

Branchial cleft cyst (cervical lymphoepithelial cyst)

Cervical lymphoepithelial cyst

Lateral neck • epithelial-lined cavity • lymphoid-rich wall

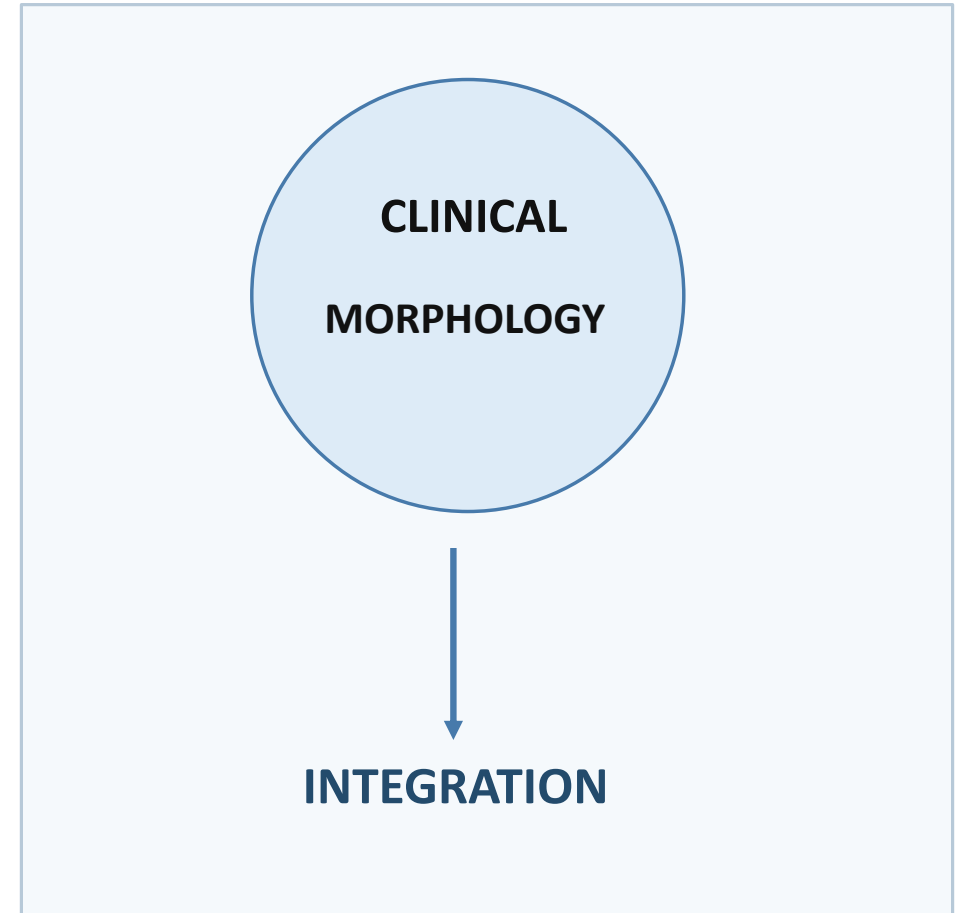
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Learning objectives

- Recognize the characteristic clinical location and age range.
- Explain epithelial lining, lymphoid stroma, and cyst contents.
- Distinguish a congenital cyst from cystic metastatic carcinoma.
- Apply morphology to targeted clinicopathologic problems.



The central diagnostic problem

- A lateral neck cyst may be developmental.
- A cystic metastatic lymph node can look similarly innocuous.
- The distinction is especially consequential in an adult.

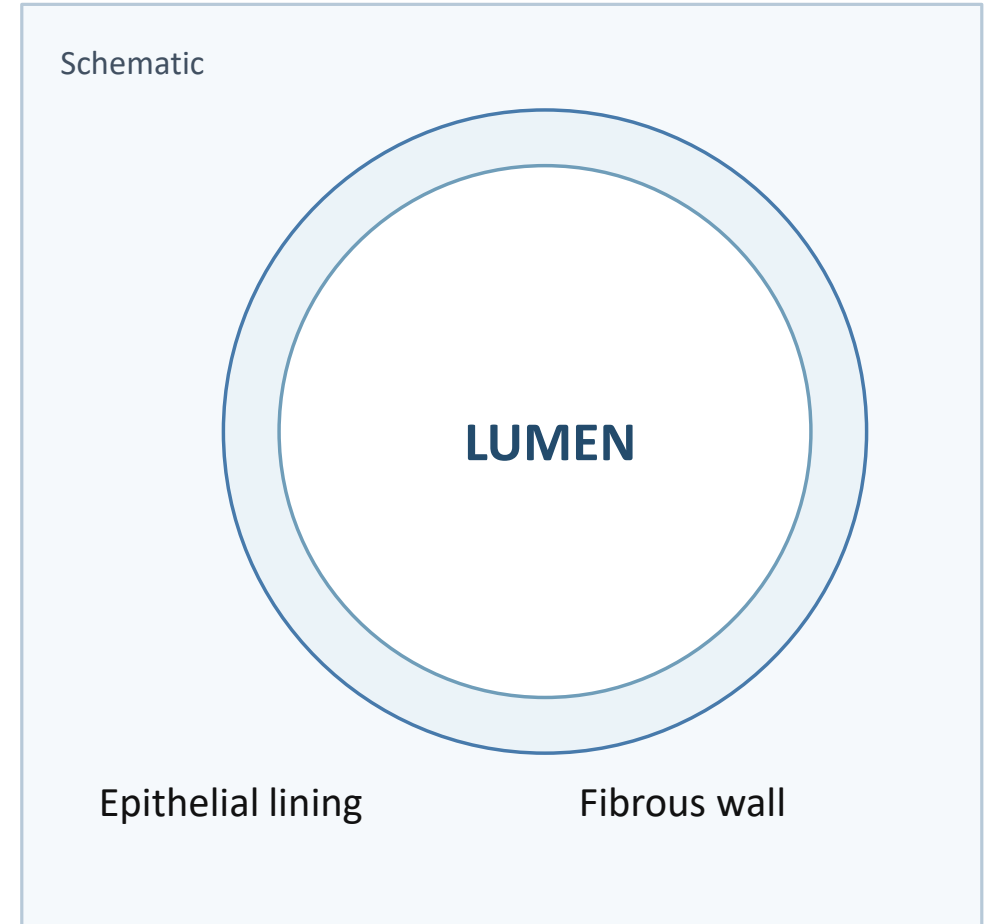
Benign cyst

**Metastatic
SCC**

Compare evidence, not a single appearance

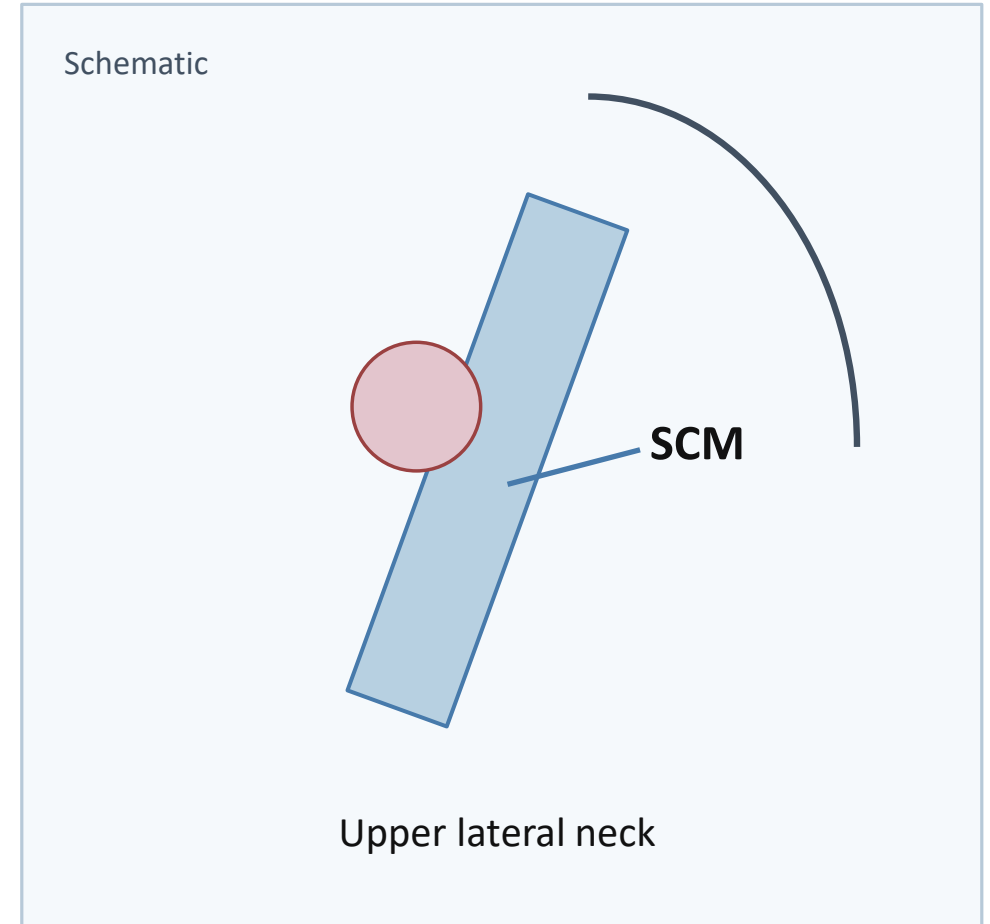
Defining a branchial cleft cyst

- Benign cystic lesion of the head and neck.
- Usually associated with remnants of the embryonic branchial apparatus.
- Also termed a cervical lymphoepithelial cyst.



The neck contains several categories of lesions

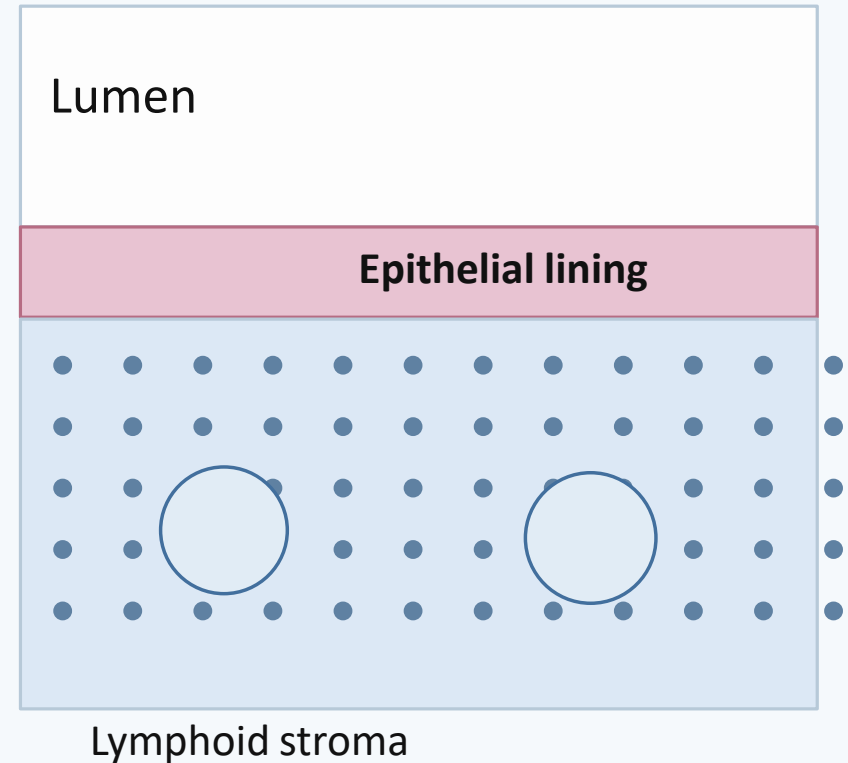
- Developmental cysts are only one cause of a cervical mass.
- Other important neck lesions may be inflammatory or neoplastic.
- Clinical location and morphology guide the initial differential.



Why the name “lymphoepithelial”?

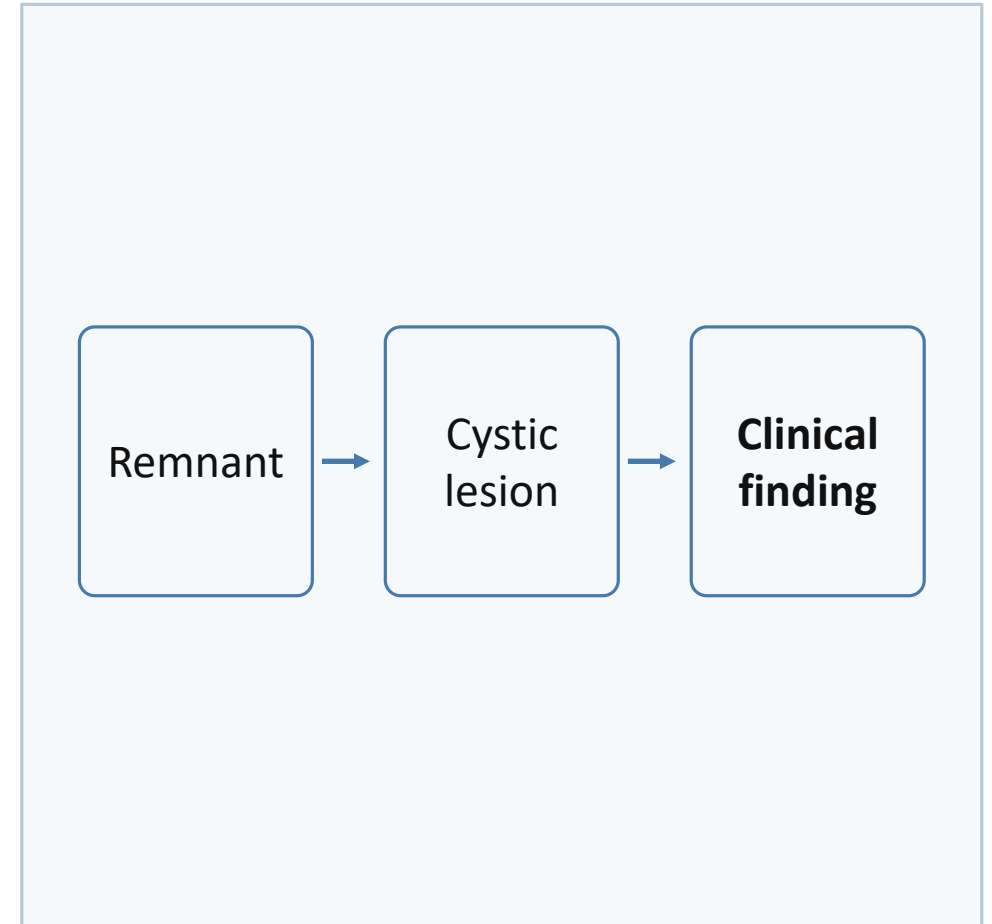
- The lumen is lined by epithelium.
- The fibrous wall typically contains lymphoid tissue.
- Prominent germinal centers are a characteristic feature.

Histology schematic — not a micrograph



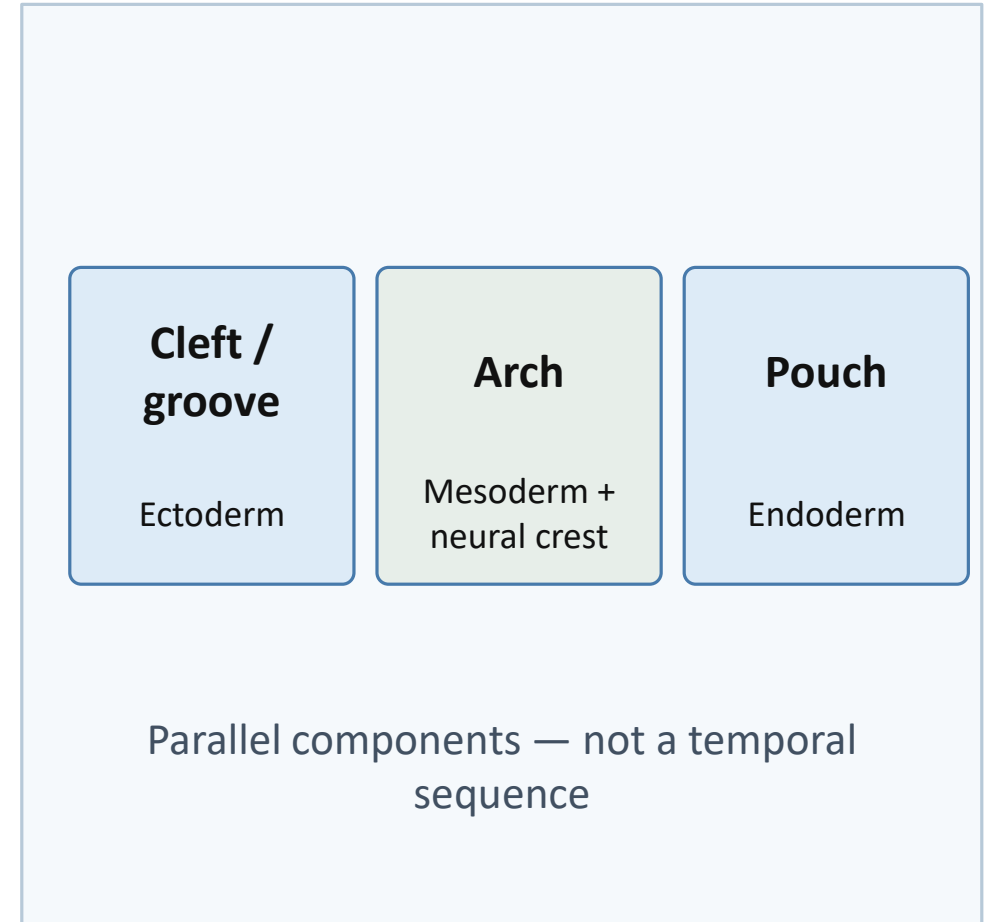
Embryologic origin: A developmental remnant

- Most lesions to remnants of the second branchial arch.
- The developmental origin explains the characteristic lateral neck distribution.
- The detailed arch/cleft/pouch terminology varies across sources.



