

Summary of Acute Inflammation

An integrated clinicopathologic review

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Learning objectives

Vessels



Leukocytes



Mediators



Resolution

- Connect vascular and cellular events to clinical signs.
- Explain recruitment, killing, and mediator effects.
- Distinguish morphologic patterns and major outcomes.

Schematic

Inflammation follows five coordinated responses

Recognize



Recruit



Remove



Regulate

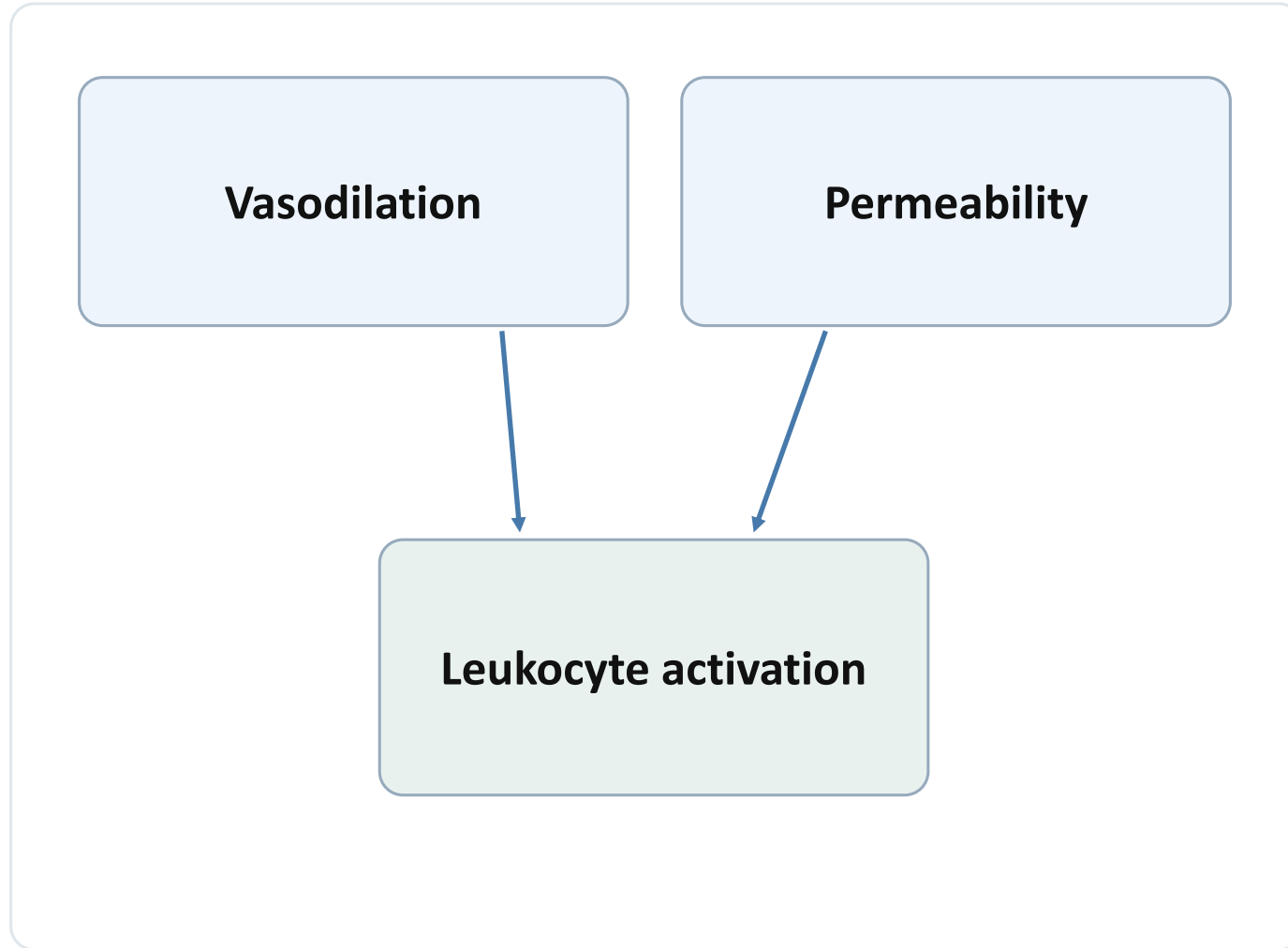


Repair

- Recognition initiates the response to injurious stimuli.
- Recruitment and removal provide antimicrobial and cleanup functions.
- Regulation and repair limit collateral damage.

Schematic

Acute inflammation has three major components



Schematic

- Small-vessel dilation increases regional blood flow.
- Increased permeability transfers protein-rich fluid into tissue.
- Leukocytes exit vessels and become activated at the focus.

The response begins with microbes or injured cells

Microbes / injured cells



Sentinel recognition

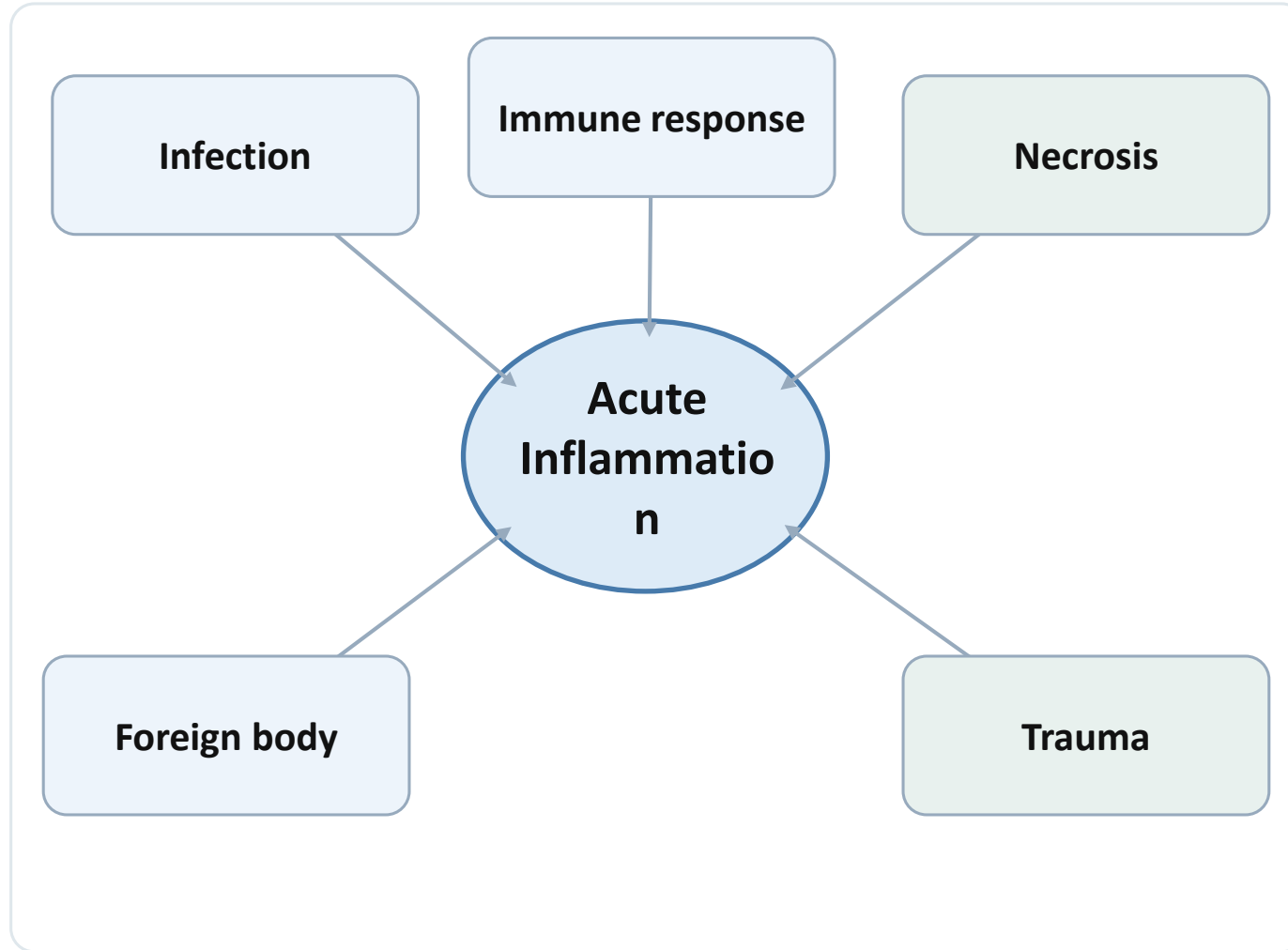


Mediator release

- Infections and necrotic tissues are important initiating stimuli.
- Resident phagocytes attempt immediate elimination.
- Sentinel cells release mediators when they sense abnormalities.

Schematic

Inflammatory stimuli are heterogeneous



Schematic

- Inflammation can follow infection or tissue necrosis.
- Foreign bodies and trauma also provoke inflammation.
- Immune responses can induce inflammation and tissue injury.

Sentinel cells connect recognition to effector responses

Tissue sentinel cells



Cytokines / lipids



Vessels + leukocytes

- Resident phagocytes and other tissue cells detect danger.
- These cells produce cytokines and lipid mediators.
- Local mediators act on vessels and recruit leukocytes.

Schematic

Microbial and damage signals activate leukocytes

Agent / damage



Activation



Phagocytosis

- Microbial products and products of injured cells stimulate recruited cells.
- Local mediators reinforce leukocyte activation.
- Activated phagocytes ingest and destroy the offending material.

Schematic

Vascular and cellular reactions operate together

Vascular arm

Flow, permeability,
endothelial activation

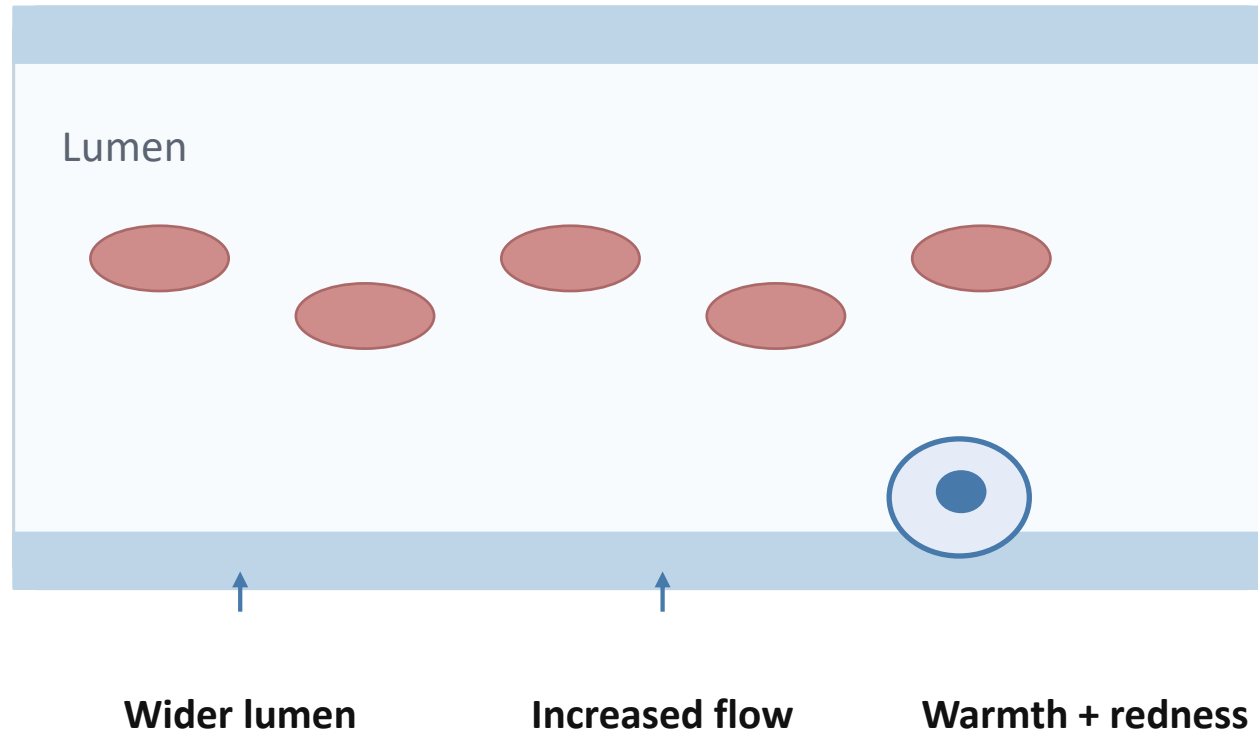
Cellular arm

Adhesion, migration,
phagocytosis

- Vascular responses deliver plasma proteins to affected tissue.
- Endothelial activation facilitates circulating cell recruitment.
- Migrating leukocytes perform the principal removal functions.

