

Spectrum of Inflammatory Responses to Infection

Morphologic patterns, pathogenic mechanisms, and
clinicopathologic interpretation

A pattern-based framework for examining infected tissues.

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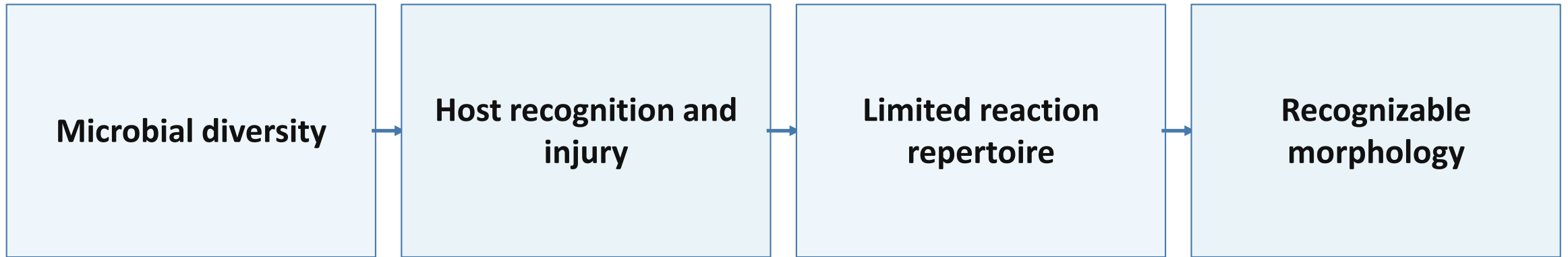
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Learning objectives

- Recognize the characteristic cellular and tissue features of each response pattern.
- Explain how pathogen virulence, host immunity, and tissue location modify morphology.
- Interpret destructive, fibrosing, mixed, and unexpectedly pauci-inflammatory lesions.
- Use histologic patterns to frame—not replace—etiologic diagnosis.

Many microbes, relatively few tissue patterns



- Distinct pathogens can trigger similar tissue responses.
- Histologic pattern is a clue to pathogenesis, not a species-level identification.

The observed lesion is a host–microbe interaction

Pathogen contributions

Microbial virulence and tropism

Chemoattractants and toxins

Intracellular persistence

Host and tissue contributions

Leukocyte number and competence

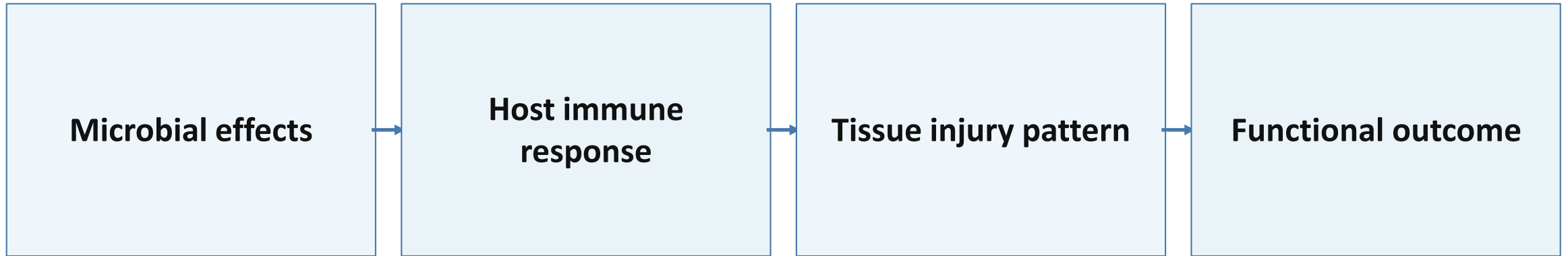
Cell-mediated immune responses

Organ architecture and duration

Five dominant patterns—and an absent response

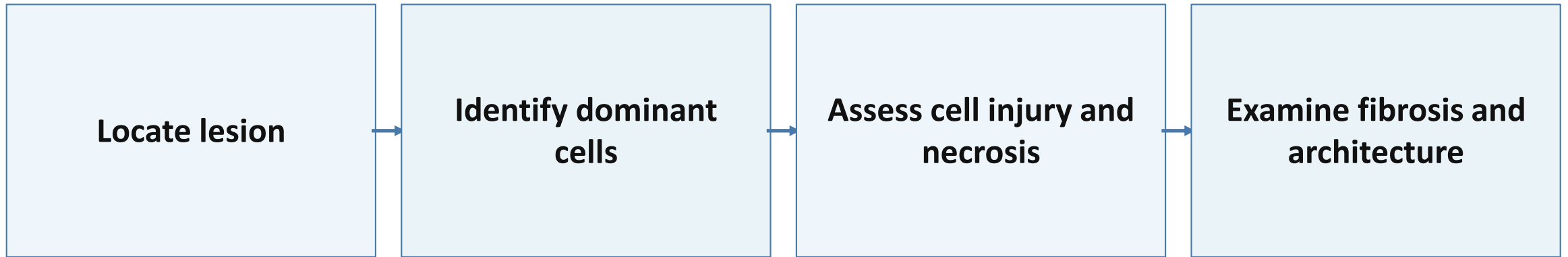
Pattern	Defining finding	Interpretive clue
Suppurative	Neutrophils; pus	Pyogenic inflammation
Mononuclear / granulomatous	Lymphocytes, plasma cells, macrophages; granulomas	Intracellular or persistent agents
Cytopathic / cytoproliferative	Cell injury, inclusions or proliferation	Commonly viral
Tissue necrosis	Destruction dominates	Toxins or cell lysis
Chronic inflammation / scarring	Fibrosis and architectural loss	Persistent or repeated injury
No reaction	Little cellular response	Severe immune compromise

Inflammation and direct injury are distinct axes



- Some tissue destruction is toxin- or pathogen-mediated.
- Some damage is caused by immunity directed against infected cells.

A practical first read of infected tissue



- Then ask whether the inflammatory response is proportional to suspected pathogen burden.
- Retain mixed infection and noninfectious mimics in the differential.

A response pattern rarely identifies one pathogen

- That few morphologic features are pathogen-specific.
- Distinct organisms can produce overlapping inflammatory infiltrates.
- The same organism can look different in immunocompetent and immunocompromised hosts.
- Morphology is best interpreted with lesion distribution and host context.

Neutropenia can conceal pyogenic inflammation

Typical leukocyte response

Pyogenic bacteria recruit neutrophils.

A conspicuous purulent exudate may develop.

Pus can draw attention to the infection.

Profound neutropenia

Rapid destruction may occur.

Little neutrophilic exudate may be present.

Sparse inflammation does not exclude bacterial infection.

Tuberculosis illustrates immune-dependent morphology

Intact cell-mediated immunity

Well-formed granulomas.

Relatively few organisms in lesions.

Organized macrophage aggregates.

Advanced T-cell deficiency

Mycobacteria may multiply profusely.

Organism-laden macrophages.

Poorly formed or absent granulomas.

