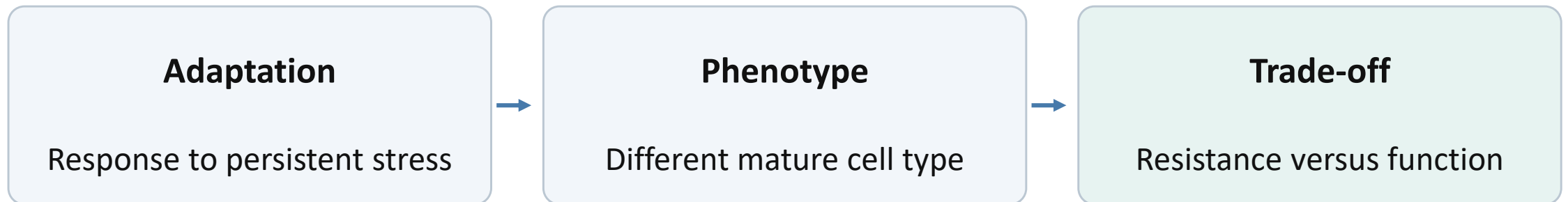


Metaplasia

Cellular adaptation, epithelial replacement and clinical consequences



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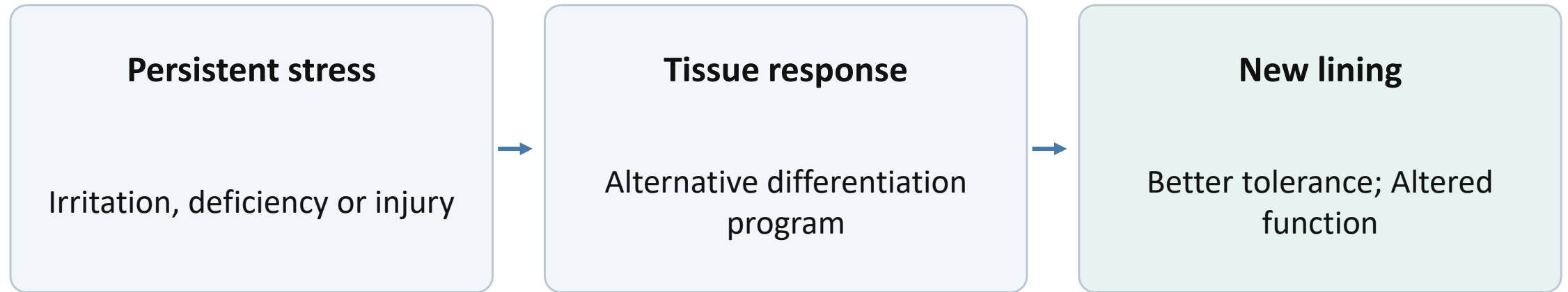
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Learning outcomes

- Define metaplasia and distinguish it from changes in cell size or number.
- Recognize squamous and columnar epithelial replacement patterns.
- Explain organ-specific benefits, functional losses and neoplastic associations.
- Distinguish epithelial from mesenchymal metaplasia.

Metaplasia sits within cellular adaptation



Definition: Replacement of differentiated cell type

- A differentiated epithelial or mesenchymal cell type is replaced by another.
- The replacement is usually a response to an adverse local environment.
- The defining feature is altered tissue identity, not simply more or fewer cells.

What changes—and what does not?

Changes

Differentiated phenotype
and tissue architecture.

May remain

An intact organ region
despite a changed lining.

Does not define it

Increase or decrease in cell
size or cell number alone.

