

Squamous Papilloma and Papillomatosis

Laryngeal squamous papilloma and recurrent respiratory papillomatosis

Structure • HPV pathogenesis • Clinicopathologic diagnosis

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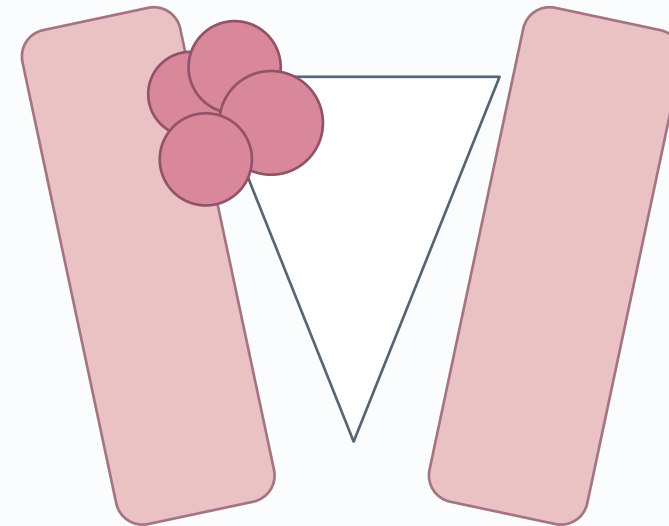
Learning objectives

- Define laryngeal squamous papilloma and recurrent respiratory papillomatosis.
- Connect HPV 6/11 to lesion distribution and recurrent disease.
- Recognize exophytic fibrovascular papillae with orderly squamous maturation.
- Differentiate papillomas from reactive nodules, dysplasia, and carcinoma.
- Explain symptoms, management goals, and vaccine prevention.

Laryngeal context: Why the site matters

- Lesions commonly involve the true vocal folds.
- Exophytic growth on the vibrating margin distorts phonation.
- Multiple lesions may also narrow the airway.

Schematic — superior view of vocal folds



Glottic lumen

Papillary lesion

Papilloma: A benign epithelial neoplasm

Benign: Orderly squamous epithelial proliferation without demonstrated invasion.

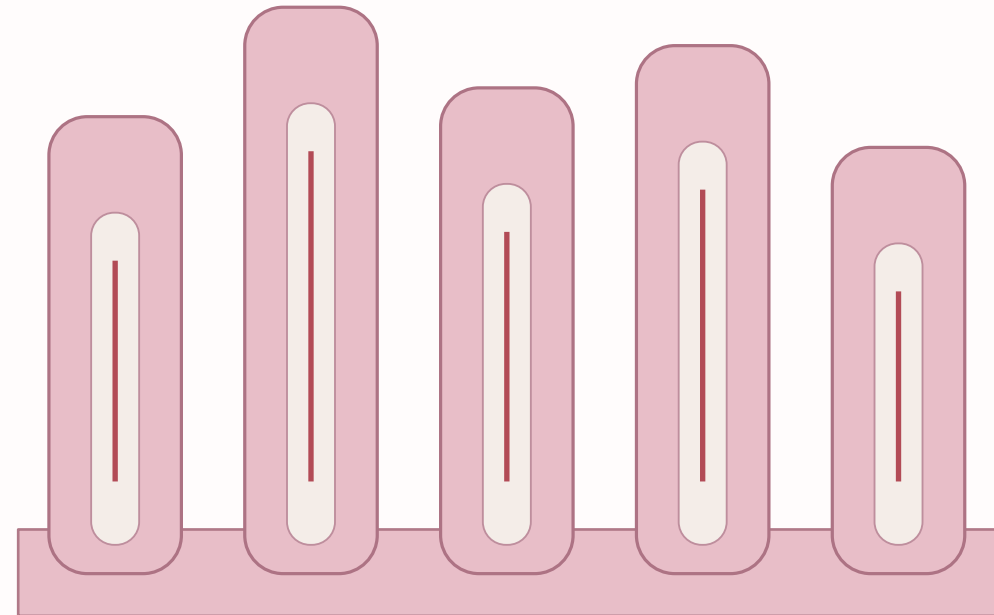
Papilloma: Outward-growing architecture forming slender projections.

Locally symptomatic does not mean intrinsically malignant.

The defining gross pattern

- Soft, exophytic lesion; Usually small and rarely exceeds 1 cm.
- Finger-like papillae create a delicate projected surface.
- Growth often arises on a true vocal fold.