Distribution changes the lesion, not its category

Distribution	Robbins example	Interpretation
Focal	Small purulent focus	A localized inflammatory reaction
Multifocal	Septic microabscesses in different organs	Dissemination can create numerous foci
Extensive	Lobar pneumonia	A large organ territory may be involved
Destructive	Necrotizing pneumonia or joint infection	Architecture and site determine consequences

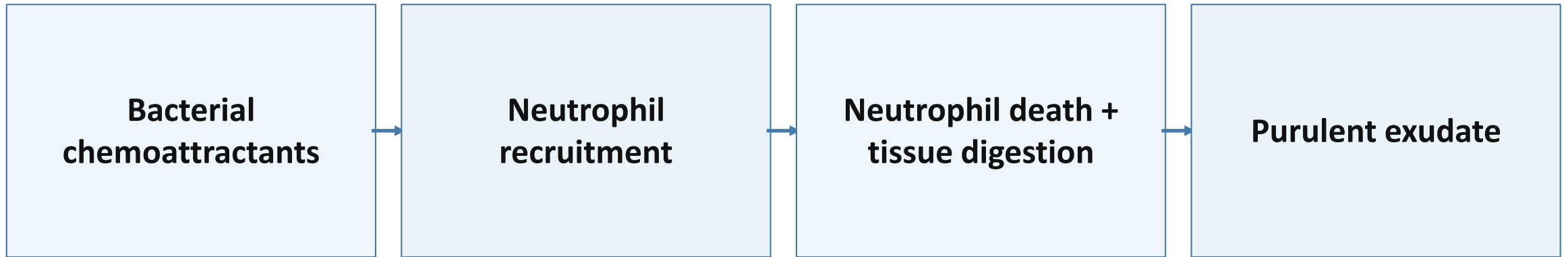
Morphologic clues across the spectrum

Look first for...	Consider...	Do not assume...
Abundant neutrophils	Suppuration	One particular bacterial species
Mononuclear infiltrate	Viral / intracellular / persistent disease	All mononuclear infiltrates are infectious
Intracellular inclusions	Cytopathic infection	An inclusion identifies every agent
Extensive necrosis	Direct toxin / lytic injury	The infiltrate must be abundant
Broad fibrous remodeling	Chronic injury	Fibrosis names the cause

Suppuration: A neutrophil-dominant reaction

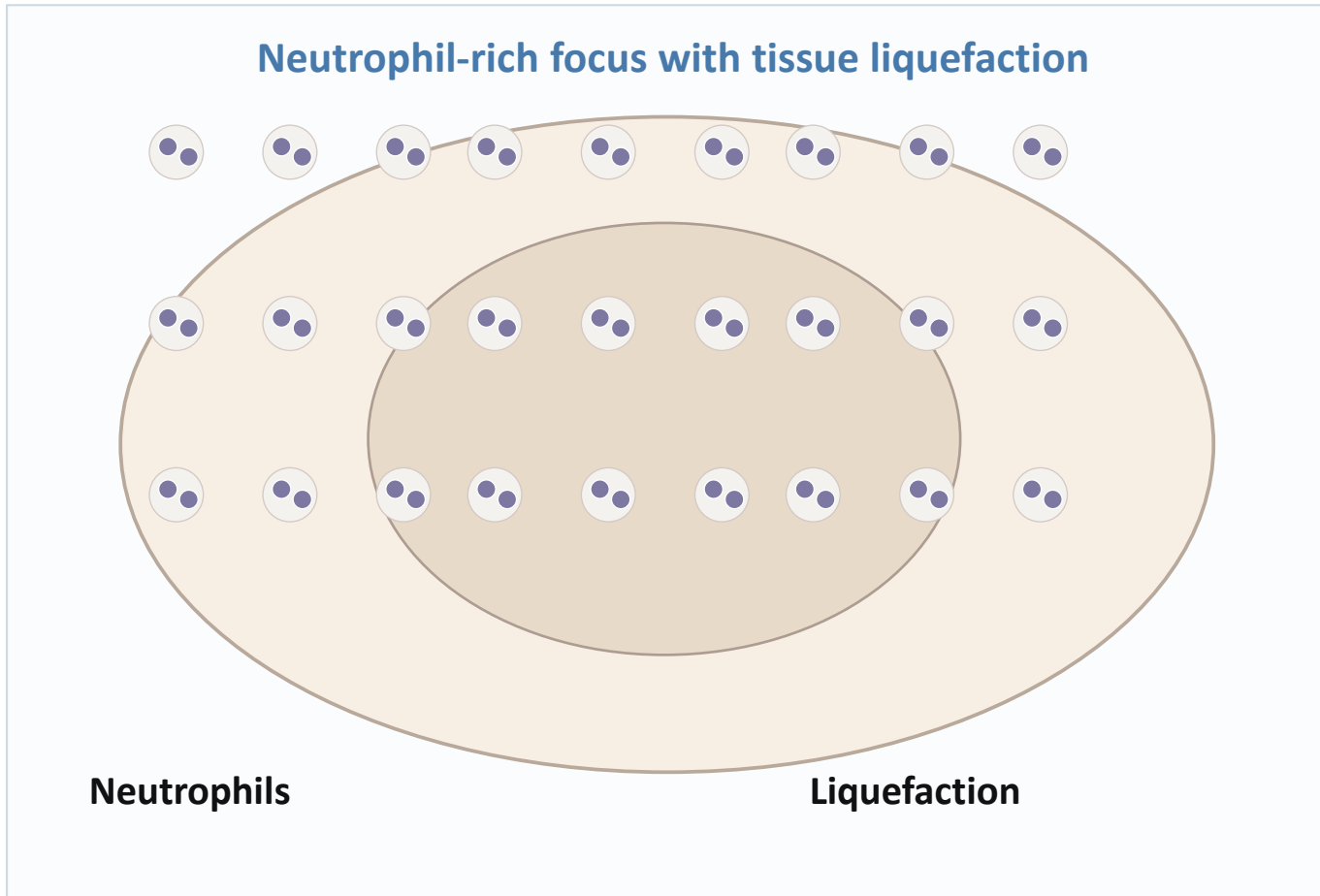
- Increased vascular permeability accompanies the acute response.
- Neutrophils accumulate at the infection site.
- Extracellular pyogenic organisms commonly evoke the pattern.
- The exudate can progress to tissue liquefaction and pus.

From pyogenic signals to pus



- The mechanism combines leukocyte influx with tissue breakdown.
- Both dying leukocytes and liquefactive necrosis contribute to pus.

Pus is a composite of cells and tissue breakdown



- Accumulated dying and dead neutrophils are central to the lesion.
- Liquefactive necrosis contributes damaged tissue to the purulent material.
- An abscess localizes this destructive inflammatory process.

Suppurative lesions vary enormously in scale

Tiny microabscesses

Small, multiple inflammatory foci.

Example: Septic dissemination from an infected heart valve.

Distribution can span multiple organs.

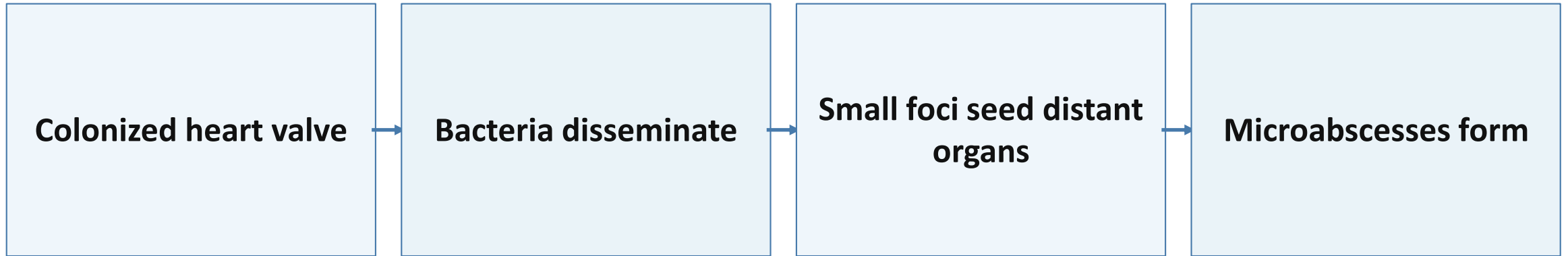
Diffuse lobar disease

Extensive airspace involvement.

Example: Lobar pneumonia.

The same broad response class can involve much of an organ.

