Inflammation and cellular responses

Is a protective response

The body's response to injury

Interwoven with the repair process

Type

Acute (sec, mins, hrs)

Chronic (days, weeks, months, yrs)

Causes of inflammation

Bacterial

Viral

Protozoal

Metazoal

Fungal

Immunological

Tumours

Chemicals, toxins etc

Radiation

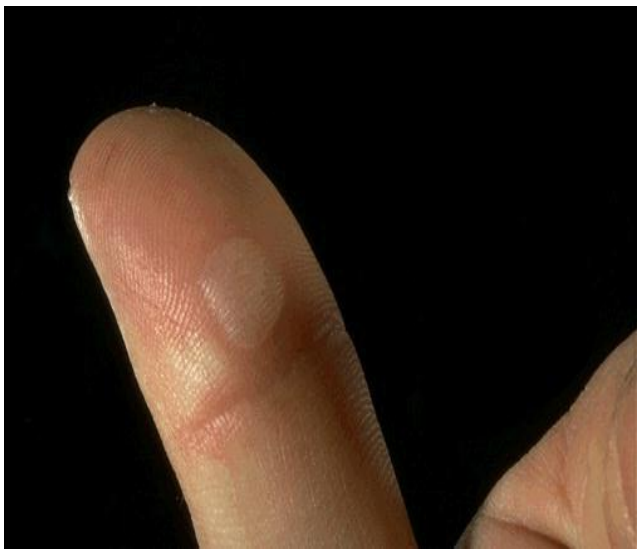
Acute inflammation

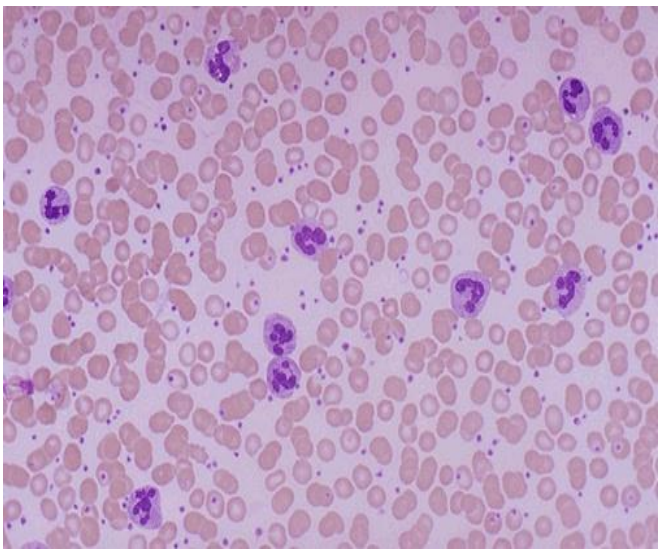
Inflammation

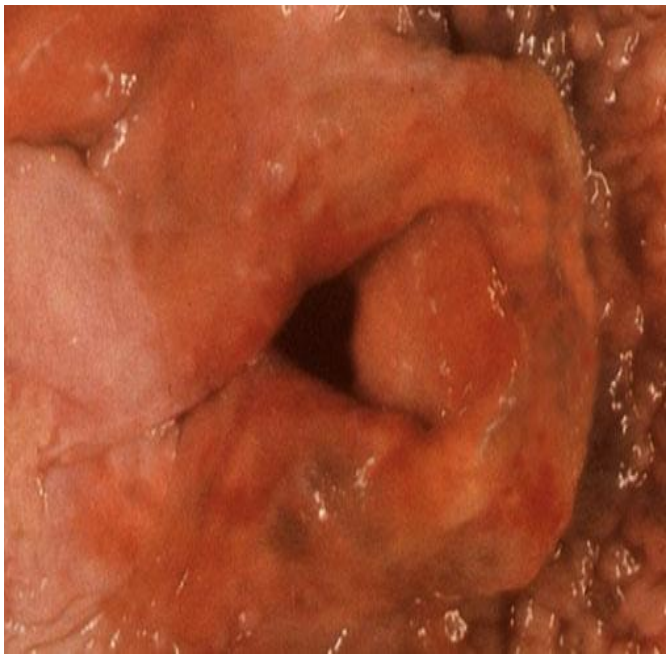
The Cardinal Signs of Acute Inflammation ■

