

Outcomes of Acute Inflammation

Resolution • Fibrosis • Chronic inflammation

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Three principal outcomes

Acute inflammatory reaction

COMPLETE RESOLUTION

Injury eliminated; Tissue architecture restored

FIBROSIS / SCAR

Lost tissue or fibrin replaced by collagen

CHRONIC INFLAMMATION

Unresolved stimulus or impaired healing

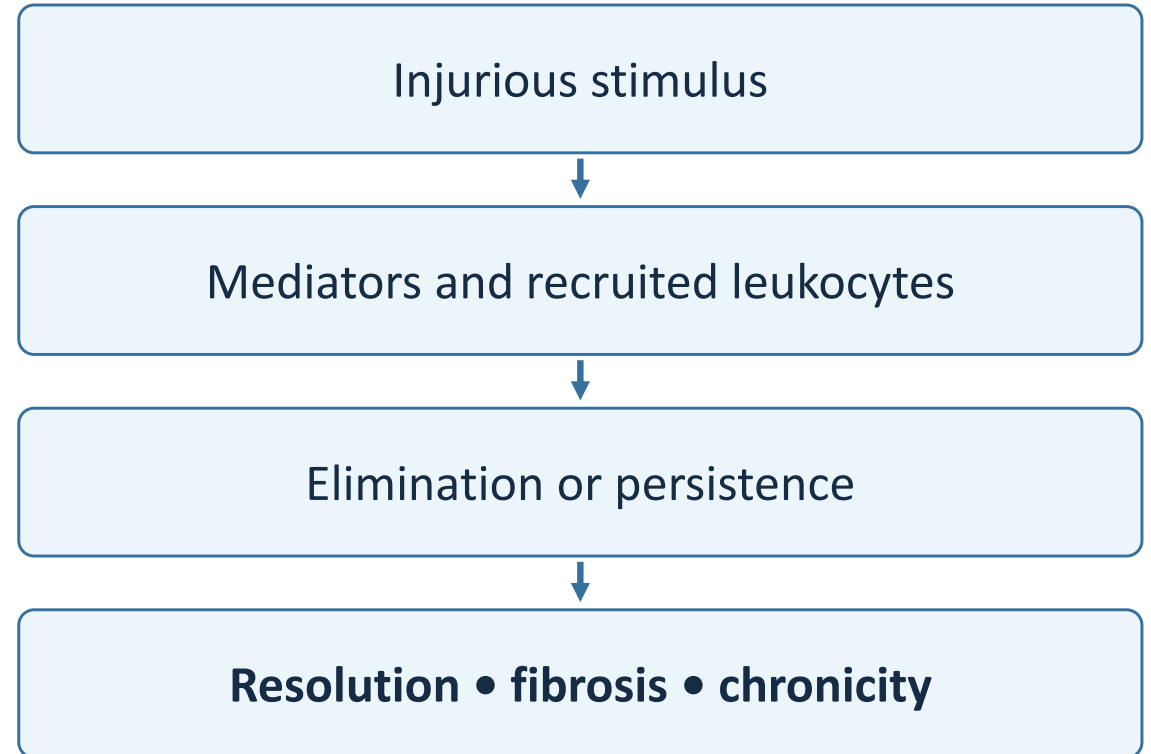
Outcome depends on the insult, injured tissue, and host response

Learning objectives

- Predict which tissue injuries resolve, scar, or become chronic
- Explain clearance and regenerative steps in resolution
- Describe organization of fibrin and collagenous scarring
- Recognize mechanisms and morphology of chronicity

Acute inflammation is a transient host response

- Recognition of microbes or dead tissue initiates inflammation
- Vascular and leukocyte responses eliminate the offender
- The response must then subside or change character



The initiating injury shapes the outcome

- The nature of the insult affects its removability
- Injury intensity affects the amount of necrosis
- Duration influences whether inflammation persists

Nature

Microbes, sterile injury,
foreign material

Intensity

Extent of parenchymal
damage

Duration

Brief insult versus
persistence

Distribution

Focal versus extensive
involvement

More extensive injury limits restitution

- Limited damage leaves viable cells and tissue support intact
- Substantial destruction increases the need for connective tissue
- The same inflammatory mediator cascade can produce different endpoints

Limited injury

Viable cells and
framework preserved

Extensive injury

Parenchyma or stromal
framework lost

Duration of the insult matters

- Transient stimuli permit the inflammatory reaction to decline
- Persistent stimuli maintain inflammatory cell recruitment
- Prolonged stimulation favors chronic inflammation

Stimulus removed → mediators fall



Short-lived neutrophils disappear



Clearance and repair can proceed

Regenerative capacity differs among tissues

- Labile epithelia can replace lost cells
- Stable tissues can proliferate after injury
- Permanent cells have little or no regenerative ability

Labile cells

Continuously renewed
epithelia

Stable cells

Quiescent but inducible
proliferation

Permanent cells

Neurons and cardiac
muscle

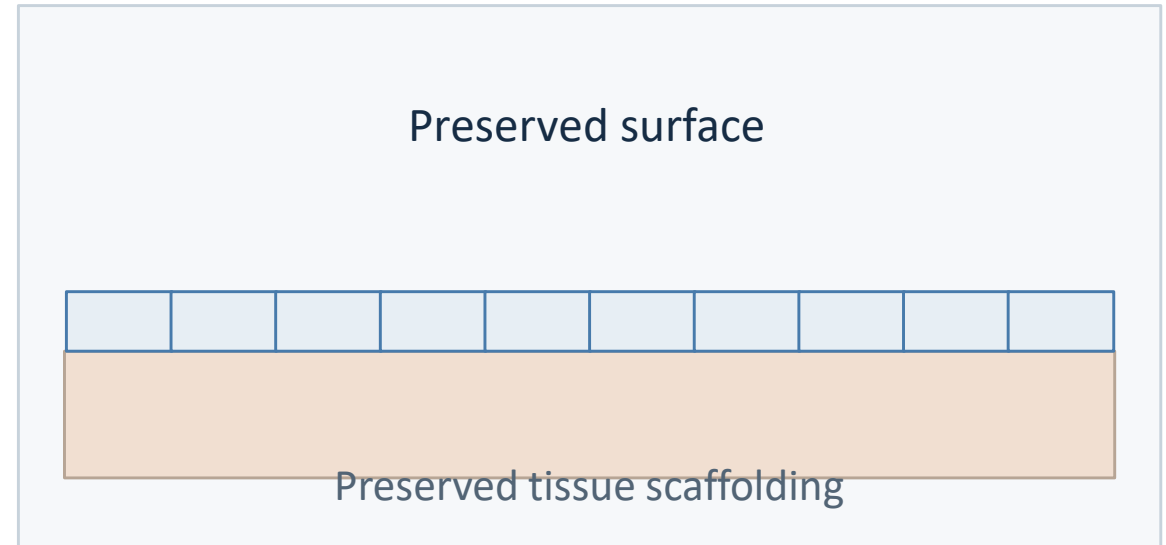
Net result

Capacity constrains
restoration

Intact extracellular matrix supports regeneration

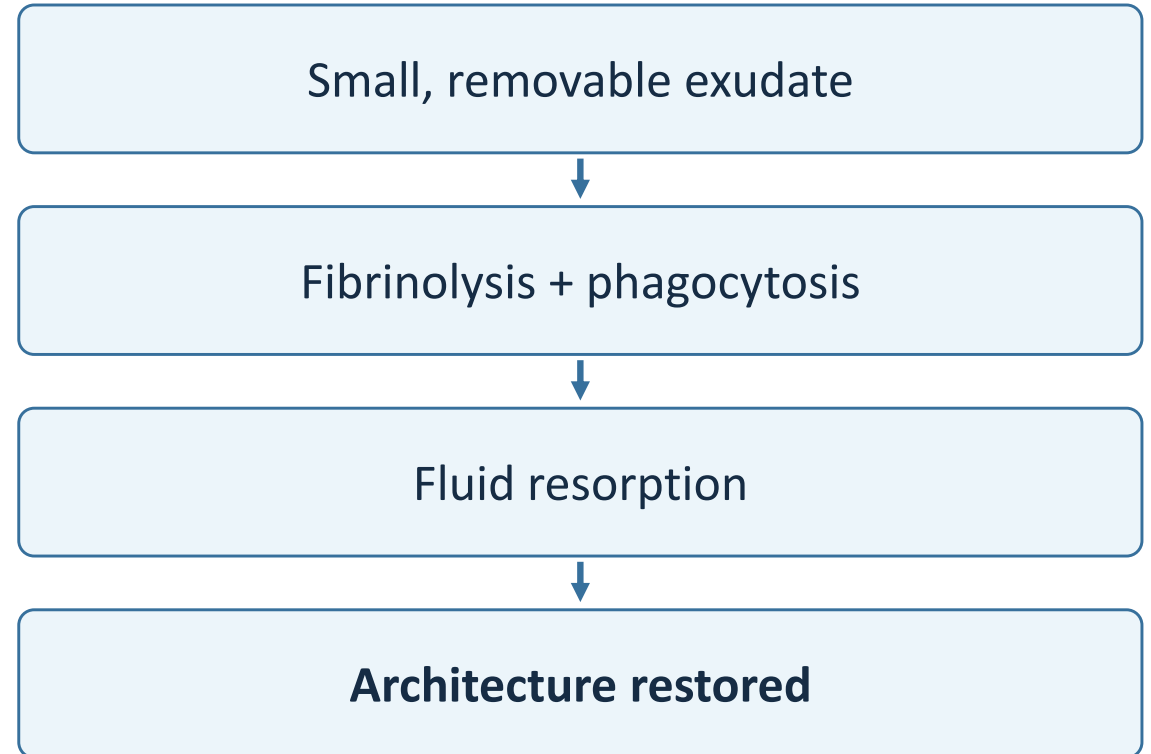
- Surviving cells need an appropriate supporting scaffold
- Mild epithelial injury may preserve underlying connective tissue
- Stromal disruption increases reliance on scar formation

Schematic tissue response



The burden of exudate influences repair

- Exudates must be removed for architecture to normalize
- Persistent fibrin may resist clearance
- Uncleared fibrin can become organized into connective tissue



Host response also modifies the outcome

- Leukocyte antimicrobial activity must be effective
- The response must turn off after clearance
- Repair depends on successful regeneration or matrix replacement