Schematic — not a photomicrograph



Fibrovascular cores

Solitary lesion versus papillomatosis

Feature	Solitary papilloma	Recurrent papillomatosis
Distribution	A single identifiable papilloma	Multiple or recurrent papillomas
Typical context	Often an adult	Can affect children or adults
Clinical course	Local lesion	Potentially repeated recurrences
Shared histology	Squamous fronds with fibrovascular cores	Same basic papillary architecture

Anatomic extent: Larynx predominates

Larynx (usual site)



Other upper airway sites



**Occasional distal airway
extension**

True vocal folds are common

Multifocal respiratory disease
may occur

Broader RRP spectrum
requires clinical assessment

HPV 6 and 11 are the principal causes

Low-risk human papillomavirus types 6 and 11 drive most laryngeal papillomas.

HPV association explains the viral etiology despite benign morphology.

Virus type alone does not provide an individual recurrence forecast.

Low-risk HPV is not synonymous with low morbidity

- HPV 6/11 usually produces benign epithelial lesions.

- Location in a narrow, functionally sensitive airway can cause serious symptoms.

- Recurrence and treatment-related scarring may dominate long-term burden.

HPV exposure and transmission routes

Exposure to HPV 6/11



**Infection of susceptible
epithelium**



**Papillomatous
proliferation**

Person-to-person contact or
perinatal exposure

Not all exposed individuals
develop disease

Benign but potentially
recurrent growth

Vertical transmission is relevant to childhood disease

- Maternal genital HPV infection provides one recognized exposure pathway.
- Passage through the birth canal is a plausible route in juvenile-onset disease.
- Perinatal exposure does not mean that every infant will develop papillomatosis.
- Mode of acquisition cannot be inferred solely from a childhood diagnosis.

Adult-onset and juvenile-onset patterns

Domain	Adult pattern	Juvenile pattern
Multiplicity	Solitary papilloma is common	Multiple lesions may occur
RRP	May occur	May occur
Clinical priority	Voice symptoms; assess extension	Voice and airway compromise
Recurrence	Variable	Can require repeated procedures

Recurrence is a clinical behavior, not a histologic grade

- A benign papilloma can recur after endoscopic removal.

- Multiple or recurring lesions support a diagnosis of respiratory papillomatosis.

- Recurrence alone must not be equated with squamous carcinoma.

Simplified HPV-associated lesion development

HPV infection



**Squamous cell
proliferation**



**Exophytic papillary
growth**

Infection of epithelium

Epithelial thickening and
maturation

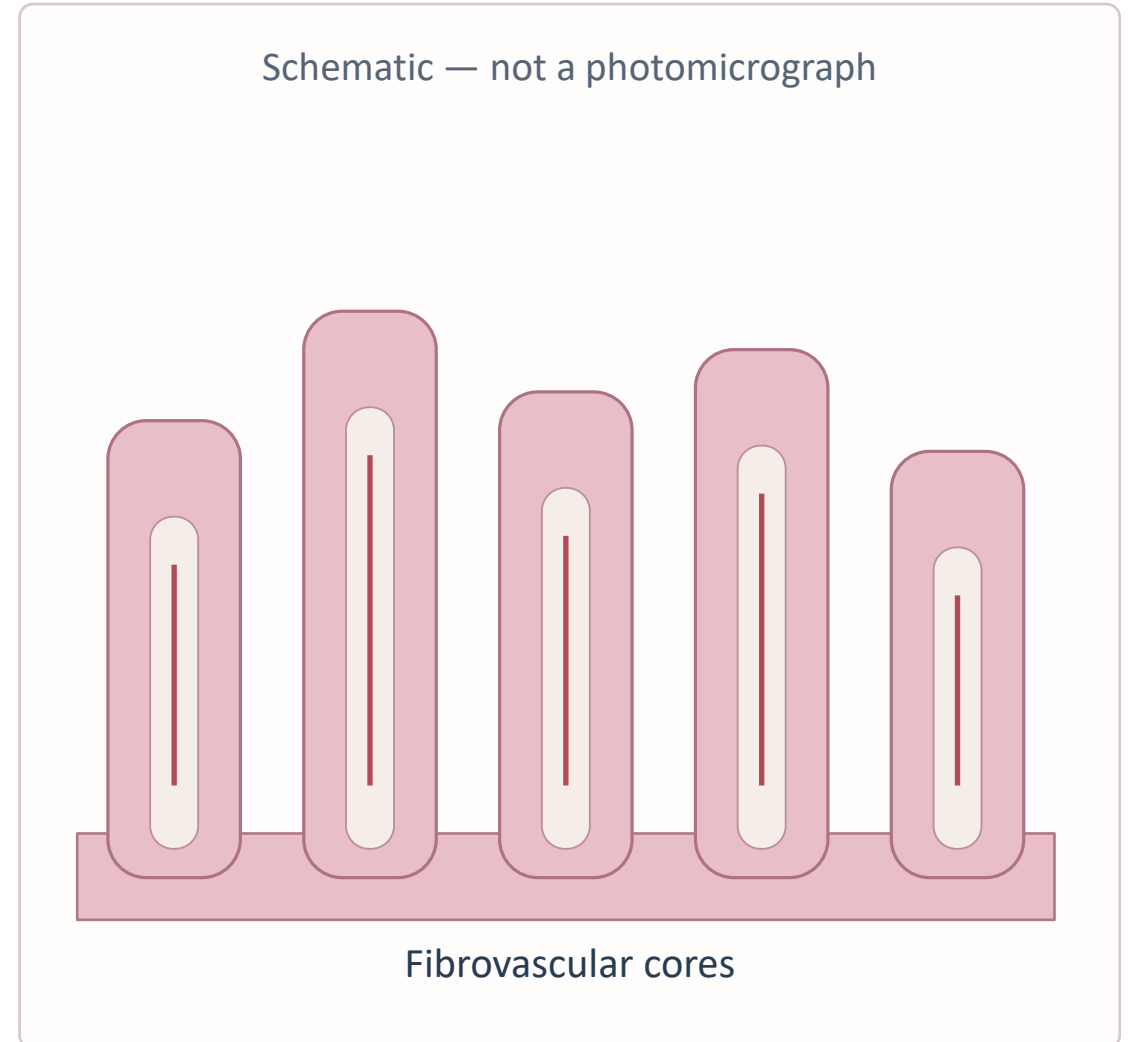
Fibrovascular stalks carry the
surface epithelium

