

# Papillary hidradenoma

Vulvar glandular tumor: clinicopathologic recognition, architecture and differential diagnosis

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## **What the learner should be able to do**

- Recognize the typical location and appearance of papillary hidradenoma.
- Explain the two-cell-layer architecture of this benign glandular tumor.
- Distinguish papillary hidradenoma from malignant and other papillary vulvar lesions.
- Use morphology before considering targeted ancillary stains.

# Glandular neoplasia in the vulva

## The anatomic context

- Vulvar skin contains modified apocrine and mammary-like secretory structures.
- Glandular lesions are distinct from epithelial squamous lesions.

## Two Robbins exemplars

- Papillary hidradenoma: Circumscribed glandular nodule.
- Extramammary Paget disease: Intraepidermal malignant glandular cells.

## Entity, nomenclature and behavior

- Papillary hidradenoma is also termed hidradenoma papilliferum.
- It is a benign epithelial adnexal neoplasm with glandular/apocrine differentiation.
- Its defining histology is a circumscribed papillary lesion with luminal and myoepithelial layers.

# Clinical-to-microscopic diagnostic logic

Vulvar nodule



Biopsy or excision



Circumscribed papillary glands



Luminal + basal layers



**Benign papillary hidradenoma**

## **Why a benign lesion may suggest carcinoma**

- The nodule may ulcerate and bleed at the skin surface.
- Ulceration is clinically alarming but not synonymous with malignancy.
- Histology determines whether tumor growth is circumscribed or infiltrative.
- Cytologic atypia and preservation of a myoepithelial layer refine the distinction.

# What does the vulvar glandular background mean?

## Robbins framework

- Modified apocrine sweat glands are present in vulvar skin.
- Breast-like glandular differentiation explains familiar epithelial patterns.

## Interpretive caution

- Mammary-like anogenital glands are discussed in later studies.
- Do not equate a breast-type morphology with a primary breast lesion.

## **Likely site: Labia and interlabial folds**

- Lesions most often on the labia majora or interlabial folds.
- The lesion is centered in the vulvar cutaneous/adnexal compartment.
- A clinical site description helps the histopathologist interpret glandular morphology.

# Usual distribution versus less typical sites

## Common setting

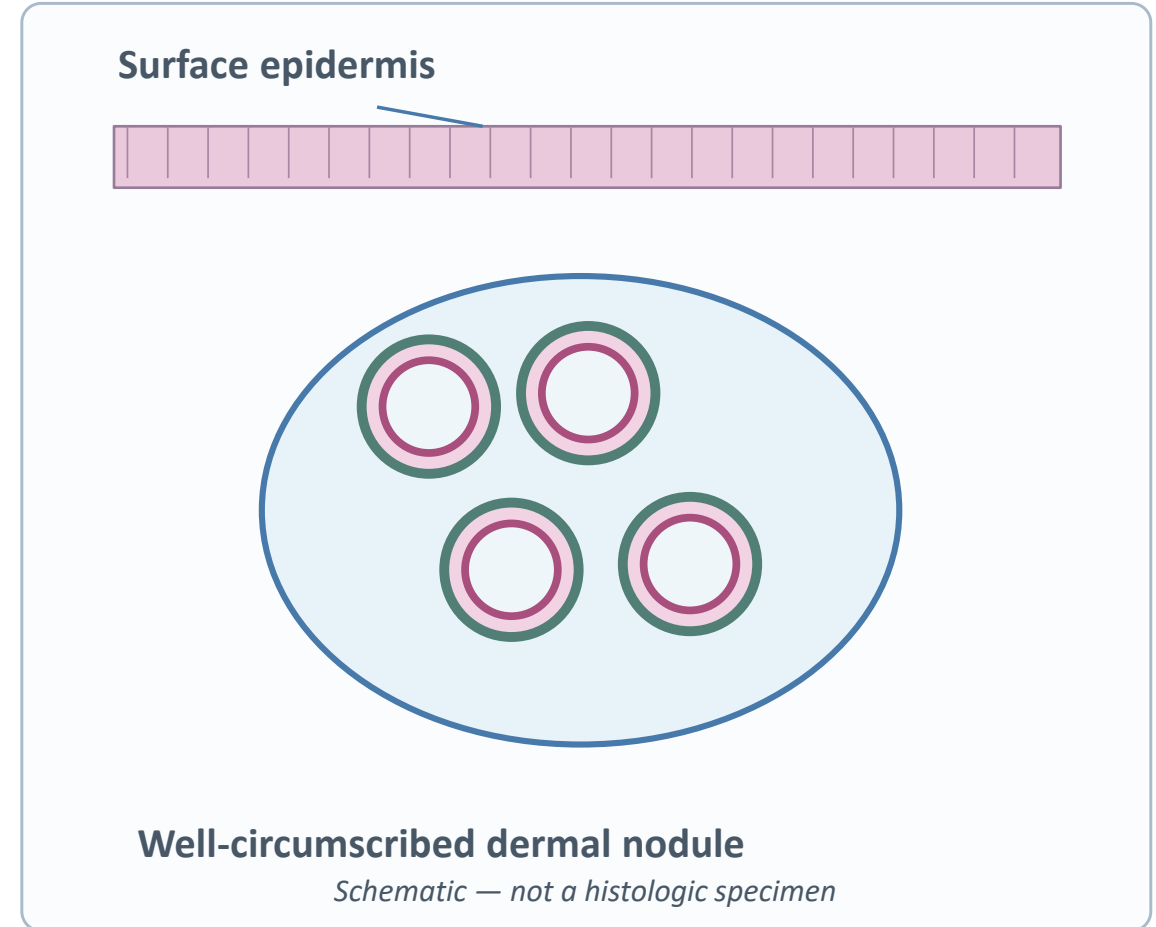
- Solitary nodule of the vulva.
- Labial or adjacent anogenital region.

## Less typical presentations

- Other anogenital sites and rare ectopic cutaneous sites have been reported.
- An unusual site requires careful morphology-based confirmation.

# Tumor sits beneath the surface

- A compact, dermal-based glandular proliferation is characteristic.
- The overlying epidermis is usually not directly continuous with the tumor.
- Surface erosion can occur without infiltrative tumor biology.



## **Clinical morphology: Circumscribed nodule**

- Papillary hidradenoma often presents as a small, sharply defined lesion.
- The surface may appear pink or red; A clinically intact surface is possible.
- It is not reliably diagnosed by naked-eye inspection alone.

