralateral breast cancer in women with a deleterious *BRCA1* or *BRCA2* mutation has been estimated to range from 10% to 65%..

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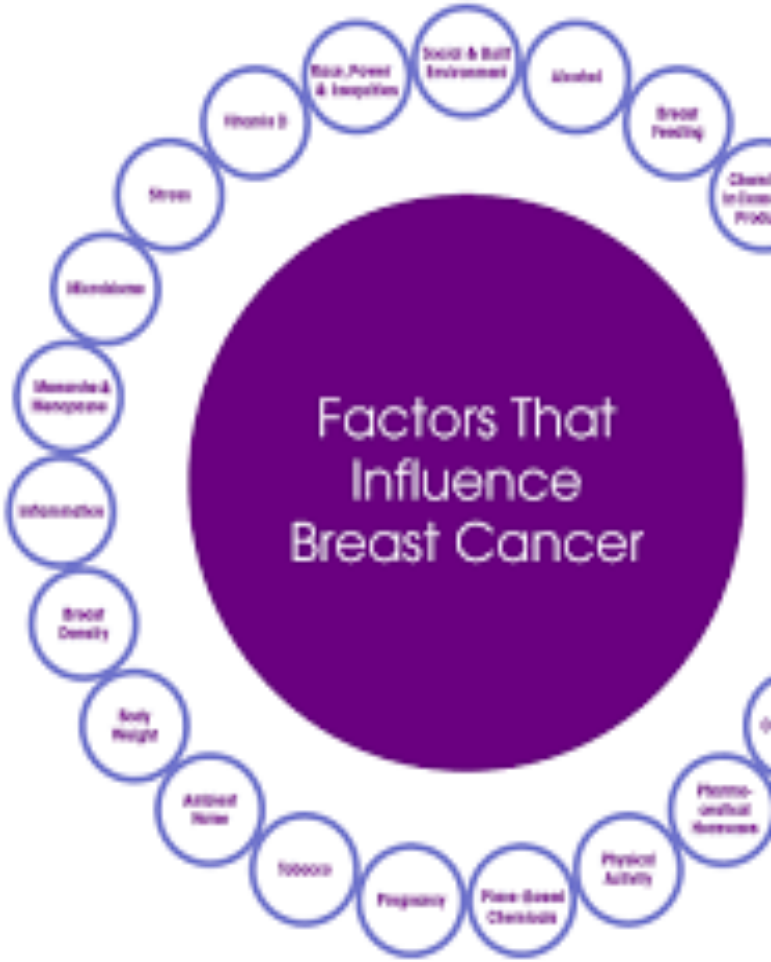
Breast cancer: inherited and familial risks

- Women with a family history of breast cancer have an increased risk of developing breast cancer.
- Approximately 15% of breast cancers are related to familial risk.
- The risk for breast cancer is significantly affected by the number of female first-degree relatives with cancer.
- risk increases for a woman the more relatives she has with breast cancer.
- The risk is threefold higher if the first-degree relative was diagnosed before age 30.



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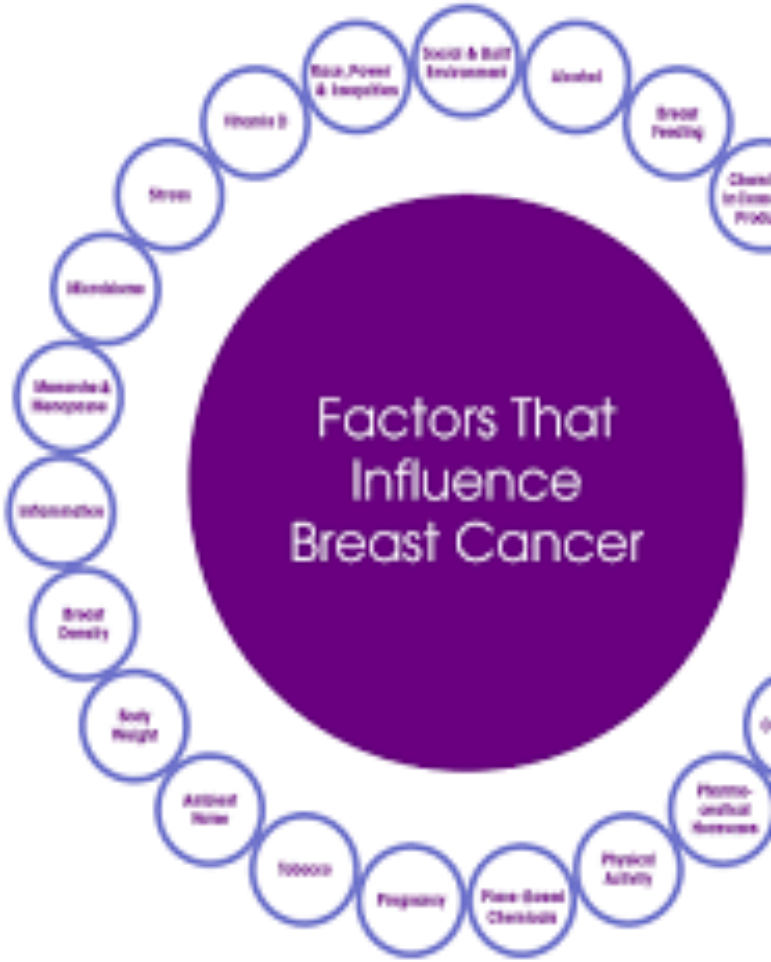
Breast cancer: radiation

- The risk of developing breast carcinoma is consistent with a linear dose-response relationship.
- This was first recognized in Japanese women who survived the atomic bombs dropped during World War II, with a high incidence of women exposed as teenagers developing breast carcinoma in their 30s.
- Other historical examples of ionizing radiation–induced breast cancer include women with a history of radiation treatments for postpartum mastitis, irradiation of the thymus in infancy, or multiple fluoroscopic examinations during treatment for tuberculosis.
- Currently, women at highest risk from radiation exposure are those who were treated with ***radiation for childhood malignancies, in particular Hodgkin lymphoma.***



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Risk assessment and prevention

- risk increases with age and with changes in both personal and family history.
- The chance of developing a malignancy can be calculated based on her risk profile.
- This profile will influence the recommendations for both her screening and for preventive measures such as chemoprevention.
- individualized counseling is the most effective approach to evaluating risk.
- Risk factors can be stratified into
  - major factors that increase relative risk greater than two times normal
  - minor factors

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Two or more first-degree relatives	Increased risk if the cancers are pre-menopausal	
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Mantle radiation for treatment of malignancy	Very high risk, which increases with age	

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Risk assessment and prevention

- A women's personal risk of developing breast cancer is divided into three levels:
  - **Average:** average risk have a personal risk of about 12% of developing breast cancer, the risk of the general population.
  - **Moderate:** personal risks from 12% to 15% of developing breast malignancy during their lifetime and have one or more minor risk factors
  - **High**: have greater than a 15% personal risk of developing breast cancer, usually from a major risk factor.
    - women have a personal risk greater than 25%, which includes women with a *BRCA* mutation and those who have had mantle radiation.
    - They are often referred to breast specialists for ongoing evaluation.