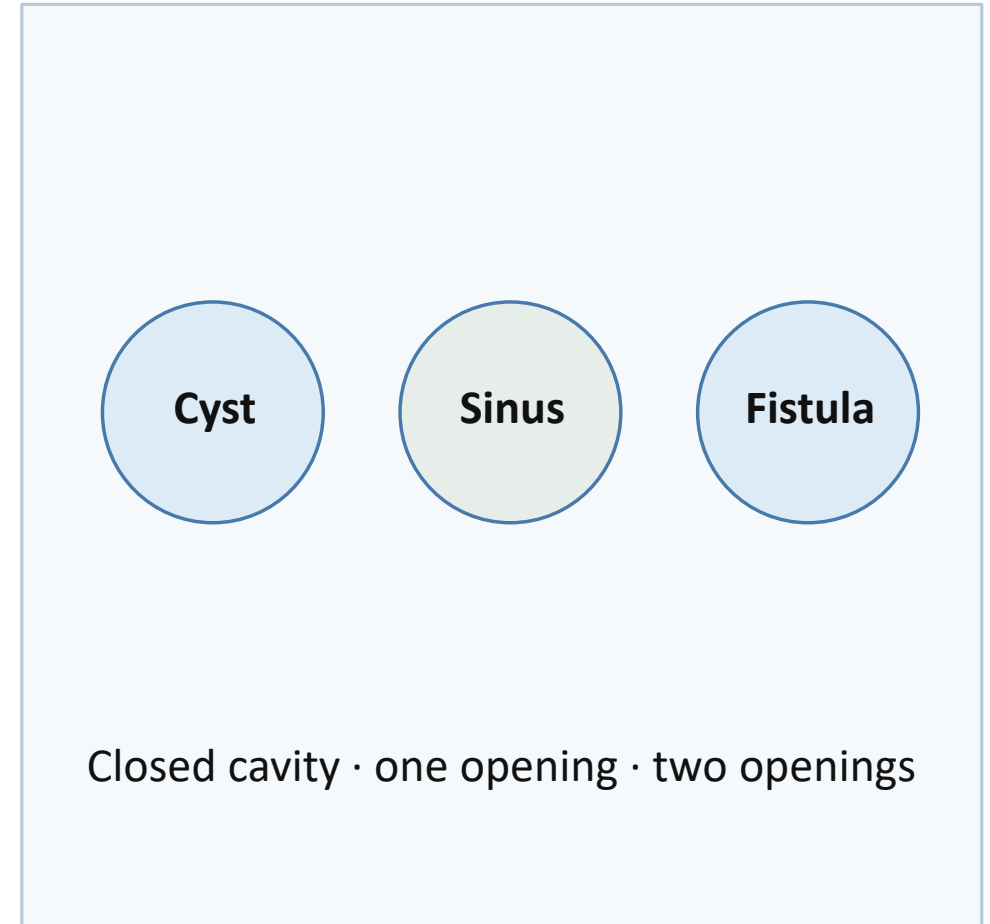
Branchial arch, cleft, and pouch are distinct

- Arches form supporting pharyngeal structures.
- Clefts or grooves are ectodermal externally.
- Pouches are endodermal internally;
Abnormal persistence can leave epithelial-lined lesions.



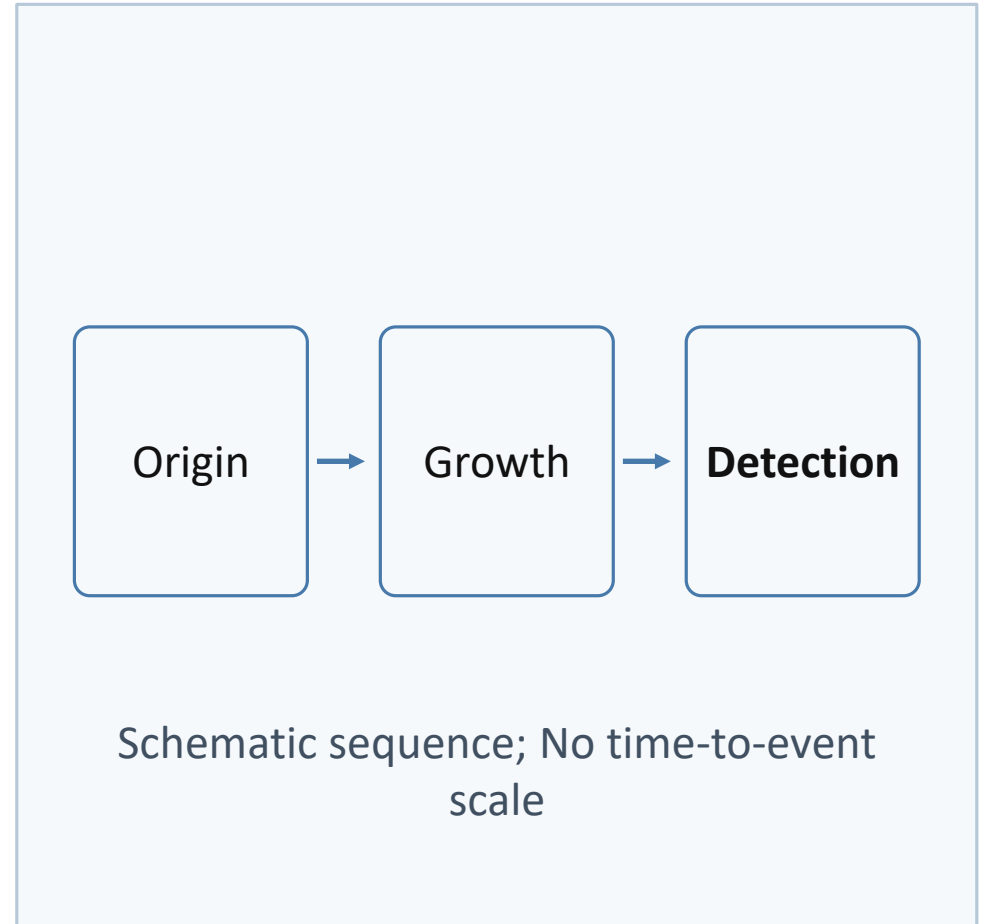
Cyst, sinus, and fistula: Different structures

- Cyst: A closed epithelial-lined space.
- Sinus: Tract with one opening.
- Fistula: Tract with two openings.



Why presentation can be delayed

- The developmental origin precedes clinical detection.
- A lesion can remain unnoticed while small.
- Progressive enlargement or inflammation can bring it to attention.



Usual age at presentation

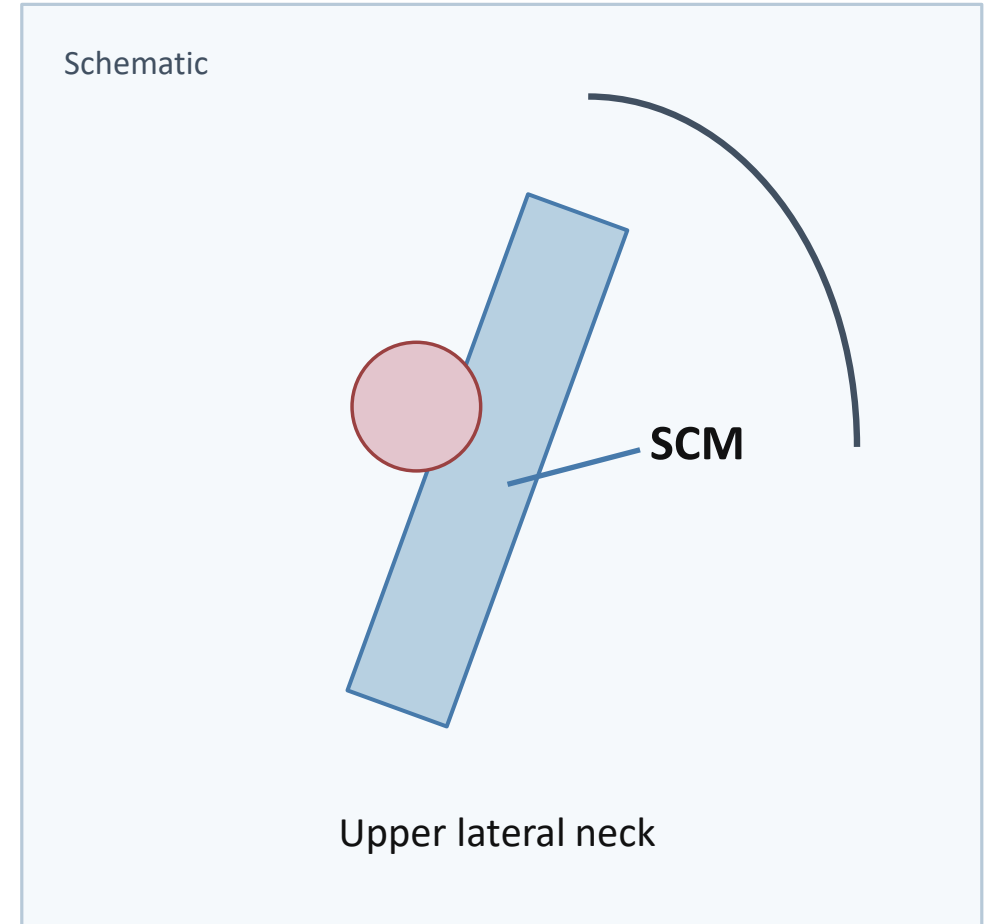
- Young adults aged 20–40 years.
- This is the common observed range, not an exclusion rule.
- Age must be interpreted with the rest of the examination.

20–40 years (common)

Age is contextual, not
exclusionary

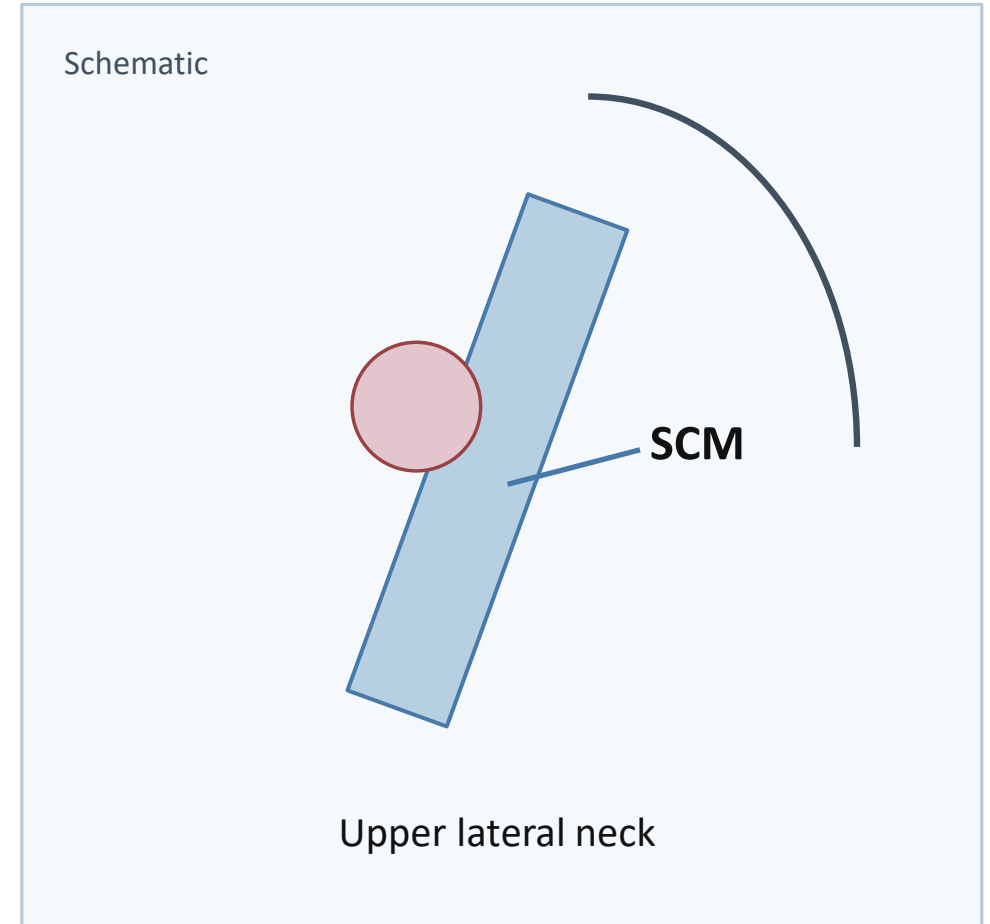
Usual site: Upper lateral neck

- Usually situated along the sternocleidomastoid muscle.
- The lesion commonly presents in the upper lateral neck.
- The site supports—but does not prove—a developmental diagnosis.



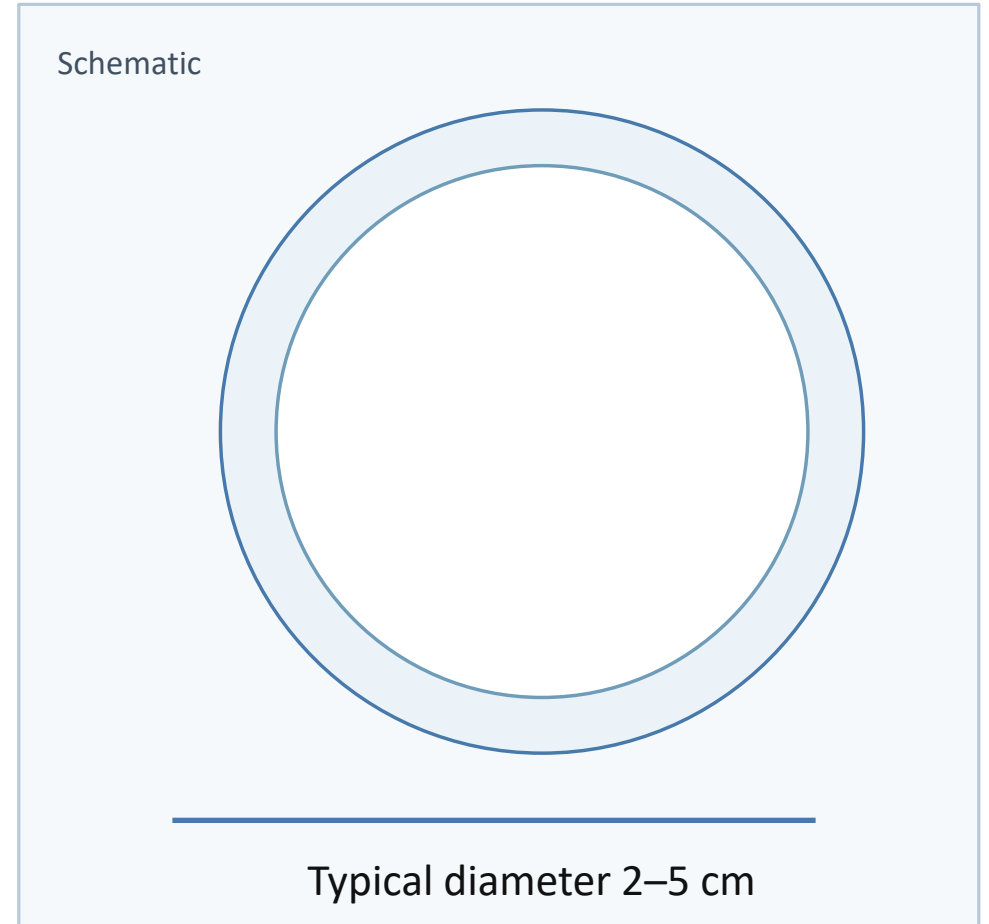
The sternocleidomastoid as a landmark

- The muscle is a practical surface landmark.
- Second-cleft-type lesions are often near its anterior border.
- Clinical examination still assesses adjacent nodes and other structures.