# Symptoms: Present or absent

## Possible incidental presentation

- Slow growth or asymptomatic course may prompt delayed evaluation.
- A well-demarcated nodule may be noticed during examination.

## Symptomatic presentation

- Ulceration or bleeding can trigger concern for carcinoma.
- Discomfort or irritation warrants examination but is not histotype-specific.

## What the 45-case series actually reports

- Wang and colleagues described 45 vulvar lesions from a multi-institutional series.
- Their observed tumor sizes were 0.3–2.0 cm.
- Reported clinical colors included pink and red.
- These are descriptive findings from that cohort, not population prevalence estimates.

# A nodule and an ulcer are different observations

## Nodule assessment

- Define size, site, mobility and clinical margins.
- Document whether a discrete mass is present.

## Surface assessment

- Note ulceration, crusting or focal bleeding separately.
- A disrupted surface does not determine the lesion's histologic grade.

## **Why clinical pattern recognition is insufficient**

- Multiple benign vulvar conditions form nodules or papillary lesions.
- Malignancy also can present as a focal ulcerated mass.
- Location and appearance narrow the differential but cannot establish the diagnosis.

# A practical diagnostic sequence

Describe lesion and site



Obtain tissue



Assess architecture on H&E



Confirm epithelial bilayer



**Resolve atypical features**

## **Tissue diagnosis: What should be documented**

- Exact anatomic location and clinical impression.
- Whether the specimen is incisional tissue or an excised mass.
- Surface ulceration and gross circumscription where assessable.
- Presence or absence of representative lesion at the deep and peripheral edges.

# Gross interpretation: Outline and contents

## Supporting benign architecture

- A sharply circumscribed nodular outline.
- A localized lesion rather than a diffuse epithelial plaque.

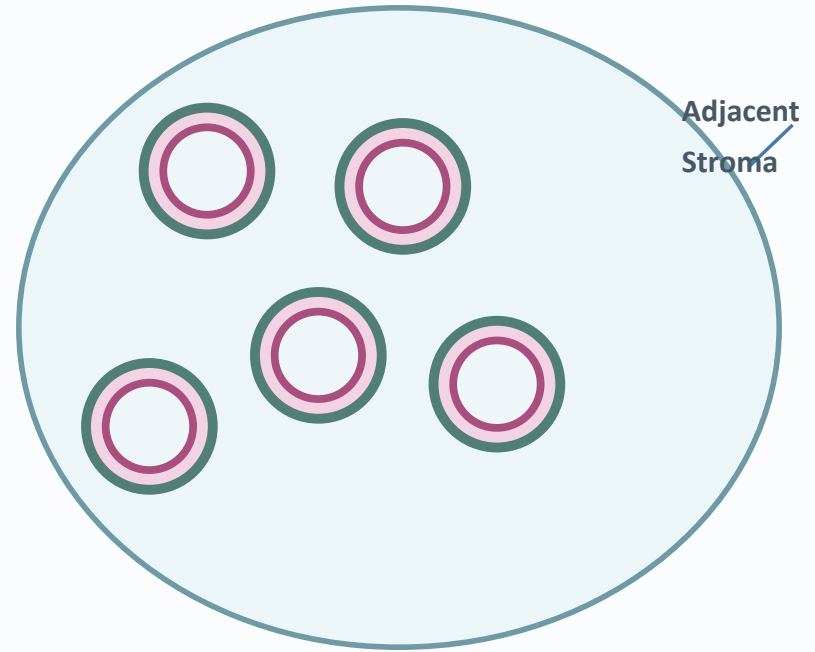
## What gross inspection cannot prove

- Papillary spaces and a myoepithelial layer require microscopy.
- A benign-looking margin alone cannot exclude an unexpected carcinoma.

# Low-power recognition: An organized border

- The lesion is typically well circumscribed within the dermis.
- Fibrous tissue can be compressed around the lesion (pseudocapsule).
- Evaluate the entire periphery for an unexpectedly infiltrative interface.

Smooth peripheral outline

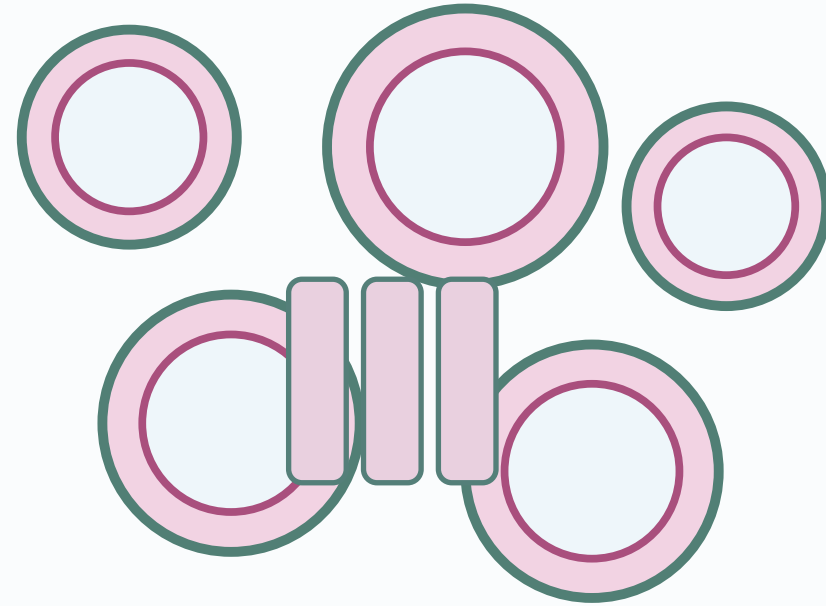


Peripheral assessment at low power

*Schematic — not a histologic specimen*

## Low power: Tubular and papillary complexity

- Tubules and dilated gland-like spaces vary in size.
- Elongated papillary fronds project into luminal spaces.
- A branching or labyrinthine configuration can still represent benign architecture.

