

Acute Inflammation

Vascular and cellular mechanisms • mediators • tissue patterns • outcomes

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What learners should be able to explain

- Connect the three defining components to local signs of acute inflammation.
- Trace neutrophils from circulation to tissue and intracellular microbial destruction.
- Relate inflammatory mediators to specific vascular and cellular effects.
- Distinguish major morphologic patterns and predict possible outcomes.

Acute and chronic inflammation are distinct responses

Acute inflammation

- Begins rapidly: Minutes to hours
- Fluid exudation with predominantly neutrophils
- Usually short-lived when stimulus is removed
- Prominent local manifestations

Chronic inflammation

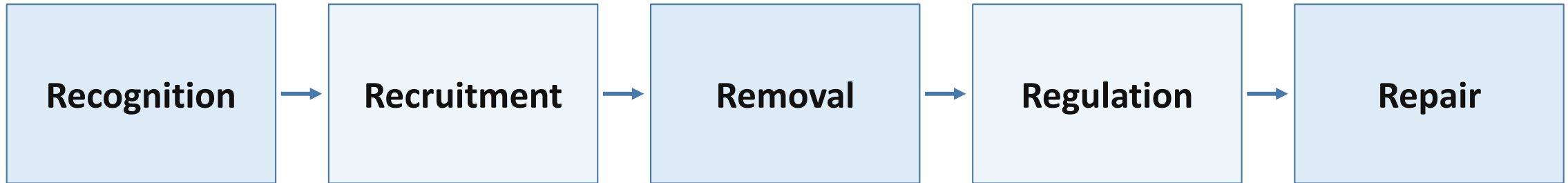
- Longer time course
- Macrophages and lymphocytes predominate
- More sustained injury and fibrosis
- Can coexist with acute inflammation

The protective purpose—and the potential cost

The central task is to deliver defense molecules and leukocytes to the focus of injury.

- Eliminate microbes, damaged cells, and foreign material.
- Extravascular proteins and activated leukocytes improve local defense.
- The same destructive products may damage surrounding healthy tissue.

Inflammation follows five coordinated tasks



- Inflammation does not end with leukocyte killing.
- Shutoff and tissue recovery are integral to effective host defense.

What can initiate an inflammatory response?

Infectious agents

Bacteria, fungi, and other microbes activate sensing pathways.

Tissue damage

Necrotic cells and tissue injury release alarm signals.

Other injurious stimuli

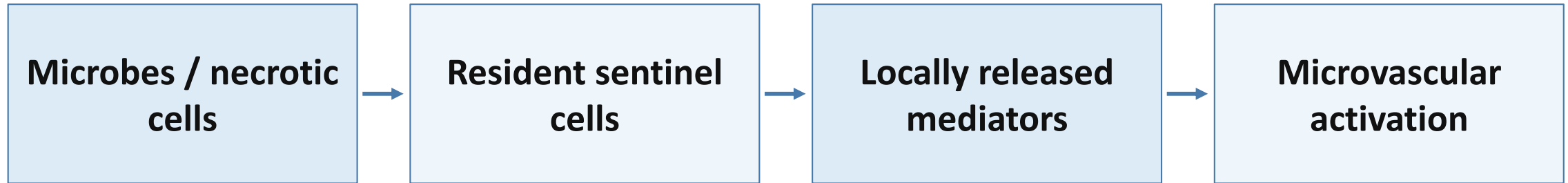
Foreign bodies, trauma, and immune reactions may elicit inflammation.

Tissue sentinels detect the offending agent

Resident macrophages, dendritic cells, and mast cells respond before circulating neutrophils arrive.

- Sentinel cells survey local tissue for microbes or abnormal material.
- Recognition triggers cytokines, lipid mediators, and other signals.
- Mediators recruit plasma proteins and circulating leukocytes.

Recognition is translated into a vascular response



- Early mediators act near the focus of injury.
- Plasma and circulating cells then gain access to extravascular tissue.

How innate receptors identify danger

- Cellular receptors can recognize conserved microbial structures.
- Sensors of cell injury respond to substances released by damaged cells.
- Complement and other circulating proteins can identify microbes.
- Recognition mechanisms initiate local effector pathways.

Three defining components of acute inflammation

1. Vasodilation

Dilation of small vessels increases regional blood flow.

2. Vascular leakage

Microvascular permeability permits plasma proteins to enter tissue.

3. Leukocyte migration

Leukocytes exit blood, accumulate, and become activated.

From detection to the inflamed tissue



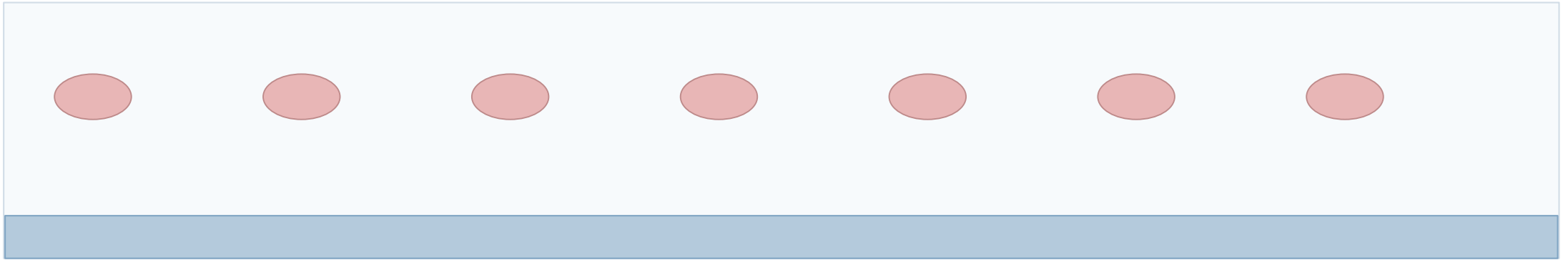
- Vascular and cellular events overlap in time.
- The response becomes self-limited if the injurious stimulus disappears.

The cardinal signs have mechanistic explanations

Clinical sign	Principal mechanism
Redness (rubor)	Vasodilation and vascular congestion
Heat (calor)	Increased local blood flow
Swelling (tumor)	Leakage and accumulation of edema fluid
Pain (dolor)	Inflammatory mediators and pressure
Loss of function	Pain and tissue injury

Why blood vessels matter in acute inflammation

Vessel lumen



Extravascular tissue

Inflammatory plasma proteins and leukocytes must cross the microvascular wall.