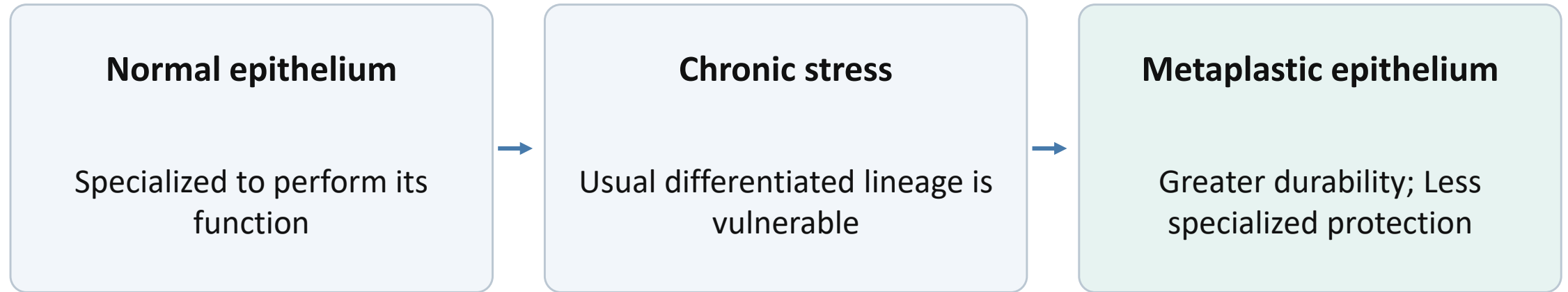
Metaplasia versus other adaptations

Response	Primary alteration	Typical trigger
Hypertrophy	Increased cell size	Greater workload
Hyperplasia	Increased cell number	Hormones / growth factors
Atrophy	Reduced cell/organ size	Reduced stimulation or supply
Metaplasia	Replacement by a different differentiated cell type	Chronic irritation or injury

The replacement is biologically purposeful—but imperfect

- The incoming cell type may be better equipped to survive the stress.
- A survival advantage does not imply preservation of specialized tissue function.
- Both benefits and costs must be evaluated in the specific organ.

The central adaptive trade-off



Reversibility is a defining potential

- Metaplasia is described as a reversible tissue change.
- Removing the stimulus can permit restoration of normal differentiation.
- Reversibility is not a guarantee that every longstanding lesion will resolve.

Why persistence matters

- Ongoing injury continues to favor a stress-resistant epithelial phenotype.
- The metaplastic lining may persist with the environmental insult.
- Persistent carcinogenic influences may promote further abnormalities over time.

Two broad categories of metaplasia

Epithelial

One epithelial lining is replaced by a different epithelial type.

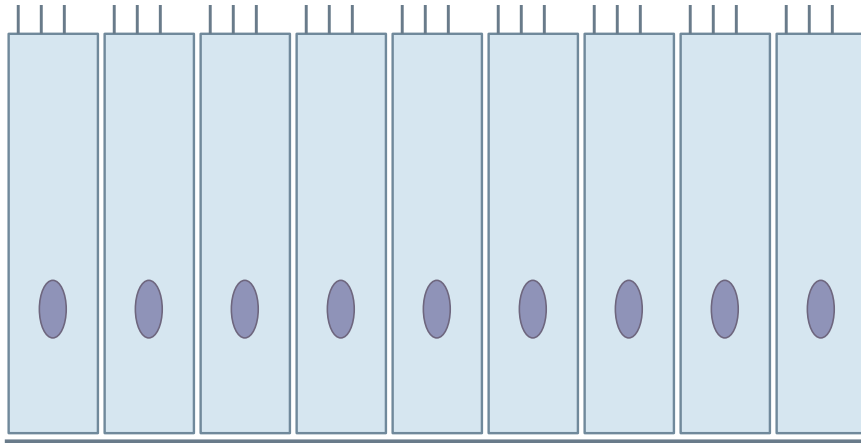
Mesenchymal

Cartilage, bone or adipose tissue appears in a site not normally containing it.

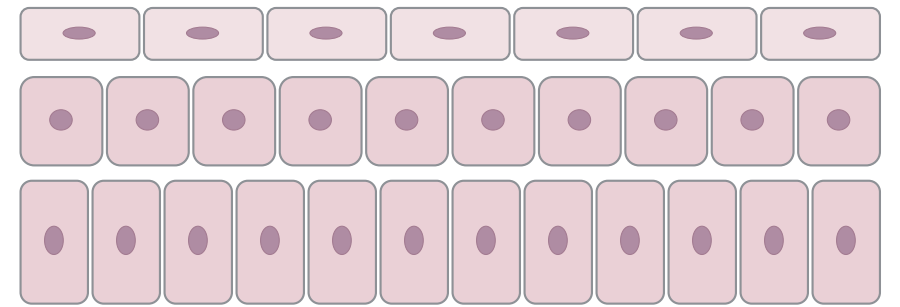
Columnar-to-squamous is a common epithelial pattern

- Normal columnar epithelium is adapted to secretion and/or ciliary transport.
- Stratified squamous epithelium tolerates repeated surface injury.
- A shift toward squamous differentiation can therefore be favored by irritation.

