ACUTE INFLAMMATION
By

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Introduction To Inflammation

Inflammation is the local response of living mammalian tissues to injury from any agent which could be microbial, immunological, physical or chemical agents.

Inflammation is of 2 types:

- **Acute Inflammation**
  - ✓ due to early response by the body
  - ✓ short duration
- **Chronic Inflammation**
  - ✓ occurs after delay
  - ✓ it is for longer duration
  - ✓ Characterised by response by chronic inflammatory cells.

Introduction To Inflammation

Table 2–1 Features of Acute and Chronic Inflammation

Feature	Acute	Chronic
Onset	Fast: minutes or hours	Slow: days
Cellular infiltrate	Mainly neutrophils	Monocytes/macrophages and lymphocytes
Tissue injury, fibrosis	Usually mild and self-limited	Often severe and progressive
Local and systemic signs	Prominent	Less prominent; may be subtle

Trigger Stimuli For Acute Inflammation

Stimuli	Description
Infections	Bacteria, viruses, fungi, parasites
Trauma	Blunt and penetrating trauma: examples include burns, frostbite, irradiation and environmental chemicals
Tissue necrosis	Examples of things that trigger necrosis include ischemia from a heart attack and physical/chemical injuries
Foreign bodies	Foreign bodies include splinters, sutures and dirt
Immune (hypersensitivity reactions)	Are triggered either against environmental substances or the body attacks itself (this process is known as autoimmune diseases: auto- meaning 'self')

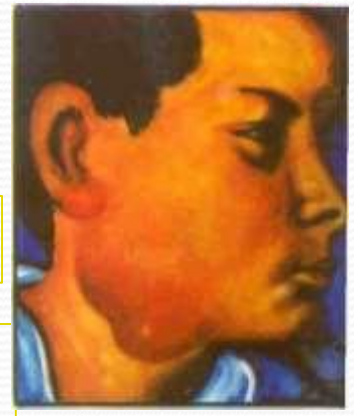
Cardinal Clinical Signs of Acute Inflammation

Acute inflammation has 5 cardinal signs:

redness (rubor)

heat (calor)

→ increased blood flow to the inflamed area



swelling (tumor) → accumulation of fluid

pain (dolor) → release of chemicals that stimulate nerve endings

loss of function → a combination of factors

Events In Acute Inflammation

The two main events of the acute inflammation are:

- **Vascular events**
- **Cellular events.**

1. Vascular events

Initial transient vasoconstriction of arterioles.

↓

Persistent progressive vasodilatation.

↓

Elevation of the local hydrostatic pressure.

↓

Increase in vascular permeability.

↓

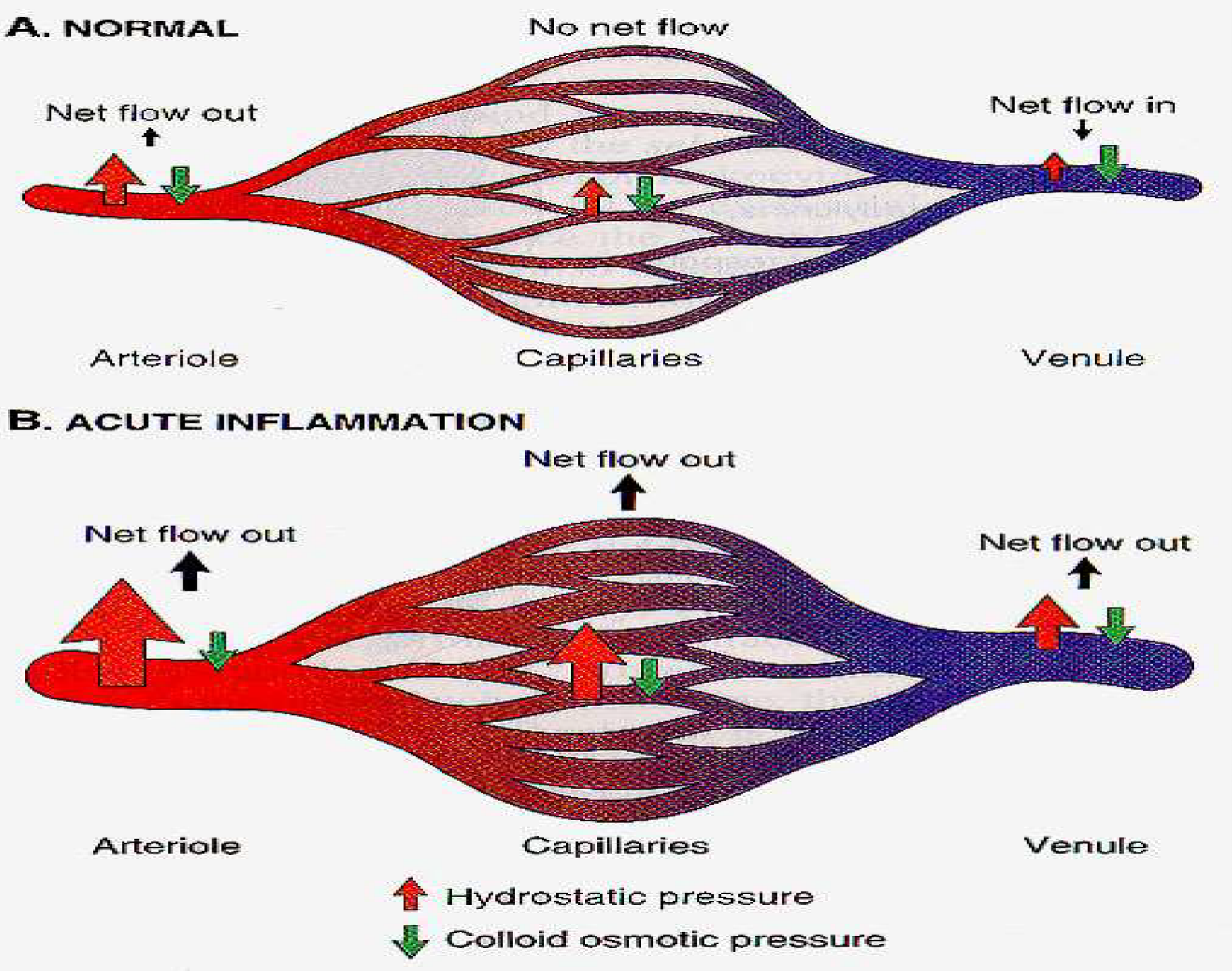
Transudation of fluid into the extracellular space.