Exophytic growth differs from stromal invasion

Architecture	Benign papilloma	Invasive carcinoma
Direction	Papillae project outward	Tumor infiltrates underlying tissue
Epithelial organization	Orderly stratification	Often disordered cytology or maturation
Stroma	Central fibrovascular cores	Desmoplastic/infiltrated tissue possible
Interpretation	Benign if no invasion	Malignant by invasive behavior

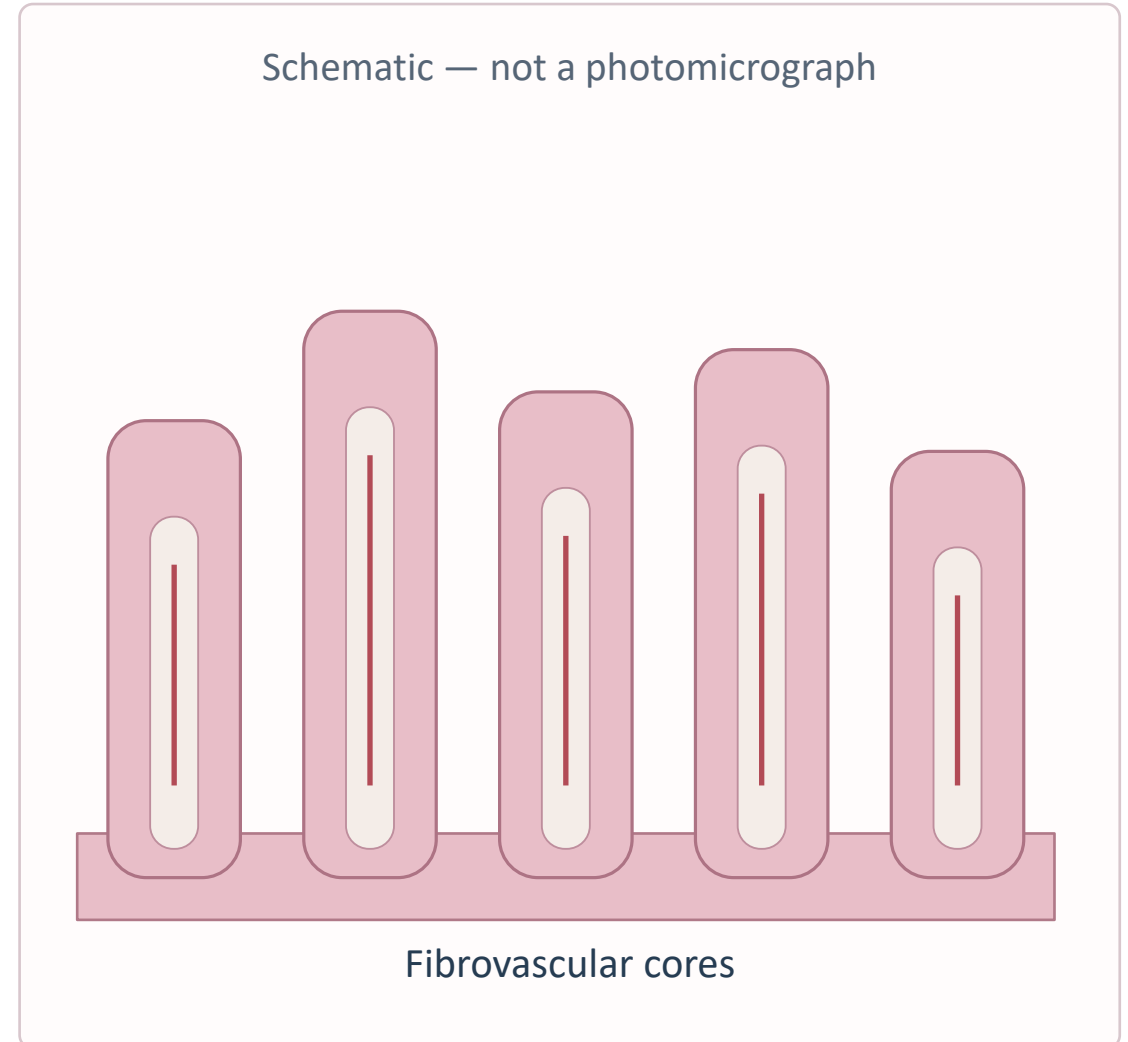
Papillary fronds are the dominant microscopic clue

