

Tissue Necrosis

Infection-driven cellular and organ injury

Pathogenesis · morphology · clinicopathologic interpretation

Dr Abu Suraih Sakhri

MBBS, MD (Pathology)

www.abusuraihsakhri.com

Learning objectives

- Recognize infection-related tissue necrosis as a dominant histologic reaction pattern.
- Explain direct toxin-, microbial-, and host-response–mediated tissue destruction.
- Contrast clostridial, diphtheritic, amebic, HSV, and HBV injury.
- Interpret necrosis relative to inflammatory infiltrates and preserved tissue architecture.

Tissue necrosis is a reaction pattern

- Necrosis refers to tissue death when substantial numbers of cells are destroyed.
- In infection, destruction may be so extensive that it dominates the histologic picture.
- It is a tissue-response pattern—not a microbiologic diagnosis by itself.
- The nature of the injury and host inflammatory response must be interpreted together.

Where necrosis fits among infectious patterns

Pattern	Dominant feature	Illustrative setting
Suppurative	Neutrophils; pus	Pyogenic bacterial abscess
Granulomatous	Epithelioid macrophages	Tuberculosis
Cytopathic	Cell injury or proliferation	Herpesvirus lesions
Tissue necrosis	Rapid tissue destruction	Clostridial gas gangrene
Chronic/scarring	Fibrosis after repetitive injury	Chronic viral hepatitis

Three routes to major tissue damage

1 Microbial exotoxins / enzymes

2 Direct microbial cytopathic injury

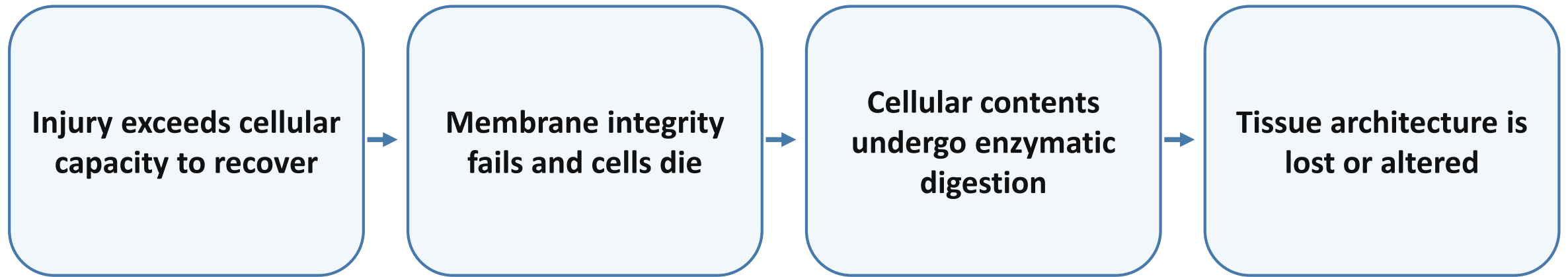
3 Host immune injury

Distinct mechanisms can produce overlapping necrosis and inflammation.

The amount of inflammation is variable

- Some fulminant infections show extensive dead tissue with relatively few inflammatory cells.
- Other necrotizing infections produce prominent inflammation around injured cells.
- Immune suppression changes the reaction: A neutropenic host may have little exudation.
- A sparse infiltrate does not exclude a destructive infection.

Necrosis: The tissue-level sequence



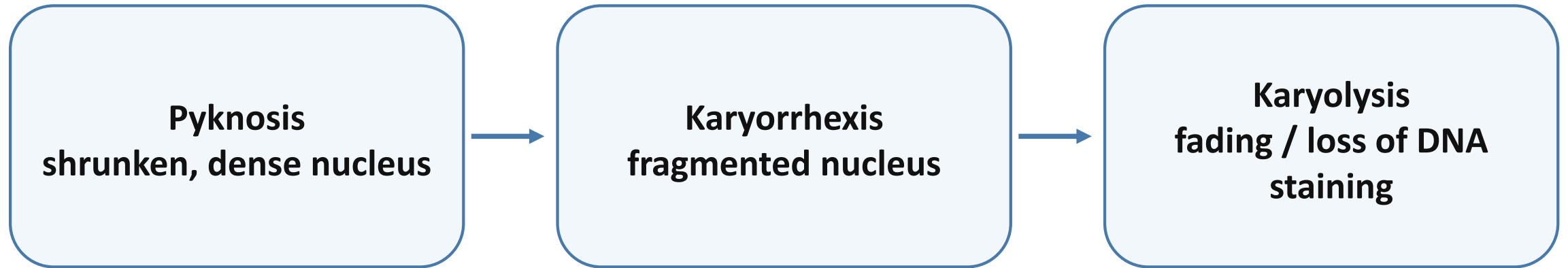
Morphology depends on the relative rates of protein denaturation and tissue digestion.

Schematic sequence

Microscopic hallmarks of dead cells

- Cytoplasm becomes more eosinophilic and often homogeneous on H&E.
- Organelles and cellular contents are degraded; Vacuolation may develop.
- The plasma membrane and organelle membranes are disrupted.
- Cells eventually become ghosts or amorphous debris, depending on tissue digestion.

Three classic nuclear changes



These are recognizable changes in necrotic cells—not organism-specific markers.

Schematic sequence

Two fundamental necrosis architectures

Finding	Coagulative	Liquefactive
Dead tissue outline	Transiently preserved	Digested and lost
Texture	Relatively firm	Viscous / liquid
Underlying mechanism	Protein/enzyme denaturation	Dominant enzymatic digestion
Typical association	Ischemia outside brain	Infections; CNS hypoxia

Why infection often causes liquefaction

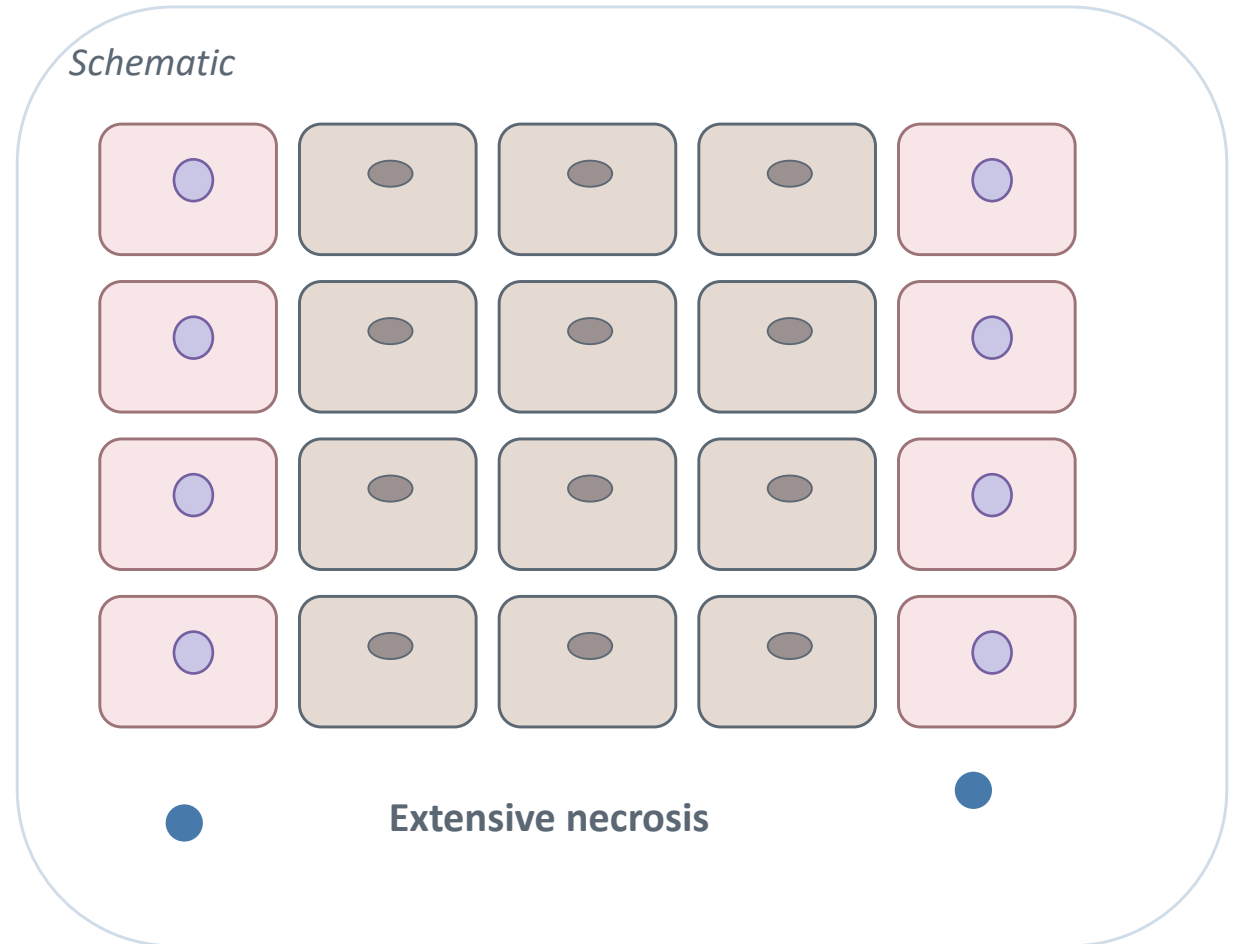
- Microorganisms recruit leukocytes and can release tissue-degrading enzymes.
- Enzymes from leukocytes and microbes digest dead cells and extracellular tissue.
- Liquefied material may become creamy yellow where leukocytes are abundant.
- This common pathway does not imply every necrotic focus contains pus.

