

Nonproliferative Breast Changes (Fibrocystic Changes)

Morphology • mechanisms • clinical correlation

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Learning objectives

- Classify nonproliferative changes within benign epithelial lesions.
- Explain cyst formation, apocrine metaplasia, stromal fibrosis, and adenosis.
- Relate microscopic changes to palpable masses, nodularity, and calcifications.
- Differentiate these changes from proliferative lesions and interpret cancer-risk grouping.

The benign epithelial lesion spectrum

Nonproliferative changes

Cysts, apocrine change, fibrosis, and adenosis.

Proliferative without atypia

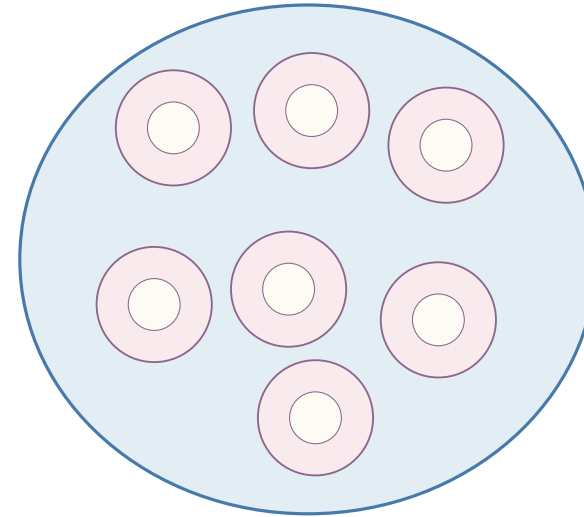
Epithelial hyperplasia or sclerosing proliferations without atypia.

Proliferative with atypia

Atypical clonal epithelial proliferations.

The terminal duct lobular unit is the key context

- Most benign epithelial lesions arise in the terminal duct lobular unit.
- Its acinar–ductal architecture provides the framework for cystic dilation and adenosis.
- Abnormalities can alter epithelial lining, acinar number, and supporting stroma.



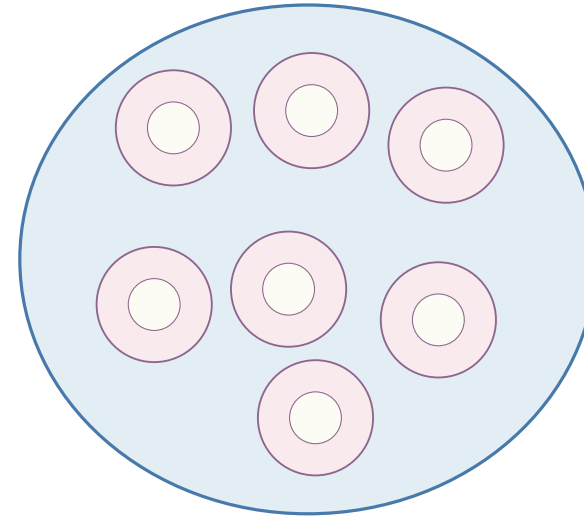
Schematic

“Fibrocystic change” is a morphologic umbrella

- A group of common breast changes rather than one discrete neoplasm.
- Three major components: Cystic change, fibrosis, and adenosis.
- Apocrine metaplasia commonly accompanies cyst formation.
- Different components can coexist within a breast.

Typical age distribution: 30–50 years

- These changes are especially common between ages 30 and 50.
- Menstrual hormonal fluctuations as a possible contributing influence.
- Hormonal association is presented as a possibility, not a proven single cause.



Schematic

Why “nonproliferative” is imperfect

Historical label

- No associated increase in breast cancer risk defines the historical category.
- The category is primarily clinicopathologic and risk-based.

Biologic nuance

- Some constituent changes include increased epithelial proliferation.
- Some may show clonal genetic aberrations.

The three core tissue responses

Cystic dilation

Expansion of acinar/lobular spaces; Often apocrine-lined.

Stromal fibrosis

Response to cyst rupture with inflammation and collagenous repair.

Adenosis

Increase in acini within an individual lobule.

Why the same process looks different clinically

Microscopic alterations

- Altered acinar lumen size
- Epithelial metaplasia
- Local secretions or calcifications

Possible presentation

- Diffuse or focal nodularity
- Palpable solitary cyst
- Mammographic calcifications

Detection is often incidental

- Benign epithelial changes are commonly found at mammography or incidentally in surgical material.
- Diffuse nodularity may reflect normal glandular tissue or fibrocystic change.
- A discrete palpable lesion requires clinical evaluation rather than diagnosis by label alone.

Read each lesion along three axes

What changed?

Space, epithelial phenotype, acinar number, or stromal repair.

What is its substrate?

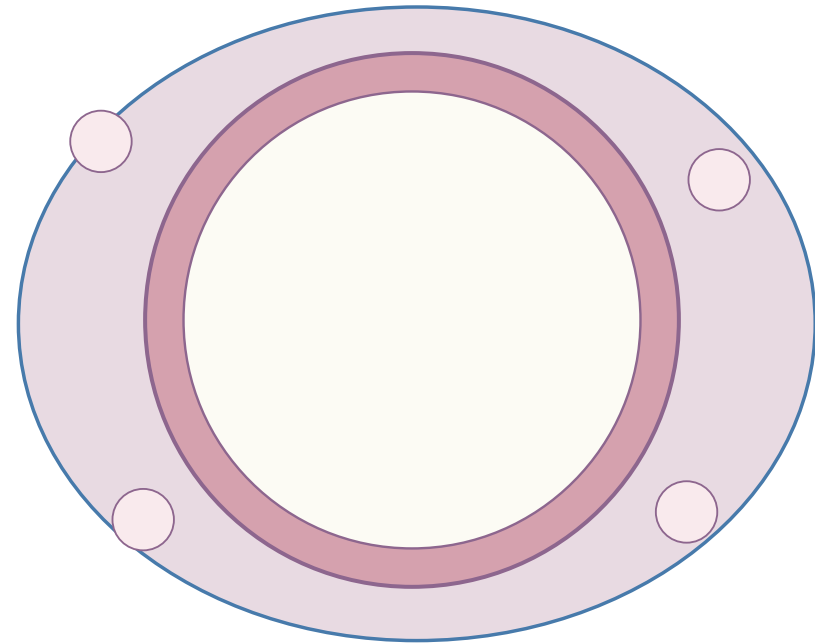
Lobule, cyst wall, or interstitial stroma.

Why is it noticed?

Palpable mass, nodularity, calcification, or incidentally.

Cysts begin with lobular dilation

- Small cysts arise through dilation of lobular structures.
- Enlarging spaces may coalesce into larger cysts.
- The architecture is one of luminal expansion, not necessarily a new solid tumor.