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Risk assessment and prevention

TABLE 15.7 Risk Levels for the Development of Breast Cancer

Level	Lifetime Risk for Breast Cancer	Recommendations for Screening
Average	12%	Yearly exams and mammograms beginning at age 40
Moderate	12%-15%	Yearly exams and mammography beginning at age 40
High	15%-20%	Yearly exams and mammography beginning at age 40; offer chemoprevention
Very high risk	>20%	Exams every 6 months; mammography alternating with MRI should be started on an individualized basis depending on the risk factor (e.g., for women with mantle radiation, imaging should begin at age 30 or 8 years after radiation is finished); offer chemoprevention

MRI, Magnetic resonance imaging.

Risk assessment and prevention

- Several models have been empirically developed to estimate a woman's risk of breast cancer.
- The most widely available and accepted tool is the Breast Cancer Risk Assessment Tool (BCRAT) developed by Dr. Mitchell Gail, which is commonly known as the **Gail model**.
  - designed for women who have never had a diagnosis of breast cancer, ductal carcinoma in situ (DCIS), or lobular carcinoma in situ (LCIS) and who do not have a strong family history suggesting an inherited gene mutation.
  - not applicable to women with more than two first-degree relatives with breast cancer and does not consider more distant relatives, the age at which relatives developed breast cancer, or a family history of ovarian cancer.
  - not useful for women with a strong family history of breast cancer on the paternal side.
  - does not estimate the risk of carrying a deleterious *BRCA1* or *BRCA2* gene.

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Risk assessment and prevention

- The **Clauss model**, developed by Elizabeth Clauss in 1994, uses data from the Cancer and Steroid Hormone Study.
  - uses first- and second-degree relatives, both maternal and paternal, to calculate risk
  - does not use risk factors beyond family history and also is not as robust in woman who are not white.
  - provides the lifetime risks for a woman over any given decade of her life.
- **Computerized risk prediction models** have been developed to assess not only the risk of breast cancer but also the risk of carrying a deleterious *BRCA1* or *BRCA2* genes
  - BRCAPRO model
  - International Breast Cancer Intervention Study or Tyrer-Cuzick model
  - BOADICEA model

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Gail Model	Tyrer-Cuzick Model
Age (35 or older)	Age
Race/ethnicity (white, black, Hispanic, Asian American [Chinese, Japanese, Filipino, Hawaiian, other], unknown)	Ashkenazi Jewish descent
Age at menarche	Age at menarche
Age at first live birth	Age at first live birth
	Menopausal status
	Age at menopause
	Use of hormone replacement therapy
	Body mass index
Number of benign breast biopsies	
Benign breast biopsy with atypical hyperplasia (excludes LCIS, DCIS, or invasive breast cancer)	Benign breast biopsy including hyperplasia with or without atypia and LCIS
Number of first-degree relatives with breast cancer	Number of first-, second-, and third-degree relatives with breast or ovarian cancer, bilateral breast cancer, and age at diagnosis
	BRCA mutation status

Abbreviations: DCIS, ductal carcinoma in situ; LCIS, lobular carcinoma in situ.

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TABLE 15.9 Professional Society Recommendations for Screening Mammography

Organization	Age to Initiate Mammography	Age to Conclude Mammography	Interval between Screenings
American Academy of Family Physicians	Routinely at ≥50 y Screening before age 50 should be individualized	Screening recommended to age 74 y Evidence insufficient for age ≥75 y	Not stated for age 40-49 y 2 y for age 50-74 y
American Cancer Society	Routinely at ≥45 y Offered for age 40-45 y	While in good health and is expected to live ≥10 y	1 y for age 45-54 y 2 y for age ≥55 y (with option of 1 y)
American College of Obstetricians and Gynecologists	Offer staring at age 40 Recommend by no later than age 50 if not already initiated	Age 75	1 or 2 y
American College of Physicians	Routinely at ≥50 y 40 y based on benefits, harms, preferences, and risk profile	When life expectancy is ≤10 y	2 y
American College of Radiology	40 y	No upper age limit	1 y for all ages
American Society of Breast Surgeons	40 y	When life expectancy is <10 y	1 y for all ages
National Comprehensive Cancer Network	40 y	When severe comorbidities limit life expectancy to ≤10 y	1 y for all ages
U.S. Preventive Services Task Force, 2017	Routinely at ≥50 y Screening before age 50 should be individualized	Screening recommended to age 74 y Evidence insufficient for age ≥75 y	2 y for age 50-74 y

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TABLE 15.8 Known Genetic Mutations in Breast Cancer and their Management

Genetic Mutation	Breast Cancer Risk	Management
ATM	Increased by 15–40%	Annual mammography starting at age 40 with consideration for breast tomosynthesis/MRI
BARD1	Limited evidence for increased risk but stronger for triple negative breast Ca.	Annual mammography starting at age 40 with consideration for breast tomosynthesis/MRI
BRCA1 *BRCA2*	Both carry increased absolute risk greater than 60%	Breast awareness starting at age 18 Clinical breast exam, every 6–12 months starting at age 25 years. Breast screening: Age 25–29 years: annual breast MRI screening with contrast or mammogram with consideration of tomosynthesis, only if MRI is unavailable or individualized based on family history if a breast cancer diagnosis before age 30 is present. Age 30–75 years: annual mammogram with consideration of tomosynthesis and breast MRI screening with contrast. Age >75 years: management should be individualized Consider risk-reducing mastectomy
BRIP1	Potential increase in risk	Management based on family history
CDH1	Increased absolute risk 41–60%	Annual mammogram with consideration of tomosynthesis or breast MRI with contrast starting at age 30
CHECK2	Increased absolute risk 15–40%	Annual mammography starting at age 40 with consideration for breast tomosynthesis/MRI
MSH2 *MLH1* *MSH6* *PMS2* *EPCAM*	Limited evidence of increased risk, absolute risk is <15%	Management based on family history

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CHEMOPROPHYLAXIS AND CHEMOTHERAPEUTIC RISK REDUCTION

- Endocrine therapy may reduce the risk of invasive or in situ breast cancers.
- women who may benefit from endocrine therapy:
  - age older than 60 years,
  - age older than 35 years with a history of lobular carcinoma in situ, ductal carcinoma in situ or atypical proliferative lesion of the breast (atypical ductal or lobular hyperplasia)
  - women 35 to 59 years with a Gail model risk of breast cancer 1.66% or more over 5 years
  - women with known *BRCA1* or *BRCA2* mutations who do not undergo prophylactic mastectomy.