Liquefactive necrosis is not synonymous with pus

Feature	Purulent bacterial abscess	Amebic hepatic lesion
Digested tissue	Present	Present
Neutrophils	Often abundant	May be scant at margins
Typical agent	Pyogenic bacteria	Entamoeba histolytica
Interpretive priority	Recognize neutrophil-rich suppuration	Recognize destructive lesion with few leukocytes

Low inflammation does not mean low injury

- Histologic cell counts can underestimate injury when destruction is rapid.
- Toxin-rich or amebic lesions may have extensive necrosis with limited infiltrates.
- Neutropenia can additionally suppress the usual suppurative response.



Interpret the tissue reaction in context

- Ask: Is tissue architecture preserved, liquefied, ulcerated, or replaced by debris?
- Ask: Are neutrophils, lymphocytes, or macrophages predominant—or scarce?
- Ask: Does the location suggest muscle, upper-airway, colon, brain, or liver injury?
- Do not infer the pathogen solely from one inflammatory pattern.

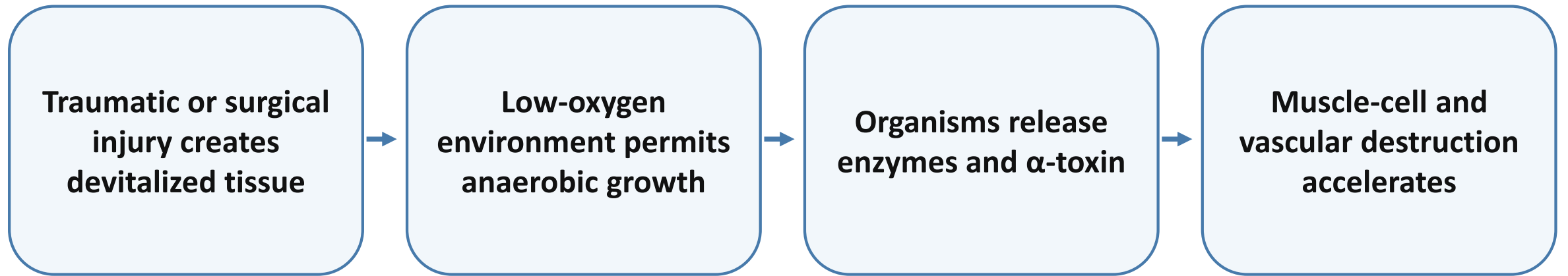
Exotoxins can dominate the lesion

- Exotoxins are secreted bacterial proteins capable of injuring host cells.
- Some are degradative enzymes; Others disrupt intracellular regulatory pathways.
- Direct molecular effects can outpace the recruitment of inflammatory cells.
- *Clostridium perfringens* and *C. Diphtheriae* exemplify severe toxin-linked necrosis.

Mechanistic distinction among bacterial toxins

Class / example	Primary action	Tissue consequence
Tissue-degrading enzymes	Break down matrix or cell proteins	Invasion; tissue destruction
C. perfringens α -toxin	Membrane phospholipase activity	Myonecrosis; hemolysis
Diphtheria toxin	EF-2 inactivation	Death of affected epithelial cells
Botulinum / tetanus toxins	Block transmitter release	Paralysis, not neuronal necrosis

Clostridial myonecrosis: Permissive environment



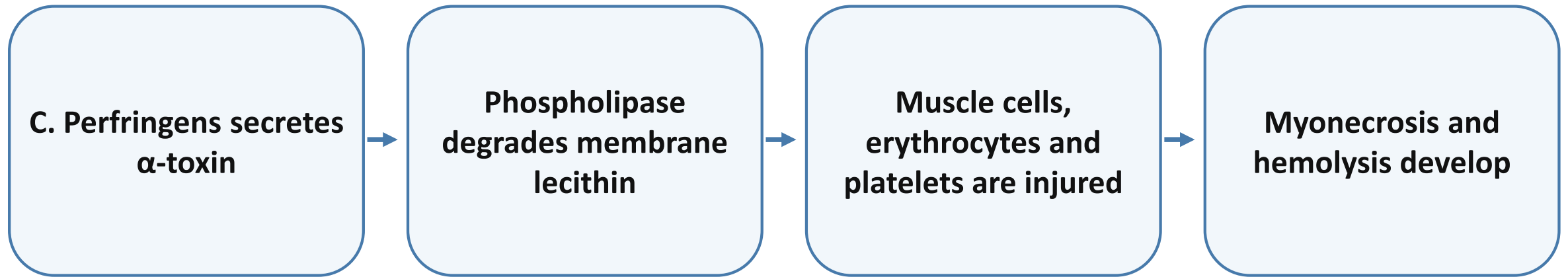
The source emphasizes pre-existing dead tissue as a prerequisite for *C. Perfringens* growth.

Schematic sequence

Clostridium perfringens: Relevant biology

- An anaerobic, spore-forming gram-positive bacillus.
- Along with *C. Septicum* and others, it causes traumatic or surgical wound myonecrosis.
- Necrotic low-oxygen tissue supports bacterial growth.
- Toxin production and tissue-degrading enzymes contribute to rapid spread.