- Multiple slender projections are visible at low magnification.
- Each projection contains a central supportive stromal core.
- Stratified squamous epithelium covers each frond.



Fibrovascular core: Structure and function

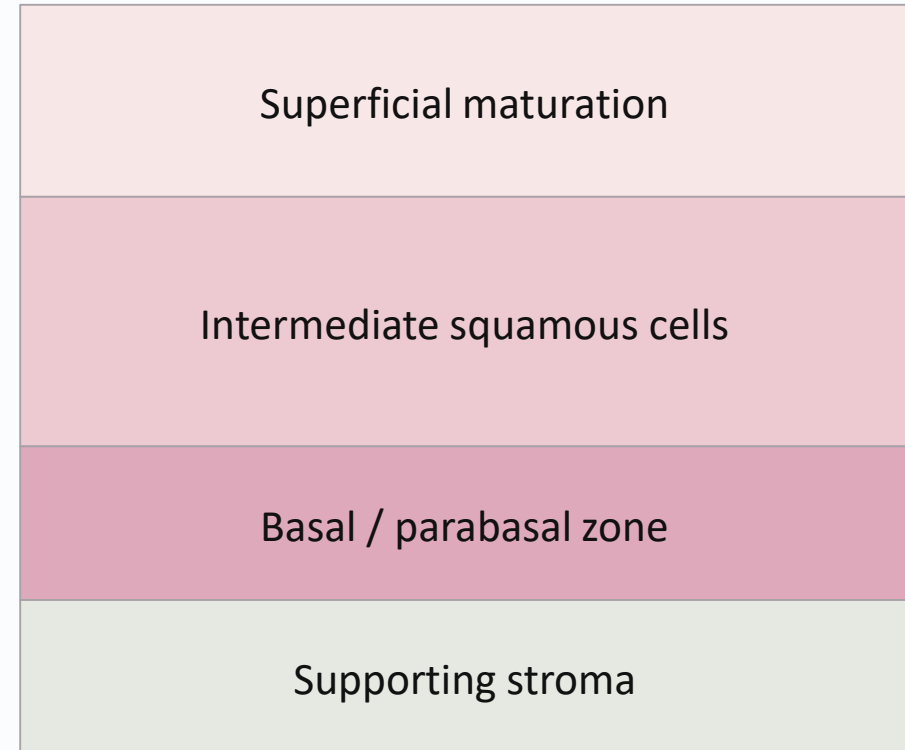
- Connective tissue provides the scaffold for each projection.
- Small vessels course within the core.
- The surface epithelium rests over the core rather than invading it.



Orderly squamous stratification

- Basal cells rest along the epithelial–stromal interface.
- Suprabasal cells mature toward the luminal surface.
- Preserved maturation supports a benign lesion when invasion is absent.