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Table Key Pharmacologic Interventions for Breast Cancer Risk Reduction

Drug	Dose	Recommendations	Not recommended
Tamoxifen	20 mg daily for 5 yrs	Should be discussed as an option to reduce the risk of invasive BC, specifically ER-positive, in any woman aged ≥35 yrs at increased BC risk or with LCIS	Not for women with a history of DVT, pulmonary embolus, stroke, or TIA; during prolonged immobilization; or in women who are or may become pregnant, or are nursing mothers; not for use in combination with hormone therapy
Raloxifene	60 mg daily for 5 yrs	Should be discussed as an option to reduce the risk of invasive BC, specifically ER-positive, in postmenopausal women aged ≥35 yrs at increased BC risk or with LCIS	Not for BC risk reduction in premenopausal women, or for women with a history of DVT, pulmonary embolus, stroke, or TIA, or during prolonged immobilization
Exemestane	25 mg daily for 5 yrs	Discuss as an alternative to tamoxifen or raloxifene to reduce the risk of invasive BC, specifically ER-positive, in postmenopausal women aged ≥35 yrs at increased BC risk or with LCIS or atypical hyperplasia	Not for BC risk reduction in premenopausal women

CHEMOPROPHYLAXIS AND CHEMOTHERAPEUTIC RISK REDUCTION

- Tamoxifen and raloxifene, both **selective estrogen receptor modulators**, are proven options that can decrease the risk of breast cancer in high-risk women
- Tamoxifen blocks the effects of endogenous estrogens in both the normal breast and the one with breast cancer.
- USPSTF data showed a **reduction in the risk of invasive breast cancer** (RR, 0.70; 95% CI, 0.59 to 0.82), primarily noted in ER-positive breast cancer.

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Detection and diagnosis

- The classic sign of a breast carcinoma is a solitary, solid, immovable, dominant breast mass with irregular borders.
- Axillary adenopathy is a potential sign of more advanced locoregional disease.
- Nipple discharge is an even less common symptom of breast cancer.
- Findings suggestive of inflammatory breast cancer include erythema, skin thickening, and skin edema causing the appearance of an orange peel (peau d'orange).
- With increased screening, many cancers and in situ lesions are found before any symptoms are experienced.

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Detection and diagnosis

- The kinetics of growth in breast carcinoma is the basis for the recommendations for screening and detection:
  - The average breast mass doubles in volume every 100 days, and the diameter doubles every 300 days.
  - A breast carcinoma grows for 6 to 8 years before reaching a diameter of 1 cm, after which it doubles in less than another year.
  - The mean diameter of a breast mass discovered by women who perform BSE at monthly intervals is 2 cm.

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Detection and diagnosis

- Three potential screening modalities include **BSE, CBE, and imaging with mammography.** BSE has the major advantages of no cost to the patient and convenience.
- BUT studies have failed to show a beneficial effect of regular BSE in rates of breast cancer diagnosis, mortality, or tumor stage or size → BSE is not recommended as a screening tool.
- CBE and mammography are complementary procedures, and therefore the effectiveness of CBE in screening by itself is difficult to assess.

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Detection and diagnosis

- As part of the screening process, the sensitivity of CBE was estimated to be 54% and specificity 94%
- **Mammography is the primary choice in screening for breast cancer**.
- Ultrasound is used as an adjunct to mammography for diagnostic follow-up of an abnormality seen on screening mammography.
- Additional imaging techniques include MRI and tomosynthesis.

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Detection and diagnosis: Breast examination

- **SBE (self breast examination)**
  - In premenopausal women, a few days immediately after a menstrual period are the best time to detect changes in normal lumps or texture of the breasts.
  - Postmenopausal women or women who have had a hysterectomy can perform BSE on the same calendar days each month if they choose.
  - The examination is best done in both supine and up- right positions using the finger pads of the three middle fingers. Three different levels of pressure (light, medium, and firm) are used to examine the breast.

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Detection and diagnosis: Breast examination

- **CBE (clinical breast examination)**
  - ACOG recommends CBE for everyone every 3 years from age 20 to 39 and annually thereafter.
  - complete breast examination involves putting the patient in both sitting and supine position;
  - inspecting and palpating all quadrants of the breasts, nipples, axilla, supraclavicular areas, and adjacent chest wall.
  - Palpation should use the pads of the first three fingers placed together, exerting firm but gentle pressure.

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Detection and diagnosis: Mammography

- Screening mammography is the detection of cancer before it is clinically palpable and less likely to have progressed to the regional nodes or distant metastases.
- Mammography may identify cancer up to 4 years before it comes clinically evident.
- The 5-year survival rate for women whose breast cancer is believed to be localized to the breast with negative axillary nodes is approximately 99% versus 84% with regionalized disease (when axillary nodes are involved).

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Detection and diagnosis: Mammography

- Screening mammography is the primary imaging technique for breast cancer detection and the only breast imaging method found to reduce breast cancer–related mortality.
- In contrast to screening mammography, diagnostic mammography is performed when women have complaints such as breast pain, a palpable lump (or mass), nipple discharge
- Once a woman has developed carcinoma of one breast, her risk is approximately 1% per year of developing cancer in the other breast.

