
Hyperplasia–Dysplasia–Carcinoma Sequence

Laryngeal squamous epithelium: precursor morphology, risk and clinical significance

Dr Abu Suraih Sakhri

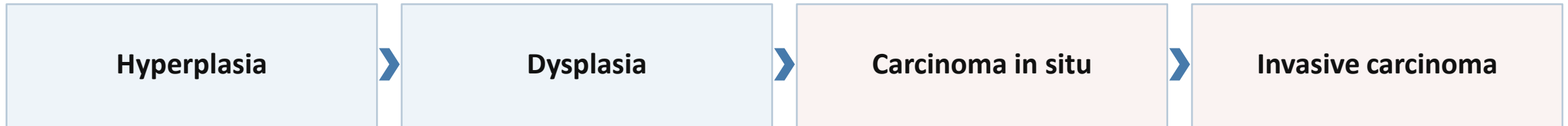
MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Distinguish hyperplasia, dysplasia, carcinoma in situ, and invasive carcinoma.
- Interpret visible laryngeal lesions without equating color or texture with histologic grade.
- Relate tobacco, alcohol and other exposures to epithelial change and cancer risk.
- Apply biopsy findings, progression-risk estimates and clinical stage to case interpretation.

The spectrum is epithelial, not merely gross



A morphologic spectrum; Progression is not inevitable in every lesion

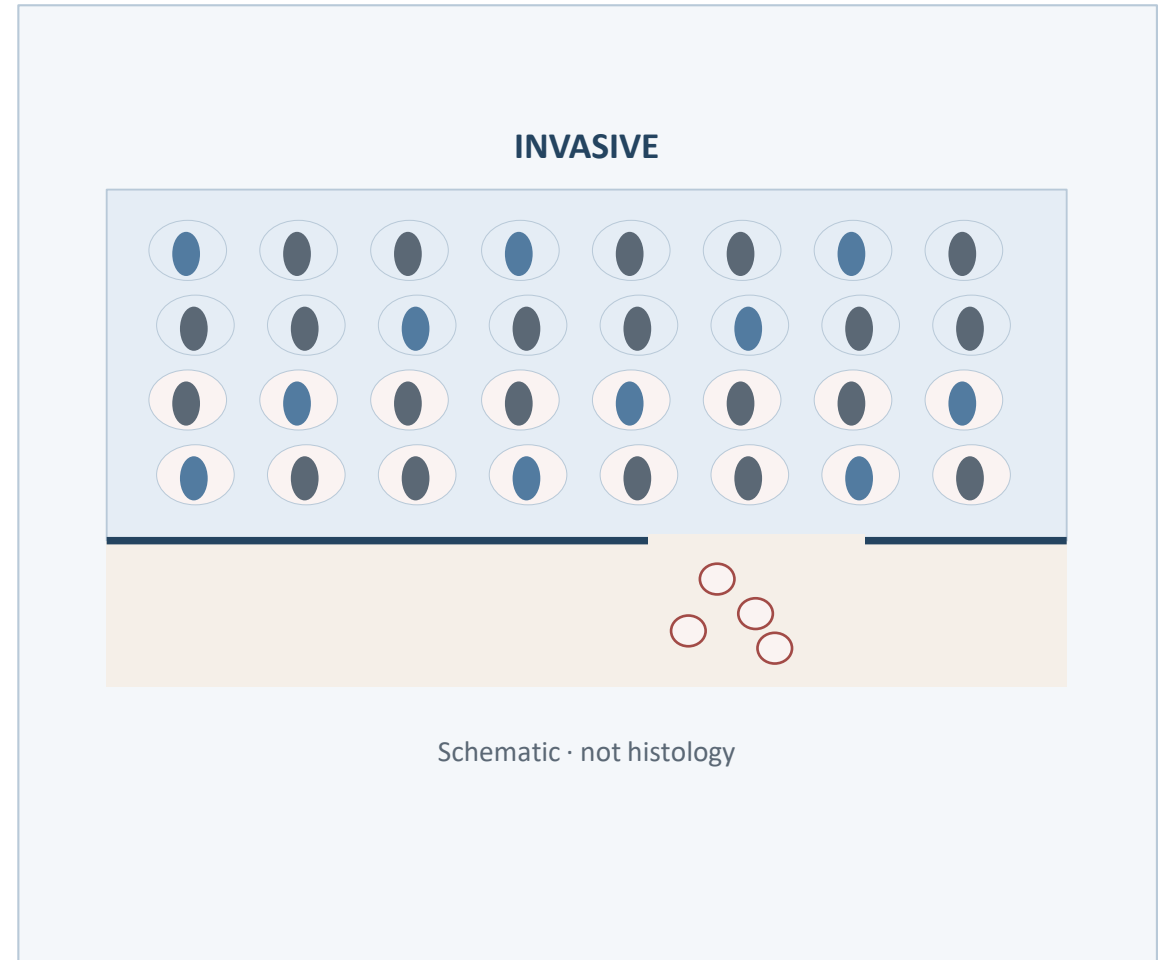
- An individual lesion cannot be placed on this continuum reliably by laryngoscopic appearance alone.
- Biopsy provides the histologic information needed to assess dysplasia.

Four terms answer different questions

Term	What changes?	Key distinction
Hyperplasia	Epithelial cell number / thickness	Orderly growth may remain nondysplastic
Dysplasia	Cellular atypia and disordered maturation	Premalignant change with variable risk
Carcinoma in situ	Full-thickness severe atypia	Basement membrane remains intact
Invasive carcinoma	Malignant growth extends into stroma	Basement membrane breached

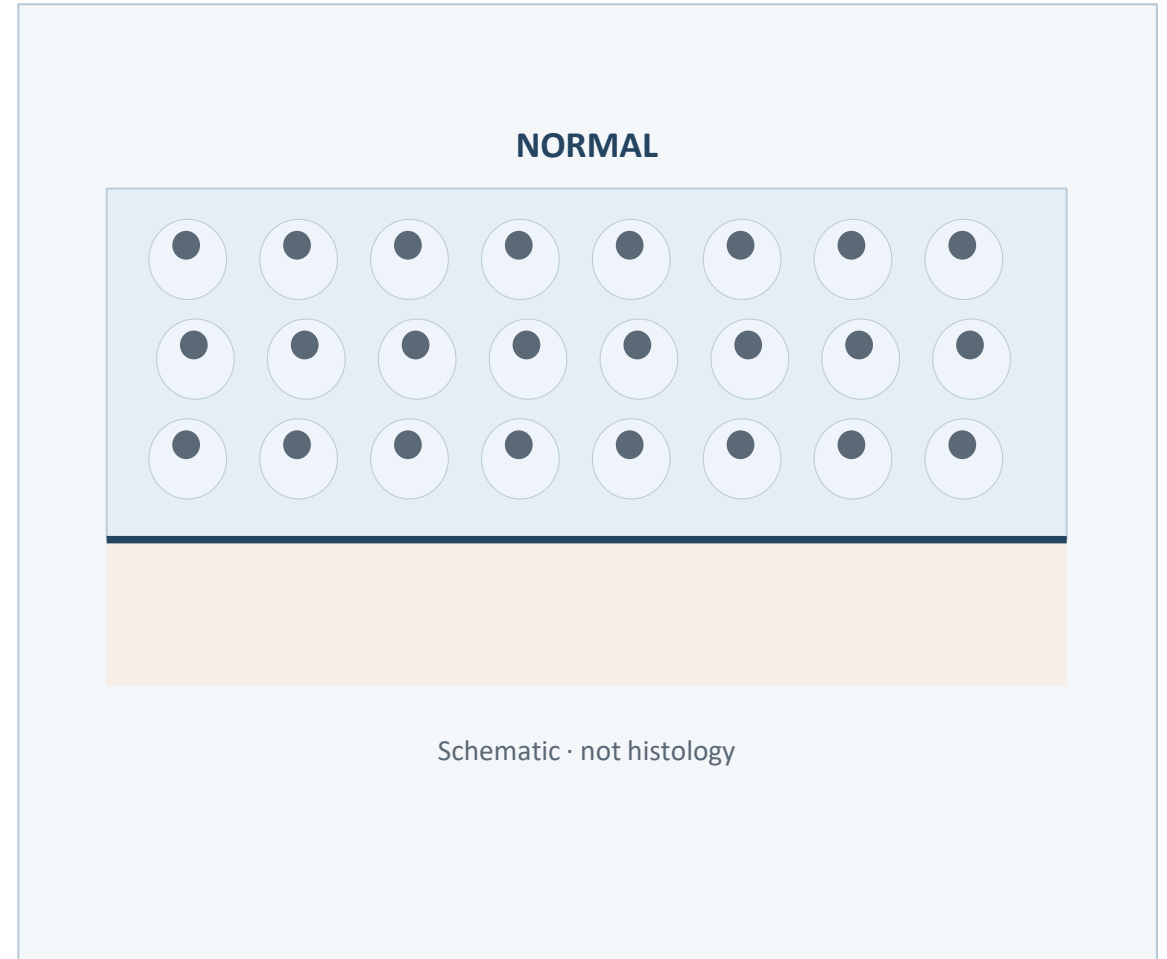
The basement membrane is the critical boundary

- Dysplasia and carcinoma in situ remain confined to the epithelial compartment.
- Invasive carcinoma crosses the basement membrane into underlying tissue.
- Surface irregularity alone cannot establish whether invasion has occurred.