Schematic

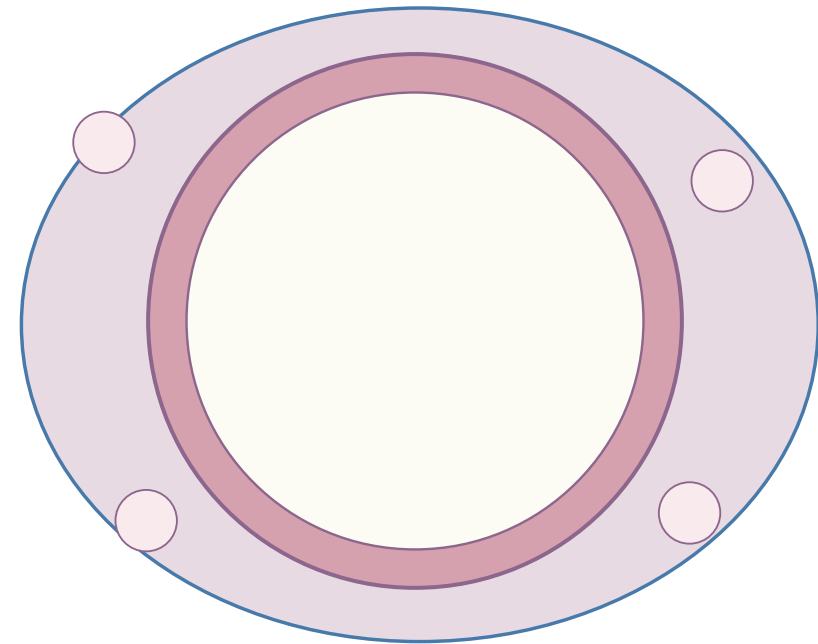
Small cysts can merge into larger spaces



Cyst size helps explain why some are incidental and others are clinically apparent.

A typical unopened cyst contains turbid fluid

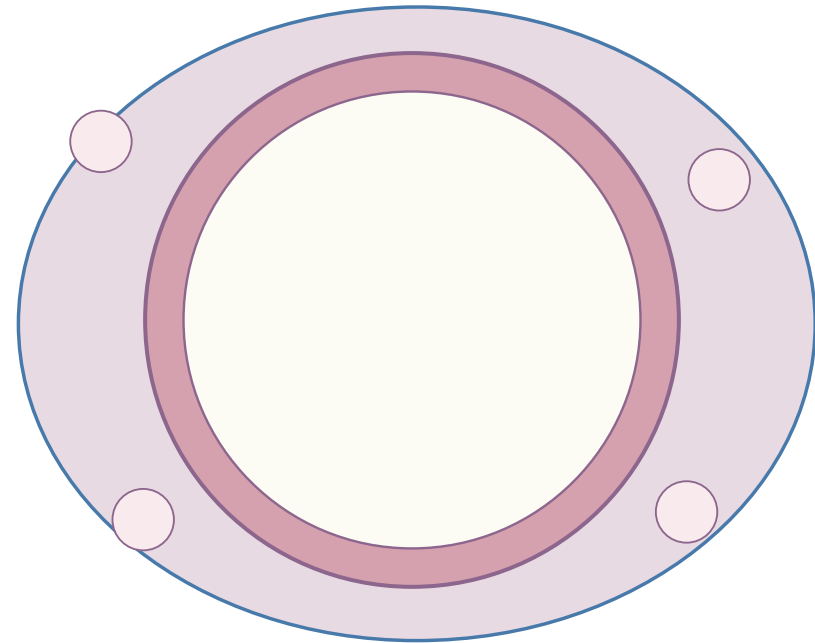
- Contents may be semitranslucent, brown, or blue tinged.
- The gross appearance underlies the term “blue-dome cyst.”
- This description concerns typical cyst fluid, not a universal appearance.



Schematic

The cyst lining may become flattened

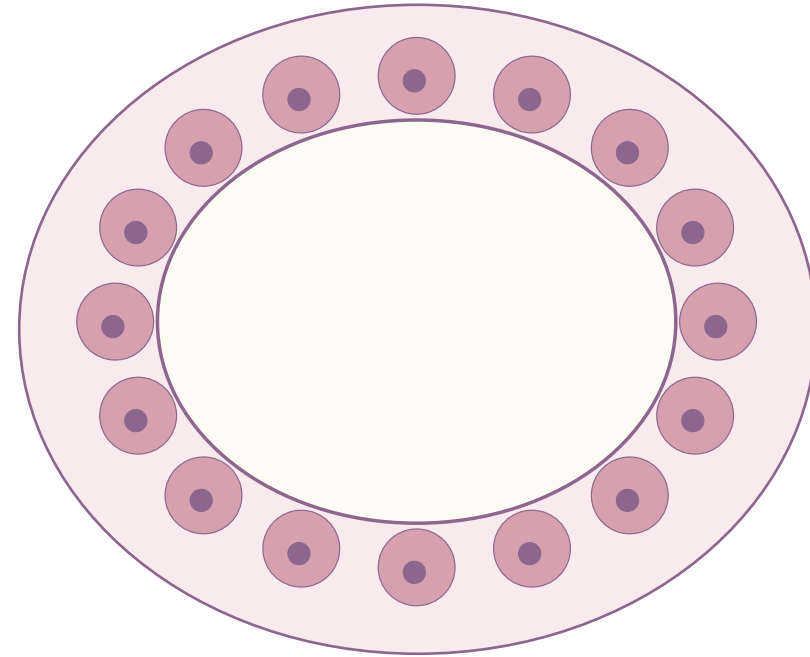
- One lining pattern is flattened, atrophic epithelium.
- Expansion can coexist with epithelial attenuation.
- A thin lining does not exclude a prominent gross cyst.



Schematic

A second lining pattern is apocrine metaplasia

- The cyst lining can instead comprise metaplastic apocrine cells.
- Apocrine epithelium resembles that of normal sweat glands.
- This cell change is part of the nonproliferative lesion spectrum.



Schematic

Two epithelial appearances in a cyst wall

Flattened / atrophic

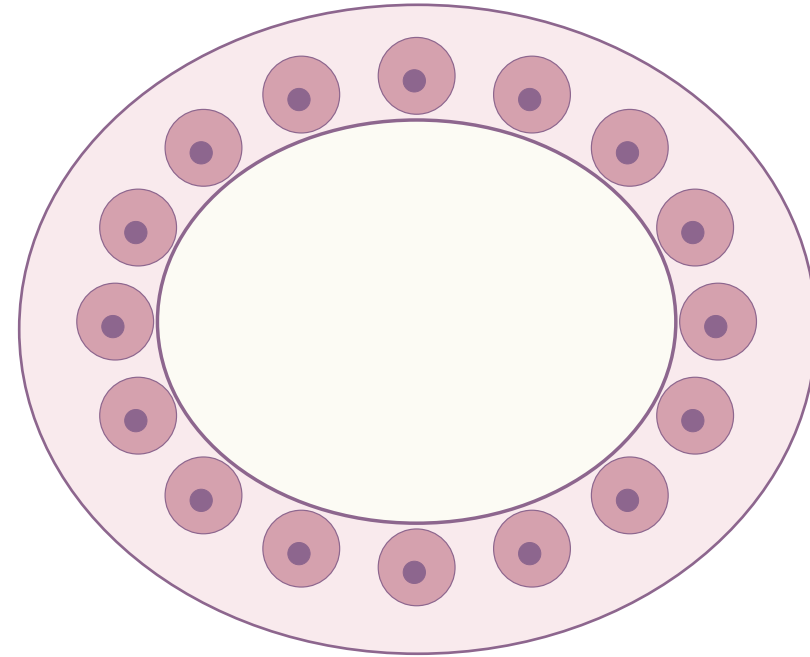
- Low-profile cells
- Thin-appearing lining
- Seen in cystically expanded lobules

Apocrine metaplasia

- Plump epithelial cells
- Abundant eosinophilic cytoplasm
- Granular cytoplasmic texture