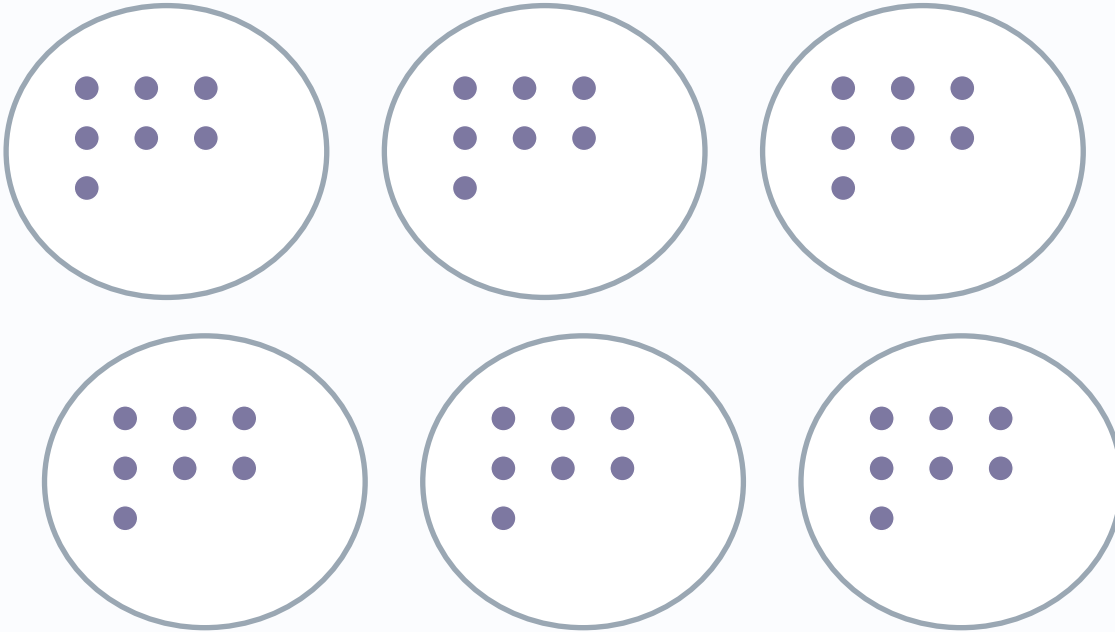
Septic microabscesses: A disseminated pattern



- Source example: Bacterial sepsis secondary to a colonized valve.
- The relevant morphology is multiple small purulent foci, not a single large mass.

Pneumonia: Filling airspaces need not destroy walls

Preserved airspace walls with intraluminal exudate



Outlined alveolar walls remain continuous

- Streptococcus pneumoniae usually spares the alveolar walls.
- Lobar pneumonia can therefore resolve with preserved architecture.
- Exudate distribution and wall integrity answer different questions.

Necrotizing pneumonia produces a different outcome

Streptococcus pneumoniae

Alveolar walls usually spared.

Pneumonia may resolve completely.

Architecture can remain intact.

S. Aureus / Klebsiella pneumoniae

Alveolar walls may be destroyed.

Abscesses may form.

Healing may leave scars.

Location modifies the consequence of infection

Bacterial pharyngitis

S. Pyogenes may cause acute pharyngeal inflammation.

The lesion can resolve without sequelae.

A mucosal site may retain integrity.

Acute bacterial joint infection

Untreated inflammation may rapidly destroy the joint.

Anatomic confinement magnifies functional cost.

Early recognition of tissue destruction is critical.

Neutrophils do not measure microbial severity alone

- An exuberant infiltrate requires intact leukocyte recruitment.
- A muted infiltrate may reflect neutropenia rather than a benign lesion.
- Necrosis, lesion distribution, and host immune status modify interpretation.
- The pathogenic organism is not defined by the mere presence of pus.

Purulent pattern: Interpret three dimensions

Dimension	Question	Why it matters
Cells	Are neutrophils conspicuous?	Defines suppurative morphology
Architecture	Are walls or tissue frameworks destroyed?	Predicts scar formation
Distribution	Small foci, abscesses, or diffuse organ involvement?	Informs spread and functional effect
Host	Is neutrophil recruitment impaired?	Avoids a false-negative inflammatory inference

Applied case: Destructive pulmonary infection

ILLUSTRATIVE SCENARIO

A lung sample contains dense neutrophilic exudate with abscess formation and loss of alveolar walls.

What distinguishes this lesion from a potentially fully resolving lobar exudate?

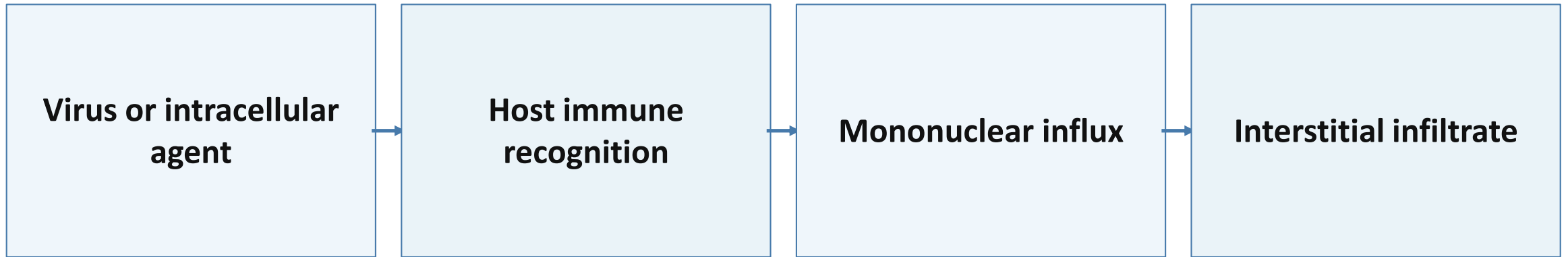
Destruction of alveolar walls; Healing may require fibrosis rather than restoration of intact architecture.

Rationale: Destructive *S. Aureus* / *Klebsiella pneumoniae* infection with usual wall preservation in pneumococcal lobar pneumonia.

Mononuclear infiltrates: Cells reveal host strategy

- Lymphocytes, plasma cells, monocytes, and macrophages may predominate.
- This is common in chronic inflammation.
- An acute mononuclear interstitial pattern often accompanies viral or intracellular infection.
- The dominant cell lineage reflects the host response to the agent.

Acute mononuclear inflammation may be interstitial



- Viruses, intracellular bacteria, and intracellular parasites.
- Spirochetes and helminths can also elicit chronic inflammatory responses.

Lymphocytes and plasma cells are not interchangeable

Predominantly lymphocytic

Cell-mediated immune response may dominate.

Examples: HBV infection and viral brain infection.

Often directed toward infected cells.

Plasma-cell-rich

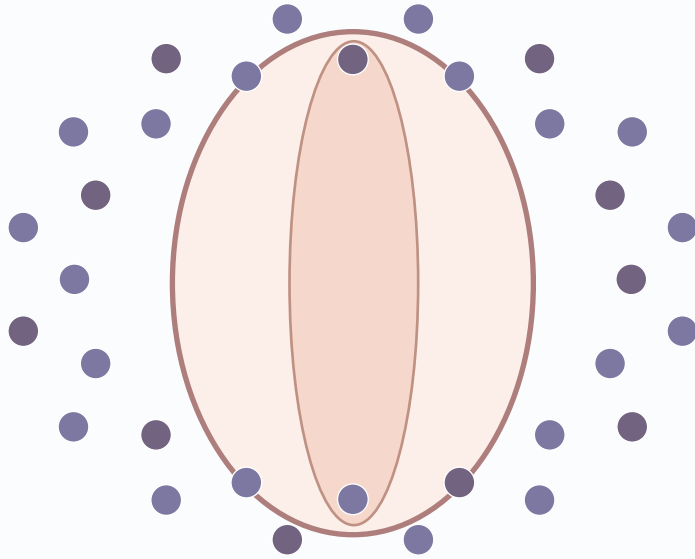
Prominent humoral-effector cell component.