Defense

Removal of offending agent

Control

Antiinflammatory stop signals

Cleanup

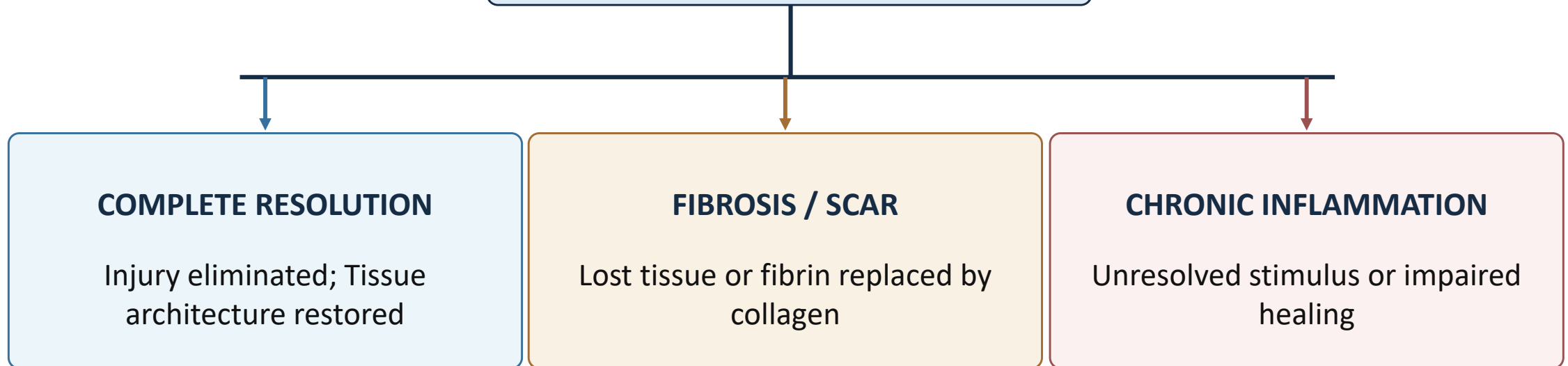
Debris and exudate clearance

Repair

Cell and matrix responses

A practical outcome decision tree

Acute inflammatory reaction



Outcome depends on the insult, injured tissue, and host response

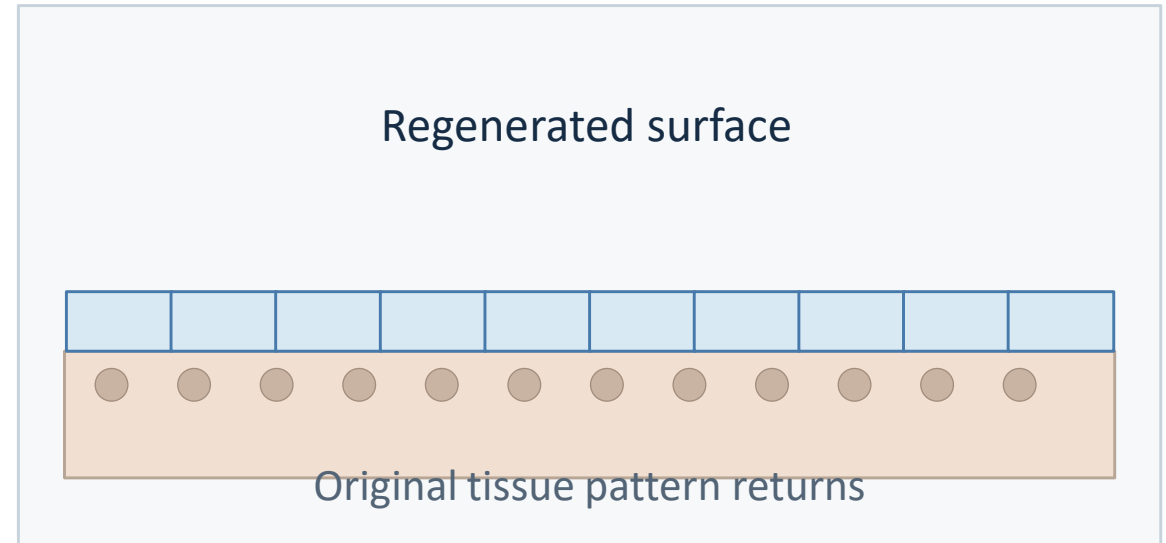
Comparing outcomes across four dimensions

Feature	Resolution	Fibrosis	Chronicity
Trigger	Brief, removed	Major injury / fibrin	Persistent or unhealed
Tissue fate	Restored pattern	Collagen replacement	Ongoing injury + repair
Key cells	Macrophages; Regenerating cells	Fibroblasts; Endothelium	Macrophages; Lymphocytes
Final state	Near-normal	Scar	Prolonged inflammation

Resolution restores normal architecture

- Successful inflammation ends after offender elimination
- Debris, microbes, and edema fluid are removed
- Damaged parenchymal cells regenerate when possible

Schematic tissue response



Conditions favoring complete resolution

- The injurious agent is quickly removed
- Tissue damage is limited or short-lived
- Damaged cells have adequate regenerative potential

Short duration

Inflammatory stimulus
ends

Little necrosis

Limited tissue
destruction

Viable cells

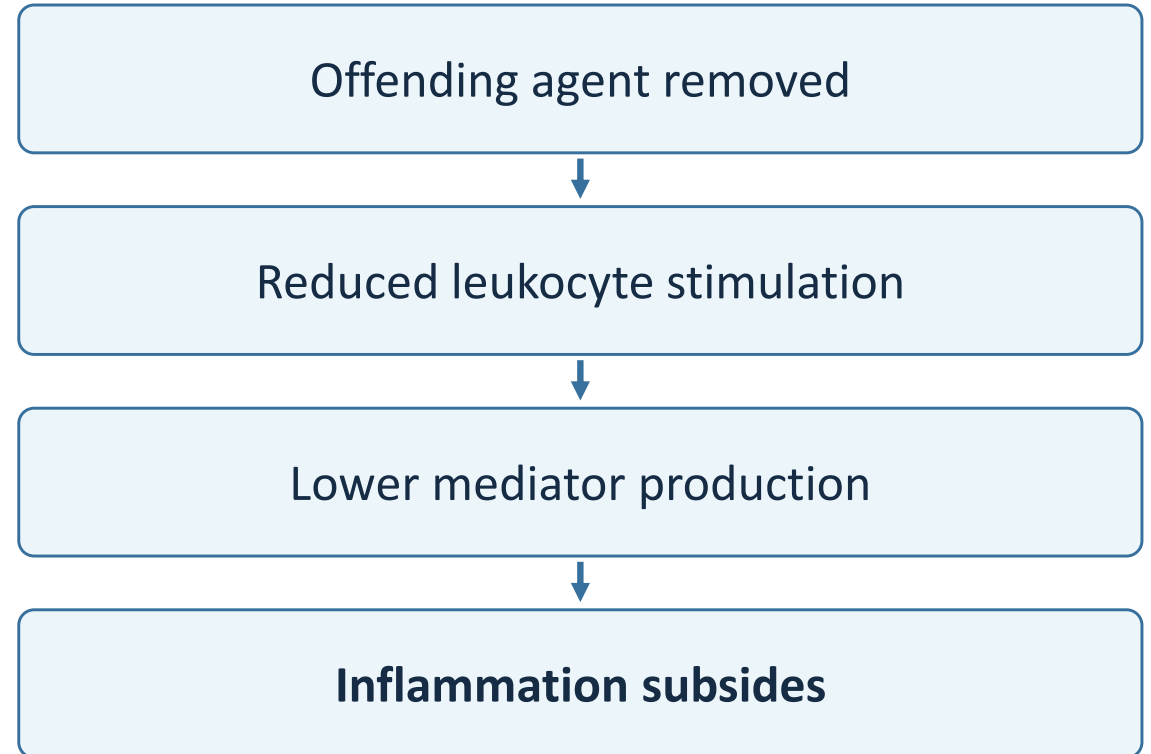
Parenchymal
regeneration

Preserved matrix

Normal organization
returns

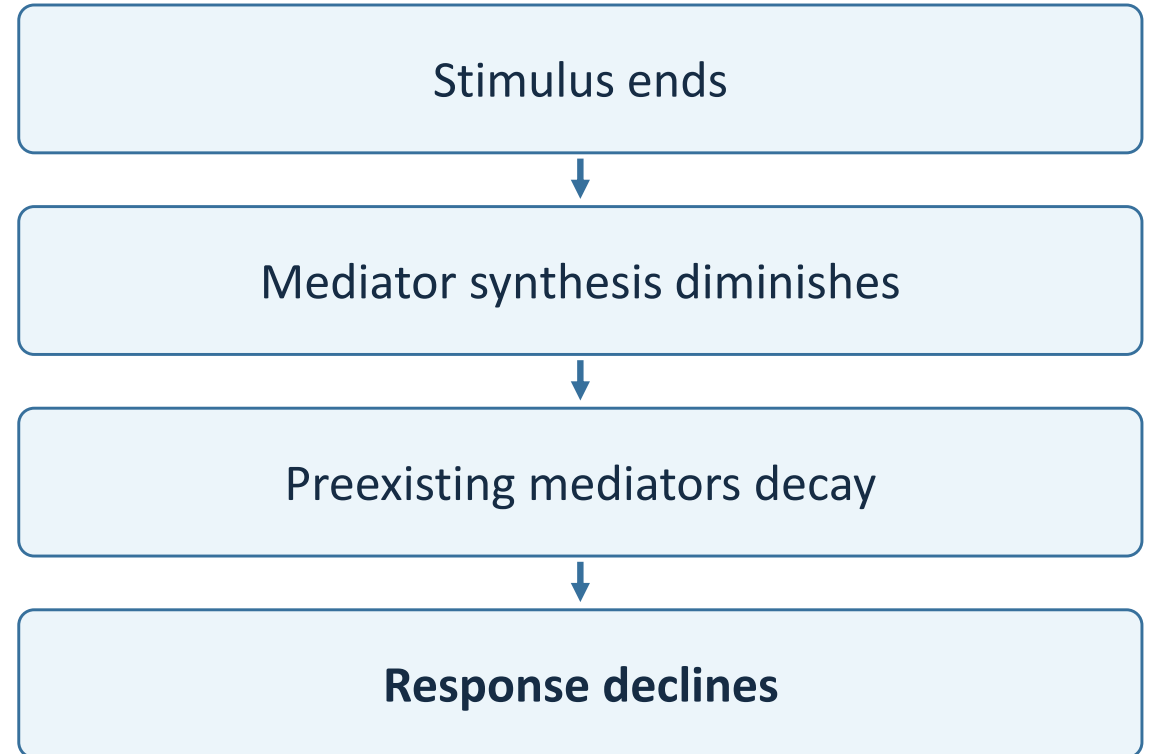
Removal of the insult permits shutdown

- Microbes or debris activate sentinel and recruited cells
- Elimination reduces continued inflammatory stimulation
- Active inflammatory mediator production declines



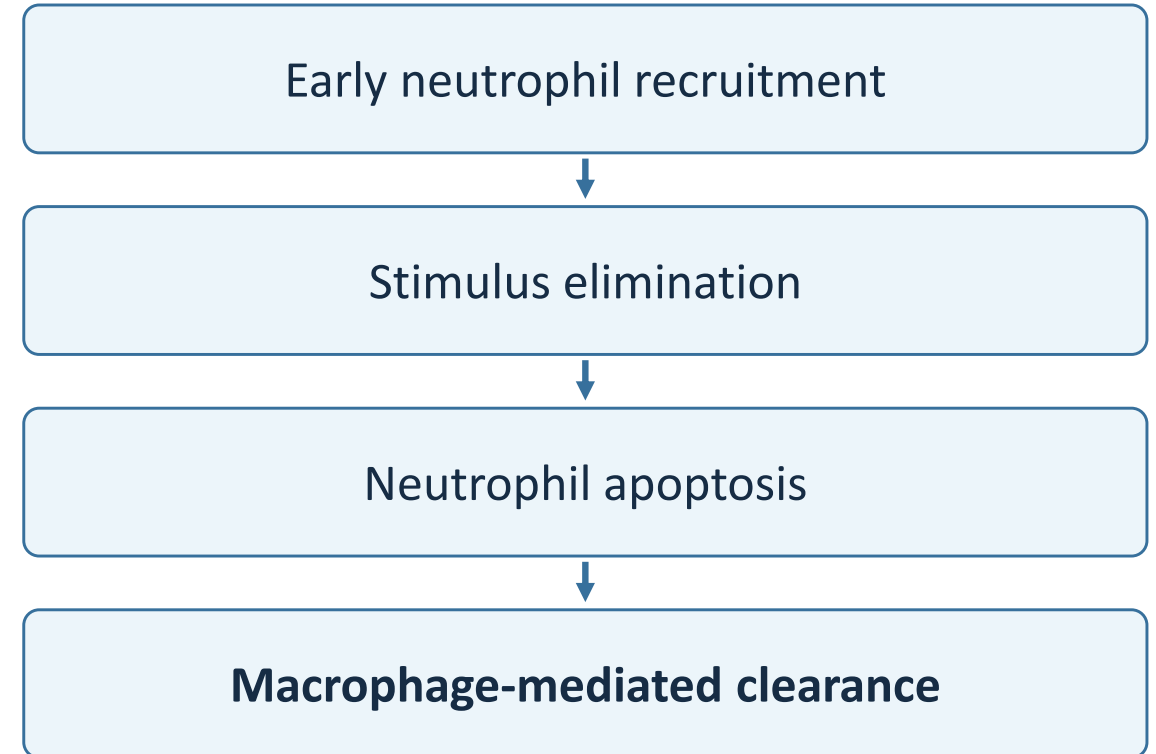
Inflammatory mediators are short-lived

- Production depends on ongoing stimulation
- Many mediators are rapidly degraded
- Disappearance of signals reduces vascular and leukocyte activation



