

Chemical and Infectious Esophagitis

Etiology · tissue injury · diagnostic morphology

Clinical pathology teaching lecture

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Learning objectives

- Identify principal chemical, iatrogenic, and infectious causes of esophageal mucosal injury.
- Correlate ulcer patterns and biopsy findings with Candida, HSV, and CMV.
- Recognize the distinctive vascular and epithelial changes of irradiation injury and GVHD.
- Use clinicopathologic context to distinguish these disorders from reflux injury.

The shared target is squamous mucosa

Common tissue compartment

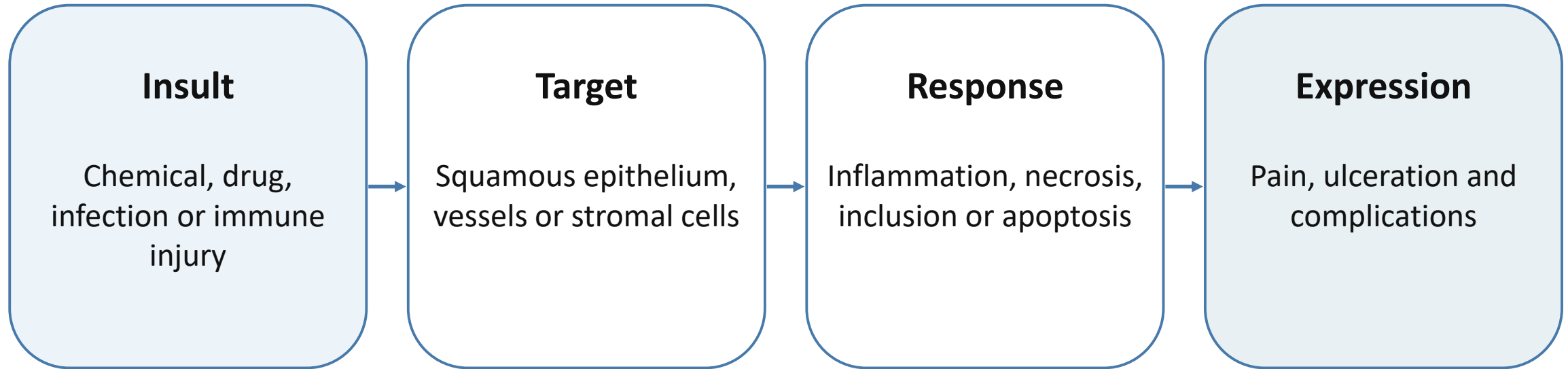
Stratified squamous epithelium of the esophagus

Exposure to luminal irritants

Injury from therapy or
immune disease

Direct microbial infection

Etiology determines the tissue response



The dominant histologic clue depends on the causal process.

Major classes of esophagitis in this topic

Direct chemical

Corrosive agents, alcohol, heat and smoking

Localized medication

Pills that lodge and dissolve

Treatment-related / immune

Chemotherapy, irradiation and graft-versus-host disease

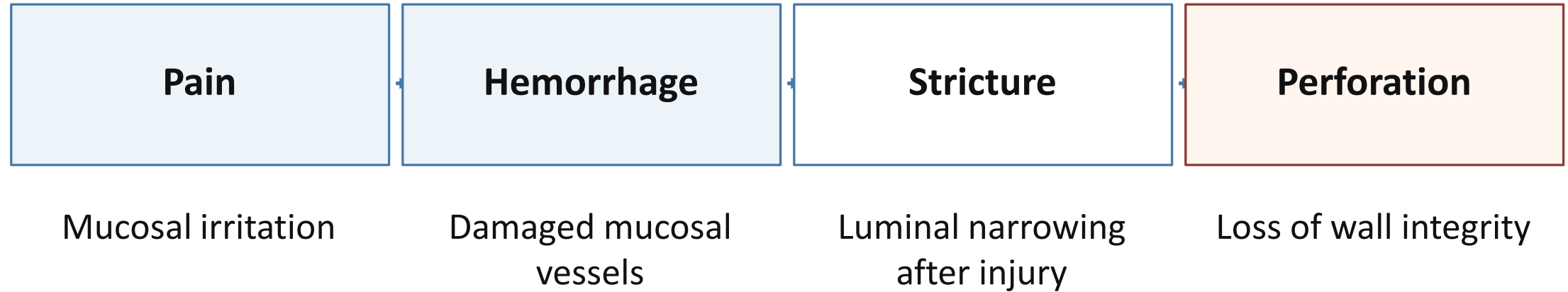
Infectious

Viruses, Candida and other pathogenic organisms

Odynophagia is a central symptom

- Odynophagia means pain on swallowing.
- Chemical and infectious esophagitis may produce acute or persistent discomfort.
- Symptoms alone do not establish the etiology or severity of tissue injury.

Clinical consequences span a broad spectrum



Recognize severe disease

Potentially serious complications

Hemorrhage · stricture · perforation

These appear in severe cases.

A mild symptomatic course is also possible.

Histologic and clinical severity can differ.

Irritants capable of chemical injury

Ingested agents

Alcohol, corrosive acids and alkalis

Physical exposure

Excessively hot liquids

Tobacco exposure

Heavy smoking

Consumer products

Household cleaners and related corrosives

How corrosive injury occurs

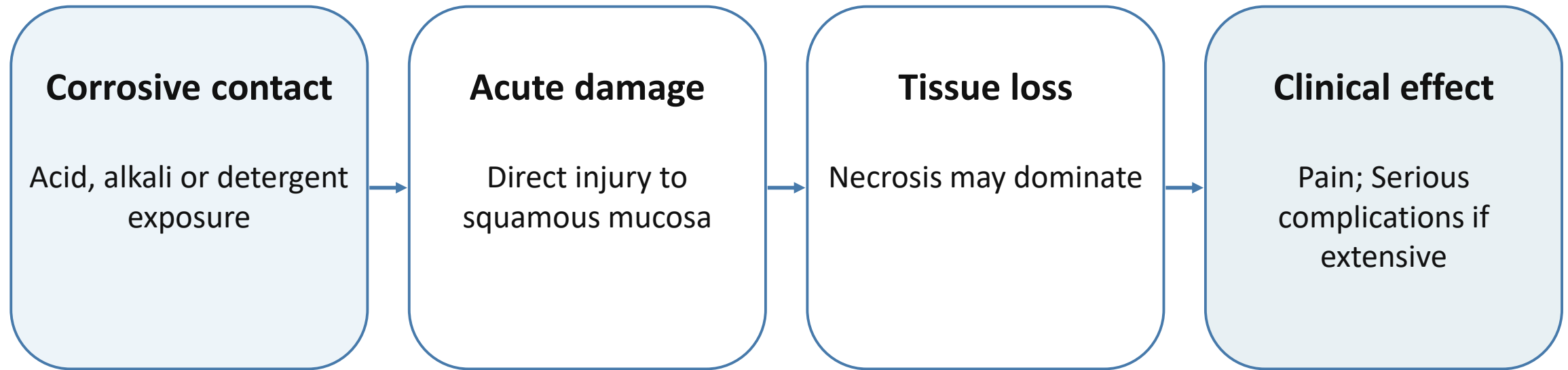
Exposure setting

- Accidental ingestion
- Intentional ingestion
- Cleaning products or other corrosives