Example: Primary and secondary syphilitic lesions.

Inflammatory pattern can be perivascular in skin.

Syphilis: Lymphoplasmacytic inflammation

Perivascular mononuclear aggregate



Vessel

Mononuclear cells

- Secondary syphilis in dermis.
- A perivascular lymphoplasmacytic infiltrate is described.
- Endothelial proliferation accompanies the illustrated lesion.

Viral hepatitis: Lymphocytes signify host injury

- HBV is a Robbins example of a lymphocyte-predominant lesion.
- Lymphocytes reflect cell-mediated responses to infected cells or pathogens.
- The inflammatory infiltrate is therefore part of the injury mechanism.
- Pattern recognition does not independently demonstrate viral identity.

Viral brain infection can be lymphocyte-rich

- Viral infections of the brain as lymphocyte-predominant examples.
- The cell type directs the differential toward immune-mediated responses to intracellular infection.
- Later development of destructive necrosis can coexist with inflammation.
- The location of injury determines major neurologic consequences.

Mycobacterium avium in AIDS: Macrophage dominance

Effective host containment

Organized inflammatory responses can limit expansion.

Pathogen-associated lymphocyte responses may be effective.

Infiltrate morphology follows immune competence.

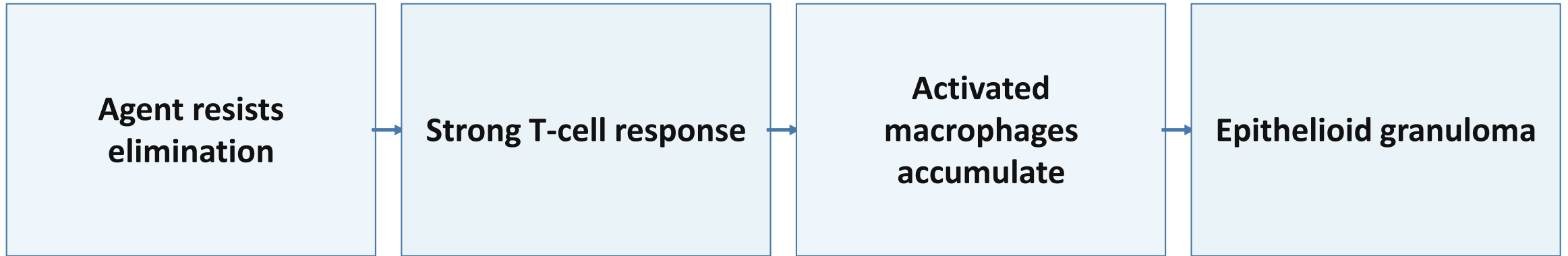
Profound immune deficit

Macrophages may become filled with M. Avium complex organisms.

The immune response fails to control microbial growth.

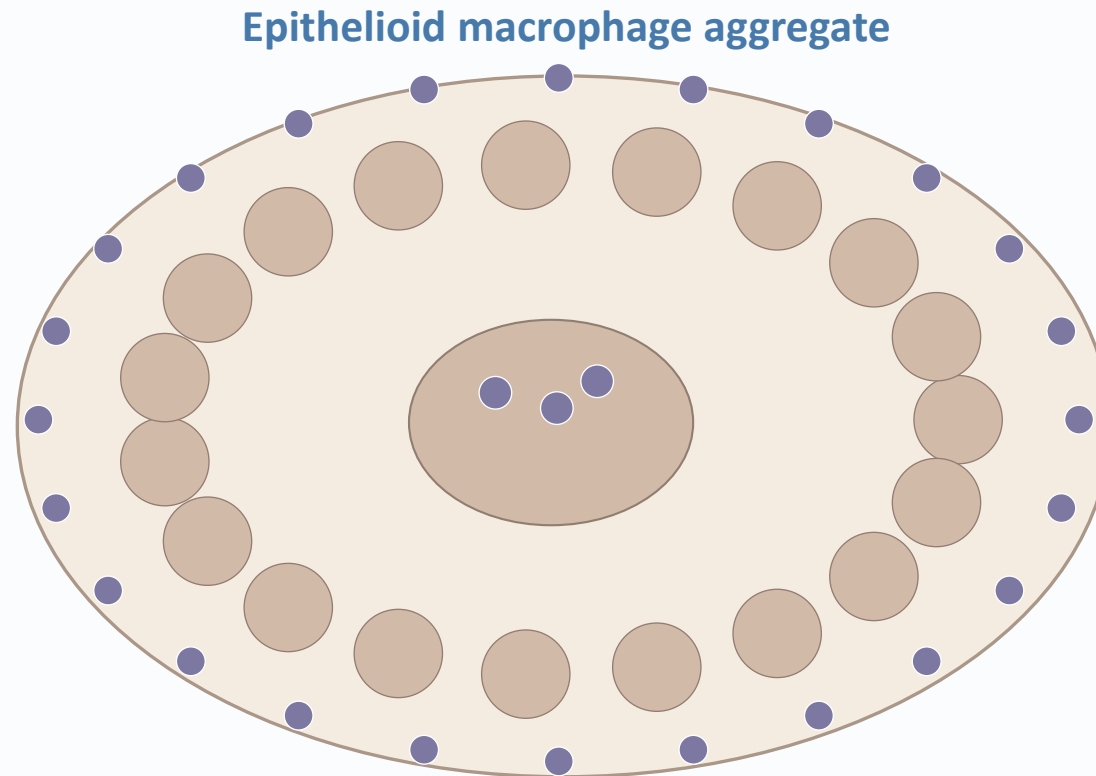
Macrophage abundance need not imply effective eradication.

Why a persistent infection may become granulomatous



- M. Tuberculosis, Histoplasma capsulatum and schistosome eggs.
- Granulomatous inflammation is a specialized mononuclear response.

Granuloma: Epithelioid macrophage aggregation



Epithelioid macrophages + outer mononuclear cells

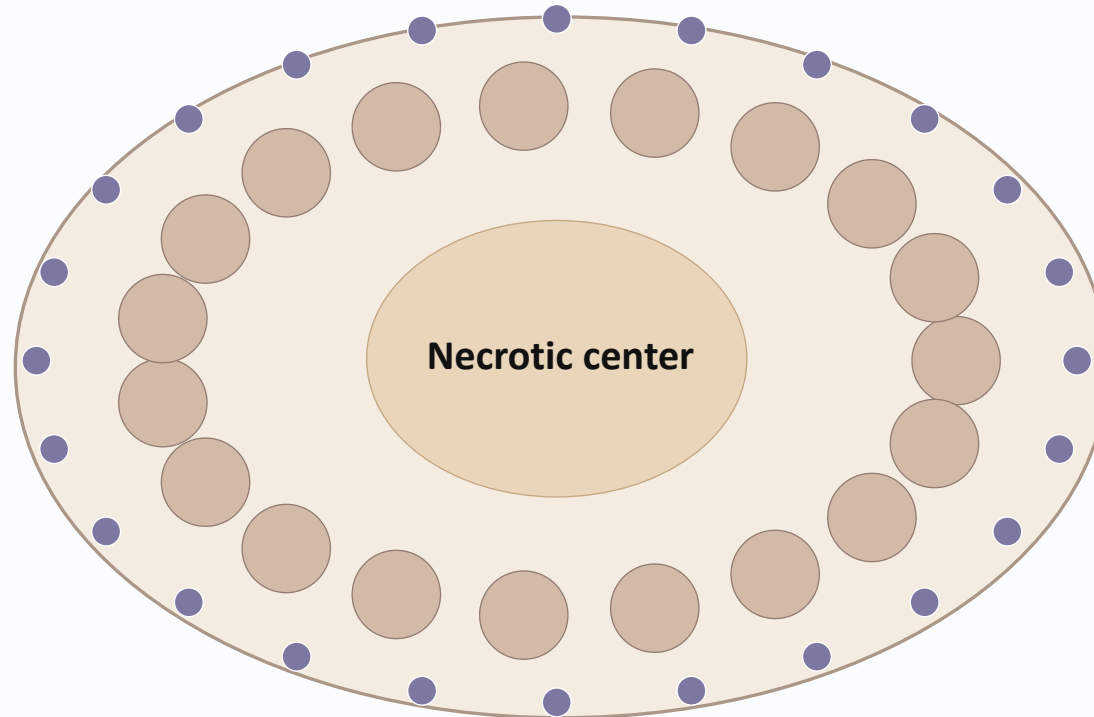
- Activated macrophages cluster into cohesive aggregates.
- “Epithelioid” describes epithelial-like cytomorphology, not epithelial origin.
- Some macrophages fuse into multinucleated giant cells.