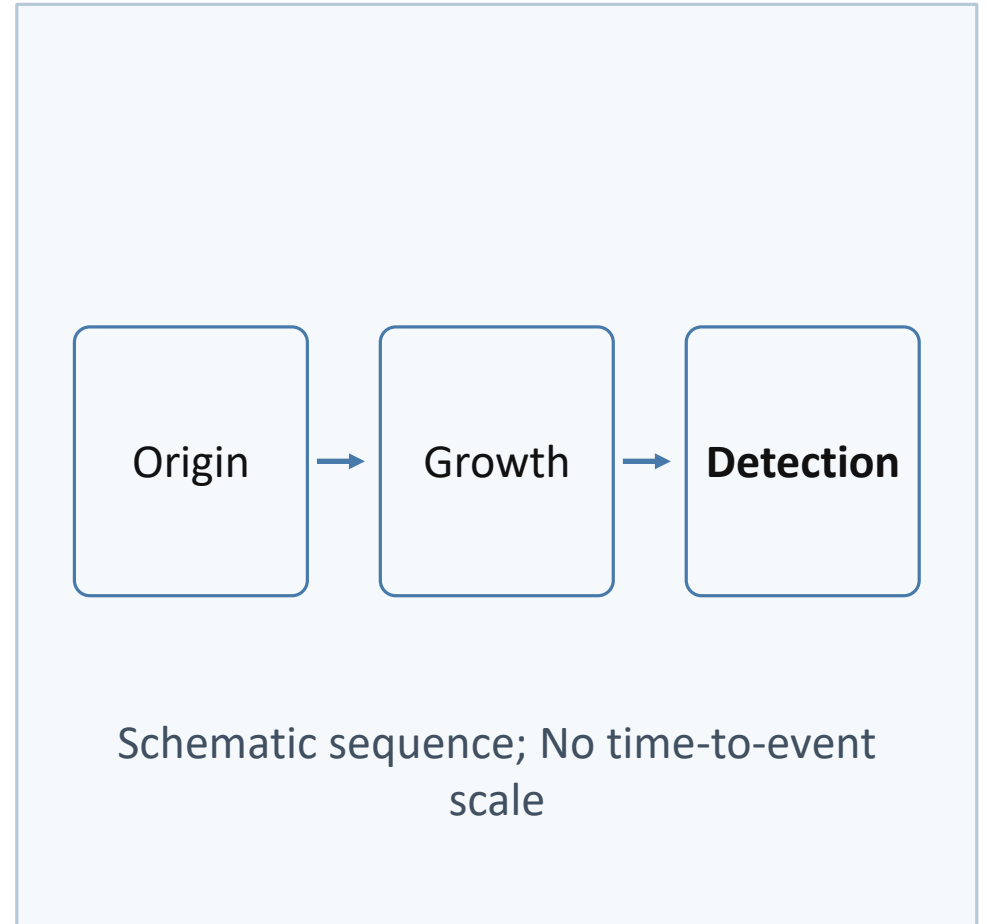
Typical size

- The reported usual diameter is 2–5 cm.
- The description concerns common morphology, not a strict diagnostic cutoff.
- Size alone does not determine biologic behavior.



Natural evolution: Gradual enlargement

- The cysts generally enlarge slowly.
- They are well circumscribed rather than infiltrative.
- A change in behavior warrants reassessment rather than assumption.



A typical clinical vignette

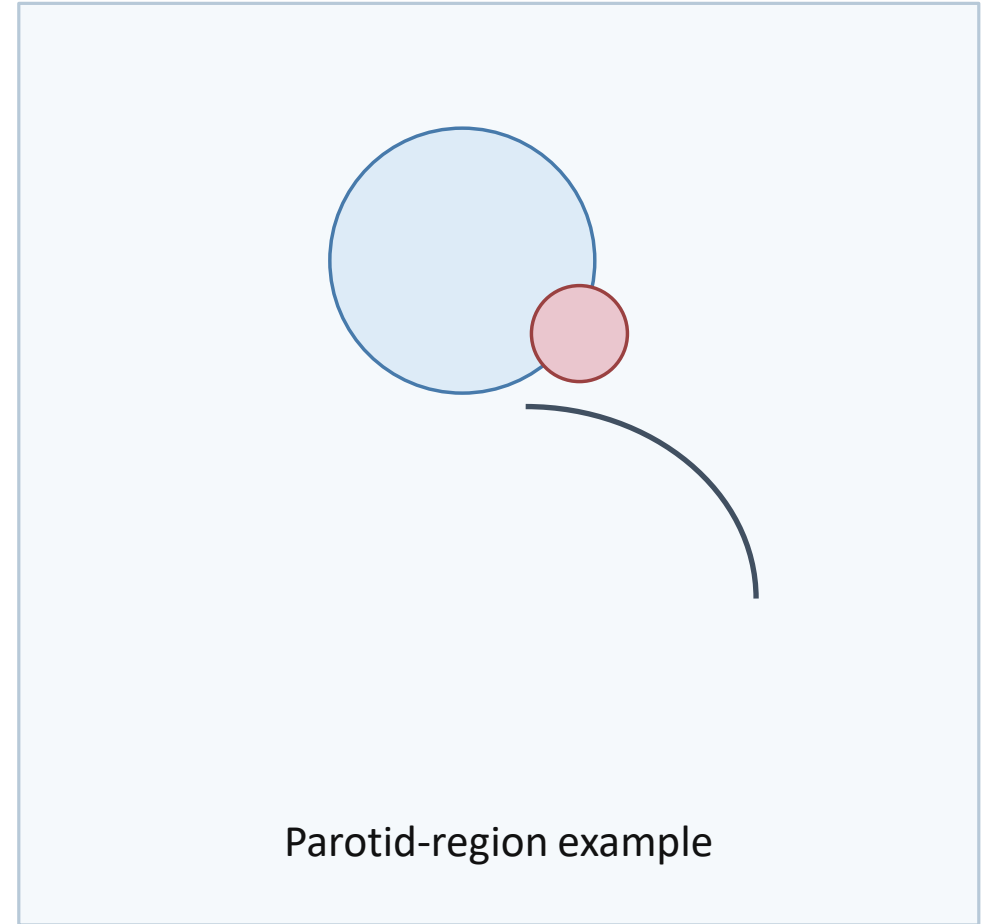
- Young adult with a slowly enlarging lateral neck swelling.
- Upper neck location along sternocleidomastoid.
- Imaging and tissue evaluation are individualized to the diagnostic concern.

Clinical problem

What finding changes
The interpretation?

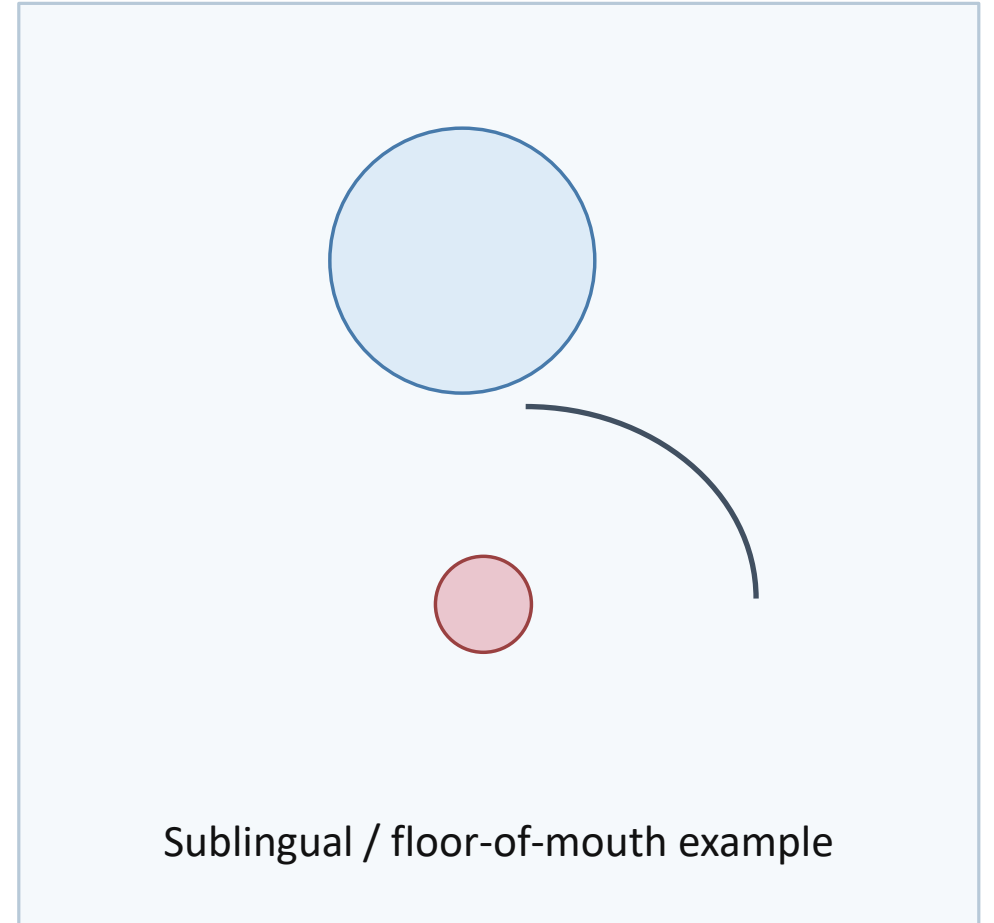
Unusual site: The parotid region

- Similar lymphoepithelial cystic lesions may occur in the parotid gland.
- The same epithelial–lymphoid organization may be relevant.
- A parotid mass has its own differential diagnosis.



Unusual site: Floor of the mouth

- Robbins also mentions the oral cavity beneath the tongue.
- Location changes the practical differential diagnosis.
- Morphology must be considered alongside the sampled anatomical compartment.



Why site and age are complementary

- A lateral site fits the classic pattern.
- Age helps set diagnostic suspicion.
- Neither variable alone can exclude cystic metastatic carcinoma.

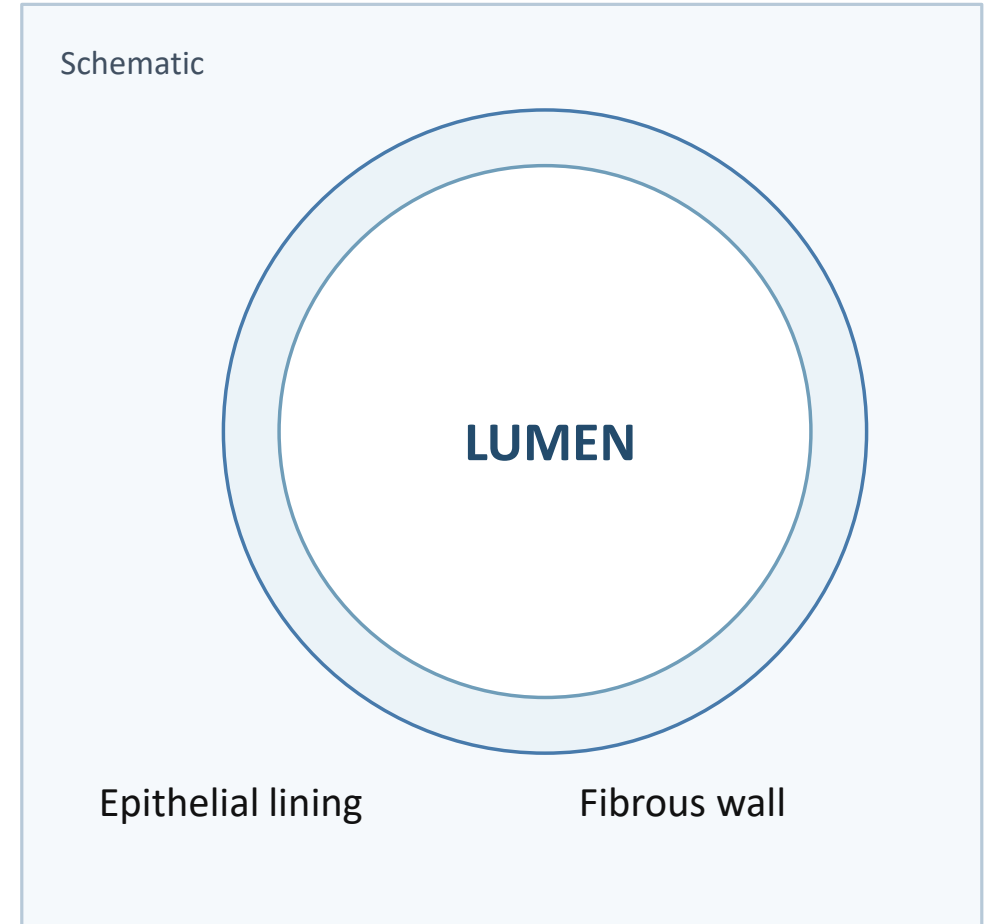
Pattern

Context

Compare evidence, not a single appearance

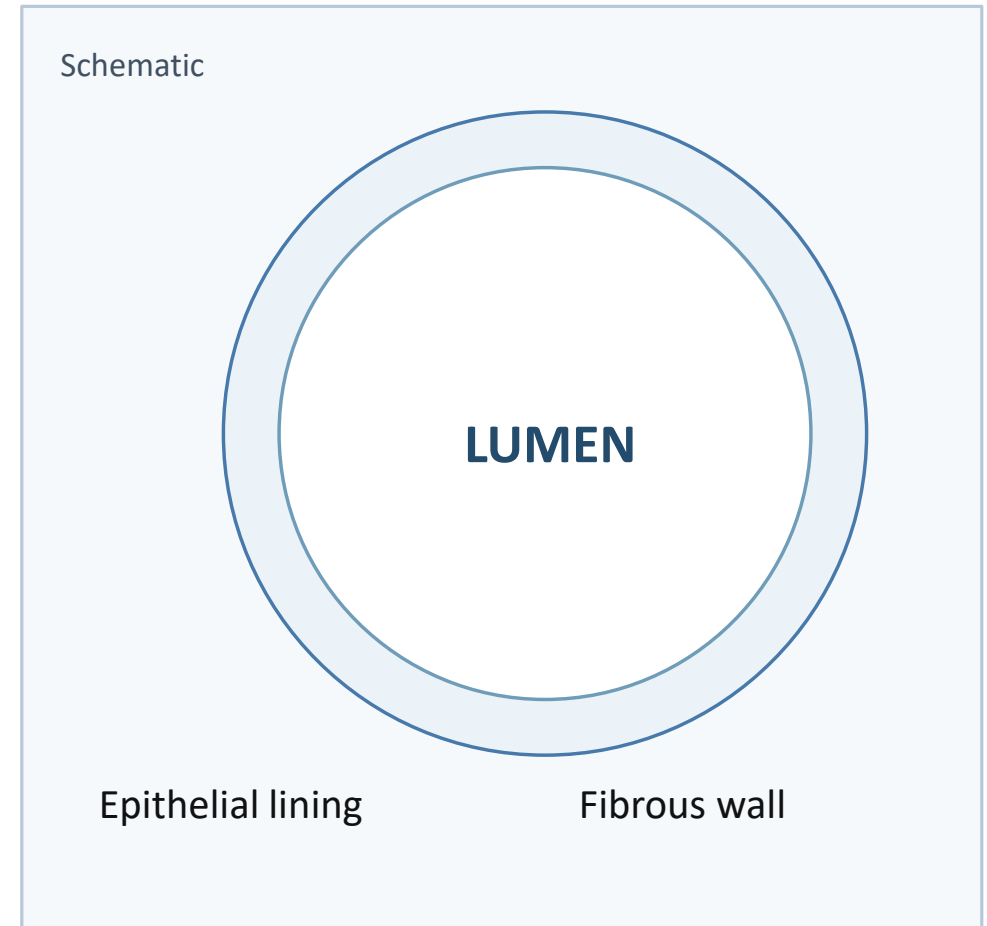
Gross appearance: Sharply defined cyst

- The lesion is typically well circumscribed.
- A cystic lumen is enclosed by a fibrous wall.
- The gross specimen is usually separable by excision.



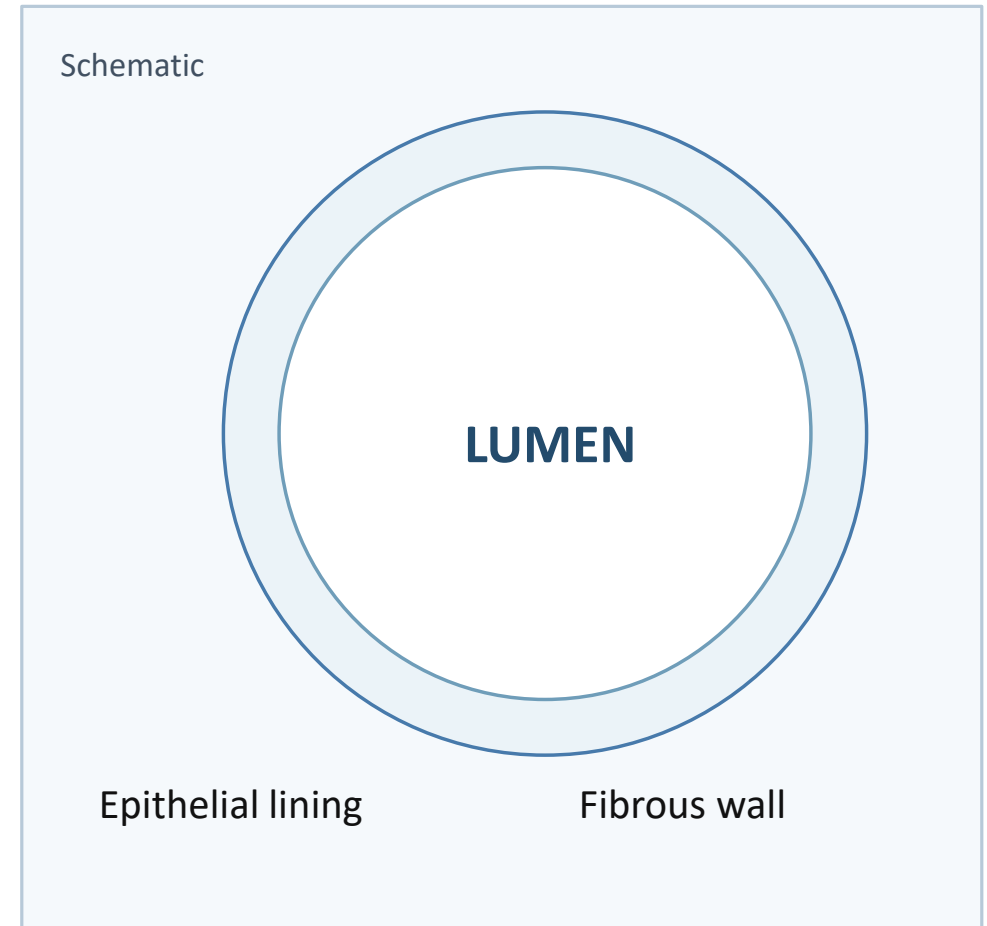
Cyst contents: Clear, watery fluid

- Watery contents are.
- The appearance of fluid varies between lesions.
- Fluid character alone cannot establish diagnosis.