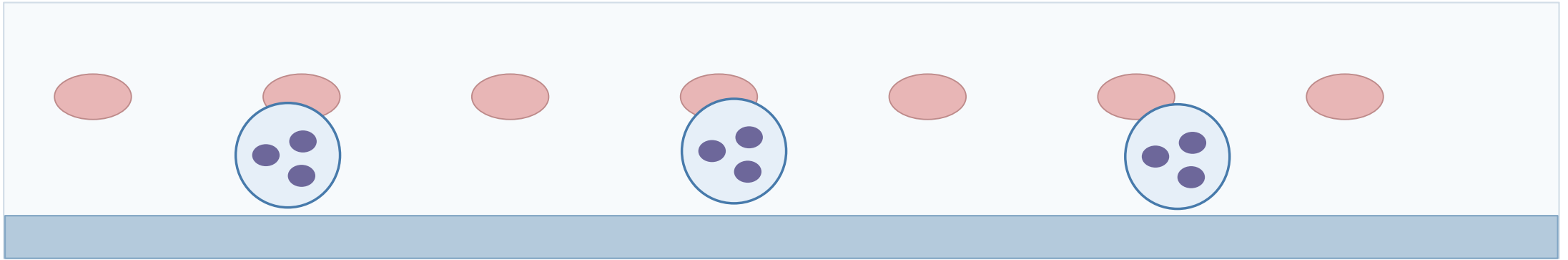
Vasodilation is an early vascular event

Vasoactive mediators relax vascular smooth muscle and increase local perfusion.

- Histamine is a major early mediator of vasodilation.
- Small vessels, including arterioles, show increased flow.
- Increased perfusion produces warmth and erythema.

Loss of fluid promotes stasis and margination

Vessel lumen



Leukocytes redistribute toward endothelial surface

Extravascular tissue

Hemoconcentration and slower flow favor leukocyte contact with endothelium.

Edema and exudation are not synonyms

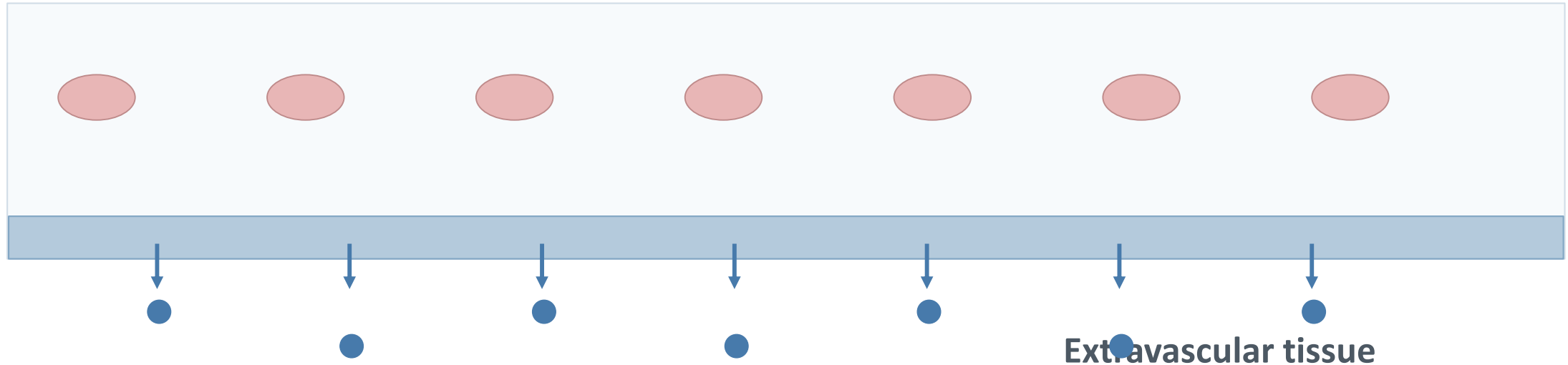
- Exudation is escape of fluid, proteins, and sometimes cells from blood vessels.
- An exudate is protein-rich fluid produced by inflammatory vascular leakage.
- Edema means increased interstitial or serous-cavity fluid, of either type.
- A transudate results from hydrostatic or oncotic imbalance without increased permeability.

Exudate versus transudate

Feature	Inflammatory exudate	Noninflammatory transudate
Protein content	Relatively high	Relatively low
Cellular material	May contain leukocytes / debris	Few or no cells
Mechanism	Microvascular permeability ↑	Hydrostatic / oncotic imbalance
Implication	Supports inflammation	May reflect systemic fluid imbalance

Leakage transfers plasma proteins into tissue

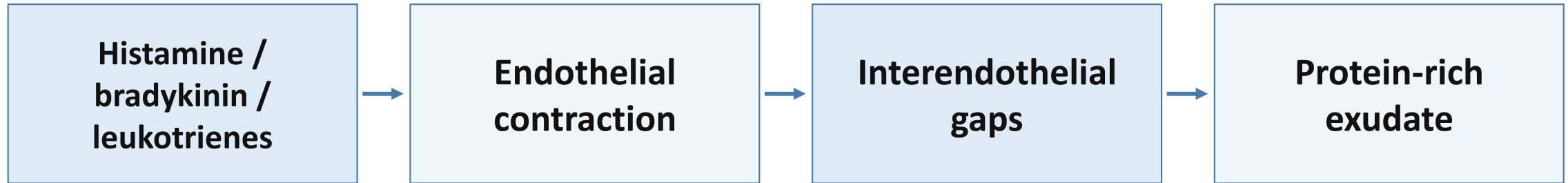
Vessel lumen



Protein-rich fluid enters the tissue after endothelial barrier disruption

Fluid accumulation is a consequence of an altered endothelial barrier.

Immediate transient permeability: Endothelial gaps



- The classic response is rapid and usually short-lived.
- Postcapillary venules are a principal site of this leakage.

Endothelial contraction and endothelial injury differ

Mediator-driven gap formation

- Rapid onset following mediator release
- Contraction creates intercellular openings
- Often transient and reversible
- Characteristic of histamine-associated leakage

Direct endothelial injury

- Severe burns, toxins, or microbial damage
- Necrosis and endothelial detachment
- Potentially sustained vascular leakage
- Can be amplified by recruited neutrophils

Delayed and sustained vascular leakage

Not every permeability response is immediate and transient.

- Some mild insults yield delayed leakage after several hours.
- Direct endothelial damage produces longer-lasting barrier failure.
- Multiple permeability mechanisms may coexist in the same injury.

Local lymphatics respond to inflammation

Drain excess fluid

Lymphatics help remove edema fluid and restore interstitial balance.

Carry cellular material

Lymphatic channels carry inflammatory cells and microbial material.