α -Toxin targets cellular membranes



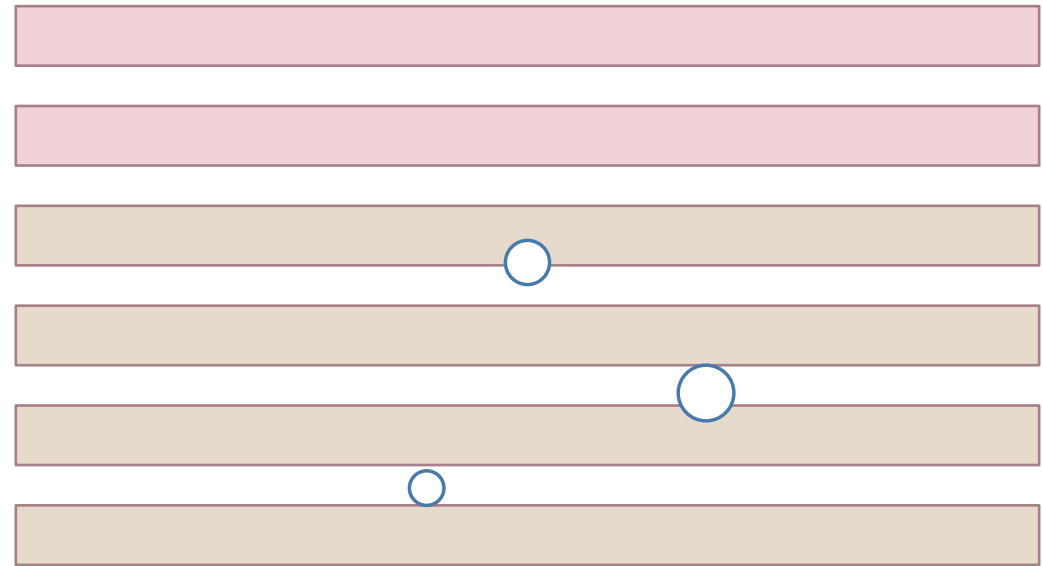
The same toxin also has sphingomyelinase activity linked to nerve sheath injury.

Schematic sequence

Why clostridial muscle injury progresses rapidly

- Extracellular matrix degradation promotes spread through tissues.
- Phospholipid membrane injury destroys muscle cells.
- Vascular injury and thrombosis coexist with myonecrosis.
- Bacterial fermentation accounts for gas bubbles in tissue.

Schematic



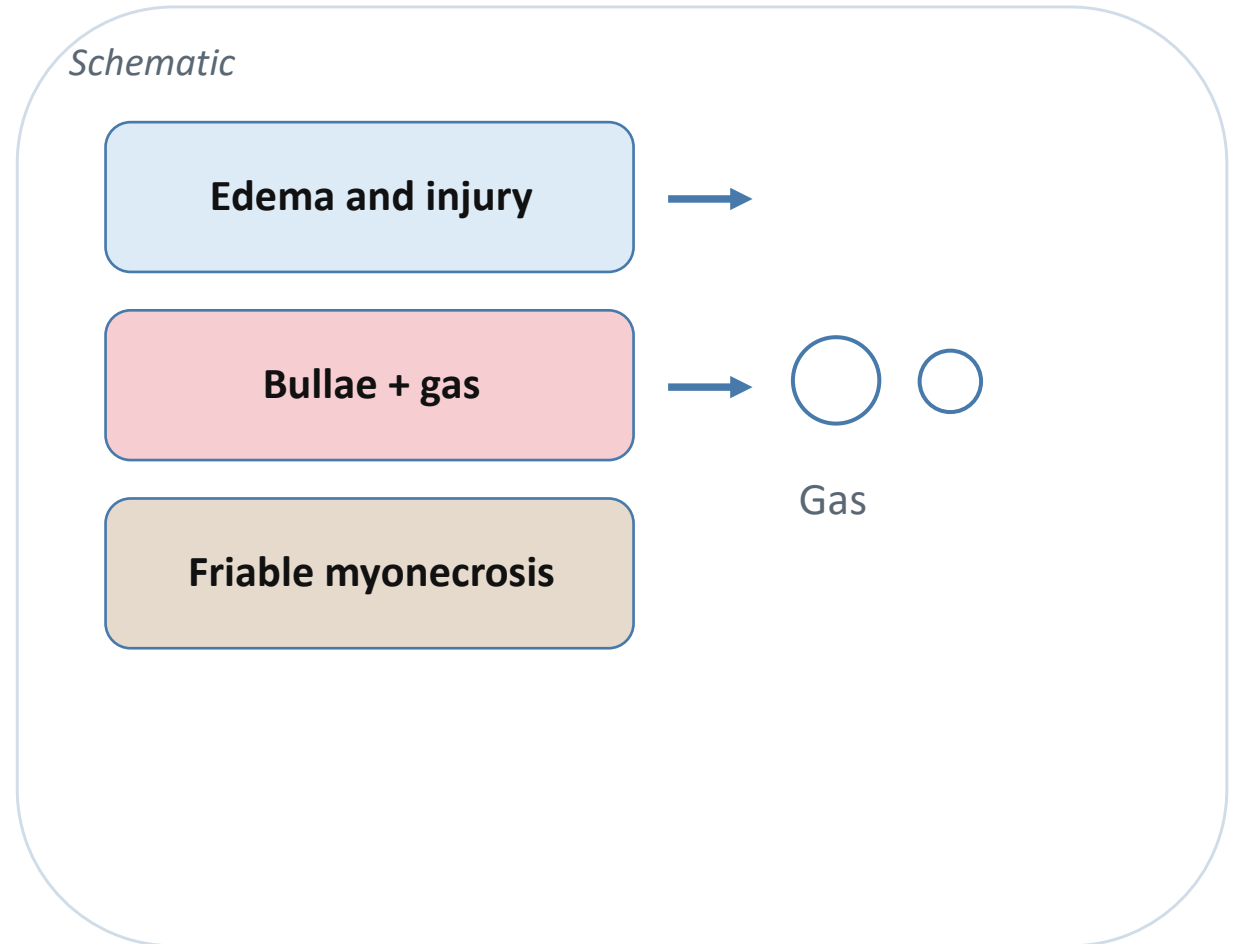
Devitalized muscle

Clostridial cellulitis versus gas gangrene

Feature	Clostridial cellulitis	Gas gangrene
Distribution	Primarily soft tissue	Prominent skeletal muscle necrosis
Lesion character	Foul-smelling, thin discolored exudate	Edema, bullae, gas, friable muscle
Microscopy	Necrosis out of proportion to neutrophils	Severe myonecrosis, hemolysis, thrombosis
Clinical gravity	Treatable with debridement and antibiotics	Life-threatening process

Gas gangrene: Gross morphological sequence

- Marked edema accompanies acute muscle injury.
- Overlying skin may develop large bullae.
- Gas bubbles appear within necrotic tissue.
- Muscle becomes soft, blue-black and friable.