Neutrophil turnover supports termination

- Acute inflammatory exudates are initially neutrophil-rich
- Neutrophils have a limited lifespan in inflamed tissues
- Their apoptosis contributes to inflammatory termination



Active stop signals complement passive decline

- Stopping mediator production is not the entire story
- Inflammation induces mechanisms that limit the reaction
- These signals help prevent collateral tissue damage

Passive decline

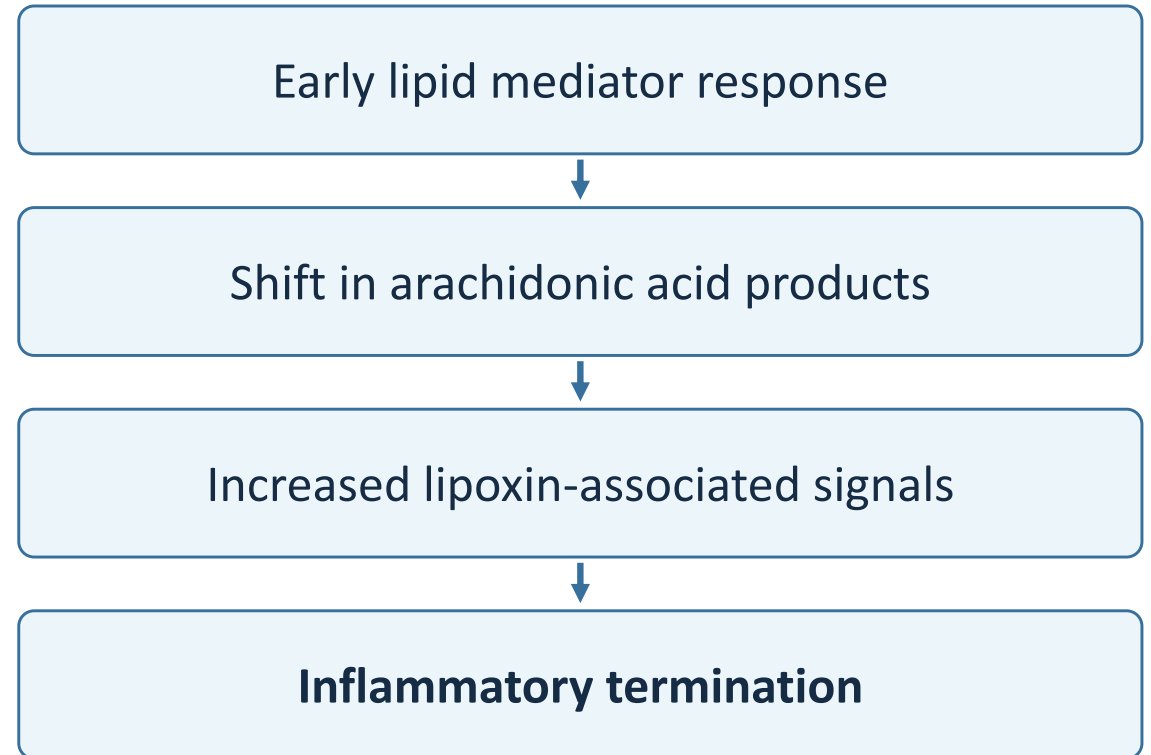
Stimulus disappears;
Mediators decay

Active termination

Lipoxins; Anti-inflammatory cytokines

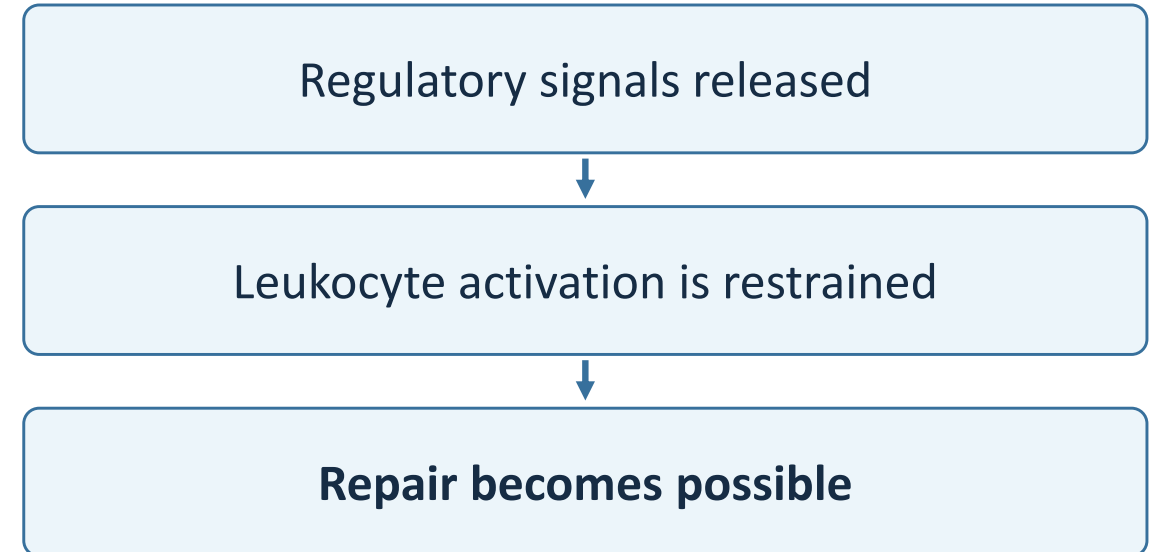
Lipid mediator switching promotes termination

- Leukotrienes are pro-inflammatory lipid mediators
- The response may switch toward lipoxin generation
- Lipoxins are associated with anti-inflammatory regulation



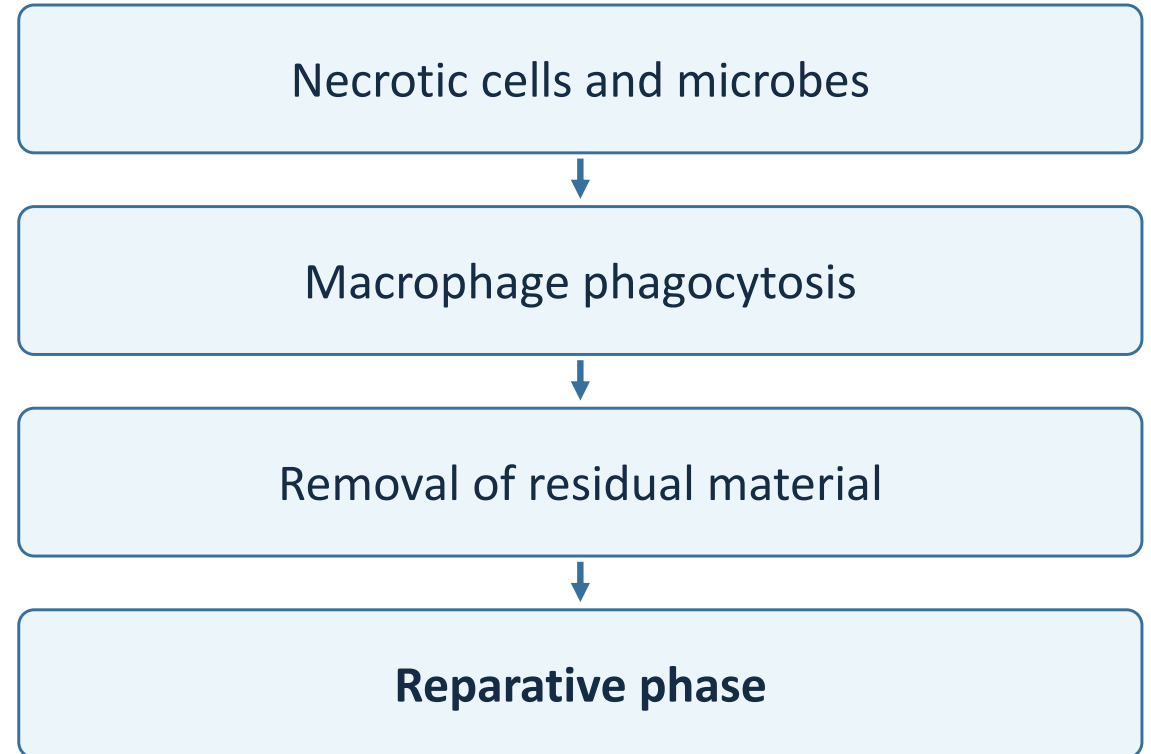
IL-10 and TGF- β restrain inflammation

- Macrophages and other cells generate anti-inflammatory signals
- IL-10 limits inflammatory responses
- TGF- β limits inflammation and also participates in tissue repair



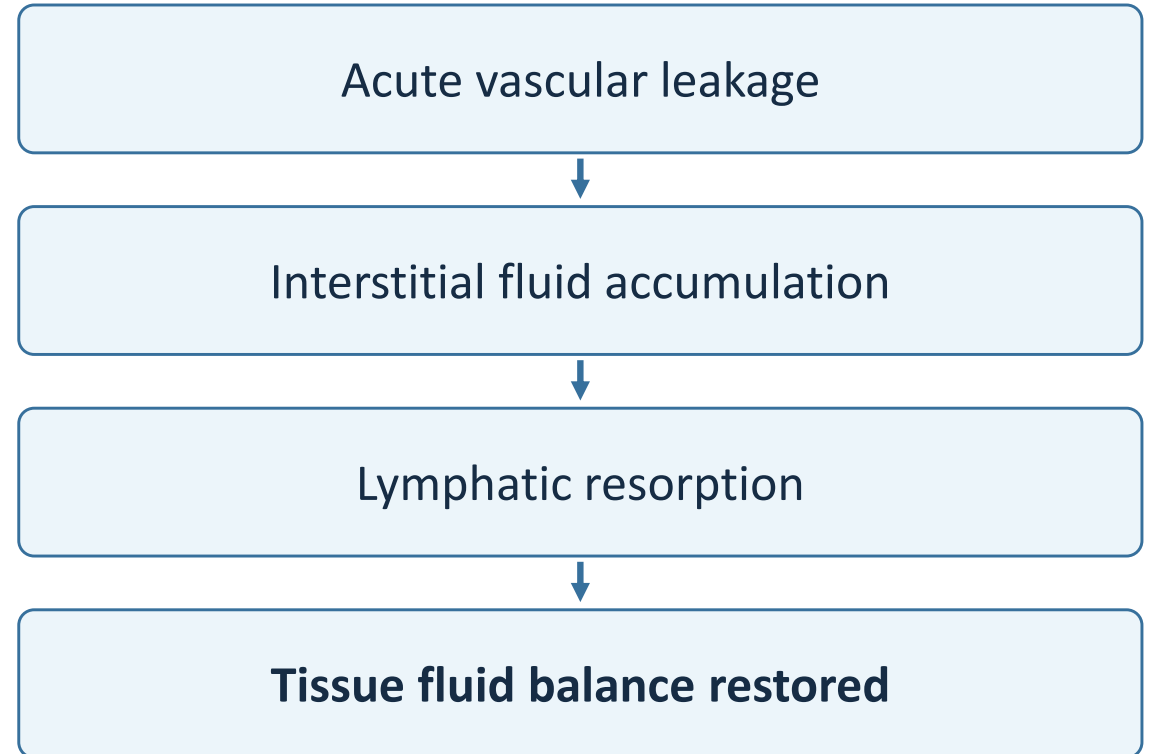
Macrophages clear the inflammatory residue

- Phagocytes remove microbes and cellular debris
- Macrophages are prominent in cleanup and repair
- Clearance creates conditions for tissue regeneration