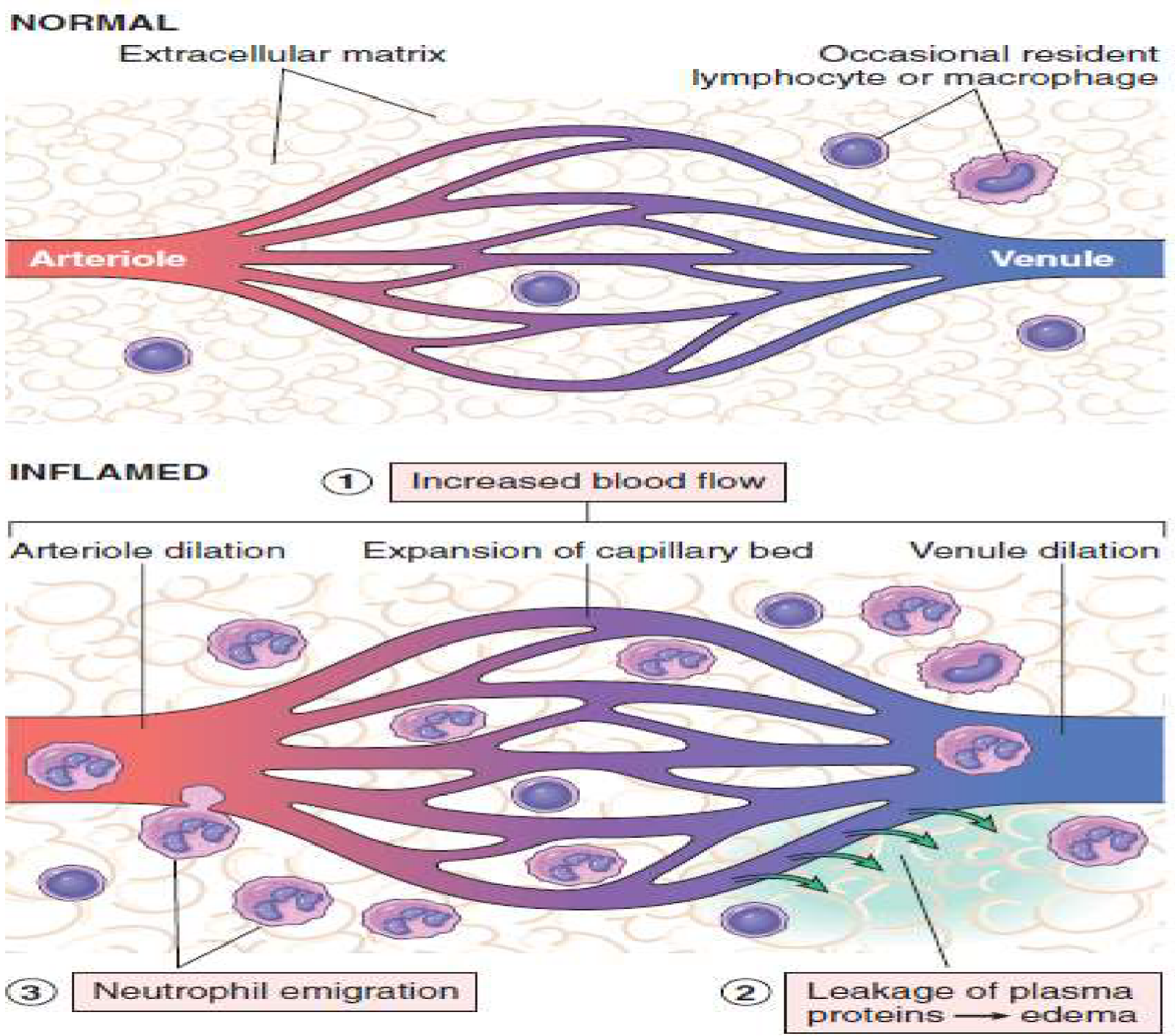
↓

Slowing or stasis of microcirculation.

↓

Leucocytic margination.


A. NORMAL
No net flow
Net flow out
Net flow in
Arteriole
Capillaries
Venule
B. ACUTE INFLAMMATION
Net flow out
Net flow out
Net flow out
Arteriole
Capillaries
Venule
Hydrostatic pressure
Colloid osmotic pressure


NORMAL
Extracellular matrix
Occasional resident lymphocyte or macrophage
Arteriole
Venule
INFLAMED
1 Increased blood flow
Arteriole dilation
Expansion of capillary bed
Venule dilation
3 Neutrophil emigration
2 Leakage of plasma proteins → edema

Causes of increased vascular permeability

- *Endothelial cell contraction →intercellular gaps in postcapillary venules .*
- *Endothelial injury*
  - *Direct*
  - *Leukocyte induced*
- Increased transcytosis of fluid
- Leakage from new blood vessels

Direct Endothelial Injury

- Immediate sustained response - Occurs immediately and lasts until vessel repaired.
- Results of severe injuries (burns) orinfections.
- *Results in vascular leakage by causing* endothelial cell necrosis and detachment.