Apocrine cells have granular eosinophilic cytoplasm

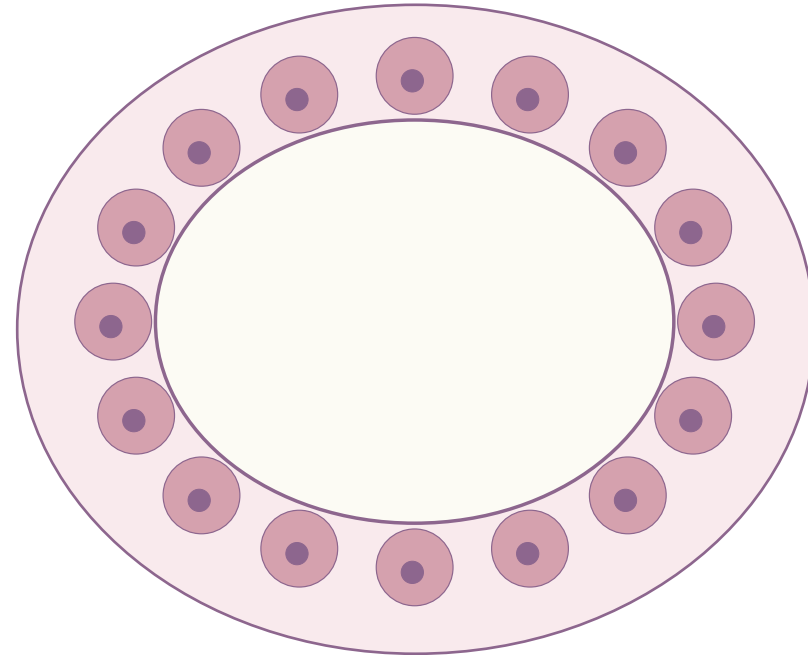
- Abundant cytoplasm is a defining microscopic clue.
- Granularity and pink staining help recognize the cell phenotype on H&E.
- The appearance resembles sweat-gland apocrine epithelium.



Schematic

A cyst wall may contain different epithelial patterns

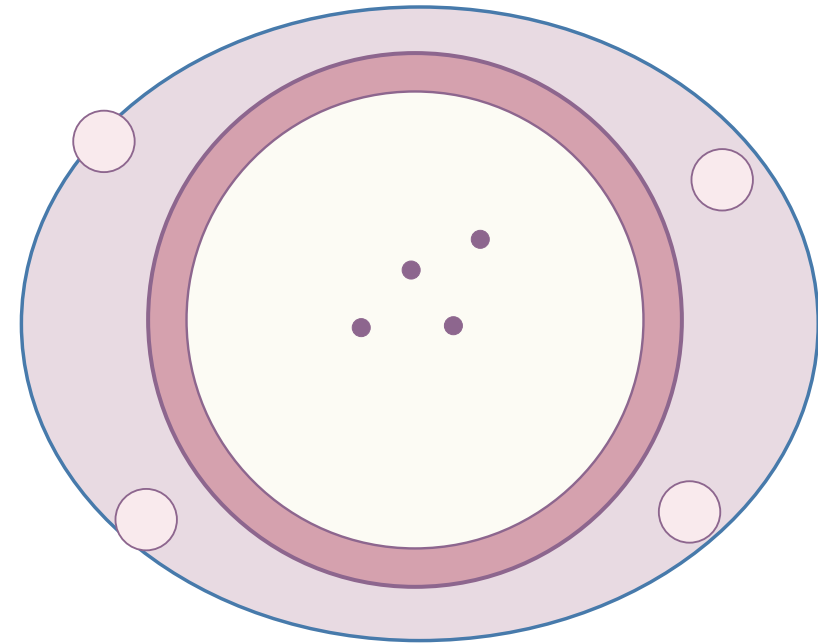
- Cystic morphology refers to luminal enlargement.
- Epithelial lining phenotype is a separate microscopic observation.
- Therefore, “cyst” and “apocrine metaplasia” are compatible, not competing diagnoses.



Schematic

Calcifications frequently accompany cystic change

- Calcification is a common finding in fibrocystic cysts.
- The textbook figure describes deposits on secretory debris within cyst lumens.
- Calcifications may bring a benign lesion to radiologic attention.



Schematic

Calcification: Tissue observation versus imaging clue

Histologic location

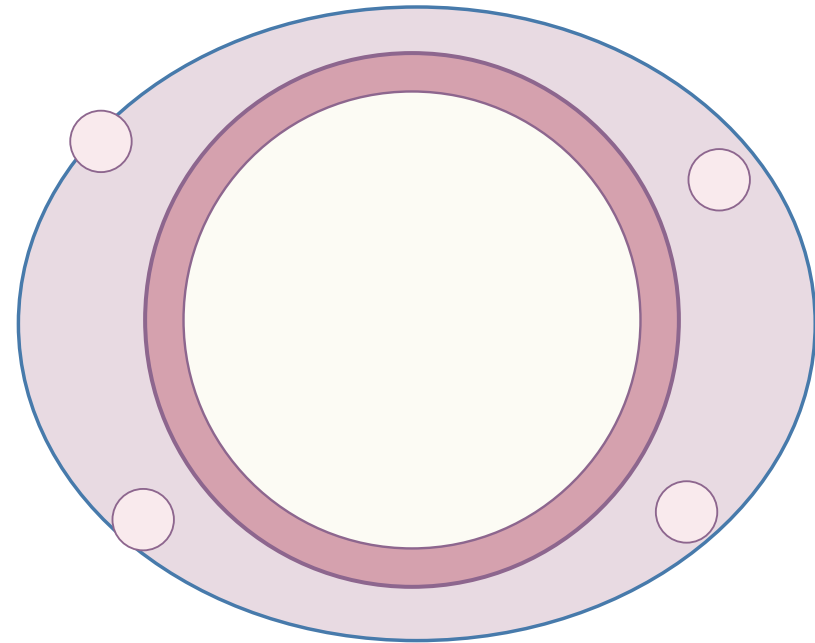
- Intraluminal deposits
- Association with secretory material
- Can accompany apocrine-lined cysts

Clinical detection

- Visible as mammographic calcifications
- Can prompt sampling or correlation
- Not a diagnosis of malignancy by itself

A single firm cyst can simulate a mass

- Many cysts cause no concern; Solitary firm cysts may be palpable.
- The physical presentation can lead to concern for an underlying tumor.
- The diagnostic question is whether the finding is a simple cyst or a persistent solid lesion.



Schematic

Aspiration can demonstrate a fluid-filled cyst



Disappearance of the mass after aspiration as confirmation.

Aspiration provides a structure–symptom correlation

- Before aspiration: A cavity filled with fluid can be felt as a mass.
- After fluid removal: The cavity collapses and the palpable mass resolves.
- The change in physical finding supports the cystic basis of the mass.

Three distinct observations about a breast cyst

Gross

Turbid brown/blue fluid in an expanded cavity.

Microscopic

Flat atrophic or apocrine epithelial lining; Calcification may be seen.

Clinical

May be found as a solitary palpable mass; Aspiration can resolve it.

Application: The solitary “blue-dome” lesion

CLINICAL / MORPHOLOGIC STEM

A 39-year-old patient has a discrete breast lump. At examination a cystic lesion is suspected; Aspiration evacuates brown-tinged fluid and the mass disappears.