Normal epithelium has orderly maturation

- Basal epithelial cells mature as they move toward the surface.
- Nuclear and cytoplasmic patterns vary in an orderly manner through the epithelial thickness.
- Mitoses are ordinarily concentrated toward the basal compartment.



Metaplasia is not synonymous with dysplasia

Alteration	Definition	Implication
Metaplasia	Replacement of one differentiated cell type by another	Adaptive response; not necessarily dysplastic
Dysplasia	Disordered epithelial maturation with cytologic atypia	A premalignant morphologic change
Carcinoma in situ	Severe full-thickness epithelial atypia without invasion	Preinvasive carcinoma

Squamous metaplasia can follow chronic injury

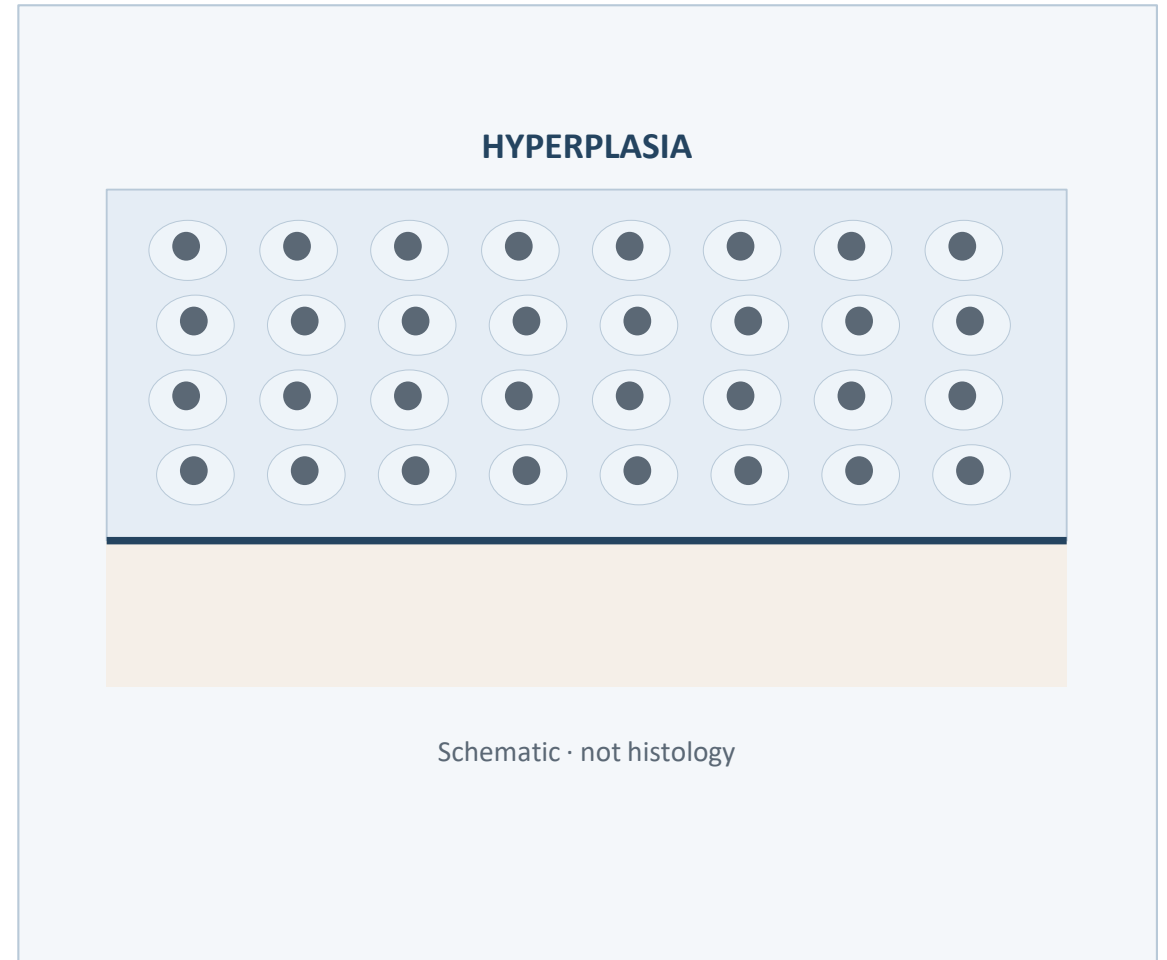
- Chronic smoking-associated laryngitis with squamous epithelial metaplasia.
- A metaplastic epithelium can remain orderly or can subsequently show dysplastic change.
- Metaplasia and dysplasia must not be reported as interchangeable diagnoses.

Important distinction

An adaptive cell-type change is not, by itself, a histologic diagnosis of cancer.

Hyperplasia means increased epithelial growth

- The laryngeal sequence may begin with epithelial thickening.
- Cell layering can increase without the disordered maturation characteristic of dysplasia.
- Hyperplasia is therefore a morphologic descriptor, not automatically a premalignant lesion.



Nondysplastic hyperplasia carries very low risk

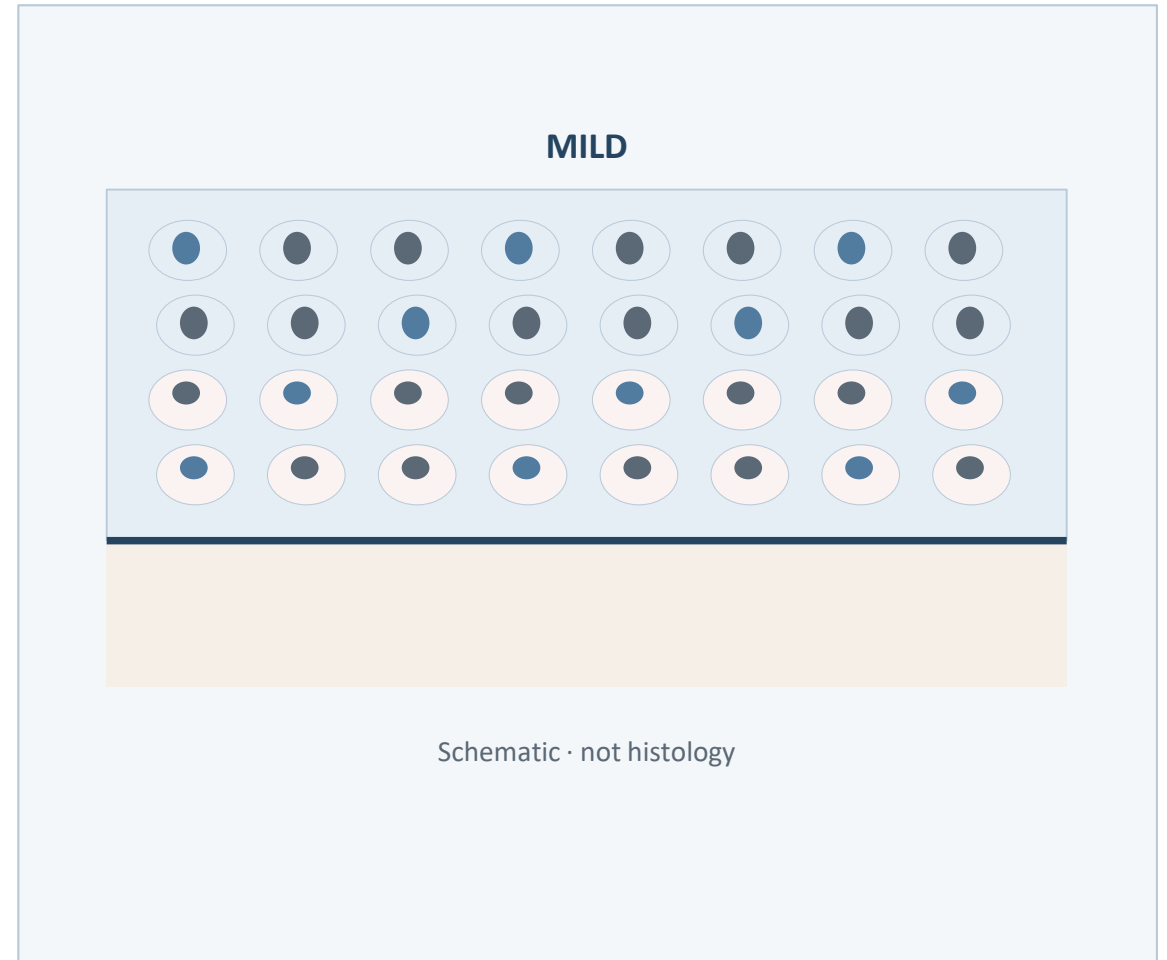
- Almost no malignant-transformation potential for nondysplastic laryngeal hyperplasias.
- This statement applies to the histologic category, not to an unbiopsied white plaque.
- Sampling and pathologic interpretation determine whether dysplasia is absent.