Leukocyte Dependent Endothelial Injury

- Endothelial cells may also be damaged as a consequence of leukocyte accumulation along the vessel wall.

- Activated leukocytes release many toxic mediators that may cause endothelial injury or detachment.

2.Cellular Events

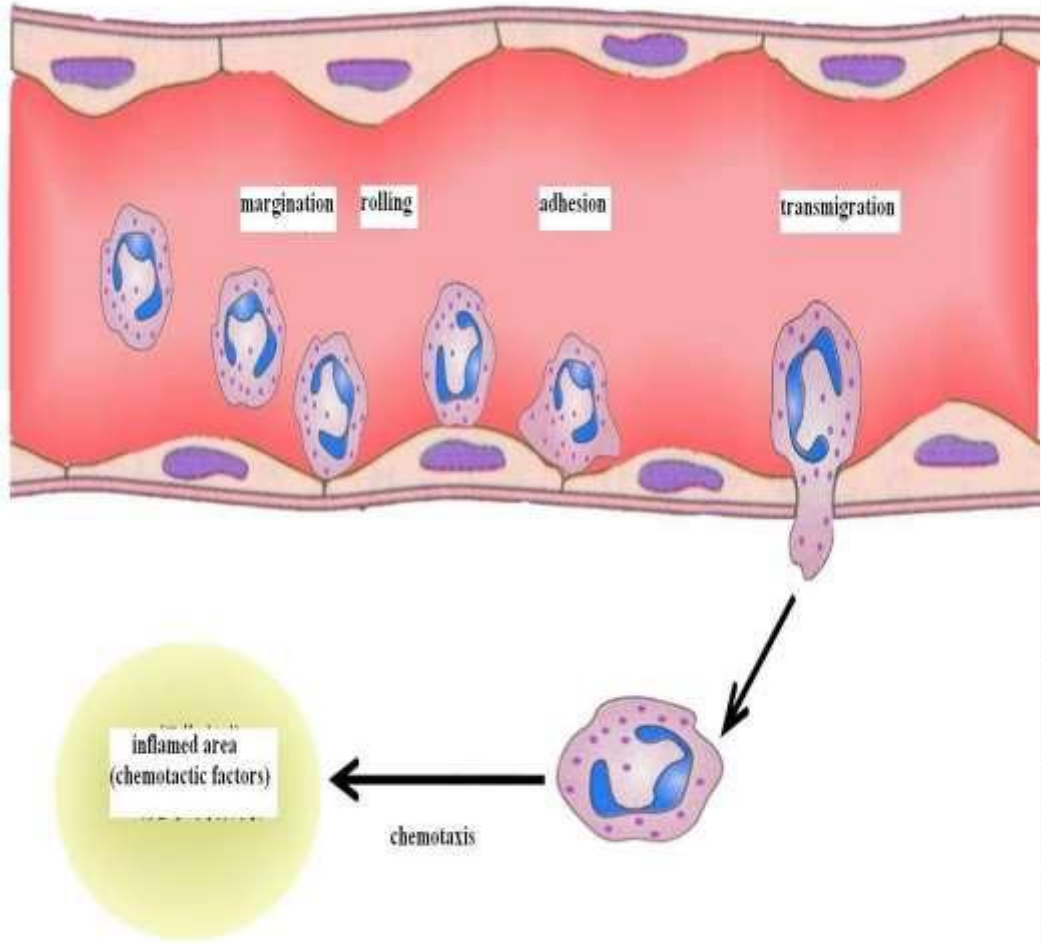
- Leukocyte Recruitment to site of injury

Extravasation → Sequence of events in therecruitment of leukocytes from the vascular lumen to the extravascular space.