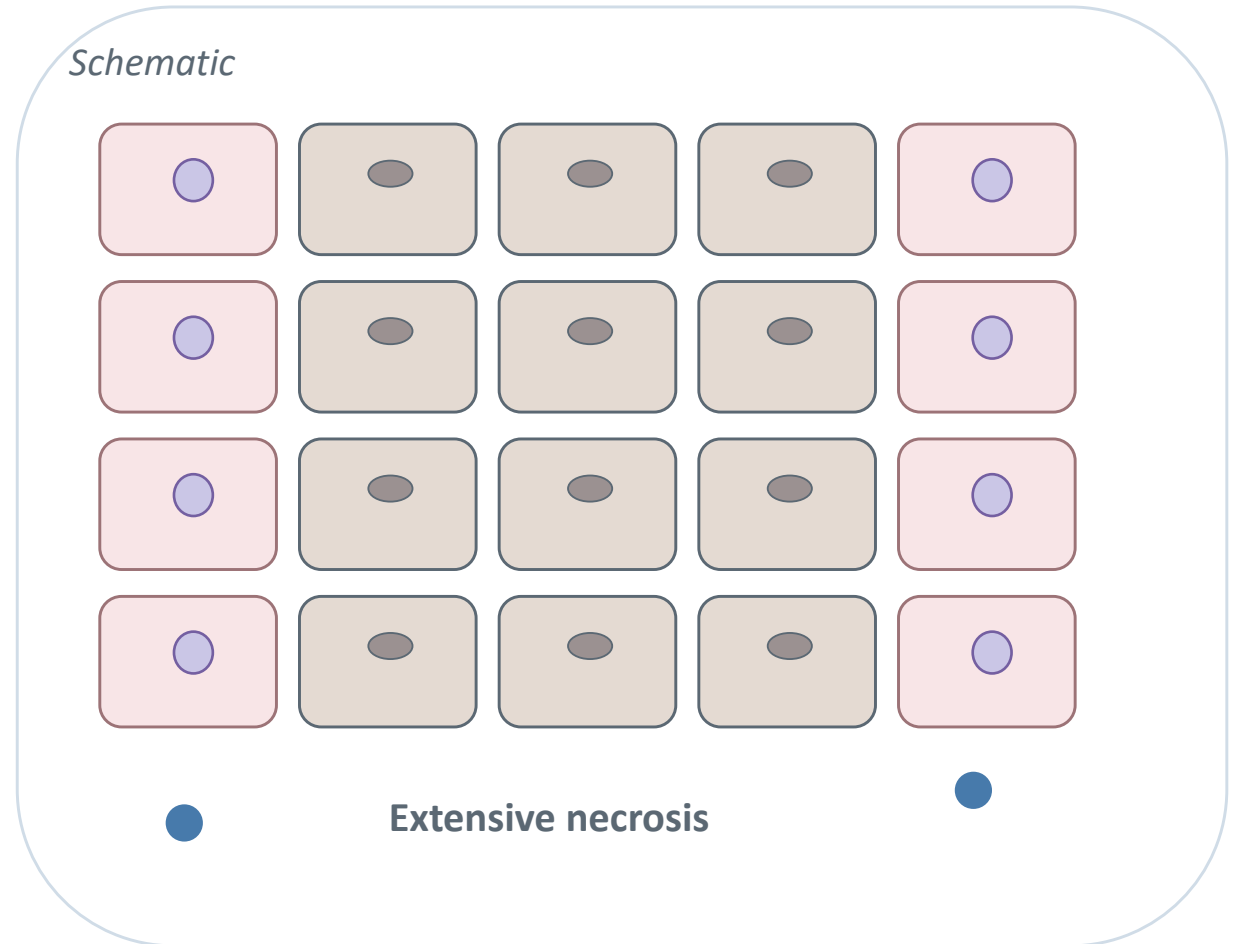


Gas gangrene: What a section may show

- Severe myonecrosis is the dominant tissue event.
- Extensive hemolysis and vascular damage are described.
- Vascular thrombosis accompanies progression.
- An extensive exudate may paradoxically contain few inflammatory cells.

Disproportionate necrosis is a histologic clue

- Look for destruction of muscle architecture.
- Compare the severity of necrosis with the density of neutrophils.
- Sparse inflammation in a rapidly progressing lesion is compatible with clostridial disease.



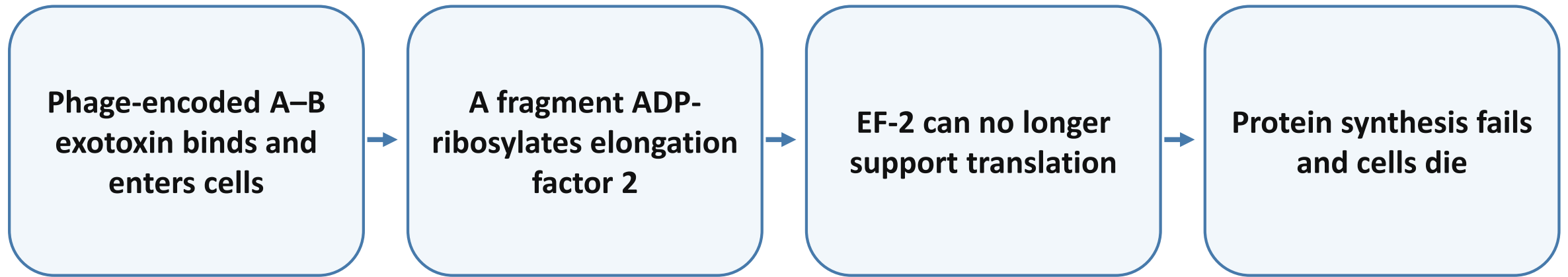
Clostridial infection: Clinical-pathologic urgency

- The textbook calls gas gangrene life-threatening.
- Rapidly evolving myonecrosis may follow trauma or surgery.
- The tissue effects stem from enzyme activity, membrane damage and vascular injury.
- This is a destructive lesion rather than merely a large accumulation of pus.

Diphtheria: A surface infection with toxin injury

- *Corynebacterium diphtheriae* can proliferate on upper respiratory mucosa.
- Toxin causes epithelial necrosis and a fibrinosuppurative reaction.
- Bacterial invasion is localized, yet toxin can distribute systemically.
- Necrosis and inflammation together produce the pseudomembrane.

Diphtheria toxin: A precise intracellular lesion



Diphtheria necrosis is mechanistically distinct from phospholipase-driven clostridial myonecrosis.

Schematic sequence

How a pseudomembrane forms

- Bacteria attach to respiratory mucosa.
- Exotoxin kills surface epithelial cells.
- Dense fibrin and inflammatory exudate coagulate over the ulcerated surface.
- The gray-black pseudomembrane is not viable tissue.

Schematic

Coagulated fibrin + dead epithelium

Ulcerated mucosal surface

Inflamed, vascularized mucosa

Not a true viable membrane

The underlying tissue remains inflamed

- Necrotic epithelium is associated with a dense fibrinosuppurative exudate.
- Underlying tissue contains prominent neutrophils.
- Vascular congestion, interstitial edema and fibrin exudation are present.
- This illustrates why necrosis can coexist with marked rather than sparse inflammation.

Why the diphtheritic membrane is dangerous

- A tough membrane adheres to ulcerated, vascularized mucosa.
- Sloughing may cause bleeding.
- Airway compromise or asphyxiation may follow.
- The danger is anatomic as well as toxin-mediated.

Local and distant lesions in diphtheria

Location	Observed injury	Mechanistic significance
Upper airway mucosa	Necrotic epithelium; pseudomembrane	Local toxin action
Myocardium	Fatty change; focal myofiber necrosis	Systemic toxin distribution
Nerves	Polyneuritis; myelin / axonal injury	Systemic toxic effect
Liver / kidney / adrenal	Occasional focal cell necrosis	Remote organ injury

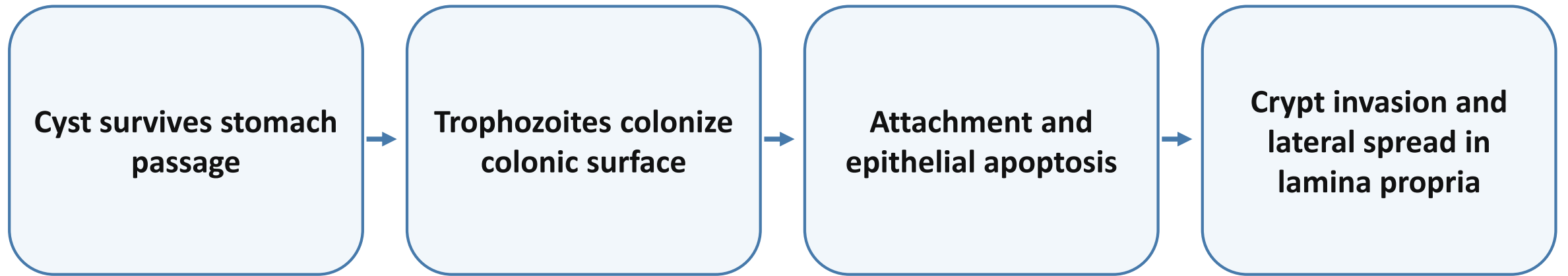
Two exotoxins, two histologic phenotypes

	C. perfringens	C. diphtheriae
Principal vulnerable site	Muscle / soft tissue	Respiratory epithelium
Molecular attack	Membrane phospholipids	Protein translation via EF-2
Dominant structural change	Widespread myonecrosis	Epithelial necrosis and membrane
Inflammatory context	May be cell-poor	Underlying tissue neutrophil-rich

Amebiasis: Invasive protozoal tissue destruction

- *Entamoeba histolytica* is transmitted by the fecal–oral route.
- The organism colonizes the colonic epithelial surface after cyst ingestion.
- Trophozoites attach, injure and penetrate mucosa.
- Invasion can extend beyond the colon and produce destructive liver abscesses.