Schematic

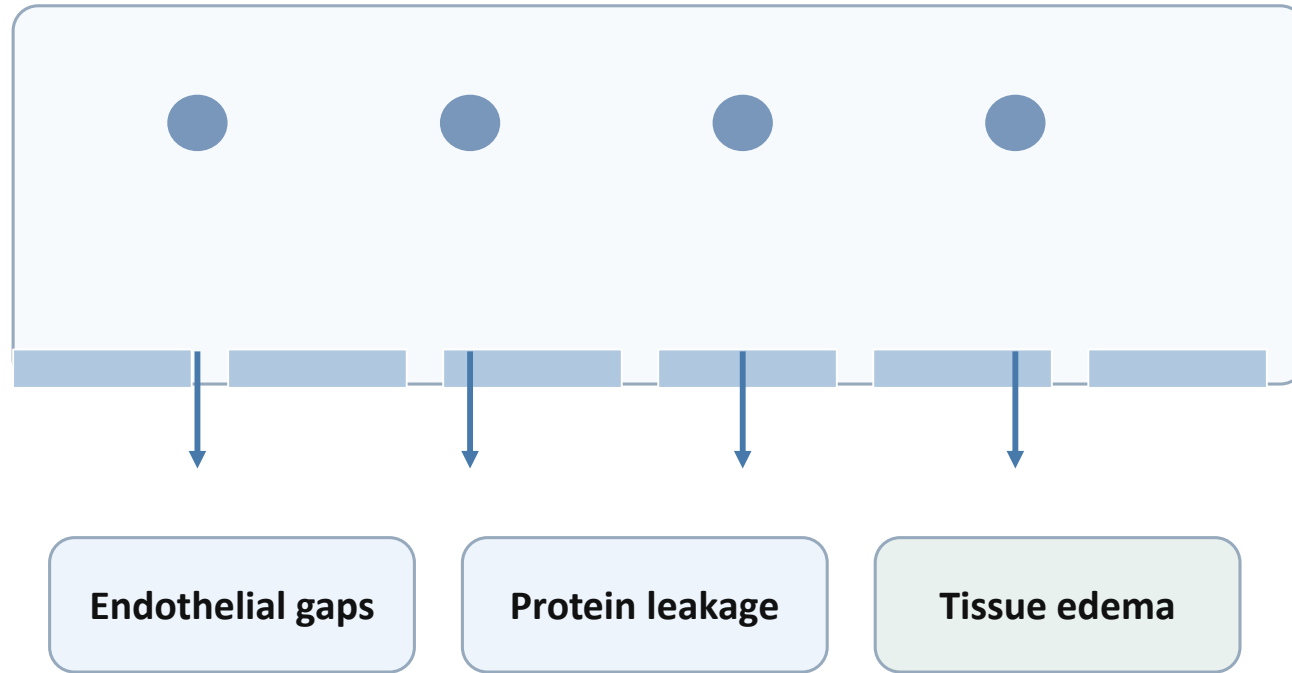
Vasodilation increases local blood flow



Schematic

- Histamine acts early on vascular smooth muscle.
- Vasodilation increases inflow into the inflamed area.
- The resulting hyperemia contributes to warmth and redness.

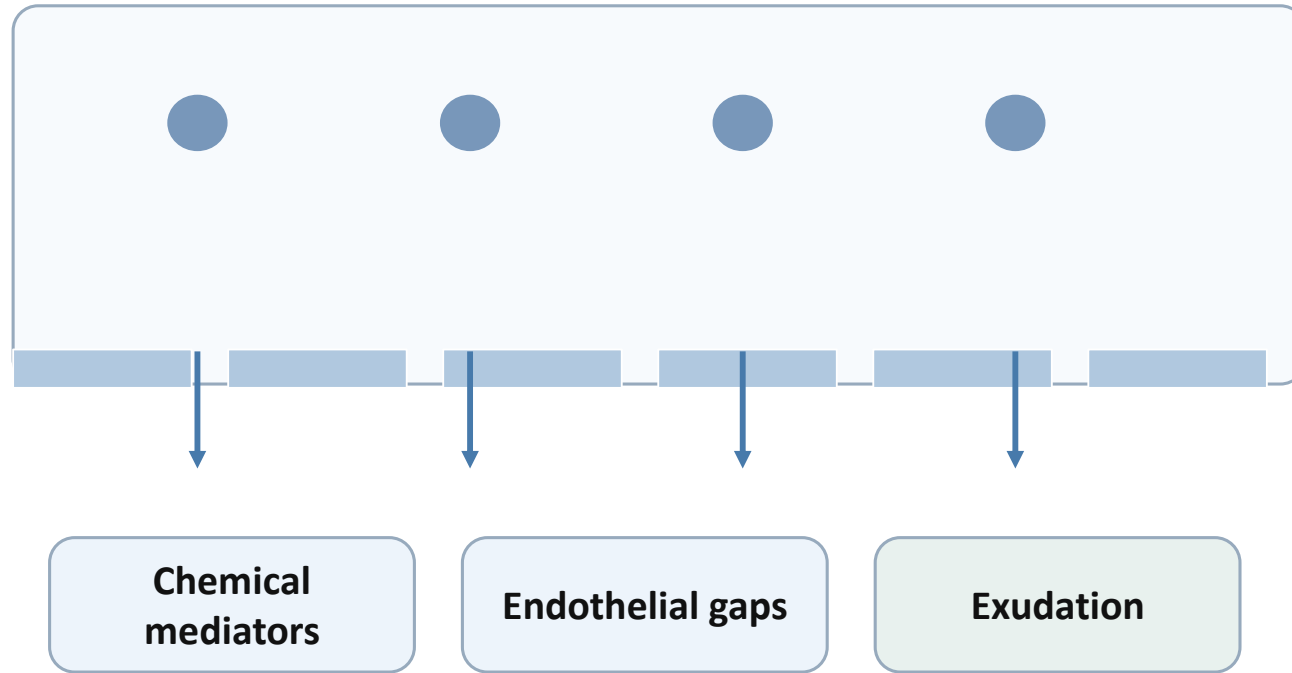
Vascular leakage delivers plasma proteins



Schematic

- Inflammatory mediators increase endothelial permeability.
- Protein-rich exudate escapes into the interstitial space.
- The same process contributes to tissue swelling.

Endothelial gaps are a common cause of leakage



Schematic

- Endothelial contraction opens intercellular gaps.
- Histamine, bradykinin, and leukotrienes can induce contraction.
- This response usually occurs rapidly and is transient.

Direct endothelial injury can sustain leakage

Severe injury



Endothelial damage



Sustained leakage

- Severe injuries can produce endothelial necrosis and detachment.
- Microbes and toxins may damage endothelium directly.
- Adherent neutrophils can further amplify endothelial damage.

Schematic

Inflammatory exudate differs from transudate

Feature	Exudate	Transudate
Mechanism	Permeability increase	Hydrostatic / oncotic imbalance
Protein	Relatively high	Relatively low
Cells / debris	May be present	Little or none

- Exudate implies increased vascular permeability.
- Transudate reflects hydrostatic or oncotic imbalance without inflammation-driven permeability.
- The mechanisms—not merely the presence of edema—distinguish them.

Edema describes excess fluid, not its cause

Inflammatory edema

Vascular leakage →
protein-rich exudate

Noninflammatory edema

Pressure imbalance →
transudate

- Edema may occur in interstitial tissue or serous cavities.
- Inflammatory edema often contains protein-rich exudate.
- Noninflammatory processes can also produce edema.

Fluid loss slows blood flow and promotes stasis

Plasma leakage



Hemoconcentration



Stasis

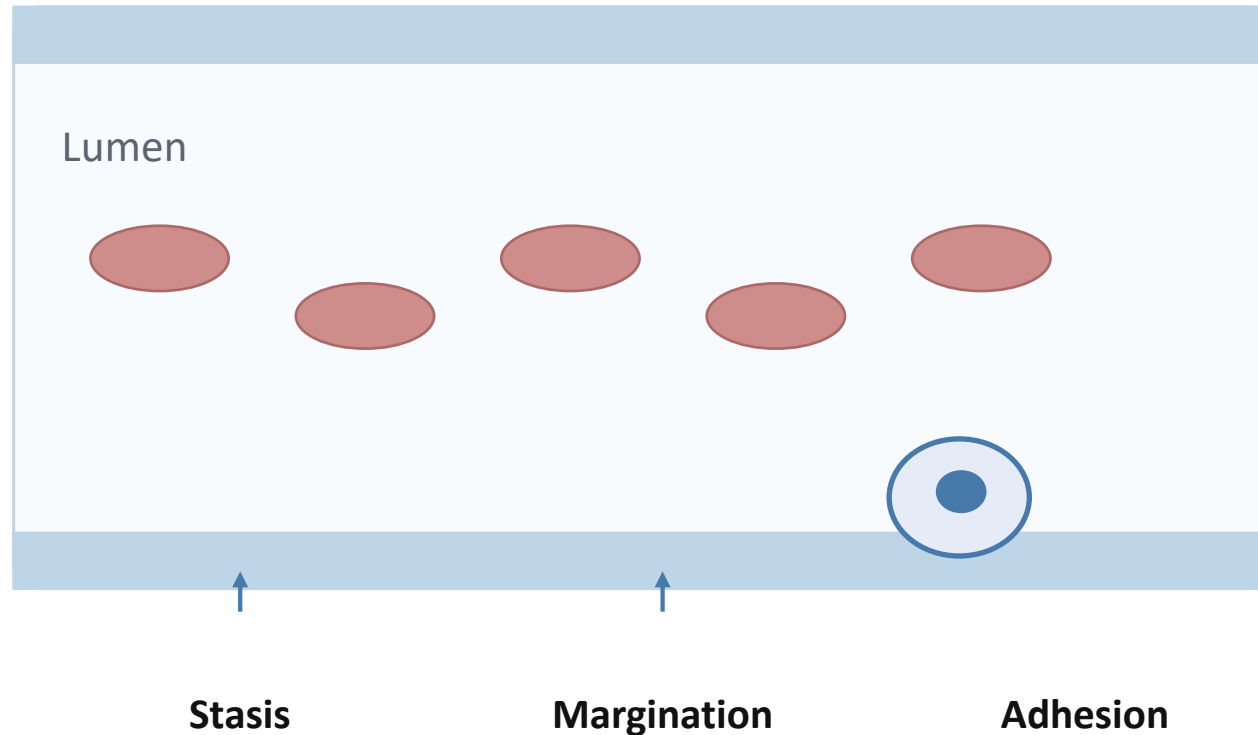


Margination

- Leakage decreases the fluid component within vessels.
- Microvascular blood becomes concentrated and flows more slowly.
- Stasis increases contact between circulating leukocytes and endothelium.

Schematic

Stasis prepares the endothelium–leukocyte interface



Schematic

- In flowing blood, leukocytes tend to be displaced toward vessel walls.
- Activated endothelium expresses adhesive molecules.
- These changes enable rolling and subsequent firm adhesion.

Leukocyte recruitment is a multistep journey

Margination



Rolling



Firm adhesion



Transmigration

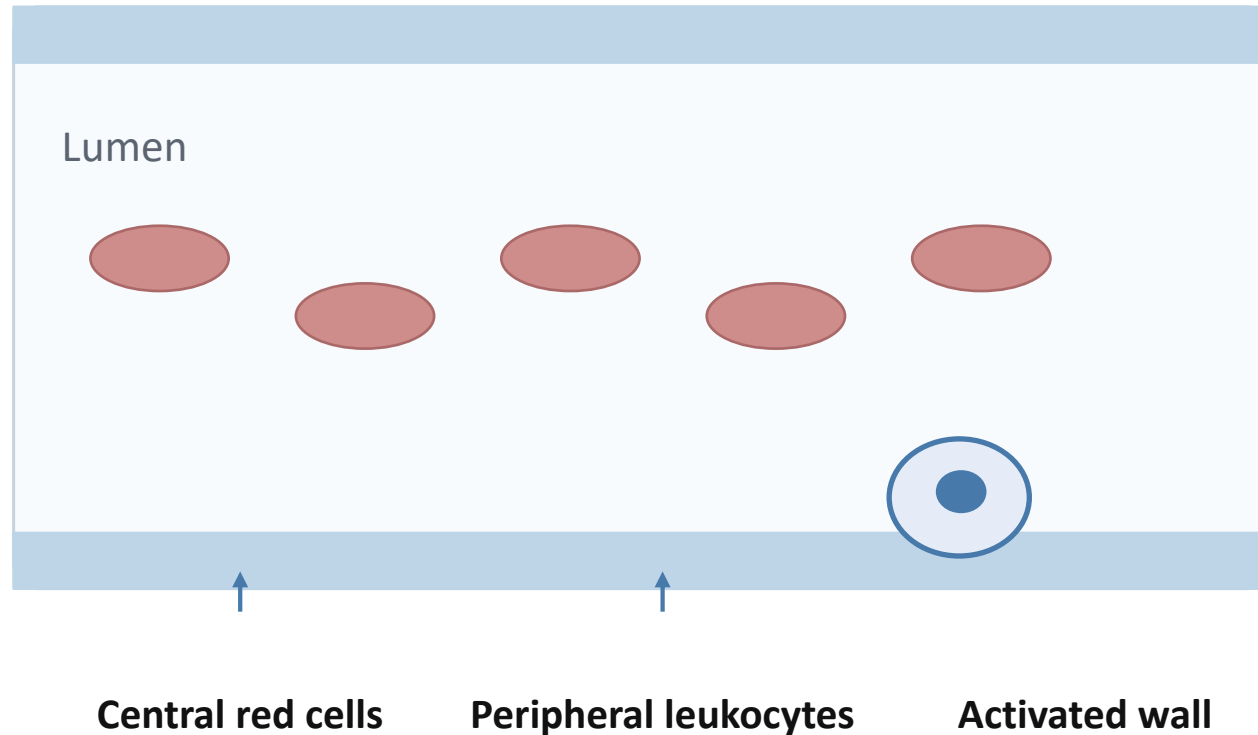


Chemotaxis

- Cells first margined, roll, and adhere to the endothelium.
- They then cross the vessel wall.
- They follow chemotactic signals to the injured tissue.