Multinucleated giant cells are fused macrophages

- Granulomatous inflammation can include macrophage fusion.
- The resulting large multinucleated cells occur within macrophage aggregates.
- Giant cells support a granulomatous reaction but are not organism-specific.
- Interpret giant cells together with necrosis and overall lesion architecture.

Granulomas can contain central necrosis

Granuloma with optional central necrosis



Epithelioid macrophages + outer mononuclear cells

- Tuberculosis-associated granulomas may develop central necrosis.
- Necrosis and epithelioid macrophage aggregation are separate features.
- Not every granuloma in infection is necrotizing.

Granulomatous and diffuse mononuclear patterns

Diffuse interstitial infiltrate

Mononuclear cells distributed through interstitium.

Examples include viral and intracellular infections.

No requirement for macrophage clustering.

Organized granuloma

Cohesive aggregates of activated macrophages.

Often strong T-cell response to persistent antigens.

May have giant cells and necrosis.

An organized granuloma requires an able host

Immunocompetent tuberculosis

Granuloma organization generally preserved.

Relatively few mycobacteria visible.

Cell-mediated immunity shapes lesion.

Advanced AIDS with tuberculosis

Profuse bacillary multiplication can occur.

Macrophages may fail to form granulomas.

Loss of organization is a host clue.

Applied case: Identifying the dominant lineage

ILLUSTRATIVE SCENARIO

A dermal lesion shows a perivascular infiltrate rich in lymphocytes and plasma cells, with endothelial proliferation.

Which example has this constellation?

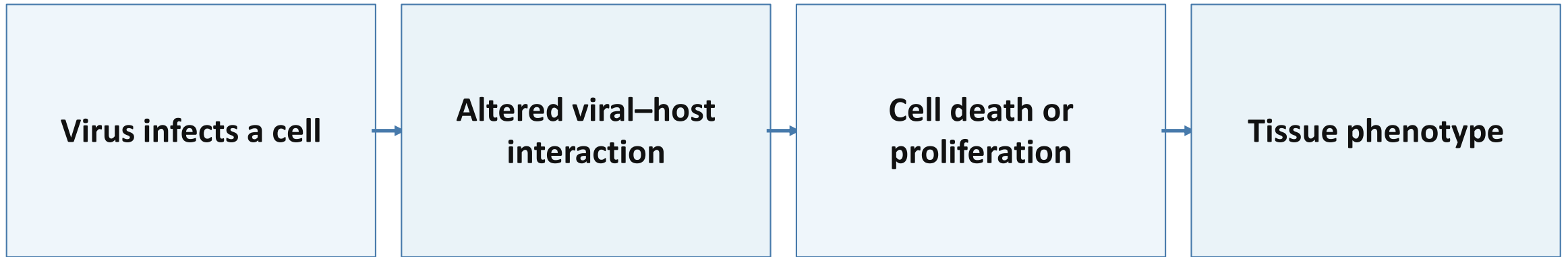
Secondary syphilis is the textbook illustration.

Rationale: The source figure caption describes a perivascular lymphoplasmacytic infiltrate and endothelial proliferation; The pattern is not exclusive to syphilis.

Cytopathic reactions emphasize infected-cell changes

- Often caused by viral infections.
- Cell injury, necrosis, or proliferation can predominate over exudation.
- Some lesions show relatively few inflammatory cells.
- Intracellular inclusions and multinucleation are morphologic clues.

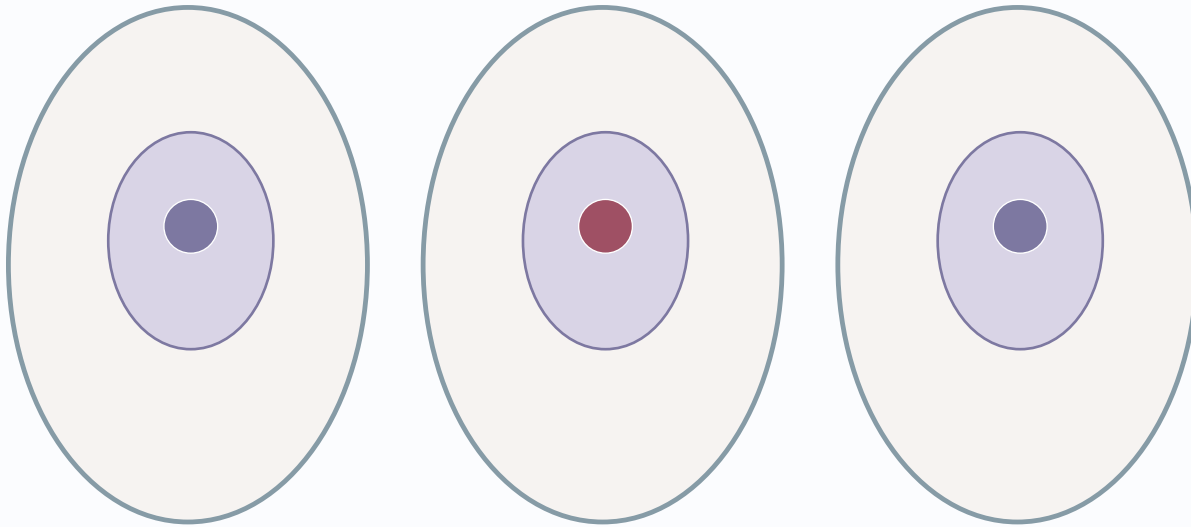
Viral infection can drive divergent cell outcomes



- The spectrum includes inclusions, syncytia, blisters, warts, and some neoplasms.
- Different viruses need not produce every outcome.