Possible tissue outcome

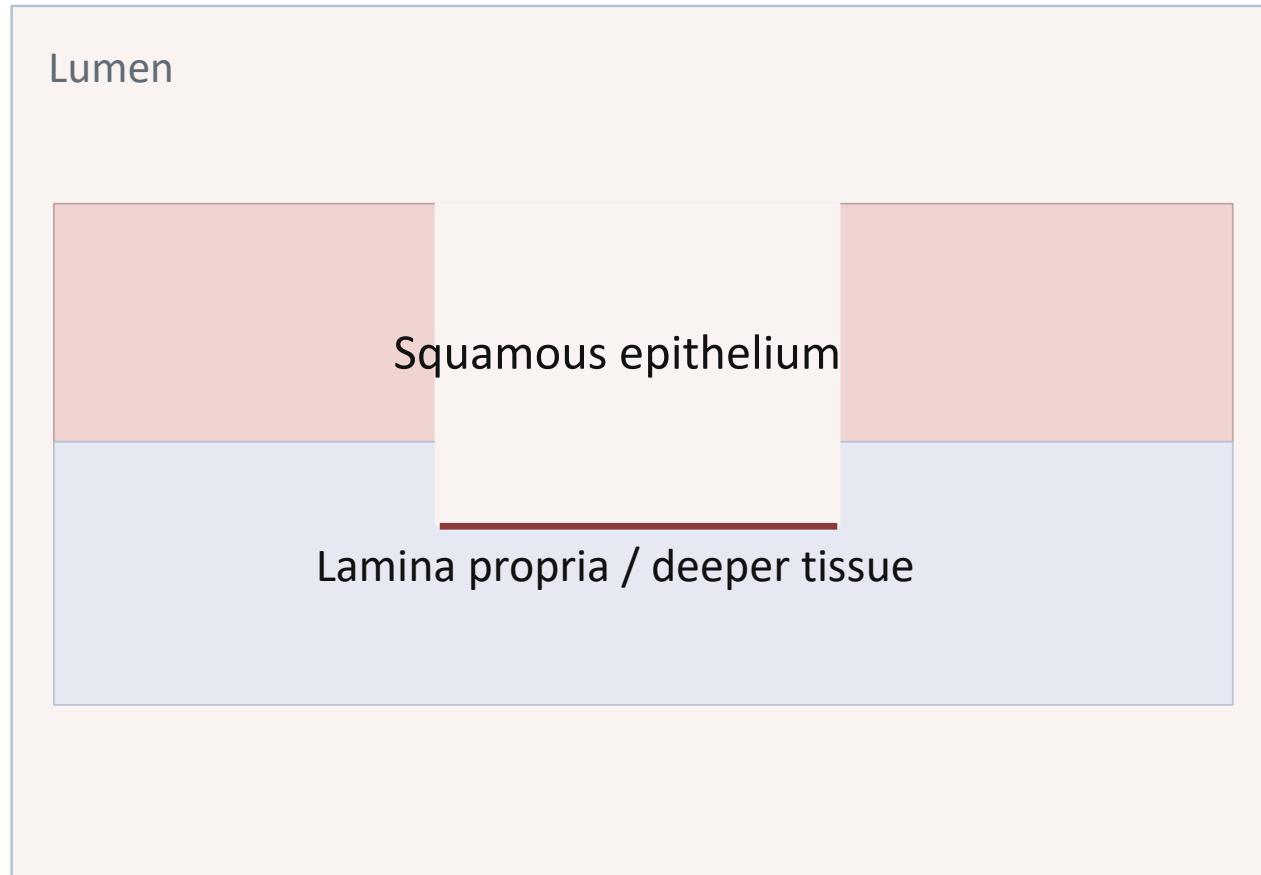
- Acute mucosal damage
- Extensive necrosis in severe injury
- Subsequent hemorrhage, stricture or perforation

Conceptual sequence of caustic injury



A causal schematic; The book does not prescribe a single uniform histologic pattern for all agents.

Chemical necrosis can dominate the lesion



Loss of epithelium

Ulceration exposes underlying tissue;
Etiologic features must be sought in
the residual tissue and ulcer bed.

Teaching schematic—not a histologic specimen

A histologic caution in corrosive injury

Do not require abundant neutrophils

Acute necrosis may occur with few or no neutrophils

Described after lye ingestion

Also described with acids

Also described with
detergents

Necrosis and inflammation are distinct observations

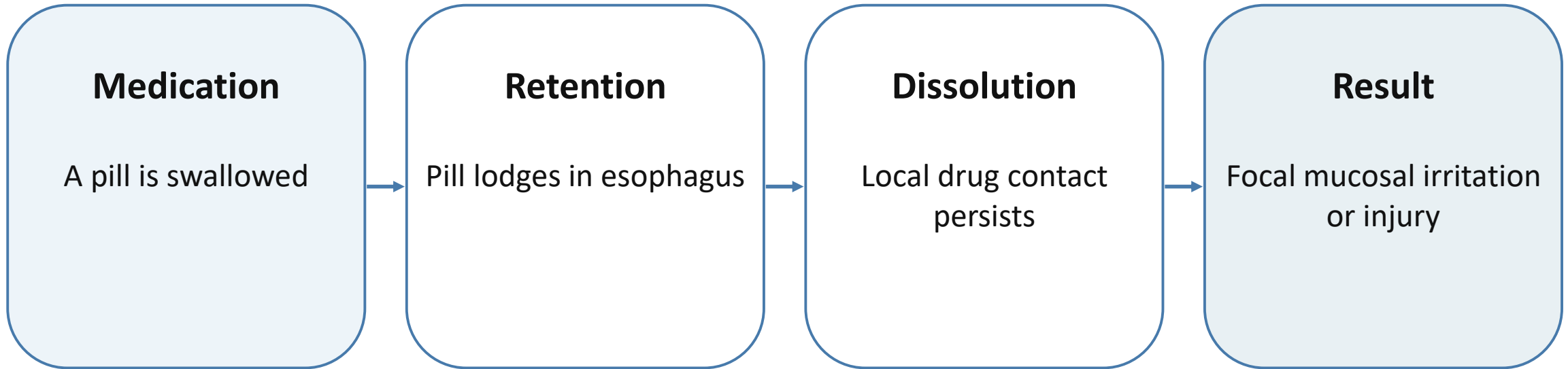
Evidence of tissue death

- Necrotic epithelium or wall tissue
- Loss of viable mucosal integrity
- Can be prominent in acute caustic injury

Evidence of inflammatory response

- Dense neutrophils commonly occur
- They are not uniformly present
- Absence does not exclude severe chemical injury

Why a retained pill can cause injury



This is the defining sequence of pill-induced esophagitis in the source.