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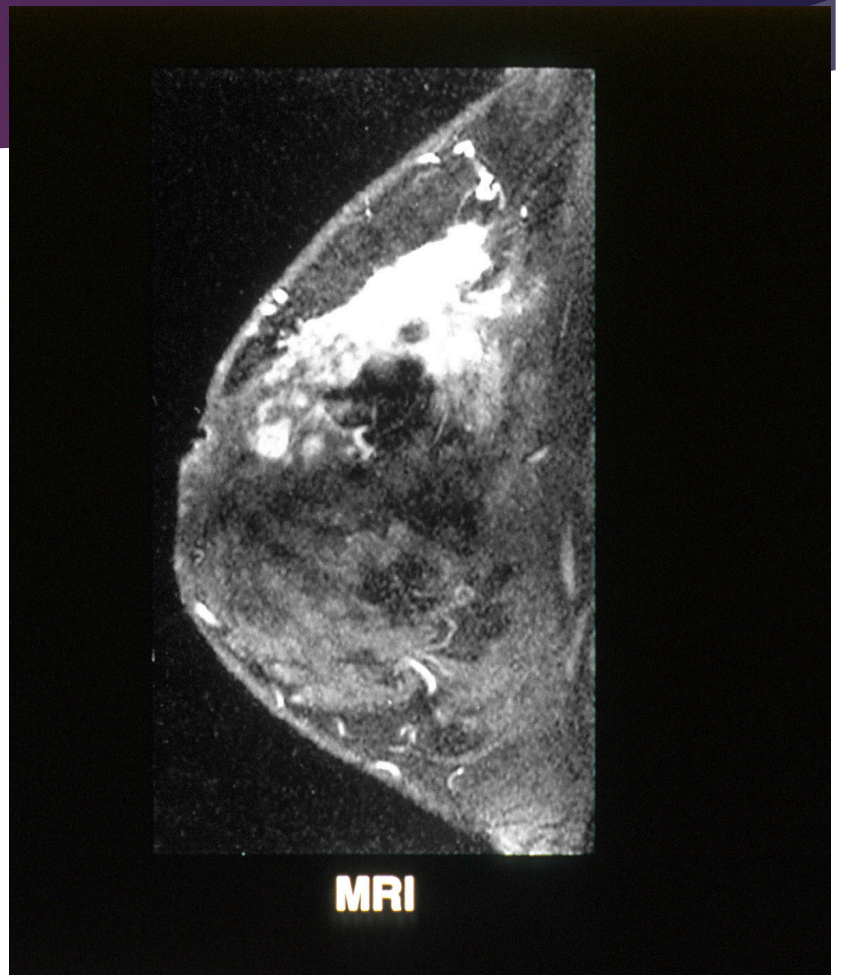
BI-RAD class	Description	Probability of malignancy	Follow-up
0	Needs additional	N/A	Additional imaging evaluation +/– prior imaging for comparison
1	Negative	0	Routine mammography screening
2	Benign	0	Routine mammography screening
3	Probably Benign	< 2%	Short interval followup or continued surveillance mammography
4 4A 4B 4C	Suspicious Low suspicion Moderate suspicion High suspicion	>2 % but < 95% >2 % but ≤10% >10 % but ≤50% >50 % but < 95%	Biopsy/Tissue diagnosis
5	Highly Suspicious	≥ 95%	Biopsy/Tissue diagnosis
6	Known/Proven Malignancy	N/A	Surgery when appropriate
BI-RADS Breast Imaging Reporting and Data Systems			

Fig. 15.16 BI-RAD (Breast Imaging Reporting and Data Systems) classification of mammographic lesions. (From Pazdur R, Coia LR, Hoskins WJ, Wagman LD, eds. *Cancer Management: A Multidisciplinary Approach.* 4th ed. Melville, NY: Cligott Publishing Group; 2006:143.)

Detection and diagnosis: MRI

- does not use ionizing radiation.
- Malignant tumors with increased tumor angiogenesis are differentiated from benign tumors based on the rapid uptake and release of contrast
- reported sensitivity of MRI ranges from 71% to 100%.
- especially useful in women with dense fibroglandular breasts and implants.
- Women with a 20% or higher lifetime risk of breast cancer should be scheduled for annual MRI and mammogram screening, usually alternating every 6 months.



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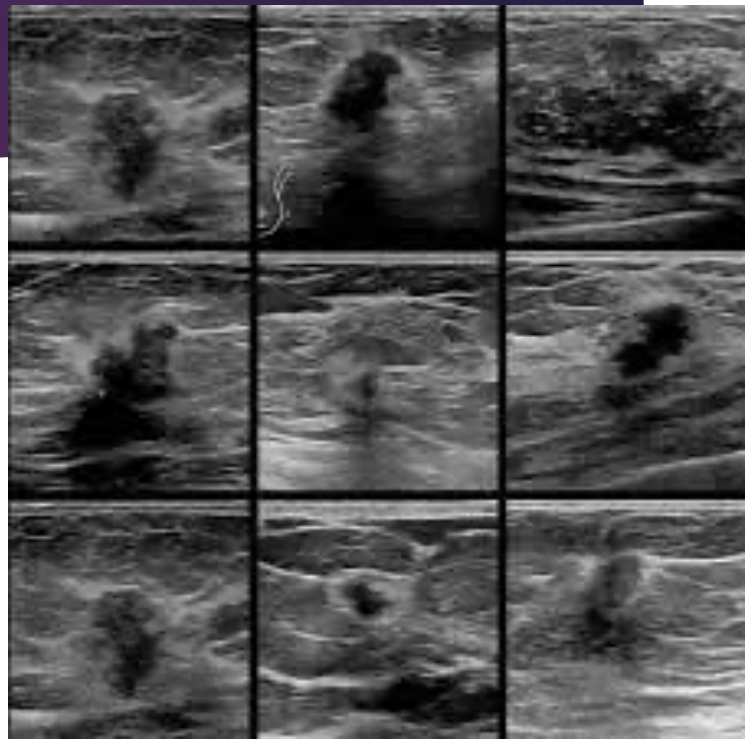
Detection and diagnosis: Ultrasound

- often used in the diagnostic follow-up of an abnormal screening mammogram.
- It should **not be used by itself as a screening tool** in average risk women; ultrasound **should not be used as a sole imaging technique for breast disease.**
- Useful for:
  - women with dense breasts may benefit from the addition of ultrasound to screening mammography.
  - differentiating cystic from solid masses.
  - examining the axilla and determining lymph node status.
  - guide needle aspiration or direct core needle biopsy.
  - localize tumors intraoperatively without a guidewire with excellent success rates
  - pregnant women with focal breast symptoms or findings



https://radiologyassistant.nl/breast/ultrasound/ultrasound-of-the-breast

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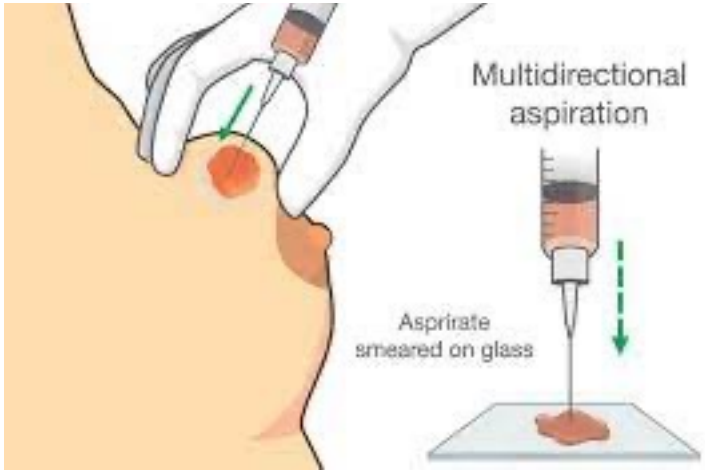
Evaluation of breast mass

https://medscope.umaryland.edu/apps/Interactive%20Dissector/Clinical_Procedure
ClinicalProcedure_BreastExam.html