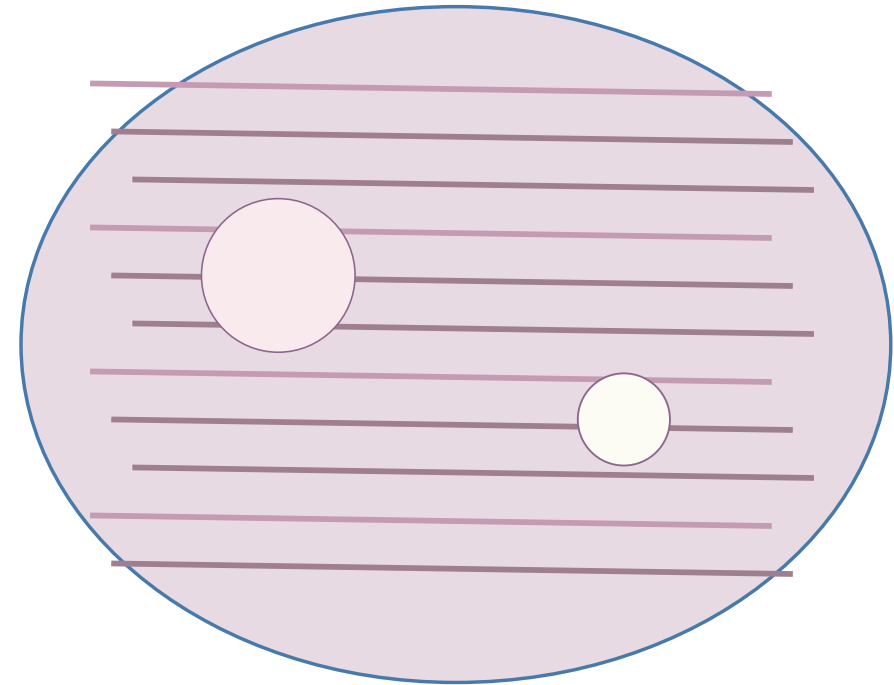
INTERPRETATION

- Lobular dilation produces the fluid-filled cavity.
- Cyst fluid may be brown or blue tinged.
- Disappearance after aspiration supports a cyst.

Most consistent process: Nonproliferative cystic change.

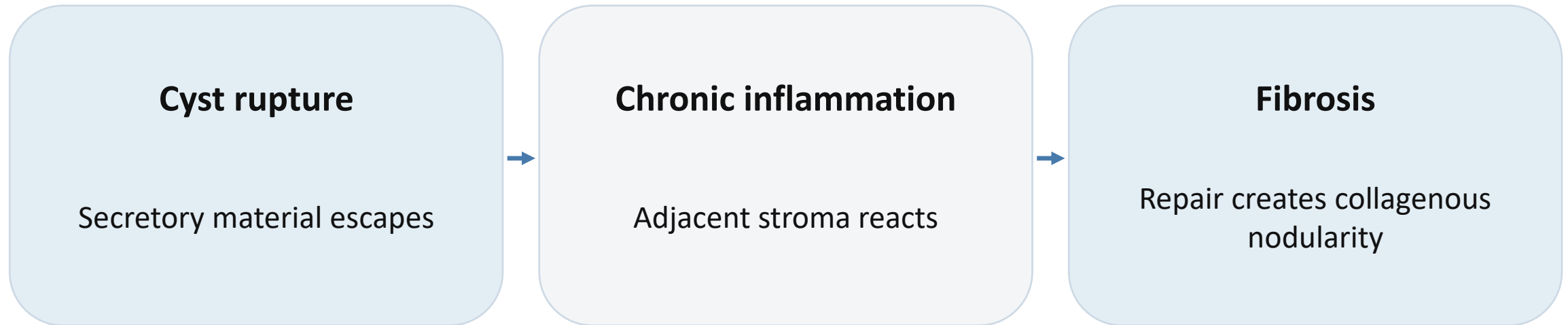
Fibrosis commonly follows rupture of a cyst

- Cysts may rupture and release secretory material into the stroma.
- Material outside the epithelial-lined space induces a tissue response.
- Fibrosis is therefore linked to prior cystic injury in this context.



Schematic

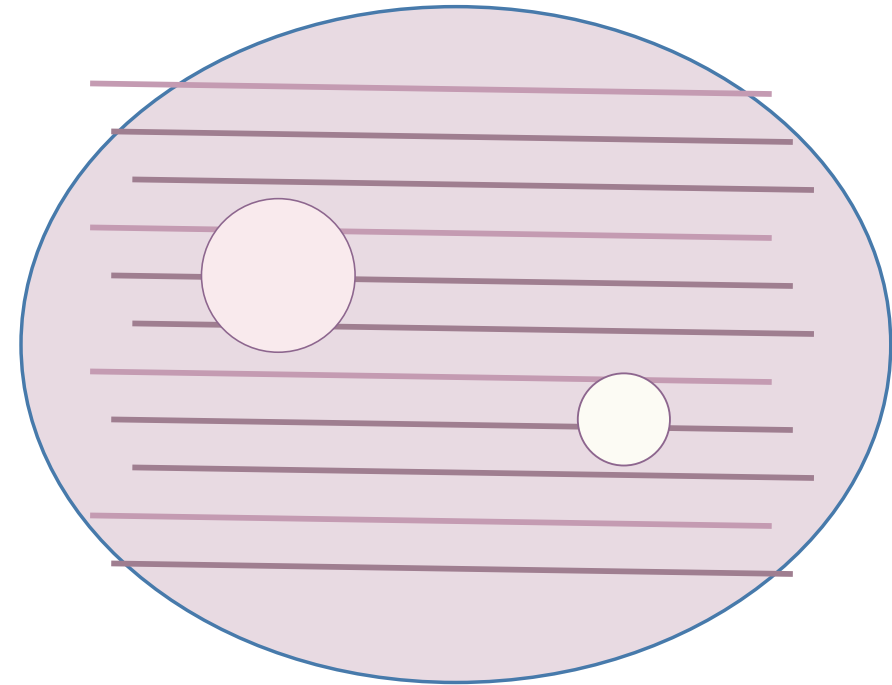
Rupture connects cystic change to stromal scarring



This is the source-defined mechanism for many palpable fibrocystic nodules.

Extravasated secretions drive inflammation

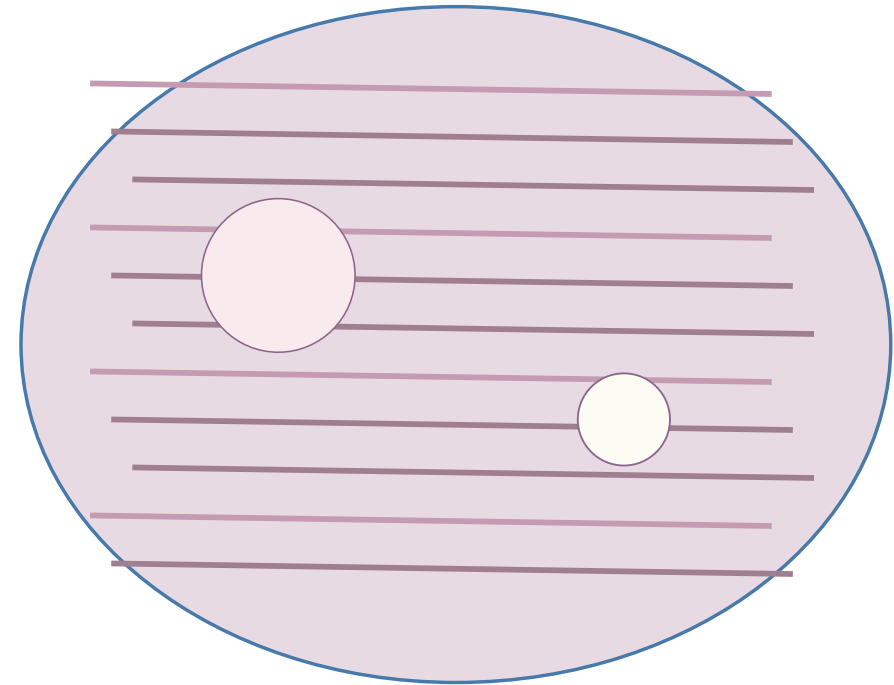
- Secretory material is normally contained within a lined lumen.
- Rupture relocates it into adjacent interstitium.
- The tissue develops a chronic inflammatory reaction around released material.