Normal respiratory lining versus squamous replacement



Ciliated columnar lining



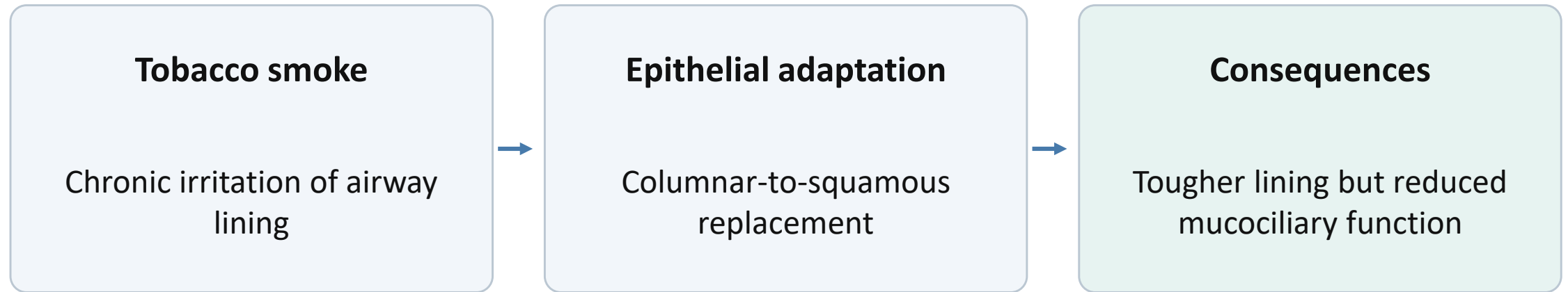
Stratified squamous lining

Original epithelial schematic — not a photomicrograph

The normal tracheobronchial lining has specialized defenses

- Ciliated cells transport luminal material along the airway surface.
- Mucus traps inhaled particles and infectious material.
- The epithelial architecture contributes to protection against infection.

Cigarette smoke can drive respiratory squamous metaplasia



Histologic concept: What replaces what?

- A ciliated columnar surface is replaced by stratified squamous cells.
- The new epithelial phenotype is recognized by multiple cell layers.
- The absence of normal ciliary architecture has functional consequences.

Respiratory metaplasia: Morphology and function

Feature	Usual airway lining	Squamous metaplasia
Epithelial pattern	Columnar, ciliated	Stratified squamous
Mucus transport	Supported by ciliary action	Ciliary transport lost
Injury tolerance	Vulnerable to chronic smoke injury	Relatively resistant surface
Clinical concern	Normal infection defense	Protective trade-off and cancer risk context

Loss of cilia is a mechanistic functional deficit

- Ciliary activity is one component of airway defense.
- Replacing ciliated cells abolishes that normal epithelial mechanism locally.
- Structural protection and physiological protection are not equivalent.

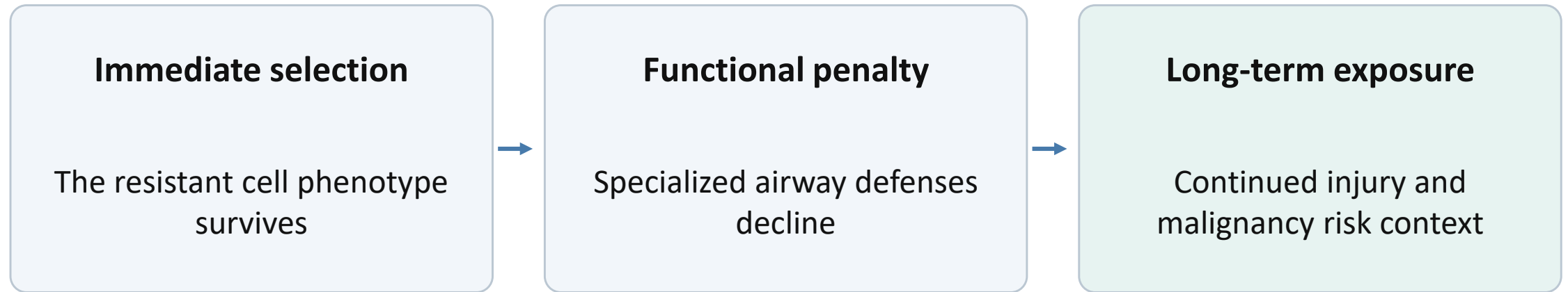
Loss of mucus secretion compounds the trade-off

- Normal respiratory epithelium contributes mucus to airway clearance.
- Squamous replacement sacrifices specialized secretory function.
- Reduced mucus–ciliary defense may facilitate respiratory infection.