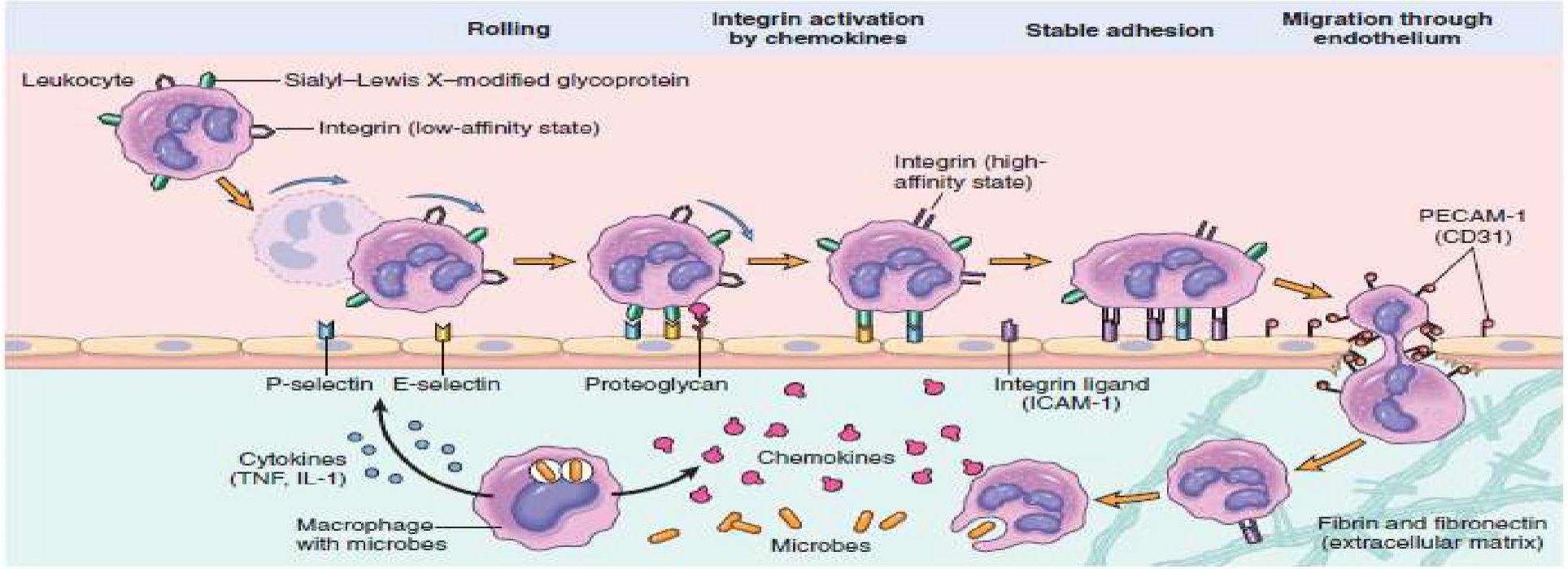
- Leukocyte Activation at the site of injury
- *Phagocytosis of particles* →Process of engulfment of
- solid particulate material by the leukocytes (neutrophils and monocytes)

Extravasation

- Margination → leukocytes assume peripheral portion of lumen
- Rolling & Adhesion → leukocytes tumble slowly along the endothelium and adhere transiently, detach and bind again.
- Diapedesis – Transmigration of leukocytes across the endothelium.
- Chemotaxis – leukocyte migration towards the site of injury (locomotion oriented along a chemical gradient)



Role of endothelial molecules in acute inflammation



Endothelial molecule	Major role
P-selectin	Rolling
E-selectin	Rolling and Adhesion
ICAM-1 (Integrin – β1)	Adhesion, Arrest & Transmigration
VCAM-1 (Integrin – β2)	Adhesion
PECAM-1 (CD-31)	Diapedesis

Chemical Mediators of Inflammation

Cell derived		Plasma protein derived
Preformed	Newly synthesized	
Histamine	Prostaglandins	Complement proteins
Serotonin	Leukotrienes	Kinins
Lysosomal enzymes	Platelet activating factor	Proteases activated during coagulation
	Nitric Oxide	Factor XII
	Cytokines	

Chemical Mediators of Inflammation

Vasodilation	↑ Vascular permeability	Chemotaxis, Leukocyte activation	Pain	Tissue damage
Prostaglandins	Vasoactive amines	C5a	Prostaglandins esp PGE2	Neutrophils and macrophage lysosomal enzymes
Nitric oxide	C3a, C5a	LTB4	Bradykinin	O2 metabolites
Histamine	Bradykinin	Chemokines	Substance P	Nitric oxide
	Leukotrienes	IL-8		
	PAF	TNF		
	Substance P	Bacterial products		
	VEGF			

Chemotaxis

Both exogenous and endogenous substances can be chemotactic for leukocytes (Chemoattractants)

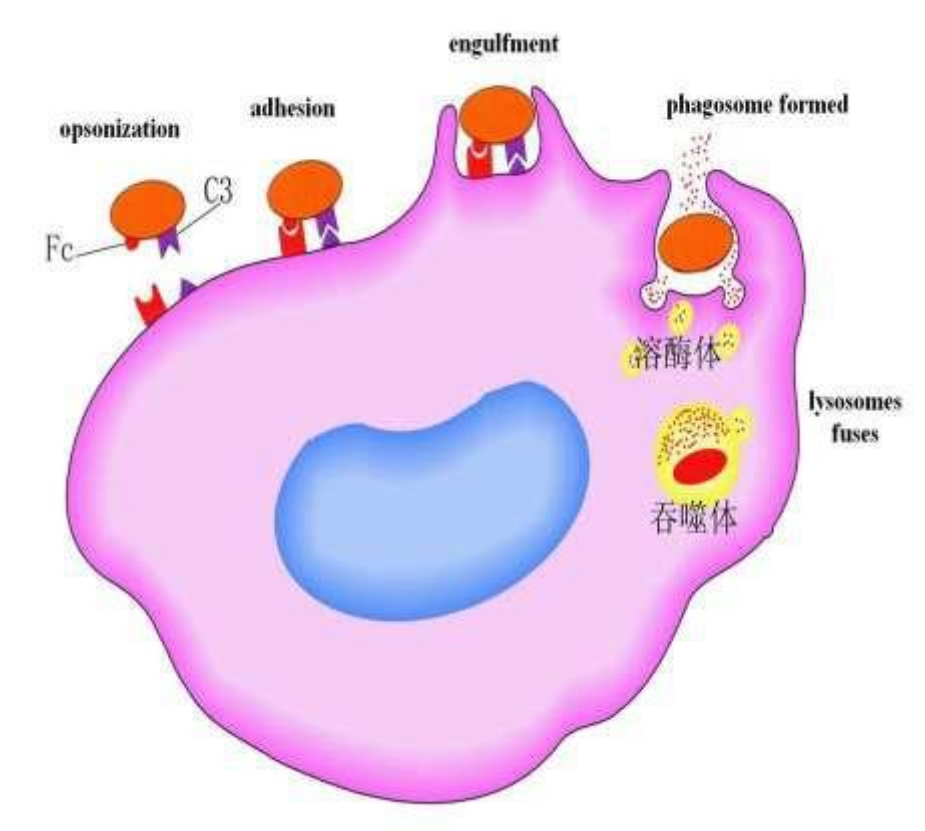
- Bacterial products, peptides with ***N-formylmethionine termini.***
- Cytokines, especially those of the ***chemokine family, IL-8.***
- Components of the complement system, particularly **C5a.**
- Products of the lipoxygenase pathway of arachidonic acid (AA) metabolism, particularly leukotriene B4 (**LTB4**).