Pill-induced esophagitis: Anatomic clue

Predisposing local feature

Preexisting esophageal stricture

Pill-induced lesions often arise at sites of a stricture.

The retained material creates a localized exposure.

Evaluate the causal role of an underlying luminal narrowing.

Caustic versus pill-related esophagitis

Dimension	Corrosive exposure	Pill retention
Typical circumstance	Ingestion of acid, alkali or cleaner	Medication lodges and dissolves
Injury distribution	Depends on direct mucosal contact	Localized to retention site
Named morphologic point	Necrosis may lack neutrophils	Often at preexisting strictures
Severity	May be severe	Described as often less severe

Iatrogenic and systemic noninfectious causes

Cytotoxic therapy

Chemotherapy-associated mucosal injury

Radiotherapy

Vascular injury contributes to mucosal damage

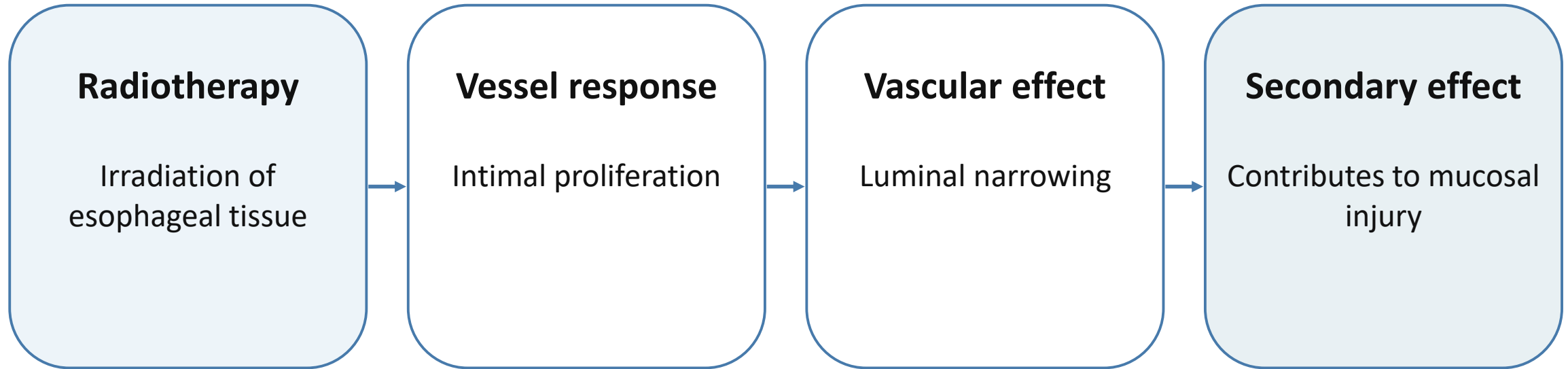
Immune-mediated

Graft-versus-host disease

Other systemic disease

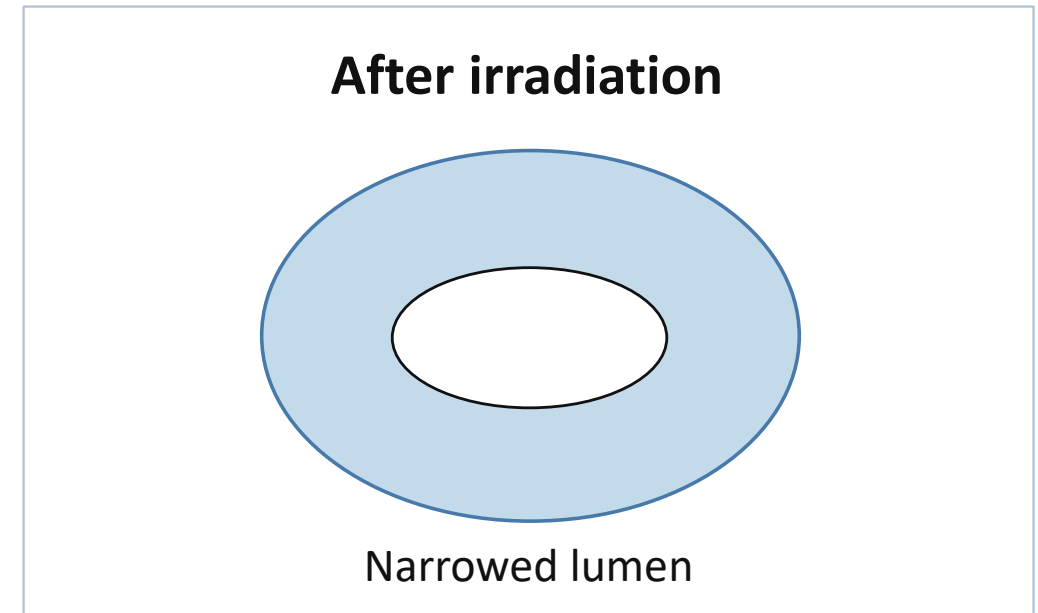
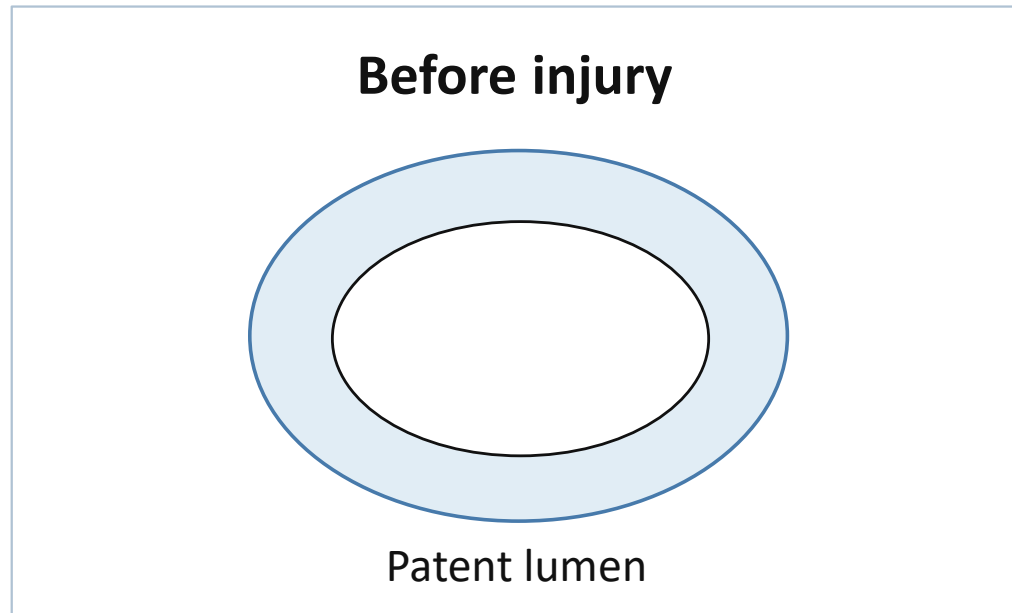
Desquamative disorders and rare Crohn involvement

Radiation injury is partly vascular



A vascular mechanism of radiation esophagitis

Radiation-associated injury to submucosal and mural vessels



Intimal proliferation → luminal narrowing → contributes to mucosal damage

What radiation-damaged vessels show

- Intimal proliferation develops within submucosal and mural vessels.
- The vascular lumen becomes narrowed.
- Esophageal mucosal injury is partly secondary to this vascular damage.
- The book explicitly relates this pattern to irradiation injury in other tissues.