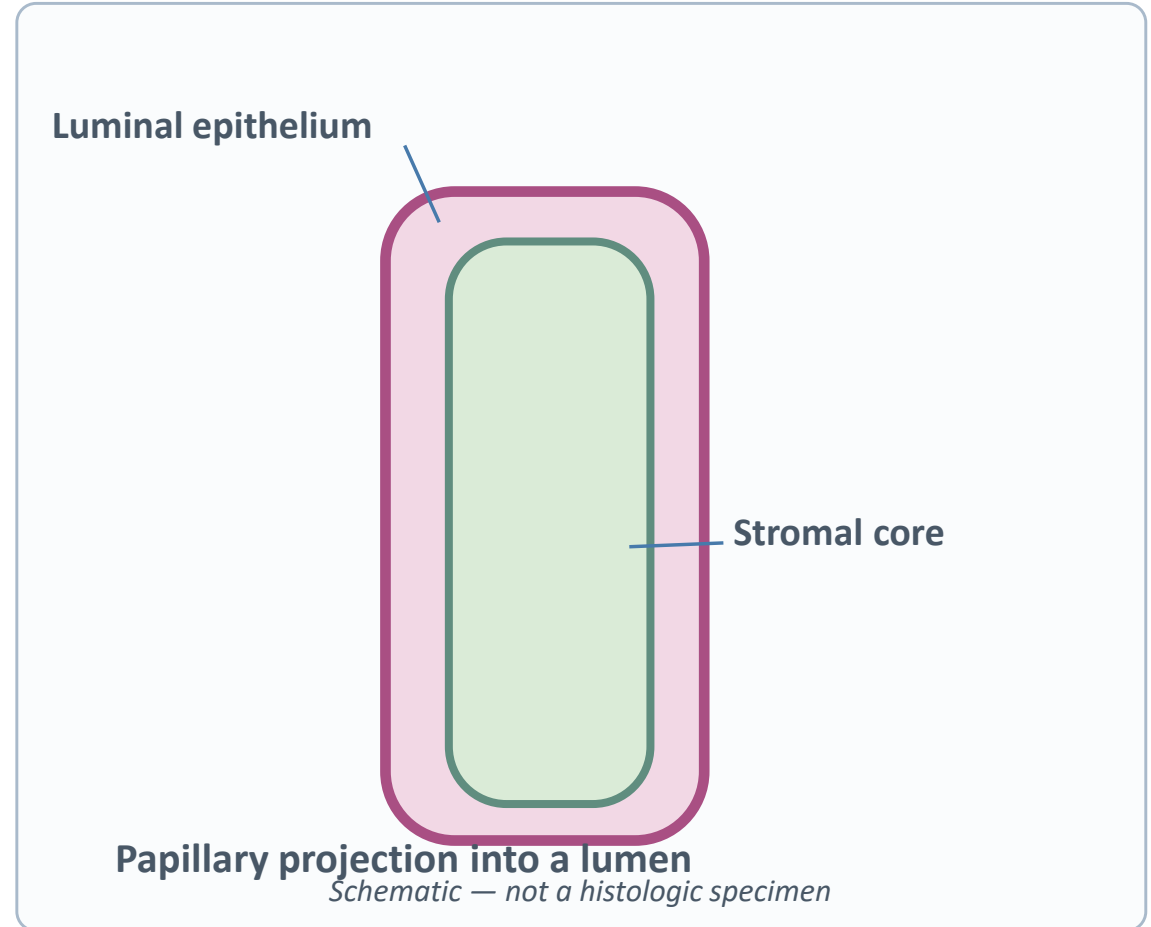


**Tubules, luminal spaces and folded fronds**

*Schematic — not a histologic specimen*

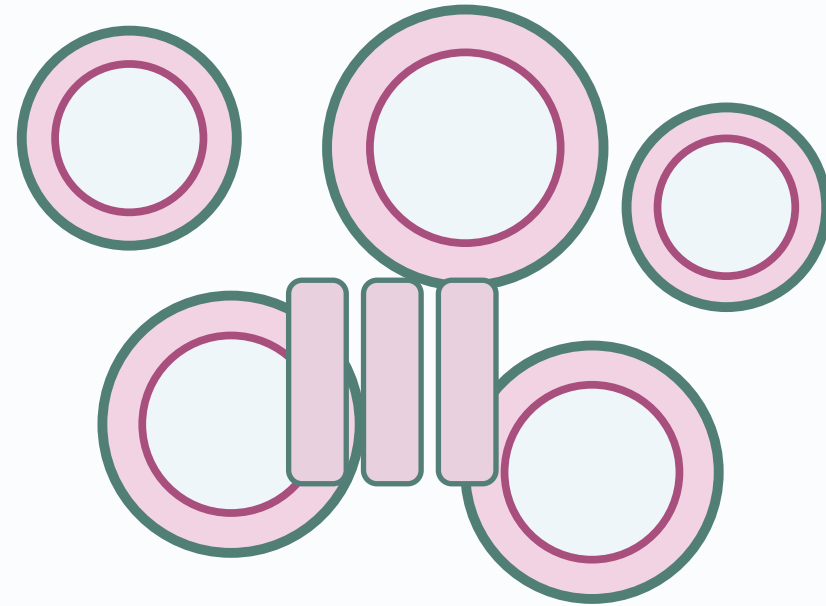
# Papillary fronds: Epithelial surfaces around cores

- A papilla projects into a lumen from its supporting connective tissue.
- Broad papillae may contain recognizable stromal or fibrovascular cores.
- Identify luminal lining cells separately from subjacent myoepithelial cells.



# Cystic and glandular spaces

- Secretory lumina are lined by a luminal epithelial population.
- Papillary structures fold into some lumina, giving a complex glandular profile.
- Architectural complexity alone is not evidence of stromal invasion.