Schematic

Margination brings leukocytes close to the vessel wall



Schematic

- Slower microvascular flow favors peripheral displacement of leukocytes.
- Endothelial surfaces become receptive to binding.
- Margination precedes selectin-mediated rolling.

Rolling depends predominantly on selectins

Selectin binding



Transient adhesion



Rolling

- Selectins mediate relatively weak, reversible cell attachment.
- Repeated adhesion and release produce rolling movement.
- Rolling creates time for leukocyte activation at inflamed endothelium.

Schematic

Chemokines activate leukocyte integrins

Chemokine signal



Integrin activation



Firm adhesion

- Endothelium displays chemokines to rolling leukocytes.
- Chemokine signaling increases integrin binding capacity.
- Activated integrins prepare the cell for stable adhesion.

Schematic

Firm adhesion depends predominantly on integrins

Rolling

Selectins • transient
contacts

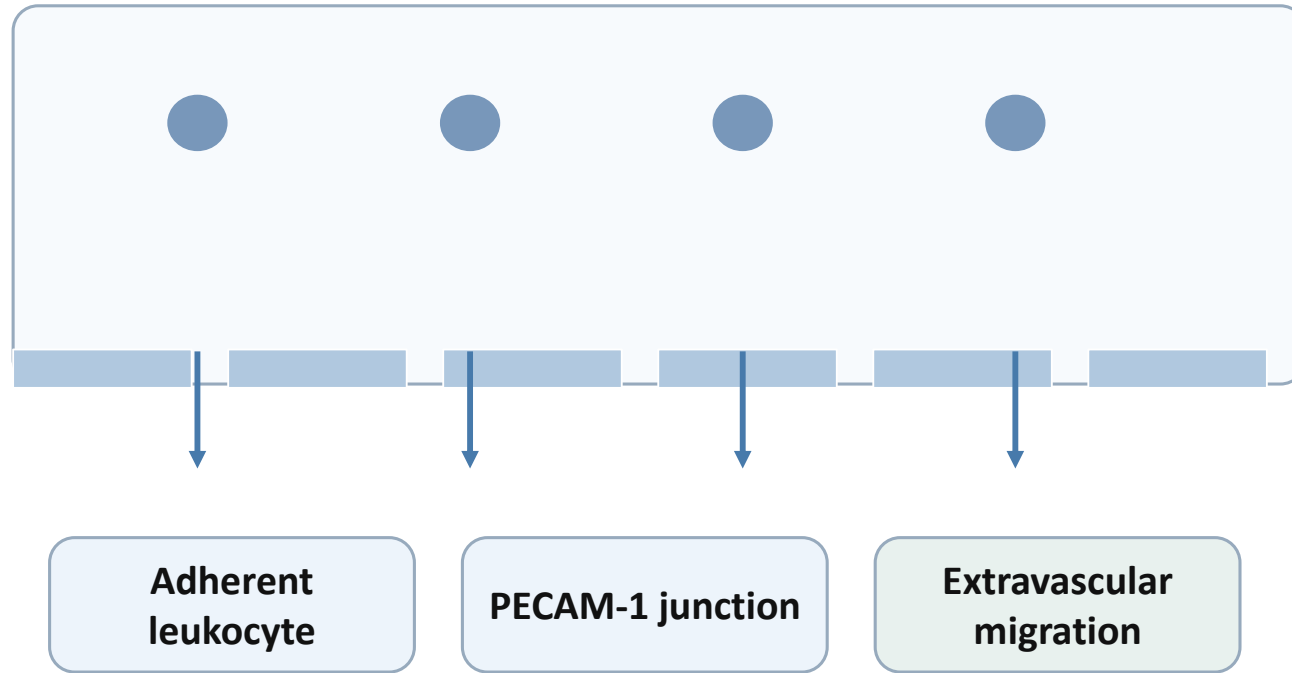
Adhesion

Integrins • stable
binding

- High-affinity leukocyte integrins bind endothelial ligands.
- ICAM-1 is an important endothelial integrin ligand.
- TNF and IL-1 promote endothelial activation and recruitment.

Schematic

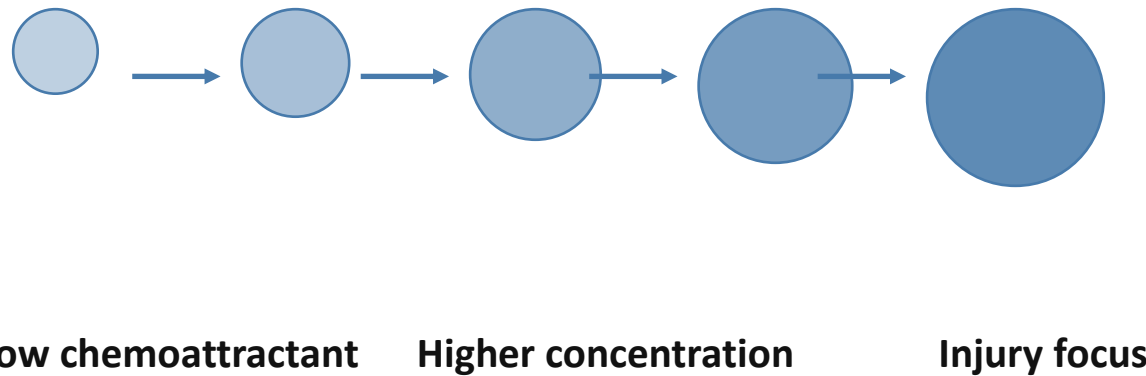
Diapedesis moves leukocytes across endothelium



Schematic

- Transmigration occurs mainly in postcapillary venules.
- Junctional molecules include PECAM-1 (CD31).
- Cells cross the basement membrane and enter tissue.

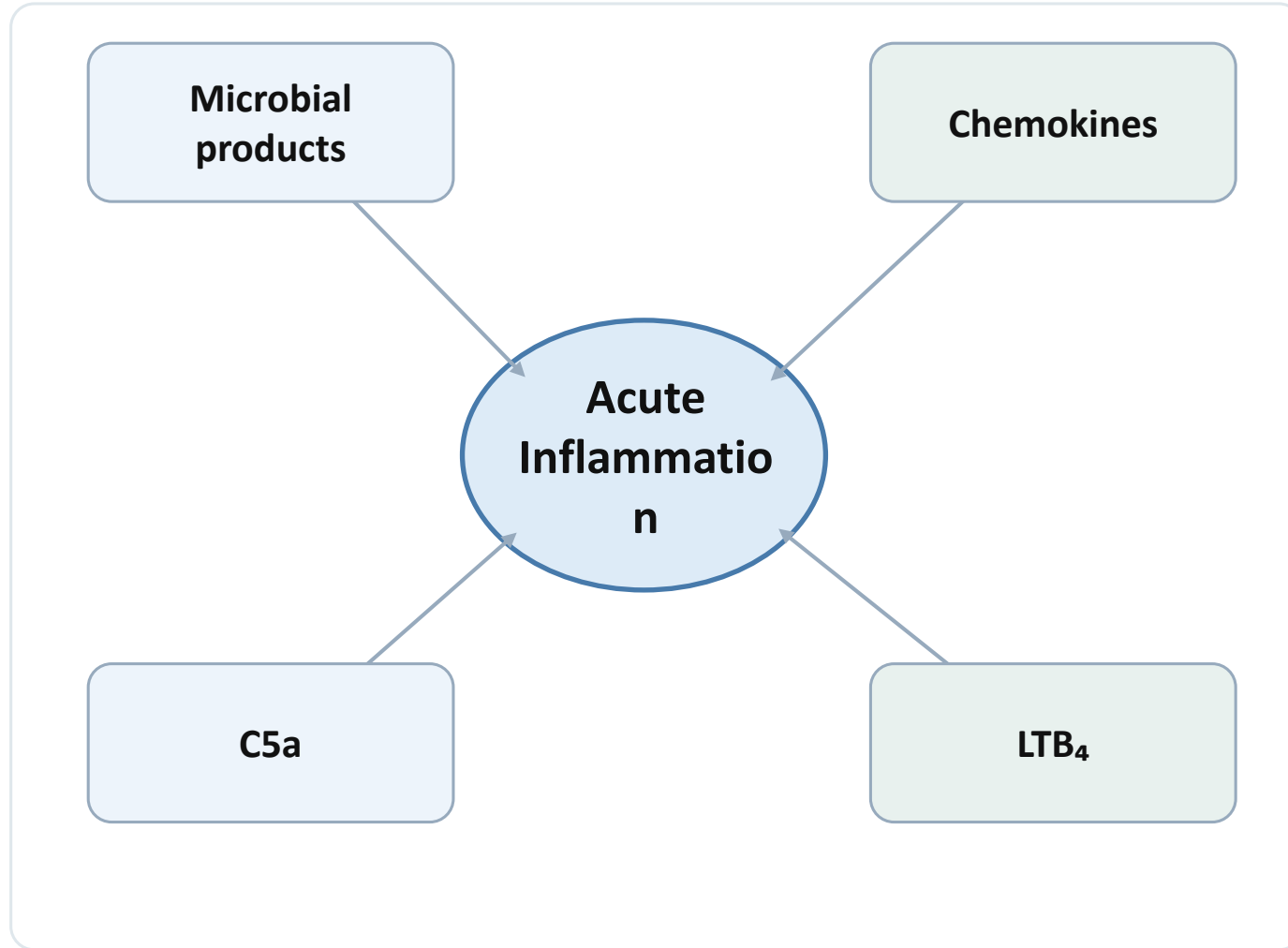
Chemotaxis directs cells toward the stimulus



- Leukocytes migrate along chemical concentration gradients.
- Leading-edge actin polymerization supports cell movement.
- Direction is toward infection, tissue damage, and chemoattractants.

Schematic

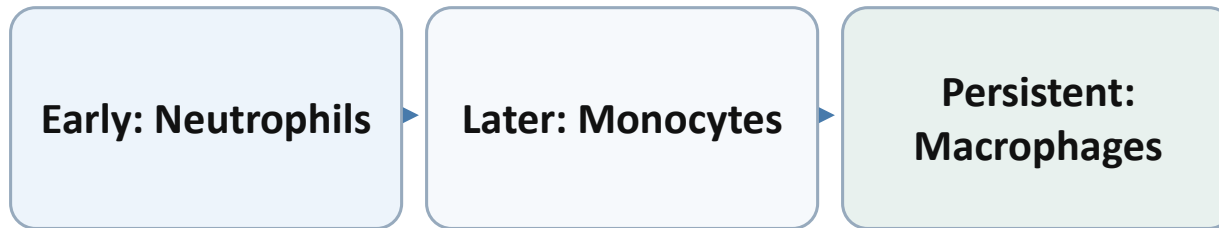
Several signals attract leukocytes



Schematic

- Bacterial products provide exogenous chemoattractants.
- Chemokines such as CXCL8/IL-8 act locally.
- Complement C5a and leukotriene B₄ are endogenous attractants.

Neutrophils typically precede macrophages



Schematic

- Neutrophils commonly predominate during the first 6–24 hours.
- Monocytes become more prominent in the next 24–48 hours.
- The infiltrate varies with the agent and duration of inflammation.