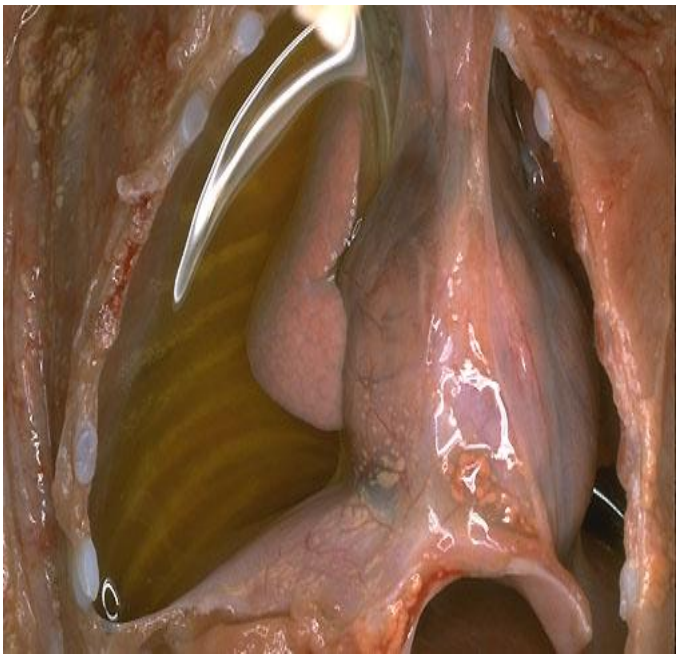
RUBOR, CALOR, TUMOR, FUNCTIO LAESA

Cardinal signs of inflammation









<u>The basis of the five cardinal signs</u>

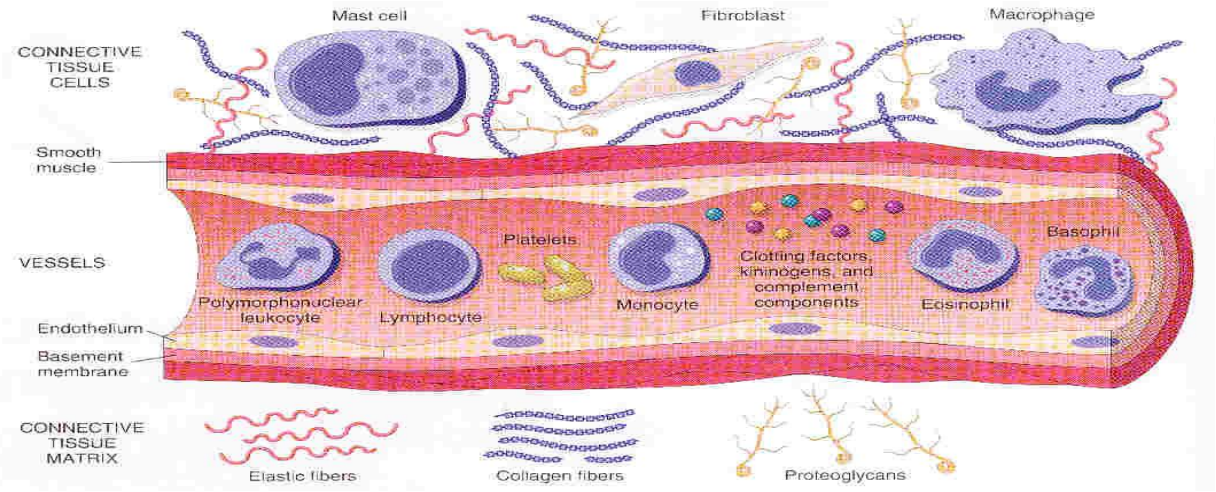
Increased blood flow due to vascular dilatation gives **redness** and **heat.**

Increased vascular permeability gives oedema causing **tissue swelling.**

Certain chemical mediators stimulate sensory nerve endings giving **pain.** Nerves also stimulated by stretching from oedema.