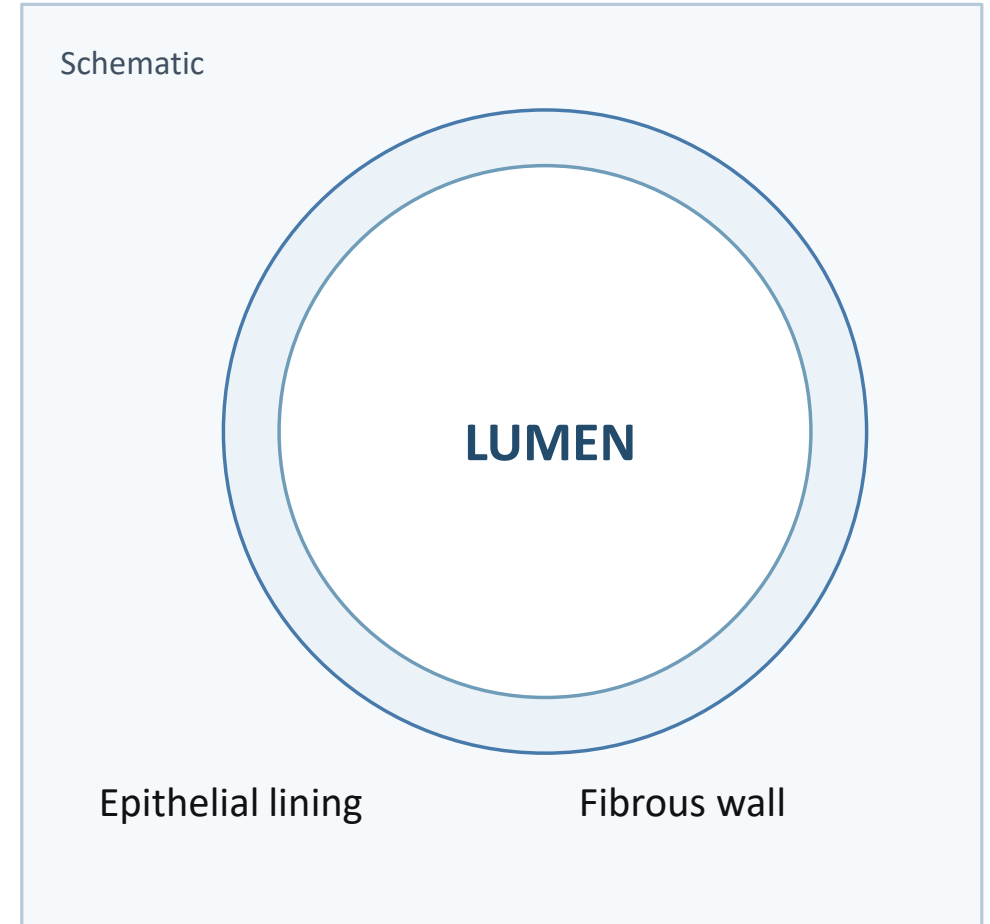
Cyst contents: Mucinous material

- Mucinous contents also occur.
- Columnar-type epithelium may contribute to the secretory phenotype.
- Content variation does not negate the diagnosis.



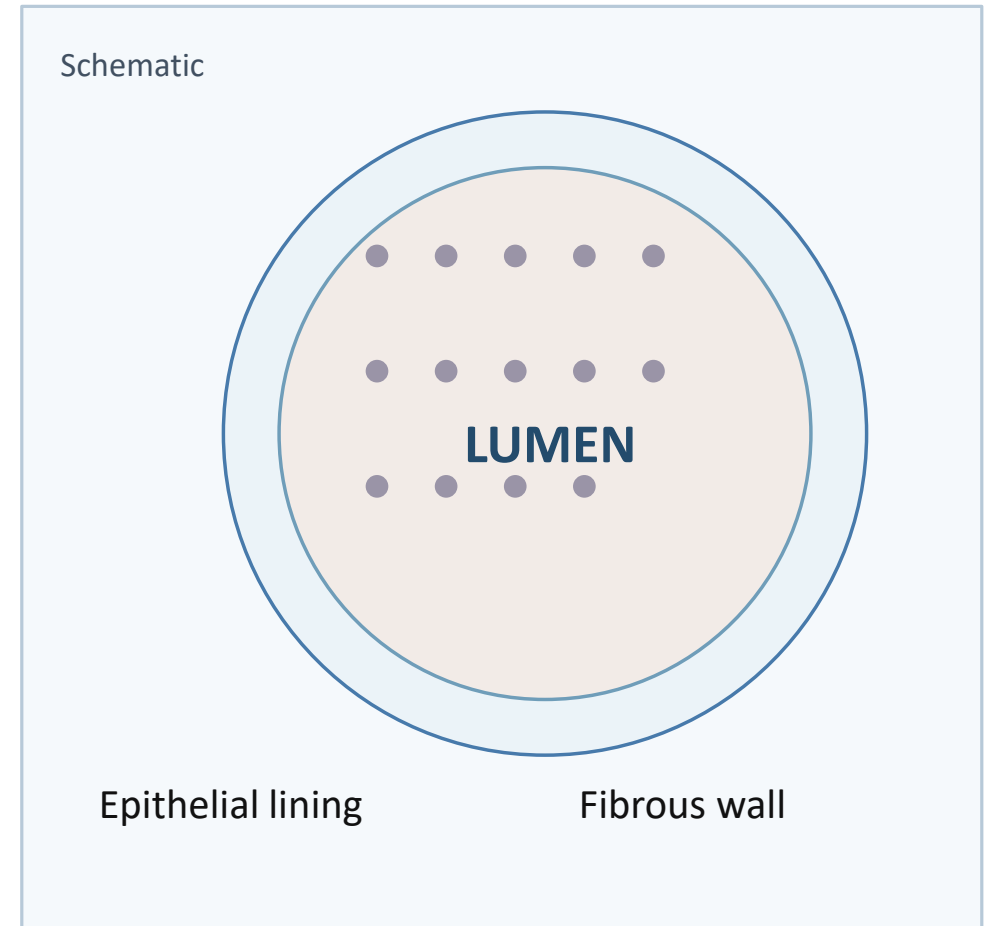
Cyst contents: Exfoliated cells

- Desquamated epithelial cells may accumulate within the lumen.
- These cells reflect turnover of the epithelial lining.
- Cytology can sample cellular debris rather than the entire wall.



Cyst contents: Granular debris

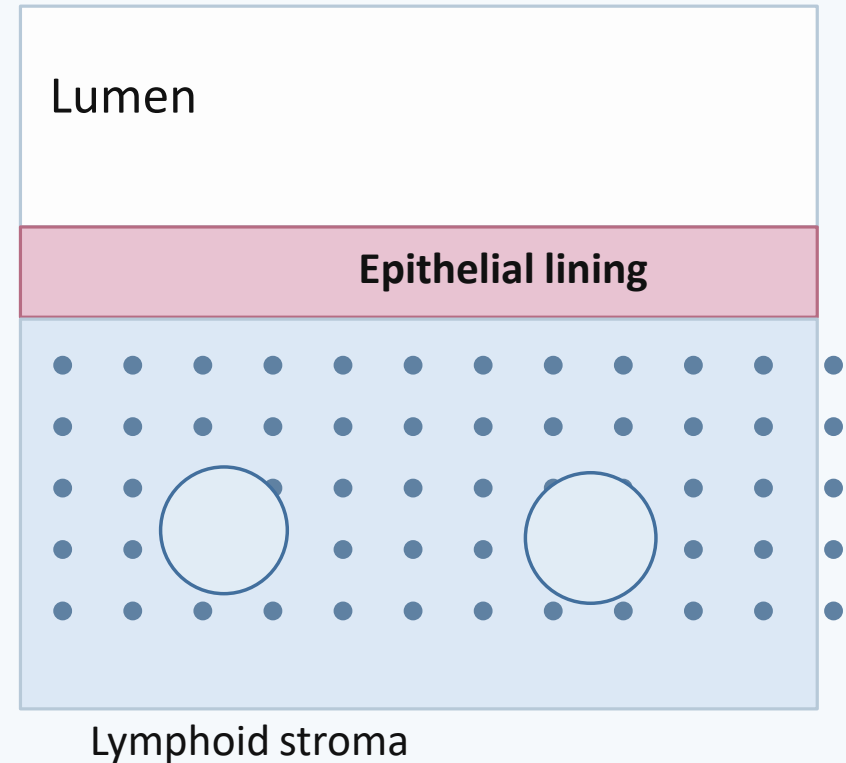
- Granular cellular debris is a documented component.
- It should not automatically be mistaken for tumor necrosis.
- Interpret debris in relation to lining and wall histology.



Two recognized epithelial linings

- Stratified squamous epithelium is common.
- Pseudostratified columnar epithelium is also described.
- The cyst wall is not defined by one lining subtype alone.

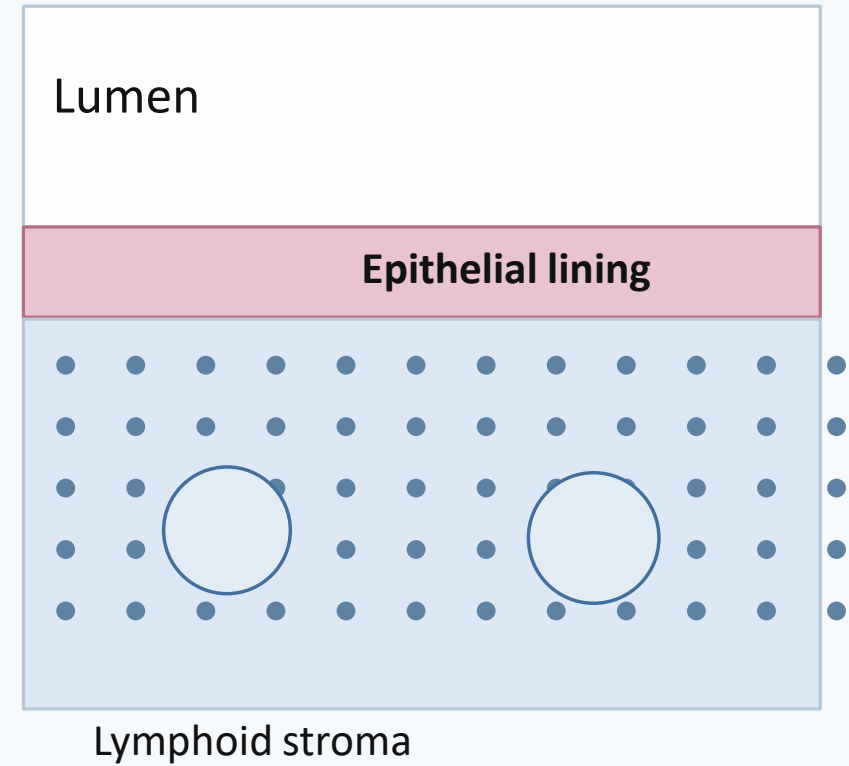
Histology schematic — not a micrograph



Squamous-lined branchial cyst

- Identify a stratified epithelial lining at the luminal surface.
- Assess epithelial maturation and absence of malignant cytology.
- Look immediately outside the lining for lymphoid tissue.

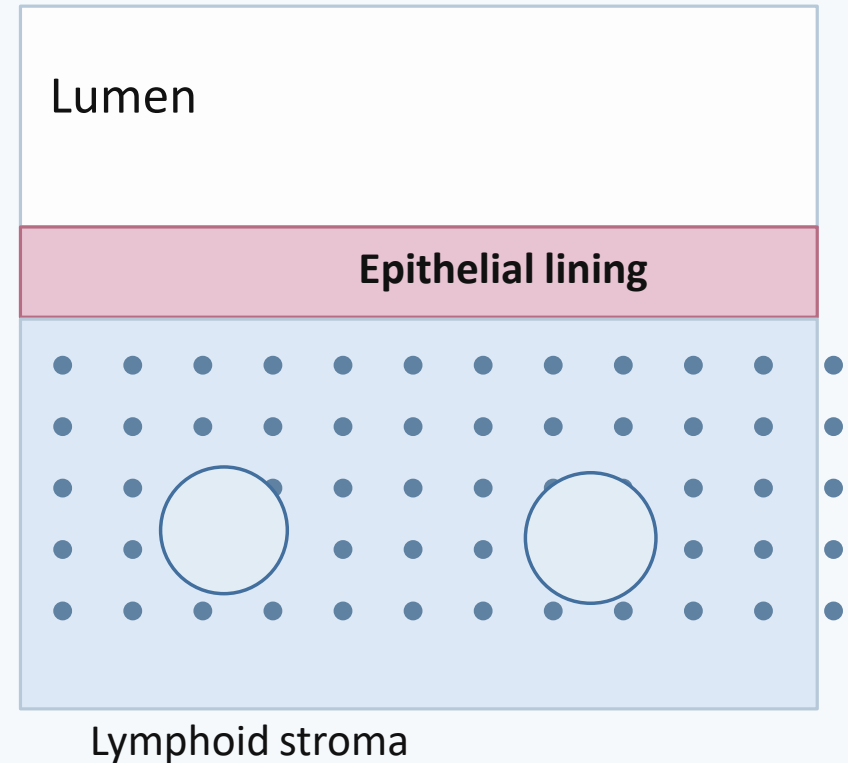
Histology schematic — not a micrograph



Pseudostratified columnar-lined cyst

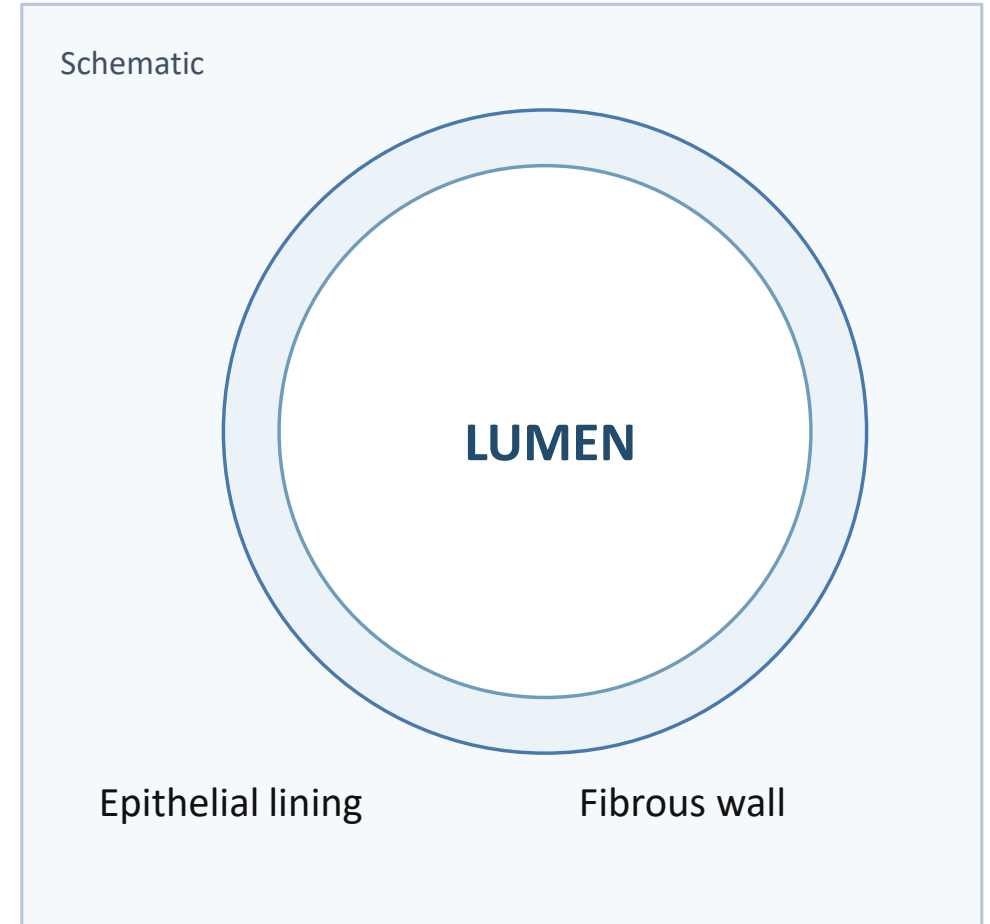
- An alternate lining can be pseudostratified columnar epithelium.
- This variation must be distinguished from the hallmark lymphoid stroma.
- Do not reject a diagnosis solely for a nonsquamous lining.