Risk interpretation

Visible thickening does not establish nondysplastic histology.

Dysplasia denotes disordered epithelial growth

- Cellular atypia and loss of orderly differentiation define the concept.
- Dysplastic changes predominantly affect epithelial cells.
- Grade helps estimate subsequent malignant-transformation risk.



Cytologic clues to dysplasia

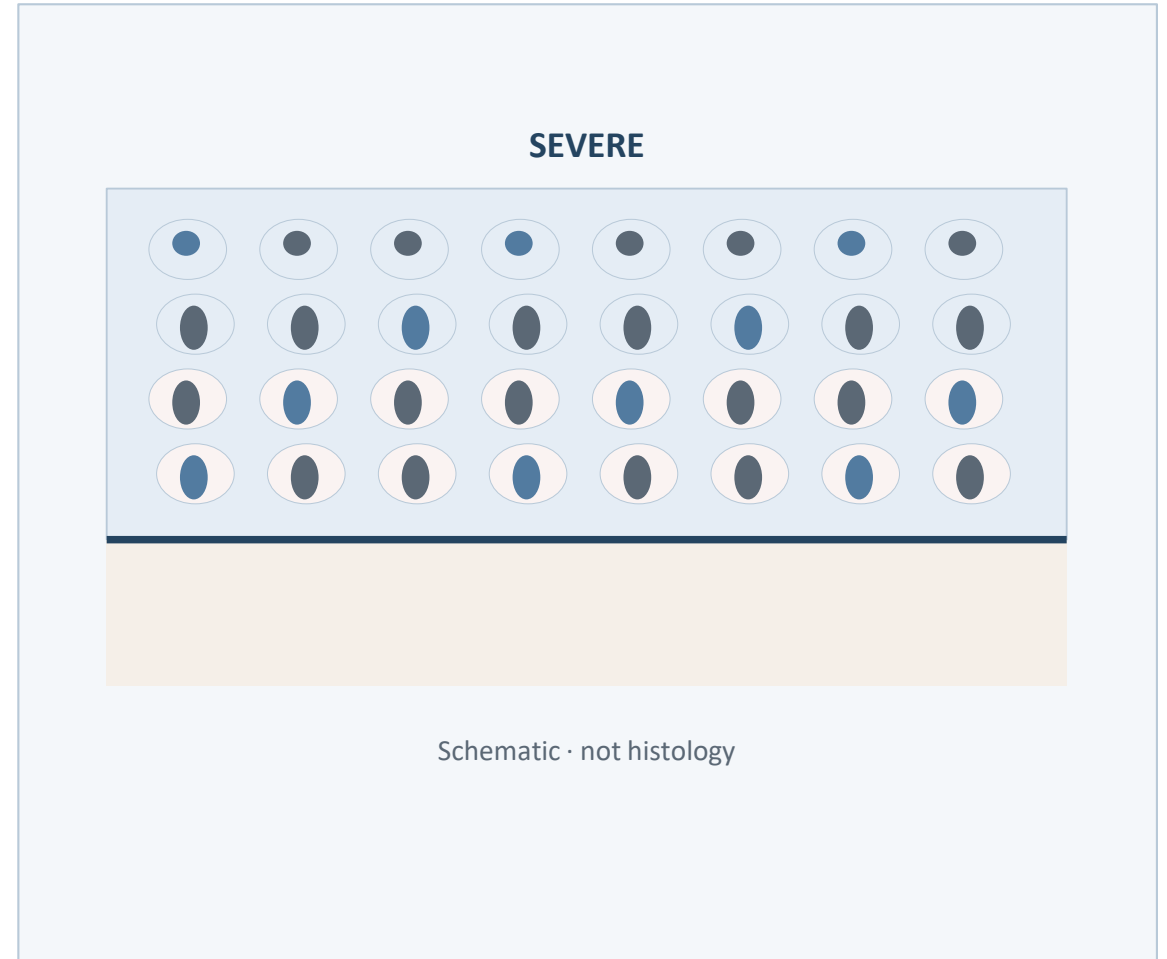
- Pleomorphism: Variability in cellular and nuclear shape.
- Larger, hyperchromatic nuclei and increased nuclear-to-cytoplasmic ratio.
- These changes must be interpreted in their tissue architecture.

Microscopic reasoning

Atypical nuclei must be interpreted with epithelial maturation and mitotic distribution.

Loss of maturation is an architectural clue

- Normal stratification shows progressive maturation from basal to superficial cells.
- Dysplasia disrupts that gradient, partially or extensively.
- The degree of architectural disorder contributes to the histologic impression.



Mitotic distribution changes with dysplasia

- Normal squamous epithelium predominantly shows mitoses near the basal layer.
- Dysplastic epithelium may show increased mitotic figures at higher levels.
- Atypical mitoses reinforce malignant cytologic concern but do not alone define invasion.

Correlation

Assess nuclear features,
architecture and mitoses together.