Reactive nodes

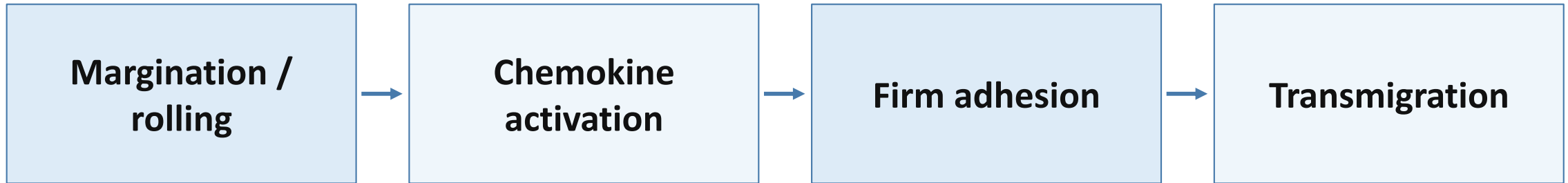
Regional lymph nodes may enlarge as immune responses develop.

The effector cells of acute inflammation

Neutrophils and macrophages are the dominant phagocytic cells.

- They ingest microbes, necrotic cells, and other unwanted material.
- Neutrophils arrive early and provide rapid antimicrobial activity.
- Macrophages clear debris and contribute to subsequent repair.

Leukocyte recruitment is a multistep cascade



- After leaving the vessel, cells follow chemical gradients in tissue.
- Cell adhesion is controlled by endothelial and leukocyte molecules.

Margination brings leukocytes to the vessel wall

- In rapidly flowing blood, red cells occupy the central axial stream.
- Stasis redistributes leukocytes toward the endothelial surface.
- Contact allows subsequent tethering and rolling interactions.

Selectins mediate rolling, not stable arrest

Endothelial selectins

Activated endothelium displays P-selectin and E-selectin.

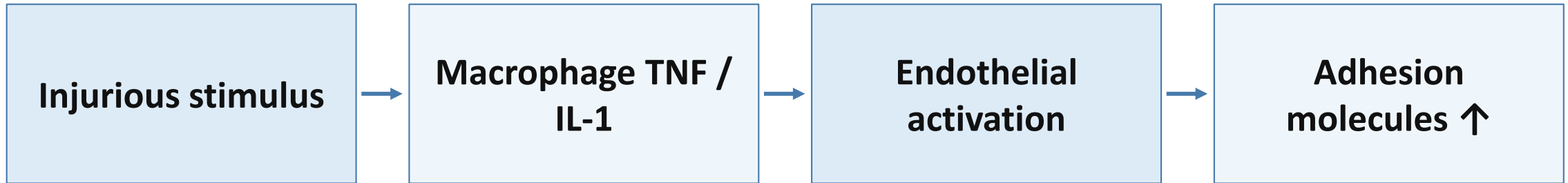
Leukocyte ligands

Carbohydrate-bearing ligands bind selectins transiently.

Functional outcome

Repeated weak attachments slow cells and produce rolling.

Inflammatory cytokines activate endothelium



- The endothelial surface changes from antiadhesive to leukocyte-binding.
- Chemokine display helps activate passing cells.

Chemokines switch leukocyte integrins to high affinity

Rolling creates time for leukocytes to encounter endothelial chemokines.

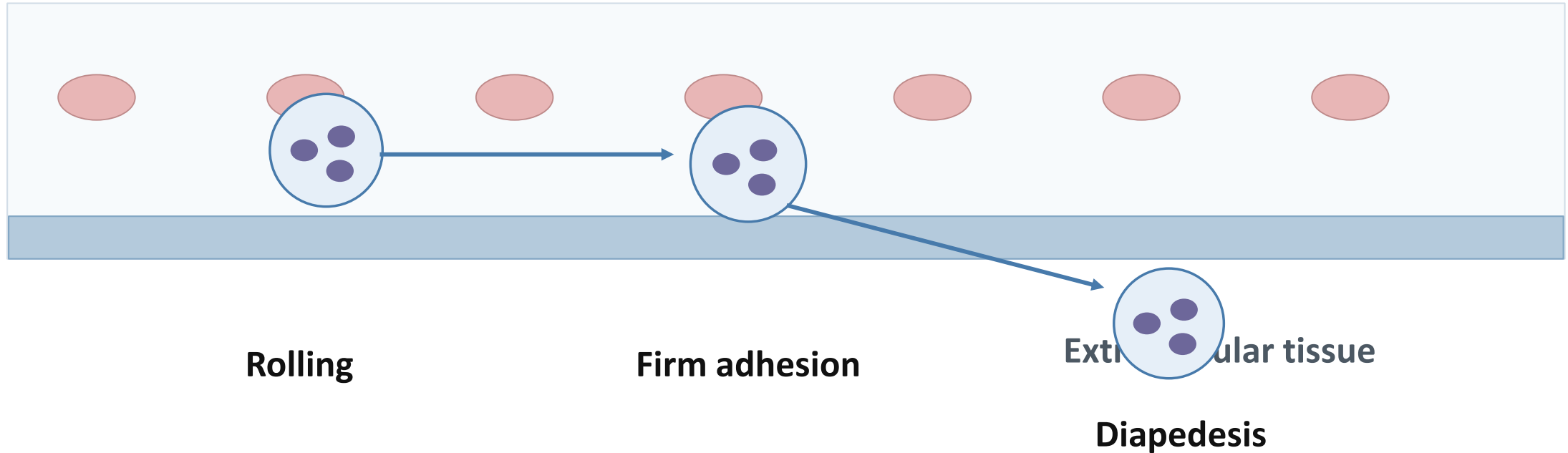
- Chemokine signals act through leukocyte G protein–coupled receptors.
- Inside-out signaling increases the binding capacity of integrins.
- Activated integrins interact strongly with endothelial ligands.

Stable adhesion requires integrins and endothelial ligands

Leukocyte surface	Endothelial surface	Result
High-affinity integrins such as LFA-1 and Mac-1 bind firmly.	Immunoglobulin-family ligands include ICAM-1.	Neutrophils stop rolling and prepare to cross the vessel wall.

Transmigration: Crossing a postcapillary venule

Vessel lumen



PECAM-1 (CD31) participates in junctional migration; Basement membrane is traversed.

Chemotaxis directs cells within the tissue

Chemotaxis is directed migration along a concentration gradient.

- Chemoattractants activate leukocyte G protein–coupled receptors.
- Actin polymerization at the leading edge drives cell movement.
- The gradient directs cells toward microbes or damaged tissue.