Viral inclusion bodies: Visible intracellular aggregates

Conceptual virus-associated inclusion

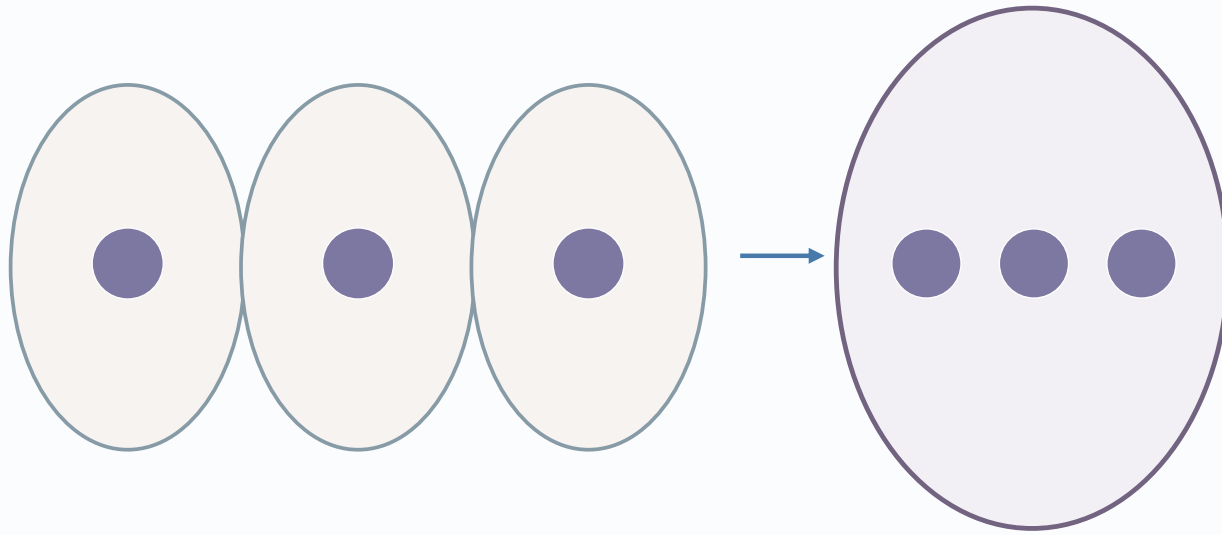


Conceptual inclusion

- Some replicating viruses form aggregates visible as inclusions.
- Robbins examples include herpesviruses and adenovirus.
- Inclusion morphology is a clue requiring corroboration, not a universal viral signature.

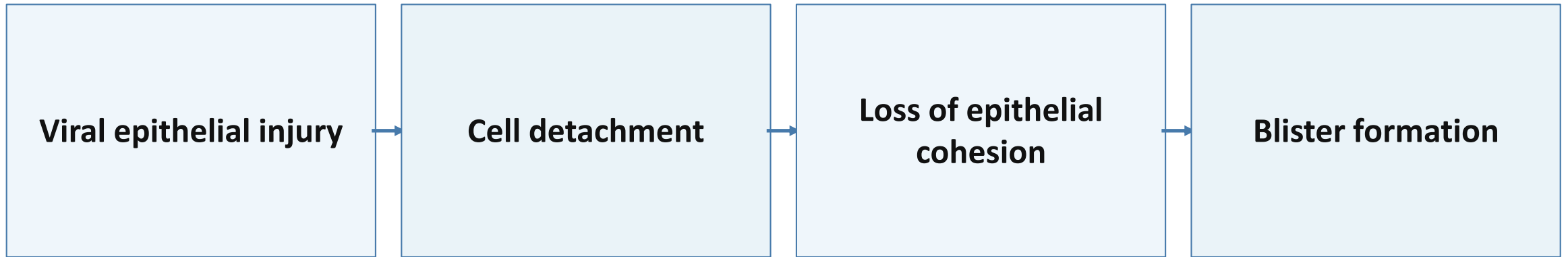
Polykaryons result from virus-induced cell fusion

Cell fusion into a multinucleated polykaryon



- Some viruses induce infected cells to fuse.
- The resulting multinucleated cells are termed polykaryons.
- Examples: Measles and herpesviruses.

Focal epithelial cell injury can produce blisters



- A herpesvirus-associated mucosal blister.
- This is an injury pattern, not a pathogen-identifying finding in isolation.

HPV-associated lesions show epithelial proliferation

- Cytoproliferation can dominate rather than tissue necrosis.
- Venereal warts are the example attributed to HPV.
- A proliferative phenotype does not imply malignant transformation in every lesion.
- Oncogenic strains of HPV can also contribute to malignant neoplasms.

Molluscum contagiosum: Another proliferative pattern

- Umbilicated papules caused by poxviruses.
- A proliferative epithelial response can be the salient tissue feature.
- The gross surface contour is a clinical clue, not a definition of all cytopathic lesions.
- Compare with blister formation from epithelial injury.

Viral oncogenesis is a distinct eventual outcome

Acute cytopathic injury

Cell necrosis or detachment may be conspicuous.

Blisters and viral inclusions may occur.

Host inflammatory cells can be sparse.

Cytoproliferative / neoplastic change

Increased epithelial proliferation may dominate.

HPV can cause warts.

EBV and oncogenic HPV can contribute to malignancy.

Not all viral lesions look lymphocyte-rich

Mononuclear host response

Inflammatory lymphocytes often prominent.

HBV and viral CNS disease are examples.

Host immunity can contribute to damage.

Dominant viral cellular phenotype

Inclusions, syncytia, or proliferation dominate.

Inflammatory infiltrate can be sparse.

Direct cellular changes may lead the diagnosis.

Applied case: A multinucleated epithelial cell

ILLUSTRATIVE SCENARIO

An epithelial sample contains fused multinucleated cells with limited surrounding inflammation.

Which broad Robbins response pattern should be considered?

A cytopathic–cytoproliferative reaction with polykaryon formation.

Rationale: Measles and herpesviruses are textbook examples, but the finding alone does not establish species.

Tissue necrosis may overwhelm the inflammatory picture

- In some infections, tissue destruction is the dominant histologic change.
- Powerful exotoxins can cause rapid, extensive injury.
- Direct pathogen-mediated destruction can precede or exceed leukocyte recruitment.
- Inflammatory cellularity and tissue damage are therefore not proportional.

Two routes to necrosis-dominant infection

Toxin-mediated destruction

Rapid injury by potent microbial exotoxins.

Examples: C. Perfringens; C. Diphtheriae.

Necrosis may be disproportionate to infiltrate.

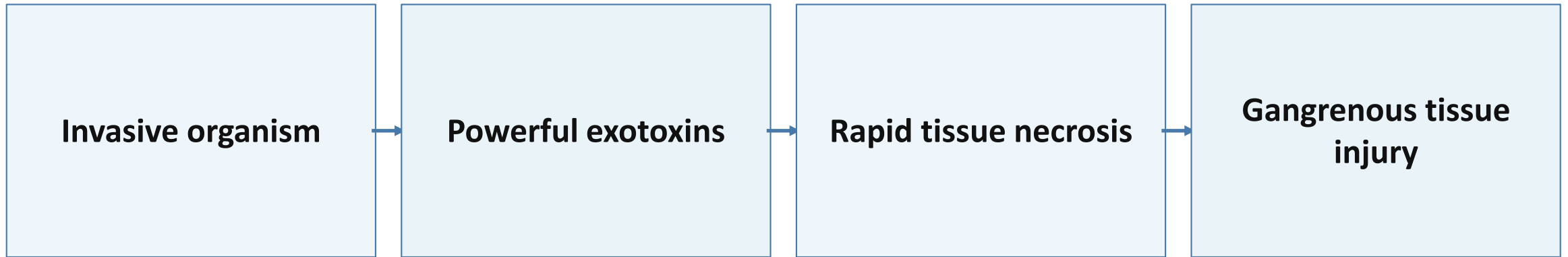
Host-cell destruction

Widespread destruction of infected host cells.

Examples: HSV-associated temporal injury; HBV-associated hepatic injury.

Inflammation may coexist.

Clostridium perfringens: Toxin-dominant damage



- C. Perfringens in the necrosis response category.
- The slide does not assert a histologic stain or specific gas morphology absent from the source.

Corynebacterium diphtheriae: Severe local injury

- C. Diphtheriae secretes a potent exotoxin.
- Rapid and severe necrosis can dominate the lesion.
- The abundance of inflammatory cells may be less informative than destruction.
- Necrosis is a reaction category shared with other mechanistic routes.