Dysplasia grade is a histologic assessment

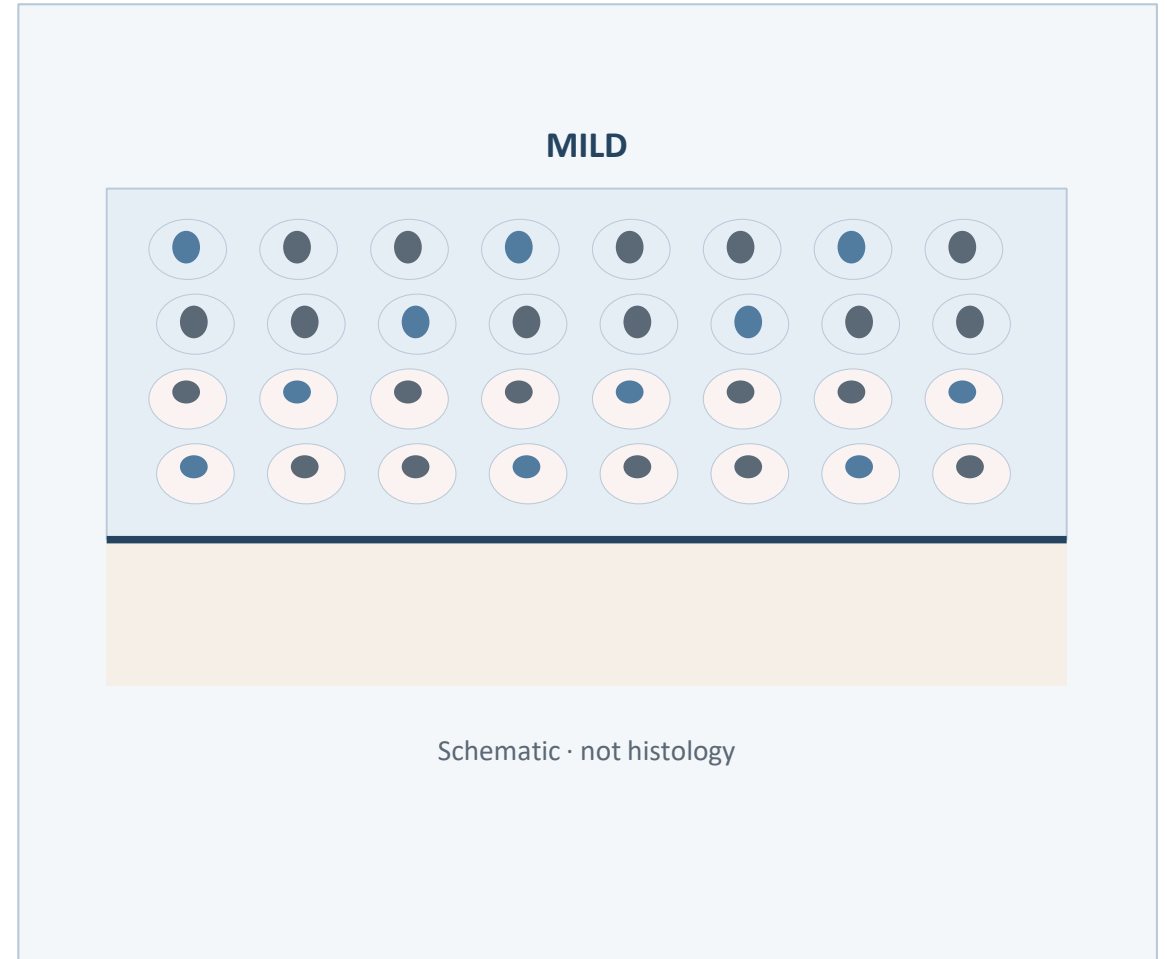
- Robbins relates transformation risk to the initial grade of dysplasia.
- Gross surface color and thickness cannot establish a reliable grade.
- Only histologic evaluation can grade dysplasia.

Key diagnostic rule

Laryngoscopy identifies a lesion;
Tissue evaluation characterizes its
dysplastic grade.

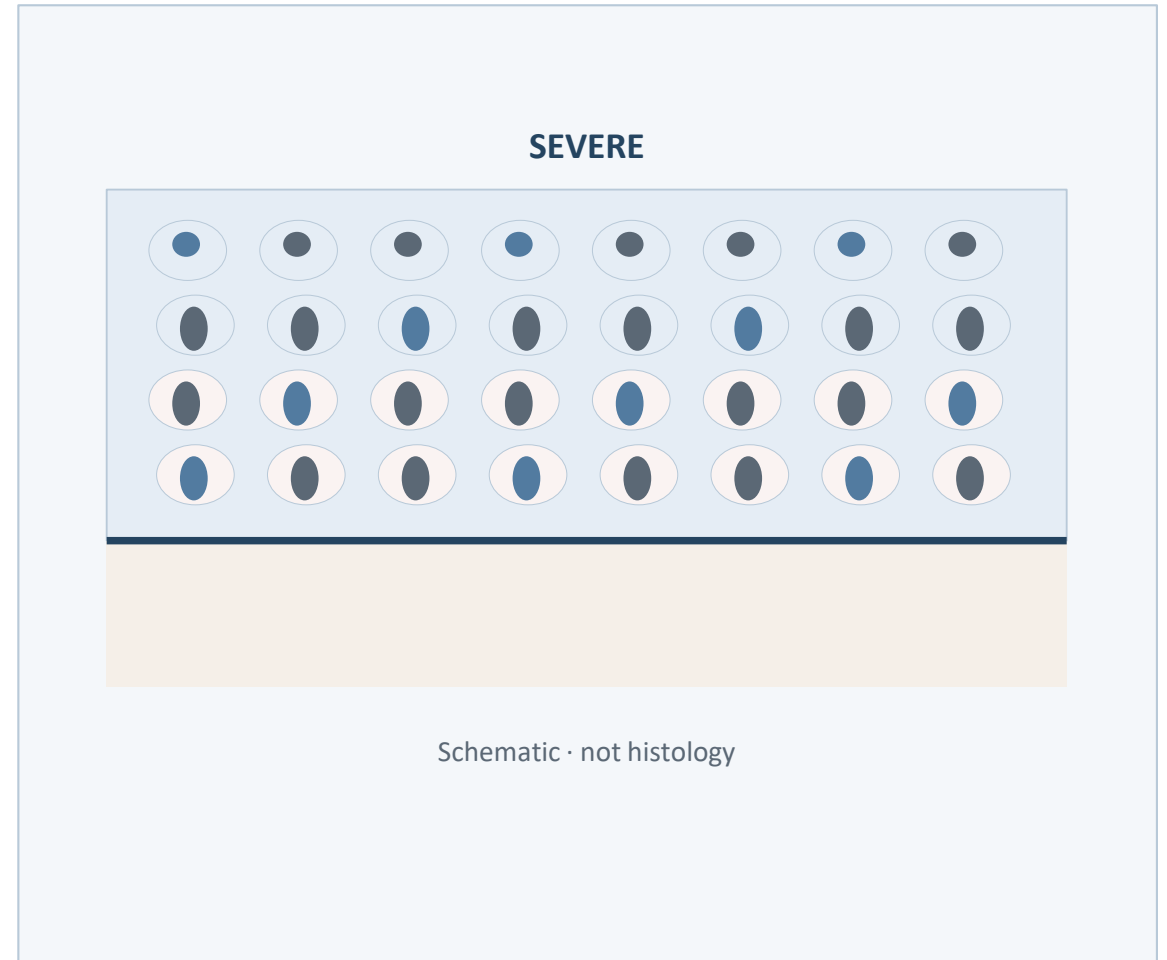
Mild dysplasia: Lower but nonzero risk

- Mild dysplasia is a histologic precursor category with relatively low transformation risk.
- Robbins gives a 1%–2% example over 5–10 years.
- Low risk must not be misconstrued as zero risk or as a prediction for an individual patient.



Severe dysplasia: Higher transformation risk

- The initial severe dysplasia category carries greater malignant-transformation risk.
- Robbins provides an illustrative 5%–10% estimate.
- A severe biopsy result warrants different concern from nondysplastic hyperplasia.



Quantitative risk must retain its context

Mild dysplasia

1%–2%

Over 5–10 years example

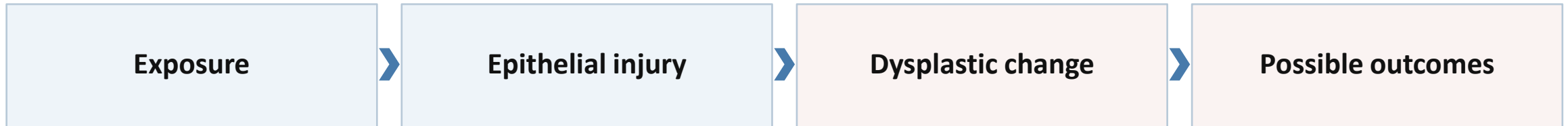
Severe dysplasia

5%–10%

Higher risk in the same source discussion

- These figures are source-reported examples, not a personalized risk calculator.
- Do not treat grade-associated risk as proof that a given lesion will progress.