- The evaluation of a breast mass includes a triple test:
  - clinical examination
  - imaging,
  - tissue sampling.
- This triple test may be an alternative to excisional biopsy.
- If triple test confirm the same benign process, the patient can be advised regular monitoring of the mass.
- However, if any of triple test indicate cancer, a biopsy should be performed.



https://www.gleneagles.com.sg/health-plus/article/guide-bre

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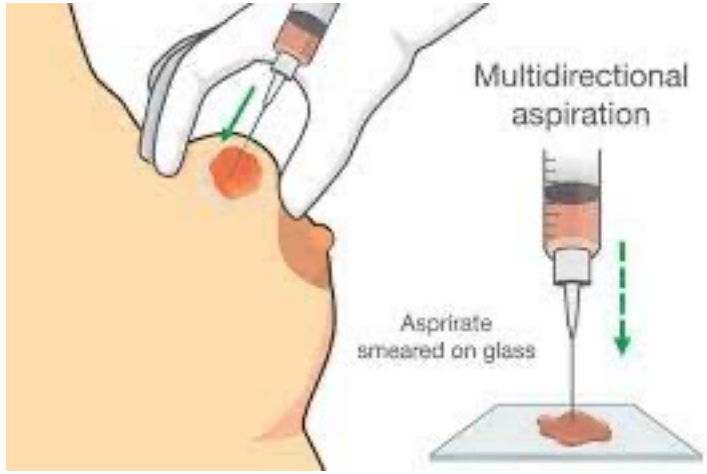
Breast tissue sampling: Fine Needle Aspiration

- least invasive first-line sampling technique: office-based procedure.
- appropriate for new, well- circumscribed, usually tender masses that are thought to be simple (not complex) cysts, and evaluation of ipsilateral axillary lymph nodes.
- If the lesion is not palpable, ultrasound guidance may be used to localize the lesion.
- A small (18- to 21-gauge) needle is used when performing an FNA.
- The breast mass is secured with one hand, and the other hand introduces the needle attached to a 10- or 20-mL syringe into the mass.
- A biopsy should be performed on cysts that recur within 2 weeks or that necessitate more than one repeat aspiration.



https://www.gleneagles.com.sg/health-plus/article/guide-breast-biopsy

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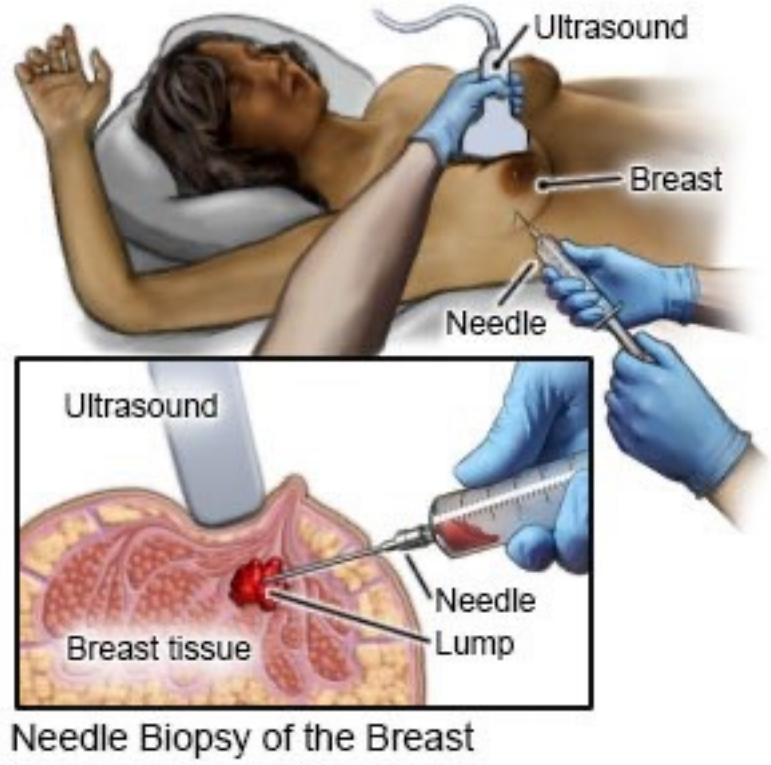
Breast tissue sampling: Core Needle Biopsy and Excisional biopsy

- retrieves more tissue than FNA, permitting the differentiation between invasive versus in situ cancer.
- provides adequate tissue for more definitive histologic assessment, including tumor grade angiolymphatic invasion, hormone receptor status, genomic analysis or cancer profiling.
- Excisional biopsy should be reserved for certain situations when a diagnosis is not established using the diagnostic triad.
- Core needle biopsy is usually performed using a **larger needle (9 to 14 gauge) than FNA.**
- Core needle biopsy may be performed with ultrasound, mammographic, or MRI guidance.



Needle Biopsy of the Breast

https://www.drugs.com/cg/core-needle-breast-biopsy.h

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Classification

TABLE 15.11 Simplified Classification of Breast Carcinoma Based on Histology

Type of Carcinoma	Percentage of All Cases Diagnosed
Ductal carcinoma	
In situ	5
Infiltrating	70
Infiltrating with uniform histologic appearance	10
Medullary, colloid, comedo, tubular, papillary	
Lobular carcinoma	
In situ	3
Infiltrating	9
Inflammatory carcinoma	2
Paget disease	1

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Classification of breast malignancies: Ductal carcinoma in situ (DCIS)

- noninvasive lesion; cellular abnormalities are limited by the basement membrane of the breast ducts.
- not usually detectable by palpation.
- Diagnosis is confirmed with a core needle biopsy
- The goal of treatment is to prevent the development of invasive cancer.
- Treatment approaches include surgery, radiation therapy, and adjuvant endocrine therapy.
- Mastectomy is curative for more than 98% of DCIS patients.
- Breast-conserving surgery (lumpectomy, partial mastectomy) followed by radiation therapy has shown equivalent survival compared with mastectomy.
- Chemoprevention with either a SERM or aromatase inhibitor is recommended for women with ER-positive DCIS who have undergone breast conservation therapy to reduce the risk of developing additional invasive or noninvasive breast cancers.

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Classification of breast malignancies: Lobular carcinoma in situ (LCIS)

- **A** noninvasive lesion arising from the lobules and terminal ducts of the breast.
- women with LCIS are at an increased risk of developing breast cancer.
- LCIS has a greater tendency to be bilateral and multifocal.
- NCCN guidelines recommend re-excision in cases where LCIS is diagnosed by core needle biopsy.
- In cases in which LCIS is diagnosed on an excisional biopsy, obtaining histologically negative margins is not mandatory because LCIS is often multicentric.
- Breast cancer chemoprevention with a SERM or an aromatase inhibitor may be indicated for women diagnosed with LCIS.