Do not equate all iatrogenic mechanisms

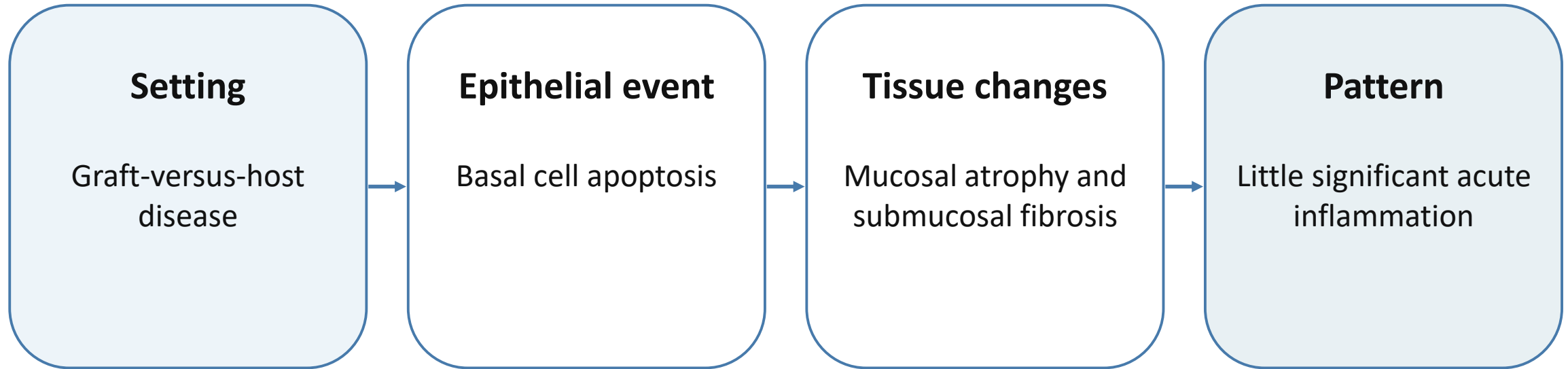
Cytotoxic chemotherapy

- Identified by Robbins as a cause of injury
- The assigned passage does not give a defining microscopic pattern
- Review treatment history alongside the biopsy

Radiation therapy

- Intimal thickening is specifically described
- Submucosal and mural vessel lumina narrow
- Vascular injury helps explain mucosal damage

GVHD: A different mode of injury



Esophageal GVHD: Microscopic triad

Structure	Described change	Interpretive value
Basal epithelial layer	Apoptosis	Epithelial injury clue
Mucosa	Atrophy	Reduced epithelial thickness
Submucosa	Fibrosis	Chronic tissue remodeling
Acute inflammatory cells	Not prominent	Distinctive relative to purulent lesions

Why GVHD can be missed as infection

Clinical context

GVHD is a recognized noninfectious cause

Dominant cell lesion

Basal epithelial apoptosis

Structural effects

Mucosal atrophy and submucosal fibrosis

Negative pattern

Significant acute inflammation is not required

Uncommon associated inflammatory disorders

Desquamative skin disorders

- Bullous pemphigoid
- Epidermolysis bullosa
- Esophageal morphology resembles lesions at other sites

Crohn disease

- Esophageal involvement is rare
- Appearance parallels disease elsewhere
- Requires clinicopathologic correlation

Noninfectious injury: Distinguishing clues

Entity	Source-described mechanism or clue
Corrosive esophagitis	Contact injury and possible necrosis without neutrophils
Pill-induced esophagitis	Pill lodged and dissolved; often a preexisting stricture
Radiation injury	Vascular intimal proliferation; narrowed lumina
GVHD	Basal apoptosis, atrophy, submucosal fibrosis
Desquamative / Crohn involvement	Morphology mirrors lesions at other body sites

Host status changes the infection differential

Otherwise healthy individuals

- HSV is the most frequent infection identified in this group
- A viral cause remains plausible despite immunocompetence
- Do not presume all esophageal infection implies immunosuppression

Debilitated or immunosuppressed patients

- Infections are more frequent
- HSV, CMV and fungal organisms are recognized
- Host context helps prioritize morphology

Infectious agents identified by Robbins

Viral

Herpes simplex virus and cytomegalovirus

Common fungal

Candida species

Other fungal

Mucormycosis and aspergillosis

Bacterial

Pathogenic bacteria may invade damaged mucosa

The dominant fungal cause

Among esophageal fungal infections

Candidiasis is the most common

Gray-white
pseudomembranes

Fungal hyphae and
inflammatory cells

Risk increased in
compromised hosts

Microbes in ulcers: Colonizer or pathogen?

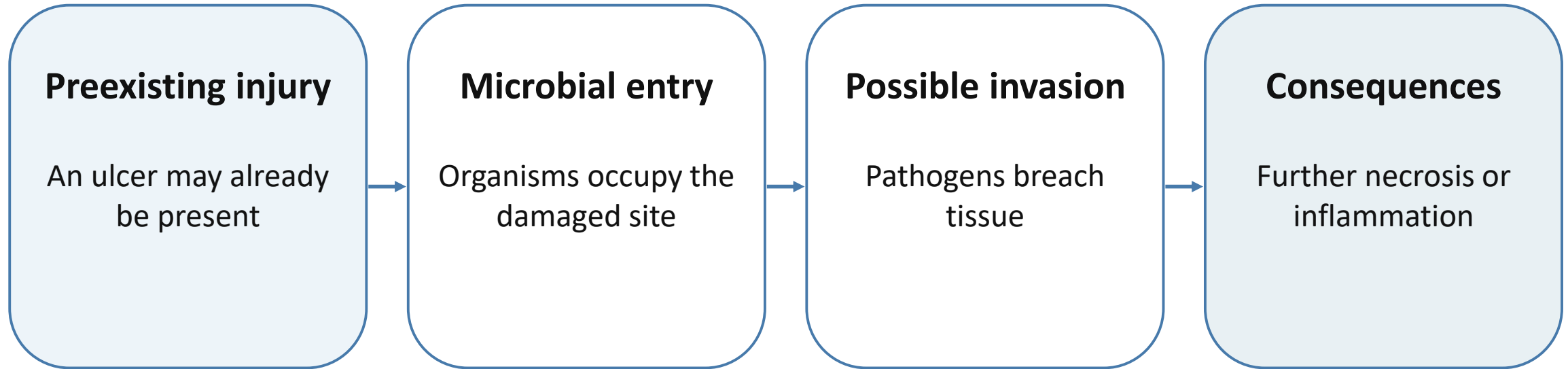
Incidental organisms

- Oral bacteria may occur in ulcer beds
- Their presence alone need not establish causation
- Context and tissue damage matter

Invasive pathogens

- Pathogenic fungi or bacteria may invade
- Invasion can produce mucosal necrosis
- A true invasive process is mechanistically different

Infection may be primary or superimposed



The role of pathogenic bacteria and fungi

- Infection by bacteria or fungi may initiate injury or complicate a preexisting ulcer.
- Nonpathogenic oral bacteria are frequent in ulcer beds.
- True invasive pathogenic bacteria and fungi can produce necrosis.
- The source attributes roughly one tenth of infectious cases to pathogenic bacteria and fungi as a group.