Lymphatics remove excess edema fluid

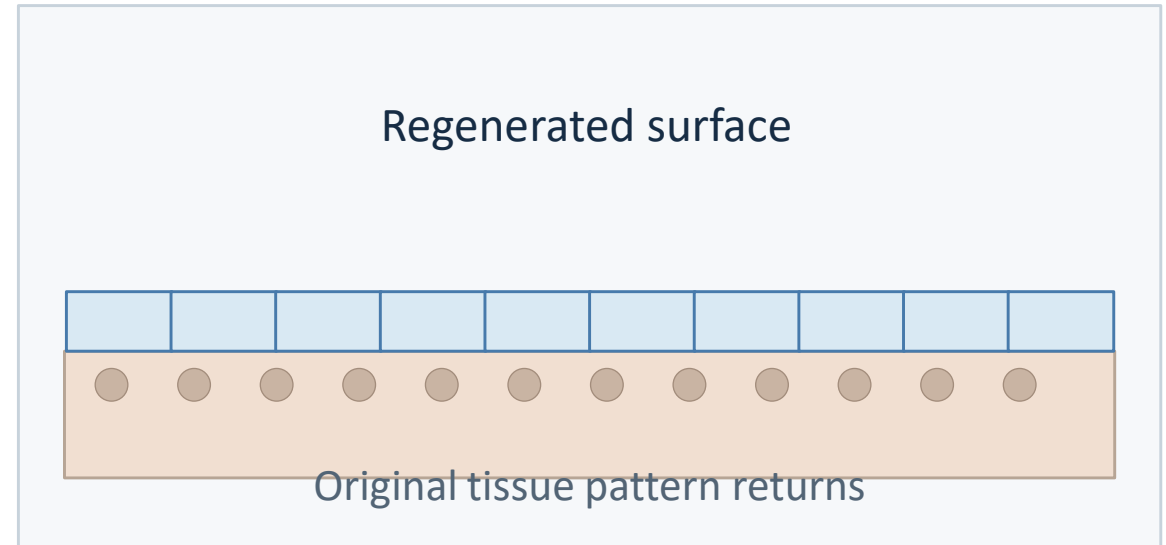
- Vascular permeability creates protein-rich exudation
- Fluid must be resorbed for normal architecture to return
- Lymphatic drainage contributes to edema clearance



Regeneration requires surviving cellular sources

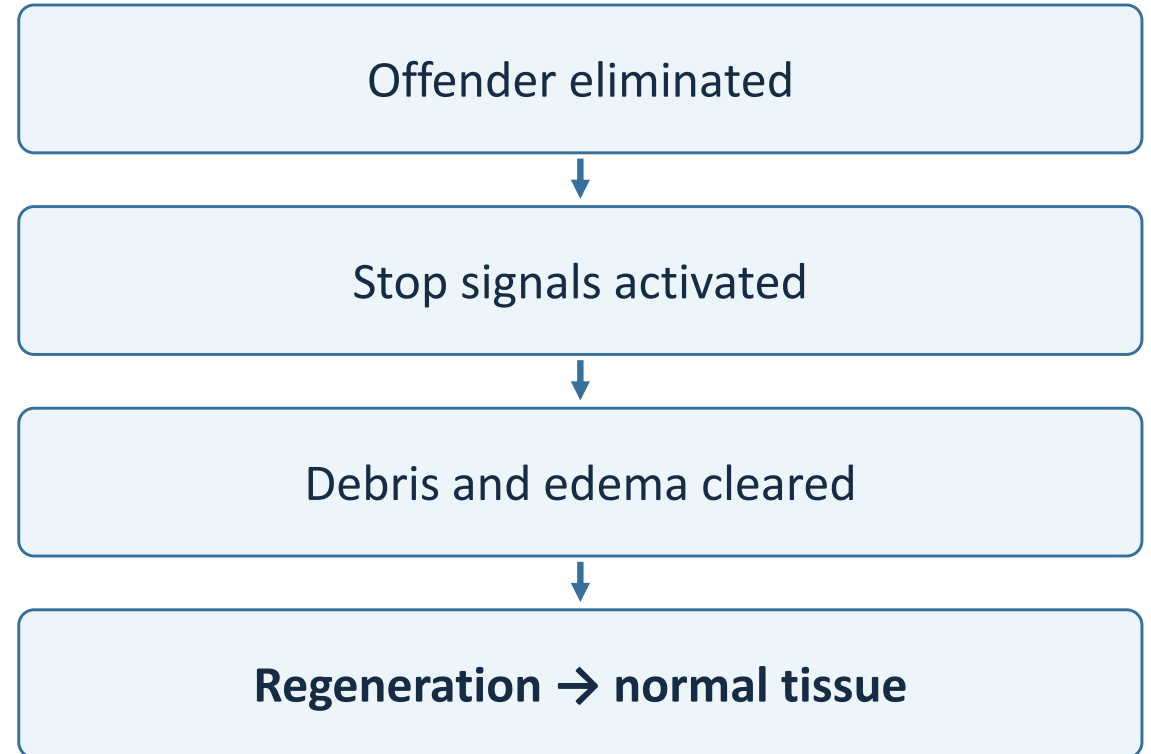
- Surviving mature cells may proliferate
- Stem or progenitor cells can replace injured populations
- Cell–extracellular matrix interactions support correct restitution

Schematic tissue response



Resolution has a recognizable sequence

- Eliminate the cause and restrict new inflammatory recruitment
- Remove neutrophils, necrotic material, and edema
- Replace injured cells without permanent architectural distortion



Inflammatory cessation is not identical to resolution

- Stopping leukocyte recruitment ends active inflammation
- Complete resolution additionally clears residual exudate
- Return of normal architecture requires restitution of damaged cells

Inflammation stopped

Mediator and cell
recruitment decline

Resolution achieved

Debris removed; Tissue
restored

Serous-space exudates may resolve

- Proteolytic digestion can liquefy inflammatory exudates
- Macrophages and resorption mechanisms clear material
- Absent tissue necrosis, normal architecture may return

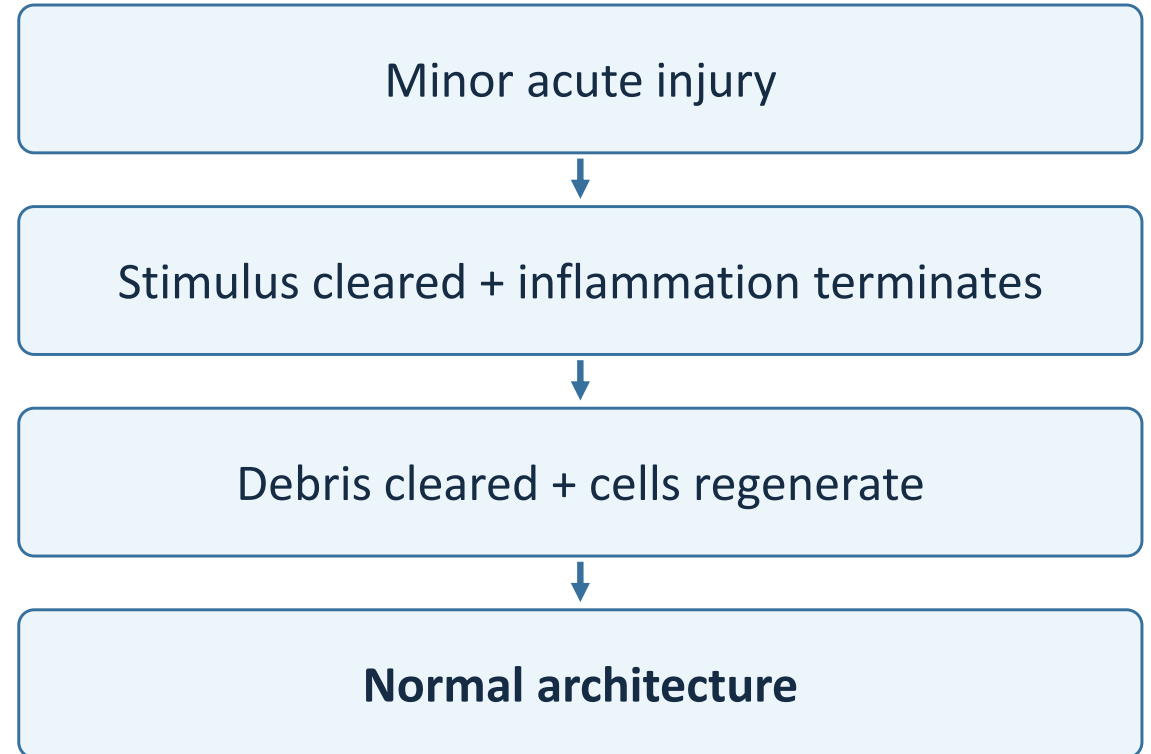
Removable exudate



Proteolysis and clearance permit resolution

A successful resolution pathway

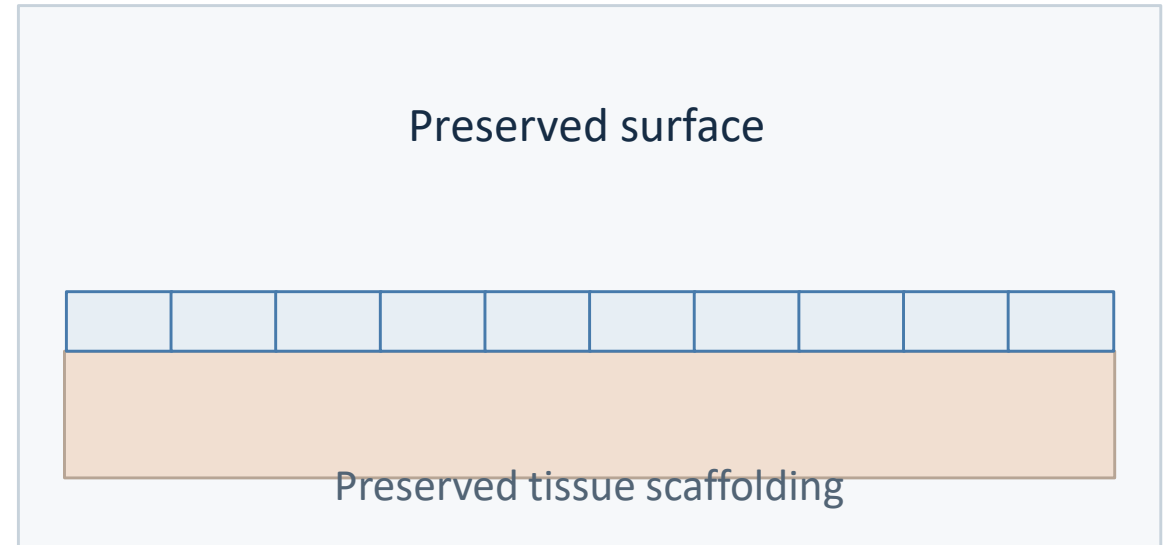
- Preserved framework enables ordered cell replacement
- Macrophages and lymphatics clear what inflammation produced
- The endpoint is near-complete structural and functional recovery



Why superficial epithelial injury often resolves

- The underlying stromal scaffold may be preserved
- Surviving epithelial cells or stem cells can proliferate
- Restitution may occur with minimal connective tissue replacement