Squamous epithelium resists the irritant at a cost

- A stratified squamous surface withstands adverse exposure better.
- Protection from direct epithelial injury increases.
- Normal cilia-dependent clearance and secretion are lost.

Adaptation does not equal a healthy outcome



Epithelial metaplasia may provide a substrate for cancer

- Squamous carcinoma in areas of bronchial squamous metaplasia.
- The chronic causal exposure also supplies carcinogenic influences.
- Metaplasia itself is not synonymous with a carcinoma or a required cancer stage.

Vitamin A deficiency is another squamous-metaplasia trigger

- Retinoic acid influences epithelial differentiation.
- Vitamin A deficiency can cause squamous changes in respiratory epithelium.
- The cornea can also develop squamous metaplasia, threatening vision.

Retinoid-related epithelial sites

Respiratory epithelium

Abnormal squamous differentiation replaces protective specialization.

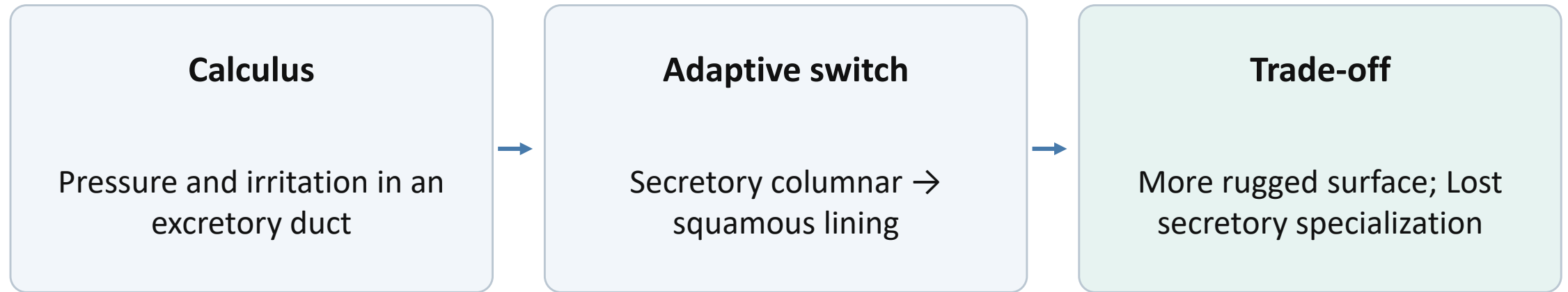
Cornea

Squamous change compromises a surface critical to vision.

The corneal example illustrates organ-specific harm

- Different tissues rely on different specialized surface properties.
- Squamous metaplasia is not universally beneficial despite stress tolerance.
- Loss of a transparent functional surface can profoundly impair vision.

Ductal calculi: Chronic mechanical irritation



Ducts where squamous metaplasia can occur

Duct system	Normal lining	Irritant described by Robbins
Salivary gland duct	Secretory columnar epithelium	Stones
Pancreatic duct	Secretory columnar epithelium	Stones
Bile duct	Secretory columnar epithelium	Stones

The salivary-duct example: Irritation rather than smoke

- A ductal stone creates local pressure and persistent irritation.
- The normal secretory duct lining is susceptible to that injury.
- Squamous replacement emphasizes resistance to the local mechanical stress.

The pancreatic-duct example follows the same logic

- The native ductal lining is specialized secretory columnar epithelium.
- A calculus can impose repeated pressure and irritation.
- Squamous metaplasia represents a changed differentiation phenotype.

The biliary-duct example extends the general principle

- Biliary excretory ducts can be exposed to chronic stone-related irritation.
- The epithelium can respond by adopting stratified squamous differentiation.
- The common mechanism is sustained stress, not a particular organ identity.

Why the same metaplasia appears in different organs

Airway

Chemical irritation: Habitual smoking.

Ducts

Mechanical pressure and irritation: Stones.

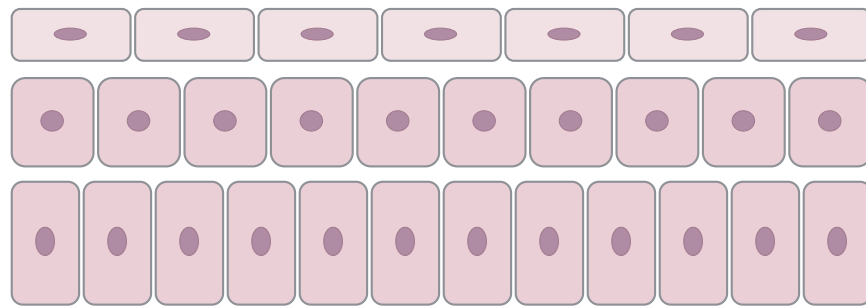
Cornea

Altered differentiation cue: Vitamin A deficiency.