Candida: Characteristic endoscopic appearance

Macroscopic hallmark

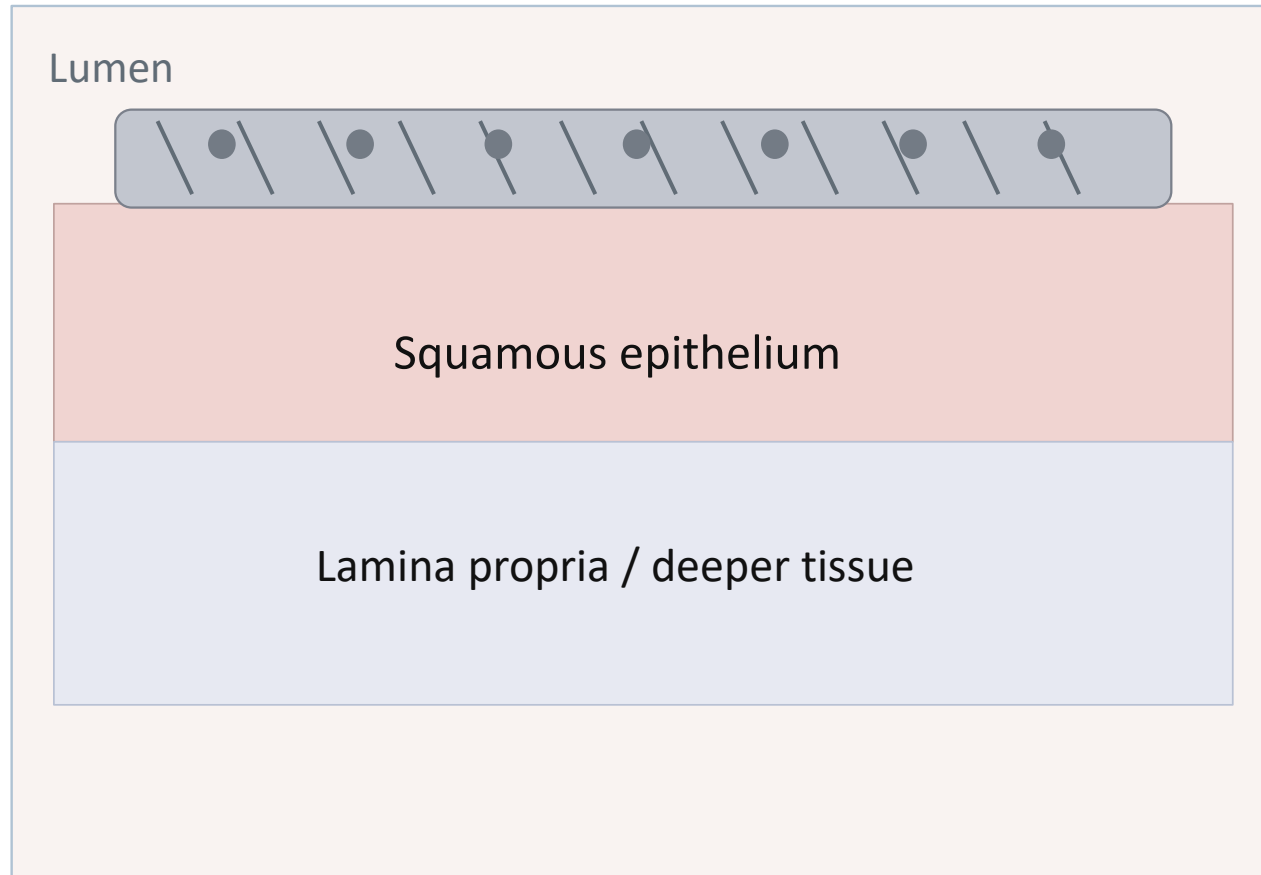
Adherent gray-white pseudomembranes

Adherent to esophageal
mucosa

May form a conspicuous
surface coating

Link the gross appearance to
its composition

What forms a candidal pseudomembrane



Adherent surface material

Gray-white pseudomembrane containing fungal hyphae and inflammatory cells

Teaching schematic—not a histologic specimen

Microscopic substrate of pseudomembranes

- Densely matted fungal hyphae form the structural component.
- Inflammatory cells intermingle with the fungal material.
- The pseudomembrane covers the esophageal mucosal surface.
- This appearance contrasts with discrete viral ulcers.

Fungal inflammation versus viral ulceration

Candida pattern

- Adherent gray-white surface pseudomembrane
- Hyphae mixed with inflammatory cells
- Fungal invasion may cause necrosis