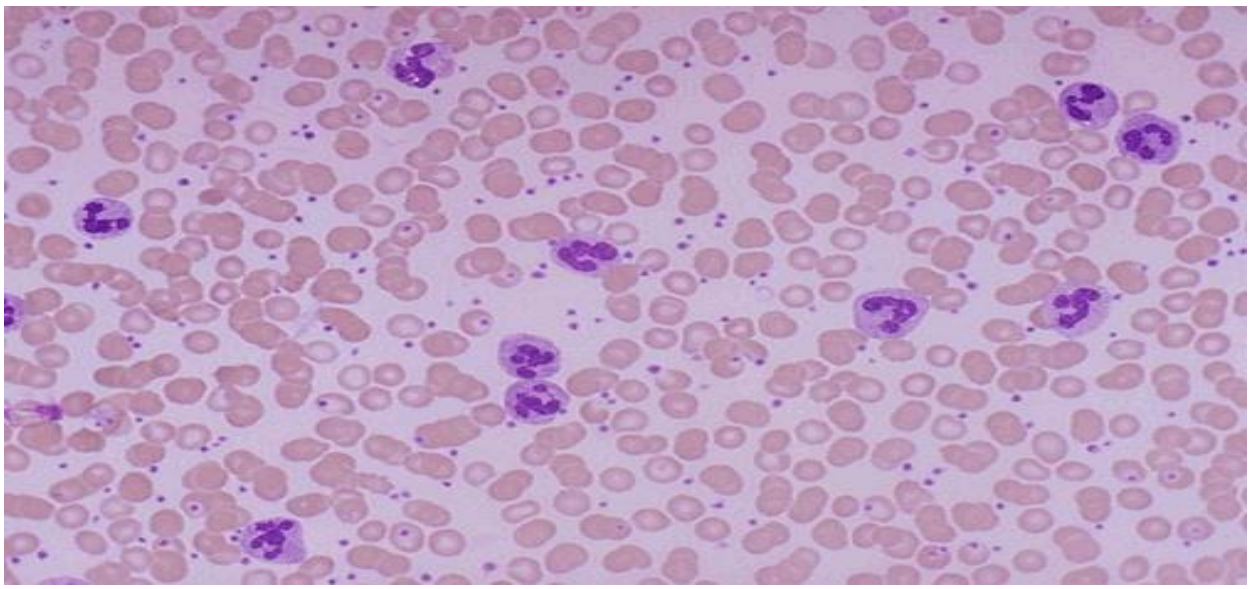
Pain and swelling result in loss of **function.**

Components of acute and chronic inflammation

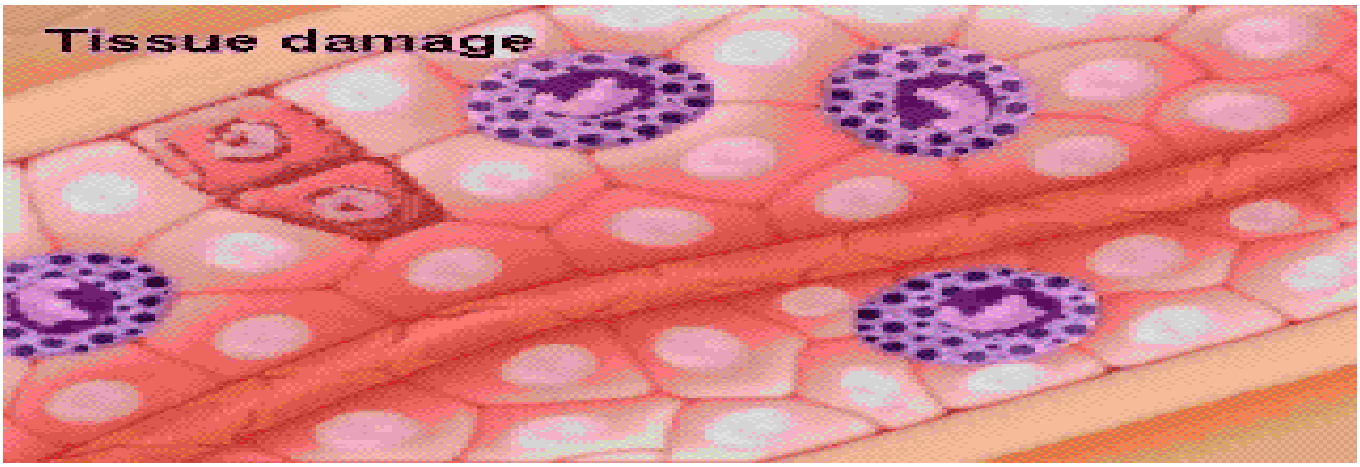


Cell of the acute inflammatory response

Polymorphonuclear leukocyte ■



The process of inflammation



The phases of inflammation

- FIRST THERE IS VASCULAR DILATATION followed by exudation of protein-rich oedema fluid which floods the area, dilutes toxins, allows immunoglobulins to opsonise bacteria and provides substrate (fibrinogen) for fibrin scaffold.
- SECOND THERE IS ACTIVE EMIGRATION OF POLYMORPHS through vessel wall and along the chemotactic gradient to the site of injury
- THE VASCULAR PHASE OF INFLAMMATION

  Fluid escapes from vessels because of endothelial cell (EC)

  retraction, opening up gap-junctions.