Amebic colonic invasion

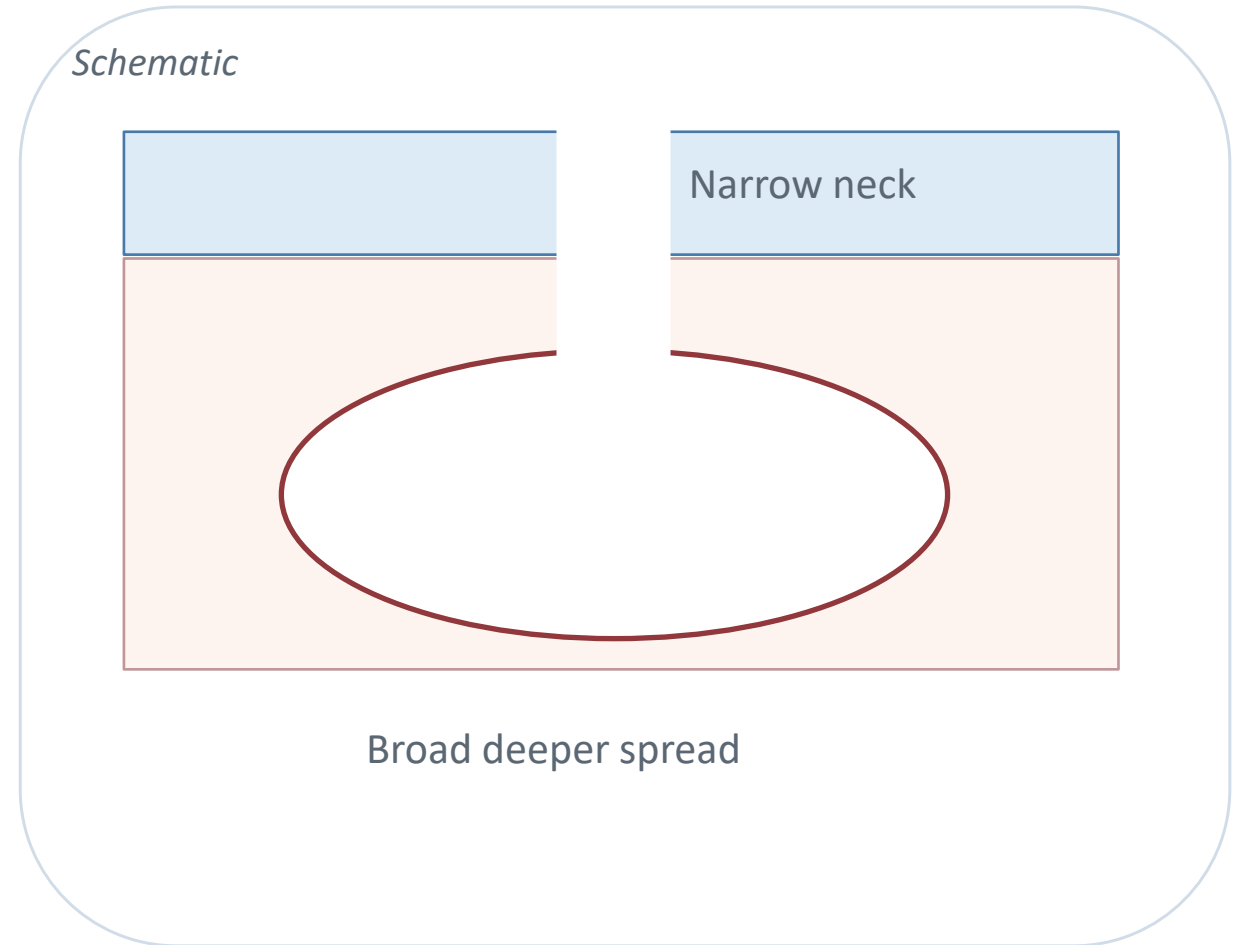


The invasive geometry helps explain a flask-shaped ulcer.

Schematic sequence

The flask-shaped amebic ulcer

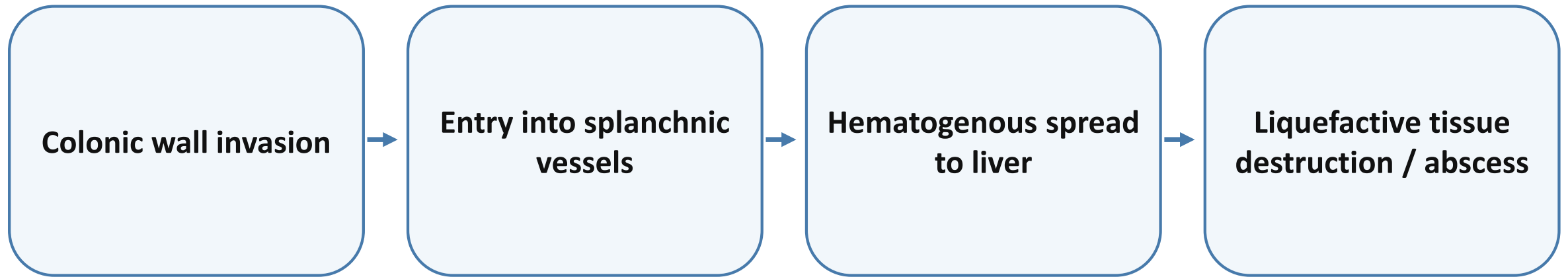
- Surface opening is relatively narrow.
- Destruction extends laterally within deeper mucosa.
- The resulting broad base under a narrow neck creates the flask profile.
- This diagram illustrates described geometry, not a histologic specimen.



Microscopic recognition has a specific pitfall

- Amoebas may resemble macrophages in both size and appearance.
- The organism must be considered in the context of the ulcer and tissue destruction.
- Morphologic resemblance alone can make histologic diagnosis difficult.
- Do not diagnose the agent merely from a necrotic surface.

From colonic invasion to liver abscess



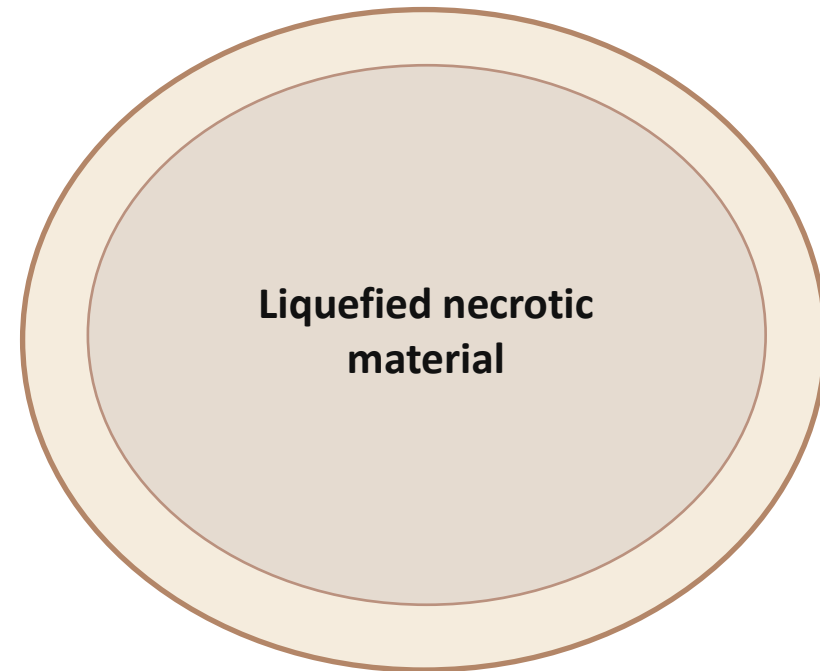
Spread may follow clinically apparent or subsequently resolved intestinal illness.