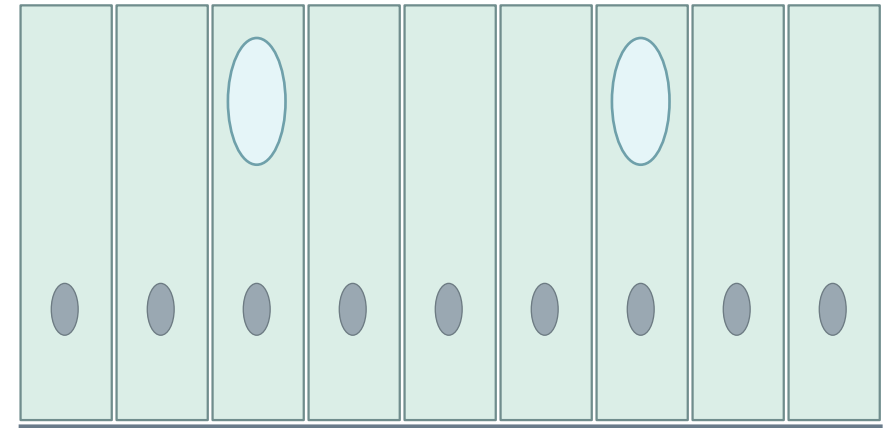
Metaplasia can also reverse the squamous–columnar direction

- The direction of epithelial replacement depends on the local insult.
- Squamous epithelium may be replaced by columnar epithelium.
- Barrett esophagus is Robbins' principal reverse-direction example.

Barrett pattern: Squamous-to-intestinal-type columnar



Normal esophageal squamous



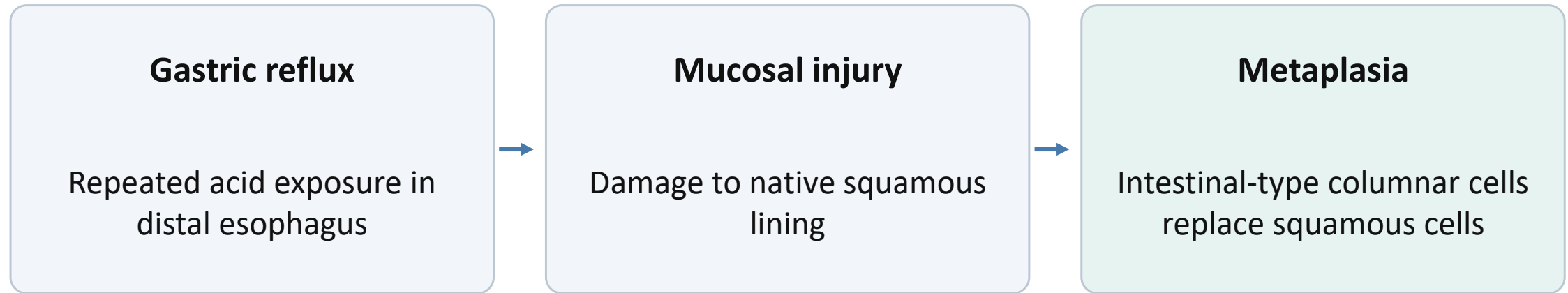
Metaplastic columnar (intestinal-type)

Original epithelial schematic — not a photomicrograph

The normal esophageal lining is stratified squamous

- The esophageal mucosa normally carries a protective squamous surface.
- It is not specialized to tolerate prolonged exposure to gastric acid.
- Chronic reflux provides an adverse environment favoring a different lining.

Barrett esophagus: Reflux-associated epithelial replacement



Barrett esophagus is not simply inflamed squamous mucosa

- Its defining tissue response is altered epithelial identity.
- Metaplastic columnar cells replace the previous squamous lining.
- The example demonstrates a different adaptive direction than the bronchus.

Goblet cells provide a recognizable intestinal phenotype

- Intestinal metaplasia may contain mucin-filled goblet cells.
- Their morphology supports identification of intestinal differentiation.
- Diagnostic definitions involving nongoblet cells vary.