In most forms of acute inflammation,

- ✓ *Neutrophils predominate in the inflammatory infiltrate during the first 6 -24 hrs*
- ✓ *Neutrophils are replaced by monocytes in 24 -48 hrs.*

Phagocytosis

- Phagocytosis is defined as the process of engulfment of solid particulate material by the cells (cell-eating).
- The cells performing this function are called *phagocytes*.
- Degranulation and the oxidative burst destroy the engulfed particle



Phagocytosis

There are 2 main types of phagocytic cells:

i. Polymorphonuclear neutrophils (PMNs) which appear early in acute inflammatory response.

ii. Circulating monocytes and fixed tissue mononuclear phagocytes, commonly called as macrophages.

Phagocytosis

Neutrophils and macrophages upon reaching the tissuespaces produce several proteolytic enzymes—

- Lysozyme
- Protease
- Collagenase
- Elastase
- Lipase
- Proteinase
- Gelatinase
- Acid hydrolases.

These enzymes degrade collagen and extracellular matrix.

Phagocytosis

Phagocytosis of the microbe by polymorphs and macrophages involves the following 3 steps:

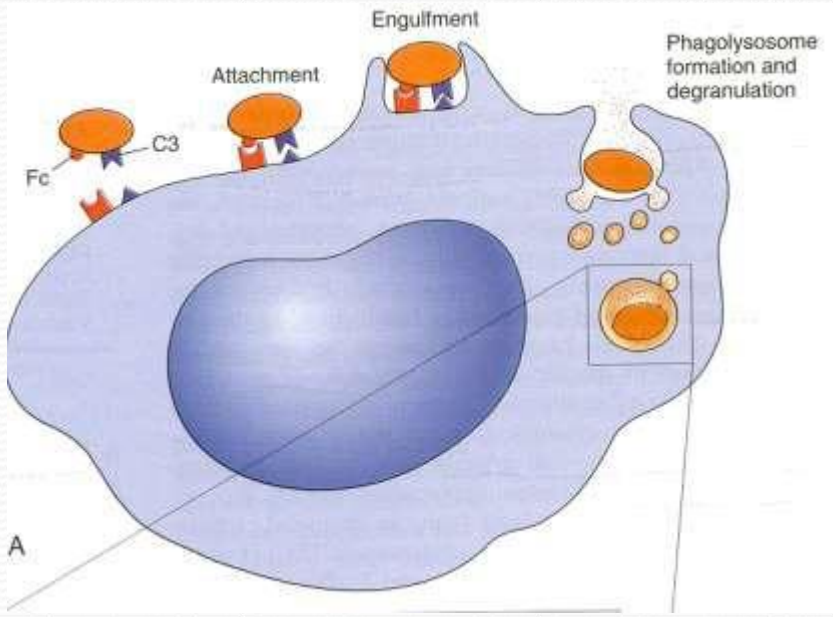
I. Recognition and attachment – Opsonisation (C3b, Fc fragment of IgG)

II. Engulfment – Phagolysosome formation.

III. Killing and degradation-

i. O_2 dependent - by
   - ✓ O_2 free radicals
   - ✓ Lysosomal granules

ii. O_2 independent – by
   - ✓ Lysozymal hydrolases
   - ✓ Lacoferrin
   - ✓ Major Basic Proteins
   - ✓ Defensins.
   - ✓ Nitric Oxide.