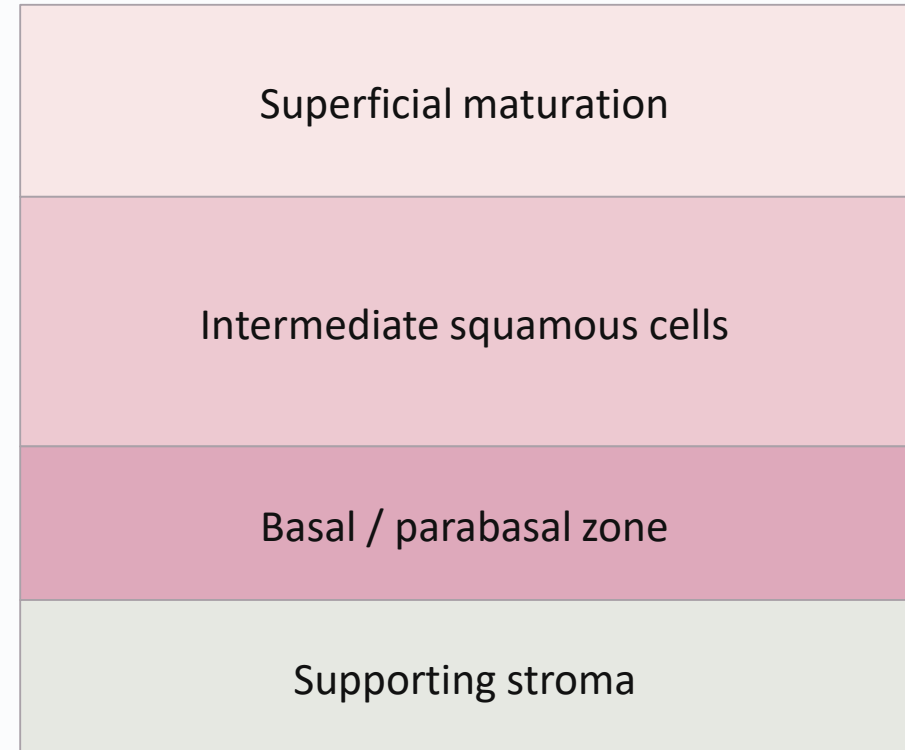
Schematic — orderly epithelial maturation



Surface and basal zones: Avoid overinterpretation

- Epithelial thickness can vary among papillary projections.
- Basal/parabasal proliferation may be accentuated.
- Evaluate architecture, maturation, cytology, and invasion together.

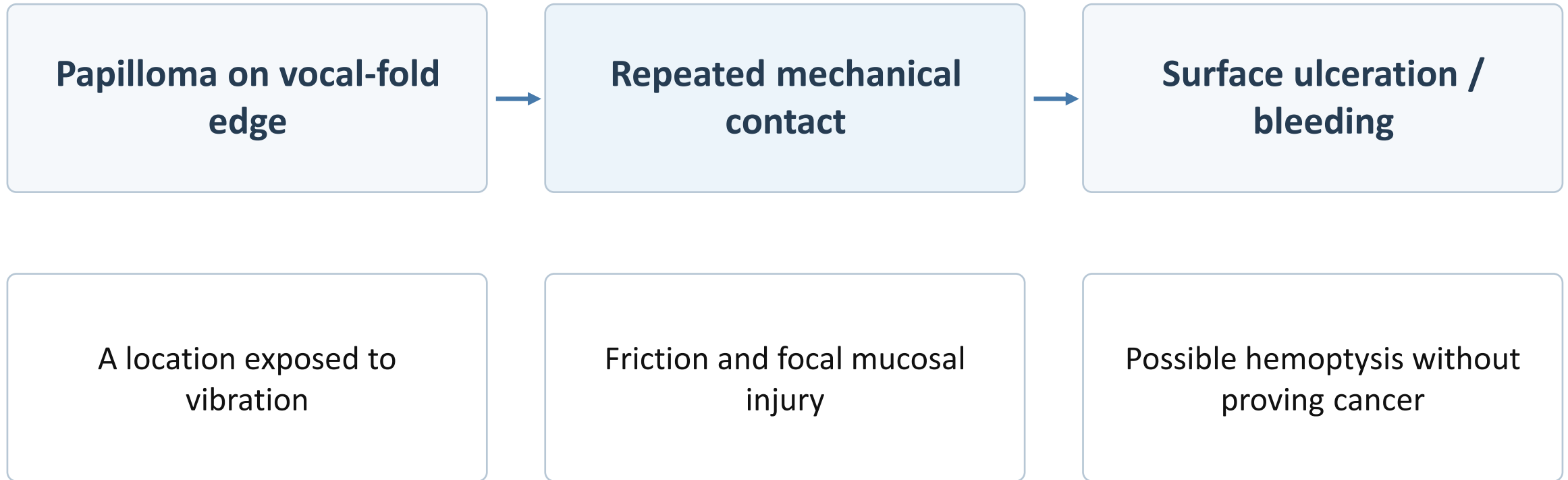
Schematic — orderly epithelial maturation



Koilocytosis: A supporting HPV-related finding

- Some papillomas exhibit superficial koilocytes.
- Koilocytes show perinuclear clearing and characteristic nuclear changes.
- The feature supports an HPV effect but is not required in every fragment.
- Exophytic fibrovascular architecture remains diagnostically central.

Trauma can change the appearance of a benign lesion



Ulceration does not automatically signify malignancy

- An injured papilloma can show erosion and bleeding.

- Interpret ulceration with the entire epithelial pattern.

- Concerning cytology or destructive infiltration still requires separate assessment.