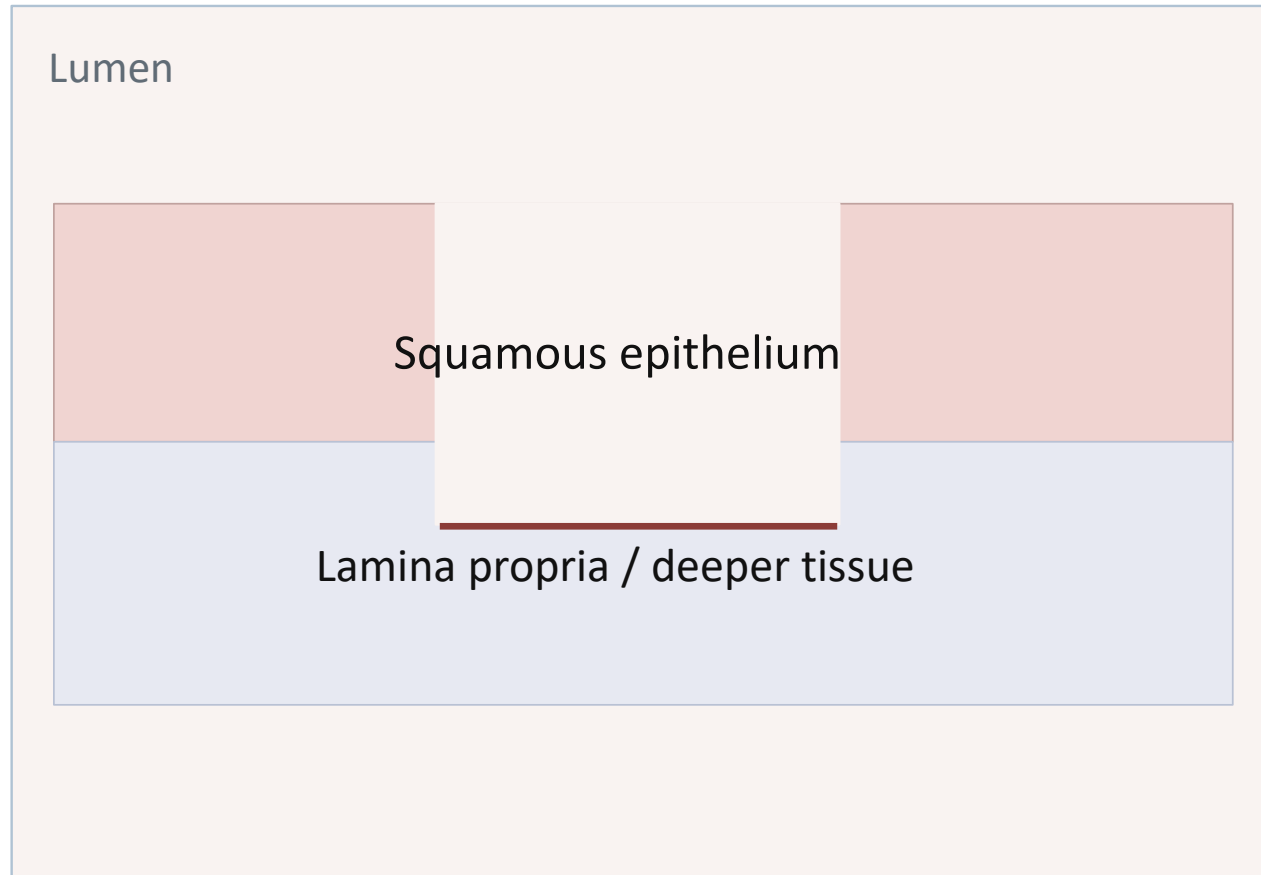
Viral pattern

- Discrete punched-out ulcers
- Virus-specific changes in host cells
- Cell identity separates HSV from CMV

Less frequent esophageal fungi

- Mucormycosis among uncommon infectious causes.
- Aspergillosis can also involve the esophagus.
- The assigned excerpt does not provide organism-specific endoscopic or microscopic criteria for either mold.
- Do not substitute Candida morphology for all fungal etiologies.

The viral pattern begins with a discrete ulcer



Loss of epithelium

Ulceration exposes underlying tissue; Etiologic features must be sought in the residual tissue and ulcer bed.

Teaching schematic—not a histologic specimen

Viral infection: A gross pattern clue

Endoscopic / gross morphology

Discrete “punched-out” ulcers

The pattern raises suspicion for viral etiology.

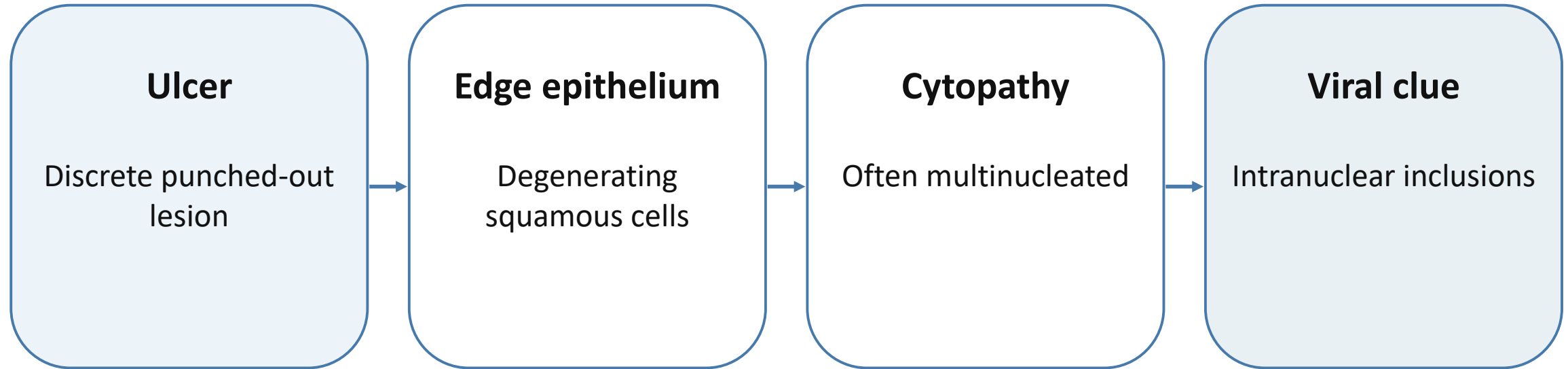
Herpes viruses can produce punched-out ulcers.

Interpret morphology with biopsy cellular changes.

HSV esophagitis: Clinical context

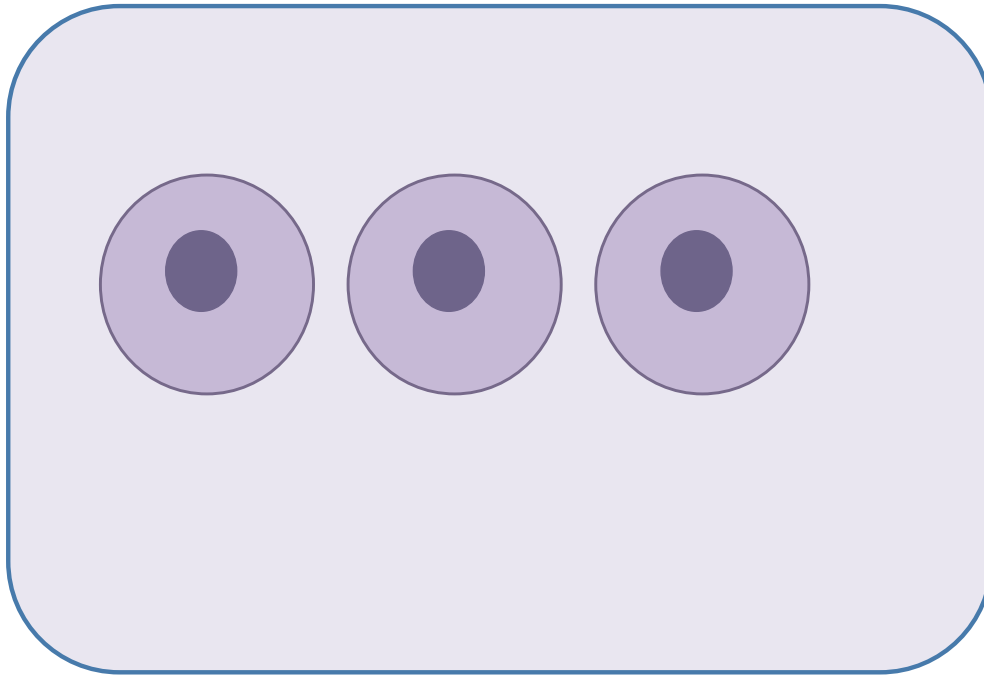
- HSV is the most frequent named infectious cause in otherwise healthy individuals.
- HSV also occurs in debilitated or immunosuppressed patients.
- Its characteristic histologic target is the squamous epithelium at ulcer edges.