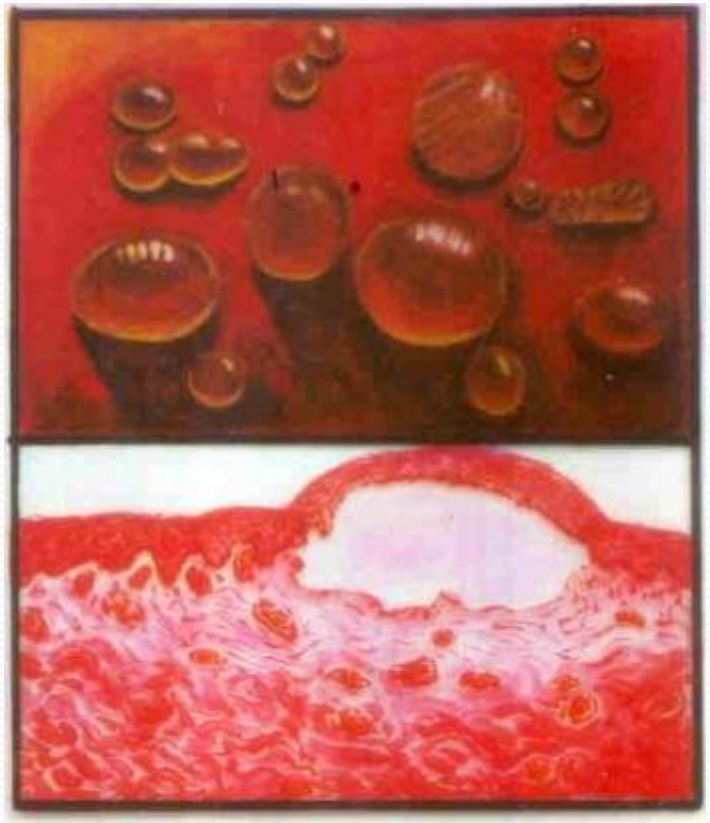


- MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION

MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION

Serous inflammation

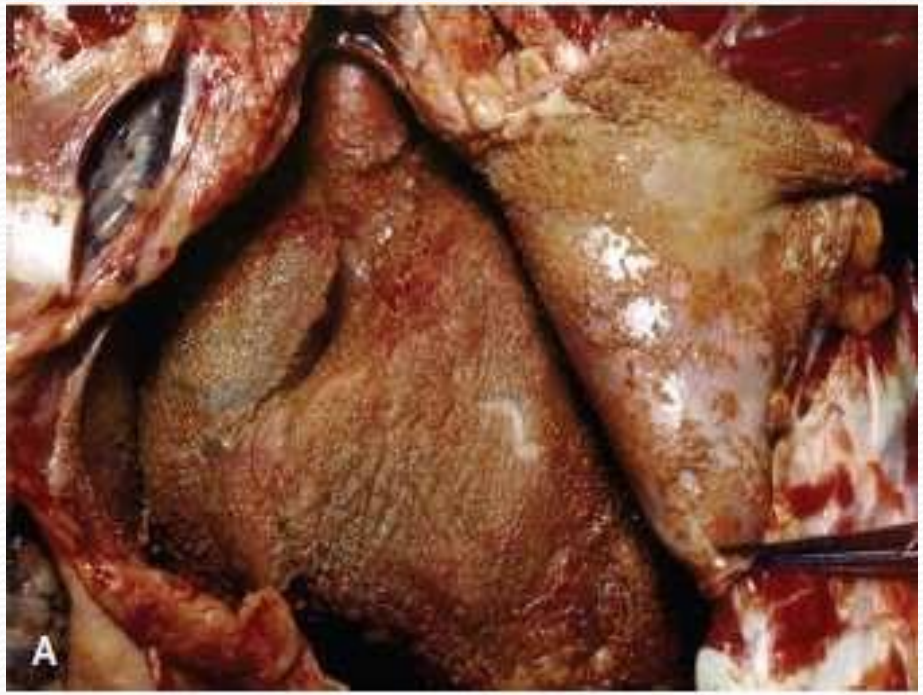
- Accumulation of excessive clear watery fluid with a variable protein content.
- Occurs in skin, and in peritoneal, pleural and pericardial cavities
- eg The skin blister resulting from a burn or viral infection is a good example of the accumulation of a serous effusion either within or immediately beneath the epidermisof the skin



MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION

Fibrinous inflammation

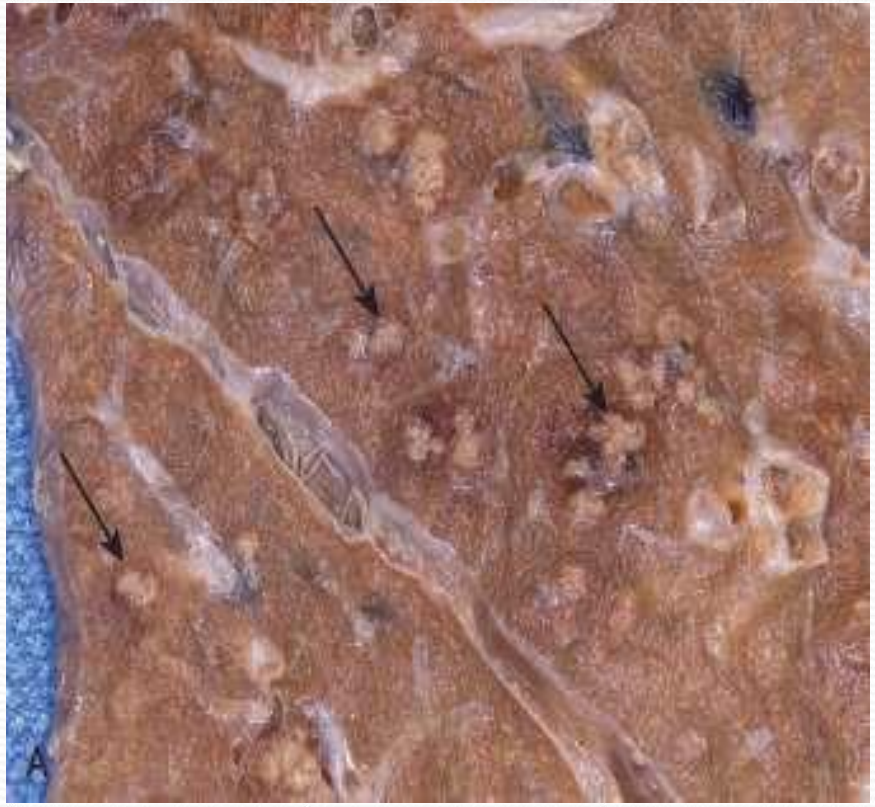
- Large amounts of fibrinogen pass the vessel wall, and fibrins are formed in the fluid exudate of extracellular spaces.
- eg Fibrinous pericarditis in which fibrin is deposited on the pericardium.



MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION

Suppurative (purulent) inflammation

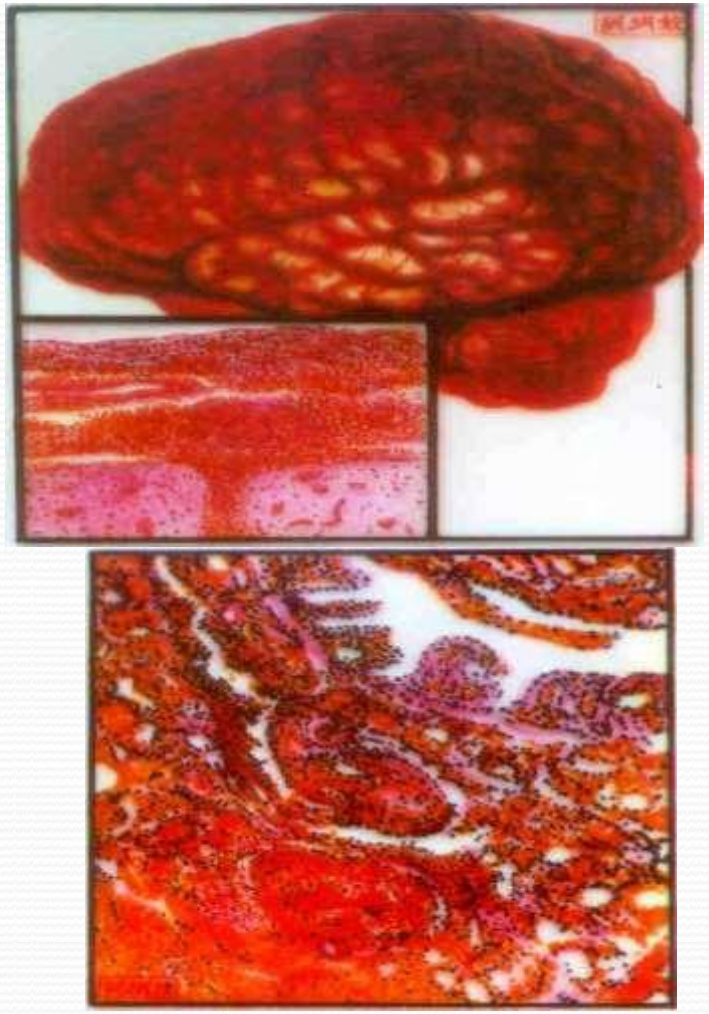
- The formation of purulent exudates or pus.
- Pus is made up of neutrophils, necrotic cells and edema fluid.
- Abscess is a localized collection of purulent inflammation accompanied by liquefactive necrosis.
- eg Multiple bacterial abscesses in the lung (*arrows) in a case of bronchopneumonia*



MORPHOLOGIC PATTERNS OF ACUTE INFLAMMATION

Hemorrhagic inflammation

Marked hemorrhage is the predominant pathological change



FATE OF ACUTE INFLAMMATION

Resolution

- ✓ Complete return to normal tissue following acute inflammation.

Repair

- ✓
  - Healing by regeneration in case of superficial tissue loss Healing by fibrosis in case of extensive tissue loss
- ✓

Suppuration

- Result of extensive tissue necrosis by pyogenic bacteria

↓

Intense neutrophil infiltration with fragments of necrotic tissue, cell debris & fibrin

↓

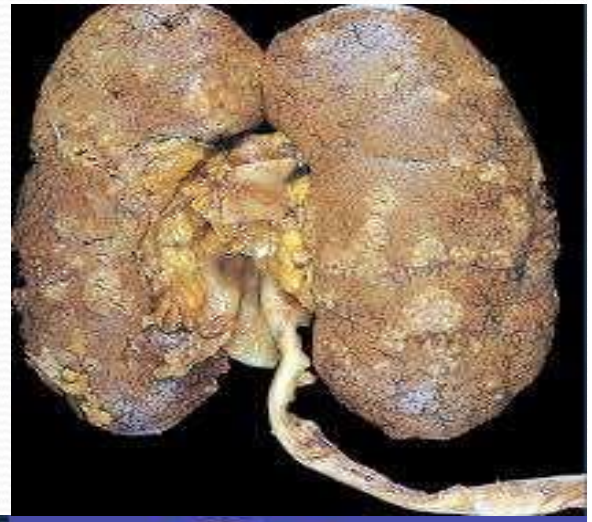
Pus/abscess.