  The vessels which are normally involved are the post-capillary

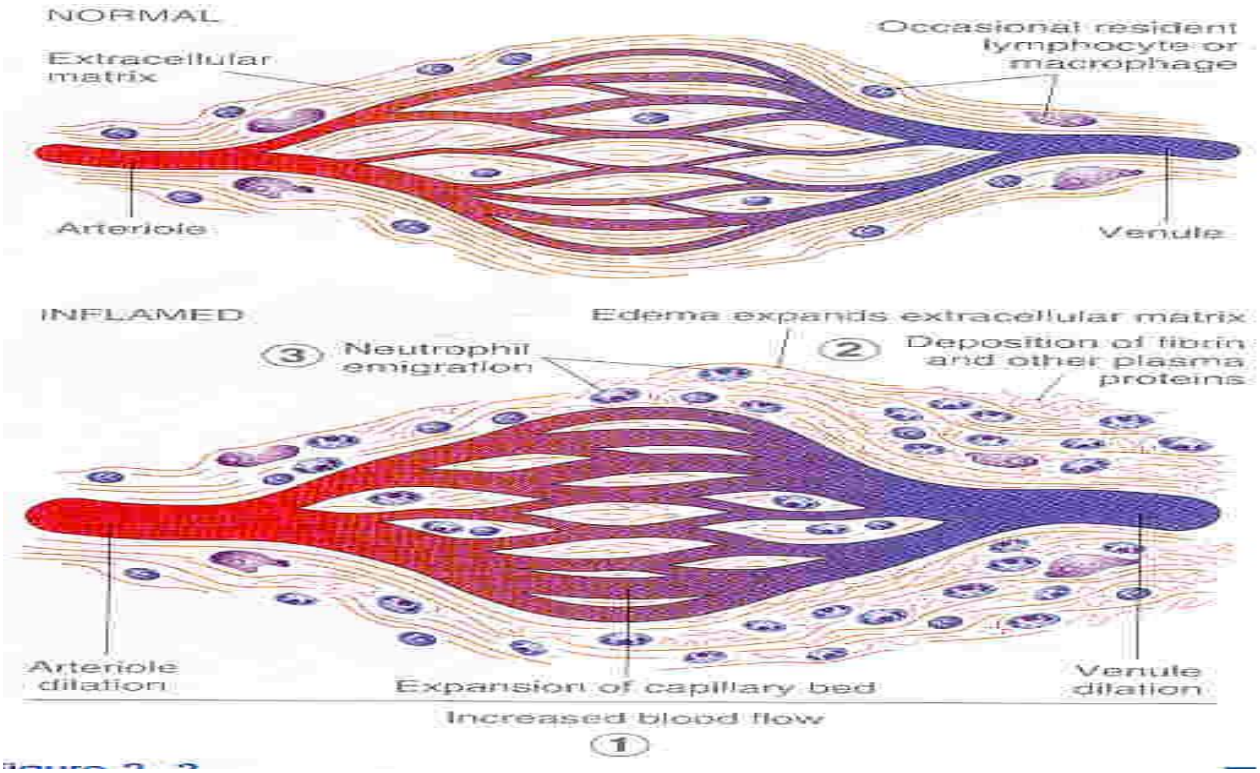
  venules where the EC have high affinity receptors for histamine.

  Severe EC injury leads to leakiness of <u>all</u> vessels

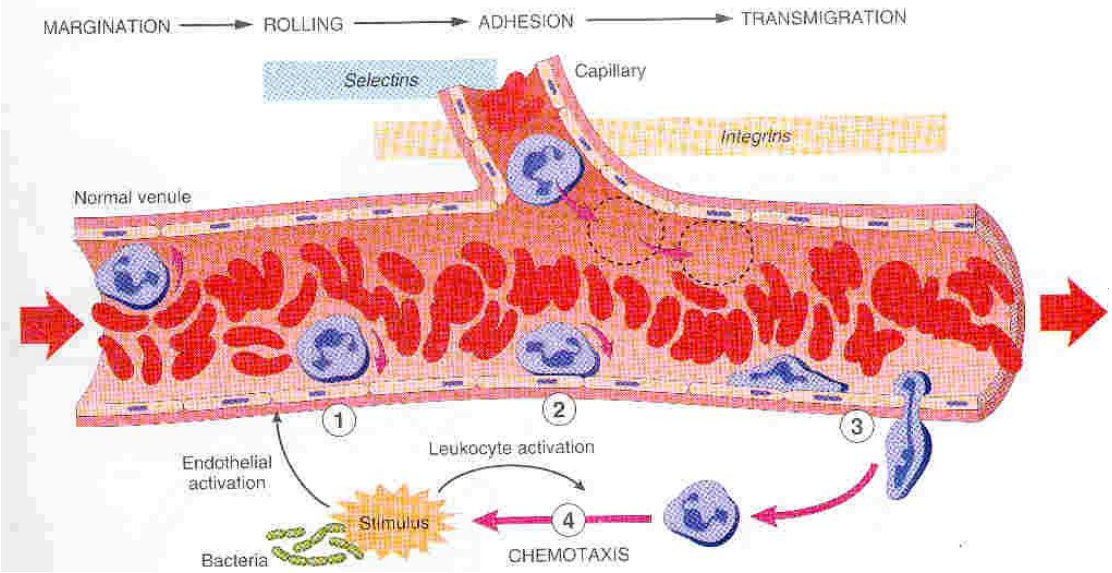
  capillaries, venules and arterioles - giving acute local oedema,