Macrophages also support tissue repair

Clear debris



Produce growth factors



Promote repair

- Neutrophils and macrophages ingest microbes and dead tissue.
- Macrophages persist longer in many inflammatory settings.
- Macrophage-derived growth factors contribute to repair.

Schematic

Phagocytosis proceeds through three linked steps

Recognition



Engulfment

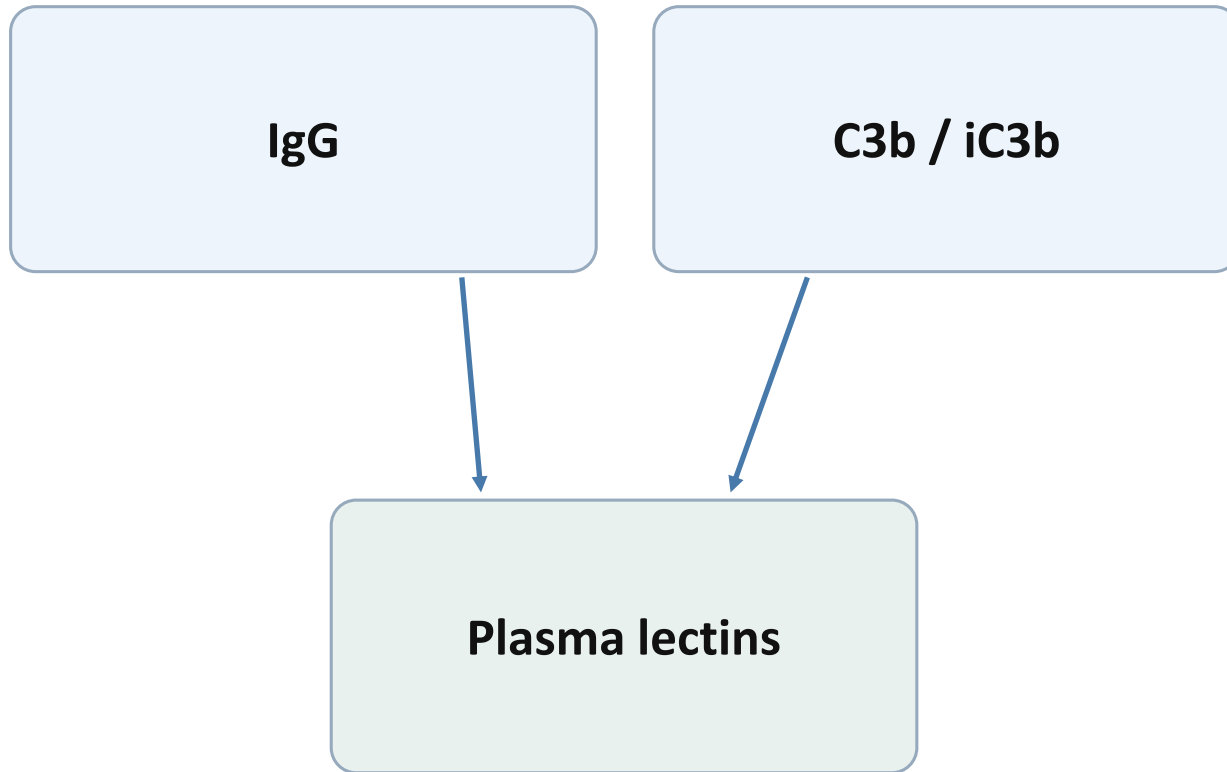


Killing + digestion

- A phagocyte recognizes and attaches to a target.
- Engulfment creates a membrane-bound phagosome.
- Microbial killing and digestion follow.

Schematic

Opsonization improves phagocyte recognition

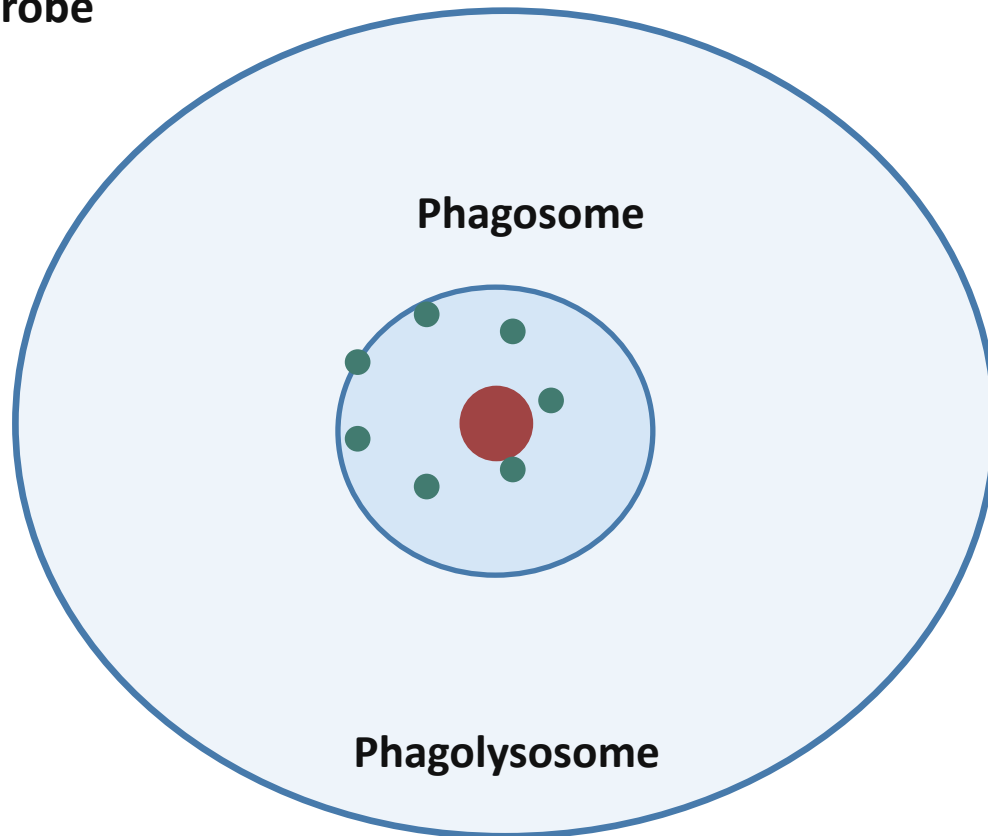


Schematic

- IgG antibodies are important opsonins.
- Complement C3b/iC3b enhances uptake.
- Plasma lectins can also coat microbes for recognition.

The phagolysosome localizes destructive products

Microbe



- Cytoplasmic extensions enclose the ingested target.
- Phagosomes fuse with lysosomal compartments.
- Destructive enzymes are concentrated around the ingested material.

Schematic

Reactive oxygen species participate in killing

Oxidase activation



Reactive oxygen species

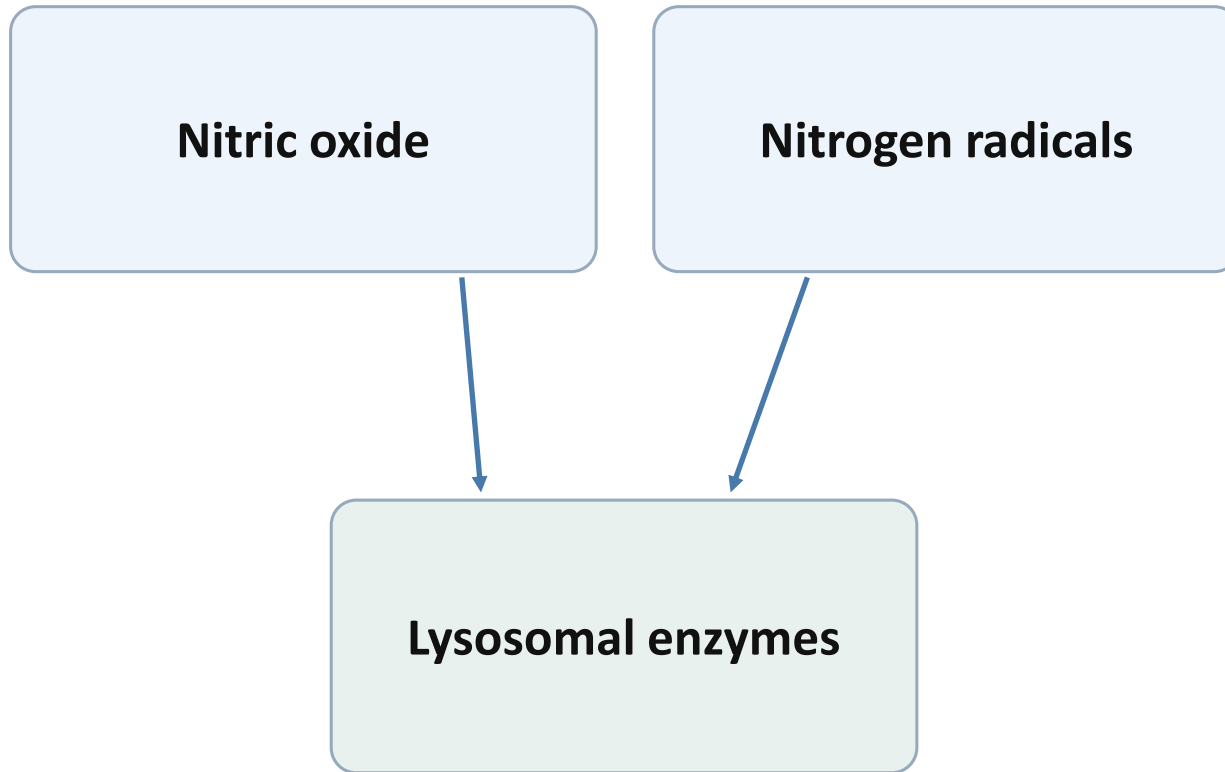


Microbial injury

- Activation of phagocyte oxidase generates reactive oxygen intermediates.
- These products act in intracellular antimicrobial compartments.
- Antioxidant defenses help limit oxidative injury to host cells.

Schematic

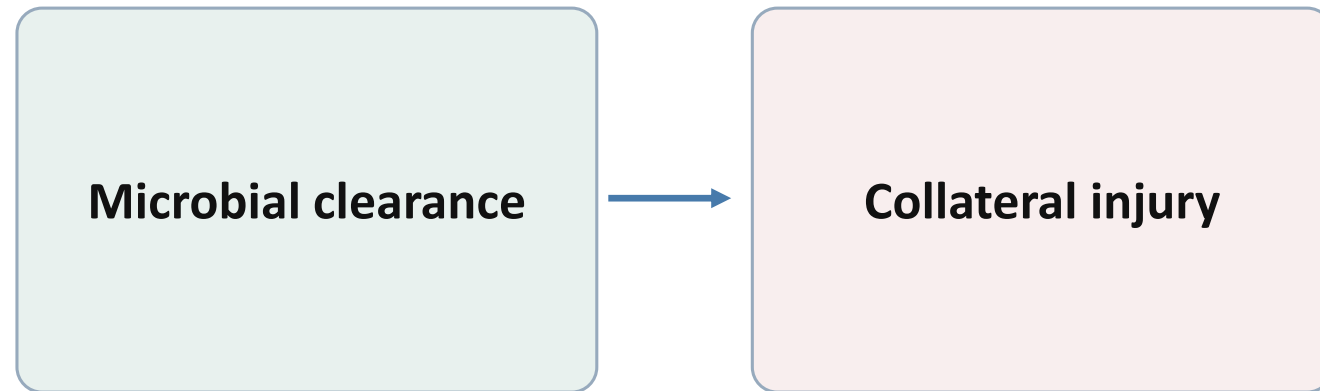
Nitric oxide and enzymes add antimicrobial activity



Schematic

- Inducible nitric oxide synthase generates NO in activated phagocytes.
- Nitrogen-derived intermediates damage microbial constituents.
- Lysosomal enzymes degrade ingested material.

Leukocyte products can also injure host tissue



- Released proteases and reactive intermediates damage normal tissue.
- Phagocytic defense therefore carries an injury risk.
- Collateral damage can amplify the inflammatory reaction.