HSV morphology: From ulcer to cell



HSV inclusions occur in squamous epithelial cells

Degenerating squamous epithelial cell at ulcer margin



Multinucleation

Intranuclear viral inclusions

Cellular site: Squamous epithelium

Simplified schematic—not a microscopy image

Where the HSV diagnostic clue resides

Location is as important as appearance

Ulcer margin squamous cells

Degeneration of epithelial
cells

Multinucleation may be
present

Nuclear viral inclusions

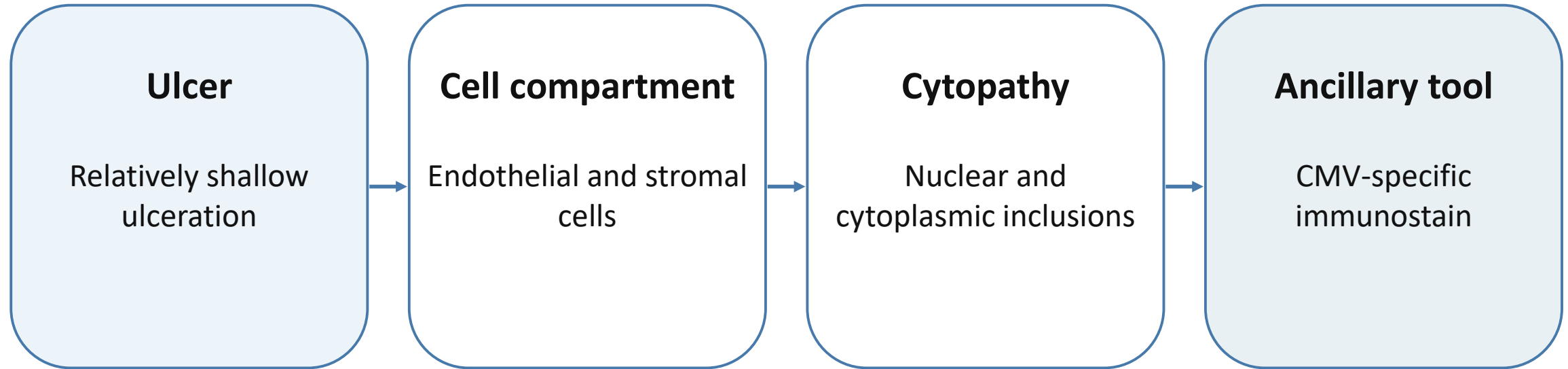
HSV biopsy interpretation: Source-based logic

- Examine viable squamous epithelial tissue bordering the ulcer.
- Look for degenerating, sometimes multinucleated cells.
- Identify intranuclear inclusions consistent with herpesvirus effect.
- Viral immunohistochemistry can support the morphologic diagnosis.

CMV esophagitis: Host and lesion

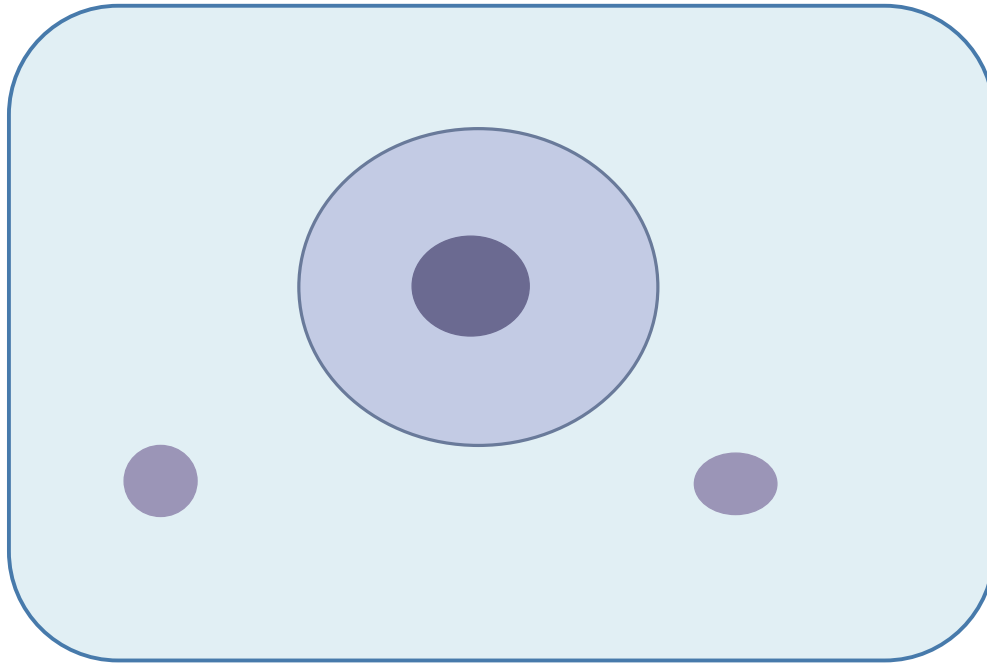
- CMV is among the important pathogens in immunosuppressed or debilitated patients.
- Its ulcers are shallower than herpetic punched-out ulcers.
- The diagnostic cellular changes involve capillary endothelium and stromal cells.

CMV morphology: Trace the host cell



CMV inclusions occur in endothelial and stromal cells

Capillary endothelial / stromal cell in an ulcer



Nuclear inclusion

Cytoplasmic inclusions

Cellular site: Endothelium / stroma

Simplified schematic—not a microscopy image

HSV and CMV: Localization of infected cells

HSV

- Degenerating squamous epithelium
- Changes at ulcer margins
- Usually intranuclear inclusions
- Multinucleated cells may be seen

CMV

- Capillary endothelial cells
- Ulcer stromal cells
- Nuclear plus cytoplasmic inclusions
- Ulcers described as shallower

A diagnostic matrix for the viral causes

Characteristic	HSV	CMV
Gross ulcer	Discrete / punched-out	Shallower ulceration
Primary cells described	Squamous epithelium	Endothelial and stromal
Cell location	Ulcer margins	Ulcer-associated stroma/vessels
Inclusional pattern	Nuclear; multinucleation often	Nuclear and cytoplasmic
Ancillary method	Virus-specific IHC	Virus-specific IHC

Viral immunohistochemistry

When morphology suggests HSV or CMV

Virus-specific antigen stains are useful adjuncts

The diagnosis begins with
tissue pattern.

Immunostains add antigen
specificity.

Use results in the context of
the observed cellular lesion.