Histology schematic — not a micrograph



The fibrous capsule forms the outer wall

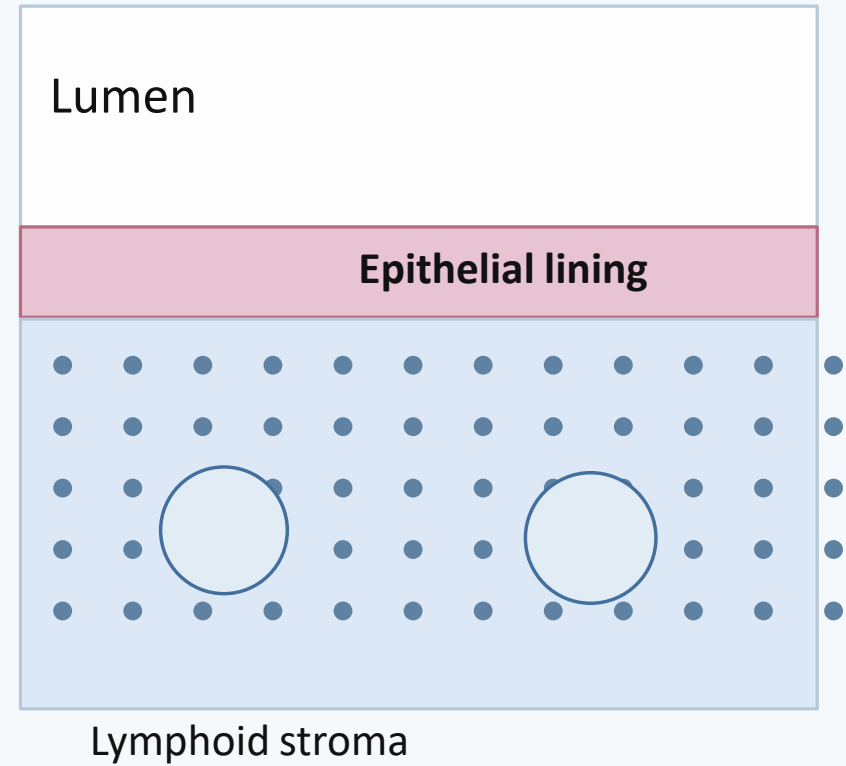
- The epithelial lining rests within a fibrous cyst wall.
- Fibrosis defines the cavity and encloses stromal elements.
- The wall provides critical diagnostic context beyond free cyst fluid.



Lymphoid tissue is characteristic

- The fibrous wall usually contains lymphoid tissue.
- Lymphoid tissue is not synonymous with a metastatic lymph node.
- Evaluate the architecture and epithelial component together.

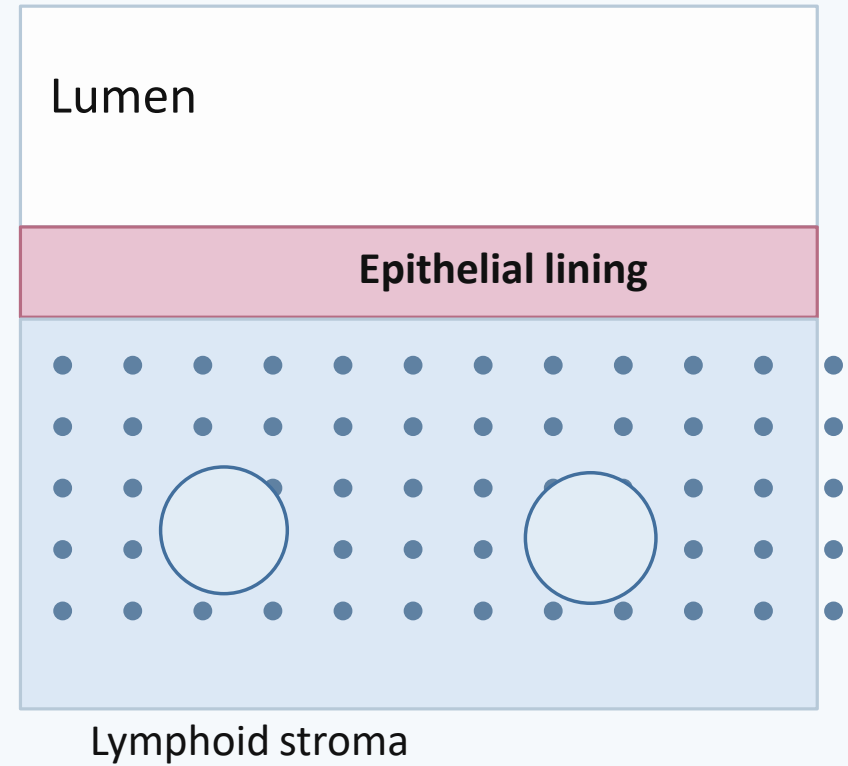
Histology schematic — not a micrograph



Germinal centers are a high-yield clue

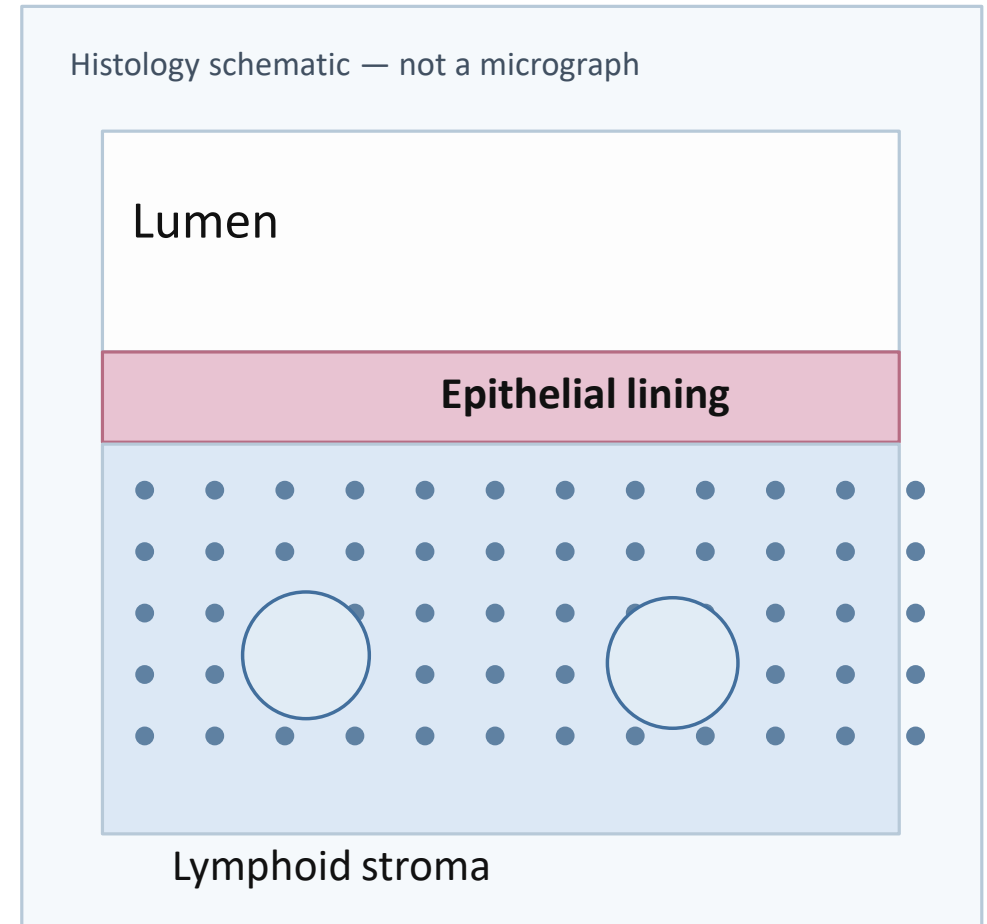
- Prominent germinal centers can be present within lymphoid aggregates.
- Their presence is consistent with reactive lymphoid architecture.
- A bland epithelial lining plus follicles supports the pattern.

Histology schematic — not a micrograph



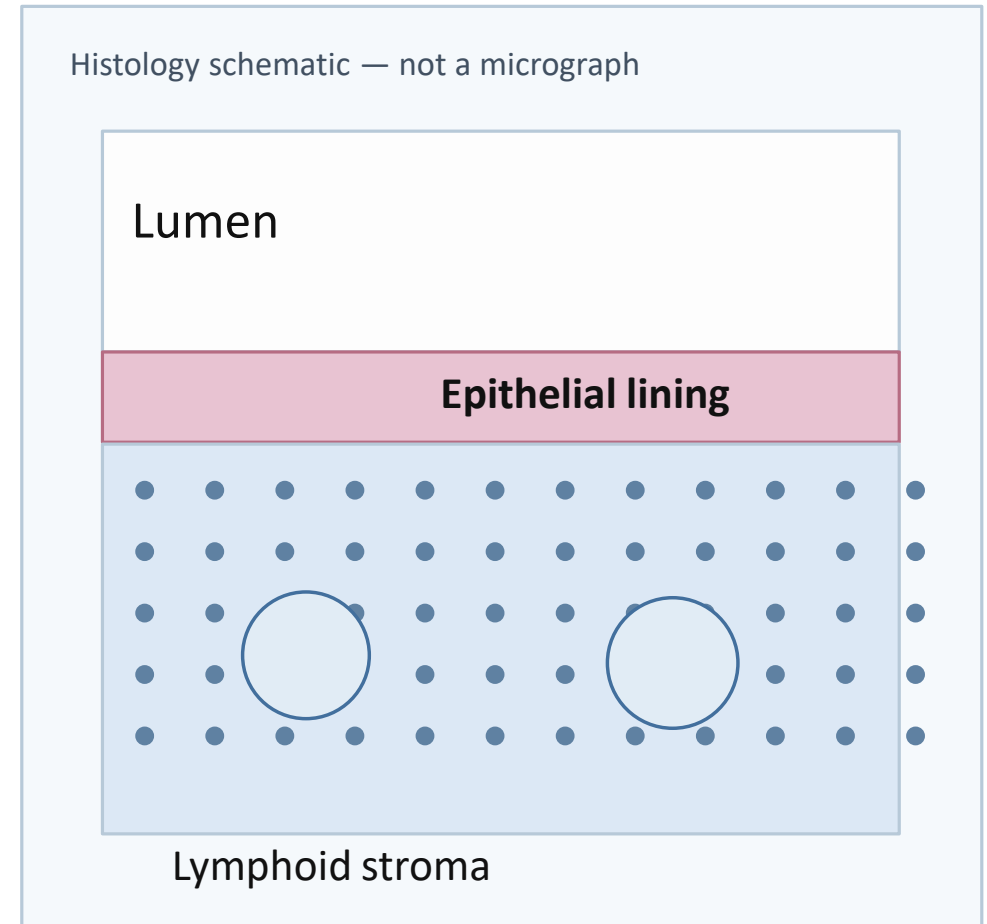
Reconstruct the low-power histologic pattern

- Cystic lumen → epithelial lining → fibrous wall.
- Lymphoid follicles appear within the wall.
- Low-power architecture should be established before cytologic detail.



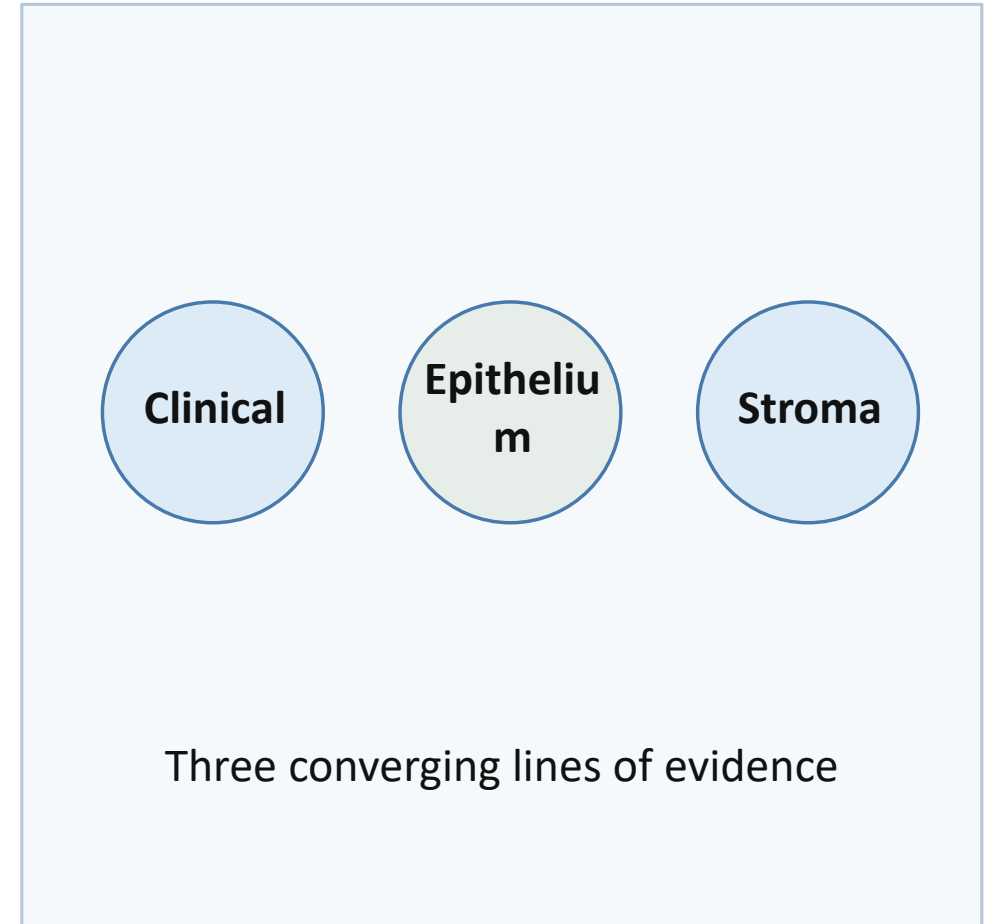
High-power examination: Epithelial blandness

- Review the lining for orderly maturation and cytologic atypia.
- Bland epithelium fits a non-neoplastic cyst.
- Disordered atypical epithelium requires a wider differential.



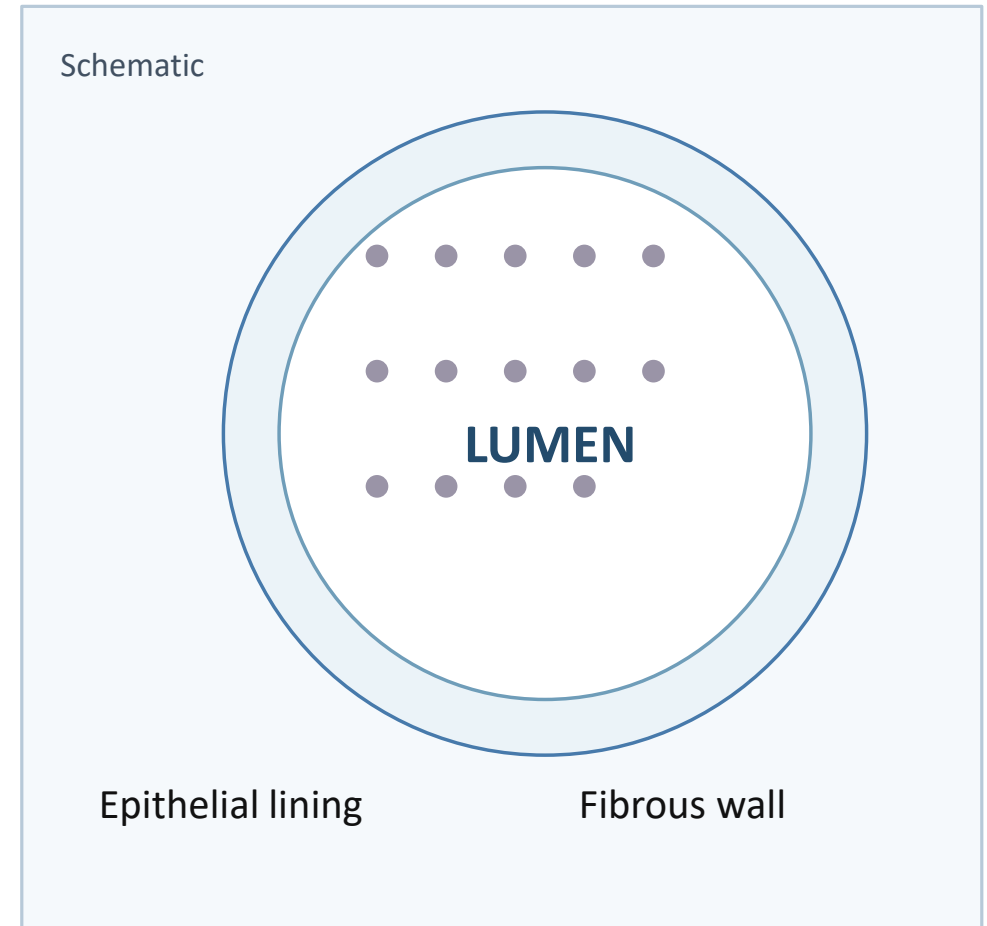
A complete histologic diagnosis is integrated

- Anatomic site and age provide clinical context.
- Lining type identifies the epithelial component.
- Lymphoid-rich fibrous wall supplies the key morphologic correlation.



Diagnostic pitfall: Cyst fluid is incomplete

- Luminal material may contain mainly keratinous or cellular debris.
- Aspirates may underrepresent the cyst wall.
- An indeterminate sample should not generate false reassurance.