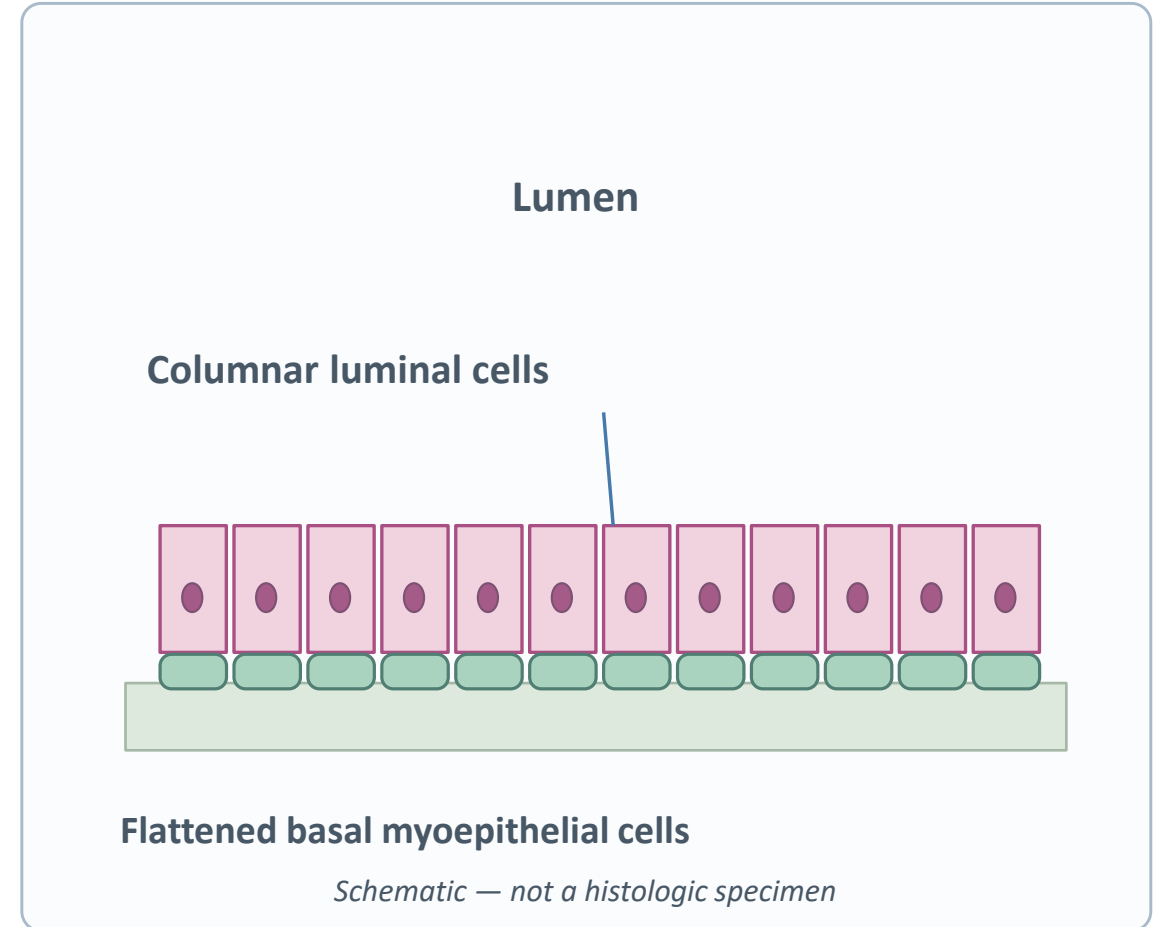


**Tubules, luminal spaces and folded fronds**

*Schematic — not a histologic specimen*

# The diagnostic two-cell-layer motif

- Upper layer: Columnar secretory cells facing the lumen.
- Lower layer: Flattened or cuboidal myoepithelial cells along the basal interface.
- Both layers can be followed around benign papillary profiles.



# Luminal cells and basal myoepithelial cells

## Luminal compartment

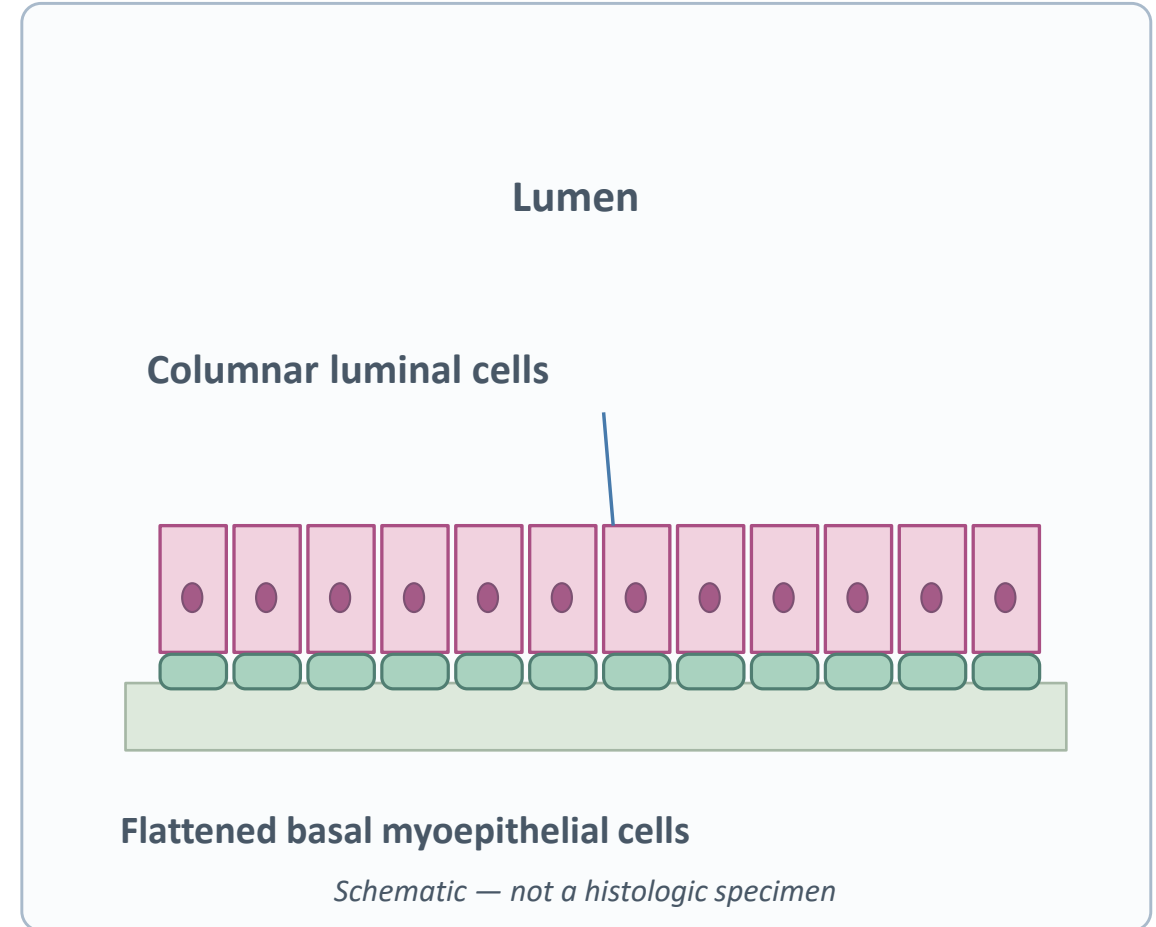
- Tall columnar glandular cells.
- Secretory differentiation; Luminal or apical cytoplasm.

## Basal compartment

- Flattened/cuboidal myoepithelial elements.
- An epithelial–stromal interface maintained around glands.