Dysplasia does not imply inevitable progression



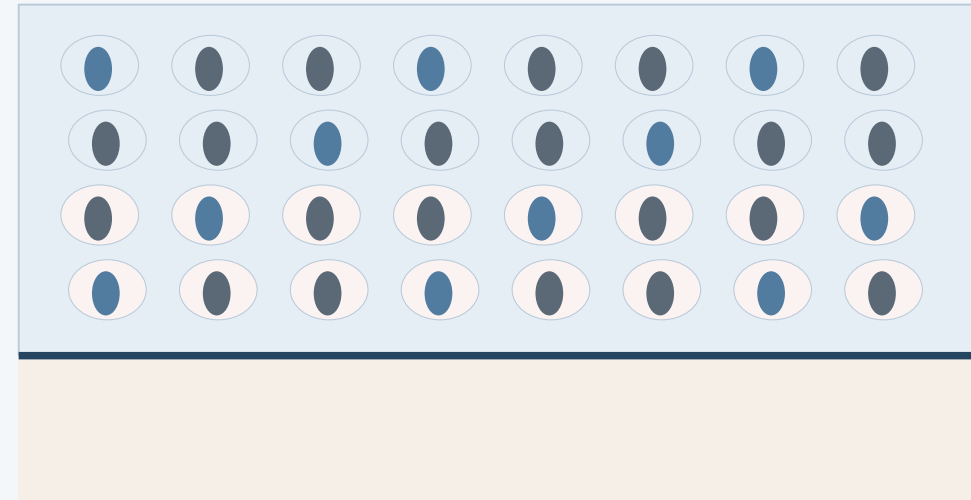
Possible outcomes include persistence, regression, or progression

- Dysplasia can regress when inciting causes are removed.
- Premalignant morphology indicates potential for progression, not deterministic fate.

Carcinoma in situ is preinvasive cancer

- Severe atypia involves the entire epithelial thickness.
- The basement membrane is not penetrated.
- The boundary between in situ and invasive disease is a tissue relationship, not a surface-color distinction.

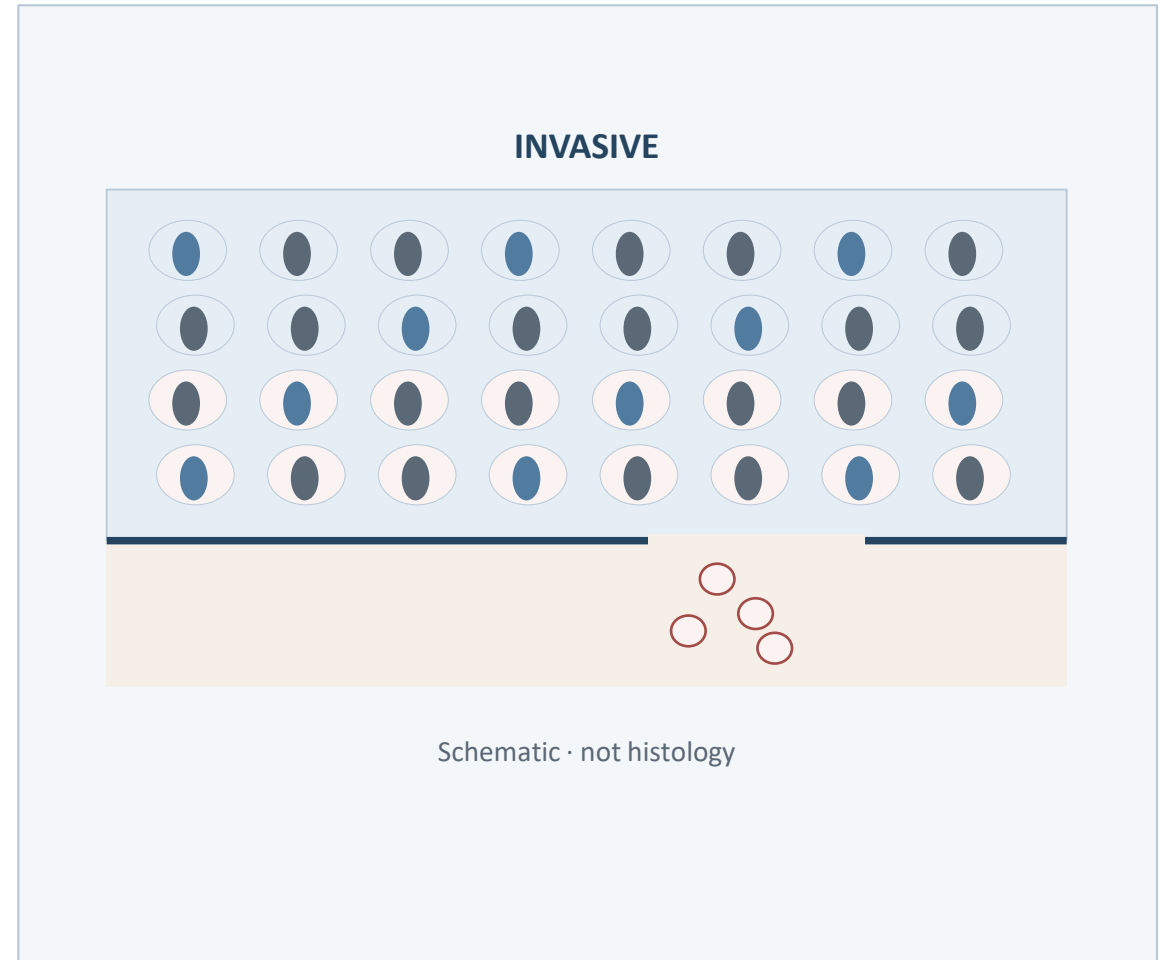
CARCINOMA IN SITU



Schematic · not histology

Invasive carcinoma crosses into stroma

- Malignant squamous epithelium extends beyond the basement membrane.
- The distinction requires attention to the epithelial–stromal interface.
- Invasion fundamentally changes the pathologic category.



Adjacent mucosa may show precursor change

- Laryngeal SCC may coexist with squamous hyperplasia, dysplasia or carcinoma in situ in nearby mucosa.
- Repeated carcinogen exposure can affect a mucosal region rather than one isolated point.
- This observation supports careful evaluation of surrounding epithelium in specimens.

Tissue context

Neoplastic and non-neoplastic epithelial changes may coexist within the same specimen.

Repeated carcinogen exposure is central



- The pathologic spectrum occurs in a tissue repeatedly exposed to environmental insults.

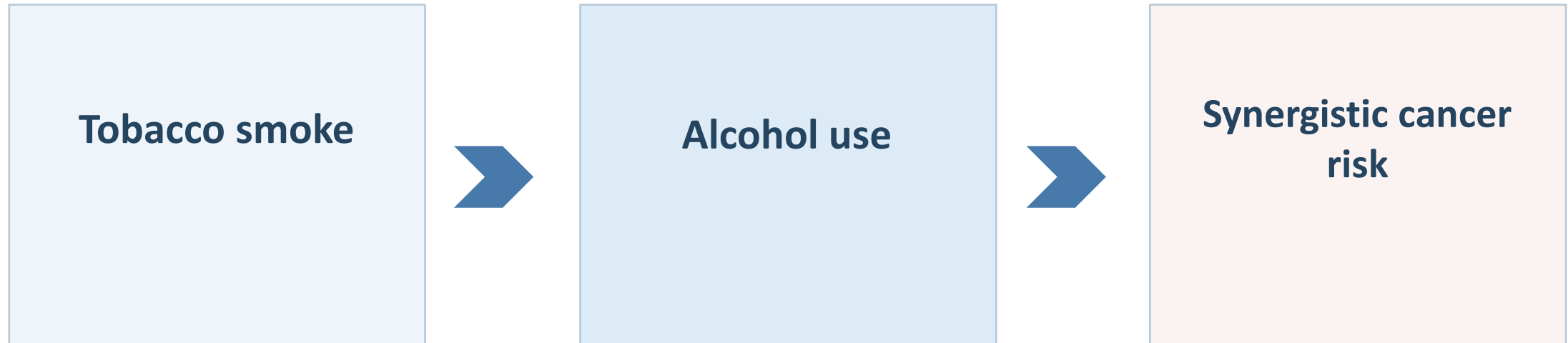
Tobacco is the dominant exposure

- Laryngeal carcinoma is most often related to tobacco smoke.
- Risk increases with exposure.
- A history of chronic smoking is a major clinical context, not a histologic diagnosis.

Tobacco-associated risk

Greater exposure is associated with greater cancer risk.

Alcohol and tobacco act synergistically

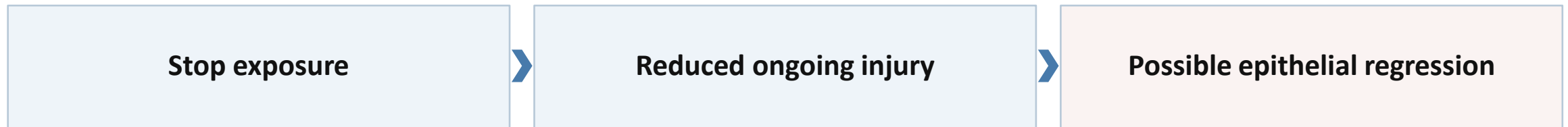


- The combined exposure increases cancer risk substantially beyond either exposure considered alone.