Major chemoattractants for neutrophils

Source	Representative chemoattractant	Consequence
Bacteria	N-formylated peptides	Directed migration
Chemokines	IL-8 / CXCL8	Chemotaxis and activation
Complement	C5a	Chemotaxis and activation
Arachidonic acid	LTB4	Chemotaxis and activation

Early neutrophils and later macrophages

Neutrophils

- Commonly dominate at 6–24 hours
- Rapidly recruited, numerous in blood
- Short lifespan; Undergo apoptosis
- Strong phagocytic and microbicidal response

Monocytes / macrophages

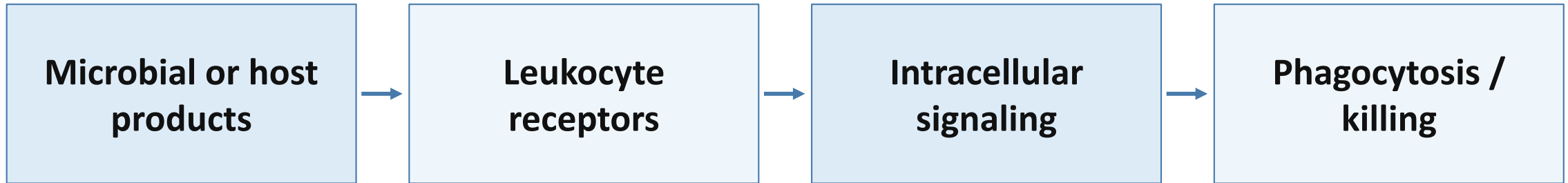
- Often increase at 24–48 hours
- Differentiate into tissue macrophages
- Can persist and proliferate locally
- Clear debris and support tissue repair

The cellular timeline is stimulus-dependent

The neutrophil-to-macrophage sequence is a useful pattern—not a rigid rule.

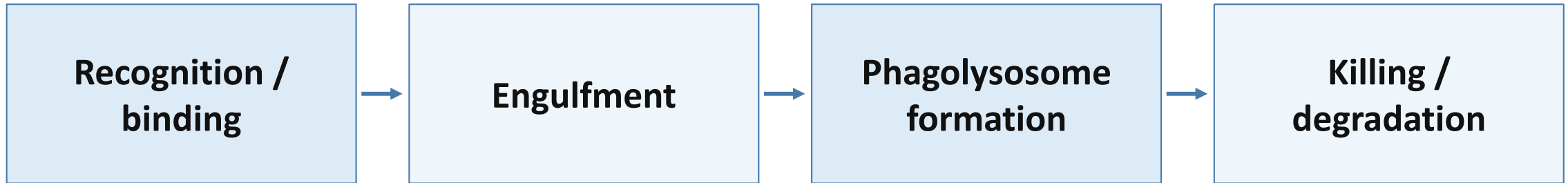
- Some bacterial infections sustain neutrophilic recruitment.
- Lymphocytes can appear early in viral inflammation.
- Eosinophils may predominate with helminths and some allergies.
- Interpret cellular composition together with time and etiology.

Leukocyte activation follows recognition



- Different receptors converge on effector functions.
- Activation can also provoke extracellular mediator release.

Phagocytosis has three sequential stages

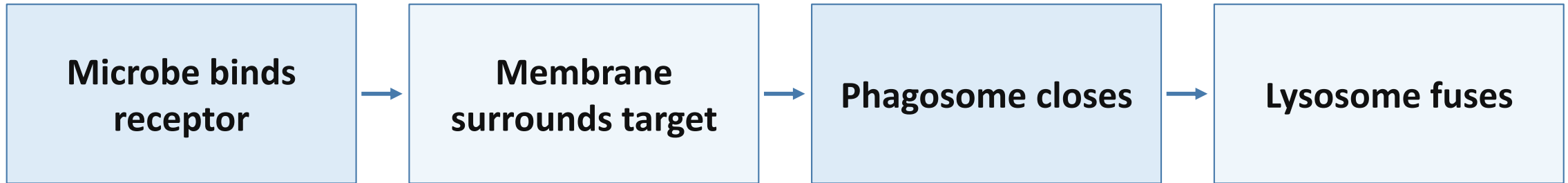


- Efficient ingestion usually depends on surface receptors and opsonins.

Opsonins improve phagocytic recognition

- Opsonins coat particles and enhance binding to phagocytes.
- Major opsonins include IgG, C3b/iC3b, and plasma lectins.
- Phagocytes express receptors that recognize these bound molecules.
- Receptor-mediated binding triggers engulfment.

How a phagosome becomes a destructive compartment



- The resulting phagolysosome concentrates microbicidal mechanisms.
- Actin remodeling is required for engulfment.

Three main intracellular killing systems

Reactive oxygen species

NADPH oxidase initiates oxygen radical generation.

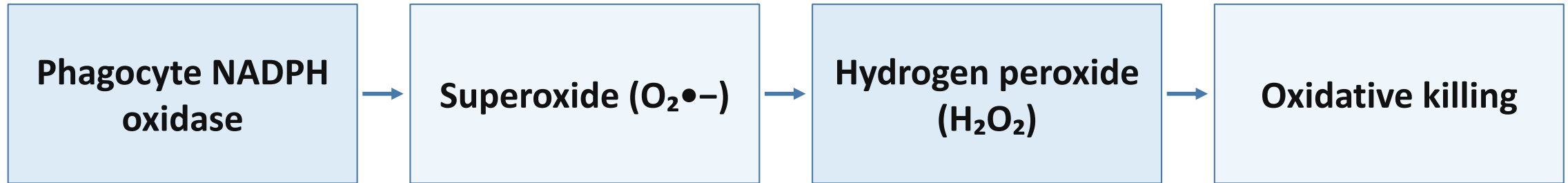
Reactive nitrogen species

Inducible nitric oxide synthase contributes reactive nitrogen products.

Lysosomal components

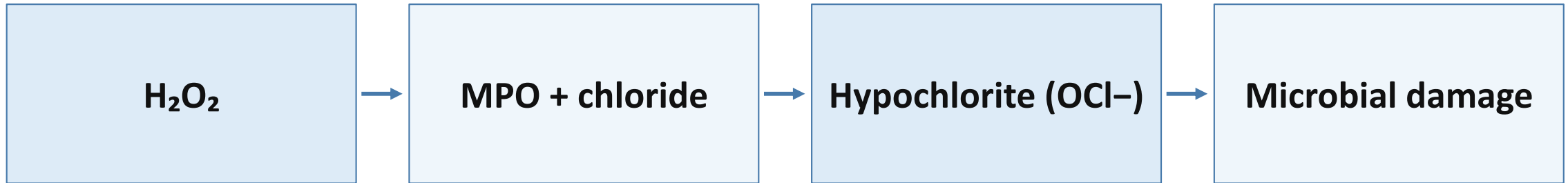
Granule enzymes and antimicrobial proteins degrade ingested targets.