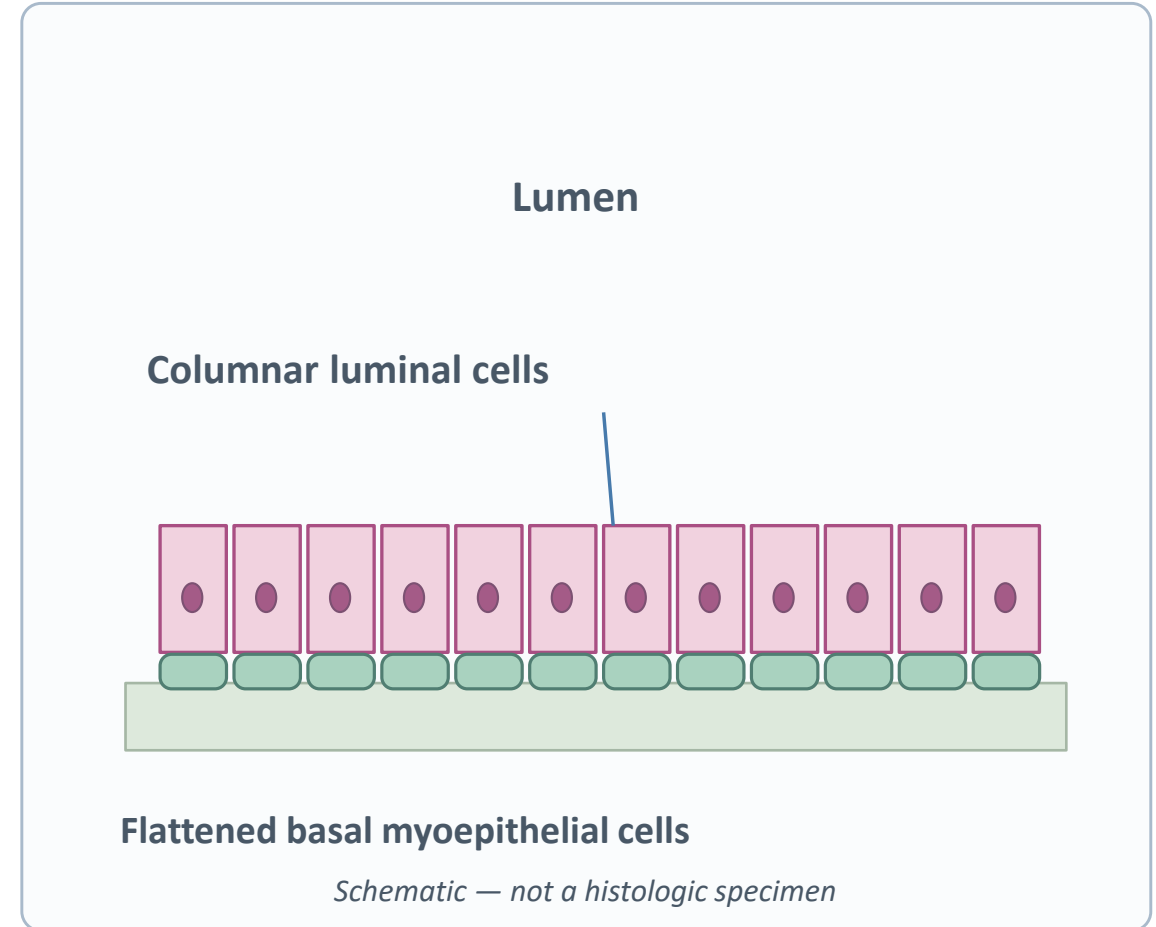
# The luminal cell layer

- Tall, often columnar cells border a gland lumen.
- The apical surface may exhibit apocrine-type secretory changes.
- Bland cytology supports benign interpretation alongside architecture.



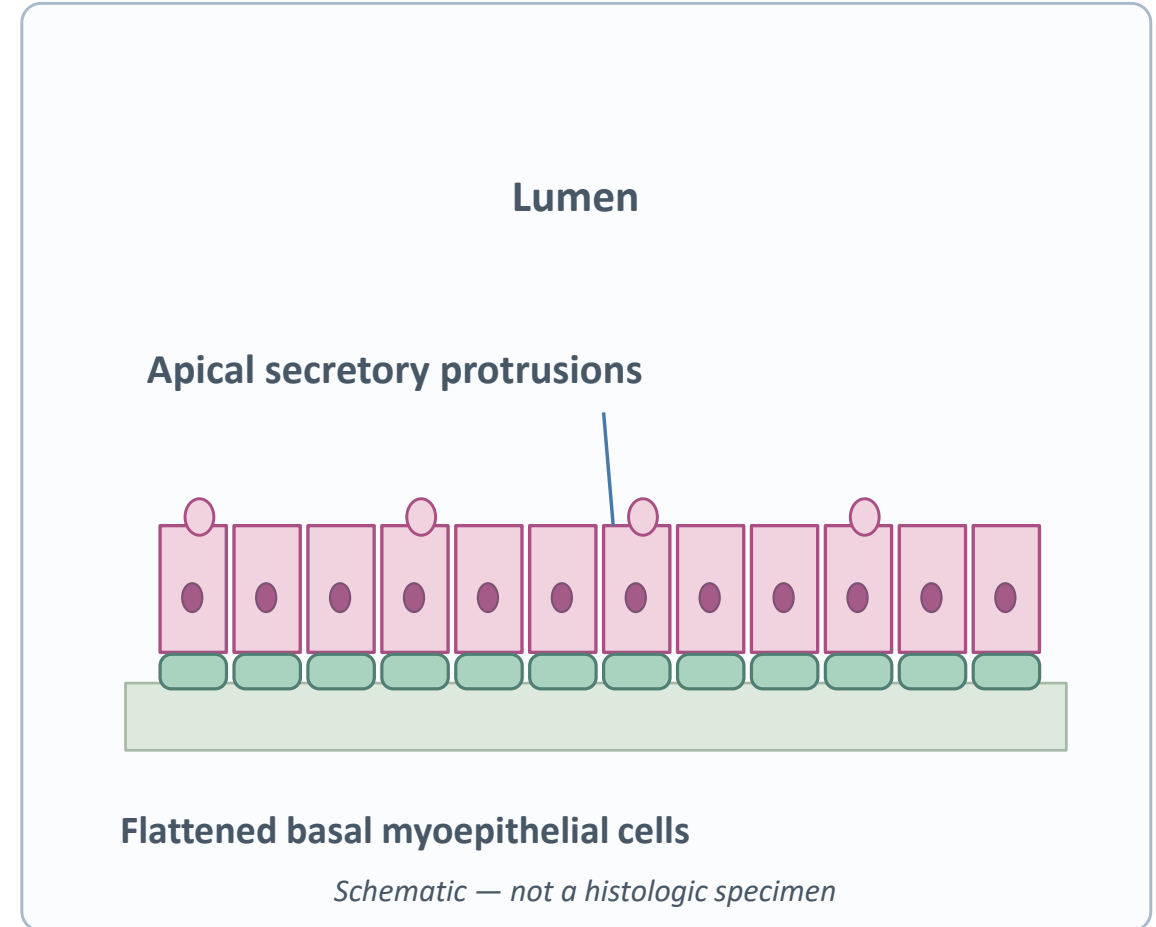
# The myoepithelial layer

- Basal cells lie outside the secretory columnar layer.
- These elements are characteristic of secretory adnexal gland structures.
- Recognizing them is more meaningful than counting layers in isolation.