Barrett mucosa has a recognizable gross appearance

- Metaplastic mucosa may appear red and velvety at endoscopy.
- It can extend proximally from the gastroesophageal junction.
- Endoscopic location and biopsy interpretation complement each other.

Bronchus and Barrett: Opposite directions

Property	Bronchial metaplasia	Barrett metaplasia
Usual epithelium	Ciliated columnar	Stratified squamous
Replacement	Stratified squamous	Intestinal-type columnar
Common stress	Tobacco smoke	Gastric reflux
Associated carcinoma	Squamous cell carcinoma	Adenocarcinoma

Barrett metaplasia is clinically important because of risk

- The metaplastic area is associated with increased risk of adenocarcinoma.
- This does not mean that most individuals with Barrett develop cancer.
- Dysplasia is a separate concerning change that may appear in Barrett mucosa.

Metaplasia and dysplasia must be evaluated separately

- Metaplasia concerns epithelial lineage replacement.
- Dysplasia concerns abnormal cellular maturation and architecture.
- A tissue may be metaplastic without showing dysplasia.

Dysplasia displays cytologic and architectural disorder

- Dysplastic cells can have pleomorphic, hyperchromatic nuclei.
- Epithelial maturation may become disorganized.
- Mitotic activity and its distribution may be abnormal.

Why metaplasia is not carcinoma in situ

Feature	Metaplasia	Carcinoma in situ
Primary concept	Changed differentiated lineage	Full-thickness severe dysplasia
Architecture	Replacement phenotype	Marked disordered maturation
Basement membrane	No invasive behavior implied	Not penetrated by malignant epithelium
Cancer status	Adaptive alteration	Preinvasive cancer

An additional organ example: Gastric intestinalization

- Intestinal-type replacement in atrophic gastric mucosa.
- Gastric glandular epithelium may be replaced by goblet-cell-containing cells.
- The site, associated injury and expected native epithelium determine interpretation.

Anatomic context determines metaplasia terminology

Esophagus

Squamous lining becomes intestinal-like columnar in Barrett esophagus.

Stomach

Gastric glandular lining can undergo intestinalization with chronic injury.

Mesenchymal metaplasia is a different tissue phenomenon

- Cartilage, bone or adipose tissue may develop in an abnormal location.
- The replacement occurs among differentiated mesenchymal tissue phenotypes.
- Unlike epithelial forms, these changes are not clearly an adaptive protective response.

The tissue types of mesenchymal metaplasia

Osseous

Bone develops in tissue ordinarily lacking bone.

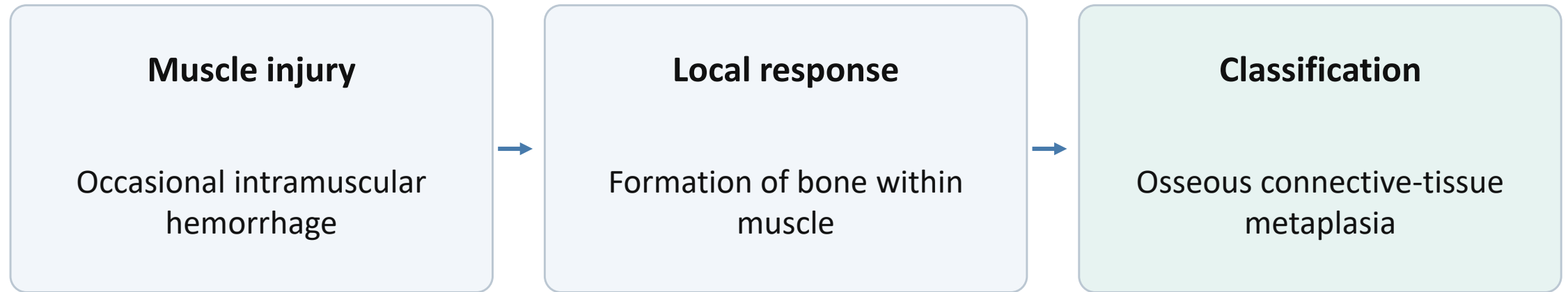
Chondroid

Cartilage appears at an ectopic site.

Adipose

Adipose tissue develops where it is not normally present.

Myositis ossificans: An illustrative mesenchymal example



Myositis ossificans is not epithelial metaplasia

- The newly appearing tissue is bone rather than a surface epithelial lining.
- Its setting can be prior injury or hemorrhage in muscle.
- The standard epithelial durability explanation is less applicable.