Schematic

Excess leukocyte activation perpetuates injury

Leukocyte activation



Toxic product release



Tissue injury

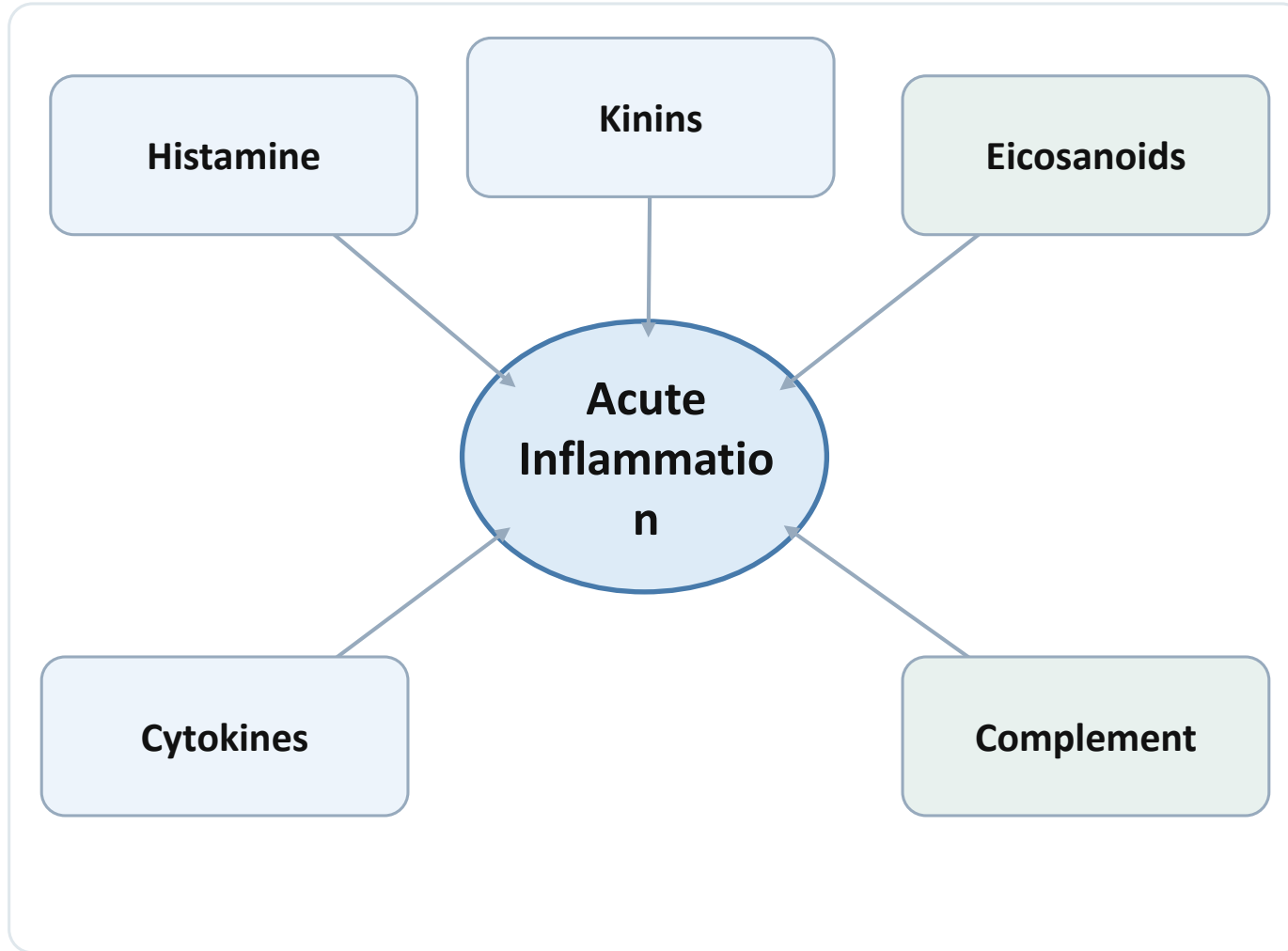


More inflammation

- Persistently activated leukocytes release inflammatory mediators.
- Extracellular release of toxic metabolites is not target-specific.
- Tissue damage can generate new inflammatory stimuli.

Schematic

Mediators convert recognition into visible inflammation



Schematic

- Cell-derived mediators act locally on vessels and leukocytes.
- Plasma-derived systems generate biologically active fragments.
- Multiple mediators may reinforce or oppose one another.

Histamine is an early vascular mediator

Mast cell activation



Histamine

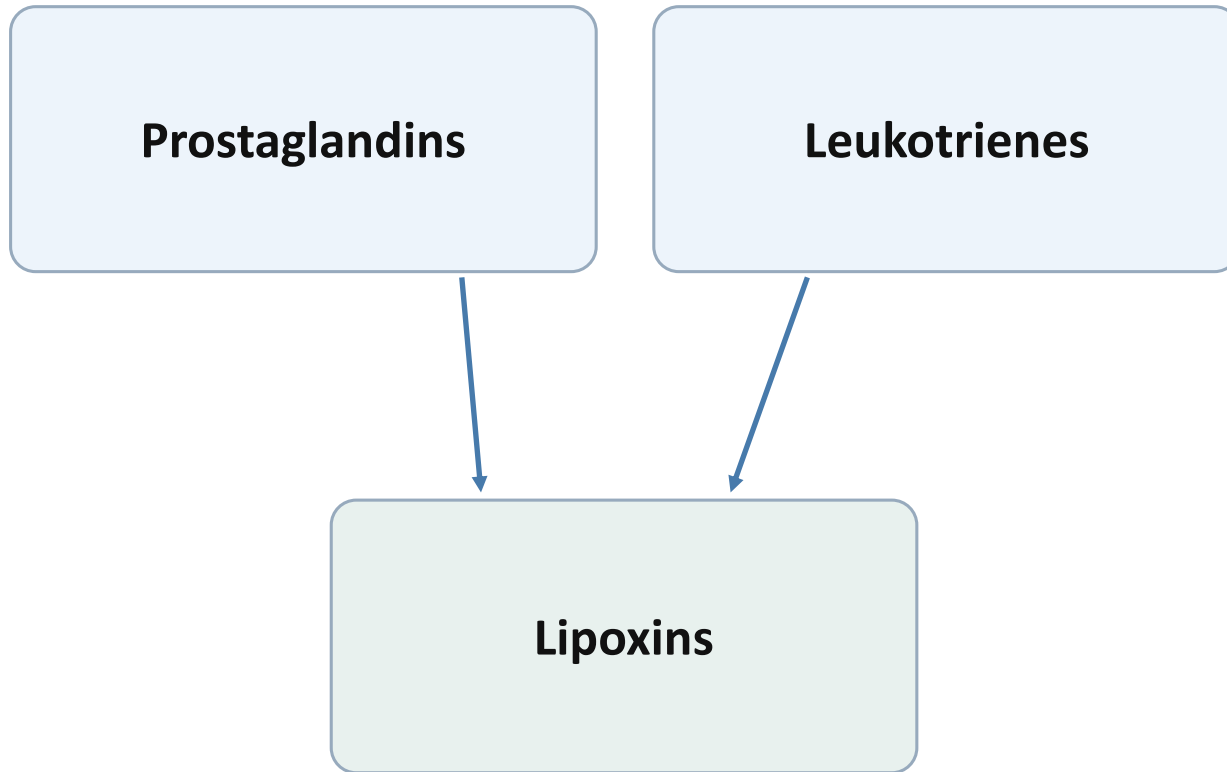


Dilation + leakage

- Mast cells contain preformed histamine near vessels.
- Histamine promotes arteriolar dilation and venular permeability.
- Mast cell degranulation may be triggered by injury or complement.

Schematic

Eicosanoids coordinate several inflammatory effects



- Arachidonic acid is converted into prostaglandins and leukotrienes.
- Different eicosanoids alter vessels, leukocyte responses, and pain.
- Lipoxins counterbalance selected proinflammatory effects.

Schematic

Prostaglandins contribute to pain and fever

Prostaglandin synthesis



Vascular / sensory effects



Pain + fever

- Prostaglandins participate in inflammatory vascular reactions.
- PGE₂ is associated with pain sensitization and fever.
- Mediator effects depend on the specific prostaglandin species.

Schematic

Leukotrienes have distinct functions

LTB₄

Leukocyte chemotaxis
and activation

LTC₄ / LTD₄ / LTE₄

Vascular leakage and
smooth-muscle effects

- LTB₄ promotes leukocyte recruitment and activation.
- LTC₄, LTD₄, and LTE₄ increase vascular permeability.
- Their effects differ from prostaglandin-mediated responses.

Schematic

Lipoxins help constrain neutrophil recruitment

Proinflammatory signals



Lipid mediator switch



Reduced recruitment

- A switch toward lipoxin synthesis is a termination mechanism.
- Lipoxins antagonize selected leukotriene effects.
- Regulation is active—not simply exhaustion of mediators.

Schematic

TNF and IL-1 activate endothelial recruitment machinery

Macrophage signals



TNF + IL-1



Endothelial activation

- Activated macrophages and other cells produce TNF and IL-1.
- Both promote endothelial adhesion molecule expression.
- Their effects enhance leukocyte adhesion and emigration.

Schematic

Chemokines provide both activation and direction

CXCL8 and others



Adhesion activation

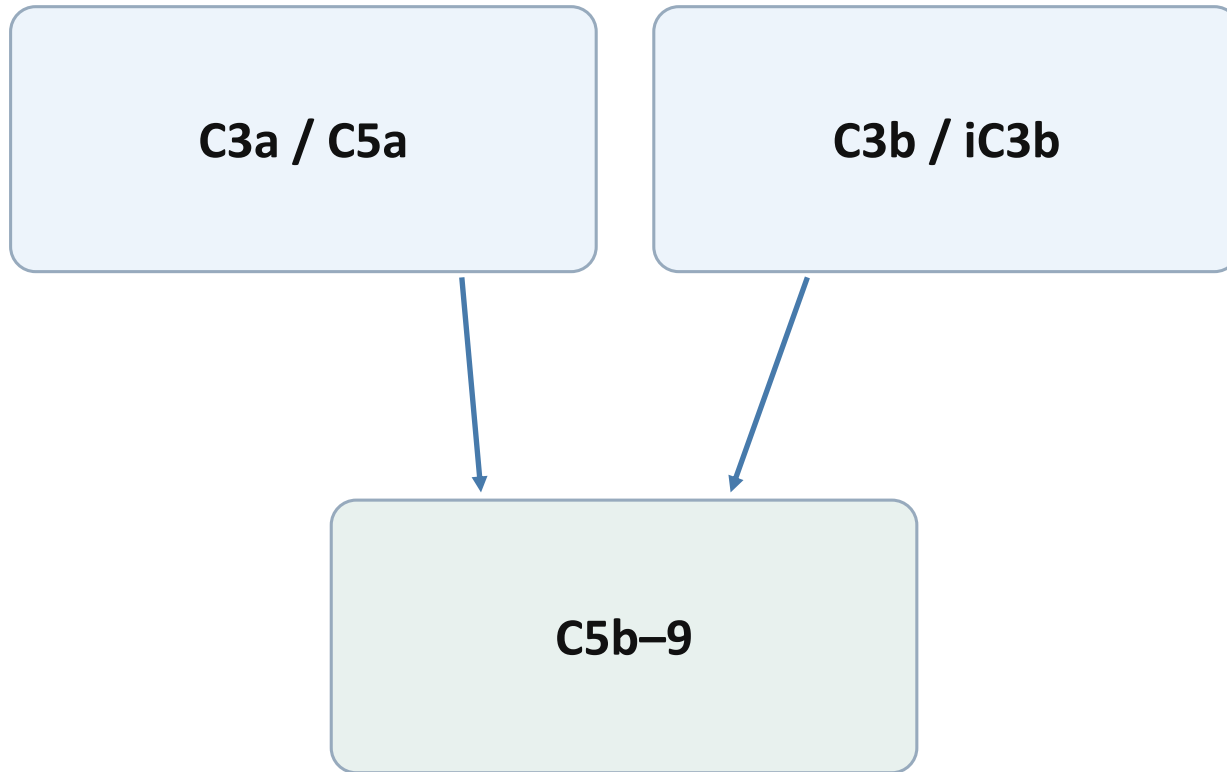


Tissue chemotaxis

- CXCL8/IL-8 attracts and activates neutrophils.
- Chemokines increase integrin binding during recruitment.
- Chemokine gradients direct migration through tissue.

Schematic

Complement links recognition and elimination



Schematic

- C3a and C5a can augment vascular inflammation.
- C5a attracts leukocytes; C3b/iC3b serves as an opsonin.
- Terminal complement components can cause membrane lysis.

Bradykinin connects vascular leakage and pain

Kinin generation



Vascular effects



Pain

- Kinin activation generates inflammatory peptides.
- Bradykinin acts on the vasculature and contributes to pain.
- It is one of several mediators responsible for local symptoms.