Respiratory burst: NADPH oxidase pathway



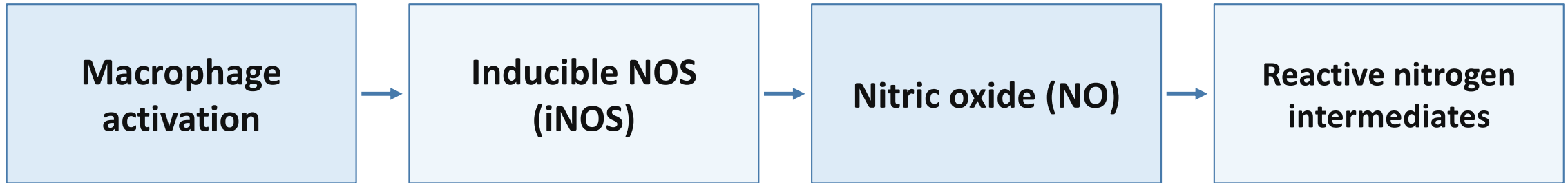
- Assembly of oxidase components follows phagocyte activation.
- The respiratory burst increases cellular oxygen consumption.

Myeloperoxidase creates a potent microbicidal oxidant



- Myeloperoxidase is abundant in neutrophil azurophilic granules.
- MPO deficiency alone has limited clinical impact because killing systems overlap.

Nitric oxide contributes to microbial killing



- NO can react with superoxide to form peroxynitrite.
- These reactive species damage microbial proteins, lipids, and nucleic acids.

Lysosomal enzymes require controlled compartmentalization

Microbicidal molecules are effective—but potentially destructive to host cells.

- Lysosomes fuse with phagosomes to deliver degradative enzymes.
- Acid hydrolases and granule components participate in digestion.
- Extracellular release can damage nearby tissue.

Neutrophil extracellular traps (NETs)

DNA-based scaffold

Activated neutrophils may release chromatin as extracellular traps.

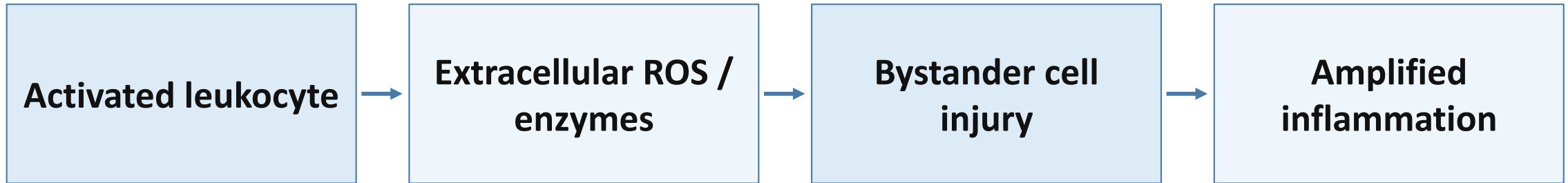
Antimicrobial components

Microbes can be trapped together with granule antimicrobial proteins.

Potential cost

Extracellular neutrophil products can contribute to host injury.

Why host defense can injure normal tissue



- Collateral damage is a recognized cost of microbial elimination.
- Excessive or misdirected responses can dominate the disease process.

Inflammatory mediators come from two sources

Preformed cell stores

Histamine can be released rapidly from mast-cell granules.

New cell synthesis

Cytokines and eicosanoids are generated after stimulation.

Plasma precursors

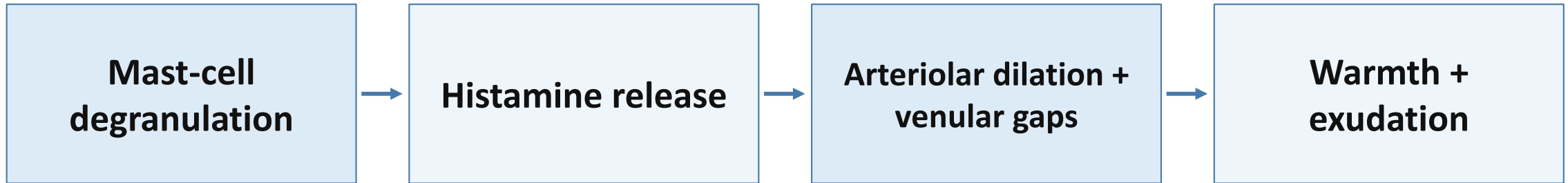
Complement and kinin pathways are activated from circulating precursors.

Mediator networks amplify and restrain inflammation

Inflammatory mediators are not simply “on/off” signals.

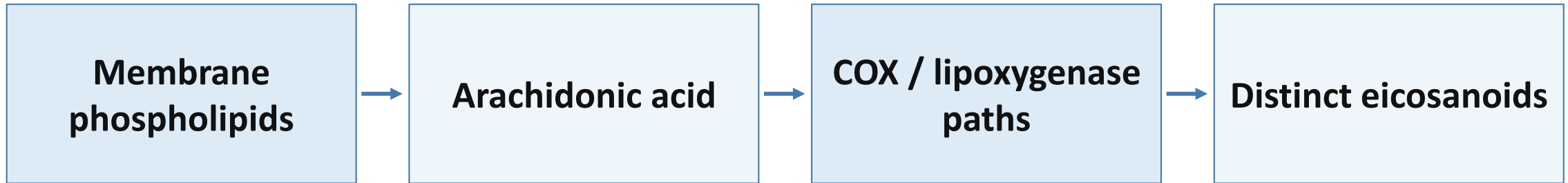
- One mediator can provoke release of additional mediators.
- Different mediators often have overlapping actions.
- Short half-lives and enzymatic inactivation restrict their effects.
- Opposing mediators actively limit the response.

Histamine links mast-cell activation to vascular change



- Antigen-bound IgE and complement fragments can provoke degranulation.
- Histamine acts prominently through H1 receptors.

Arachidonic acid generates different mediator families



- Prostaglandins, thromboxane, leukotrienes, and lipoxins have different effects.
- Enzyme branch determines biological output.