  e.g. blister formation after a burn.

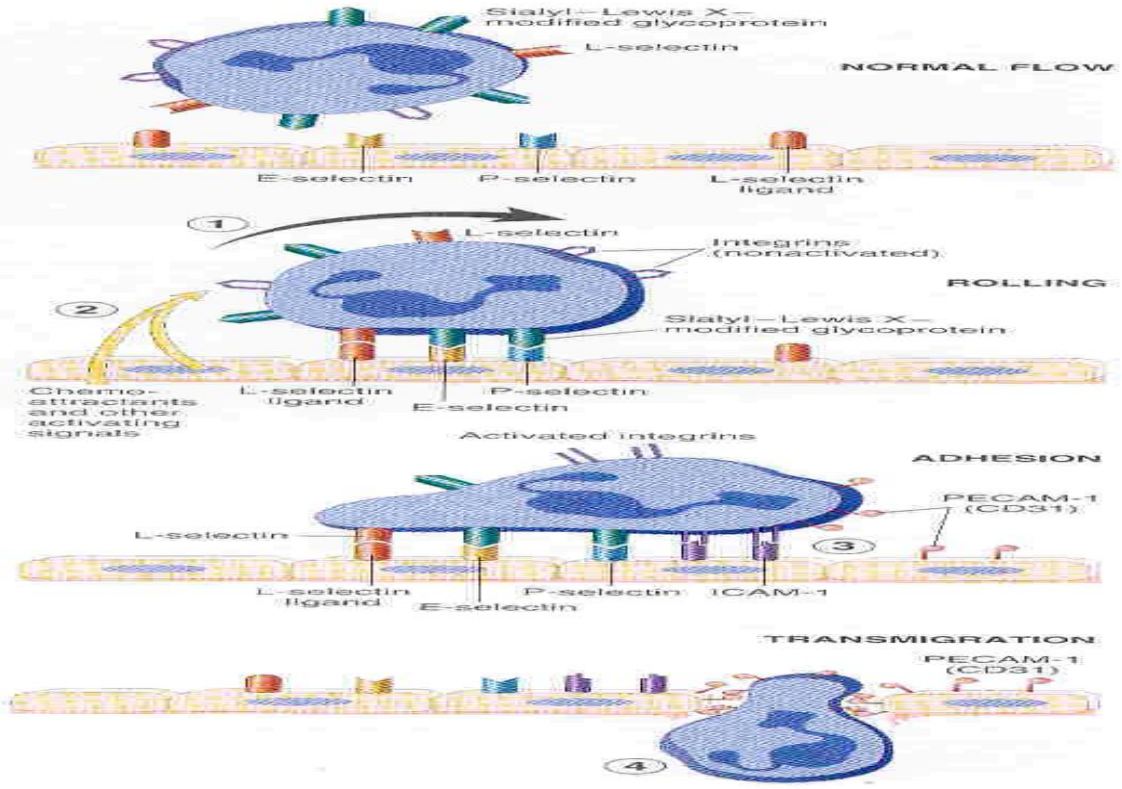
  Local vascular manifestations of acute inflammation