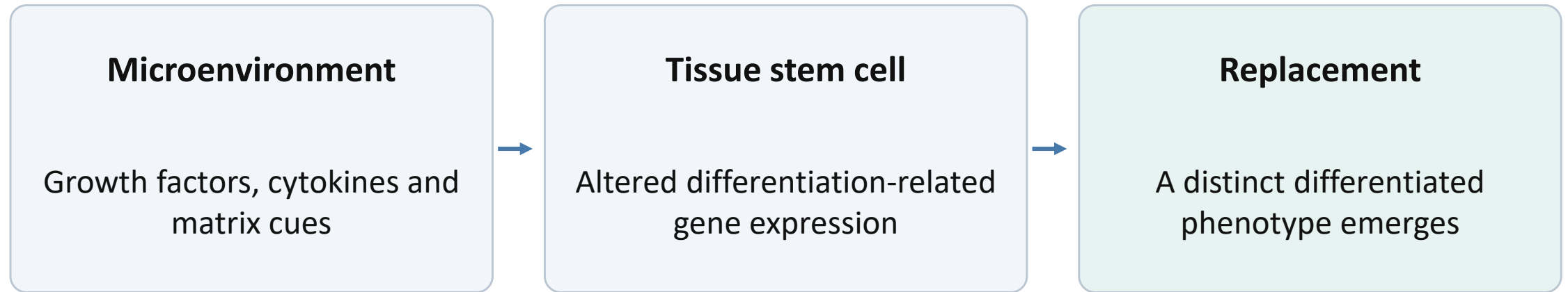
The neoplastic implications are category-dependent

- Persistent epithelial metaplasia-inducing exposure with malignancy risk.
- The textbook does not describe increased cancer risk from mesenchymal metaplasia.
- Avoid transferring the epithelial risk narrative to ectopic bone or cartilage.

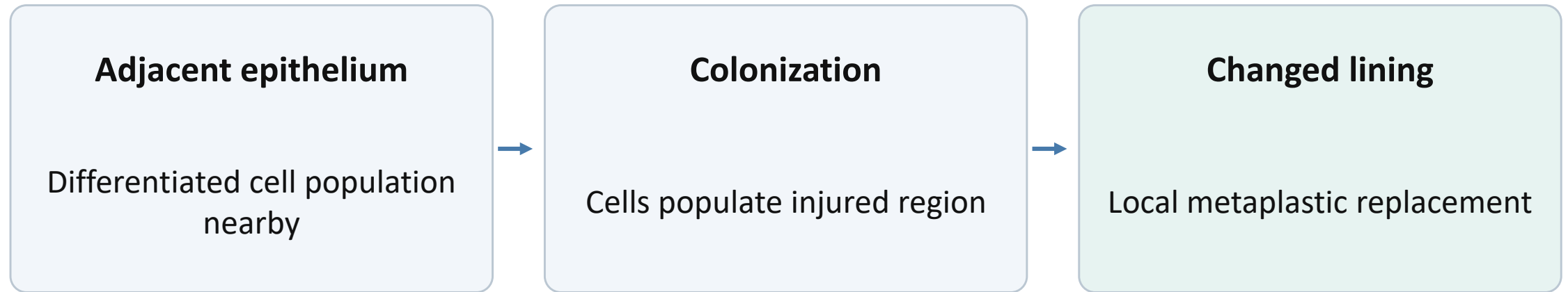
Mechanism: Direct conversion of mature cells is not the model

- Reprogramming of local stem cells or adjacent-cell colonization.
- A changed differentiation program yields cells with the replacement phenotype.
- Metaplasia should not automatically be described as one mature cell directly changing into another.