Entamoeba histolytica causes destructive lesions

Colon

Destructive ulceration can occur.

Tissue injury is prominent.

Relatively scant inflammatory cells may be present.

Liver

Abscesses with extensive tissue destruction.

Liquefactive necrosis is emphasized.

Inflammatory infiltrate may remain limited.

Herpes simplex virus can destroy temporal tissue

- Severe destruction of the temporal lobes as an HSV example.
- Viral injury and associated inflammation can coexist.
- Localization in the brain amplifies functional consequences.
- A necrosis-dominant pattern may overlap with cytopathic changes.

Hepatitis B: Inflammation and hepatocellular loss

Lymphocyte-rich response

Lymphocytes reflect cell-mediated antiviral immunity.

Inflammatory infiltrates may be prominent.

Represents a mononuclear reaction.

Severe necrotic response

Widespread loss of host cells may occur.

Severe hepatic necrosis can dominate.

The same infection can occupy multiple pattern categories.

Necrosis is not synonymous with suppuration

Purulent necrosis

Neutrophils and liquefactive tissue destruction form pus.

Abscesses typify localized suppuration.

Leukocyte-rich morphology is a defining clue.

Necrosis-dominant lesion

Direct toxins or cell lysis may dominate.

Inflammatory cells can be few.

Severe damage does not require a neutrophil-rich exudate.

Applied case: Necrosis with sparse inflammation

ILLUSTRATIVE SCENARIO

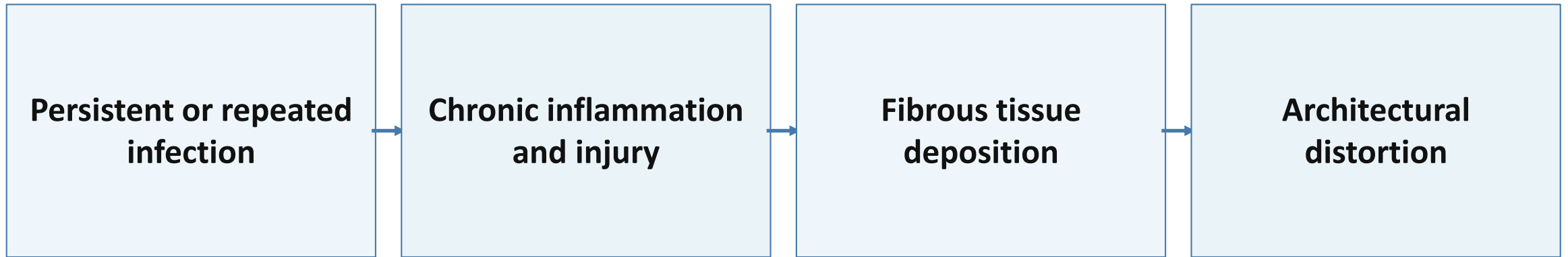
A biopsy from a severely destructive infection shows broad necrosis but only a small inflammatory infiltrate.

Does the sparse infiltrate exclude a serious infection?

No. Toxin-driven necrosis, direct cell destruction, or immune impairment can all diminish the apparent inflammatory response.

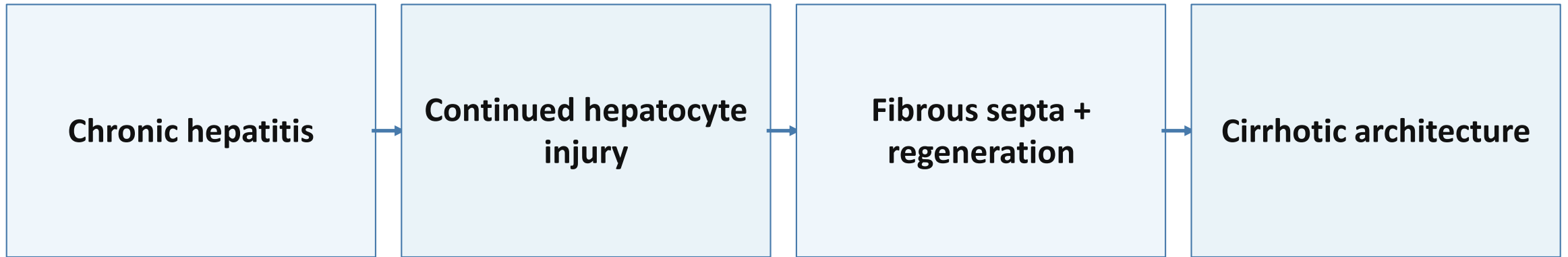
Rationale: Rapidly necrotizing infections and absent reactions in immunocompromised hosts as distinct situations.

Chronic injury can reorganize an organ by fibrosis



- Scarring may follow tissue destruction or become the principal cause of dysfunction.
- Scar location matters as much as the amount of inflammation.

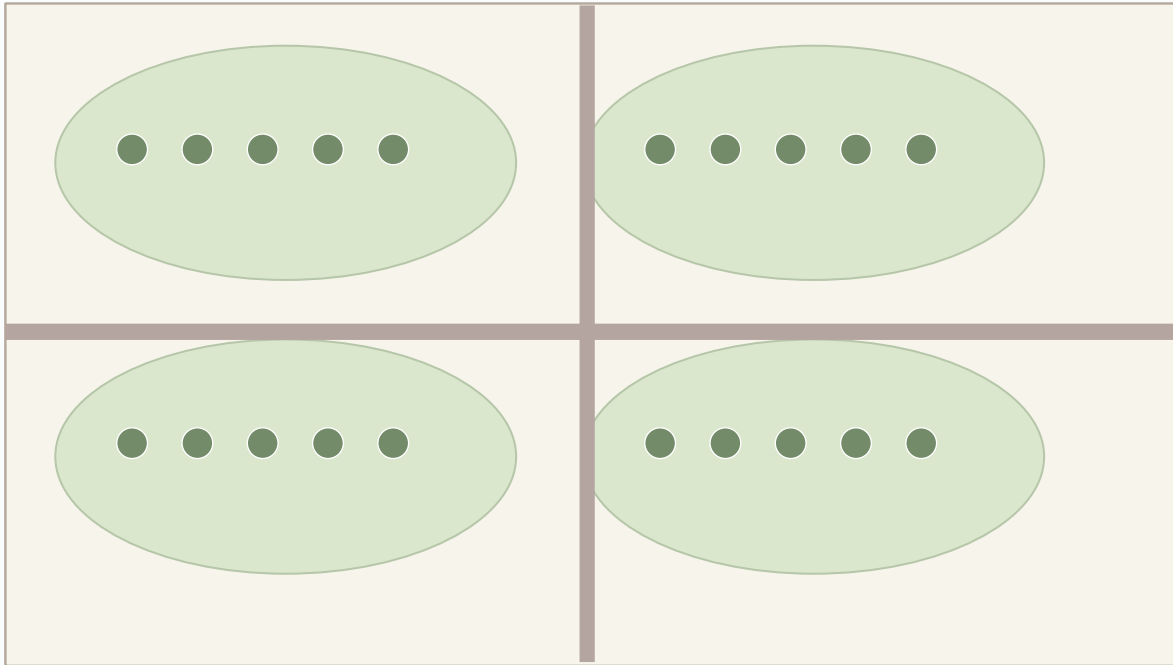
Chronic HBV can culminate in cirrhotic remodeling



- Fibrous septa surrounding nodules of regenerating hepatocytes.
- The altered architecture changes intrahepatic blood flow.

Cirrhosis: Septa and nodules explain dysfunction

Fibrous septa partition parenchymal nodules



Parenchymal nodules separated by fibrous bands

- Dense fibrous bands partition regenerating hepatocyte nodules.
- Normal liver architecture is lost.
- Blood-flow patterns change because the vascular–parenchymal arrangement is distorted.