Other factors can contribute to risk

Exposure	Source-supported relationship	Interpretive limit
Nutritional factors	May increase laryngeal cancer risk	Robbins does not quantify effect here
Asbestos exposure	May increase risk	No effect estimate supplied
Irradiation	May increase risk	Depends on clinical context
High-risk HPV infection	May increase risk	Do not conflate with HPV 6/11 papillomas

Smoking cessation may reverse precursor change



Smoking cessation acts on the initiating exposure

- Before malignant transformation, epithelial abnormalities often regress after tobacco cessation.
- Reversal is possible, not guaranteed, and does not replace histologic assessment of suspicious lesions.

Do not infer gene pathways from appearance

- Squamous carcinogenesis to accumulating molecular changes across time.
- The selected laryngeal section does not specify a gene-by-gene molecular sequence.
- A schematic continuum must not be mistaken for a universal ordered mutation pathway.

Scope control

Morphologic progression is supported; A deterministic molecular timeline is not specified by this excerpt.

Visible epithelium has several appearances



Smooth focal thickening



White rough keratosis



Irregular / ulcerated lesion

- Clinical morphology is variable even within the laryngeal precursor spectrum.

Smooth thickening is nonspecific

- Focal mucosal thickening is part of the reported clinical spectrum.
- Smooth appearance cannot demonstrate histologic absence of dysplasia.
- A lesion must be interpreted with history, examination and tissue findings.

Surface versus tissue

A smooth surface is not the same as an orderly microscopic epithelium.

White mucosa may reflect keratosis

- White, roughened laryngeal surfaces associated with keratosis.
- White color describes a gross finding; It does not grade the epithelium.
- Histologic assessment distinguishes orderly keratinizing change from dysplasia.

Interpretive caution

Gross leukoplakic appearance does not map one-to-one onto a single histologic diagnosis.

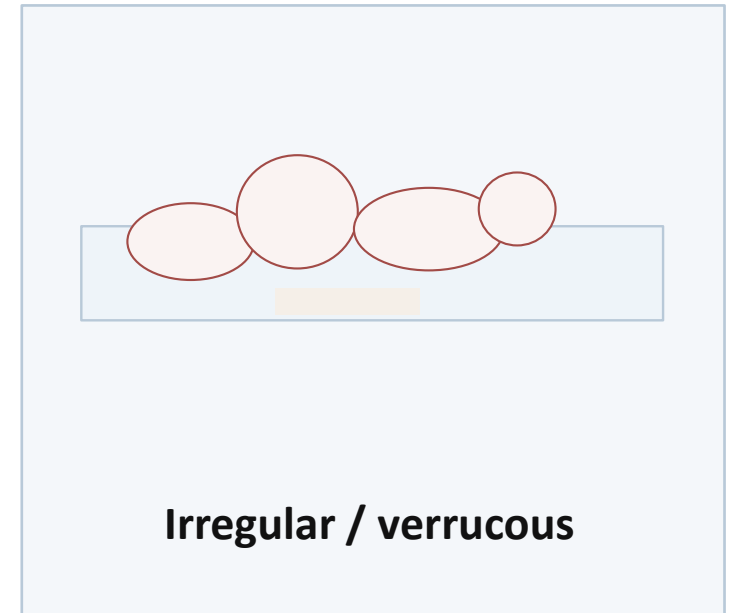
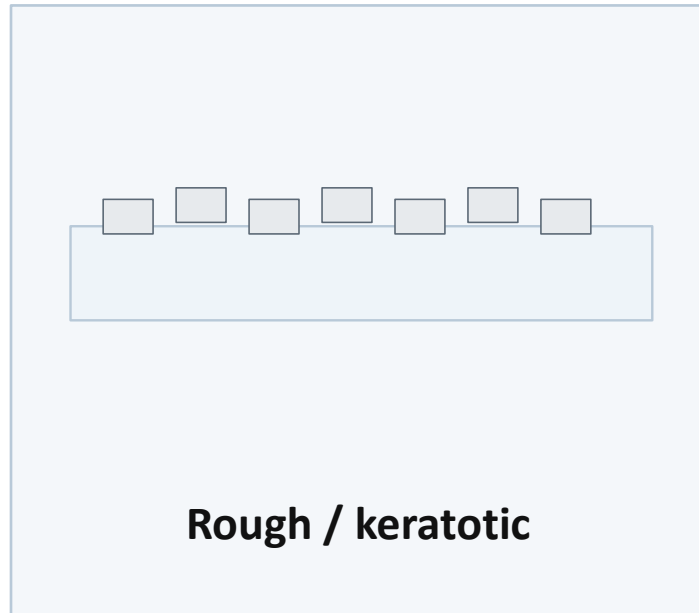
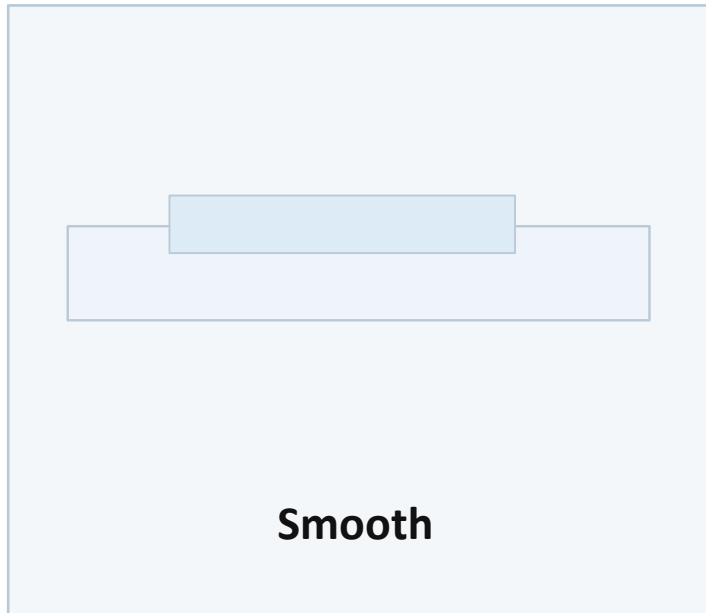
Red mucosa also lacks specific grade information

- The source describes focal erythematous laryngeal surfaces.
- Redness may prompt examination but cannot independently diagnose carcinoma.
- The same diagnostic rule applies: The histologic compartment and atypia matter.