# Apocrine secretion: What to look for

- Apical snouts or focal decapitation-type secretion may be seen.
- This suggests secretory/apocrine differentiation of luminal cells.
- The feature is supportive rather than a stand-alone diagnostic criterion.



# Cytologic findings supporting benignity

## Reassuring features

- Relatively orderly luminal epithelium.
- Minimal cytologic atypia and preserved layering.
- No convincing destructive infiltration.

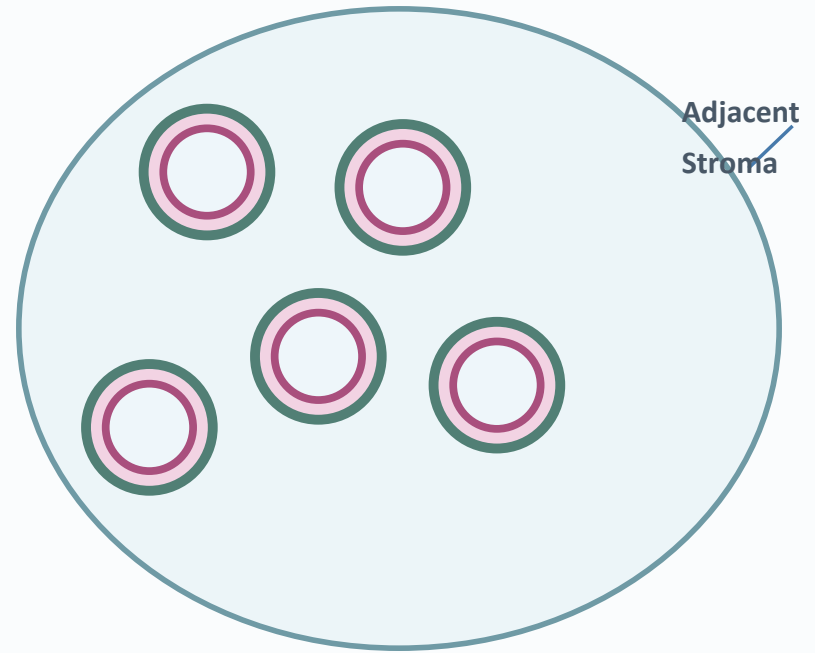
## Concerning departure

- Striking nuclear atypia or atypical mitoses.
- Tumor necrosis or irregular infiltrative glands.
- Loss of an organized epithelial–myoepithelial profile.

# Tumor–stroma interface

- A compact lesion has a boundary recognizable at scanning magnification.
- Compression of adjacent collagen may create a pseudocapsule.
- Do not mistake a curved papillary fold for infiltration into stroma.

**Smooth peripheral outline**



**Peripheral assessment at low power**

*Schematic — not a histologic specimen*

# The surface and tumor can be disconnected

## Typical relationship

- A dermal tumor without direct continuity with the epidermis.
- The epidermis may be preserved or locally eroded.

## Different diagnostic pattern

- An exophytic lesion continuous with epidermis suggests a different papillary process.
- Intraepidermal spread of malignant glandular cells suggests Paget disease.

# Why Robbins invokes intraductal papilloma

## Shared architecture

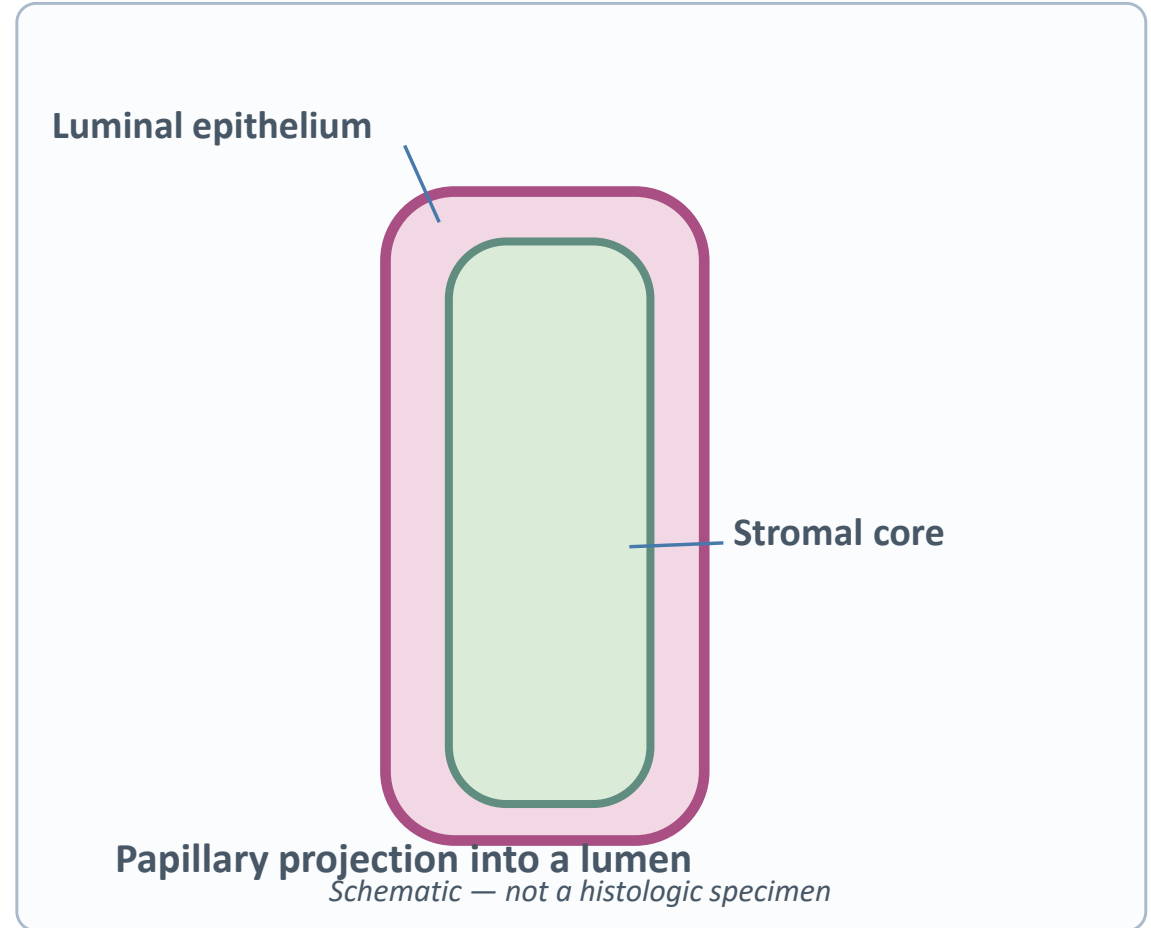
- Papillae and glandular spaces.
- Luminal epithelium plus an underlying myoepithelial population.