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Classification of breast malignancies: Infiltrating Lobular carcinoma

- constitute approximately 10% to 15% of invasive lesions
- second most common type of invasive breast cancer.
- characterized by the uniformity of the small, round neoplastic cells that infiltrate the stroma and adipose tissue in a single-file fashion
- more commonly ER positive.
- excised breast tissue often has a normal consistency and no mass lesion is grossly evident.

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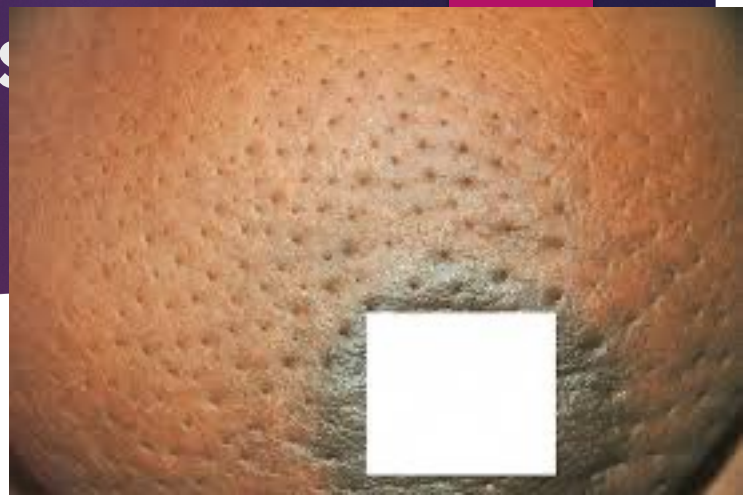
Classification of breast malignancies: Inflammatory Breast Cancer

- rare and accounts for approximately 1% to 5% of breast cancers.
- recognized clinically as a rapidly growing malignant carcinoma with highly angiogenic and angioinvasive characteristics.
- Because of its aggressive features, most inflammatory breast cancers are diagnosed as either stage III or IV, and most are invasive ductal carcinomas.
- Infiltration of malignant cells into the dermal lymphatics of the skin produces a clinical picture that appears like a skin infection (hence called "inflammatory")
- The breast is firm, warm, and enlarged with thickened, erythematous, peau d'orange skin



https://www.thestkittsnevisobserver.com/seek-medattention-observe-abnormality-around-breasts/

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Inflammatory Breast Cancer

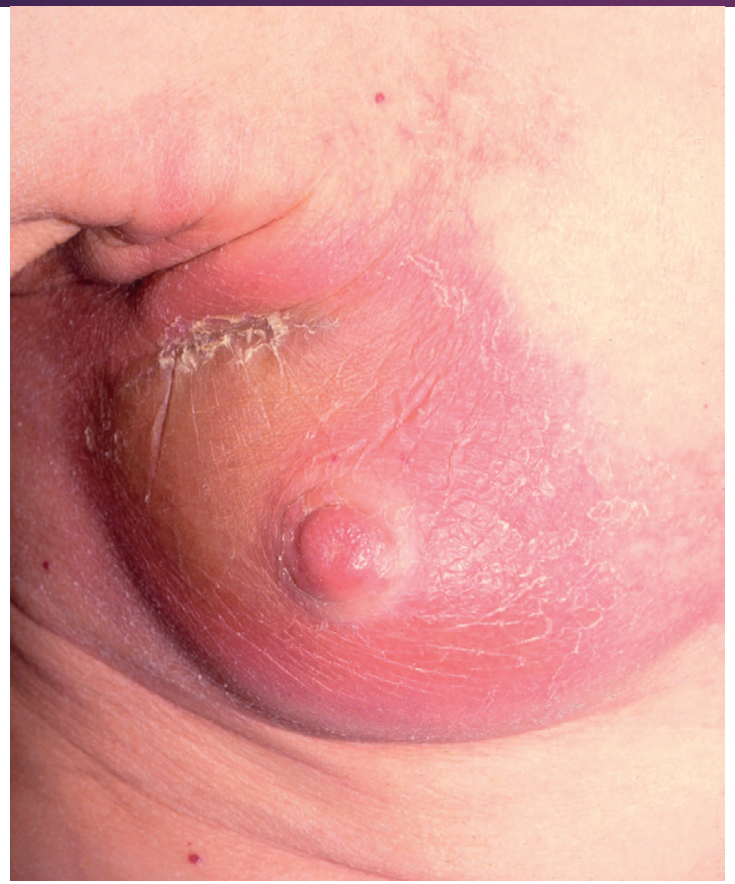

Fig. 15.21 Inflammatory breast carcinoma—cellulitic-appearing plaque. (From Marks J, Miller J. *Lookingbill and Marks' Principles of Dermatology.* 4th ed. Philadelphia: Saunders; 2006.)

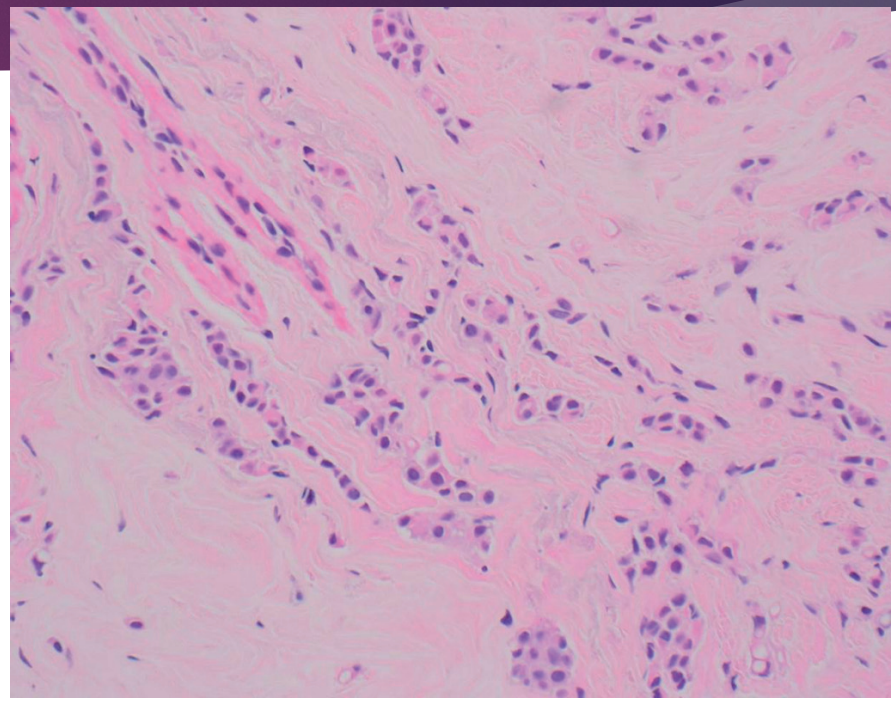

Fig. 15.20 Infiltrating lobular carcinoma of the breast. Neoplastic cells infiltrating the stroma and adipose tissue in a single-file fashion. (Courtesy Panagiotis J. Tsakalakis, MD.)