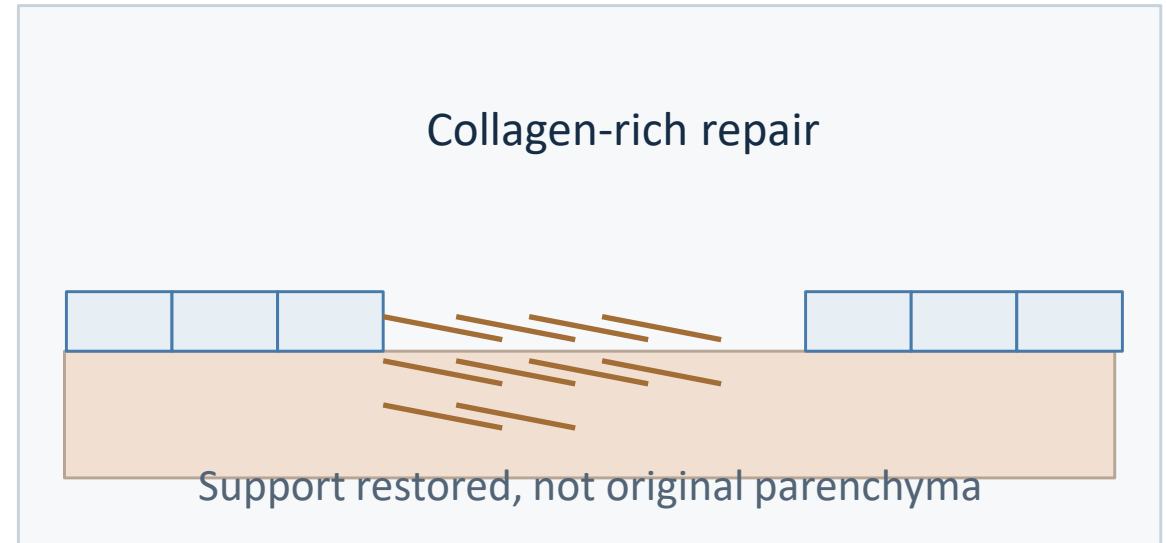
Schematic tissue response



Fibrosis replaces lost tissue with connective tissue

- Repair cannot always regenerate the original parenchyma
- Collagen-rich connective tissue provides structural support
- A scar repairs a defect but does not replicate native architecture

Schematic tissue response



Three conditions favor scarring

- Substantial tissue destruction
- Injury in tissue incapable of regeneration
- Abundant fibrin that cannot be adequately cleared

Severe damage

Necrotic loss of native tissue

Poor regeneration

Limited surviving cell proliferation

Scaffold injury

ECM cannot support restitution

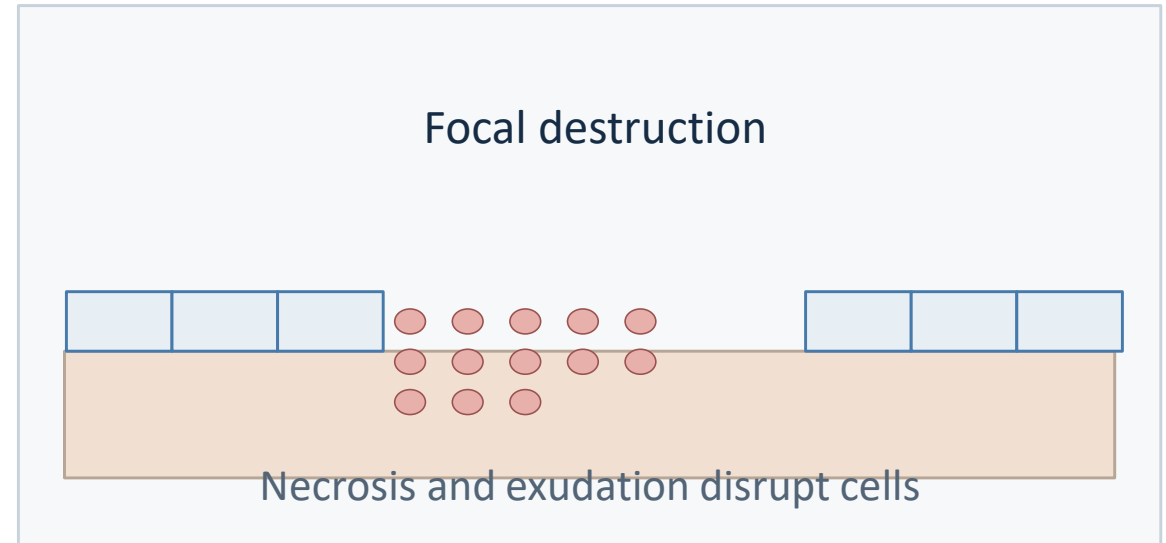
Persistent fibrin

Organization of exudate

Destruction can outstrip regeneration

- Necrosis removes functional parenchymal cells
- Destruction may extend into supporting connective tissue
- Connective tissue deposition fills the persistent defect

Schematic tissue response



Nondividing cells predispose to permanent loss

- Regeneration depends on the proliferative potential of cells
- In permanent tissues, injured specialized cells are not readily replaced
- Connective tissue repair compensates for loss but may impair function

Regenerating tissue

Surviving cells rebuild
parenchyma

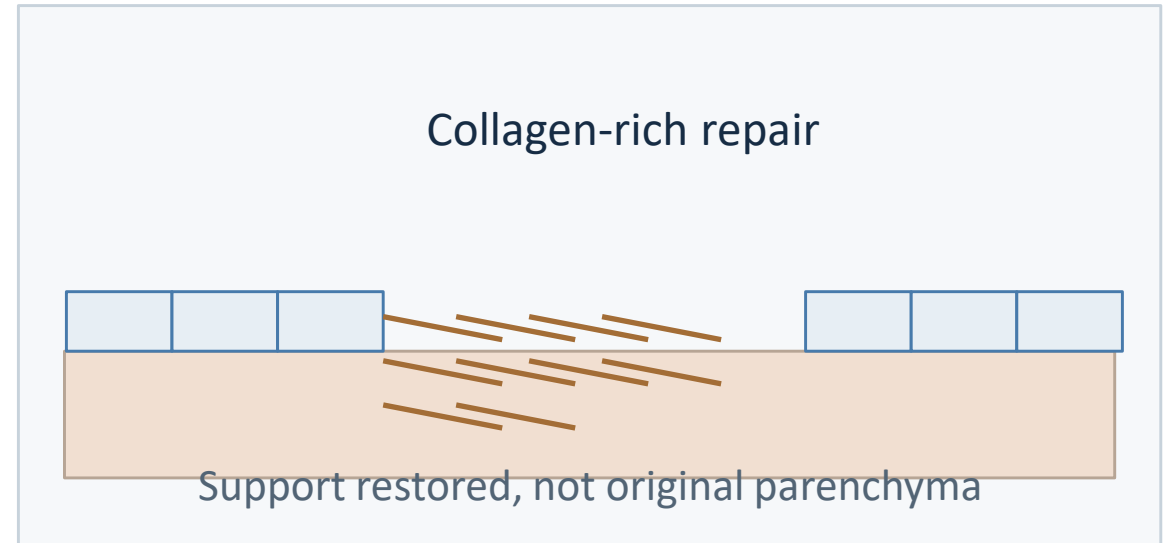
Permanent-cell tissue

Scar replaces missing
cells

Damaged stromal framework changes the repair mode

- Extracellular matrix organizes tissue architecture
- Loss of the supporting framework impairs orderly restitution
- Scar formation becomes necessary even if some cells can divide

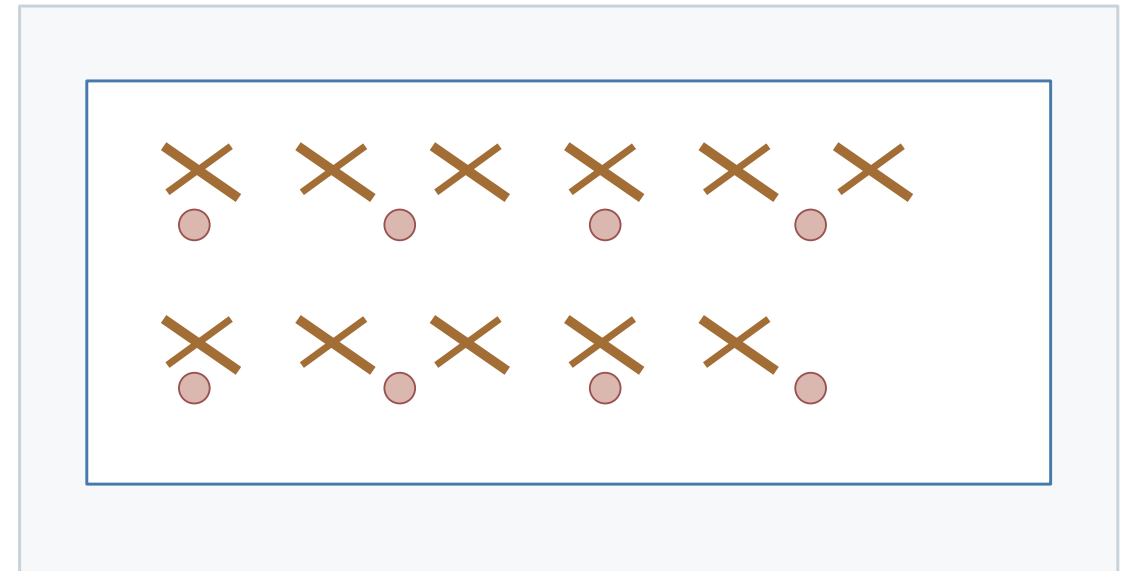
Schematic tissue response



Persistent fibrin provides a substrate for organization

- Abundant fibrin can accumulate in tissues or serous spaces
- If it is not cleared, fibroblasts and blood vessels grow into it
- The exudate is converted into fibrous tissue