## Important distinction

- Breast papilloma is located within a mammary duct.
- Papillary hidradenoma arises in vulvar glandular/adnexal tissue.

# Breast analogy: Fibrovascular branching

- Intraductal papilloma as branching papillae inside a duct.
- A central fibrovascular core is a useful architecture concept.
- The epithelial bilayer—not the organ name—explains the resemblance.



# Structural comparison: Vulvar and breast papillomas

| Feature            | Papillary hidradenoma                 | Intraductal papilloma          |
|--------------------|---------------------------------------|--------------------------------|
| Usual site         | Vulvar dermis / anogenital skin       | Mammary duct                   |
| Arrangement        | Circumscribed papillary/tubular tumor | Papillary tumor within duct    |
| Epithelial support | Luminal + myoepithelial layers        | Luminal + myoepithelial layers |
| Teaching role      | Vulvar glandular differential         | Morphologic comparator         |

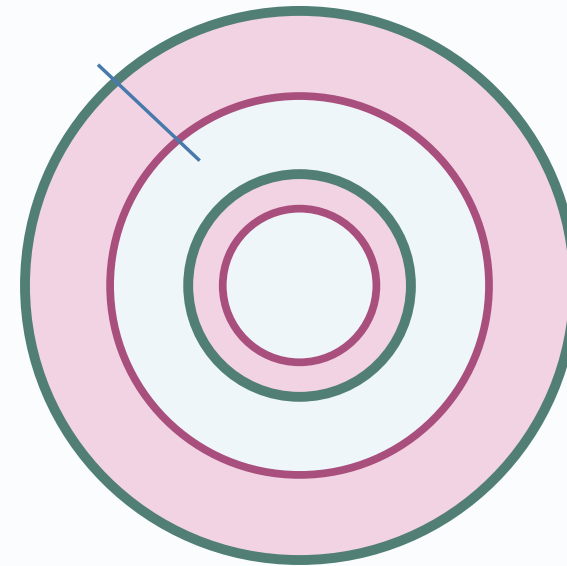
## **H&E: A reproducible reading order**

- First: Identify whether the lesion is dermal and circumscribed.
- Second: Search for cystic spaces and papillary fronds.
- Third: Identify columnar luminal and basal myoepithelial layers.
- Fourth: Evaluate atypia, mitoses, necrosis and peripheral invasion.

# High power: Avoid mistaking folded glands for atypia

- A tortuous gland may intersect the section plane many times.
- Distinguish a genuine solid epithelial expansion from a tangential fold.
- Follow papillary cores and cell-layer polarity across adjacent profiles.

Tangential cut



Repeated gland profiles may reflect section plane

*Schematic — not a histologic specimen*

## **When ancillary stains add value**

- Routine H&E is generally sufficient in classic cases.
- Immunohistochemistry can clarify the luminal and myoepithelial compartments.
- Select markers to test a specific problem rather than stain indiscriminately.

## Luminal immunophenotype: Supportive markers

| Marker    | Expected use                              | Interpretive limit          |
|-----------|-------------------------------------------|-----------------------------|
| CK7       | Demonstrates glandular luminal epithelium | Not specific for this tumor |
| EMA / CEA | Support glandular differentiation         | Not proof of benignity      |
| GCDFP-15  | Supports apocrine differentiation         | Can be focal                |
| ER / PR   | May be expressed by luminal cells         | Variable; Not a requirement |

## Myoepithelial markers: Basal compartment

| Marker              | Compartment illustrated                       | Caution                         |
|---------------------|-----------------------------------------------|---------------------------------|
| P63                 | Nuclear staining in basal myoepithelial cells | Interpret with location         |
| S100                | May label myoepithelial cells                 | Not specific by itself          |
| Smooth muscle actin | Supports basal myoepithelial phenotype        | Requires morphology correlation |
| CD10                | Additional reported basal marker              | Not uniquely diagnostic         |

# Why an IHC panel is not the diagnosis

## Helpful result

- CK7-positive luminal cells.
- P63-positive basal cells around glands.
- Architecture remains circumscribed and orderly.

## Unhelpful shortcut

- One positive glandular stain cannot classify all papillary lesions.
- A focal/negative apocrine stain cannot alone exclude a classic tumor.

# Problem-solving use of IHC

H&E architecture



Question: Is basal layer intact?



Choose a myoepithelial marker



Correlate basal pattern with glands



**Integrated interpretation**

# The essential positive morphologic constellation

- Dermal-based, circumscribed nodule.
- Branching tubules, papillae and occasional cystic lumina.
- Luminal columnar cells overlying basal myoepithelial cells.
- Absence of overt malignant cytology or destructive stromal invasion.

# Atypical findings require a broader diagnosis

## Expected features

- Orderly two-cell-layer glands.
- Pushing/circumscribed border.
- No marked atypia or conspicuous atypical mitoses.

## Escalation features

- Infiltration, marked nuclear polymorphism, conspicuous mitoses.
- Extensive necrosis or unexpectedly solid expanses.
- Correlate with sampling and additional histology.