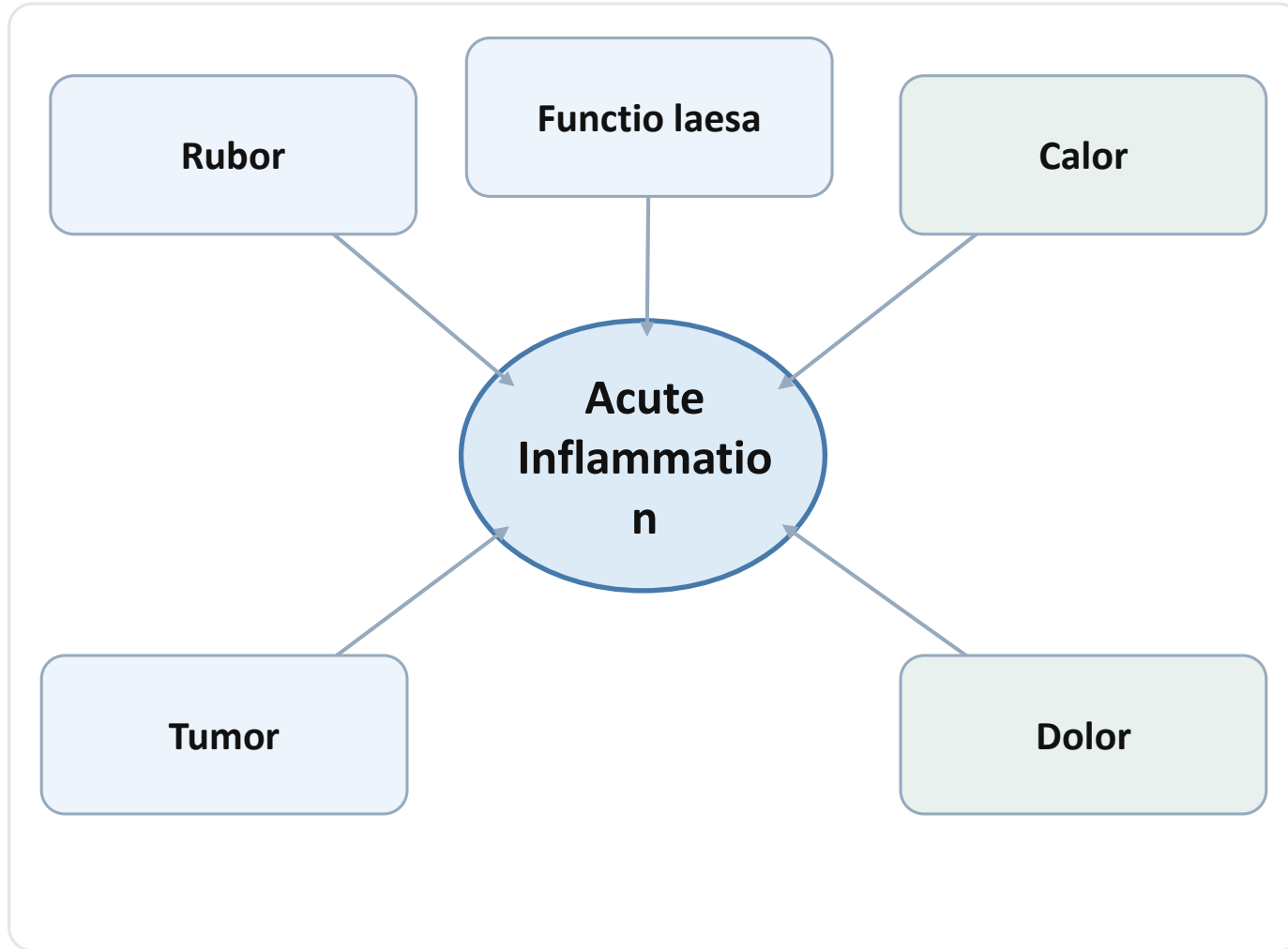
Schematic

Multiple mediators converge on the same endpoints

Effect	Representative mediators
Vasodilation	Histamine
Permeability	Histamine; LTC ₄ / LTD ₄ / LTE ₄
Recruitment	TNF; IL-1; chemokines; C5a; LTB ₄
Pain	Prostaglandins; bradykinin

- Histamine and leukotrienes can increase leakage.
- TNF, IL-1, and chemokines regulate recruitment.
- Prostaglandins and bradykinin contribute to pain.

The cardinal signs express vascular and cellular events



Schematic

- Rubor and calor principally reflect increased regional blood flow.
- Tumor reflects accumulation of extravascular fluid.
- Dolor and functio laesa arise from pain and tissue injury.

Redness and warmth reflect hyperemia

Vasodilation



Hyperemia



Rubor + calor

- Small vessels dilate in response to inflammatory mediators.
- Increased local perfusion produces erythema and warmth.
- This finding represents a vascular response rather than pus formation.

Schematic

Swelling reflects extravascular fluid accumulation

Leakage



Exudate



Edema (tumor)

- Permeable small vessels permit protein-rich fluid escape.
- Fluid accumulates in interstitial spaces as edema.
- Swelling can limit the mechanical function of affected tissues.

Schematic

Pain and lost function have multiple causes

Inflammation + damage



Pain (dolor)

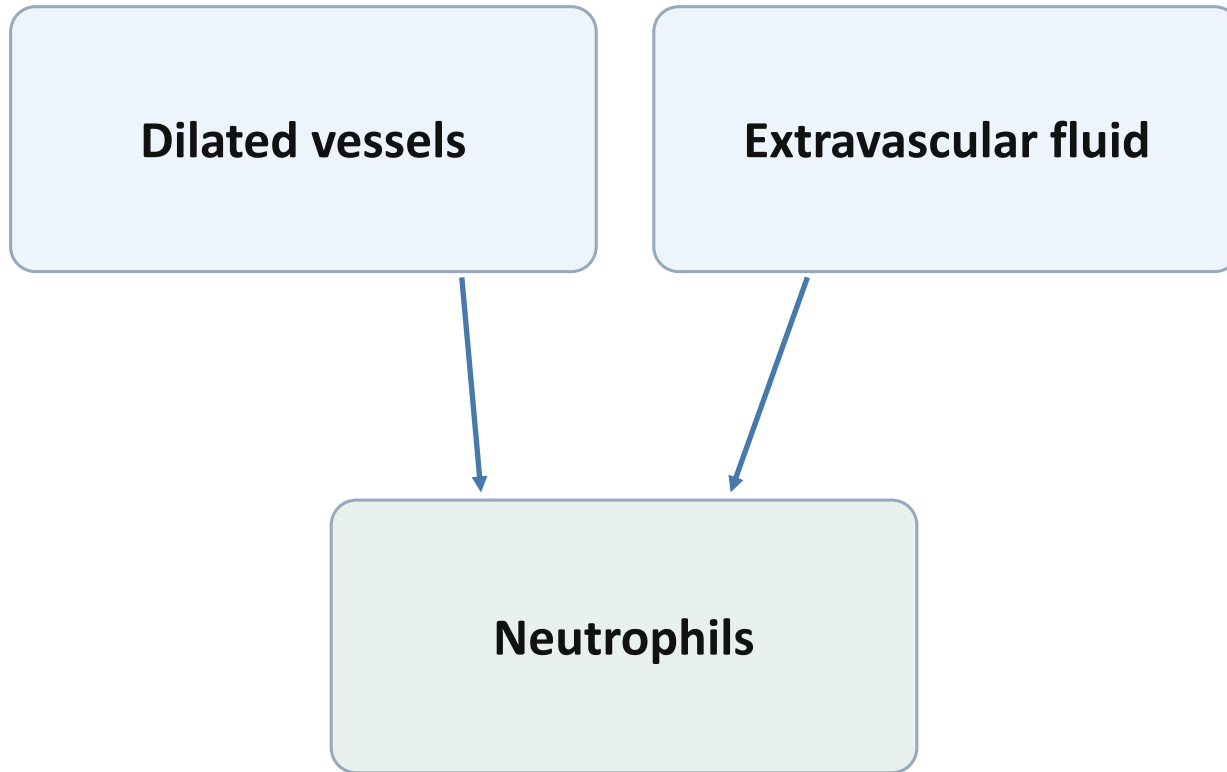


Impaired function

- Prostaglandins, neuropeptides, and cytokines contribute to pain.
- Damage to tissue also generates nociceptive stimuli.
- Loss of function follows from pain and structural injury.

Schematic

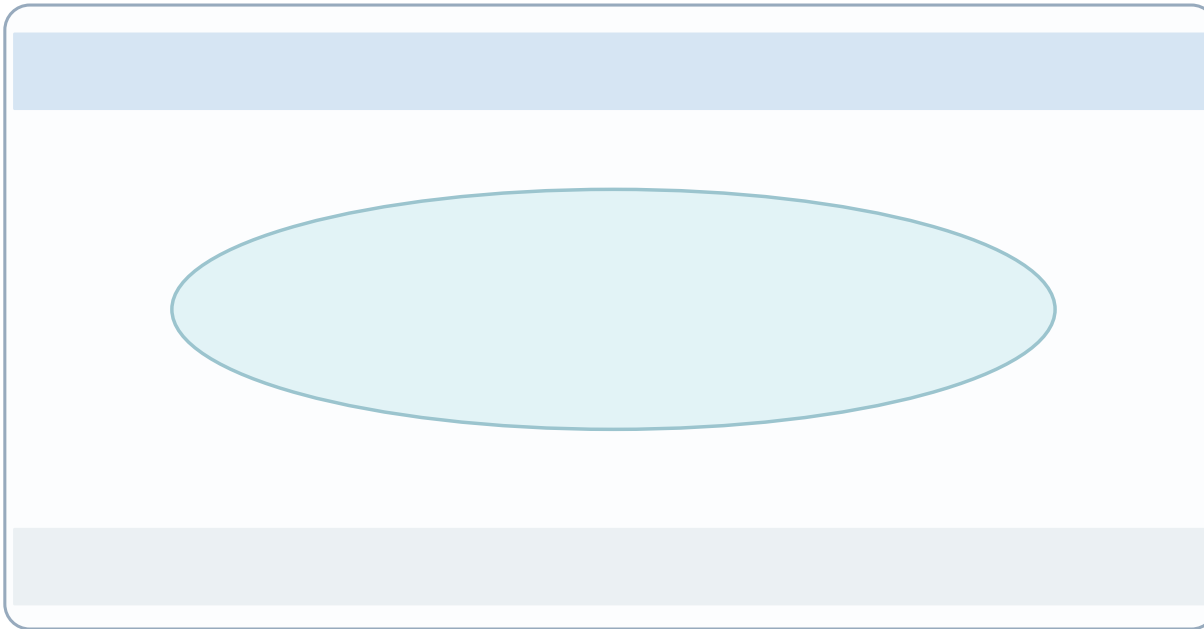
Microscopy reflects vessels, fluid, and leukocytes



Schematic

- Dilated small vessels are a cardinal morphologic feature.
- Extravascular fluid accumulates in inflamed tissues.
- Neutrophils commonly dominate early cellular infiltrates.

Serous inflammation produces relatively cell-poor fluid



Surface injury

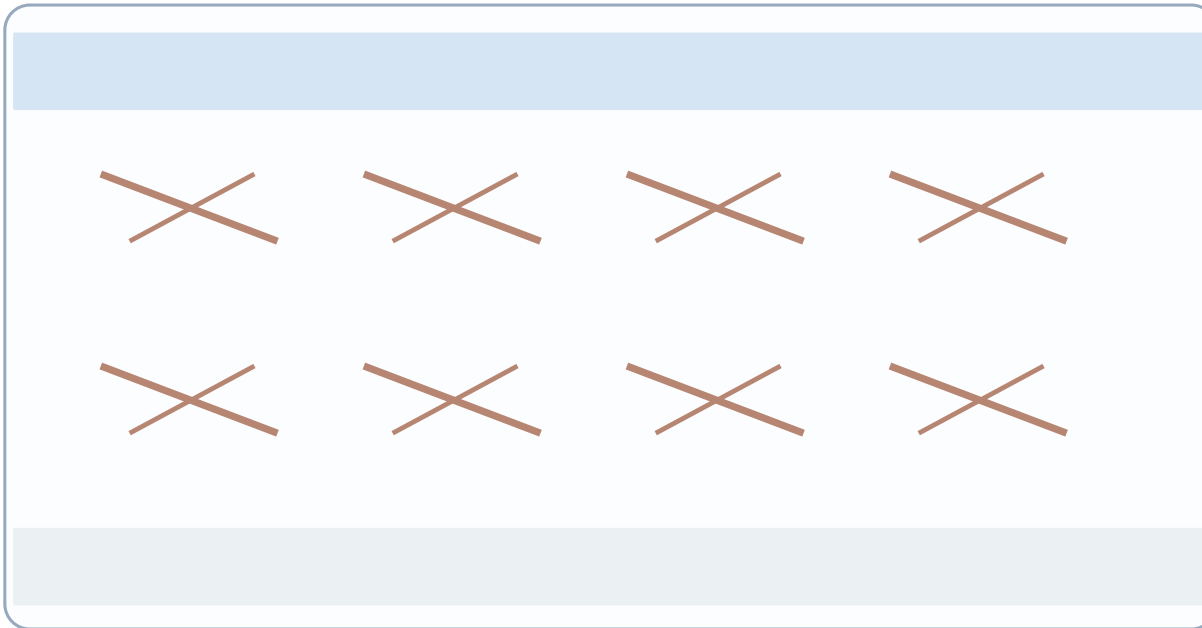
Fluid collection

Serous pattern

Simplified schematic; Not a tissue micrograph

- Serous exudation may create a blister or a body-cavity effusion.
- Such fluid generally lacks large numbers of leukocytes or microbes.
- A skin blister from a burn is a classic morphologic example.