Stem-cell reprogramming model



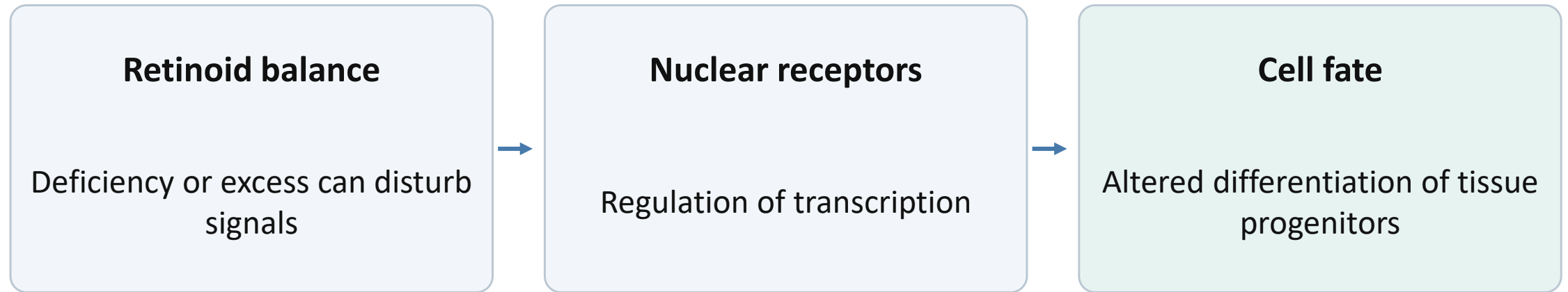
An alternative origin: Colonization from adjacent tissue



Local microenvironmental signals guide the response

- Cytokines and growth factors can alter lineage commitment.
- Extracellular-matrix signals contribute to the differentiation environment.
- The tissue context helps determine which replacement phenotype emerges.

Retinoic acid acts through gene regulation



Recognition framework: Type, trigger, consequence

Pattern	Principal trigger	Important interpretation
Respiratory squamous	Habitual smoking	Loss of ciliary and mucus protection
Ductal squamous	Stone-related irritation	Local epithelial adaptation to pressure
Barrett columnar	Chronic reflux	Adenocarcinoma association
Mesenchymal bone	Muscle injury / hemorrhage	No increased cancer risk described

How to identify metaplasia on a biopsy

- First establish the normal epithelial or mesenchymal identity of that anatomic site.
- Then identify a differentiated phenotype inappropriate for the location.
- Interpret the change alongside evidence of sustained injury or repair.

Avoid two diagnostic category errors

- Reactive injury without a changed lineage does not, by itself, establish metaplasia.
- Metaplastic replacement does not, by itself, establish dysplasia.
- Assess abnormal differentiation and cytologic atypia as separate observations.

Application: Chronic cough in a smoker

Clinical vignette

A bronchial biopsy from a habitual smoker shows replacement of ciliated columnar cells by layered squamous cells.

Pathologic interpretation

Bronchial squamous metaplasia

The epithelial shift favors a rugged surface but sacrifices mucociliary protection.

Application: Reflux-associated esophageal change

Clinical vignette

Distal esophageal biopsy after long-standing reflux shows intestinal-type columnar cells replacing the usual squamous lining.

Pathologic interpretation

Barrett-type intestinal metaplasia

A reverse epithelial replacement pattern occurs under chronic gastric reflux.

Application: Ductal obstruction

Clinical vignette

A duct repeatedly irritated by a calculus develops a stratified squamous epithelial lining instead of its usual secretory columnar epithelium.

Pathologic interpretation

Stone-associated squamous metaplasia

Mechanical irritation and pressure are sufficient triggers in several excretory duct systems.

Application: Post-hemorrhagic muscle lesion

Clinical vignette

Bone develops in muscle after a focal episode of intramuscular hemorrhage.

Pathologic interpretation

Mesenchymal (osseous) metaplasia

Myositis ossificans illustrates ectopic bone formation, not replacement of an epithelial lining.

Integrated map of metaplasia

Question	Key answer	Relevant contrast
What changes?	Differentiated tissue phenotype	Not merely cell size or number
Why?	Stress-favored alternative lineage	Functional cost may occur
Where?	Epithelia and mesenchymal tissues	Site determines clinical meaning
Cancer relevance?	Context-dependent epithelial association	Not equivalent to dysplasia

Four durable principles

- Metaplasia is a potentially reversible replacement of differentiated tissue identity.
- The replacement phenotype can survive an insult yet diminish normal function.
- Bronchial and esophageal epithelial metaplasia point in opposite directions.
- Assess dysplasia and cancer risk separately from the metaplastic change.

Source material and image interpretation

Primary

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. Chapter 2, “Metaplasia,” printed p. 55.

Context within Robbins

Chapter 2: “Mechanisms of Metaplasia” (pp. 55–56).

Chapter 7: “Metaplasia, Dysplasia, and Carcinoma In Situ” (p. 241).

Chapter 17: “Barrett Esophagus” (pp. 691–692).

Chapter 14: gastric intestinalization in pernicious anemia.

All epithelial illustrations are original, editable schematics—not microscopy specimens.