Textbook comparison: Thyroglossal duct cyst

- Thyroglossal cyst originates from the thyroid descent pathway.
- It favors the anterior midline rather than the upper lateral neck.
- Its wall may contain thyroid remnants.

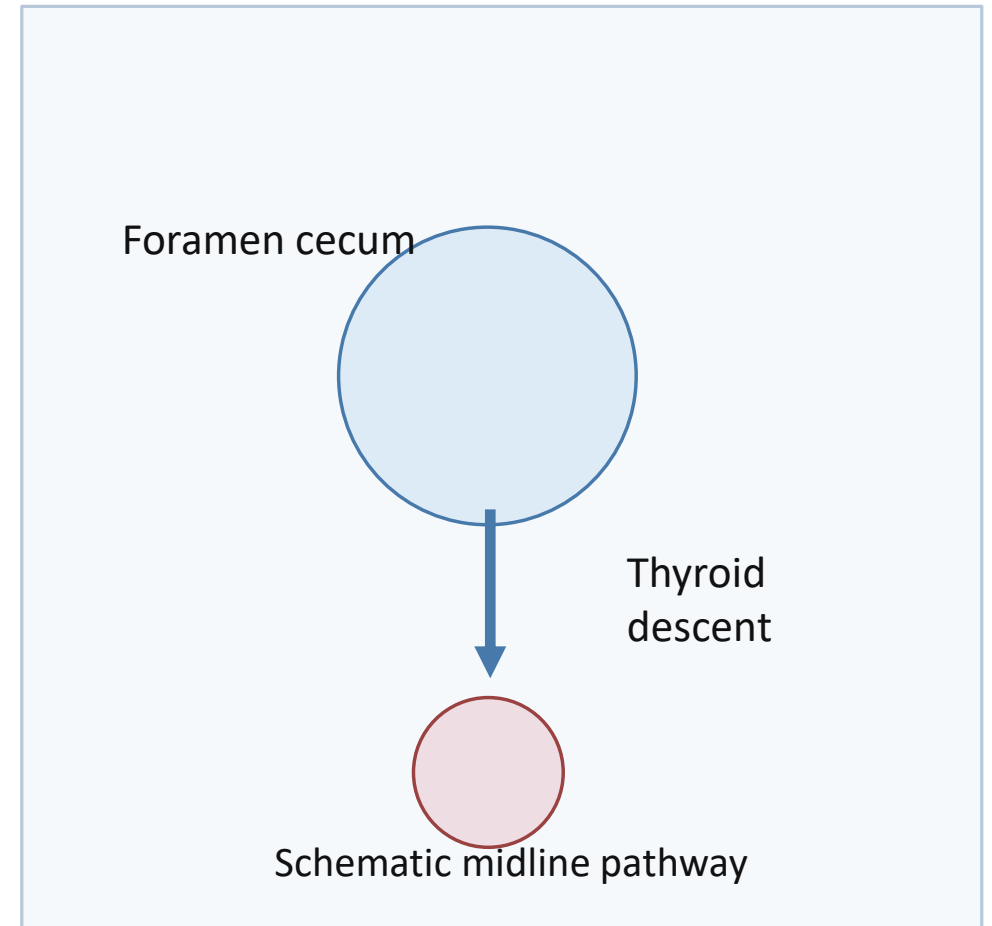
Branchial

Thyroglossal

Compare evidence, not a single appearance

Embryology explains the midline comparator

- The thyroid develops near the foramen cecum.
- It descends to the anterior neck.
- Persistence of that tract creates a thyroglossal duct cyst.



Compare cyst-wall components

- Branchial cyst: Lymphoid tissue with germinal centers is typical.
- Thyroglossal cyst: Thyroid follicles/remnants may occur.
- Both lesions can have squamous or columnar-type linings.

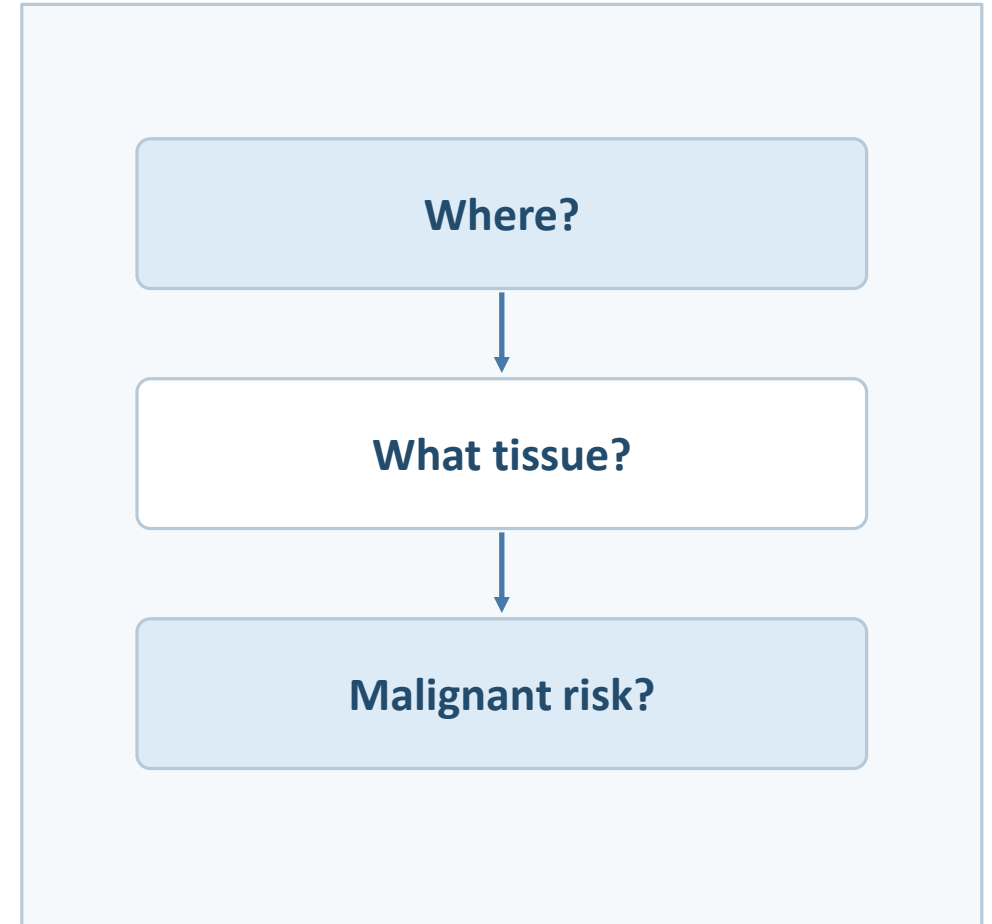
Branchial

Thyroglossal

Compare evidence, not a single appearance

Cystic neck lesions: A structured differential

- Developmental epithelial cyst.
- Cystic or necrotic lymph node, including metastatic carcinoma.
- Other cystic soft-tissue or salivary lesions according to site.



Branchial cysts are generally benign

- The entity as a benign lesion.
- They usually do not undergo malignant transformation.
- Benign nature cannot be presumed before correct classification.

Benign cyst

**Metastatic
SCC**

Compare evidence, not a single appearance

Primary “branchiogenic carcinoma” is problematic

- A carcinoma arising in a true branchial cyst is exceptional and contested.
- An apparent cystic neck carcinoma more often represents metastasis.
- Search for an upper aerodigestive primary when appropriate.

Cystic mass

**Diagnostic
risk**

Compare evidence, not a single appearance

The crucial mimic: Cystic metastatic SCC

- Most cystic squamous carcinomas of the neck are metastatic.
- Upper aerodigestive tract primaries must be considered.
- An apparently smooth-walled cyst does not exclude malignancy.

Benign cyst

**Metastatic
SCC**

Compare evidence, not a single appearance

Clinical extension: Evidence-based adult evaluation

- A persistent adult neck mass may be malignant.
- Risk is assessed with history, examination, and appropriate testing.
- The 2017 AAO-HNS guideline addresses this diagnostic pathway.

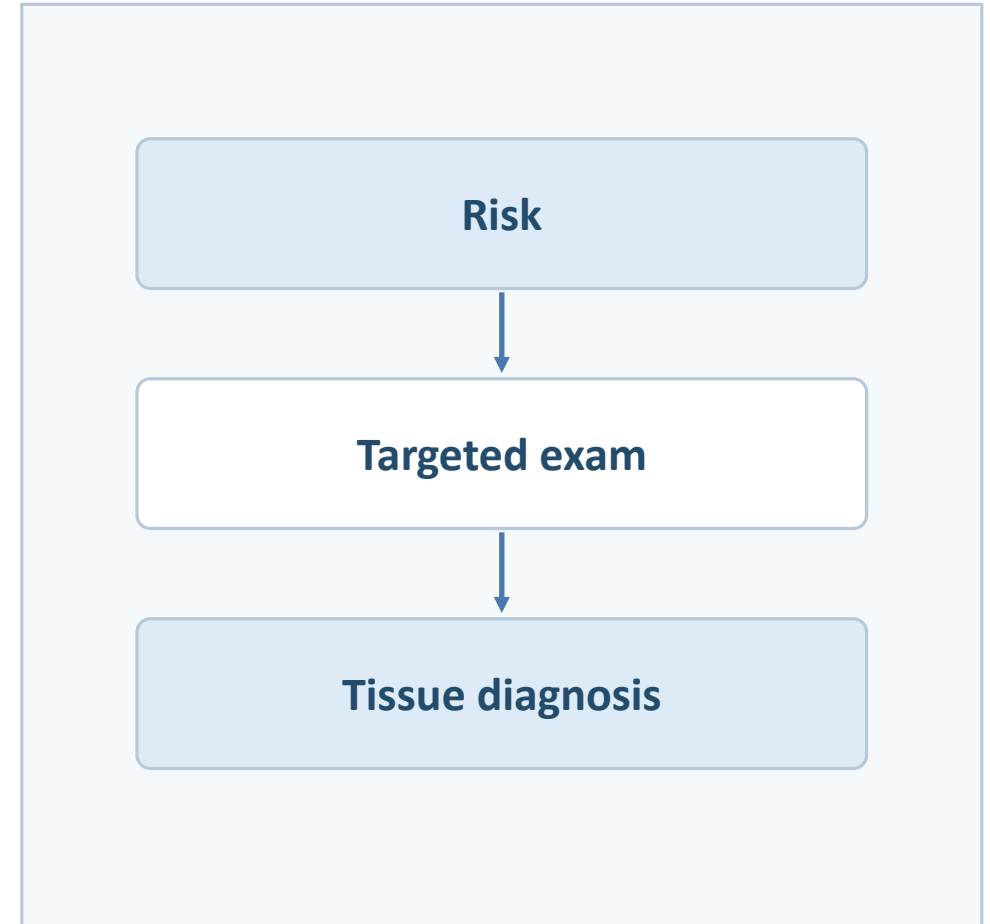
Cystic mass

**Diagnostic
risk**

Compare evidence, not a single appearance

Adult risk assessment comes before reassurance

- Assess duration, growth, symptoms, and physical findings.
- Determine whether the patient is at increased risk for malignancy.
- Avoid routine reassurance from cystic texture or imaging alone.



Targeted mucosal examination

- Examine the pharynx, base of tongue, and laryngeal mucosa in at-risk adults.
- An occult primary can produce the first visible neck finding.
- Refer for a targeted specialist examination when indicated.

Base of tongue

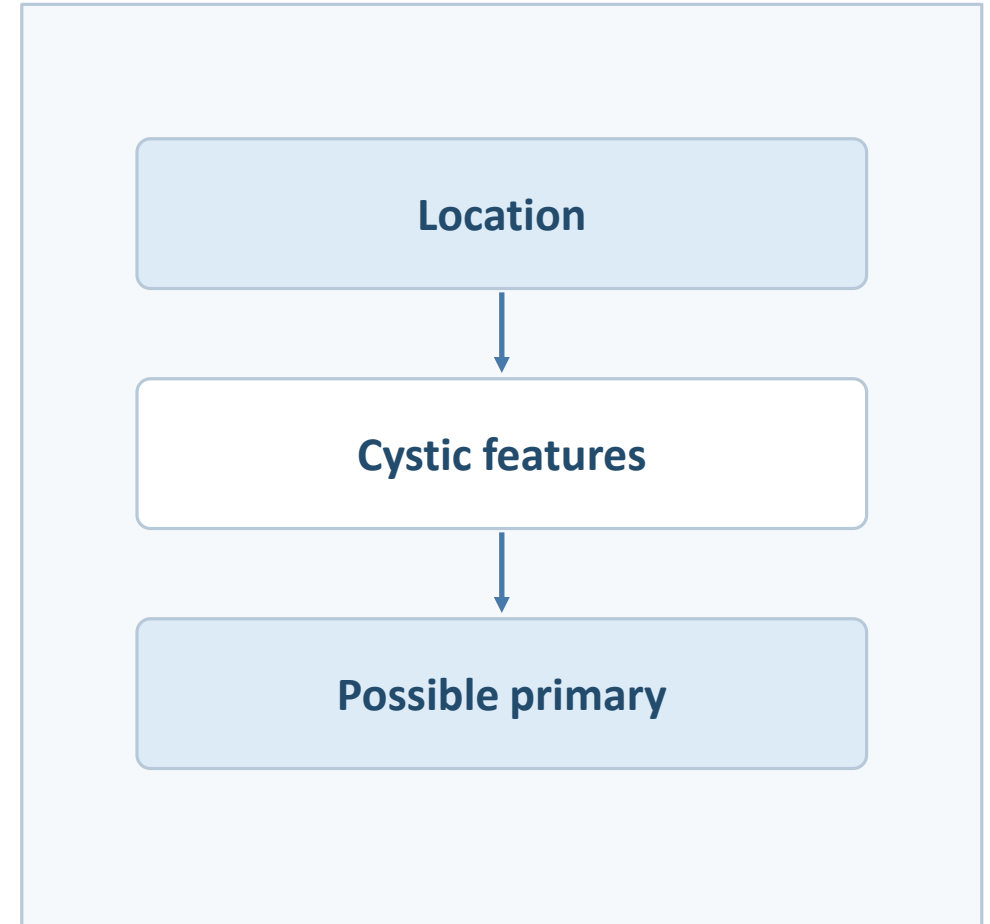
Pharynx

Larynx

Targets of specialist mucosal examination

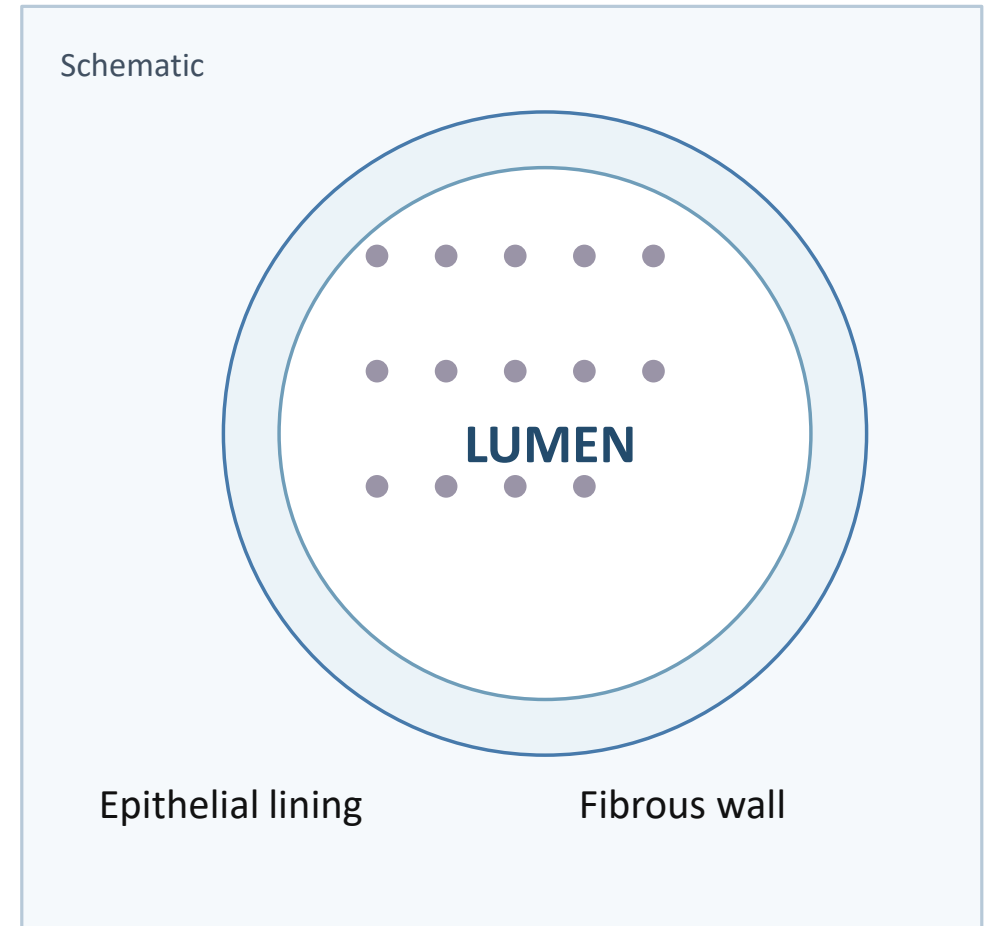
Cross-sectional imaging in an at-risk adult

- Contrast-enhanced CT or MRI is recommended for a higher-risk adult mass.
- Imaging assesses anatomy and guides further evaluation.
- A cystic imaging phenotype alone is not diagnostic of benignity.