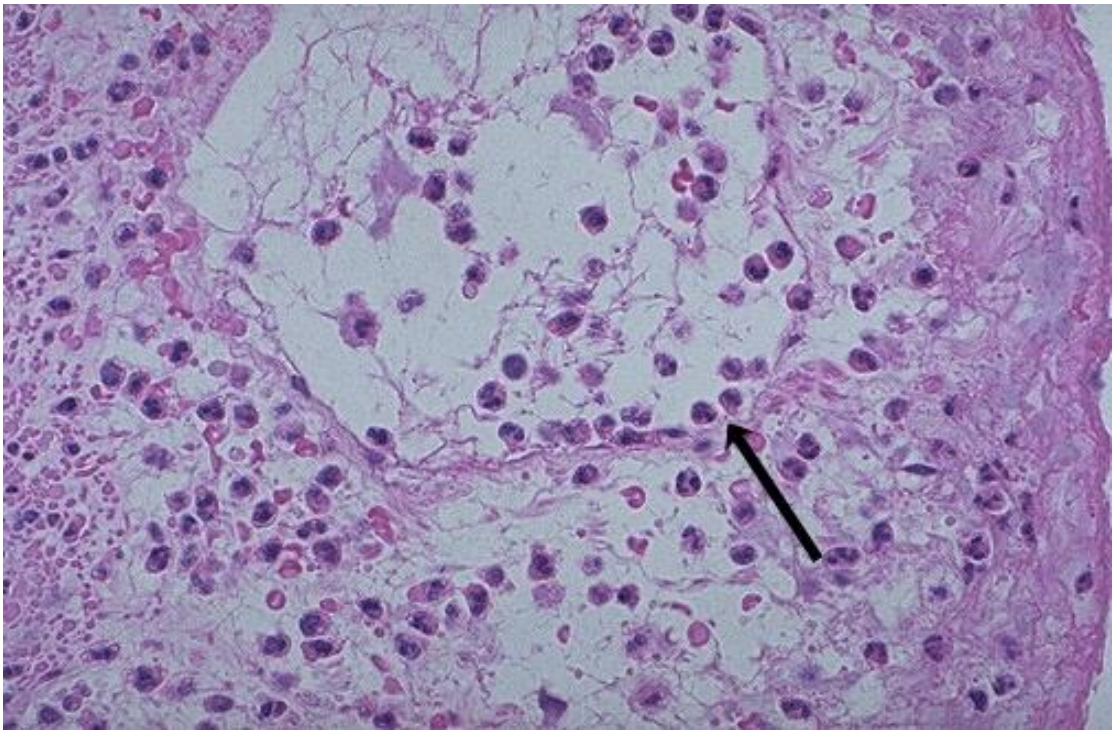
Leukocyte migration in inflammation



Molecules modulating endothelial-neutrophil interactions

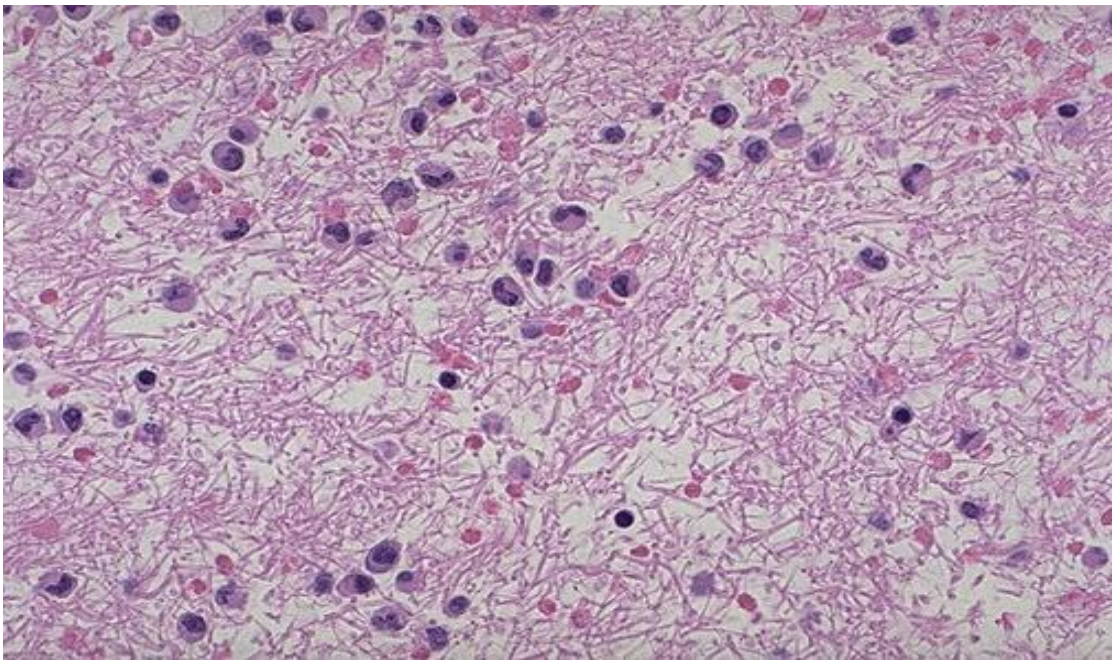


Acute inflammation: tissue effects



Pavementation and diapedesis

Acute inflammation: tissue effects



Inflammatory cells in protein exudate

Chemical mediators of inflammation

- Vasoactive amines,: (Histamine, Serotonin (5-HT))
- Neuropeptides, : (Substance P).
- Plasma proteases and the complement system: (Action of Hageman factor)
- Arachidonic acid metabolites ,: (Prostaglandins, Leukotrienes , Lipoxins)
- Cytokines: (IL-1, TNF etc.)
- Chemokines (CXC and CC)
- Nitric oxide and oxygen-derived free radicals