Do not overinterpret ulcer shape

- A punched-out ulcer suggests a viral cause; It is not a stand-alone organism identification.
- HSV and CMV differ principally by their infected cell populations and inclusion patterns.
- Ancillary virus-specific IHC can clarify difficult morphology.

Rapid morphologic pattern recognition

Adherent white surface material

Consider candidal pseudomembrane

Viral ulcer + squamous inclusions

Favor HSV-associated changes

Viral ulcer + endothelial/stromal inclusions

Favor CMV-associated changes

Basal apoptosis with little acute inflammation

Consider GVHD

Neutrophils: A useful but nonspecific clue

Setting	Source-described inflammatory pattern
Most chemical/infectious injury	Often dense neutrophilic infiltrates
Severe acute caustic necrosis	Neutrophils may be absent
Esophageal GVHD	No significant acute inflammatory infiltrate
GERD (adjacent section)	Neutrophils less common than eosinophils

Chemical or infectious injury versus reflux

This topic

- Specific exposure or immunosuppressive context
- Chemical injury may be necrotizing
- Fungal pseudomembranes or virus-specific inclusions

Reflux esophagitis (adjacent topic)

- Distal gastric reflux is the driver
- Basal zone hyperplasia / papillary elongation
- Eosinophils may enter squamous epithelium

GVHD versus infectious ulceration

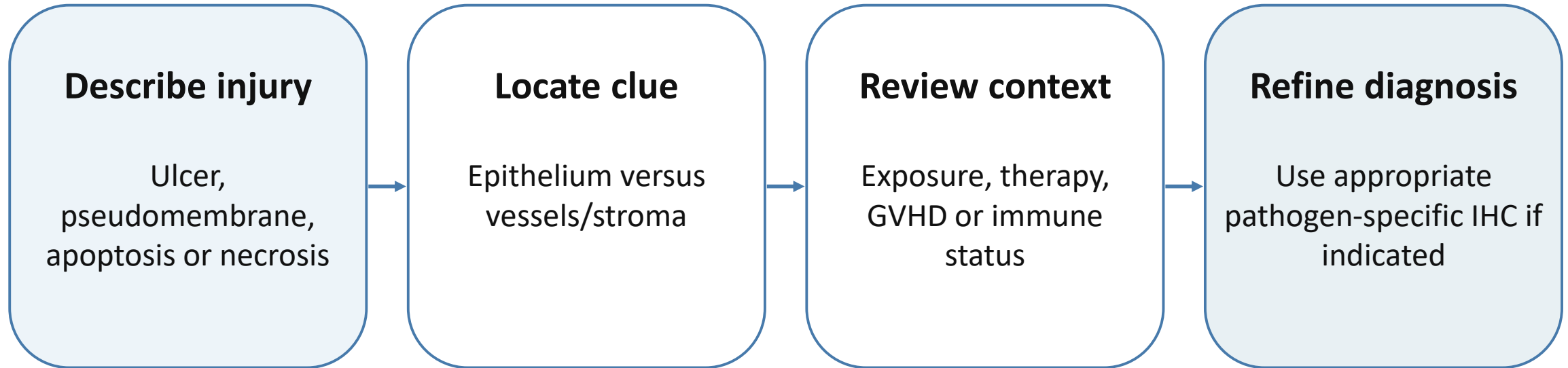
GVHD

- Basal epithelial apoptosis
- Atrophy with submucosal fibrosis
- Little significant acute inflammation

Infectious injury

- Pathogen or viral cytopathic changes
- Neutrophils often present
- Fungal invasion or viral inclusions identify cause

An editable reasoning pathway for a biopsy



Case application: Corrosive ingestion

Hypothetical teaching vignette

After ingestion of an alkaline household product, a patient develops marked odynophagia. Biopsy from a damaged region shows extensive mucosal necrosis with very few neutrophils.

Which source-based principle prevents a diagnostic error?

- A. Few neutrophils exclude serious injury.
- B. Acute caustic necrosis may lack neutrophils.
- C. Ulceration proves CMV infection.

Case interpretation: Caustic necrosis

Correct interpretation

Marked necrosis can occur without neutrophilic infiltration

Exposure provides etiologic context.

Neutrophil abundance is not a severity scale.

Correlate with risk of stricture or perforation.

Case application: Viral ulcer

Hypothetical teaching vignette

An immunosuppressed patient has esophageal ulceration. Biopsy shows enlarged infected endothelial and stromal cells containing nuclear and cytoplasmic inclusions.

Which etiologic pattern is described?

- A. CMV esophagitis
- B. HSV esophagitis
- C. Pill-induced esophagitis

Case interpretation: Infected cell type

Most consistent etiology

Cytomegalovirus (CMV)

Endothelial and stromal inclusions are the key distinction.

Nuclear and cytoplasmic inclusions are described.

Virus-specific IHC is a useful confirmatory adjunct.

Case application: Adherent surface plaques

Hypothetical teaching vignette

A debilitated patient has painful swallowing and adherent gray-white esophageal plaques. Histology shows a dense surface mat of fungal hyphae and inflammatory cells.

Which morphology is most characteristic?

- A. Candidal pseudomembrane
- B. GVHD-associated apoptosis
- C. Radiation-induced vasculopathy

Case interpretation: Candidiasis

Most consistent pattern

Candidal esophagitis

A pseudomembrane links gross and microscopic findings.

Hyphae and inflammatory cells form the surface coating.

Candida is the most common fungal cause named in the source.

Case application: Post-treatment injury

Hypothetical teaching vignette

An esophageal biopsy after irradiation demonstrates proliferation of vascular intima and narrowing of blood vessel lumina.

What mechanism contributes to the mucosal injury?

- A. Radiation-associated vascular damage
- B. HSV replication in squamous epithelial cells
- C. Pseudomembranous fungal infection

Case interpretation: Irradiation

Mechanism highlighted

Vascular compromise contributes to mucosal injury

Changes involve submucosal and mural vessels.

The lumina become narrowed by intimal proliferation.

The source emphasizes a partly secondary mucosal effect.

Five high-yield pattern–etiology links

Corrosive agent

Necrosis may be severe with absent neutrophils

Retained pill

Look for a preexisting stricture

Radiotherapy

Intimal proliferation and luminal narrowing

Candida

Adherent hyphal pseudomembrane

HSV vs CMV

Squamous inclusions vs endothelial/stromal inclusions

Consolidated clinicopathologic principles

- History of exposure or therapy narrows the noninfectious differential.
- Host immune status alters the likelihood of infectious causes.
- Gross ulcer pattern is a clue, not a complete etiologic diagnosis.
- Cellular localization and inclusion pattern are critical in viral esophagitis.
- Ancillary IHC supports, rather than replaces, morphologic assessment.

Primary reference

Robbins, Cotran & Kumar: Pathologic Basis of Disease

11th edition (2026)

Chapter 17: The Gastrointestinal Tract

Chemical and Infectious Esophagitis, pp. 689–690

Adjacent reflux text consulted only for diagnostic differentiation.