Inflammation

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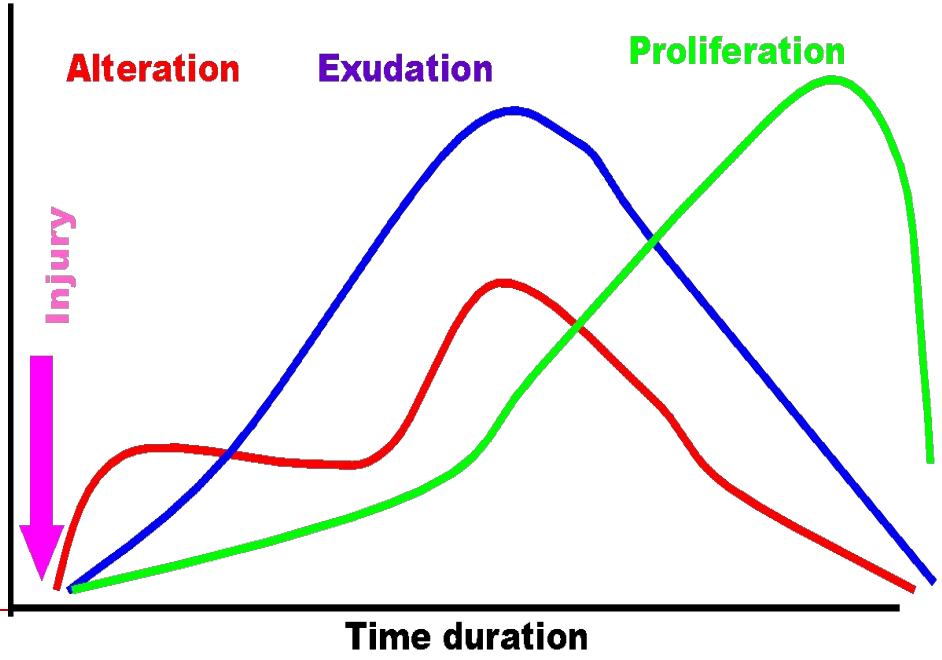
Causes of inflammation

- Exogenous Infectious factors
- Exogenous Non-infectious factors:
  - physical
  - chemical
  - biological
- Endogenous products of tissue decay
- Endogenous chemical agents

Inflammation – local manifestation of the organism general reaction to the tissue injury

Inflammation events

- Alteration (injury)
  - primary and secondary
- Exudation
  - vascular reactions
  - vascular leakage
  - leukocyte exudation
  - phagocytosis
- Proliferation



Signs of inflammation

Local:

- Calor - heat
- Rubor - redness
- Dolor - pain
- Tumor - swelling
- Functio laesa
  -loss of function

Systemic:

- peripheral blood leukocytosis
- fever
- ↑ globulins blood level
- ↑ erythrocytes sedimentation rate
- ↑ cateholamines and corticosteroids