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Classification of breast malignancies: Paget Disease

- rare, constituting 1% to 3% of new breast carcinomas
- This lesion has an innocent appearance and looks like eczema or dermatitis of the nipple.
- The clinical picture of a scaly, raw, or ulcerated lesion of the nipple and areola is usually the result of an infiltrating ductal carcinoma that invades the epidermis.
- The majority of patients (97%) also have an underlying cancer, either DCIS or invasive cancer, somewhere else in the breast.
- Punch biopsy or a full-thickness wedge biopsy of the nipple is used for diagnosis.
- Intraepithelial adenocarcinoma cells (Paget cells) are noted on histologic examination, presenting either singly or in small groups within the epidermis of the nipple.

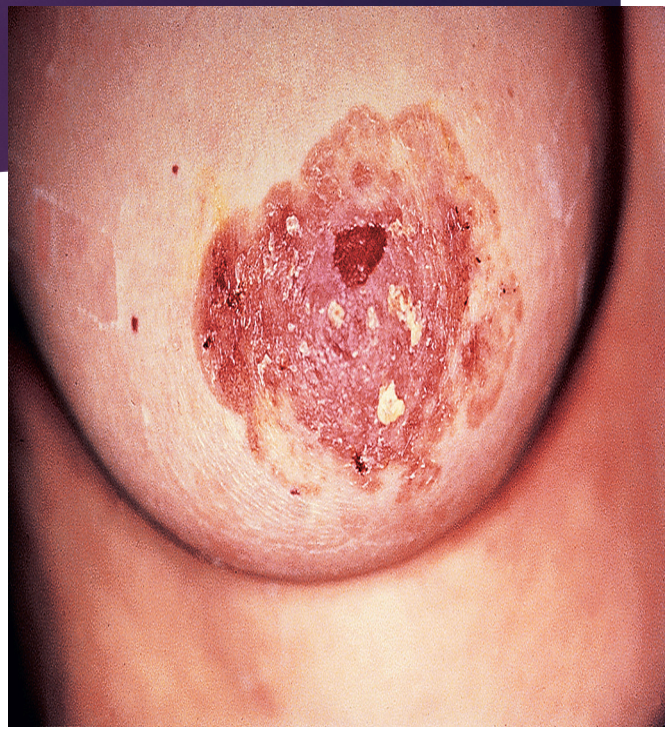

Fig. 15.22 Paget disease of the breast. Note the erythematous plaques around the nipple. (From Callen JP. Dermatologic signs of systemic disease. In: Bolognia JL, Jorizzo JL, Rapini RP, eds. *Dermatology.* Edinburgh: Mosby; 2003:714.)

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Management

- The primary algorithm of treatment is primarily determined by the tumor stage.
- The tumor-node-metastasis (TNM) system is a widely recognized staging system based on both clinical and pathologic criteria
- goal of treatment for stage 0, pure noninvasive carcinomas (LCIS, DCIS), is preventing the development of invasive disease
- In cases of invasive disease, treatment is based on the stage-appropriate guideline for invasive carcinoma.
- The major objectives of treating breast carcinoma are:
  - ✓ control of local disease
  - ✓ treatment or prevention of distant metastases
  - ✓ improved quality of life for women treated for the disease.

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TABLE 15.13 TNM Staging of Breast Cancer

PRIMARY TUMOR (T)	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Tis*	Carcinoma in situ; intraductal carcinoma, lobular carcinoma in situ, or Paget disease of the nipple with no tumor
T1	Tumor is ≤2 cm in greater dimension
T1a	Tumor is ≤0.5 cm in greatest dimension
T1b	Tumor is >0.5 cm but not more than 1 cm in greatest dimension
T1c	Tumor is more than 1 cm but not more than 2 cm in greatest dimension
T2	Tumor is >2 cm but not more than 5 cm in greatest dimension
T3	Tumor is >5 cm in greatest dimension
T4	Tumor of any size with direct extension to chest wall or skin
T4a	Extension to chest wall
T4b	Edema (including peau d'orange) or ulceration of the skin of the breast or satellite skin nodules confined to the same breast
T4c	Both T4a and T4b above
T4d	Inflammatory carcinoma
REGIONAL LYMPH NODE INVOLVEMENT (N) (CLINICAL)	
NX	Regional lymph nodes cannot be assessed (e.g., previously removed)
N0	No regional lymph node metastasis
N1	Metastasis to movable ipsilateral axillary lymph node(s)
N2	Metastasis to ipsilateral axillary lymph node(s) fixed to one another or the other structures
N3	Metastasis to ipsilateral mammary lymph node(s)
DISTANT METASTASIS (M)	
MX	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis (includes metastasis to ipsilateral supraclavicular lymph node[s])

STAGE GROUPING			
Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIa	T0	N1	M0
	T1	N1*	M0
	T2	N0	M0
Stage IIb	T2	N1	M0
	T3	N0	M0
Stage IIIa	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1, N2	M0
Stage IIIb	T4	Any N	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

From Eberlein TJ. Current management of carcinoma of the breast. *Ann Surg.* 1994;220(2):121-136.

Paget disease associated with a tumor is classified according to the size of the tumor. Chest wall includes ribs, intercostal muscles, and serratus anterior muscle but not pectoral muscle.

*The prognosis of patients with pN1a is similar to that of patients with pN0.

Management

- The **initial size of the breast carcinoma** is the single best predictor of the likelihood of positive axillary nodes.
- The **presence and number of axillary node metastasis** are the best predictors of survival.
- Women whose initial tumor is less than 1 cm in diameter and who have negative axillary nodes have excellent chances for disease-free survival. The 10-year relapse rate is less than 10%.

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Management: Surgery

- Locoregional treatment of clinical stage I, IIA, IIB, or T3N1MO (a subset of stage IIIA) invasive breast cancer includes lumpectomy (or total mastectomy 6 reconstruction) with surgical axillary staging.
- Until the 1980s, **radical mastectomy** was the standard operation for carcinoma of the breast.
- With an increased understanding that cancer of the breast is often a systemic disease and that prognosis is similar with conservative surgery, the therapeutic emphasis has changed to less radical surgery and **increased use of radiotherapy and chemotherapy**
- **Breast-conserving therapy** (**lumpectomy**, axillary **sentinel lymph node** biopsy followed by whole breast irradiation) has been shown to be equivalent to mastectomy and axillary lymph node dissection in the primary treatment of women with stages I and II breast cancer.