Prostaglandins: Selected inflammatory effects

Mediator group	Principal effect	Clinicopathologic relation
PGE ₂	Pain sensitization; fever	Pain and elevated temperature
PGI ₂ / PGD ₂	Vasodilation	Increased flow / redness
Thromboxane A ₂	Vasoconstriction; platelet effects	Vascular / hemostatic interface

Leukotrienes have distinct cellular and vascular actions

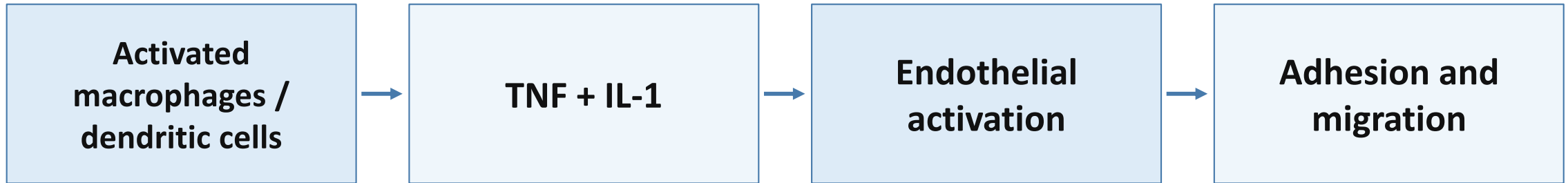
Mediator	Major effect	Interpretation
LTB ₄	Neutrophil chemotaxis and activation	Recruitment toward inflammatory focus
LTC ₄ / LTD ₄ / LTE ₄	Increased permeability	Exudation
LTC ₄ / LTD ₄ / LTE ₄	Bronchoconstriction	Airway reaction in asthma

Lipoxins help restrain further neutrophil influx

Arachidonic acid metabolites can also be anti-inflammatory.

- Lipoxins inhibit neutrophil adhesion to endothelium.
- They reduce neutrophil chemotaxis.
- A change toward resolving mediators supports termination.

TNF and IL-1 coordinate leukocyte recruitment

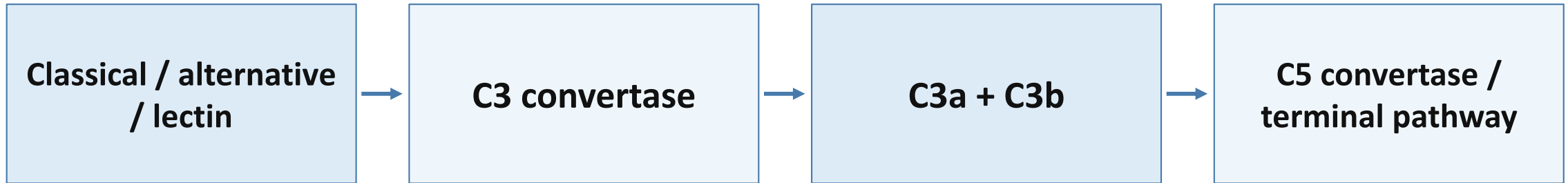


- They also stimulate other cells and contribute to systemic inflammation.
- TNF and IL-1 are powerful but potentially harmful cytokine signals.

Chemokines provide positional information

- Inflammatory chemokines form gradients that guide migrating cells.
- Chemokines presented on endothelial surfaces promote integrin activation.
- Chemokine receptors transmit signals that reorganize cell motility.

Complement activation converges on C3



- The pathways have different triggers but share central effector steps.
- Complement proteins circulate as inactive precursor molecules.

Complement has three major effector functions

Inflammation

C3a and C5a stimulate vascular reactions; C5a attracts leukocytes.

Opsonization

C3b and iC3b coat microbes and enhance phagocytosis.

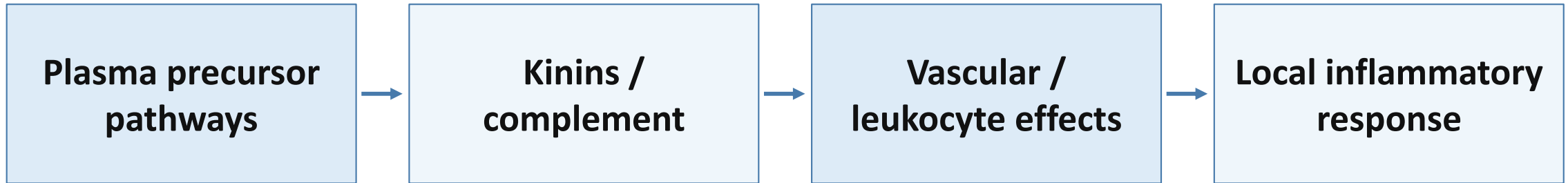
Cell lysis

C5b–C9 forms the membrane attack complex on susceptible microbes.

Mediator-to-effect map for acute inflammation

Inflammatory event	Important mediator examples
Vasodilation	Histamine; prostaglandins
Permeability ↑	Histamine; bradykinin; LTC ₄ /LTD ₄ /LTE ₄
Neutrophil chemotaxis	C5a; IL-8 / CXCL8; LTB ₄
Endothelial activation	TNF; IL-1
Pain / fever	Bradykinin and prostaglandins; cytokine effects

Other soluble mediators extend the network



- Bradykinin promotes vascular permeability and pain.
- Multiple mediators may operate simultaneously at a single site.

Morphology reflects the dominant tissue reaction

Dilated vessels

Congestion produces a visibly hyperemic focus.

Extravascular fluid

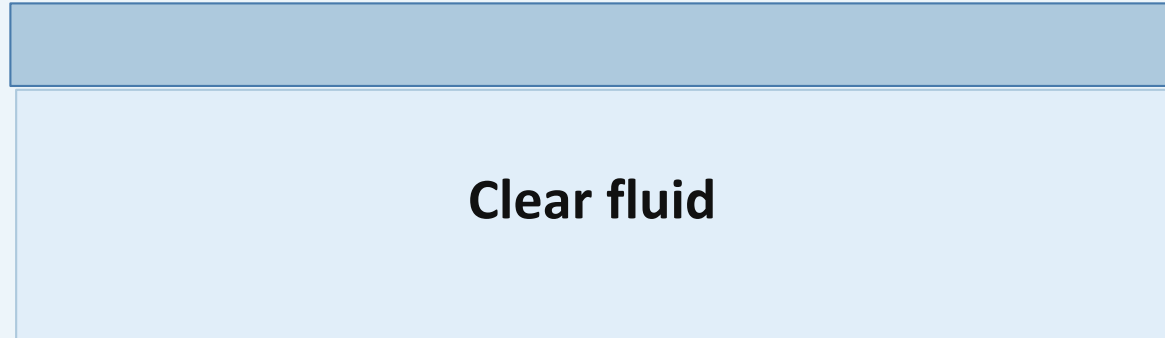
Edema results when fluid accumulates outside vessels.

Leukocyte infiltrate

Typically, neutrophils dominate early acute tissue inflammation.