Histology: Four observations to record

Growth pattern

Exophytic slender projections

Core

Central fibrovascular stroma

Lining

Orderly stratified squamous epithelium

Interface

No evidence of infiltrative growth in sampled tissue

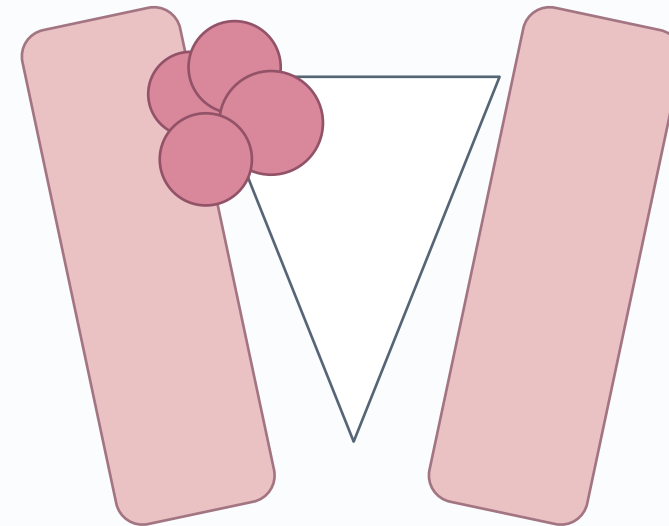
Where pathology can mislead: Fragmented biopsies

- Tangentially sectioned papillae may obscure the true projection pattern.
- Small biopsy fragments may incompletely show the epithelial–stromal boundary.
- Trauma can introduce reactive atypia that needs contextual evaluation.
- Correlate microscopic interpretation with laryngoscopic distribution.

Why small lesions cause prominent voice symptoms

- Voice depends on regular vocal-fold vibration.
- An exophytic mass alters fold contact and vibratory symmetry.
- Hoarseness can occur despite benign biology and small size.

Schematic — superior view of vocal folds



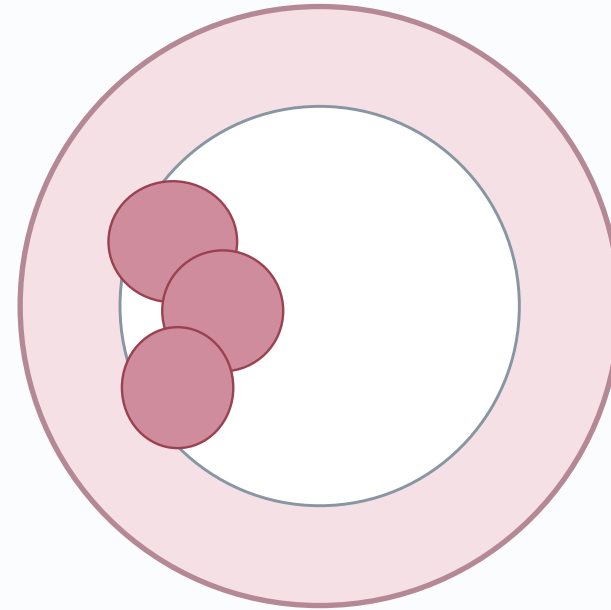
Glottic lumen

Papillary lesion

Why multiple lesions may compromise breathing

- Multifocal papillomas occupy portions of the airway lumen.
- Luminal narrowing increases airflow resistance.
- Stridor or respiratory distress requires urgent clinical assessment.

Schematic — airway cross-section



Functional narrowing

Hoarseness is the most common clinical signal

- A persistent altered voice can be the first sign of laryngeal papilloma.
- The site and surface burden affect phonation.
- Persistent symptoms warrant laryngeal visualization rather than assumptions.
- Symptom severity does not directly measure malignant potential.

Pediatric presentations may extend beyond dysphonia

- Young children may show chronic cough or noisy breathing.
- Airway narrowing can present with inspiratory stridor or breathing difficulty.
- The clinical picture can resemble common respiratory disorders.
- Anatomic evaluation is decisive when symptoms are persistent or progressive.

Hemoptysis: A mechanically plausible consequence

Papillomas on the free edge of the cord experience repeated trauma.

Ulcerated, vascular surfaces may bleed.

Hemoptysis merits evaluation; It is not a specific marker of carcinoma.

Clinical presentation depends on three variables

Site

Vocal edge versus other
airway mucosa

Burden

Single small lesion versus
multifocal growth

Course

Stable appearance versus
repeated recurrence

Laryngoscopy supplies the anatomic diagnosis

**Symptoms and
examination**



Endoscopic visualization



Biopsy when indicated

Hoarseness, stridor or other
concern

Inspect site, multiplicity, and
airway size

Confirm squamous papilloma
and assess atypia

Macroscopic recognition at laryngoscopy

- Papillomatous lesions may appear soft, pink, and lobulated.
- Surface projections give a finely papillary or wart-like appearance.
- Record whether the lesion is solitary or clustered.
- Location relative to the free vocal-fold edge helps explain symptoms.