# Papillary hidradenoma versus syringocystadenoma

| Characteristic   | Papillary hidradenoma                 | Syringocystadenoma papilliferum           |
|------------------|---------------------------------------|-------------------------------------------|
| Surface contact  | Usually no epidermal connection       | Typically connected to surface            |
| Dominant pattern | Circumscribed dermal papillary glands | Papillary lesion with surface involvement |
| Stromal reaction | May show fibrous pseudocapsule        | Plasma cells often in papillary cores     |
| Useful clue      | Two-layer glandular neoplasm          | Surface continuity + plasma cells         |

# Bartholin cyst: Clinically adjacent, morphologically different

## Bartholin duct obstruction

- Cystic process related to the Bartholin duct.
- Interpret by ductal/cyst lining and clinical site.

## Papillary hidradenoma

- Solid–cystic papillary glandular tumor.
- Recognizable luminal + myoepithelial layered proliferation.

# Squamous papilloma is not a glandular papilloma

## Benign squamous papilloma

- Papillary/exophytic lesion covered by squamous epithelium.
- No glandular secretory bilayer as defining structure.

## Papillary hidradenoma

- Papillae inside glandular lumina, often in dermis.
- Columnar secretory lining plus basal myoepithelial cells.

# Condyloma: HPV-related squamous rather than glandular

## Condyloma acuminatum

- Exophytic treelike squamous fronds.
- Koilocytic change can be present.
- Related to low-risk HPV, mainly 6 and 11.

## Papillary hidradenoma

- Dermal glandular papillary neoplasm.
- Two-layer secretory and myoepithelial architecture.
- Do not presume an HPV-driven process.

# Extramammary Paget disease has a different compartment

## Paget disease

- Malignant pale glandular cells dispersed in epidermis.
- Often visible as erythematous pruritic crusted plaque.

## Papillary hidradenoma

- Localized dermal nodule.
- Organized glands/papillae with basal myoepithelial cells.

# Vulvar adenocarcinoma: Infiltration is central

## Benign glandular papillary tumor

- Smooth boundary; Orderly bilayer.
- Little atypia; No destructive tissue invasion.

## Suspicious adenocarcinoma

- Infiltrative margins, atypical glands and cytologic malignancy.
- Myoepithelial investment often absent in invasive glandular areas.

## A focused differential decision table

| Main question                | Finding favoring hidradenoma      | Finding prompting alternative        |
|------------------------------|-----------------------------------|--------------------------------------|
| Is this squamous?            | True glandular luminal structures | Squamous-lined surface fronds        |
| Is it surface connected?     | Usually dermal and disconnected   | Epidermal continuity / Paget cells   |
| Is a basal layer present?    | Myoepithelial layer preserved     | Absent basal layer with infiltration |
| Is there destructive growth? | Circumscribed or pushing outline  | Irregular infiltrative border        |

## **Diagnostic pitfalls: Four common traps**

- Ulceration is mistaken for evidence of invasion.
- An arborizing glandular pattern is overcalled as carcinoma.
- A single positive immunostain is treated as disease-specific.
- A superficially sampled lesion cannot be assessed for circumscription.

## **Clinical management: Link action to diagnosis**

- Definitive histology commonly follows local removal of the lesion.
- For a classic completely excised benign lesion, routine follow-up can be individualized.
- Persistent, recurrent or atypical lesions warrant reevaluation and possible resampling.
- Do not apply carcinoma treatment pathways to a benign papillary tumor.

# An excision specimen answers two questions

## Classification

- Does the morphology support papillary hidradenoma?
- Are any atypical or invasive components identified?

## Completeness

- Does the specimen include the lesion boundary?
- Can margin involvement be meaningfully assessed?

## What a useful pathology report conveys

- Recognizable diagnostic term: Papillary hidradenoma (hidradenoma papilliferum).
- Location, size and specimen type when supplied.
- Any ulceration, unusual atypia or invasive component if present.
- Margin status only where specimen orientation and sampling support it.

# Case 1 · an asymptomatic vulvar nodule

## Clinical or microscopic vignette

A small, well-defined labial nodule is removed. The section shows papillary glands within the dermis; Luminal columnar cells have a basal myoepithelial layer.

**Which feature most strongly supports the proposed diagnosis?**

An organized papillary glandular proliferation with an intact two-cell-layer lining supports papillary hidradenoma.

## Case 2 · the ulceration trap

### Clinical or microscopic vignette

A vulvar nodule has a focal ulcerated surface and is referred as “rule out carcinoma.” Histology shows a circumscribed papillary tumor with bland epithelial cells.

### Does ulceration establish malignant transformation?

No. Papillary hidradenoma may ulcerate and clinically resemble carcinoma; Invasion and cytology must be assessed.

## Case 3 · a surface-connected papillary lesion

### Clinical or microscopic vignette

A papillary lesion is directly continuous with the epidermis, and several papillary cores show a conspicuous plasma-cell infiltrate.

### Which competing diagnosis should be prioritized?

Syringocystadenoma papilliferum is favored over typical papillary hidradenoma by the surface continuity and plasma-cell-rich cores.

## Case 4 · stains in context

### Clinical or microscopic vignette

A dermal papillary glandular tumor is CK7 positive in the luminal compartment and p63 positive at the basal interface. The periphery is circumscribed.

### What does this integrated pattern support?

The findings support a two-layer glandular adnexal lesion, consistent with papillary hidradenoma in the correct morphologic context.

## Case 5 · the missing layer

### Clinical or microscopic vignette

A vulvar glandular lesion contains markedly atypical epithelial cells and irregular glands infiltrating dermal collagen; Myoepithelial markers do not outline many abnormal glands.

### What is the safest diagnostic next step?

Do not force a benign diagnosis. Evaluate for an invasive adenocarcinoma or another malignant glandular neoplasm with comprehensive sampling and correlation.

## **Synthesis: Recognize a pattern, not a single clue**

- A circumscribed vulvar papillary glandular tumor is the clinical-pathologic starting point.
- Luminal columnar cells and basal myoepithelial cells provide the strongest structural signature.
- Ulceration is compatible with benignity; Infiltrative growth and marked atypia require escalation.
- Use IHC as morphology-directed support, not as a replacement for architecture.

## Three-minute final recognition checklist

| Evaluation level | Question                           | Target observation                           |
|------------------|------------------------------------|----------------------------------------------|
| Clinical         | Where is the lesion?               | Labial / interlabial nodule                  |
| Low power        | How does it interface with stroma? | Circumscribed dermal tumor                   |
| Intermediate     | Which architecture dominates?      | Arborizing papillae and tubules              |
| High power       | What lines each papilla?           | Columnar luminal + basal myoepithelial cells |
| Safety check     | Any malignant discrepancy?         | Assess invasion / atypia / necrosis          |

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