Serous inflammation: Fluid-rich, cell-poor reaction

Serous fluid



Clear fluid

Schematic — not a tissue micrograph

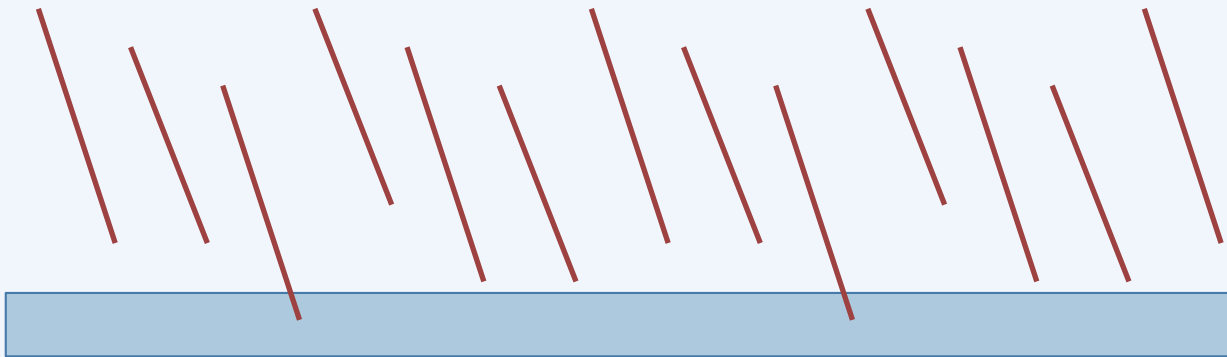
**Fluid accumulation with
few leukocytes**

The serous pattern requires context

- Serous fluid may accumulate in a blister after skin injury.
- Serous-cavity effusions may arise from inflammatory leakage or mesothelial secretion.
- An effusion is not automatically inflammatory: Noninflammatory causes also exist.

Fibrinous inflammation: Plasma fibrinogen escapes

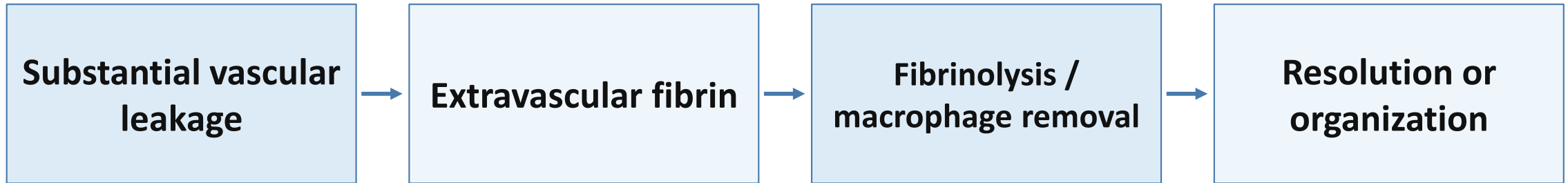
Fibrin deposition



Schematic — not a tissue micrograph

**Fibrinogen leakage →
extracellular fibrin**

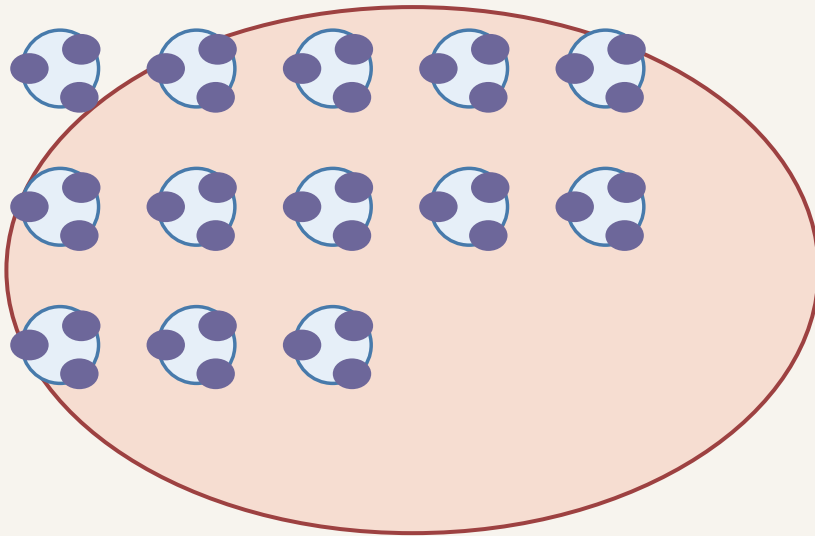
Fibrinous exudate can resolve—or organize



- Persistent fibrin promotes fibroblast and vascular ingrowth.
- Organization can produce fibrous adhesions or serosal thickening.

Purulent inflammation: Pus and liquefactive necrosis

Suppurative focus



Schematic — not a tissue micrograph

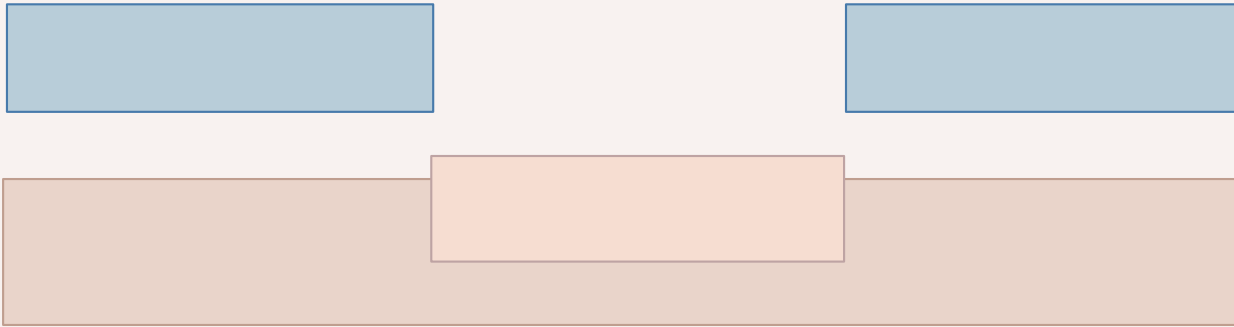
**Neutrophils + liquefied
necrotic debris**

Abscess: A localized collection of pus

- Pyogenic organisms can trigger local suppuration.
- Central necrotic fluid contains dead leukocytes and tissue debris.
- A neutrophil-rich zone and reactive vascular changes often surround it.
- Later organization may wall off the lesion and leave fibrous tissue.

An ulcer requires necrosis at or near a surface

Surface loss



Schematic — not a tissue micrograph

**Sloughing of inflamed
necrotic tissue**

Morphologic patterns: What distinguishes them?

Pattern	Dominant feature	Example in source
Serous	Relatively cell-poor fluid	Skin blister
Fibrinous	Fibrin-rich surface / cavity exudate	Pericarditis
Purulent	Neutrophils + necrotic debris	Acute appendicitis / abscess
Ulcerative	Surface tissue loss after necrosis	Peptic ulcer

Acute inflammation has three broad outcomes

Complete resolution

Stimulus eliminated; Debris and fluid cleared; Tissue regenerates.