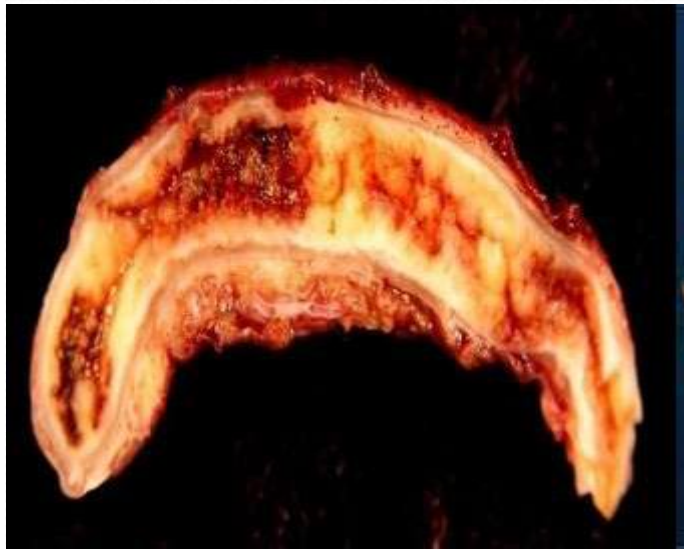
Chronic inflammation

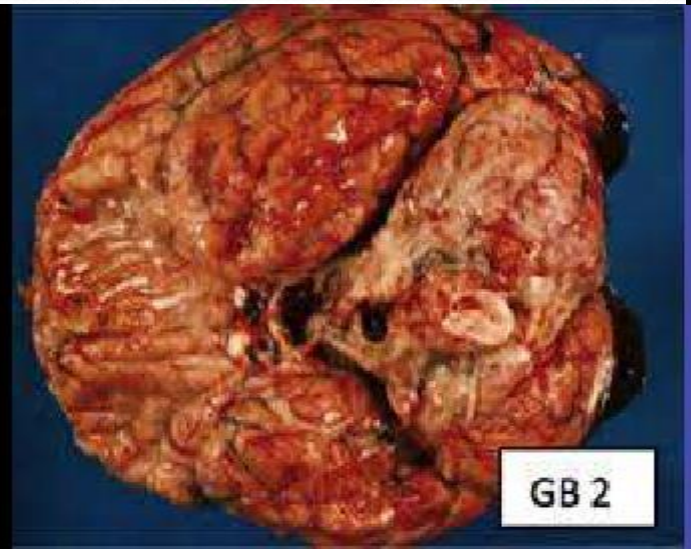
- ✓ Persisting or recurrent acute inflammation → chronic inflammation.
- ✓ Inflammation & healing proceed side by side.

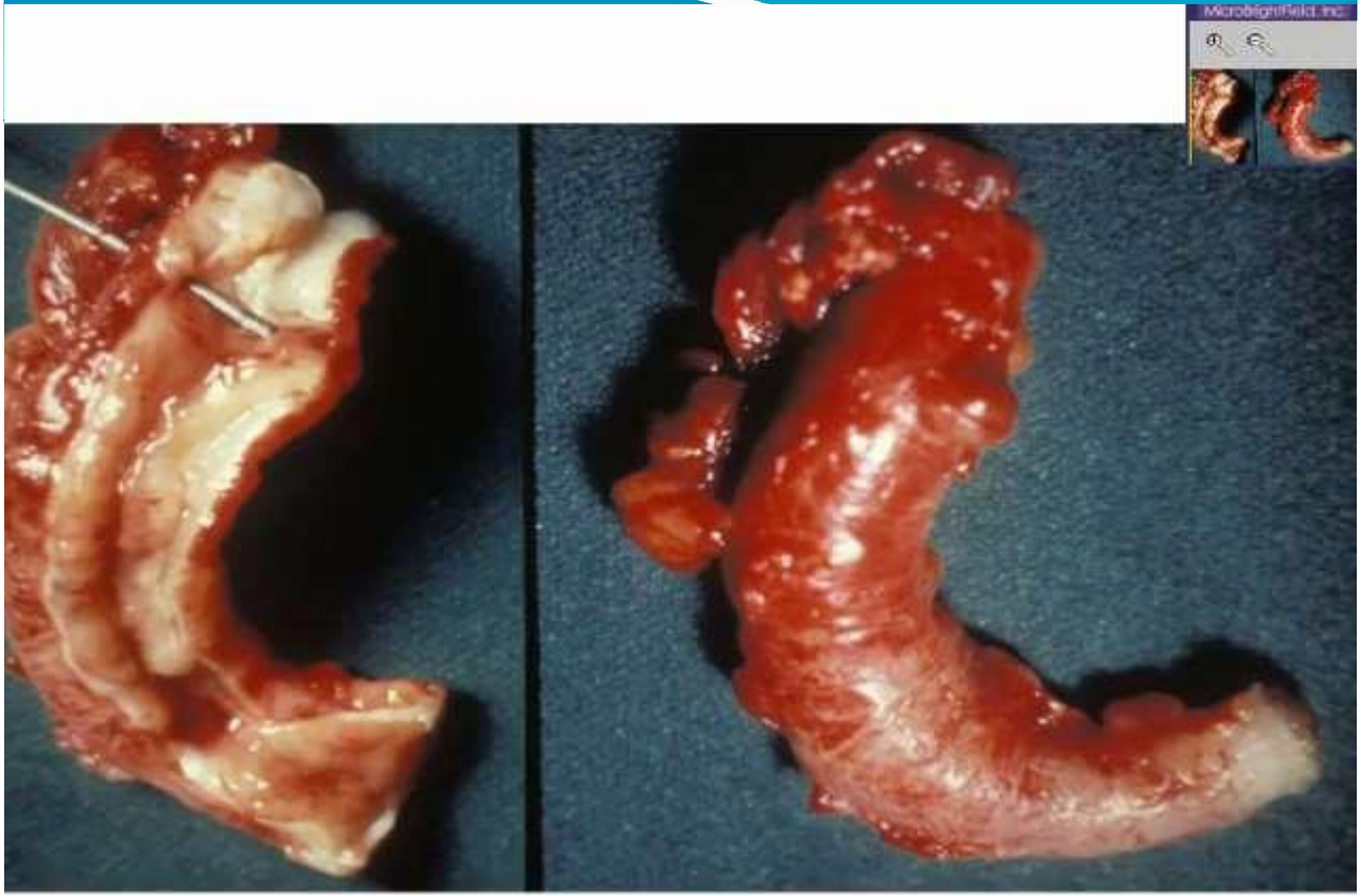
EXAMPLES OF ACUTE INFLAMMATION

- Acute appendicitis.
- Acute meningitis.
- Lobar pneumonia.
  - May spill to involve pleural cavity – EMPYEMA.
- Acute pyelonephritis.









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