Tissue diagnosis: How to examine the specimen

**Confirm papillary
architecture**



**Examine epithelial
maturation**



**Search for atypia and
invasion**

Fibrovascular cores

Orderly squamous lining

Report genuine concern
rather than recurrence alone

Histologic diagnosis does not require routine HPV typing

- In characteristic lesions, morphology and clinical context establish the diagnosis.
- HPV 6/11 is already strongly associated with recurrent papillomatosis.
- HPV ISH or PCR may be informative in selected or research contexts.
- No routine viral assay should substitute for assessing invasion.

P16 is not a stand-alone discriminator

- P16 overexpression is associated with some high-risk HPV-driven tumors.

- That framework should not be mechanically applied to HPV 6/11 laryngeal papillomas.

- A negative p16 result does not exclude a low-risk HPV papilloma.

A focused pathology report

Diagnosis

Squamous papilloma / papillomatous lesion

Morphology

Papillary fronds with fibrovascular cores

Atypia

Describe dysplasia if truly present

Sampling

State limitations when invasion cannot be assessed

Differential: Reactive vocal-fold nodule or polyp

Feature	Reactive nodule / polyp	Squamous papilloma
Surface	Typically smooth / rounded	Papillary / lobulated
Etiology	Voice strain or smoking context	HPV 6/11 association
Stroma	Loose, myxoid, fibrotic, or vascular	Discrete fibrovascular papillary cores
Histology	Reactive squamous cover over altered stroma	Squamous-lined finger-like fronds

Reactive polyps: Why the stroma differs

- Vocal-fold polyps are reactive lesions rather than HPV-driven neoplasms.

- The stromal component may be edematous, myxoid, fibrotic, or vascular.

- Architecture is generally smooth or polypoid, not slender papillary fronds.

Nodules versus polyps: Pattern recognition

Feature	Vocal-fold nodule	Vocal-fold polyp
Typical laterality	Bilateral	Unilateral
Common setting	Repeated voice strain	Voice strain / smoking
Microscopic basis	Reactive squamous cover and altered stroma	Similar reactive stromal changes
Key distinction	Not HPV papillomatosis	Not HPV papillomatosis

Papilloma versus dysplastic squamous mucosa

Feature	Papilloma	Dysplasia
Defining pattern	Exophytic fibrovascular fronds	Epithelial cytologic/architectural atypia
Cell maturation	Usually orderly	Progressively disturbed with grade
Invasion	Absent in benign papilloma	Absent in pure dysplasia
Clinical implications	Can recur	Premalignant risk depends on grade

Papilloma versus exophytic carcinoma

Diagnostic question	Papilloma favors	Carcinoma concern
Epithelial cytology	Orderly squamous cells	Significant malignant cytologic atypia
Tissue interface	No destructive invasion	Infiltrative epithelial nests / tongues
Gross appearance	Delicate, soft papillary lesion	May be irregular, ulcerated, or fungating
Decisive step	Inspect histology	Assess deep interface and invasion

The key cancer pitfall: Reactive atypia

- Inflammation, repeated trauma, and repair can distort benign epithelial cytology.
- Interpret mitoses and nuclear changes relative to epithelial layer and injury.
- Unequivocal dysplasia should be described; Do not infer it from HPV positivity.
- Concern for infiltration requires an adequately sampled epithelial–stromal interface.

Features prompting expanded assessment

Clinical change

Unexpected rapid change, ulceration or persistent worsening

Microscopy

Significant epithelial atypia or possible destructive growth

Risk context

Smoking or prior irradiation in a recurrent lesion

Next action

Correlate, re-examine deeper tissue, or resample as indicated

Risk of malignant transformation is low, not zero

Squamous carcinoma arising from papillomas as rare.

Tobacco exposure and prior irradiation are contexts of concern.

Neoplastic risk must be distinguished from the much more common risk of recurrence.

Recurrent papillomatosis is frequently a longitudinal disease

Local removal



Clinical improvement



Possible regrowth

Remove visible disease

Voice/airway can improve

Repeat evaluation and
procedures may be needed

Clinical treatment goals

Airway

Maintain adequate patency

Voice

Preserve vocal-fold function

Disease control

Reduce symptomatic burden

Tissue preservation

Limit injury from repeated intervention

Endoscopic resection is a primary approach

- Endoscopic removal as usual therapy.

- Endoscopic access permits site-directed treatment of visible papilloma.

- Surgery removes lesions but cannot guarantee permanent eradication of disease.

Tissue-sparing surgery matters in the larynx

- Surgical precision must balance lesion removal against damage to healthy vibratory mucosa.
- Repeated intervention can lead to fibrosis or impaired voice.
- Airway safety takes priority when obstruction develops.
- Operative technique is selected by the treating airway specialist.