Fibrinous inflammation deposits fibrin



Fibrinogen leakage

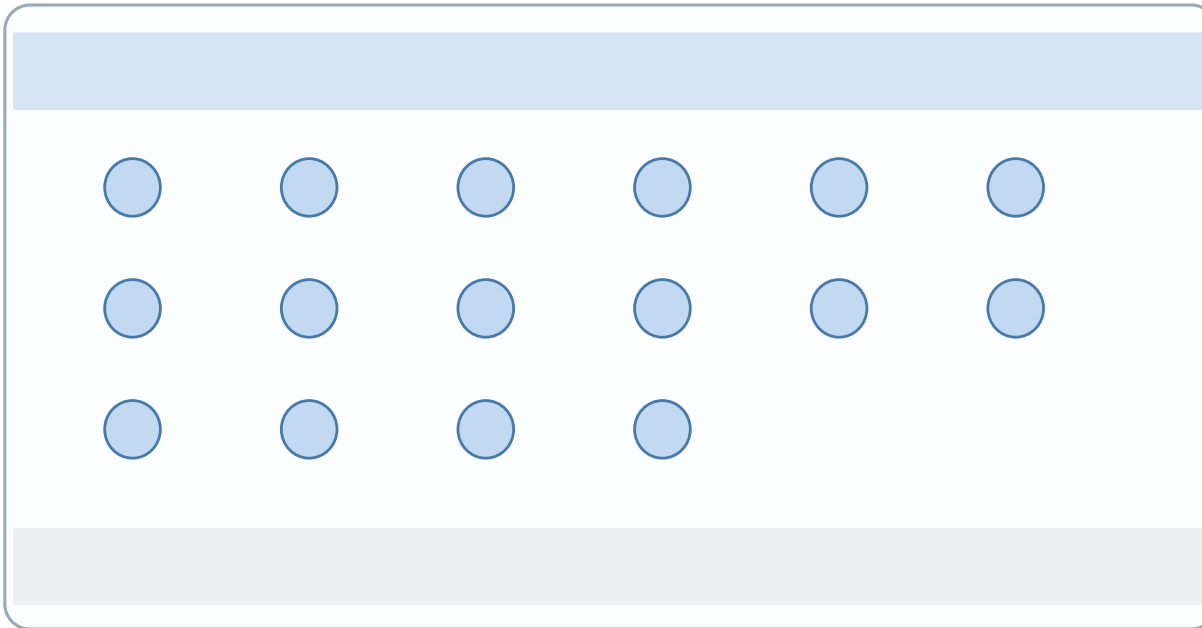
Fibrin deposition

Clearance or scar

- Greater permeability permits plasma fibrinogen to escape.
- Fibrin may collect on serosal surfaces, including pericardium.
- Persistent fibrin may organize into fibrous tissue.

Simplified schematic; Not a tissue micrograph

Purulent inflammation creates pus



Pyogenic injury

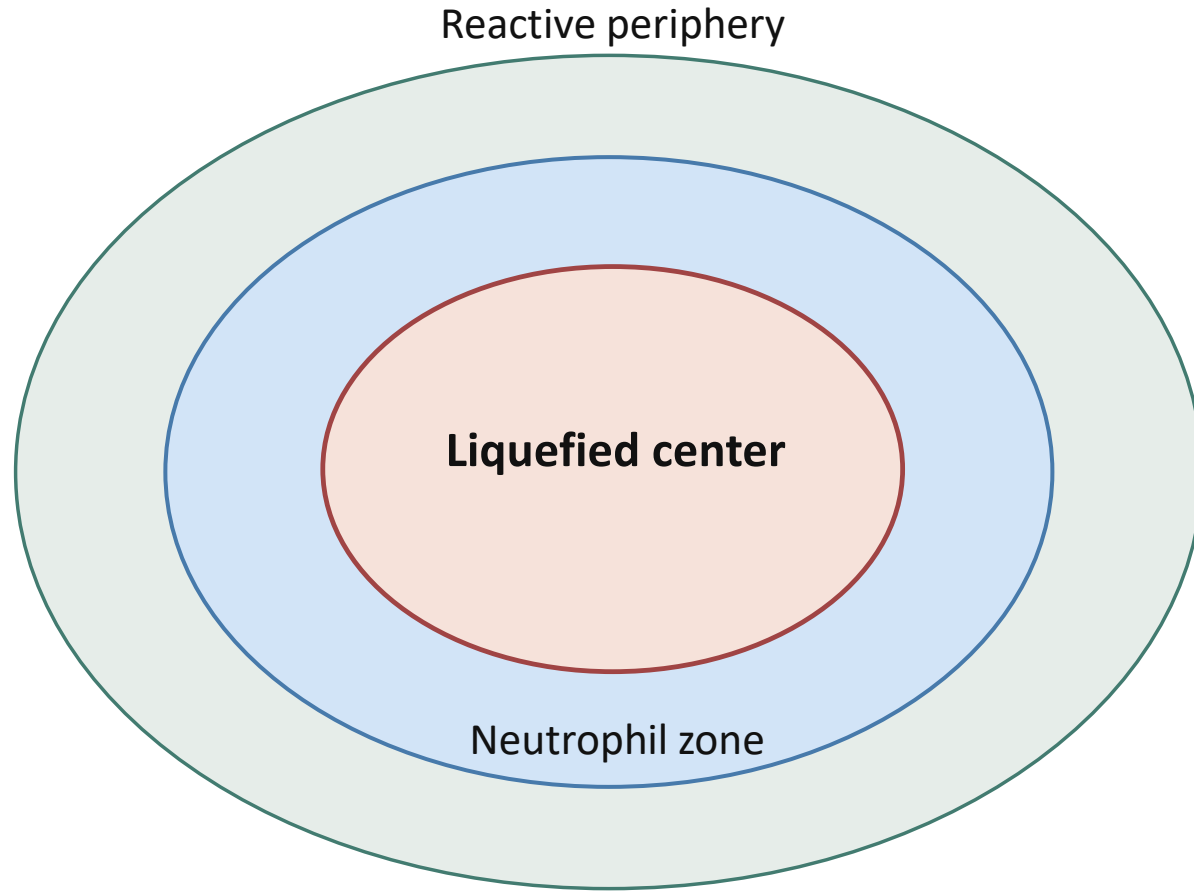
**Neutrophil-rich
exudate**

Pus

- Pus contains neutrophils and liquefied necrotic debris.
- Pyogenic bacteria frequently cause this pattern.
- Acute appendicitis is a common example of suppurative inflammation.

Simplified schematic; Not a tissue micrograph

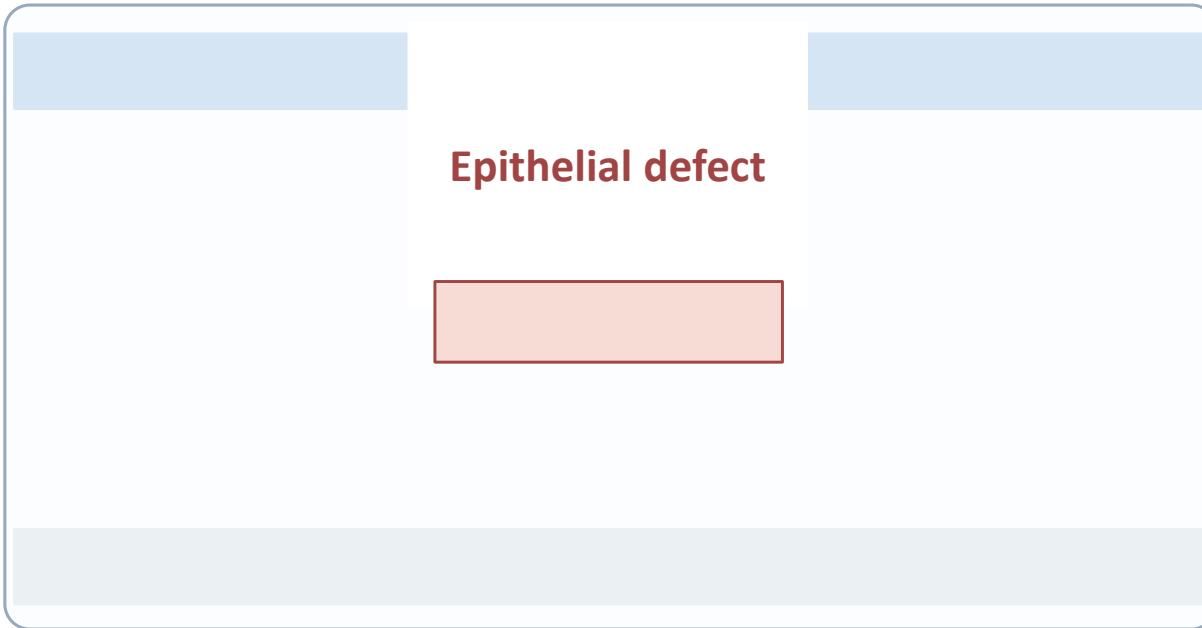
An abscess is localized suppurative inflammation



- An abscess contains a central liquefied region.
- Viable neutrophils often surround the necrotic center.
- Peripheral inflammation and repair may subsequently wall off the lesion.

Concentric schematic; Not a specimen

Ulceration combines surface loss with inflammation



Surface necrosis

Tissue loss

Inflammatory base

- An ulcer is a surface defect caused by sloughing of necrotic tissue.
- Acute inflammation may occur at its base.
- With chronicity, inflammatory cells and fibrosis can develop.

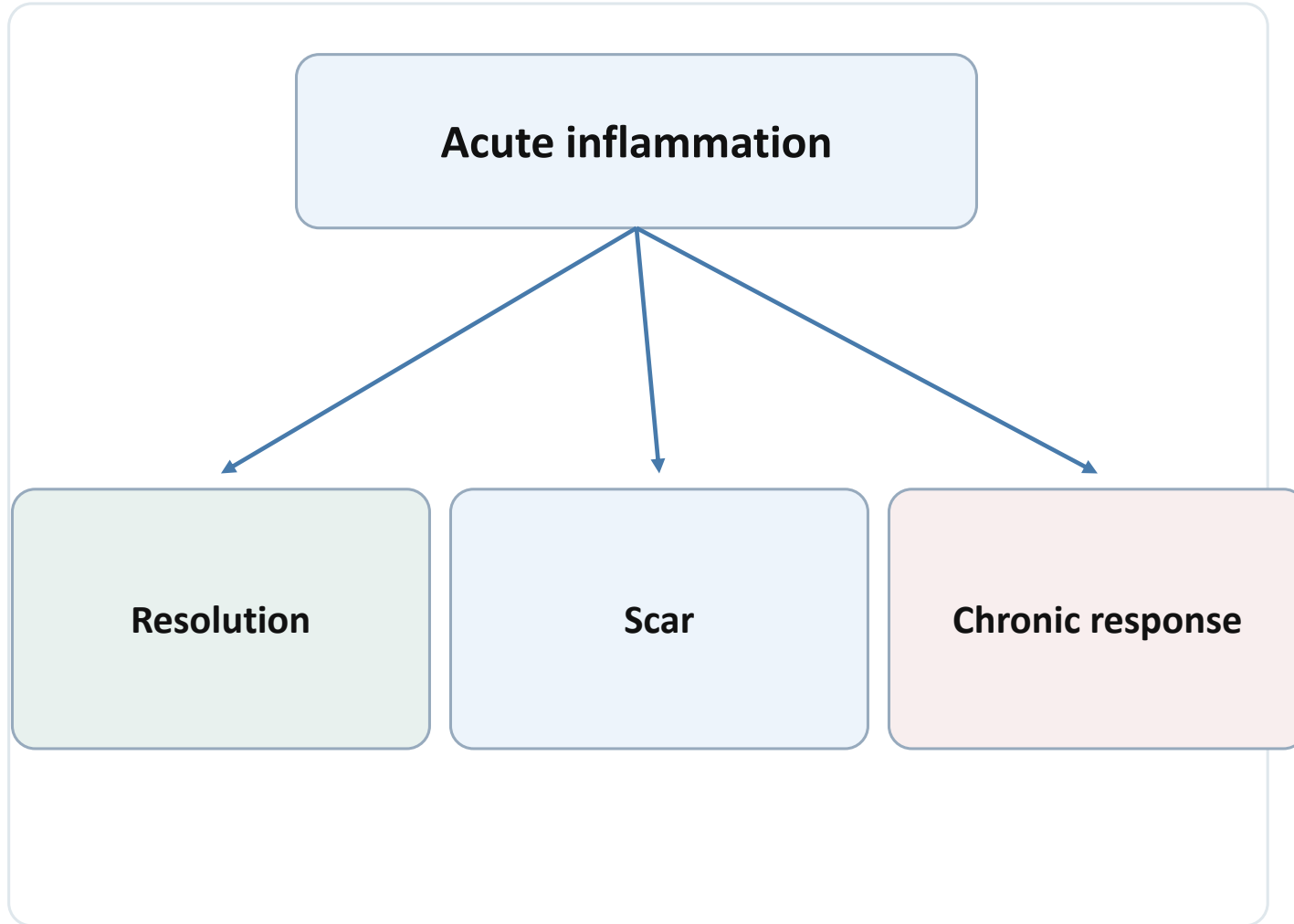
Simplified schematic; Not a tissue micrograph

The morphology helps infer the process

Pattern	Dominant material	Typical teaching example
Serous	Relatively cell-poor fluid	Skin blister
Fibrinous	Fibrin-rich exudate	Fibrinous pericarditis
Purulent	Pus: neutrophils + debris	Abscess / appendicitis

- Serous exudates emphasize fluid accumulation.
- Fibrinous exudates indicate conspicuous fibrin deposition.
- Purulent processes feature neutrophil-rich exudate and necrotic debris.