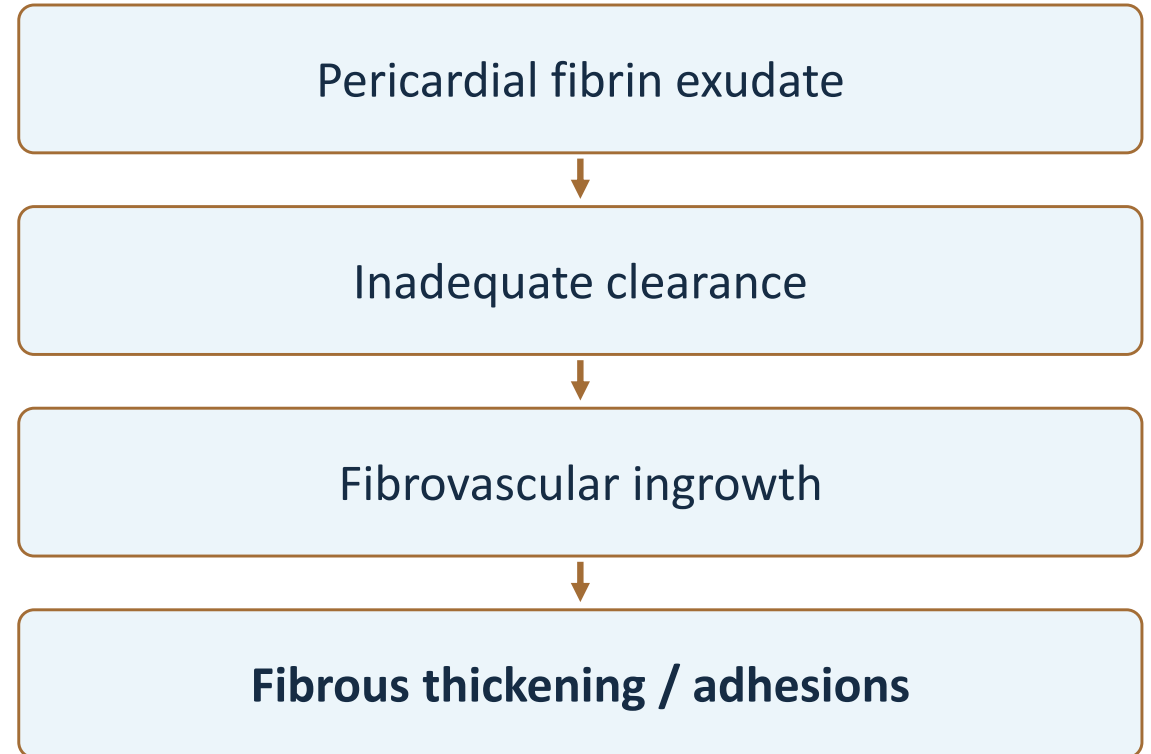
Organized fibrin exudate



Fibrovascular ingrowth converts exudate to scar

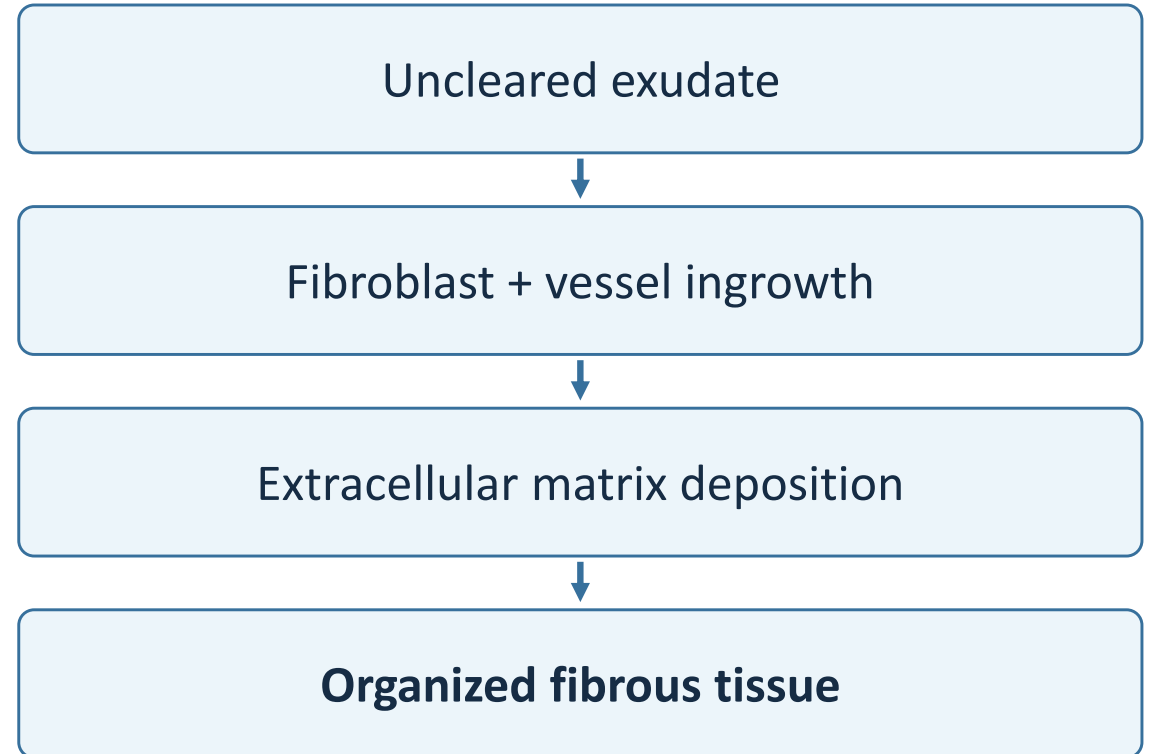
Fibrinous pericarditis may heal by fibrosis

- Fibrin can cover the pericardial surfaces
- Clearance may occur by fibrinolysis and macrophages
- Failure of clearance permits organization and thickening



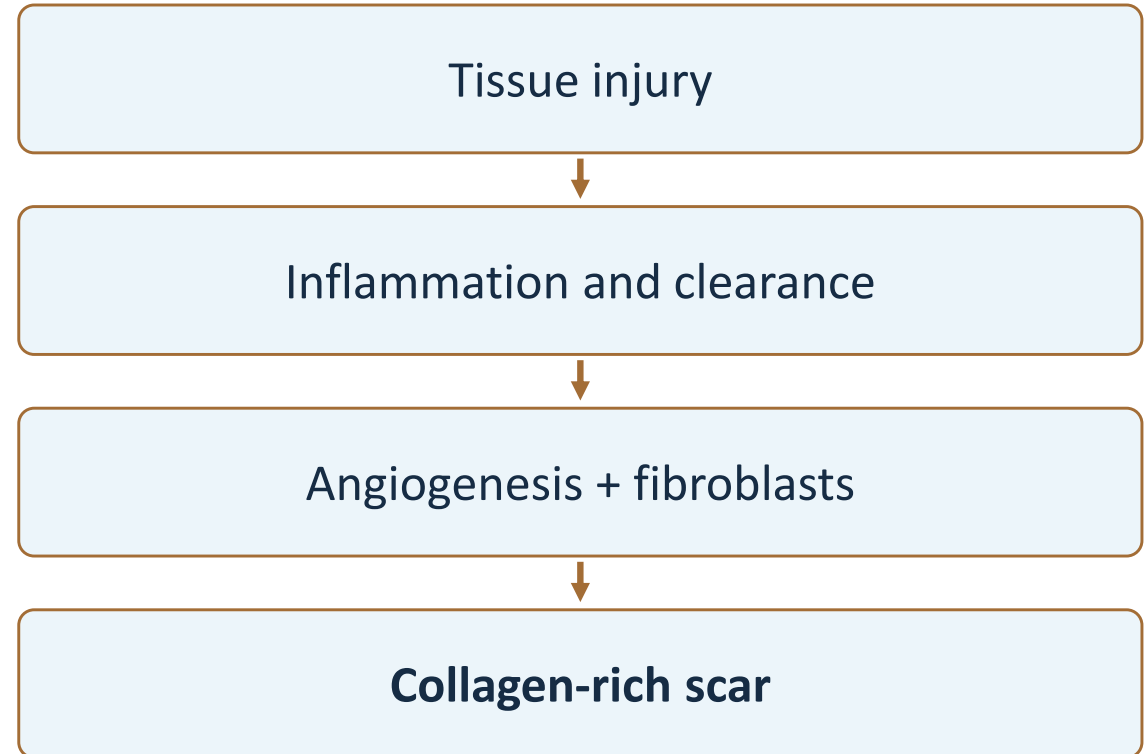
Organization means ingrowth into exudate

- Organization is not merely persistence of fibrin
- Fibroblasts and new blood vessels infiltrate the deposit
- Collagen-rich connective tissue replaces the former exudate



Scar formation involves cellular proliferation

- Inflammation initiates a reparative response
- Angiogenesis supplies new capillaries
- Fibroblasts proliferate and deposit extracellular matrix



Granulation tissue is a provisional repair matrix

- New small vessels form in injured tissue
- Activated fibroblasts accumulate
- Extracellular matrix deposition gradually becomes prominent

Endothelium

New capillary growth

Fibroblasts

Matrix synthesis

Macrophages

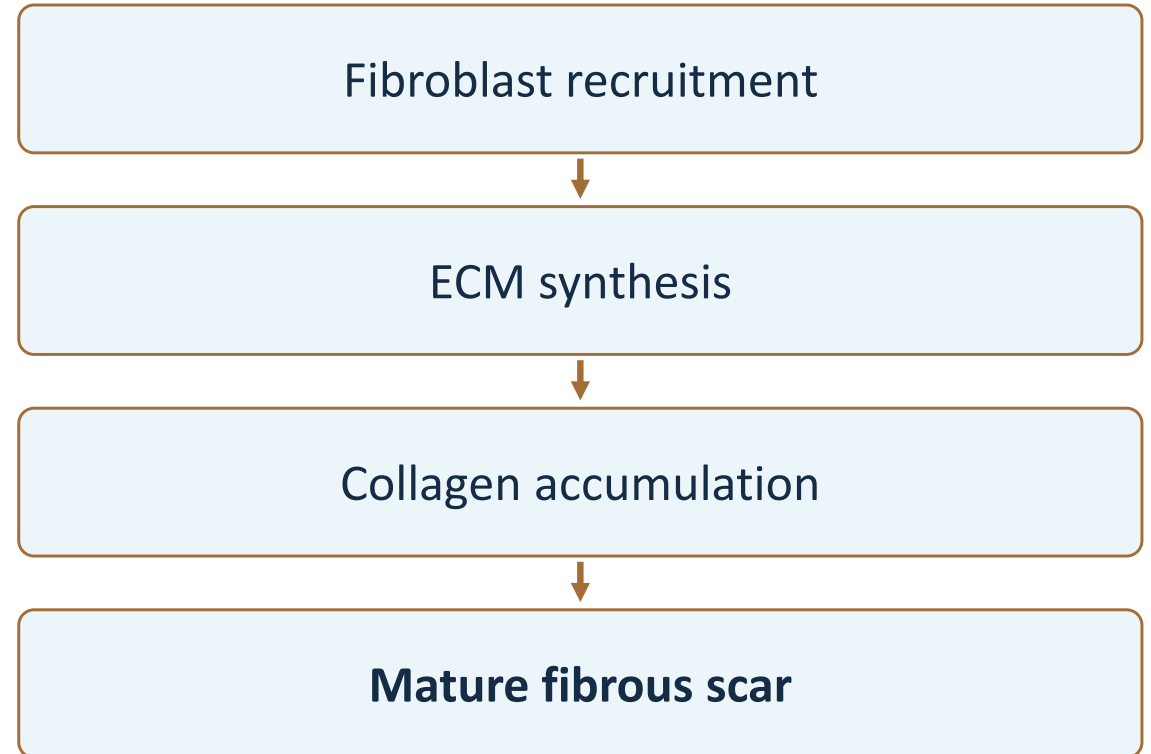
Cleanup and repair
signals

Provisional tissue

Organizes the defect

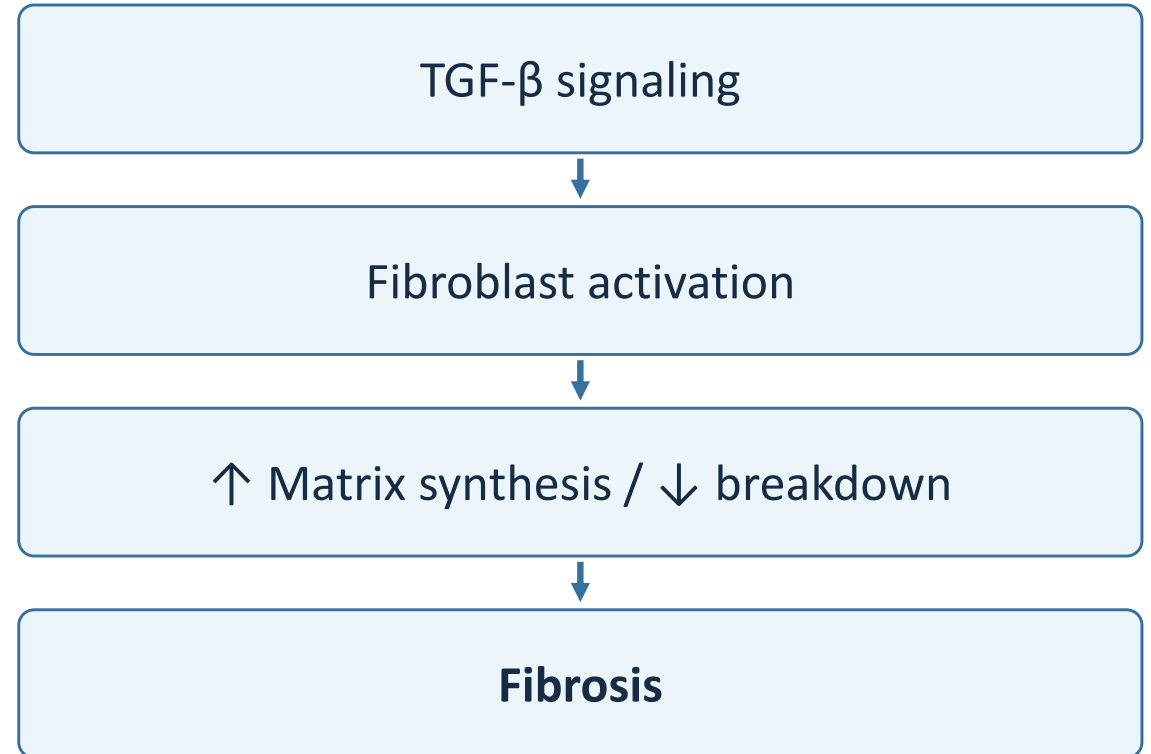
Collagen converts repair tissue into scar