Schematic

Stromal repair produces collagenous nodularity

- Fibrosis follows chronic inflammation after cyst rupture.
- Firmness or nodularity can arise from the stromal component.
- The palpable abnormality need not be produced by a solid epithelial proliferation.



Schematic

Fluid and fibrous tissue produce different findings

Fluid-filled cyst

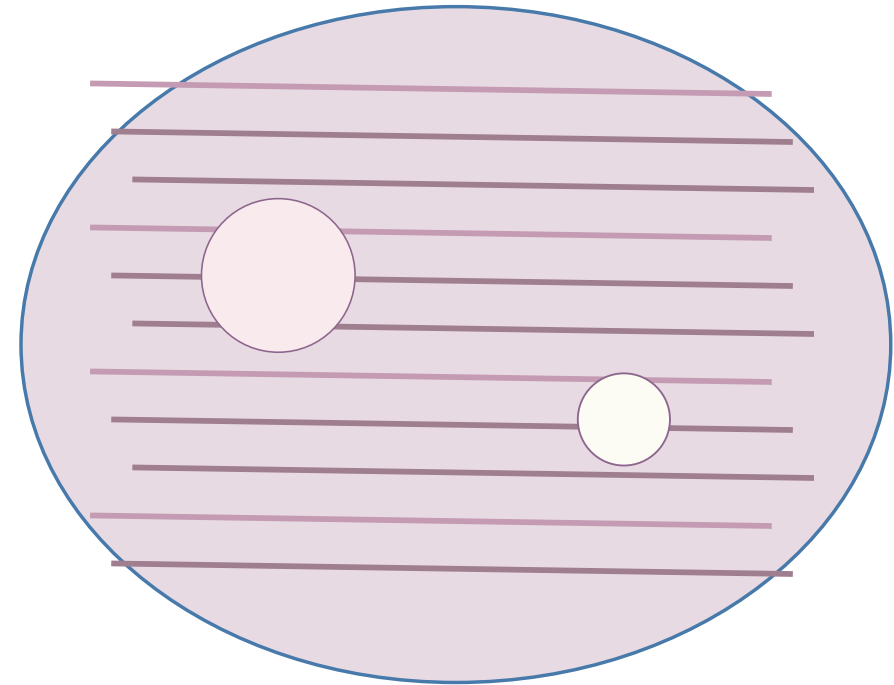
- An epithelial-lined, expanded lumen
- Luminal liquid contributes to volume
- Mass may resolve on aspiration

Fibrotic nodularity

- Stromal scarring follows chronic inflammation
- Collagen-rich tissue produces firmness
- Not simply a cavity of aspiratable fluid

The stroma is an active participant

- Fibrocystic change is not solely an epithelial abnormality.
- Ruptured cysts affect supporting interstitial tissue.
- Reactive fibrosis helps determine what is palpable.



Schematic

Application: Diffuse palpable nodularity

CLINICAL / MORPHOLOGIC STEM

A 44-year-old patient reports diffusely nodular breast tissue. Histology reveals prior cystic spaces with adjacent stromal fibrosis.

INTERPRETATION

- Cyst rupture may release material into stroma.
- Inflammation and scarring follow.
- Fibrosis explains the palpable nodularity.

Mechanistic link: Cyst rupture → stromal fibrosis.

Distinguish three components of a fibrocystic nodule

Epithelial space

Cystic dilation, sometimes apocrine-lined.

Inflammatory response

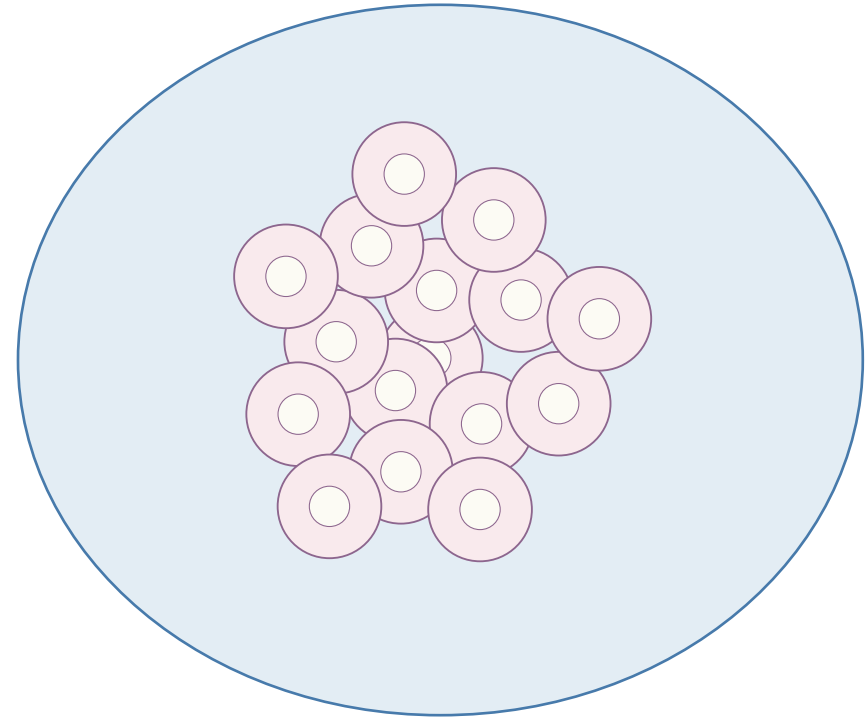
Reaction to secretory material when cysts rupture.

Stromal outcome

Collagenous fibrosis creating palpable irregularity.

Adenosis means more acini per lobule

- The defining feature is an increase in acinar number.
- The unit of comparison is an individual lobule.
- Adenosis describes glandular abundance rather than an enlarged cyst lumen.



Schematic

Normal lobule versus adenosis

Reference architecture

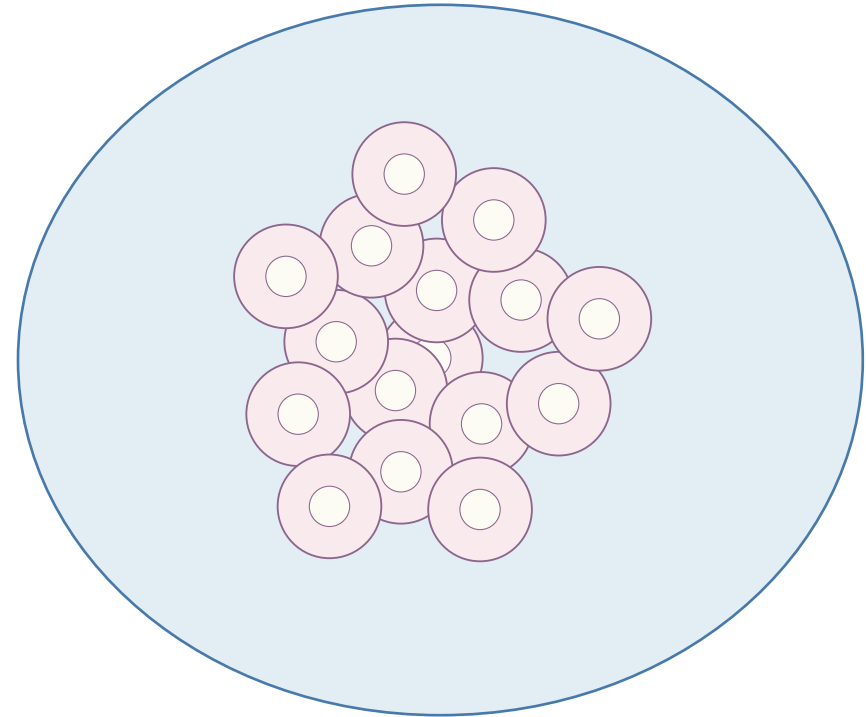
- Smaller number of acini in the lobule
- Individual acinar lumens are identifiable