Fine-needle aspiration is favored initially

- For an at-risk adult with uncertain diagnosis, use FNA rather than open biopsy.
- Results require interpretation with imaging and clinical findings.
- Insufficient fluid-only sampling does not settle the question.



The special rule for a cystic adult neck mass

- Continue evaluation until a diagnosis is established.
- Do not assume a benign branchial cyst solely because imaging shows a cyst.
- The guideline treats cystic morphology as a potential pitfall.

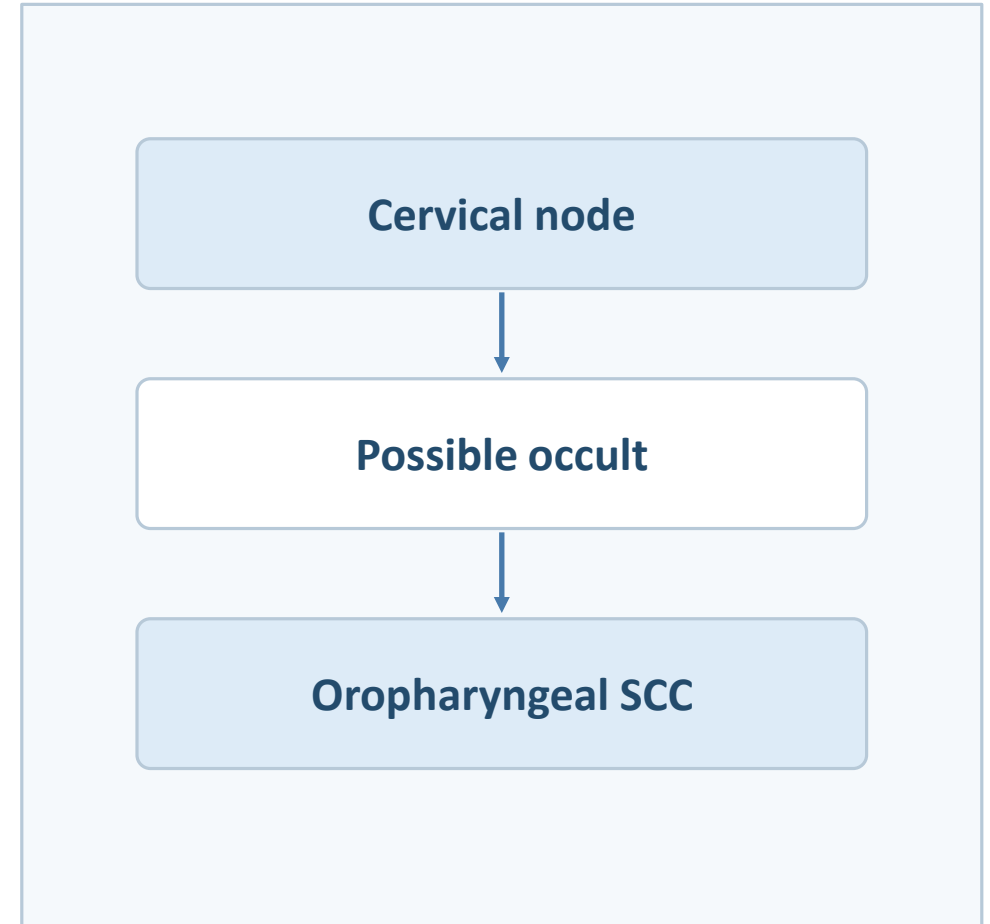
Cystic mass

**Diagnostic
risk**

Compare evidence, not a single appearance

Why HPV-related carcinoma enters the differential

- Oropharyngeal SCC can metastasize to cervical lymph nodes.
- Some metastases have a predominantly cystic presentation.
- The tonsil and base of tongue are clinically relevant primary sites.



Morphologic distinction: Bland versus atypical

- Branchial cyst: Orderly, bland epithelial lining within lymphoid wall.
- Metastatic SCC: Malignant squamous cytology may be focal or subtle in cystic samples.
- Adequate sampling and clinical work-up remain essential.

Bland lining

**Malignant
cells**

Compare evidence, not a single appearance

P16 immunostaining has diagnostic limits

- P16 is often diffuse/strong in HPV-associated oropharyngeal SCC.
- Benign branchial cyst epithelium can also show limited p16 reactivity.
- P16 alone must not be treated as an infallible classifier.

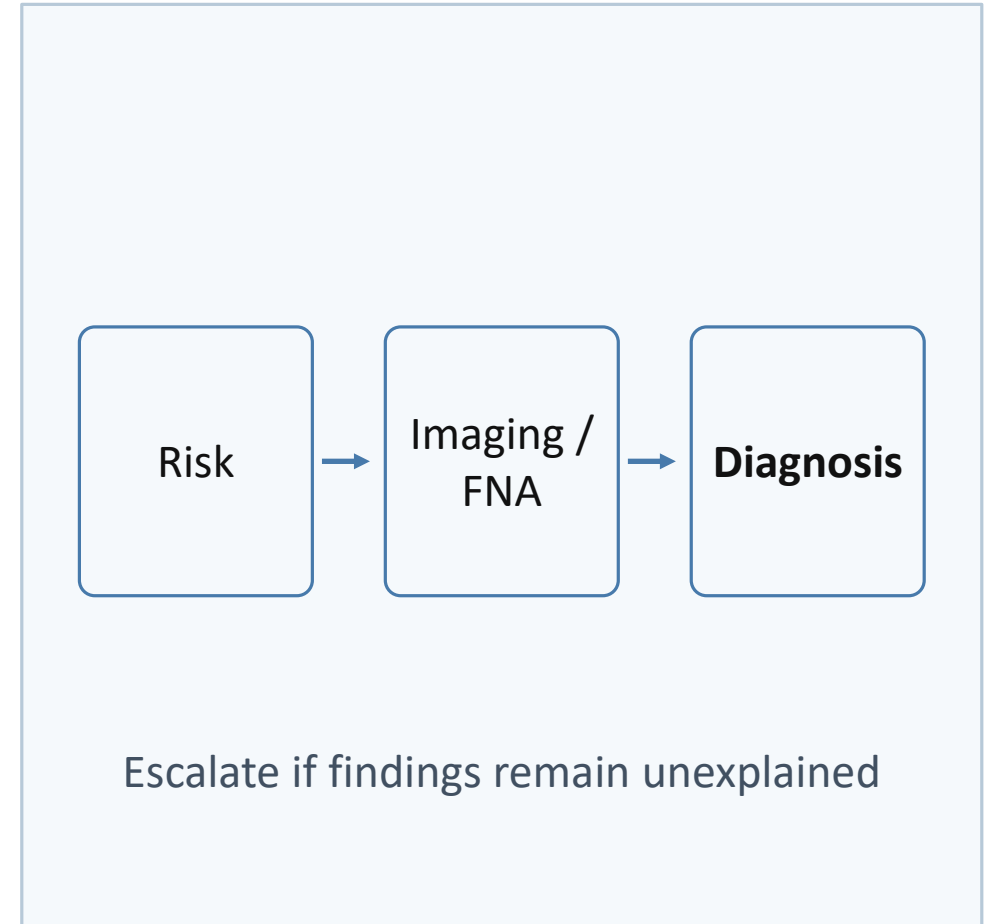
P16 pattern

HPV evidence

Compare evidence, not a single appearance

HPV-specific testing can resolve uncertainty

- WHO 5th-edition review recommends HPV-specific assessment where indicated.
- High-risk HPV RNA ISH or validated molecular tests may support origin.
- Interpret results alongside epithelial morphology and clinical findings.



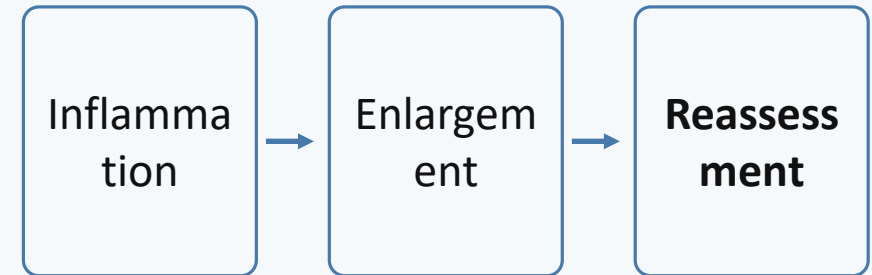
A multidisciplinary diagnostic sequence

- Identify increased clinical risk.
- Use targeted examination, imaging, and tissue sampling.
- Escalate an unresolved or discordant cystic mass.



Inflammation may change the presentation

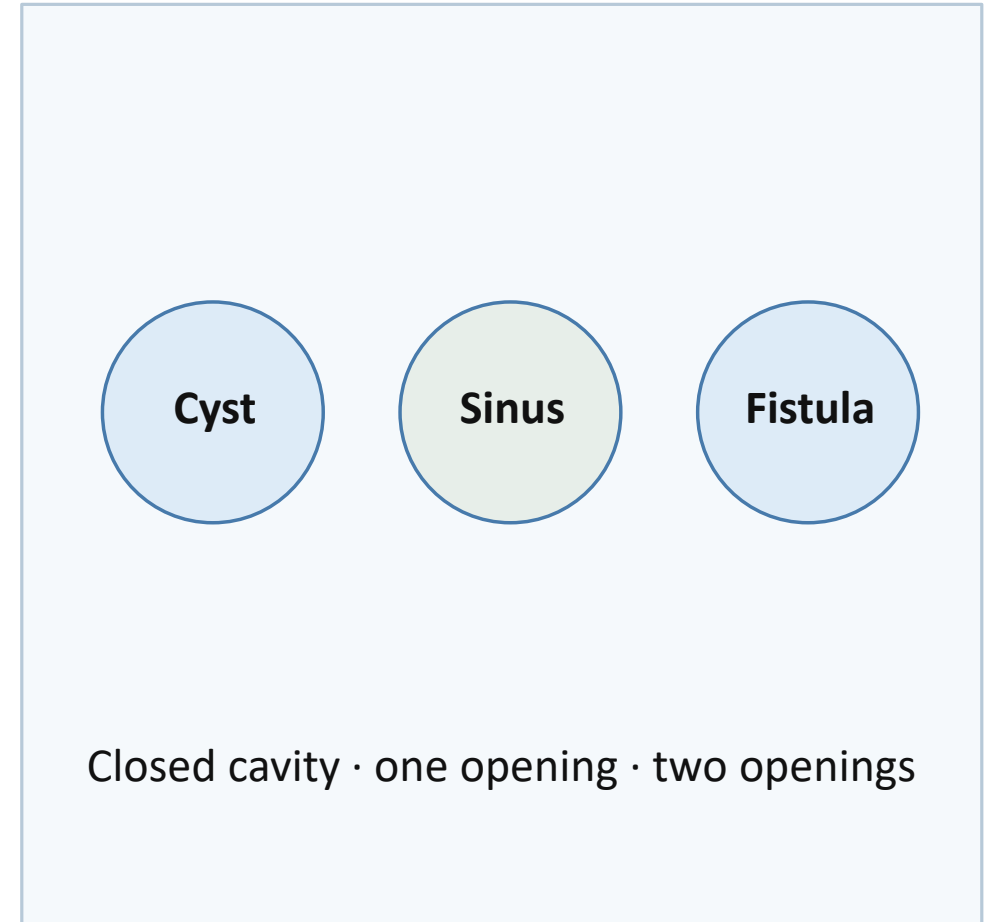
- Branchial cleft anomalies may become infected.
- Acute inflammation can cause pain, tenderness, or rapid enlargement.
- Reassess the underlying lesion after treating infection.



Schematic sequence; No time-to-event scale

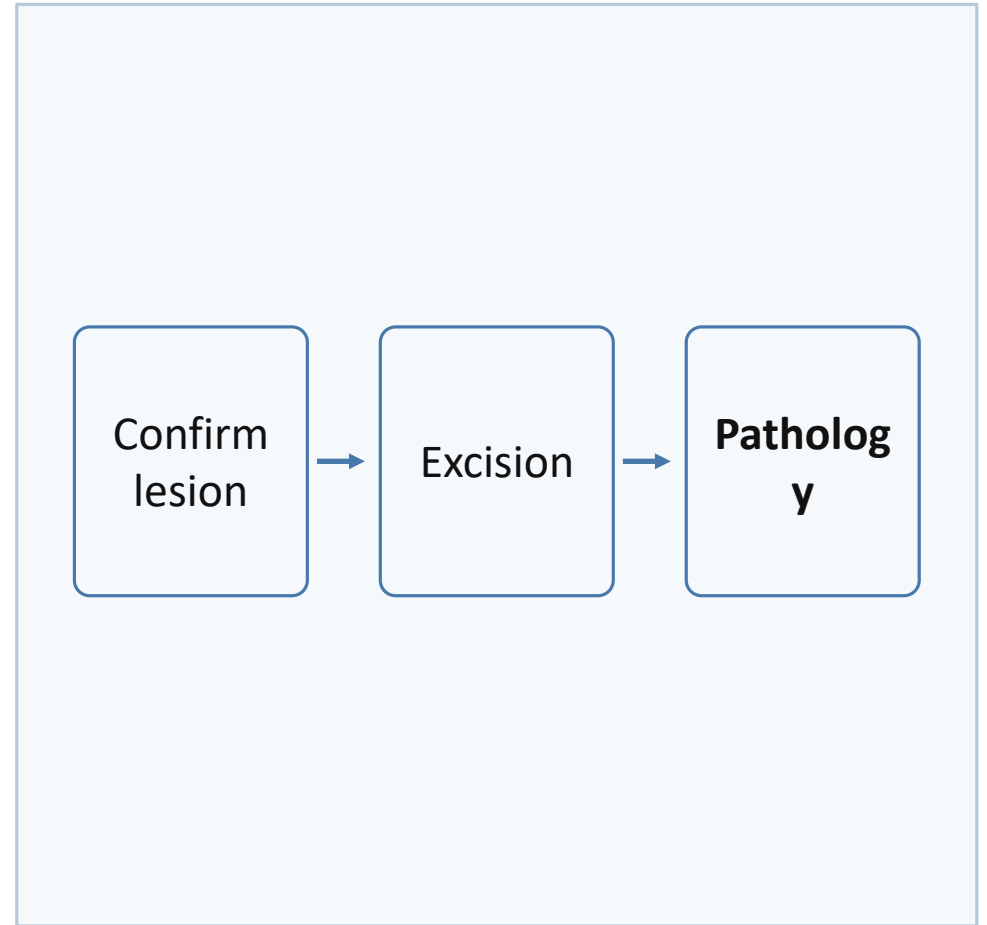
Complications affect management

- Secondary infection or abscess may require prompt care.
- Persistent tracts may lead to recurrent drainage or infection.
- Treatment planning should address the entire anomaly.



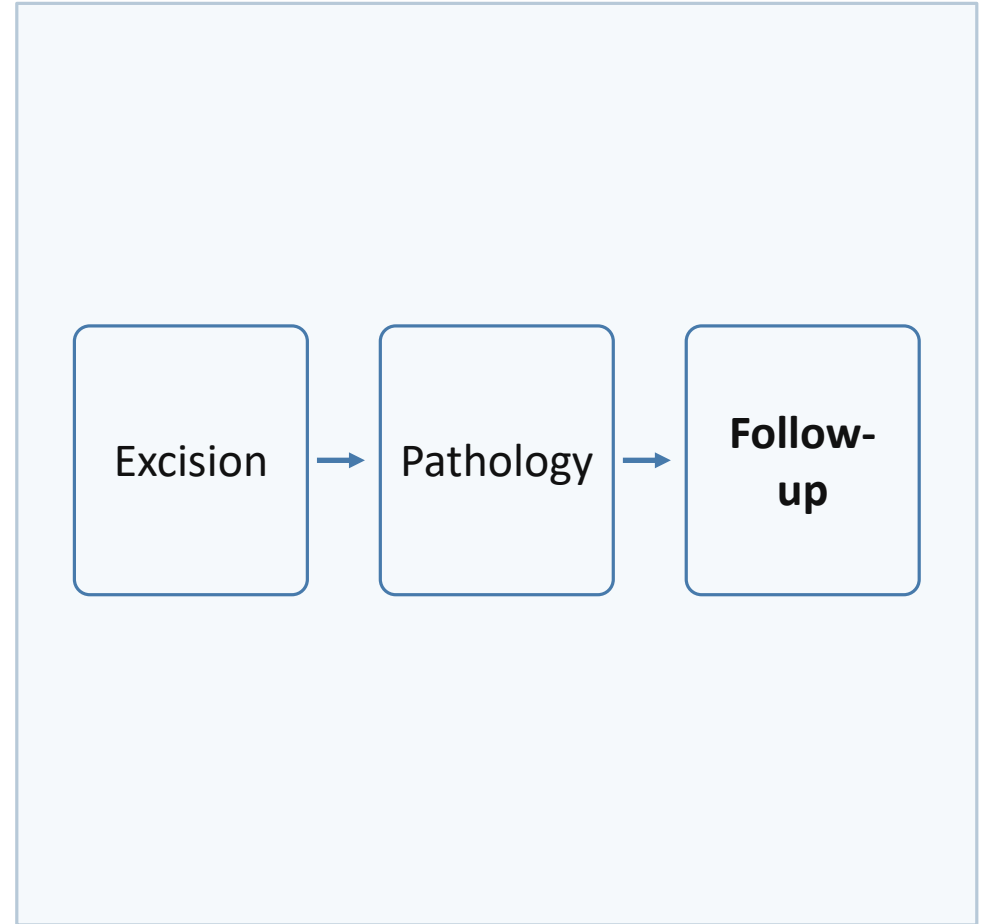
Excision is definitive for a confirmed cyst

- These lesions are readily excised.
- Complete removal treats the benign cyst.
- Exclude a malignant mimic before treating a suspicious adult mass as a simple cyst.