Schistosome eggs can drive major fibrotic injury

Liver

“Pipestem” fibrosis is a Robbins example.

Egg-associated injury may lead to marked fibrosis.

Scar can dominate organ dysfunction.

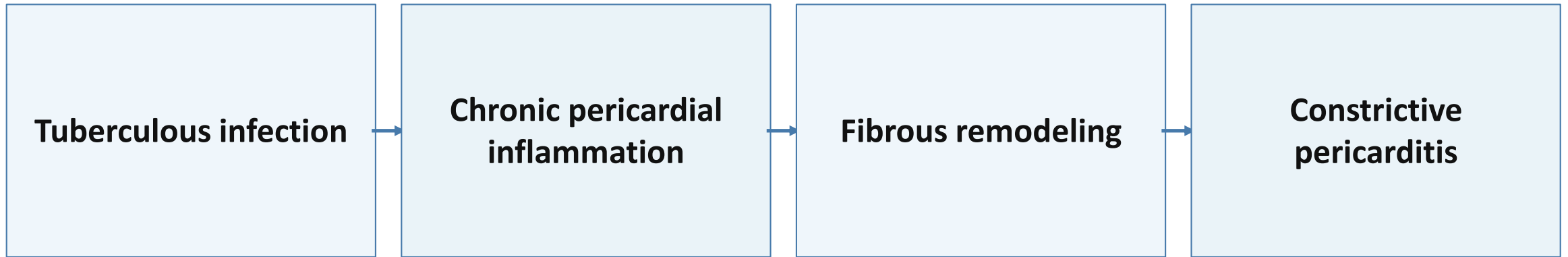
Urinary bladder

Schistosoma haematobium eggs can be present.

Extensive bladder-wall scarring may develop.

Numerous calcified eggs.

Tuberculous pericarditis can become constrictive



- This as scar-driven functional impairment.
- This is a downstream consequence, not the characteristic microscopic appearance of every TB infection.

The burden of scarring may exceed active inflammation

- Current inflammatory cellularity may be modest after prolonged disease.
- Persistent structural fibrosis can continue to impair organ function.
- Examples include cirrhosis, schistosomal scarring, and constrictive pericarditis.
- Distinguish active inflammatory injury from established architectural damage.

The “no reaction” category is a diagnostic warning

Source condition	Illustrative infection	Expected pitfall
T-cell deficiency / untreated AIDS	Mycobacterium avium complex	Abundant organisms with poor organized response
Profound neutropenia after transplantation	Mucormycosis	Little neutrophil response despite invasive infection
Profound neutropenia more generally	Pyogenic bacterial disease	Necrosis despite scant purulent exudate

Untreated AIDS: Organism expansion without containment

- Severe T-cell deficiency compromises pathogen control.
- M. Avium complex may proliferate in organism-laden macrophages.
- The expected granulomatous structure can be deficient.
- The amount of visible inflammation must be interpreted against immune competence.

Neutropenia: Absence of pus can be misleading

- The marrow-transplant mucormycosis example appears under “no reaction” in Table 8.3.
- A leukocyte-poor biopsy does not establish that tissue is uninfected.
- Pyogenic bacteria can also cause rapid necrosis without typical exudation in marked neutropenia.
- Consider organism burden and tissue destruction independently of cell count.

Scant inflammation has more than one explanation

Strong direct pathogen injury

Microbial toxins or cell lysis drive tissue damage.

Inflammation can be secondary or sparse.

Examine morphology of injury and distribution.

Inadequate host response

Deficient T cells or neutrophils alter typical reaction.

Organisms may multiply with little cellular containment.

Examine immune status and tissue organisms.

Mixed infection can generate overlapping signatures

CMV in lung

CMV causes changes in alveolar lining cells.

A cytopathic pattern can appear.

A single lung may show more than one process.

Pneumocystis spp. In lung

Pneumocystis may cause interstitial inflammation.

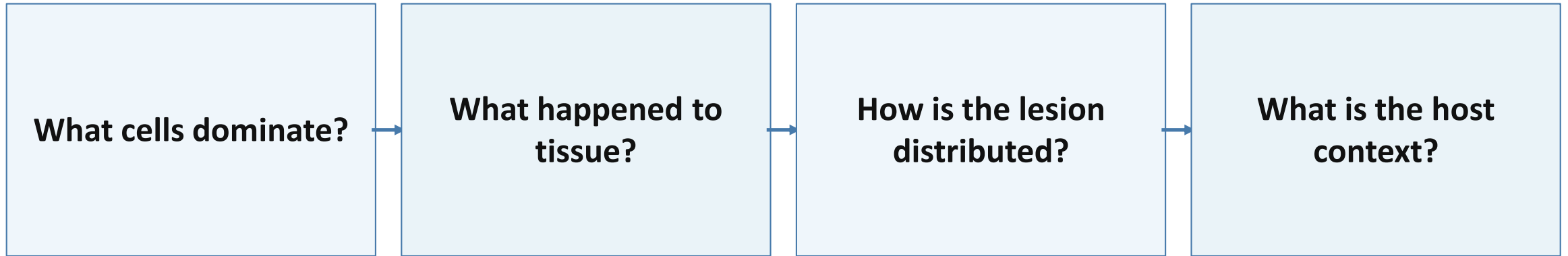
An inflammatory infiltrate can coexist with cytopathic changes.

Source example: Coinfection in an AIDS patient.

The same patterns occur without infection

- Robbins cautions that chemical and physical injury can produce similar inflammatory morphologies.
- Inflammatory disorders of unknown cause can mimic infectious patterns.
- Pattern recognition is a hypothesis-generating step, not etiologic proof.
- Negative organism evidence does not automatically define a noninfectious cause.

Integrated tissue interpretation: Four linked questions



- A destructive, lymphocyte-poor lesion in neutropenia demands different interpretation from classic suppuration.
- Architectural fibrosis adds information about persistence and accumulated injury.

Challenge: Choose the most informative feature

ILLUSTRATIVE SCENARIO

A biopsy shows fibrous septa surrounding regenerating parenchymal nodules in a patient with chronic viral hepatitis.

Is lymphocyte counting or tissue remodeling most informative for the dominant reaction pattern?

Architectural remodeling by septa and nodules identifies the chronic inflammation/scarring phenotype.

Rationale: The example echoes Robbins' description of HBV-associated cirrhosis; Activity and etiology still require additional assessment.

Pattern recognition is a differential—not a verdict

Dominant observation	Pattern category	Key interpretive qualifier
Pus and neutrophils	Suppurative	Host neutrophils must be present
Interstitial mononuclear cells	Mononuclear	Cell composition varies by pathogen/host
Epithelioid aggregates	Granulomatous	Requires appropriate T-cell-mediated organization
Inclusions or fused cells	Cytopathic	Classically viral, often relatively paucicellular
Necrosis out of proportion	Tissue necrosis	Toxins, cytolysis, or impaired response
Fibrous remodeling	Chronic/scarring	Residual injury can dominate dysfunction

Core synthesis: Read pattern, architecture, and immunity

- The major infection responses are a limited repertoire despite microbial diversity.
- Dominant cells, cell injury, necrosis, and fibrosis provide complementary clues.
- Impaired immunity can transform or virtually erase the expected reaction.
- Mixed and noninfectious lesions prevent morphologic overdiagnosis.

Primary reference and source limits

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. 2026. Chapter 8, “Spectrum of Inflammatory Responses to Infection,” pp. 311–313; Table 8.3.
- Supplied teaching extract: RCK-0224 and adjacent headings in robbins.md.
- All tissue, cellular, and mechanism illustrations are original editable schematics—not patient material, photomicrographs, or textbook figure reproductions.