Schematic sequence

The amebic liver abscess is cell-poor at its edge

- Liver lesions may contain extensive liquefied necrotic material.
- The source describes scant inflammation at the margins.
- The cavity may have a shaggy fibrinous lining.
- Extensive destruction need not produce the dense neutrophilic ring of pyogenic pus.

Schematic



Scant marginal cells

Amebic necrosis: Clinical organ manifestations

- Colonic disease may produce bloody diarrhea and abdominal pain.
- Invasive disease can lead to acute necrotizing colitis and megacolon.
- Hepatic abscesses can persist after the acute intestinal episode.
- Rare direct extension to lung or heart and hematogenous spread to other sites are described.

Amebic versus pyogenic tissue destruction

	Amebic hepatic abscess	Pyogenic bacterial abscess
Principal injurious context	Parasite invasion and tissue destruction	Neutrophil-rich bacterial inflammation
Necrosis	Extensive liquefaction	Liquefaction forming pus
Inflammatory cells	Scant at lesion margins	Typically prominent
Morphologic limitation	Cannot infer all abscesses are bacterial	Pus does not indicate a unique species

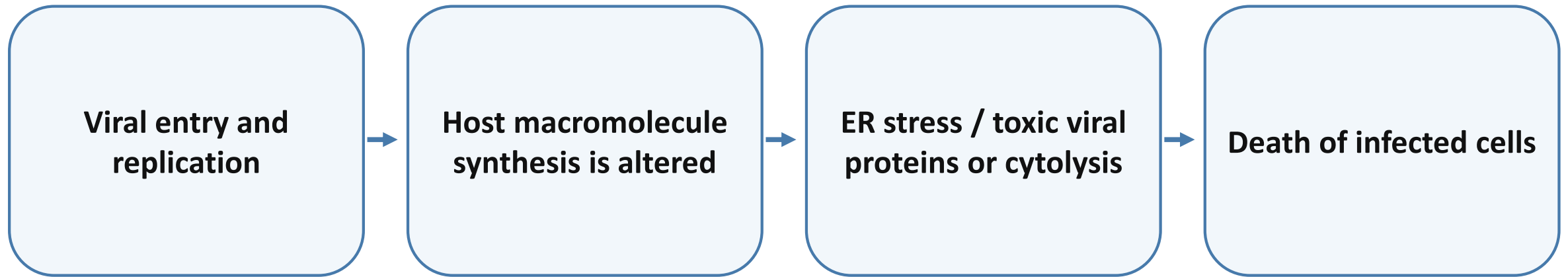
The unifying amebic teaching point

- The parasite causes colonic ulcers and liver abscesses.
- Both lesions arise through invasive tissue destruction.
- Liquefactive necrosis can be prominent even when inflammatory infiltration is modest.
- Lesion architecture and epidemiologic / clinical context matter alongside cell density.

Viruses can cause severe tissue necrosis

- Viral cell killing is not limited to minor cytopathic changes.
- Some infections produce widespread host-cell necrosis with inflammation.
- HSV destruction of temporal lobe tissue and HBV-related hepatic injury.
- Viral injury can reflect direct cytopathic activity or antiviral immunity.

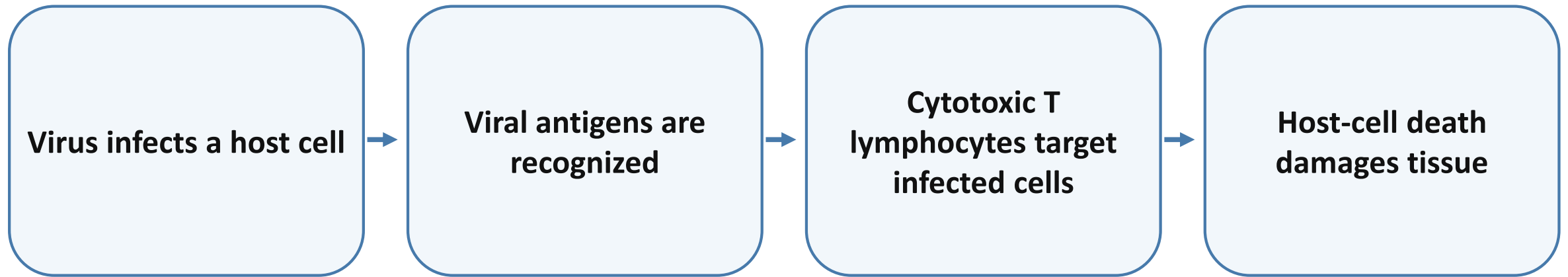
Direct virus-induced cell injury



Direct mechanisms vary across viral families; This is a general pathway, not a claim for every virus.

Schematic sequence

Antiviral immunity can also injure organs



A protective immune response may simultaneously be the principal cause of organ injury.

Schematic sequence

Direct cytopathy versus immune-mediated injury

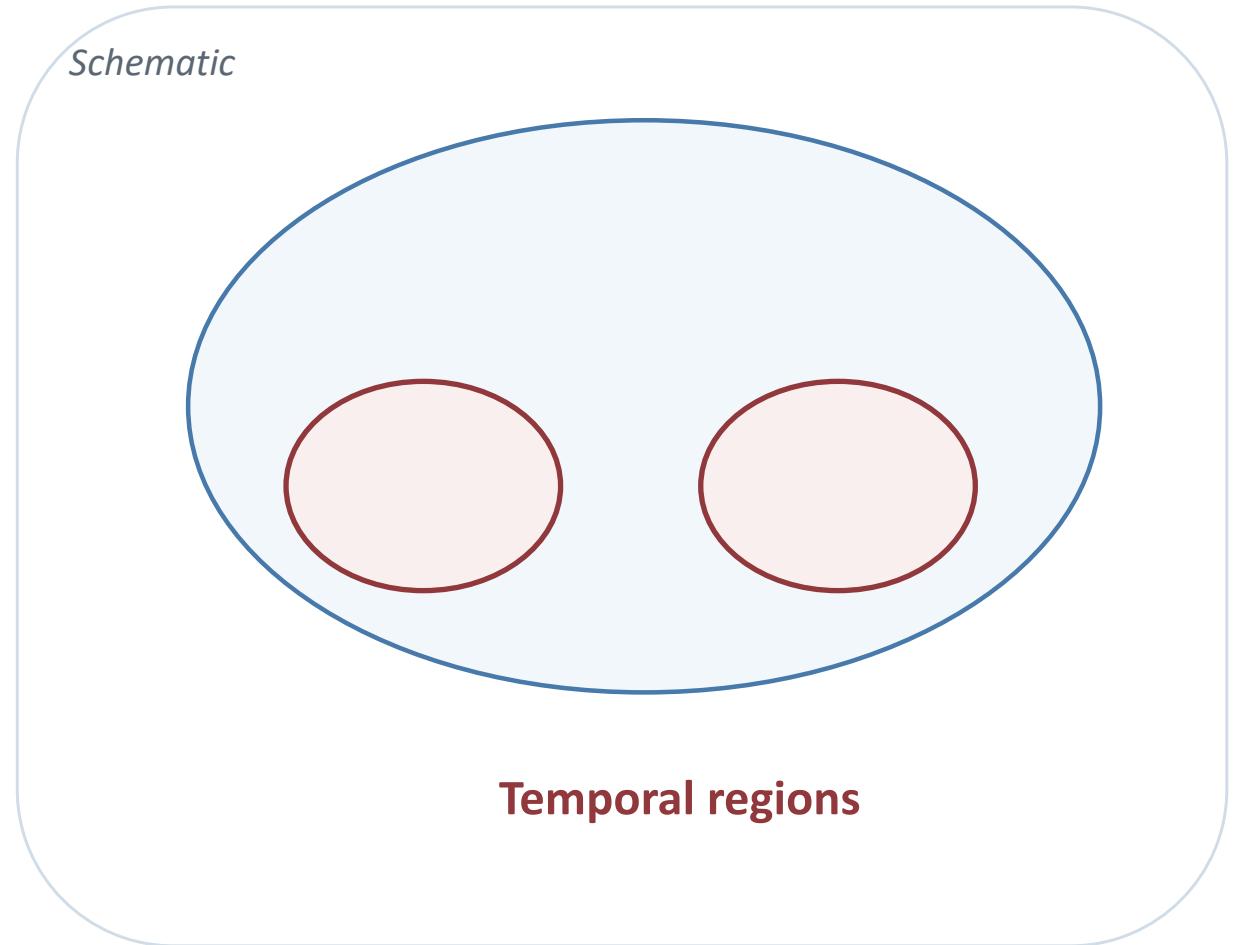
Question	Direct viral effects	Host antiviral response
Immediate injurious agent	Viral replication or proteins	Immune effector cells
Target	Infected host cell	Virus-infected host cell
Teaching example	HSV-associated cytopathic injury	HBV hepatocyte injury via CD8 ⁺ T cells
Interpretation	Identify viral cell changes if visible	Consider immune infiltrate and cell injury