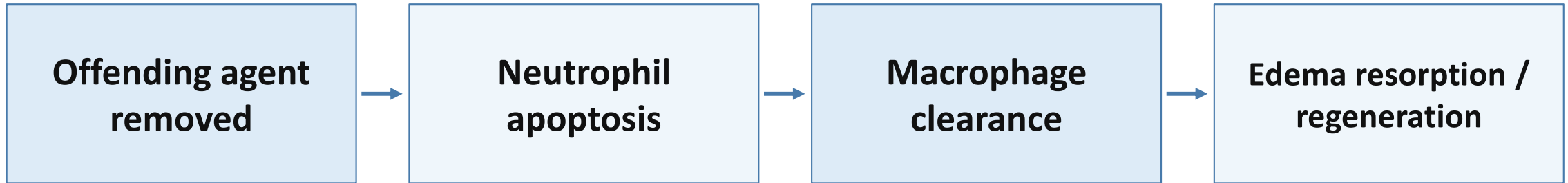
Healing with fibrosis

Severe injury, nonregenerating tissue, or persistent fibrin becomes scar.

Chronic inflammation

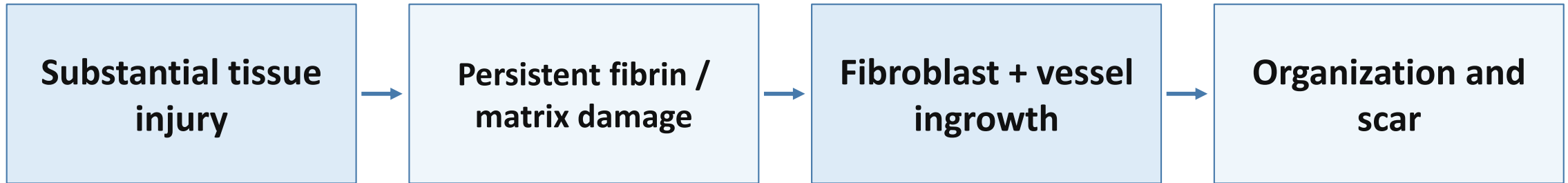
Failure to eliminate the stimulus sustains the inflammatory reaction.

Resolution requires coordinated cleanup



- Resolution is most likely after limited, short-lived injury.
- Tissue structure and function can return toward normal.

Fibrosis follows damage that cannot fully regenerate



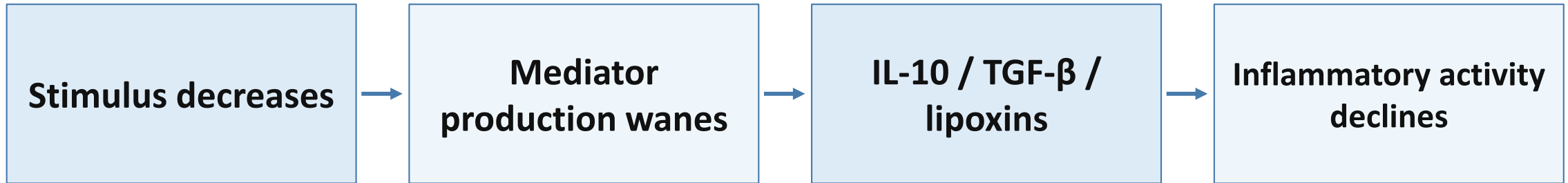
- A fibrovascular response replaces tissue that cannot be restored.
- Serosal fibrin may organize into adhesions.

Persistence can convert acute into chronic inflammation

Failure of stimulus elimination prevents complete resolution.

- A persistent agent can sustain macrophage recruitment and activation.
- Acute and chronic cell populations may overlap within lesions.
- Long-standing injury may progress to tissue destruction and fibrosis.

Active signals help terminate the acute response



- Short-lived neutrophils also disappear by apoptosis.
- The termination program limits collateral tissue injury.

Clinical application: A superficial blister

A patient develops a fluid-filled blister after a mild burn, without a thick purulent exudate.

- What morphologic pattern is most likely?
- Why can clear fluid accumulate beneath a damaged epithelial surface?
- What additional finding would suggest suppurative inflammation?

Clinical application: A localized abscess

A tissue lesion contains a central liquefied focus rich in neutrophils and cell debris.

- Identify the inflammatory pattern and the term for the localized collection.
- Explain how neutrophil products contribute to central tissue liquefaction.
- Predict one potential later outcome if tissue destruction is extensive.

Apply the vascular–cellular sequence

An acutely inflamed venule becomes congested, and neutrophils begin adhering to its endothelial surface.

- What hemodynamic change favors neutrophil margination?
- Distinguish molecules responsible for rolling and stable adhesion.
- Name the migration step mediated in part by PECAM-1.

Clinical findings can be traced back to mechanism

Red + warm

Vasodilation increases blood flow and causes vascular congestion.

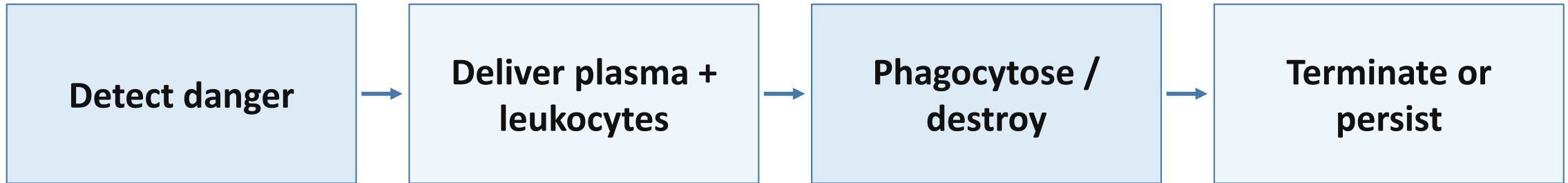
Swollen + painful

Permeability, edema, and inflammatory mediators cause these manifestations.

Neutrophil-rich

Leukocyte recruitment followed by activation produces neutrophilic exudation.

Acute inflammation, integrated



- Mechanisms are protective when spatially and temporally controlled.
- Persistent stimuli or extensive tissue injury alter the outcome.

Core concepts to retain

- The vascular triad is dilation, increased permeability, and leukocyte recruitment.
- Selectins → chemokine-mediated integrin activation → adhesion → diapedesis.
- Phagocytes use ROS, reactive nitrogen species, and lysosomal components.
- The tissue result is resolution, fibrosis, or chronic inflammation.

Primary reference

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026).
- Chapter 3: Inflammation and Repair.
- Acute inflammation and connected vascular, leukocyte, mediator, morphology, and outcome sections.