PREFORMED

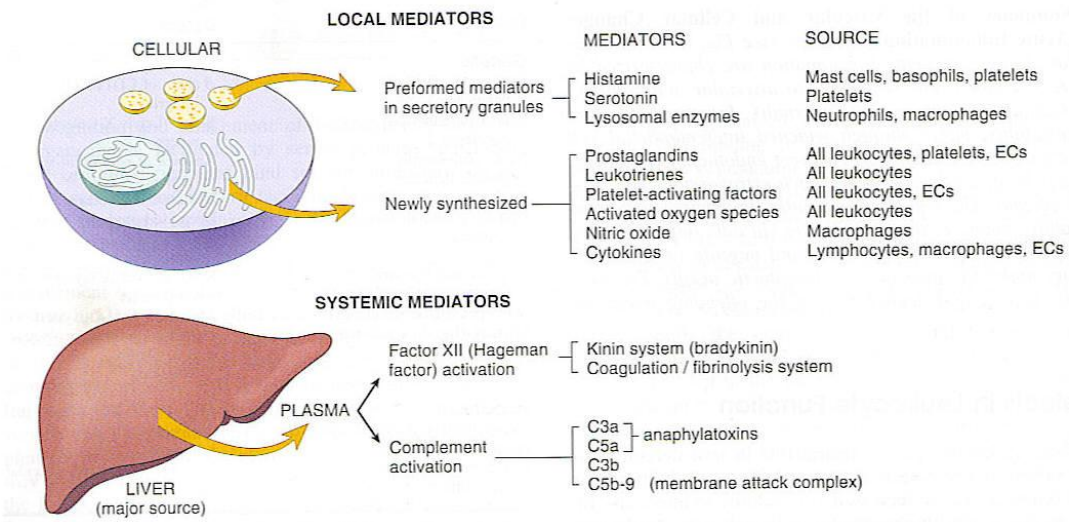
(Histamine, Serotonin)

NEWLY SYNTHESISED

(Prostaglandins, Leucotrienes, Platelet activating factor, Cytokines, Nitric oxide)

- **LOCAL AND SYSTEMIC**

Chemical mediators of inflammation (local and systemic)



Effects of mediators of inflammation

Vasodilation:

Prostaglandins, NO

Increased vascular permeability:

Histamine, serotonin, C3a, C5a, bradykinin,

Leukotrienes C4, D4, E4, platelet activating factor

Chemotaxis, leukocyte activation:

C5a, leukotriene B4, bacterial products, chemokines (IL-8)

Fever:

IL-1, IL-6, TNF, prostaglandins

Pain:

Prostaglandins, bradykinin

Tissue damage:

Neutrophil and macrophage lysosomal enzymes, oxygen metabolites NO

PHAGOCYTOSIS

Recognition and attachment

Foreign objects coated with opsonins IgG and C3b which attach toreceptors on polymorph surface.