- Fibroblasts synthesize collagen and other ECM proteins
- Matrix deposition provides mechanical support
- Progressive remodeling changes scar composition and architecture



TGF- β couples inflammation control to fibrosis

- TGF- β stimulates fibroblast migration and proliferation
- It promotes collagen and fibronectin synthesis
- It reduces extracellular matrix degradation



Scar maturation reduces vascularity

- Early repair tissue contains proliferating fibroblasts and vessels
- Collagen progressively accumulates as healing advances
- A mature scar is typically less cellular and less vascular

Early repair tissue

New vessels,
fibroblasts, provisional
ECM

Mature scar

Dense collagen, fewer
vessels

Fibrosis preserves continuity, not exact structure

- The scar may provide useful structural stability
- Lost specialized parenchymal function may remain reduced
- The amount and site of fibrosis determine functional impact

Regeneration

Native architecture and
cells restored

Fibrosis

Defect patched by
connective tissue

Scar-related dysfunction is organ-dependent

- Collagen does not always perform the function of lost tissue
- Anatomic location matters as much as scar size
- Fibrosis may alter mobility or organ mechanics

Myocardium

Cardiomyocyte loss →
scar

Serous cavity

Fibrous thickening /
adhesions

Skin

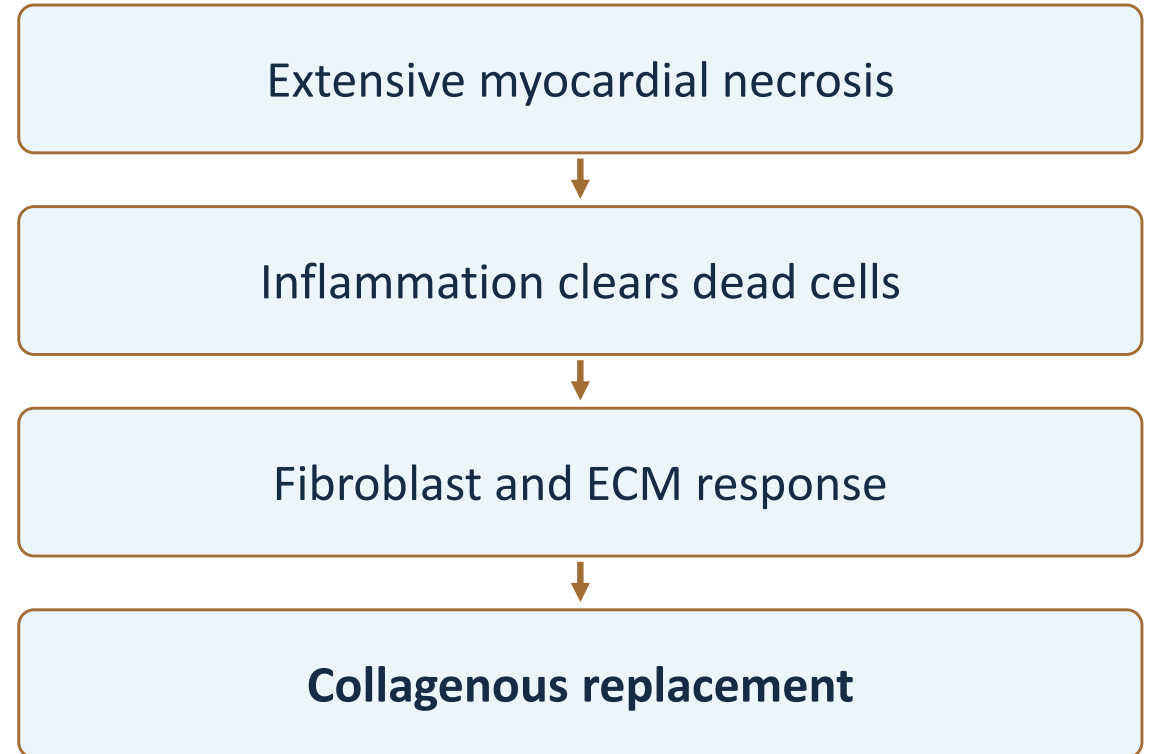
Scar substitutes for
missing dermis

Parenchyma

Reduction in native
tissue reserve

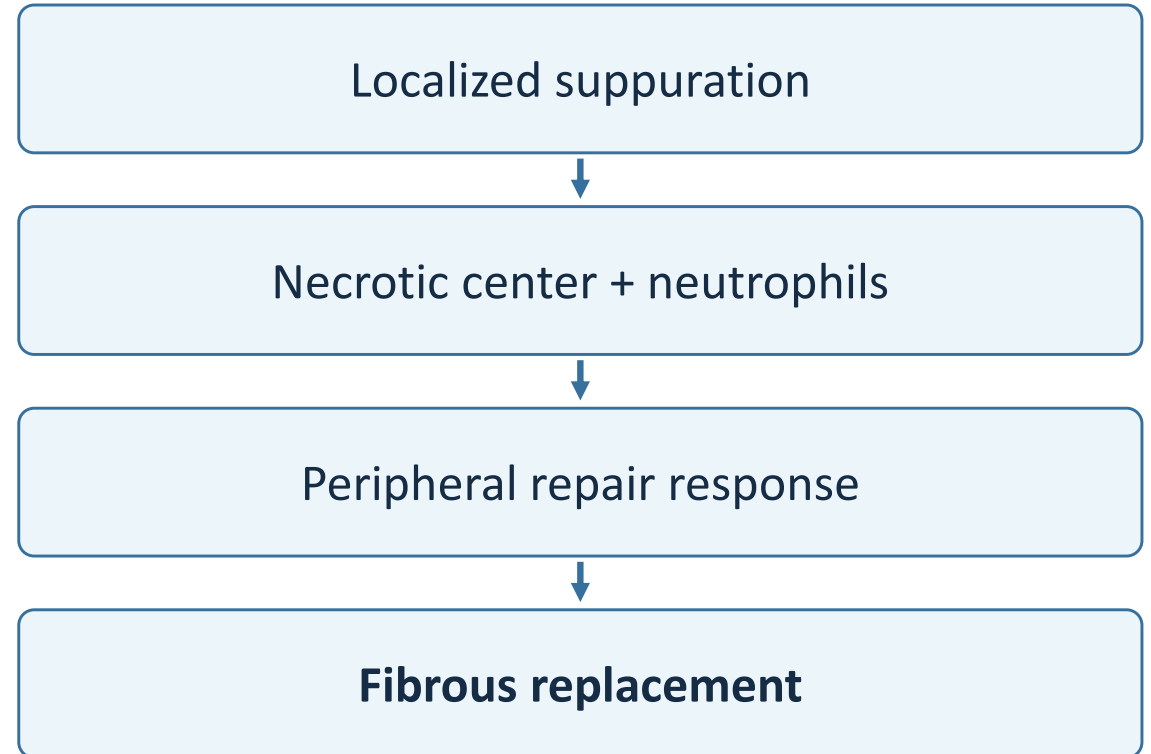
Infarcted myocardium illustrates scar replacement

- Cardiac muscle cells have very limited regenerative capacity
- Extensive ischemic necrosis destroys functional myocardium
- Fibrosis replaces the necrotic area rather than new cardiomyocytes



An abscess may end as a fibrous focus

- Pus contains neutrophils and liquefied necrotic debris
- An abscess may become surrounded by proliferating repair tissue
- Later replacement by connective tissue can leave a scar



Serous exudates: Removal versus organization

- Adequate digestion and resorption support resolution
- Larger or persistent accumulations admit granulation tissue
- Organization converts the exudate into a fibrous scar

Clearable exudate

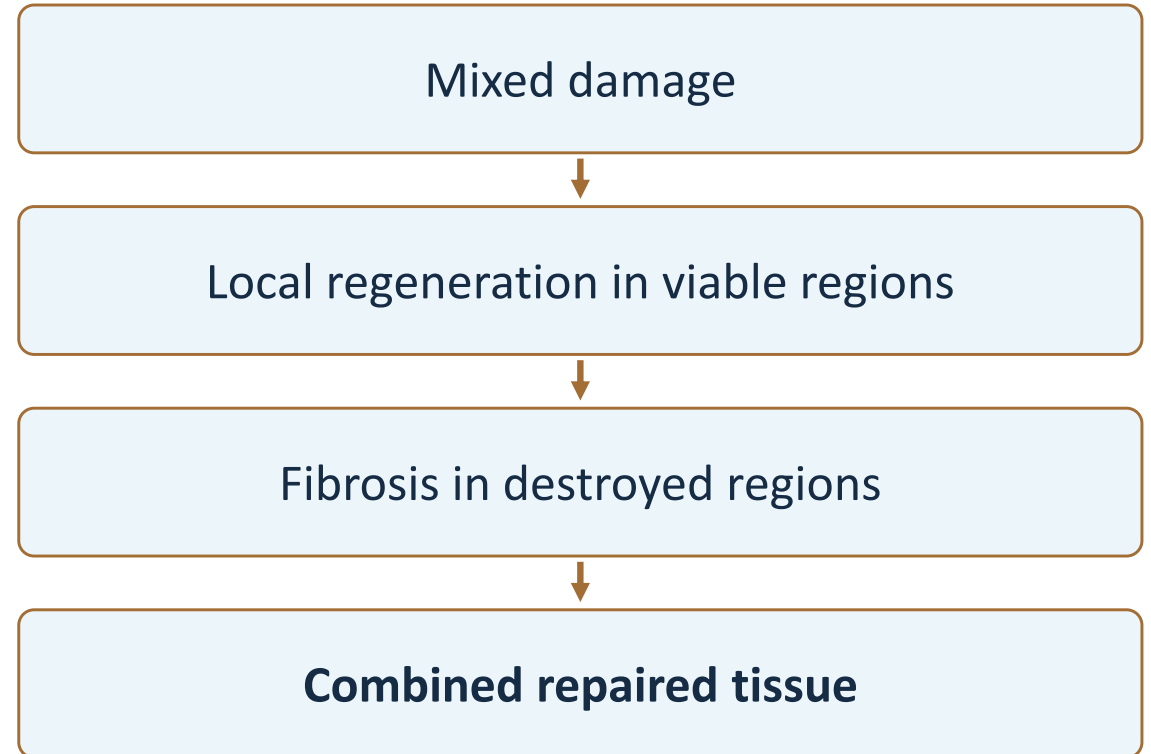
Digestion + resorption
→ resolution

Persistent exudate

Ingrowth → fibrosis /
organization

Tissue restoration and scar formation may coexist

- Repair is not always a strict either–or choice
- Some sites regenerate viable cells while other foci scar
- The proportional contribution depends on injury and tissue



Chronic inflammation is prolonged and active

- Chronic inflammation may follow unresolved acute inflammation
- Tissue injury and attempts at repair coexist
- It may also begin insidiously without a recognized acute phase