HSV: From mucosal replication to CNS involvement

- HSV-1 and HSV-2 replicate at mucocutaneous entry sites.
- The viruses travel along sensory axons and establish latency in neuronal cell bodies.
- HSV-1 encephalitis usually involves temporal lobes and orbital frontal gyri.
- CNS infection may cause extensive destruction of involved brain tissue.

HSV encephalitis: Regional vulnerability

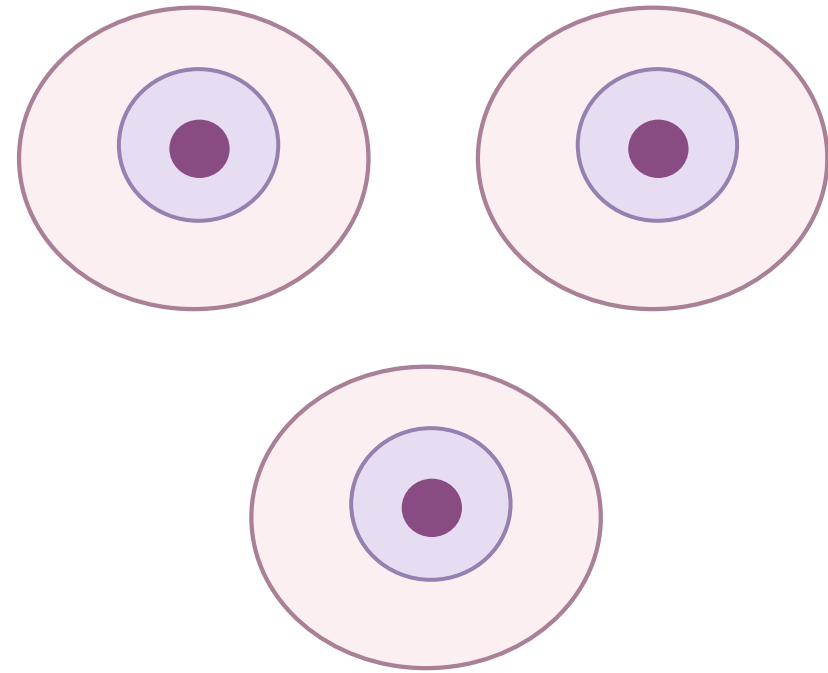
- Temporal lobes are characteristic sites emphasized.
- The excerpt describes severe tissue destruction in these regions.
- Location can be diagnostically informative but not independently definitive.



HSV cytopathic morphology

- HSV may form Cowdry type A intranuclear inclusions.
- Nuclear chromatin is displaced to the periphery.
- Infected cells can fuse into multinucleated syncytia.
- The drawing conveys nuclear relationships only; It is not microphotography.

Schematic



Intranucl. Inclusion (schematic)

HSV infection is not confined to the brain

- Cutaneous and mucosal lesions may form vesicles and erosions.
- Neonatal infection can involve necrotic foci in lungs, liver, adrenals and CNS.
- Necrotizing HSV bronchopneumonia and hepatitis are described in disseminated infection.
- Immunosuppression increases the importance of disseminated visceral HSV.

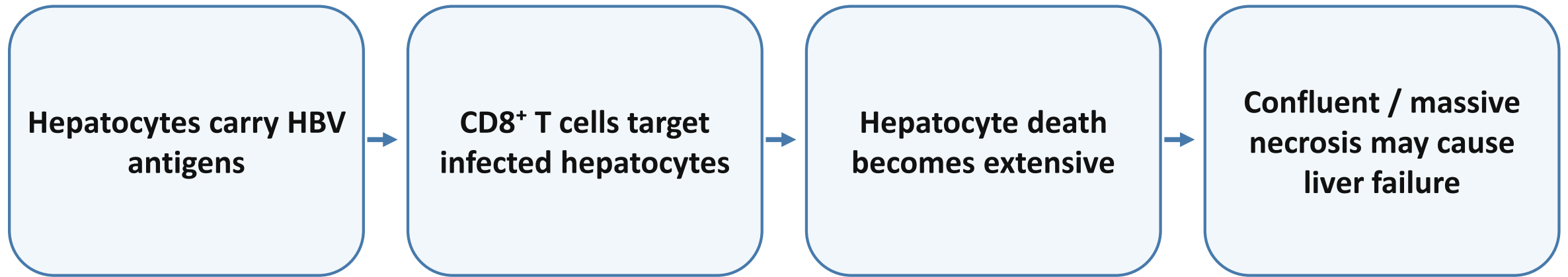
HSV: Direct cytolysis and immune-related injury

Setting	Dominant teaching mechanism	Pathologic consequence
Epithelial keratitis	Direct viral cytolysis	Superficial epithelial damage
Stromal keratitis	Host immune reaction	Inflammation and later scarring
Encephalitis	Destructive viral infection	Severe regional CNS injury
Disseminated infection	Visceral involvement	Necrotic foci in organs

HBV hepatocyte injury is largely immune-mediated

- HBV infection may be cleared, persist, or occasionally produce acute hepatic failure.
- Most hepatocyte injury is attributed to CD8⁺ cytotoxic T lymphocytes.
- High viral replication can also cause some cytopathic changes.
- The degree of immune response strongly affects disease outcome.

HBV injury: Pathogenesis to liver failure



Avoid equating infection with inevitable liver failure; This is a severe possible outcome.

Schematic sequence

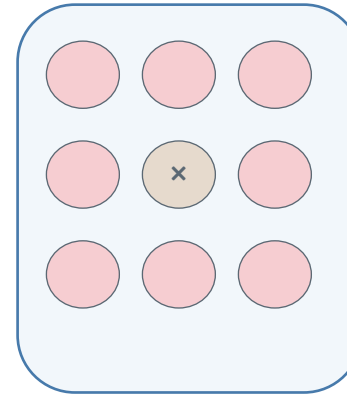
Morphology of severe viral hepatitis

- Acute viral hepatitis produces predominantly lymphocytic portal and lobular inflammation.
- Hepatocytes can undergo necrosis or apoptosis.
- Necrosis may become confluent, bridging or panlobular.
- The liver may shrink in cases associated with acute liver failure.