Adenosis

- Increased number of acini per lobule
- Preserved glandular/acinar profile
- May include intraluminal calcifications

Acini in adenosis may have columnar epithelium

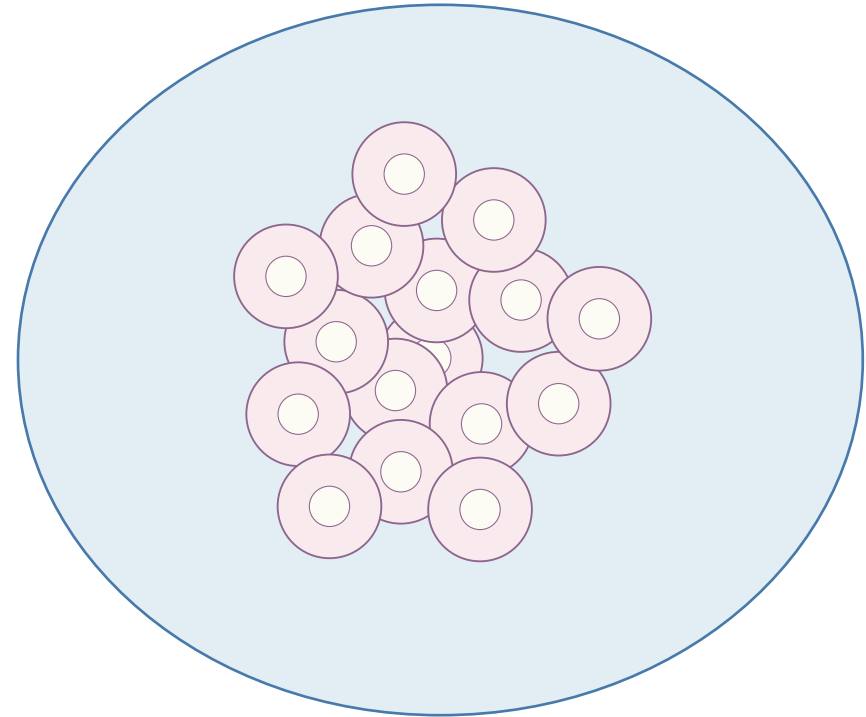
- Columnar cells lining the increased acini.
- The diagnostic feature combines epithelial lining with the count of acini.
- Increased acinar number is distinct from cyst expansion.



Schematic

Adenosis may show luminal calcification

- Calcifications occasionally occur within acinar lumina.
- Intraluminal mineralization is compatible with a benign acinar process.
- Microscopic location helps relate the finding to mammographic detection.



Schematic

Simple adenosis versus sclerosing adenosis

Adenosis in this topic

- More acini in a lobule
- Acini may be columnar-lined
- No defining compression by dense fibrosis

Sclerosing adenosis: Adjacent topic

- Increased acini plus stromal fibrosis
- Distortion and compression of glandular profiles
- Belongs to proliferative disease without atypia

Application: Increased acini without marked sclerosis

CLINICAL / MORPHOLOGIC STEM

A tissue sample shows a lobule containing more acini than expected. These acini have columnar epithelium; Occasional calcification is present.

INTERPRETATION

- The defining change is acinar number.
- Columnar lining accords with simple adenosis.
- Calcification can occur in lumens.

Best term: Adenosis within nonproliferative change.

What to count, inspect, and localize in adenosis

Count

Acini per lobule.

Inspect

Epithelial lining character.

Localize

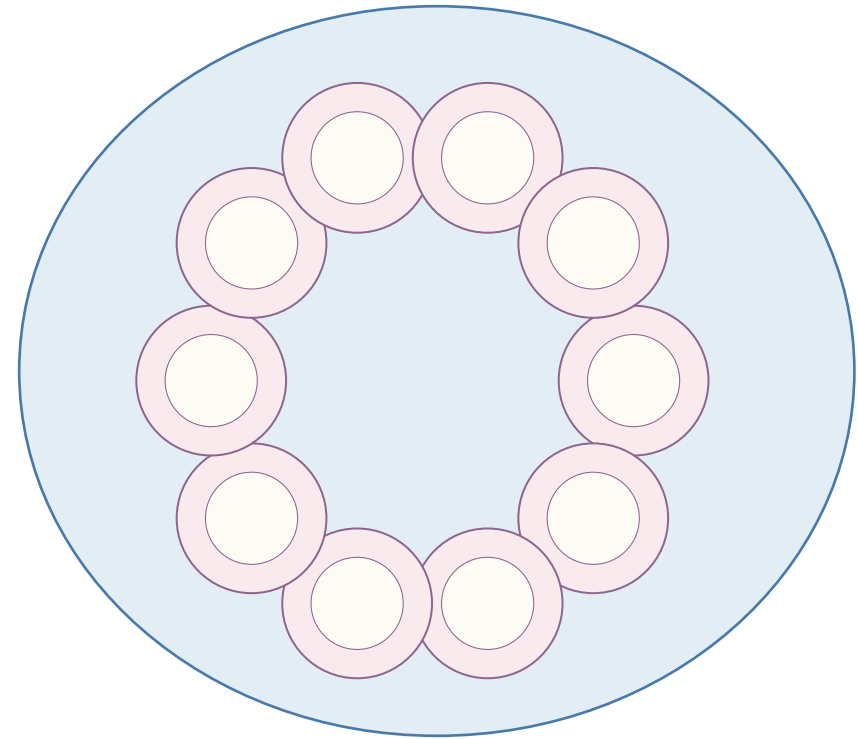
Any calcifications inside lumina.

Cysts and adenosis modify different dimensions

- Cysts: Increased luminal size as lobular spaces dilate.
- Adenosis: Increased acinar number within a lobule.
- Fibrosis: Increased stromal collagen following injury/inflammation.
- These dimensions can coexist but should be reported separately.