Management: Surgery

TABLE 15.14 Ten-Year Disease-Free Survival Rates of Women with Breast Cancer

	Conservation Surgery and Radiation	Radical or Modified Radical Mastectomy Alone
Minimal breast cancer	92%	95%
Stage I	78%	80%
Stage II	73%	65%

From Montague ED. Conservation surgery and radiation therapy in the treatment of operable breast cancer. *Cancer.* 1984;53(3 Suppl):700-704.

Management: Surgery

TABLE 15.15 Twenty-Year Follow-up Comparing Total Mastectomy, Lumpectomy, and Lumpectomy Plus Irradiation

	Total Mastectomy	Lumpectomy Alone	Lumpectomy and Irradiation
Overall survival	47% ± 2%	46% ± 2%	46% ± 2%
Cumulative incidence of a recurrence in ipsilateral breast	N/A	39.2%	14.3%
Disease free survival	36% ± 2%	35% ± 2%	35% ± 2%
Distant disease free survival	49% ± 2%	45% ± 2%	46% ± 2%

From Fisher B, Anderson S, Bryant J, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N Engl J Med.* 2002;347(16):1233-1241.

N/A, Not applicable.

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Management: Radiation

- After breast-conserving surgery, external beam whole breast irradiation is usually administered.
- whole breast irradiation resulted in a significant reduction in the 10-year risk of any first recurrence compared with breast-conserving surgery alone
- Women with positive axillary lymph nodes after mastectomy and axillary lymphadenectomy are also candidates for breast radiation therapy.
- NCCN guidelines recommend irradiation after mastectomy in women with four or more positive axillary lymph nodes and strong consideration of radiation in women with one to three positive axillary lymph nodes
- Chest wall irradiation is also recommended in women with negative nodes but with a primary tumor greater than 5 cm or positive surgical margins.

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Management: Hormonal Therapy

- Women with hormone receptor–positive breast cancer are candidates for **endocrine therapy**.
- When estrogen receptors are positive, approximately 60% of breast cancers will respond to hormonal therapy;
- If estrogen receptors are negative, less than 10% of tumors respond to hormonal manipulation.
- Progesterone receptor positivity is a sign of better differentiation and greater response to hormonal therapy.
- In general, luminal-A receptor–positive tumors are usually better differentiated and exhibit a less aggressive clinical behavior, including a lower risk of recurrence and lower capacity to proliferate.
- An 80% response rate is noted when both estrogen and progesterone receptors are present.

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Management: Hormonal Therapy

- Hormonal therapy is effective in producing a response in advanced metastatic carcinoma for approximately 1 year.
- **Tamoxifen**, a selective estrogen receptor modulator, is a commonly prescribed hormonal agent for breast carcinoma.
- Tamoxifen significantly reduces the risk of breast cancer recurrence at 15 years and the risk of breast cancer mortality at 15 years
- Treatment with tamoxifen was associated with an increased risk of thromboembolic disease, strokes, and intrauterine polyps as well as endometrial hyperplasia and carcinoma.

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Management: Hormonal Therapy

- Aromatase inhibitors (AIs) (anastrozole, letrozole, and exemestane) block the peripheral conversion of adrenal androgens to estrone.
- Ovarian suppression can also be accomplished with pharmacologic interventions that inhibit ovarian production of estrogen, such as the gonadotropin-releasing hormone (GnRH) agonists.
- AIs compared with tamoxifen were noted to reduce recurrence rates by ap- proximately 30%, have a higher risk of osteoporosis/fractures, and have a lower risk of endometrial cancer

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Chemotherapy

- Chemotherapy may be adjuvant and neoadjuvant
- recommended for the treatment of most triple-negative breast cancers, HER2-positive breast cancers, and high-risk luminal tumors.
- The benefit of chemotherapy is more pronounced in ER-negative tumors.
- Combination therapy of cytotoxic drugs is vastly superior to single-agent regimens.
- chemotherapy regimens based on anthracyclines and taxanes reduce breast cancer mortality by about one-third.

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- Triple negative breast CA:
  - ✓ negative for 3 receptors: Her2, estrogen, progesterone
  - ✓ These cancers tend to be more common in women younger than age 40, who are Black, or who have a *BRCA1* mutation.

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https://www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer/triple-negative.html

Chemotherapy

- Neoadjuvant chemotherapy may be given:
  - tochange unresectable tumors to resectable ones and decrease the extent of surgery necessary to achieve adequate resection.
  - for patients who desire breast-conserving surgery but initially are not candidates because of tumor size.
  - For patients with inflammatory breast cancer and may confer a survival benefit in this population of patients.
- HER2-positive breast cancer and triple-negative breast cancer are the most chemosensitive and are excellent subtypes for neoadjuvant chemotherapy.
  - These patients have the highest pathologic complete response rate

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Summary

- 1. Benign Breast disorders
- 2. Breast carcinoma
  - Detection and diagnosis
  - classification
  - management

Thank you!

youtube channel: Ina Irabon

www.wordpress.com: Doc Ina OB Gyne

Quiz (10 pts)

1. The most classic symptom of fibrocystic breast change.:

A. Bloody Nipple discharge
B. Cyclical breast pain
C. Nipple inversion
D. rapidly increasing size of mass

2. Best predictor of survival for cases of breast cancer

A. Initial breast mass size
B. Bloody nipple discharge
C. presence of axillary node metastasis
D. BMI and age

3. Once a woman has developed carcinoma of one breast, her risk is approximately ____% per year of developing cancer in the other breast.

A. 5%
B. 10%
C. 3%
D. 1%

Quiz (10 pts)

4. What is the most common benign neoplasm?

A. Fibroadenoma
B. Fibrocystic changes of the breast.
C. mastitis
D. phyllodes tumor

5. Hormone therapy that reduces the risk of recurrence of breast cancer and also decreases the overall mortality rate

A. Tamoxifen
B. Clomiphene
C. Gonadotropins
D. Dydrogesterone

6. The most common breast malignancy

A. Inflammatory carcinoma
B. Invasive ductal carcinoma
C. DCIS
D. LCIS

Quiz (10 pts)

7. _____is the primary choice in screening for breast cancer.

A. Breast ultrasound
B. Magnetic resonance imaging
C. Fine needle aspiration
D. Mammography

8. Women at "average risk for breast cancer" means that they have ____% lifetime risk of developing breast cancer

A. 10%
B. 15%
C. 12%
D. < 5%

Quiz (10 pts)

9. _____ is the strongest risk factor for developing breast cancer

A. Family history
B. Age
C. breastfeeding
D. hormone therapy

10. Accdg to updated guidelines, when should we start requesting mammography for routine screening for breast cancer?

A. 40
B. 50
C. 45
D. at onset of menopause