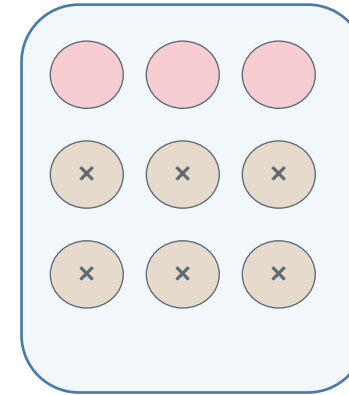
Progression from scattered to confluent injury

- Isolated dying hepatocytes may coexist with otherwise viable plates.
- Confluent necrosis indicates involvement of groups of hepatocytes.
- Bridging necrosis links vascular structures; Panlobular necrosis spans a lobule.
- These are patterns of extent, not separate pathogens.

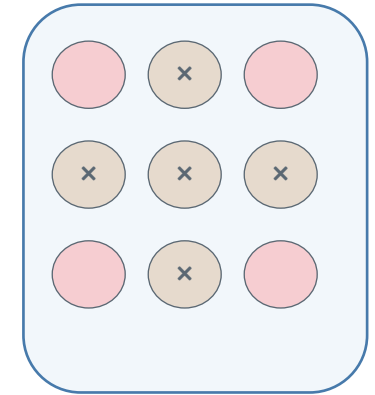
Schematic



Scattered cell injury



Confluent groups



Widespread injury

x = necrotic cell (conceptual)

Massive hepatic necrosis is an organ-level event

- Extensive hepatocyte loss compromises functional liver parenchyma.
- Acute hepatic failure with massive necrosis among HBV outcomes.
- Necrosis can progress from groups of hepatocytes to entire lobules.
- Severe anatomic destruction explains why fulminant hepatitis is clinically consequential.

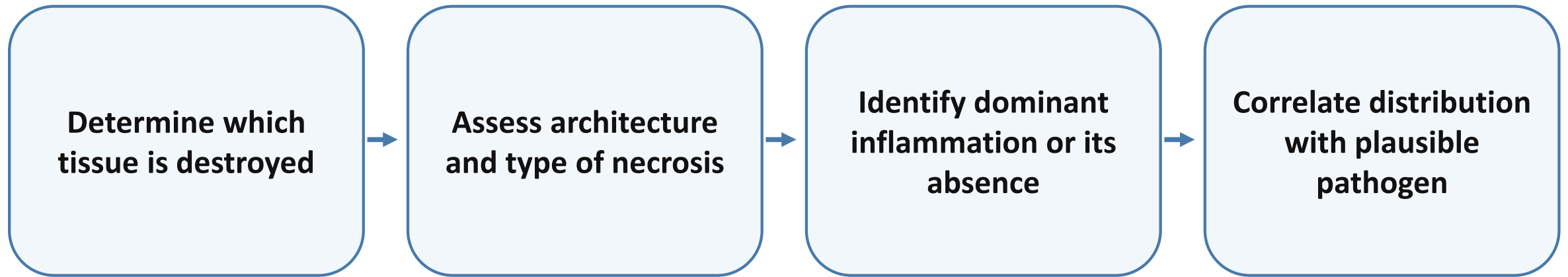
HSV and HBV: Do not equate mechanism

Dimension	HSV	HBV
Exemplar organ	Brain (temporal lobe)	Liver
Characteristic lesion	Severe regional destruction	Hepatocellular necrosis
Mechanistic emphasis	Viral cytopathic damage; inflammation	Mainly CTL-mediated hepatocyte injury
Diagnostic context	HSV cell changes / CNS localization	Portal-lobular hepatitis / serology

Five exemplar agents: A mechanistic synthesis

Agent	Principal site	Destructive mechanism
C. perfringens	Muscle / wound	Phospholipase toxin + enzymes
C. diphtheriae	Airway epithelium	EF-2 inhibition by exotoxin
E. histolytica	Colon / liver	Protozoal invasion; liquefaction
HSV	CNS / other tissues	Viral cytopathy ± inflammation
HBV	Liver	Predominantly T-cell-mediated injury

Reading a necrotizing infectious lesion



Necrosis is a pattern to be interpreted, not a stain-based species identification.

Schematic sequence

Anatomic pattern is a major discriminator

Involved tissue	Key morphological clue	Exemplar
Skeletal muscle	Extensive myonecrosis; gas / thrombosis	Clostridial gas gangrene
Upper airway	Adherent necrotic pseudomembrane	Diphtheria
Colon	Narrow-neck, broad-base ulcer	Amebiasis
Liver abscess	Liquefaction, little edge inflammation	Amebiasis
Brain temporal region	Severe tissue destruction	HSV encephalitis

Three cautions for morphology-based inference

- Necrosis patterns are not uniquely attributable to one microorganism.
- Multiple inflammatory patterns can coexist in one infected tissue.
- The host immune state can markedly change cell recruitment and lesion morphology.
- Clinical context and targeted organism identification remain essential.

Case 1 · Rapidly destructive wound lesion

Following trauma, a patient develops rapidly progressive swollen muscle with bullae and gas within diseased tissue.

Histology shows marked muscle necrosis with relatively few neutrophils.

Question: Which causal mechanism best explains the dominant pathology?

Case 1 · Mechanistic interpretation

- The pattern points toward clostridial myonecrosis.
- Anaerobic growth follows tissue devitalization.
- *C. Perfringens* α -toxin damages membranes; Enzymes facilitate spread.
- Extensive necrosis may be disproportionate to the neutrophilic infiltrate.

Case 2 · Colonic ulcer and liver cavity

A patient with dysentery has a colonic ulcer with a narrow mucosal opening and broader deeper extension.

A liver cavity contains extensive liquefied tissue but little inflammation at its edge.

Question: Why does this pattern differ from a typical pyogenic abscess?

Case 2 · Mechanistic interpretation

- Invasive *E. Histolytica* produces a characteristic flask-shaped ulcer.
- Vascular spread may seed the liver.
- Amebic liver abscesses can have extensive necrosis with scant marginal inflammation.
- Thus, liquefaction does not automatically mean neutrophil-rich bacterial pus.

Case 3 · Adherent gray airway lesion

An upper-airway lesion displays a tough gray membrane over ulcerated mucosa.

Below the membrane there is a dense neutrophilic infiltrate and vascular congestion.

Question: Explain the epithelial death and the clinical risk of membrane separation.

Case 3 · Mechanistic interpretation

- C. Diphtheriae exotoxin blocks translation by inactivating EF-2.
- Epithelial necrosis plus fibrinosuppurative exudate creates the pseudomembrane.
- The membrane rests on inflamed, vascularized mucosa.
- Sloughing may cause bleeding and airway compromise.

Case 4 · Severe necrotizing viral injury

An infection severely injures temporal lobe tissue; Another patient has diffuse hepatocellular death with lymphocytic inflammation.

Question: Which exemplar viruses are described, and must their dominant cellular injury mechanism be identical?

Case 4 · Mechanistic interpretation

- Severe temporal lobe destruction is a classic HSV example.
- Fulminant hepatic necrosis is a potential HBV-associated outcome.
- HBV hepatocyte damage is mainly cytotoxic T-cell mediated.
- Similar morphologic endpoints can result from different causal pathways.

Integrative take-home points

- Infectious tissue necrosis is a morphologic endpoint, not a diagnosis of species.
- Microbial toxins, direct cytopathy and host immunity are distinct pathways to cell death.
- Clostridial and amebic lesions can destroy tissue with sparse inflammation.
- Correlate distribution, injury architecture, inflammatory cells and clinical context.

Core source and cross-chapter context

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. 2026.
- Chapter 8: infectious tissue-reaction patterns and organism-specific pathology.
- Chapter 2: morphology and patterns of tissue necrosis.
- Chapter 17: *Entamoeba histolytica* colitis and hepatic abscess.
- Chapter 18: viral hepatitis–related hepatocyte injury.