Lactational adenoma is a special associated alteration

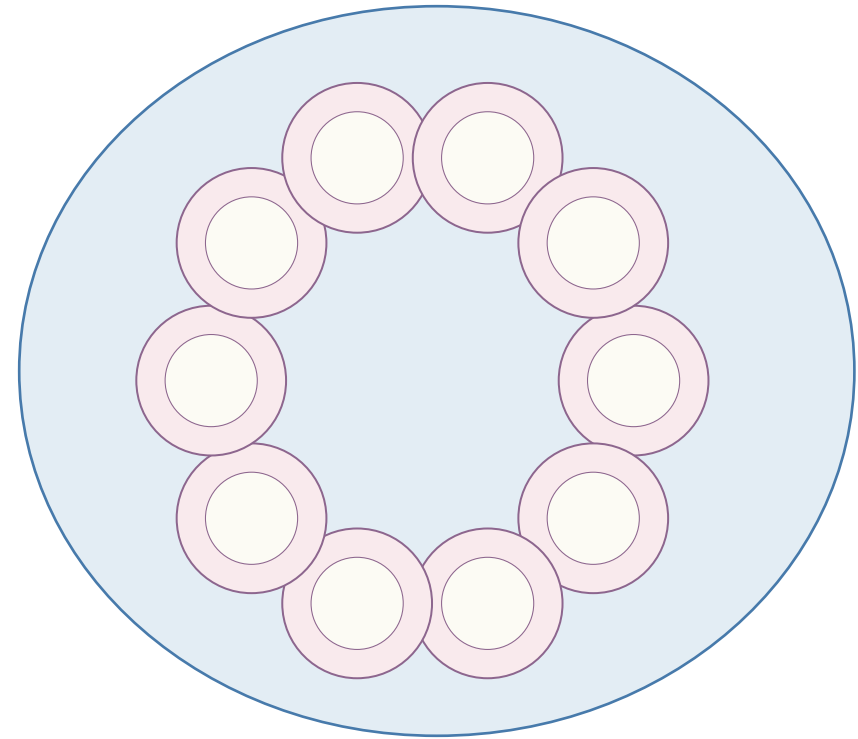
- Lactational adenoma among other “nonproliferative” morphologic changes.
- It presents as a mass during pregnancy or lactation.
- Its hormonal setting differentiates it from the typical nonlactational changes.



Schematic

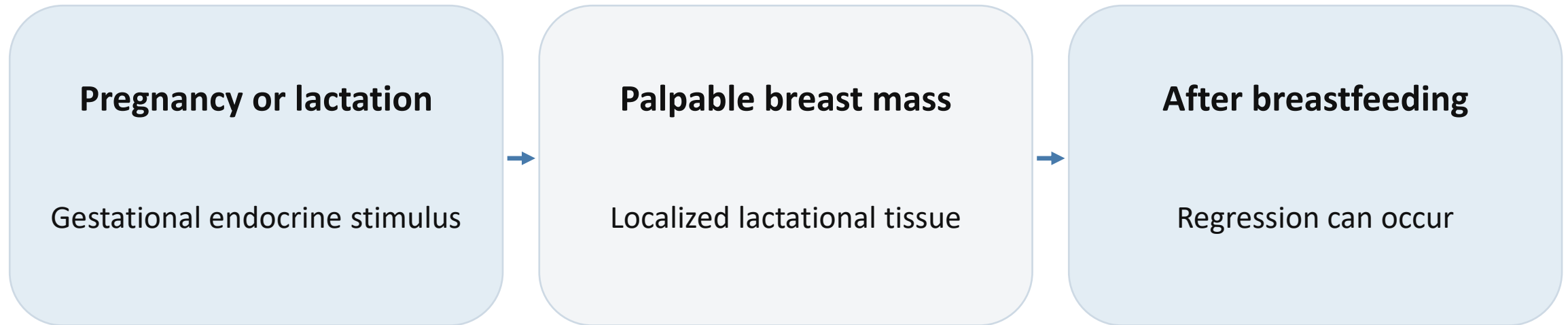
Histology resembles breast tissue in lactation

- The mass contains normal-appearing tissue with lactational changes.
- The lesion may represent an exaggerated localized response to gestational hormones.
- Robbins cautions that it may not be a true neoplasm.



Schematic

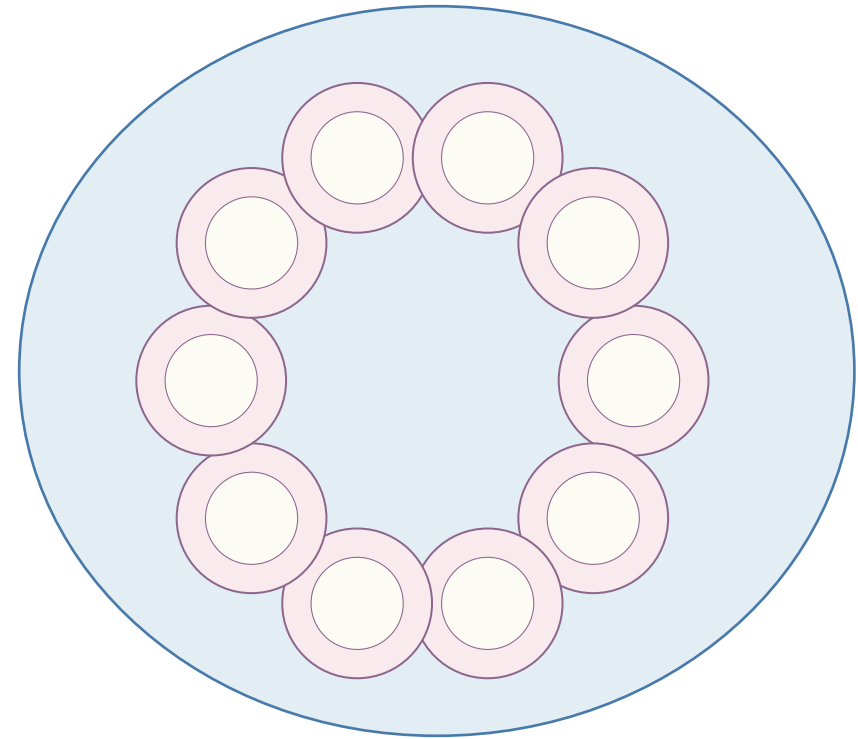
Lactational adenoma follows a characteristic setting



Natural regression supports the proposed hormone-responsive biology.

Regression after breastfeeding is a diagnostic clue

- Lactational adenomas may regress following cessation of breastfeeding.
- Natural-history observation is part of their clinicopathologic identity.
- Regression is consistent with an exaggerated gestational response.



Schematic

Lactational adenoma versus fibrocystic cyst

Lactational adenoma

- Pregnant or breastfeeding setting
- Lactational-appearing breast tissue
- Tends to regress after lactation

Fibrocystic cyst

- Lobular dilation with cyst cavity
- Flat or apocrine lining
- May produce a mass resolving on aspiration

Application: A mass during lactation

CLINICAL / MORPHOLOGIC STEM

A lactating patient has a well-defined breast mass. Sampled tissue shows normal-appearing breast epithelium with lactational changes, rather than cystic dilation.

INTERPRETATION

- Clinical setting is pregnancy/breastfeeding.
- Morphology shows a local lactational response.
- The lesion may regress after breastfeeding ends.

Most consistent lesion: Lactational adenoma.

Breast lesion groups are defined by risk

Category	Representative changes	Relative risk
Nonproliferative	Cysts, apocrine change, adenosis	1.0
Proliferative / no atypia	Sclerosing adenosis, florid UDH	1.5–2
With atypia	Atypical ductal/lobular hyperplasia	4–5
Carcinoma in situ	DCIS or LCIS	8–10

Relative risk is not histologic intensity

Pathologic appearance

- Benign changes may have prominent cysts, apocrine epithelium, or nodularity.
- Some show proliferation despite the group name.

Clinical risk category

- Nonproliferative group: Relative risk 1.0.
- Atypia elevates risk category independent of mere palpability.