Why recurrent lesions often need repeated procedures

**Viral-associated disease
persists**



**Visible papilloma
removed**



Disease may reappear

Underlying susceptibility /
infection

Anatomic burden decreases

Follow-up remains necessary

Follow-up assesses function as well as recurrence

Voice

Hoarseness or voice fatigue

Breathing

Stridor, dyspnea, airway symptoms

Anatomy

Endoscopic recurrence or extension

Histology

Resample when new suspicious features emerge

Adjuvant therapies: Separate disease control from cure

- Advanced or repeatedly recurrent RRP may require measures beyond local surgery.
- Bevacizumab and other adjuvant approaches have been evaluated in selected patients.
- The evidence and indications differ across treatments and populations.
- This lecture does not treat such approaches as an established universal cure.

HPV vaccination targets the causal viral types

Vaccine prevention



**Fewer vaccine-type HPV
infections**



**Reduced juvenile RRP
burden**

Vaccines containing HPV 6/11
antigens

Prevention of vaccine-type
infection

Population-level decline
observed after vaccine
introduction

Vaccination evidence: Separate prevention from treatment

Question	What evidence supports	What not to infer
Prevention	CDC documents decline in juvenile-onset RRP	Not a guaranteed individual preventive outcome
Established papilloma	Vaccination is not equivalent to surgical removal	No claim of certain cure
Clinical recurrence	Adjunctive vaccine studies exist	Cannot generalize all study findings

The HPV 6/11 link explains prevention logic

The same HPV types repeatedly underlie benign laryngeal papillomatosis.

A vaccine targeting these types interrupts the causal infection pathway.

CDC reports significant declines in juvenile-onset disease following vaccine introduction.

Clinical reasoning case: Persistent adult hoarseness

A 29-year-old has progressive hoarseness. Laryngoscopy shows a small, soft exophytic lesion on the true vocal fold.

- What architecture should you expect on biopsy?
- What viral types are most relevant?

Interpretation: Finger-like squamous-lined papillae with fibrovascular cores; HPV 6 and 11.

Clinical reasoning case: Child with recurrent stridor

A school-aged child develops hoarseness and recurrent noisy breathing. Endoscopy identifies multiple laryngeal papillary lesions.

- What is the likely clinicopathologic syndrome?
- What makes this condition important despite benign histology?

Interpretation: Recurrent respiratory papillomatosis; Repeated recurrence and airway compromise.

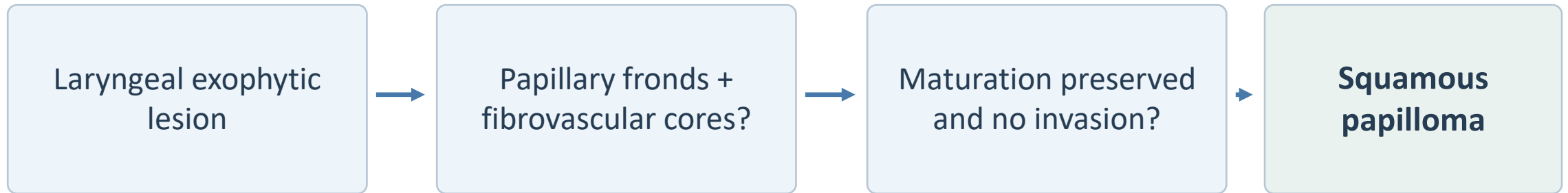
Microscopy reasoning exercise

Biopsy shows multiple slender exophytic epithelial fronds, mature squamous lining, vascular cores, and no infiltrative growth.

- What is the best morphologic diagnosis?
- Which single missing finding would most change the malignant assessment?

Interpretation: Squamous papilloma; Unequivocal destructive stromal invasion (with malignant cytology) would trigger concern.

A structured diagnostic pathway



If not: Assess reactive polyp, dysplasia, or other tumor
If not: Evaluate atypia, sampling, and carcinoma

High-yield distinctions

Finding	Interpretation
Exophytic fibrovascular squamous fronds	Supports squamous papilloma
HPV 6/11 and recurrent multiplicity	Supports respiratory papillomatosis
Rounded smooth vocal-fold lesion with myxoid stroma	Favors reactive polyp
Destructive epithelial stromal infiltration	Requires assessment for invasive SCC
Recurrent benign papilloma	Not automatically malignant

Five concepts to retain

- Laryngeal squamous papilloma is a benign, exophytic HPV 6/11–associated lesion.
- Its histologic signature is finger-like fronds with fibrovascular cores.
- Orderly squamous maturation and absent invasion support benign diagnosis.
- Multiplicity and recurrence create substantial voice and airway morbidity.
- Endoscopic control and HPV vaccination address different points in disease prevention and care.

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