Three major outcomes follow an acute reaction



Schematic

- Elimination and adequate regeneration permit resolution.
- Severe damage or unreabsorbed fibrin may lead to fibrosis.
- Persistence of the stimulus can produce chronic inflammation.

Complete resolution restores tissue architecture

Agent removed



Debris + edema cleared



Regeneration

- Macrophages clear microbes and cellular debris.
- Lymphatics remove edema fluid from affected tissue.
- Viable parenchymal cells regenerate if regenerative capacity is adequate.

Schematic

Fibrosis replaces tissue that cannot regenerate

Persistent damaged area



Organization



Scar

- Extensive destruction prevents simple restoration.
- Uncleared fibrin may become organized.
- Fibroblast and vessel ingrowth leads to fibrous scar formation.

Schematic

Persistent injury can convert acute into chronic inflammation

Unresolved cause



Continued recruitment

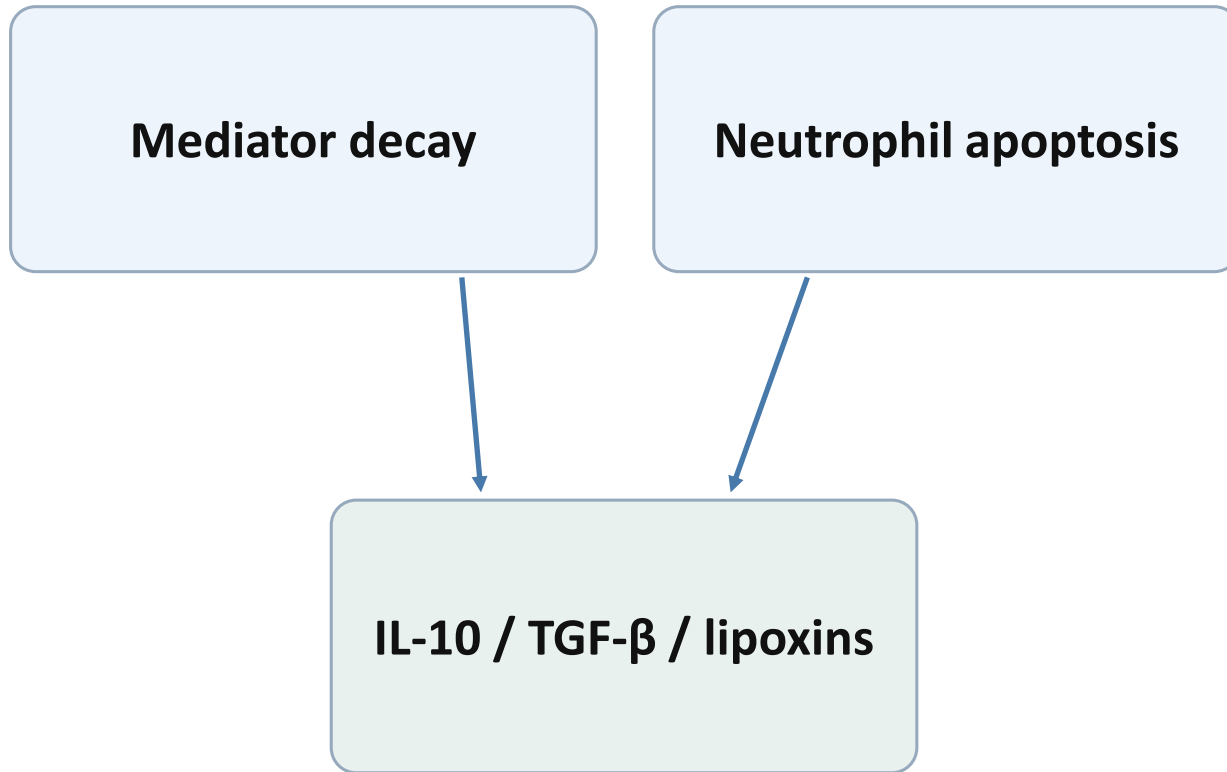


Chronic inflammation

- The offending stimulus may resist elimination.
- Normal healing may be interrupted or ineffective.
- Persistent inflammation combines damage and ongoing repair.

Schematic

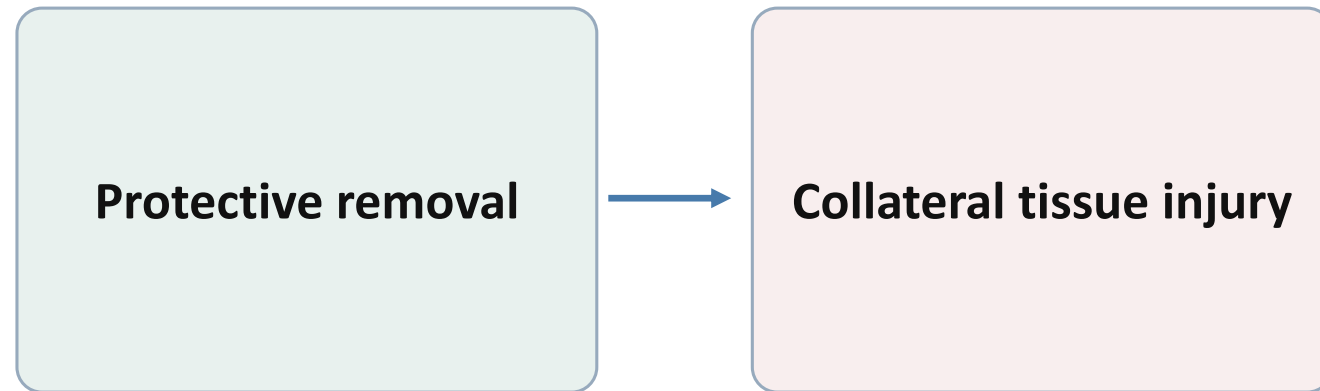
Resolution requires active antiinflammatory signals



- Stimulus disappearance limits new mediator production.
- Neutrophils are short-lived and undergo apoptosis.
- Lipoxins, IL-10, and TGF- β contribute to inhibition of inflammation.

Schematic

Host protection and tissue injury coexist



Schematic

- Inflammation is beneficial when it removes offending agents.
- The same antimicrobial products can injure host structures.
- The ultimate outcome depends on the stimulus, damage, and regulation.

Application: Why does an acutely infected wound swell?

Microbial stimulus



Vascular leakage



Edema

- Injury-associated mediators increase microvascular permeability.
- Protein-rich plasma fluid enters the affected tissue.
- The exudate produces local edema and contributes to dysfunction.

Schematic

Application: What makes an abscess purulent?

Bacterial injury



Suppuration



Localized abscess

- Pyogenic infection initiates neutrophil recruitment.
- Necrotic cells and neutrophils contribute to liquefied debris.
- The localized collection of pus defines an abscess.

Schematic

Application: Why can inflammation leave a scar?

Substantial injury



Fibrovascular ingrowth



Fibrous scar

- Deep tissue destruction may exceed regenerative capacity.
- Persistent fibrin or damaged extracellular space becomes organized.
- Connective tissue fills the defect, potentially impairing function.

Schematic

Integrated cascade: From injury to outcome

Recognition



Vascular response



Recruitment



Elimination



Regulation / outcome

- Sentinel-cell mediators initiate vascular changes and leukocyte entry.
- Activated leukocytes phagocytose agents but may also injure tissue.
- Successful control ends in resolution; Persistent damage changes the outcome.

Schematic

The five Rs unify the acute inflammatory response

Recognition



Recruitment



Removal



Regulation

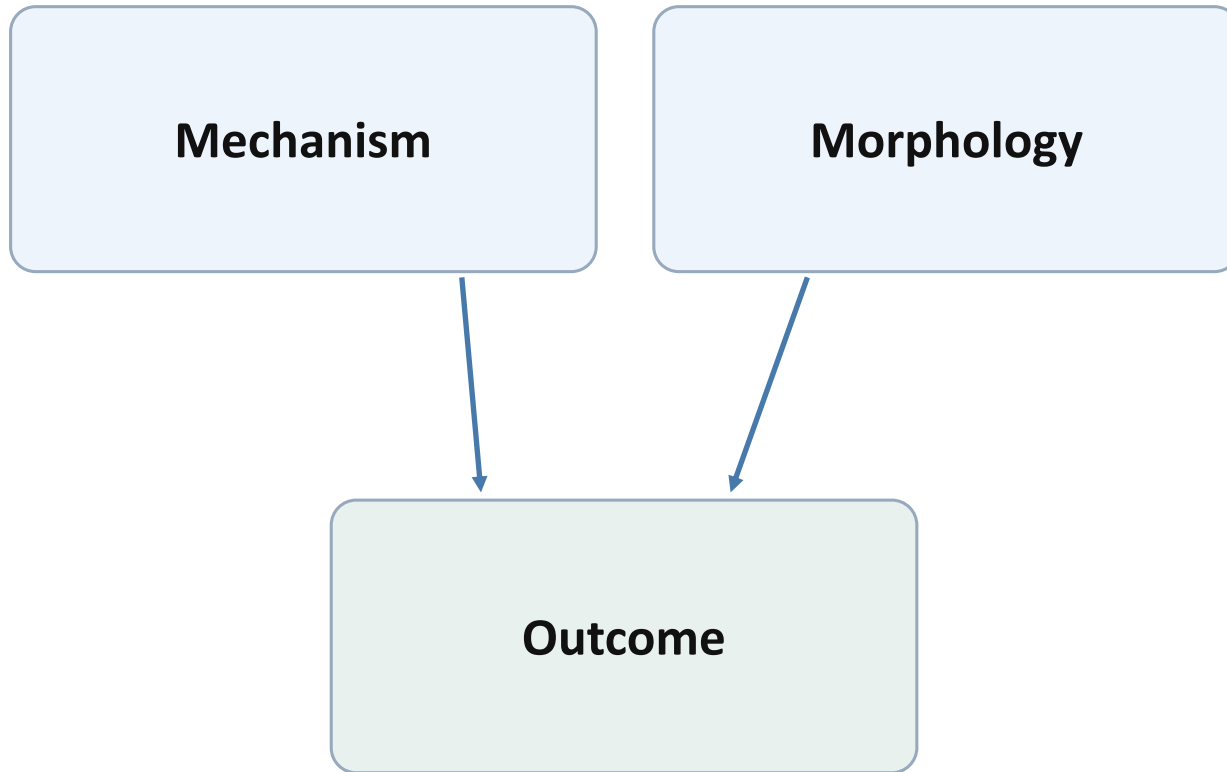


Repair

- Recognition initiates mediator-driven vascular changes.
- Recruitment and removal clear injurious agents and necrotic debris.
- Regulation and repair restore homeostasis or expose failure of resolution.

Schematic

Summary: what to retain for clinicopathologic reasoning



Schematic

- Vasodilation + leakage + leukocytes explain the core reaction.
- Selectins, integrins, chemokines, and phagocytic mechanisms connect cause to morphology.
- Morphology and persistence of injury help predict resolution, fibrosis, or chronicity.