Visible appearance

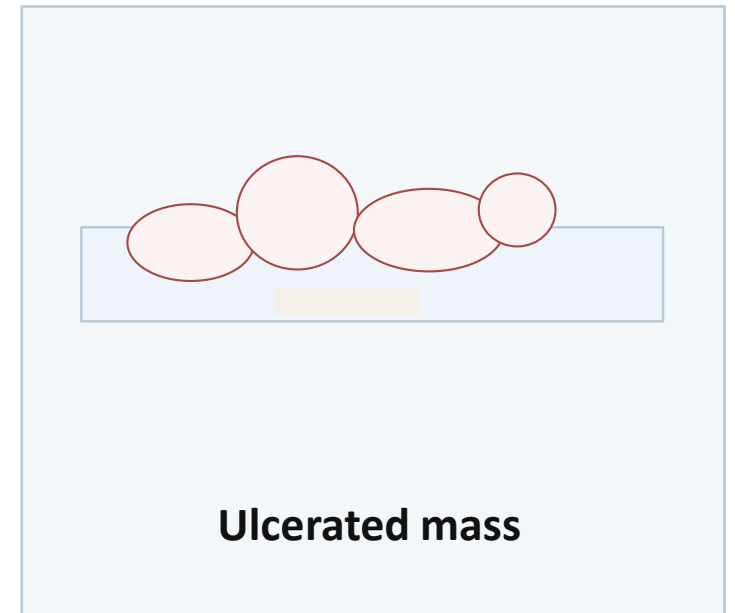
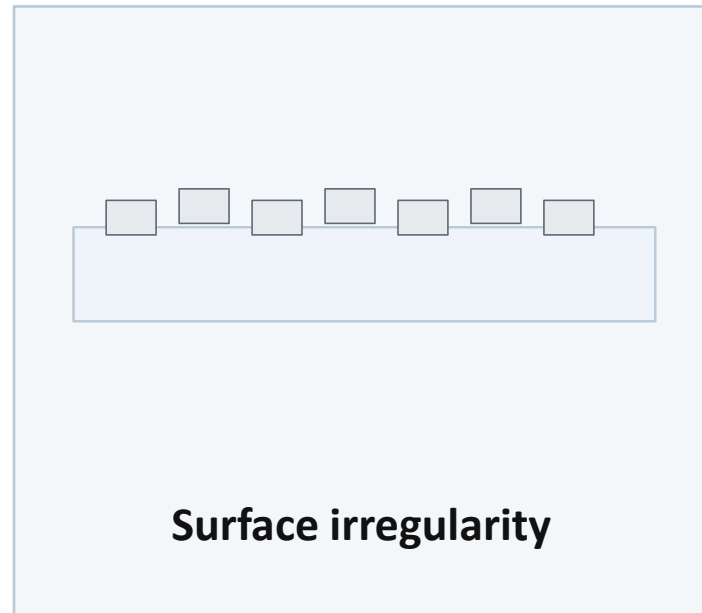
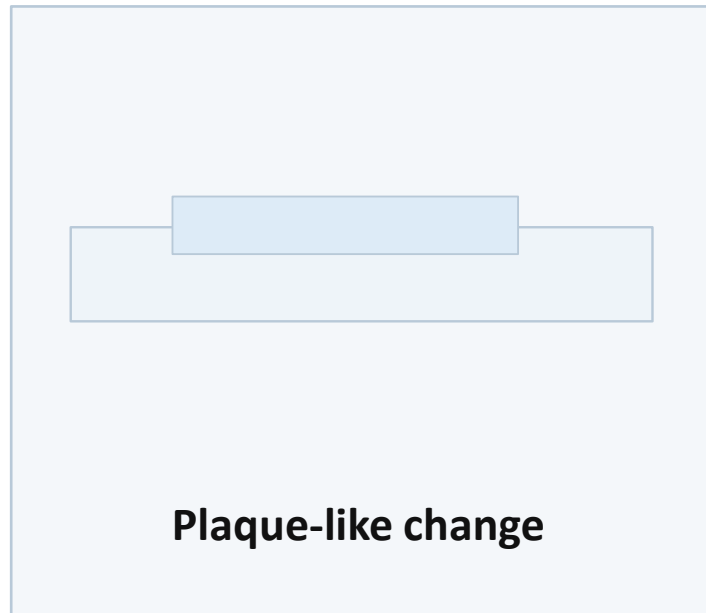
Surface color cannot establish whether the basement membrane has been breached.

Irregular and verrucous surfaces raise concern



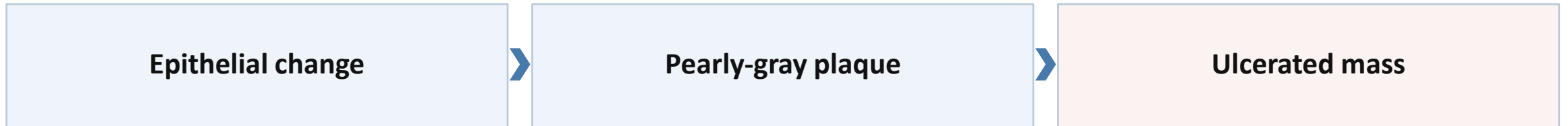
- Laryngeal lesions may be irregular, verrucous or white-pink.
- Exophytic architecture must be separated from microscopic cellular atypia.

Ulcerated fungating masses mark advanced morphology



- Laryngeal carcinoma as an ulcerated, fungating lesion.
- This pattern is worrisome for invasive malignancy but requires tissue confirmation.

The gross sequence is illustrative, not obligatory



Typical appearance described; Not an inflexible chronology

- Lesions evolving from wrinkled pearly-gray plaques to larger ulcerated masses.
- Individual tumors need not traverse visibly documented intermediate steps.

Histology answers what the surface cannot

Clinical observation	Cannot establish	Histologic evaluation addresses
White / keratotic lesion	Dysplasia grade	Cytologic atypia and maturation
Red or smooth lesion	Benignity	Architecture and dysplastic change
Irregular mass	Presence of invasion	Basement-membrane interface

The most common histologic tumor is SCC

- Approximately 95% of laryngeal carcinomas are squamous cell carcinomas.
- The remainder are not characterized by this short source excerpt.
- Avoid assuming that every laryngeal tumor is a squamous carcinoma.

~95%

Squamous cell carcinomas account
for about 95% of laryngeal
carcinomas.

Laryngeal SCC has several anatomic sites

Supraglottic

Epiglottis / aryepiglottic folds

Glottic

True vocal cords

Subglottic

Below vocal cords

Simplified regional map — not a scale anatomical drawing

Vocal cords are a frequent primary site

- Most laryngeal SCCs arise on the vocal cords.
- Tumors can also develop above or below the cords.
- Other sites discussed include the epiglottis, aryepiglottic folds and pyriform sinuses.

Anatomic site matters

Most arise on vocal cords,
but supraglottic and
subglottic sites also occur.

Histologic differentiation varies widely

- Variable degrees of anaplasia in laryngeal SCC.
- The tissue may show markedly atypical malignant squamous cells.
- Do not infer histologic grade solely from the size or ulceration of a mass.

Morphology

Anaplasia describes loss of differentiation, not clinical stage.

Bizarre mitoses and giant cells may occur

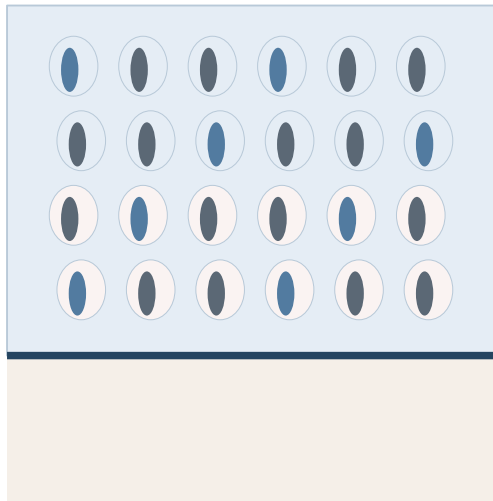
- The source identifies bizarre mitotic figures and tumor giant cells as possible findings.
- Their presence reflects atypical tumor-cell morphology.
- Absence of a particular atypical feature would not exclude malignancy.

Cytology in context

Cellular atypia is interpreted with the invasive growth pattern.

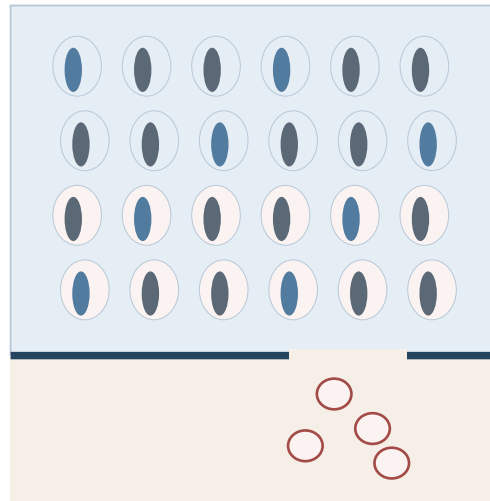
The in situ–invasive boundary is practical

CARCINOMA IN SITU



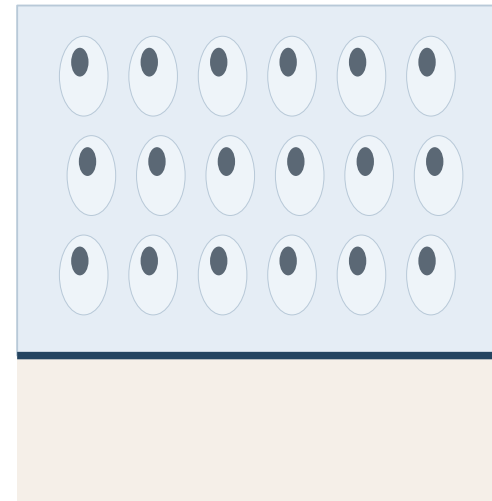
Schematic · not histology

INVASIVE



Schematic · not histology

NORMAL



Schematic · not histology

- CIS is confined to the epithelial compartment; Invasive SCC extends beyond it.