Atypia is a crucial boundary between groups

- Nonproliferative changes are grouped as lacking an elevated subsequent carcinoma risk.
- Proliferative disease without atypia has a small increase in subsequent risk.
- Proliferative disease with atypia carries a larger increase in risk.
- These are classifications of subsequent risk, not synonymous with invasive cancer.

Simple adenosis and sclerosing adenosis are not interchangeable

Simple adenosis

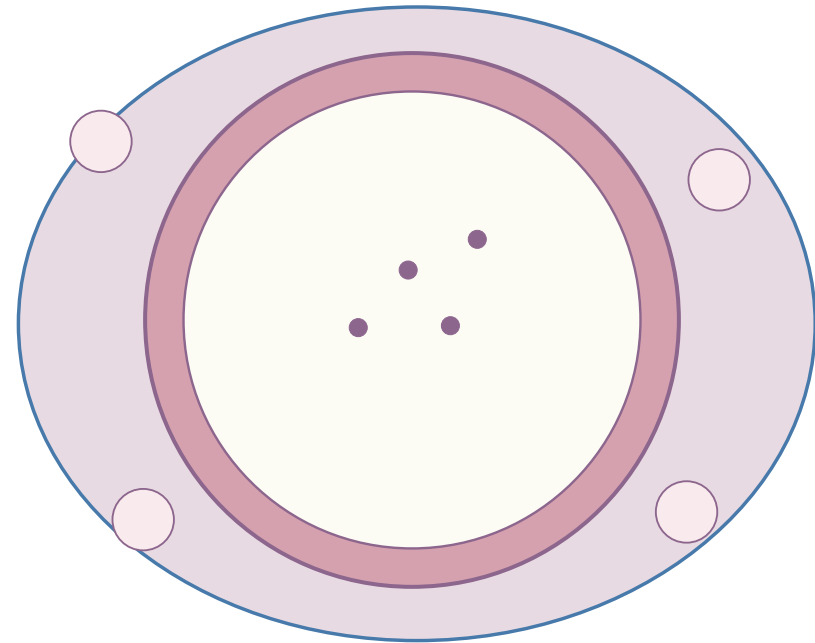
- More acini per lobule
- Belongs to nonproliferative changes
- Relative-risk category 1.0

Sclerosing adenosis

- Fibrous distortion and compression of acini
- Proliferative disease without atypia
- Higher category relative risk 1.5–2

Calcifications must be interpreted in context

- Cystic change and adenosis can contain calcifications.
- Mammography may detect them even if a lesion is not palpable.
- Calcification alone does not determine the lesion's biologic risk category.



Schematic

The lesion is approached at three scales

Patient

Palpable mass, diffuse nodularity, or incidental detection.

Image

A mass/density or calcifications may prompt assessment.

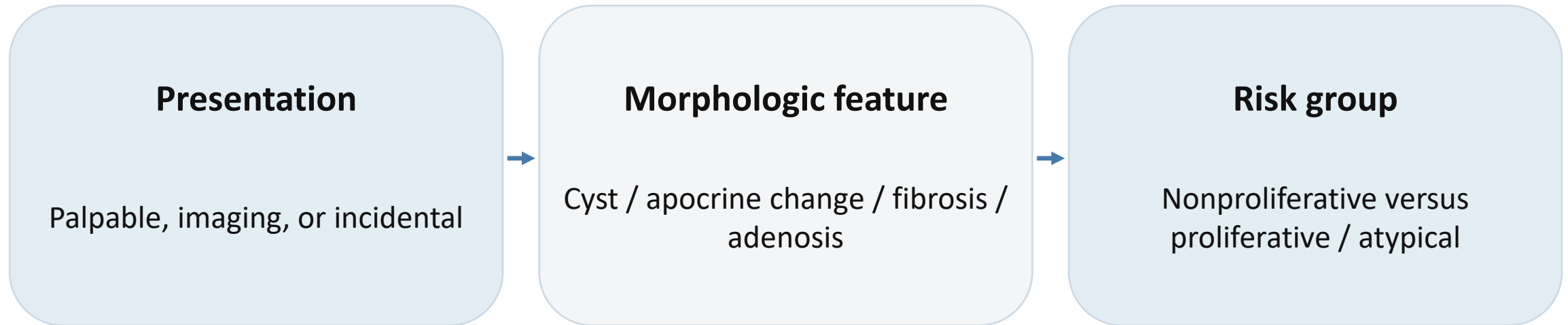
Tissue

Cyst lining, acinar number, and fibrosis establish the pattern.

The “nonproliferative” label does not mean no genetic change

- Some morphologic changes include epithelial proliferation.
- Clonal genetic aberrations may occur in some of them.
- Risk categorization remains clinically distinct from any one molecular observation.

Interpreting a benign breast finding



A diagnosis should describe the pattern before applying its risk category.

Integrative case: Calcified apocrine-lined cyst

CLINICAL / MORPHOLOGIC STEM

A mammographically detected lesion has a dilated cystic lumen, luminal mineralization and epithelial cells with abundant granular eosinophilic cytoplasm.

INTERPRETATION

- Luminal dilation identifies a cyst.
- Granular eosinophilic cells identify apocrine metaplasia.
- Calcifications can accompany this benign pattern.

Classification: Fibrocystic change; Cyst with apocrine metaplasia.

Integrative case: Cyst plus stromal scarring

CLINICAL / MORPHOLOGIC STEM

Microscopy shows an expanded lobular space, disruption of the lining and adjacent dense collagenous tissue. The breast feels nodular.

INTERPRETATION

- A prior cyst can rupture.
- Released secretion induces chronic inflammation.
- Fibrotic repair explains the clinically firm area.

Mechanism: Rupture-associated stromal fibrosis.

Integrative case: The misleading category name

CLINICAL / MORPHOLOGIC STEM

A biopsy is labeled nonproliferative fibrocystic change. A trainee argues that absolutely no epithelial proliferation can be present.

INTERPRETATION

- The term is historical and risk-based.
- Some included alterations increase epithelial proliferation.
- The label does not exclude possible clonal aberrations.

Correction: “nonproliferative” is not biologically literal.

Integrative case: Two lesions called adenosis

CLINICAL / MORPHOLOGIC STEM

Specimen A has many columnar-lined acini in a lobule. Specimen B has glandular multiplication with prominent distortion and compression by fibrosis.

INTERPRETATION

- A fits simple adenosis.
- B fits sclerosing adenosis.
- The lesions occupy different Robbins risk groups.

Specify the pattern; The word “adenosis” alone is insufficient.

Morphologic recognition checklist

Component	Defining observation	Clinical correlate
Cyst	Dilated lobular lumen; variable epithelial lining	Solitary mass; may collapse on aspiration
Apocrine change	Granular eosinophilic epithelial cytoplasm	Often lines cysts
Fibrosis	Stromal scarring after cyst rupture	Palpable nodularity
Adenosis	More acini per lobule	Occasional luminal calcifications
Lactational adenoma	Lactational-appearing tissue	Pregnancy/lactation-associated mass

Core concepts to retain

- Fibrocystic change combines cysts, apocrine metaplasia, fibrosis, and adenosis.
- Cyst rupture can cause chronic inflammation and stromal scarring.
- Simple adenosis increases acinar number; Sclerosing adenosis is a separate proliferative pattern.
- The nonproliferative category is defined by a relative-risk grouping, not a literal absence of cell proliferation.

Reference and image-use note

Primary source

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 23: The Breast, pp. 945–952; especially pp. 947–948 and Table 23.1.

All tissue drawings are original, editable schematics, not histology images. No textbook figures have been reproduced.