The importance of complete removal

- Complete surgical excision generally has excellent outcomes.
- Residual epithelial elements or associated tracts can predispose to recurrence.
- Pathologic examination documents the final diagnosis.



Case 1: Classical clinical pattern

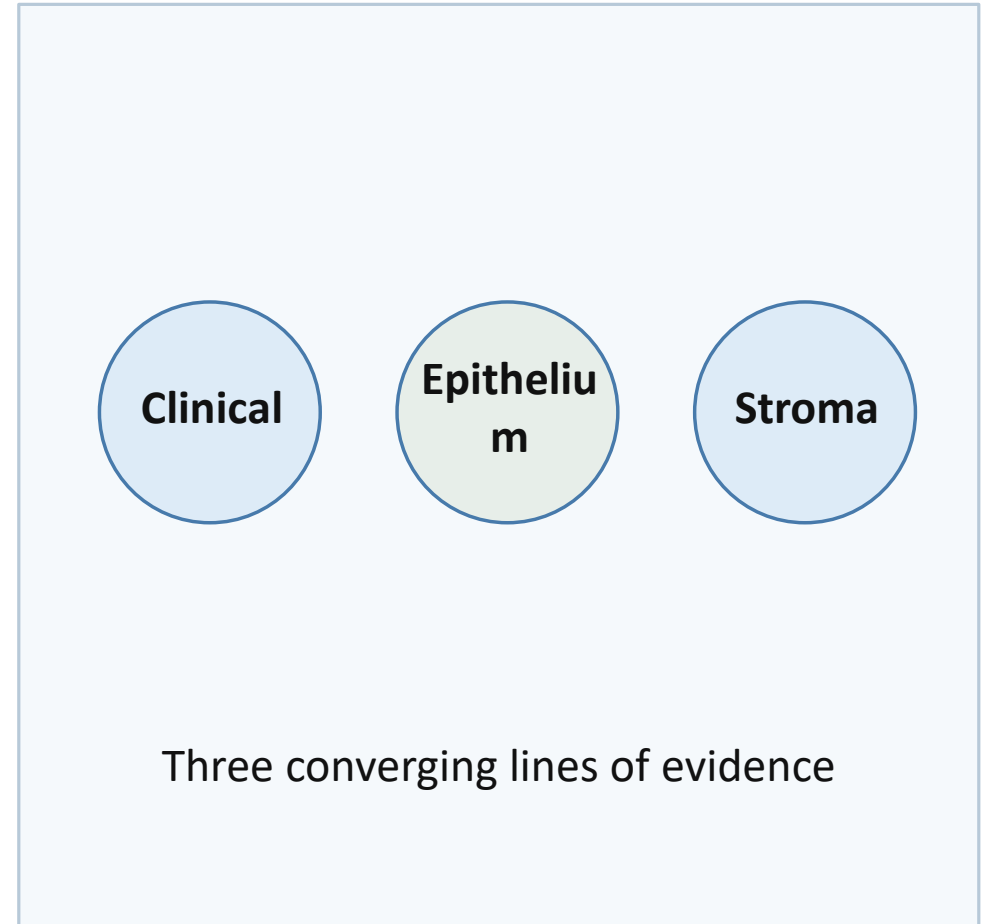
- A 27-year-old has a slowly growing, painless upper lateral neck mass.
- It lies along the sternocleidomastoid and is approximately 3 cm.
- Which clinicopathologic findings most strongly support branchial cyst?

Clinical problem

What finding changes
The interpretation?

Case 1: Defend the diagnosis

- A well-defined cyst containing a bland epithelial lining is compatible.
- Reactive lymphoid follicles in a fibrous wall strengthen support.
- Age and site are supporting—not conclusive—facts.



Case 2: Cystic mass in an older adult

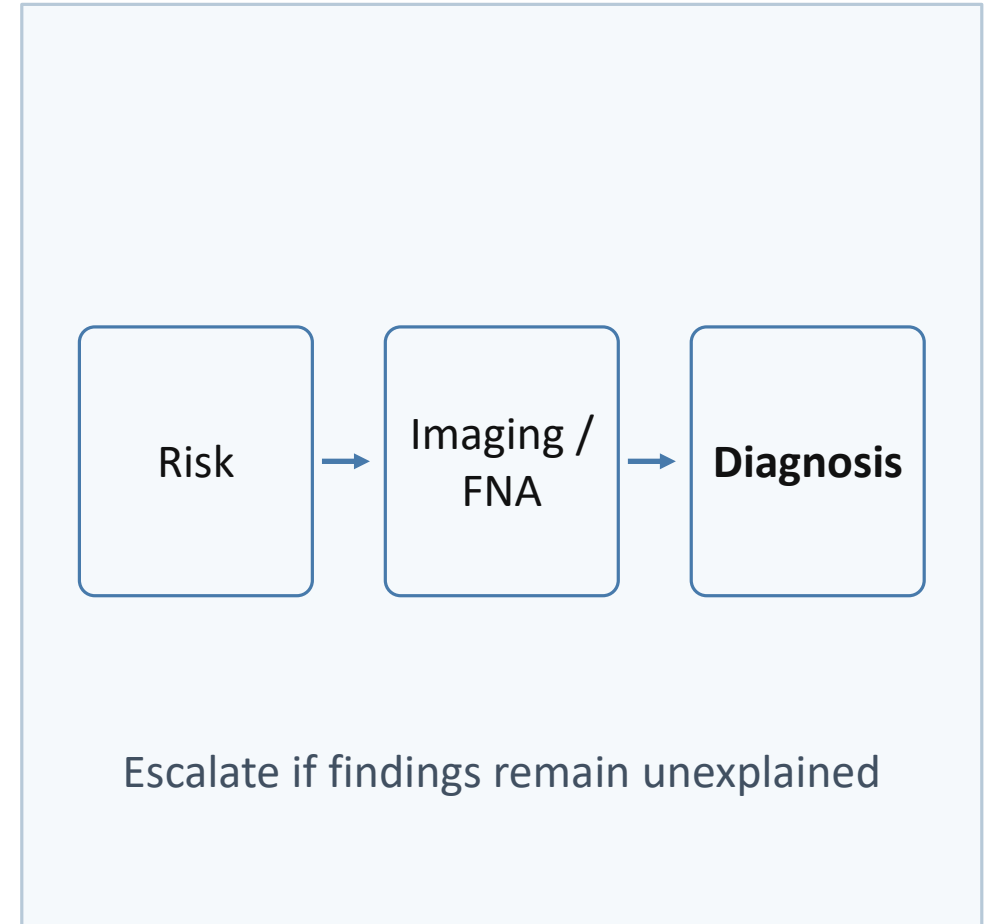
- A 58-year-old presents with a new, painless upper lateral neck cystic mass.
- An initial aspirate yields debris without representative epithelium.
- What must be excluded before a benign label is accepted?

Clinical problem

What finding changes
The interpretation?

Case 2: Next diagnostic steps

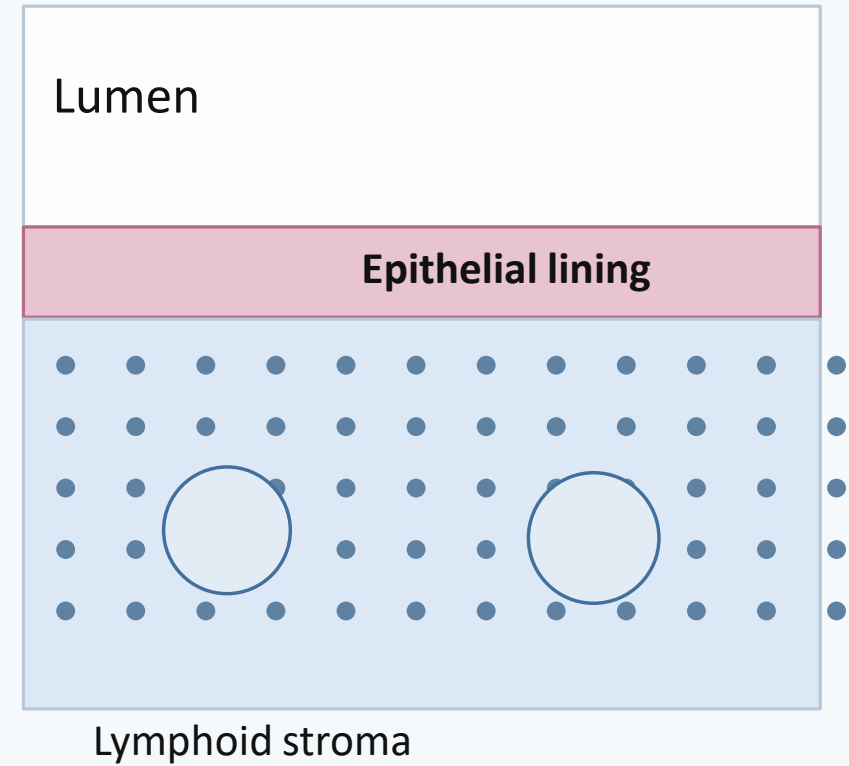
- Assess malignancy risk and upper aerodigestive mucosa.
- Obtain indicated cross-sectional imaging and adequate tissue sampling.
- Continue until a specific diagnosis is established.



Case 3: Identify the cyst wall

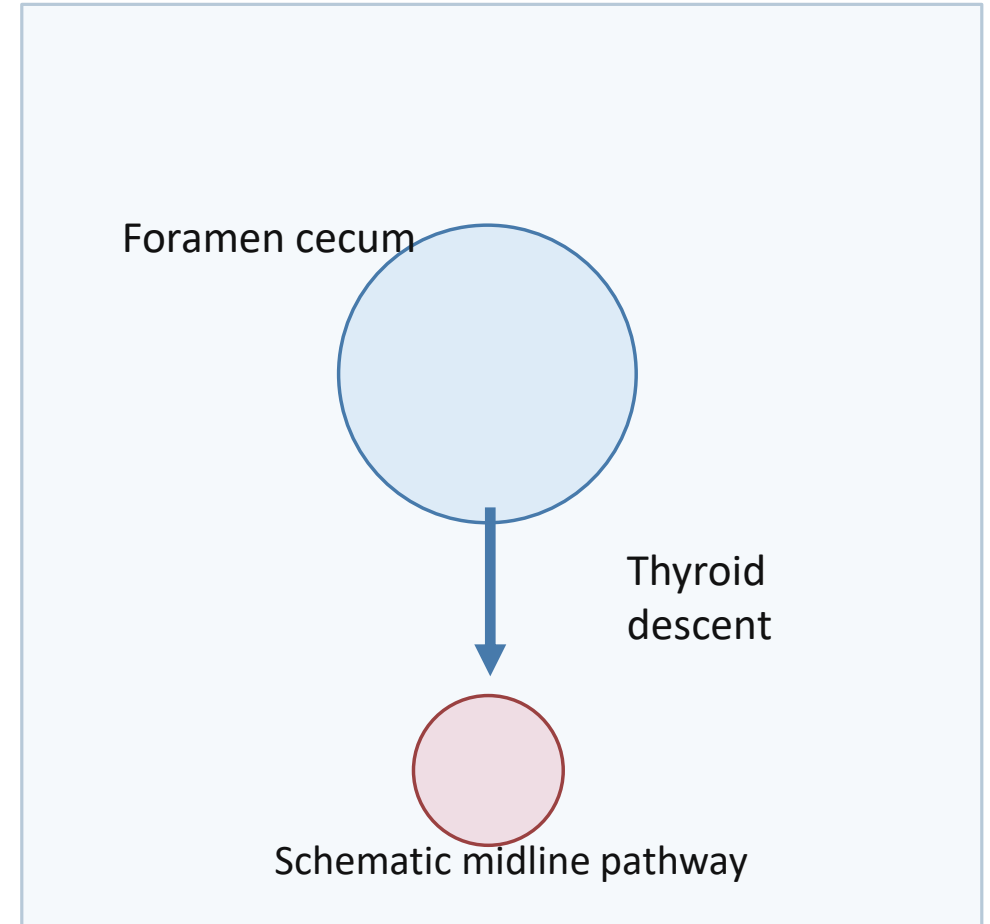
- Microscopy shows a squamous-lined cavity and fibrous stroma.
- Lymphoid follicles with germinal centers populate the wall.
- No malignant epithelial features are recognized.

Histology schematic — not a micrograph



Case 4: Midline versus lateral

- A cystic mass is located in the midline near the hyoid.
- Histology shows thyroid tissue within the cyst wall.
- Which developmental diagnosis is more plausible?



Case 5: An immunostaining trap

- A cystic neck specimen has superficial epithelial p16 staining.
- The lining is bland and HPV-specific testing is negative.
- Why is p16 reactivity alone insufficient to diagnose metastasis?

P16 pattern

HPV evidence

Compare evidence, not a single appearance

Diagnostic comparison at a glance

- Upper lateral neck with bland lining and lymphoid follicles favors branchial cyst.
- Anterior midline lesion with thyroid remnants favors thyroglossal cyst.
- Adult cystic neck SCC must be investigated as metastatic until explained.

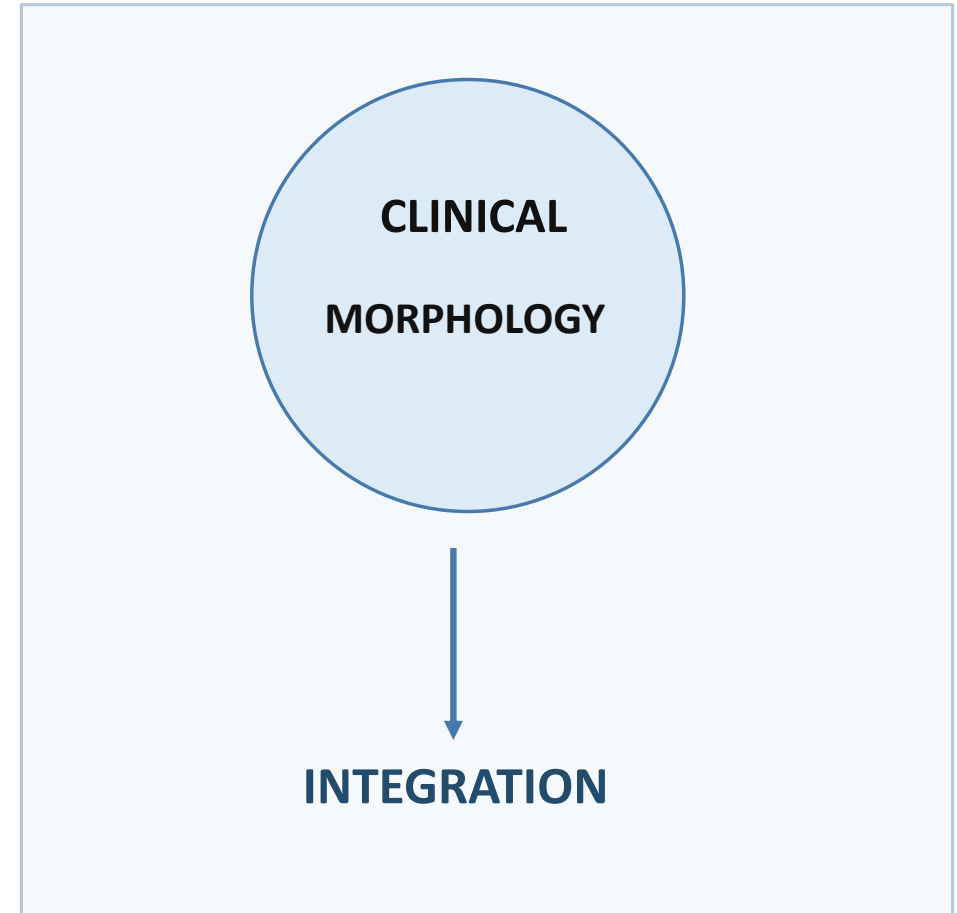
Pattern

Context

Compare evidence, not a single appearance

Five statements worth remembering

- Embryonic branchial remnants are the usual proposed origin.
- Common pattern: Young adult, upper lateral neck, 2–5 cm.
- Squamous or columnar lining + lymphoid-rich wall with germinal centers.
- Cystic metastatic SCC is the essential exclusion.
- Confirmed benign lesions are amenable to excision.



References and source boundaries

Primary textbook

Robbins, Cotran & Kumar, 11th ed. (2026), Head and Neck, p. 677

Adult clinical evaluation

AAO-HNSF Clinical Practice Guideline: Evaluation of the Neck Mass in Adults (2017)

Embryology / management

StatPearls, Branchial Cleft Cysts (updated 2025)

Differential / biomarkers

WHO head-and-neck classification update (2022); Pai et al. (2009)