Reactive vocal-cord nodules are a benign mimic

Feature	Reactive nodule / polyp	Concern in precursor-neoplastic lesions
Typical context	Voice strain or smoking	Tobacco-linked epithelial neoplasia
Gross	Small smooth protrusion	Variable plaque, verrucous, ulcerated mass
Biology	Almost nonexistent cancer risk in nodules	Risk depends on epithelial dysplasia grade

Nodules show reactive stromal change

- The covering squamous epithelium may be hyperkeratotic or hyperplastic.
- Robbins also notes occasional slight dysplasia over a loose myxoid stroma.
- Fibrosis, fibrinous change or vascularity may be present in the underlying stroma.

Distinguishing context

A reactive subepithelial stromal lesion differs from a primarily dysplastic epithelial lesion.

Squamous papilloma has a different architecture

- Laryngeal papilloma is a benign exophytic squamous neoplasm.
- Finger-like fronds contain fibrovascular cores and orderly squamous covering.
- It is usually located on the true vocal cords and is often small.

Architectural discriminator

An orderly papillomatous epithelium is not equivalent to invasive squamous carcinoma.

HPV 6/11 papillomatosis differs from HPV risk

Feature	Laryngeal papillomatosis	Carcinoma risk discussion
HPV category	Low-risk HPV 6 and 11	High-risk HPV may contribute to cancer risk
Usual diagnosis	Benign squamous papilloma	Dysplasia / invasive SCC are distinct histologies
Progression	Recurrs often; rarely becomes SCC	Risk varies with precursor histology

A lesion's appearance does not identify its cause

Finding	Possibilities supported by surrounding section	What resolves the distinction
Hoarseness	Nodule, papilloma, epithelial lesion or SCC	Clinical evaluation and tissue when indicated
Exophytic growth	Papilloma or carcinoma	Histologic architecture and atypia
Keratosis	Reactive thickening or dysplasia	Biopsy to determine the epithelial category

Clinical presentation can start with hoarseness

- Persistent hoarseness is a common early manifestation of laryngeal carcinoma.
- A vocal-cord lesion can disturb vibratory function and alter voice.
- Persistent symptoms warrant clinical attention; They do not establish carcinoma by themselves.

Persistent hoarseness

A symptom that should be correlated with examination and tissue findings.

Dysphonia and dysphagia add clinical context

- Dysphonia describes alteration of voice production.
- Dysphagia describes impaired swallowing.
- Both are among the manifestations listed for laryngeal carcinoma.

Clinical synthesis

Symptoms describe function; Histology describes the tissue diagnosis.

Cancer often presents in the sixth decade

- Laryngeal carcinoma most commonly presents in the sixth decade of life.
- Clinical context includes chronic tobacco exposure and, frequently, alcohol exposure.
- Age and exposure raise or lower suspicion but are not substitutes for pathology.

Clinical epidemiology

The source states a common age range, not a diagnostic age cutoff.

Dysplasia grade and cancer stage are different

Variable	Asks	Clinical use
Dysplasia grade	How abnormal is the intraepithelial lesion?	Source links grade with transformation risk
Histologic invasion	Have malignant cells entered underlying tissue?	Distinguishes in situ from invasive carcinoma
Clinical stage	How far has established carcinoma extended?	Robbins ties prognosis to stage

Stage drives carcinoma prognosis

- For established laryngeal carcinoma, prognosis is directly related to clinical stage.
- Severity of epithelial dysplasia should not be substituted for tumor stage.
- The supplied chapter does not provide a staging table, so no TNM criteria are asserted here.

Prognostic hierarchy

Precursor risk, invasion status and clinical stage answer different clinical questions.

Early disease can allow organ preservation

- Robbins mentions laser surgery, microsurgery and radiation therapy in early disease.
- These treatment approaches are discussed for established carcinoma, not as an automatic treatment rule for every keratotic plaque.
- Clinical management depends on the actual diagnosis and stage.

Treatment context

Treatment choice follows confirmed disease and appropriate staging.

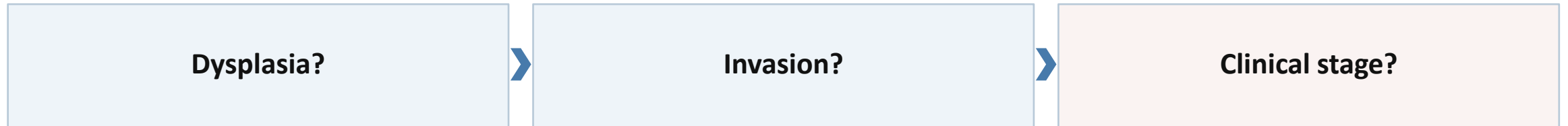
Advanced disease often requires combined therapy

- Chemoradiation, with or without laryngectomy, for more advanced or recurrent disease.
- Loss of natural voice is an important possible consequence of surgical treatment.
- This slide summarizes the textbook context; It is not an individualized regimen.

Stage-sensitive care

Different disease extents
require different treatment
strategies.

Three diagnostic questions prevent category errors



A sequence of interpretive questions, not a clinical guideline

- First: Is the epithelium orderly or dysplastic?
- Second: If malignant, is the basement membrane intact?
- Third: If invasive carcinoma, what is its clinical stage?

Case A: A persistent white vocal-cord plaque

Illustrative case: An adult smoker has persistent hoarseness and an endoscopically white focal thickening of the true vocal cord. No biopsy information is supplied.

What can be concluded from the evidence given?

- Can this lesion be called mild dysplasia because it is white and thin?
- Can a benign grade be assumed from its smooth margin?

Case A: Appearance alone cannot assign grade

- The gross description is compatible with several epithelial categories.
- Neither white color nor smooth contour establishes a histologic grade.
- The decisive missing observation is tissue architecture and cytology.

Answer

Do not diagnose or grade dysplasia from the visible plaque alone.

Case B: Severe dysplasia without invasion

Illustrative case: A laryngeal biopsy is reported as severe squamous dysplasia, without demonstrated stromal invasion. The person has ongoing tobacco exposure.

What can be concluded from the evidence given?

- Does severe dysplasia prove the patient already has invasive carcinoma?
- How should the grade-specific progression risk be interpreted?

Case B: A high-risk precursor is not invasion

- Severe dysplasia carries increased future transformation risk.
- Without documented invasion, the biopsy is not evidence of invasive SCC.
- Exposure reduction may matter, but histologic assessment remains essential.

Answer

Risk of progression and present invasive disease are distinct questions.

Case C: Tumor nests beyond the epithelial border

Illustrative case: A biopsy shows markedly atypical squamous epithelial cells in nests beneath the basement membrane, in the subepithelial stroma.

What can be concluded from the evidence given?

- What is the decisive morphologic distinction from carcinoma in situ?
- Does the biopsy alone supply the complete clinical stage?

Case C: Tissue invasion changes the diagnosis

- Extension into stroma indicates invasive carcinoma rather than in situ disease.
- Clinical staging requires information beyond the presence of microscopic invasion.
- Prognosis should be linked to clinical stage rather than a precursor dysplasia grade.

Answer

Invasion is established histologically; Clinical stage remains a separate assessment.

High-yield synthesis

Question	Key finding	Avoid this error
Which lesion has near-zero potential?	Histologically nondysplastic hyperplasia	Calling a white plaque nondysplastic by sight
What predicts transformation risk?	Initial dysplasia grade	Assuming progression is inevitable
What defines in situ disease?	Full-thickness atypia without BM breach	Equating severe dysplasia with stromal invasion
What drives carcinoma prognosis?	Clinical stage	Treating precursor grade as TNM stage

Source framework and limitations

- Primary source: Robbins, Cotran & Kumar, Pathologic Basis of Disease, 11th ed. (2026), Chapter 16, pp. 675–677.
- Supporting definitions: Chapter 7, “Metaplasia, Dysplasia, and Carcinoma In Situ.”
- The textbook excerpt supplies example transformation risks but not a complete grading algorithm or TNM staging system.
- All epithelium, surface and process diagrams are editable educational schematics, not photomicrographs.