Acute pattern

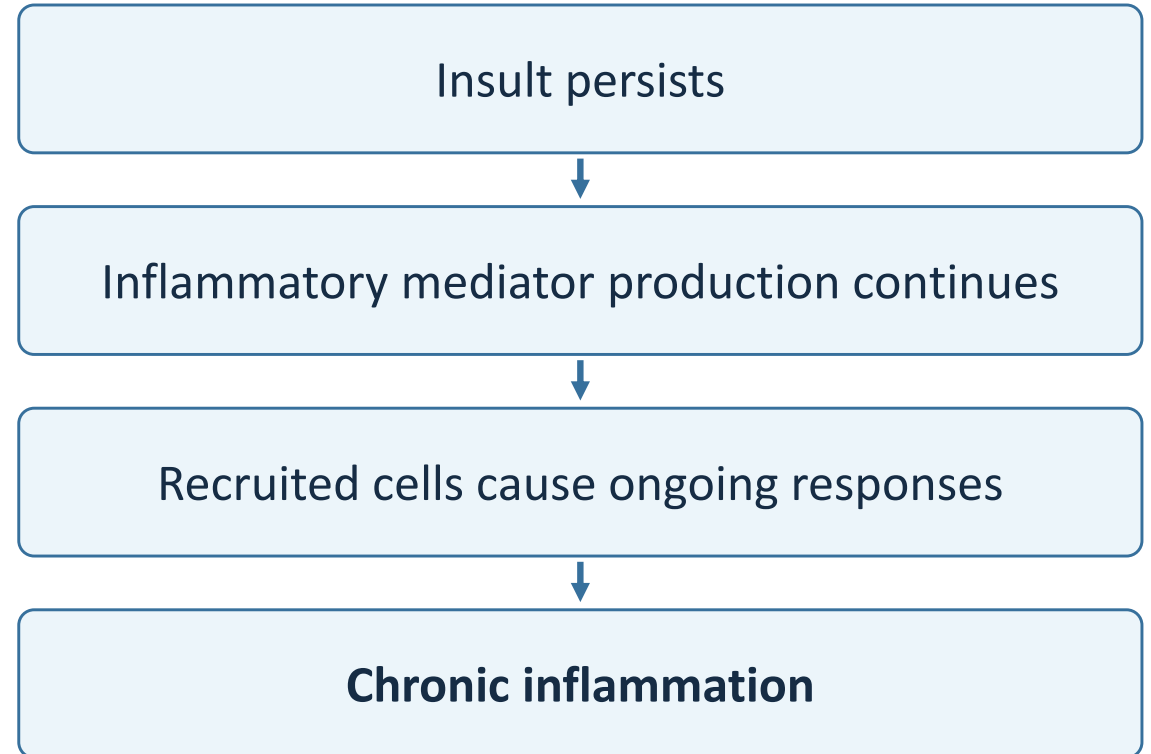
Vascular response;
Edema; Neutrophils

Chronic pattern

Mononuclear cells;
Injury; Repair

Persistence of the offender blocks resolution

- Unremoved infectious or other stimuli sustain immune activation
- Leukocyte recruitment continues instead of ending
- Persistent responses may become chronic



Disturbed healing can prolong inflammation

- Normal resolution requires effective clearance and repair
- Infection or foreign material can perpetuate inflammation
- Impaired perfusion or systemic disease may compromise repair

Infection

Stimulus remains

Foreign bodies

Persistent local reaction

Poor perfusion

Reduced healing
capacity

Diabetes

Systemic repair
impairment

The cellular infiltrate changes with chronicity

- Early acute lesions are commonly neutrophil-rich
- Monocytes/macrophages become prominent as responses evolve
- Chronic lesions include macrophages, lymphocytes, and plasma cells

Acute phase

Neutrophils; Exudation

Chronic phase

Mononuclear infiltrate

Chronic inflammation has three key morphologic features

- Mononuclear inflammatory infiltrates persist
- Tissue destruction continues through the stimulus and/or inflammation
- Angiogenesis and fibrosis show ongoing repair

Cells

Macrophages;
Lymphocytes; Plasma
cells

Destruction

Loss of parenchymal
elements

Angiogenesis

New microvessels

Fibrosis

Repair by collagen
deposition

Macrophages can sustain injury and promote repair

- Activated macrophages remove microbes and dead tissues
- They may also release mediators that perpetuate injury
- The M1/M2 distinction is a model, not a strict binary

Pro-inflammatory functions

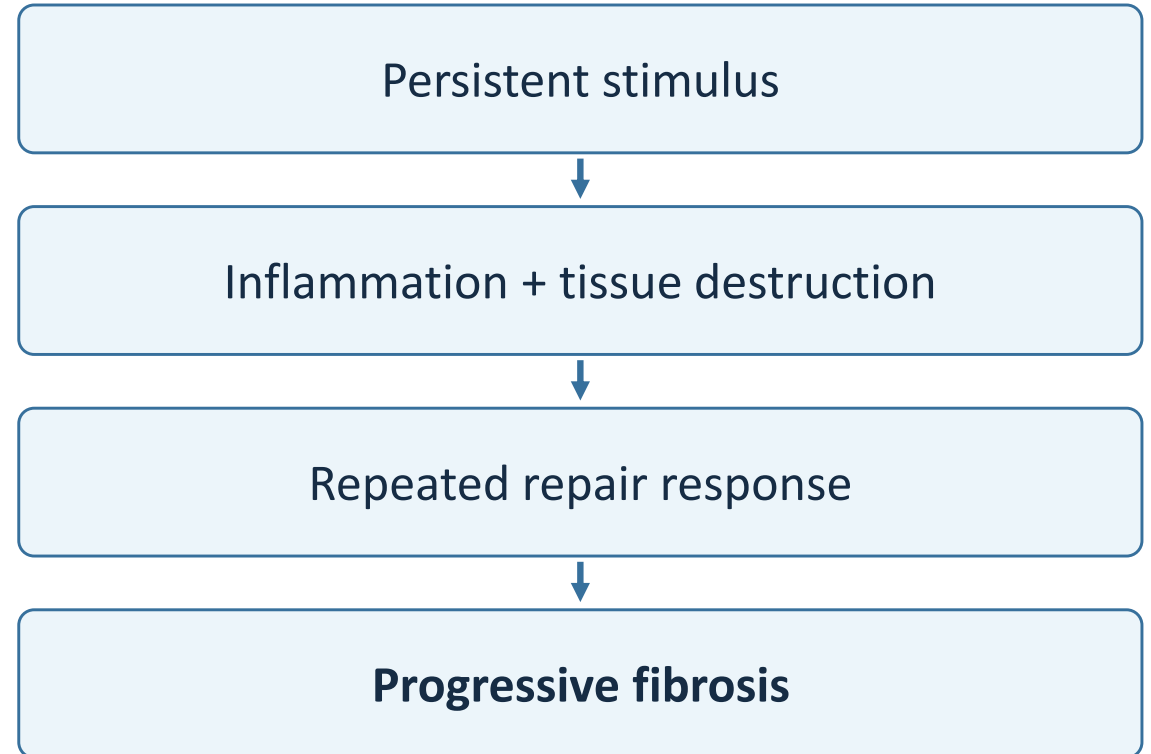
Microbial killing;
Cytokine release

Repair-associated functions

Inflammation control;
Matrix repair

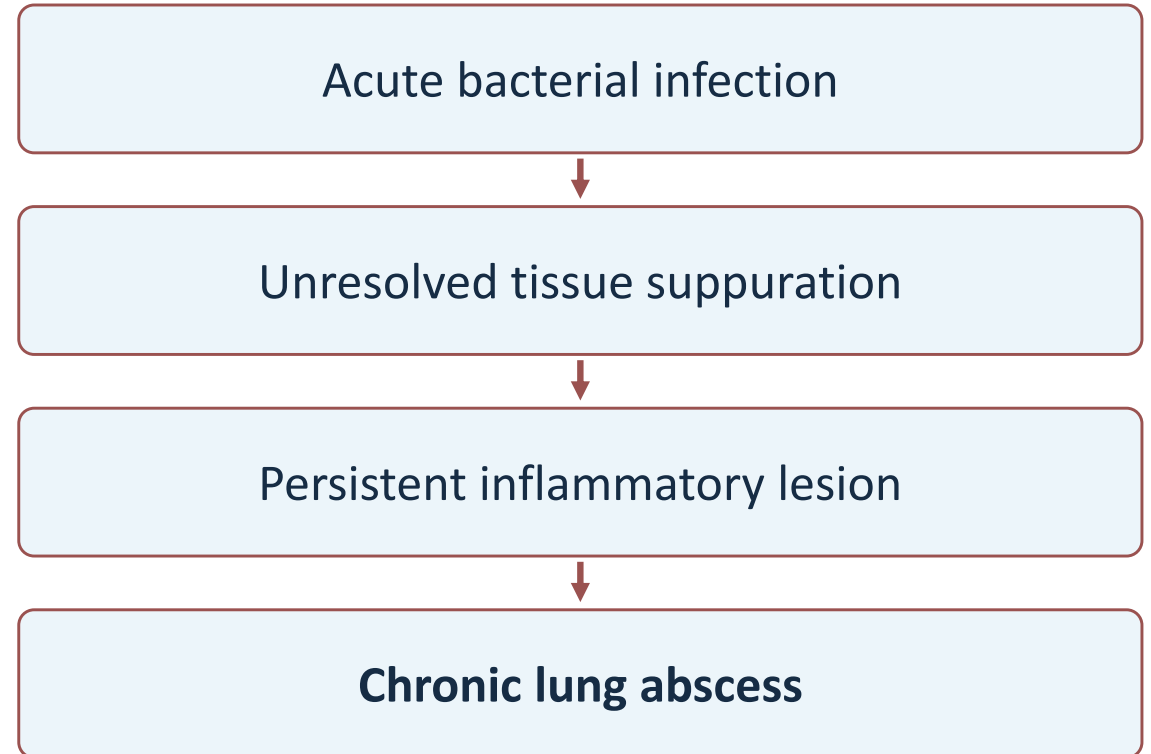
Continued injury often produces progressive fibrosis

- In chronicity, inflammation and repair overlap
- Repeated injury recruits fibroblasts and stimulates ECM deposition
- Fibrosis may dominate late lesions



A persistent bacterial abscess may become chronic

- Acute bacterial infection may fail to be eradicated
- Necrotic debris and repeated inflammation maintain the lesion
- A chronic lung abscess is a textbook example



Ulcer bases illustrate concurrent acute and chronic injury

- Acute ulcer margins may show neutrophils and vascular dilation
- Chronic ulcers develop lymphocytes, macrophages, and plasma cells
- Fibroblastic proliferation and scar form in margins and base

Acute ulcer

PMNs + dilation at
edges

Chronic ulcer

Mononuclear cells +
scarring

Case: Short-lived superficial injury

- A superficial epithelial injury removes few cells
- The underlying connective tissue scaffold remains intact
- The inciting stimulus is no longer present

Which outcome is favored, and why?

Resolution: Preserved matrix and viable epithelial progenitors favor regeneration.

Case: Persistent fibrin in a serous cavity

- A fibrin-rich exudate persists on a serosal surface
- Fibrinolytic clearance is incomplete
- Fibrovascular tissue grows into the deposit

What does this tissue response represent?

Organization: A fibrinous exudate is replaced by fibrous connective tissue.

Case: An offending agent cannot be eradicated

- An infectious stimulus persists despite early neutrophilic inflammation
- Additional inflammatory cells continue to accumulate
- Destruction and repair now coexist

What is the most likely trajectory?

Chronic inflammation because the initiating stimulus remains active.

Predict outcomes by identifying the dominant constraint

Scenario	Main constraint	Likely outcome
Transient mild injury	Little necrosis; Intact matrix	Resolution
Severe parenchymal loss	Loss exceeds regeneration	Fibrosis
Uncleared fibrin exudate	Persistent proteinaceous deposit	Organization / scar
Persistent injurious agent	Inflammation does not terminate	Chronic inflammation

An integrated model of acute inflammatory outcomes

Acute inflammatory reaction

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graph TD; A[Acute inflammatory reaction] --> B[COMPLETE RESOLUTION  
Injury eliminated; Tissue architecture restored]; A --> C[FIBROSIS / SCAR  
Lost tissue or fibrin replaced by collagen]; A --> D[CHRONIC INFLAMMATION  
Unresolved stimulus or impaired healing]
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COMPLETE RESOLUTION

Injury eliminated; Tissue architecture restored

FIBROSIS / SCAR

Lost tissue or fibrin replaced by collagen

CHRONIC INFLAMMATION

Unresolved stimulus or impaired healing

Outcome depends on the insult, injured tissue, and host response

References and scope

Core source

Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th ed. (2026). Chapter 3: Inflammation and Repair.

Sections: Outcomes of Acute Inflammation; Termination of the Acute Inflammatory Response; Chronic Inflammation; Tissue Repair.

Conceptual drawings and decision diagrams are original teaching schematics.