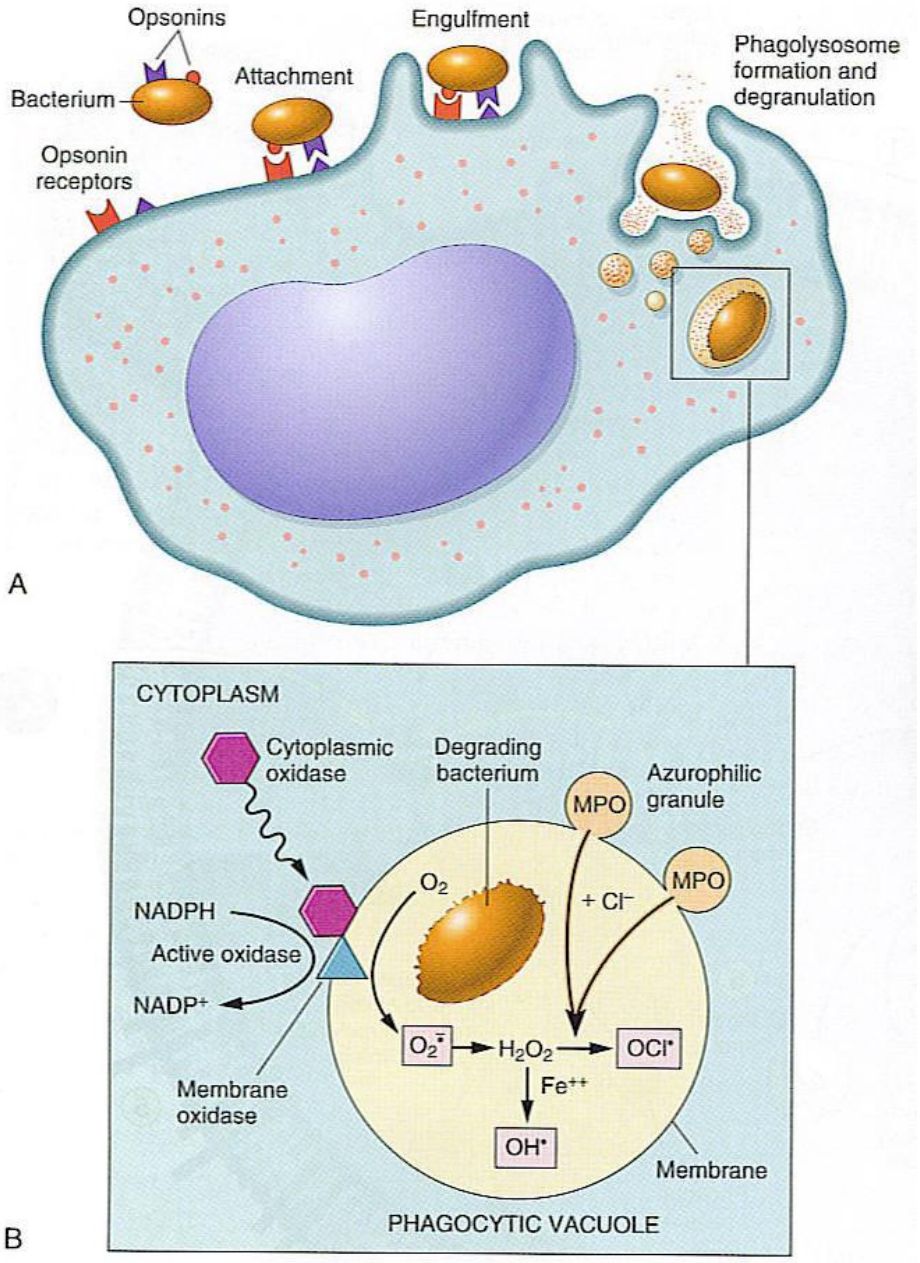
Engulfment

Cell membrane fuses around an object: at the some time lysosomes

empty into the vacuole, often before vacuole has time to seal -this gives rise to 'regurgitation during feeding' and enzymatic damage to surrounding tissue.

Killing or degradation

H_2O_2, hypohalous acid (HOC1) produced by myeloperoxidase and superoxides kill bacteria. Lysozyme digests them.

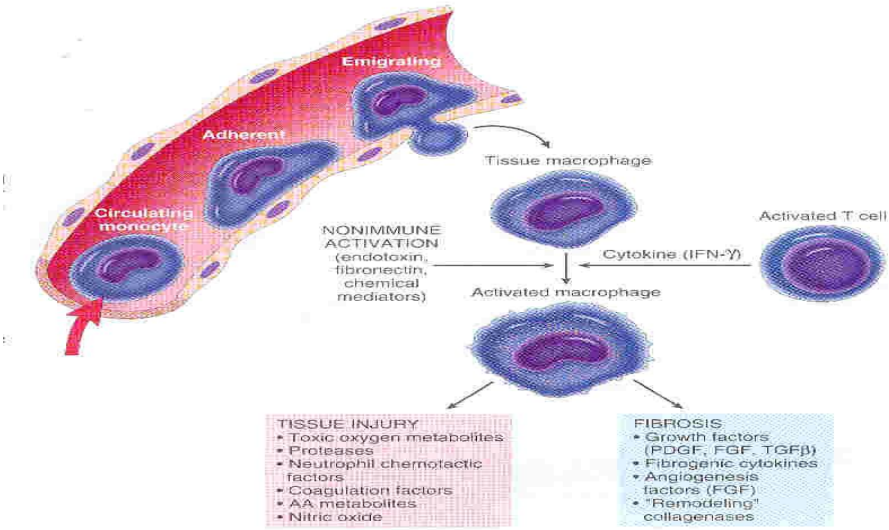


Chronic inflammation

Cells of the chronic inflammatory response

- Lymphocytes
- Monocytes/ macrophages
- Plasma cells

Maturation of circulating monocytes to macrophages



Macrophage-lymphocyte interactions in chronic inflammation