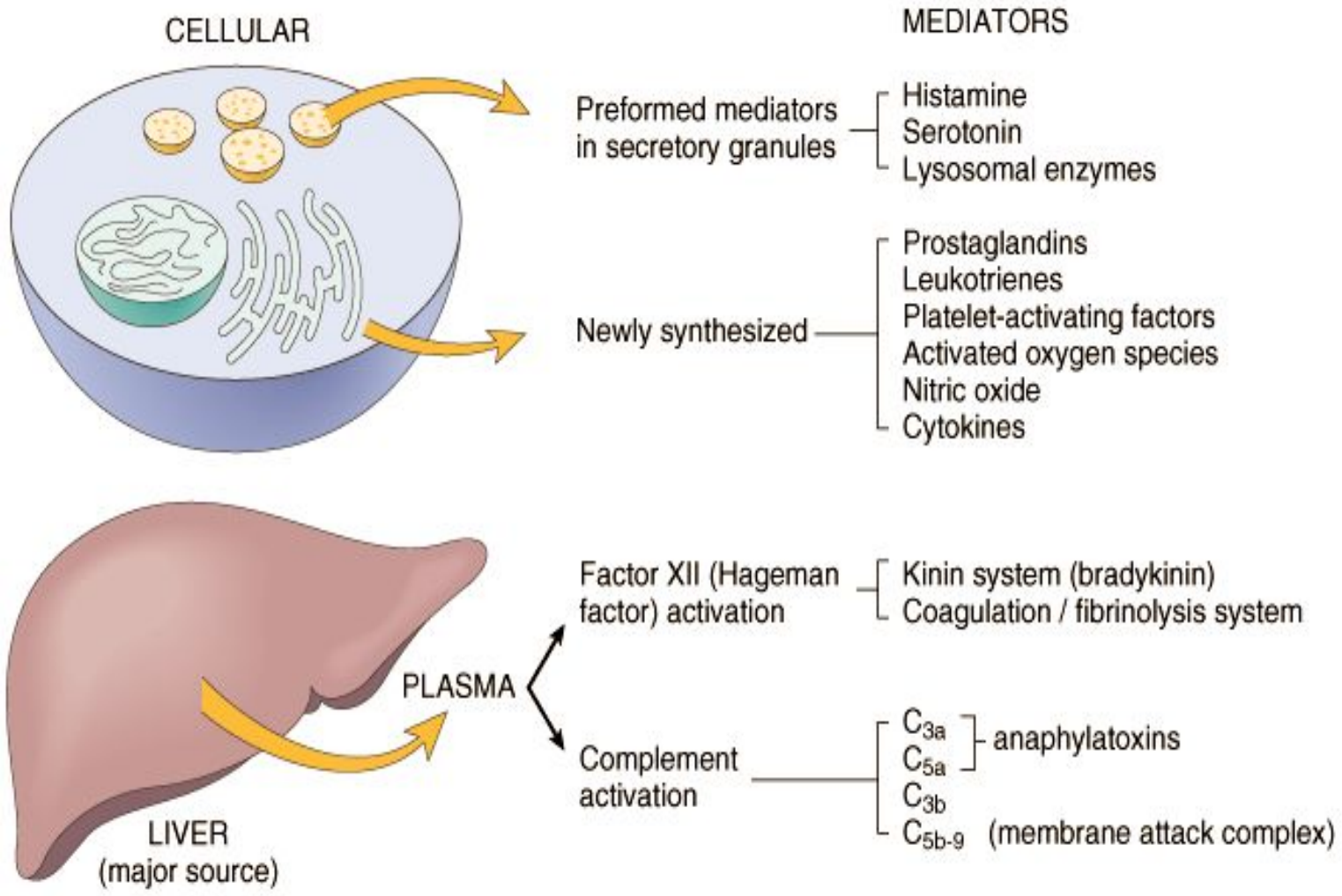
Alteration

- Primary alteration - direct action of pathogenic factor (functional and structural injury of the cells)
- Secondary alteration mechanisms:
  - disturbances of local nervous regulation and blood circulation;
  - influence of inflammatory mediators;
  - alteration of T^0, pH, oncotic, osmotic pressure;
  - lysosomal effect.

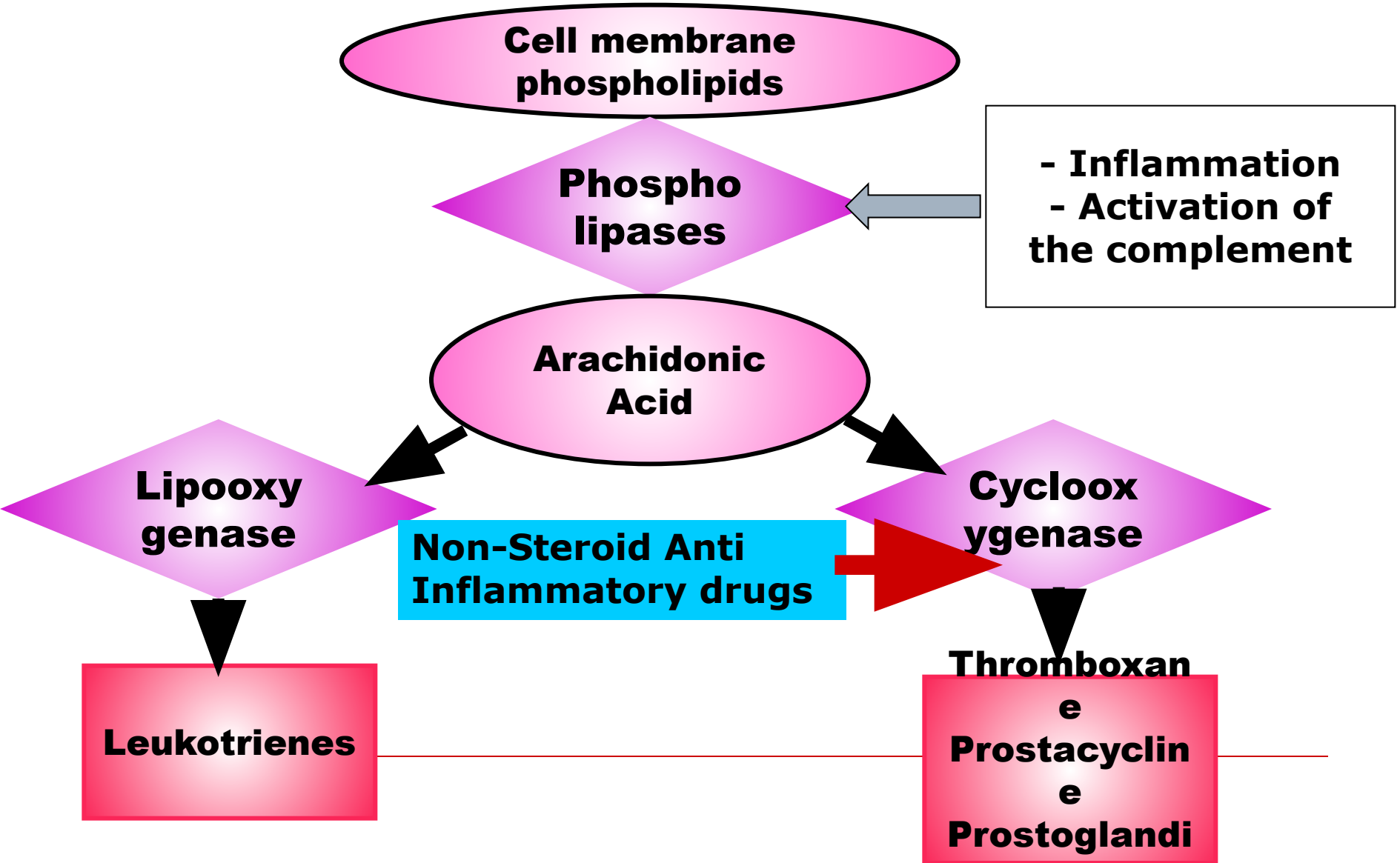
Metabolism changes

- Prevalence of catabolic processes in the early stages
- High speed of metabolic reaction (***heat***)
- Metabolic acidosis
- ↑ osmotic and oncotic pressure
- Intracellular and extracellular hyperhydration (***swelling***)
- Prevalence of anabolism – final stages

Inflammatory mediators



Arachidonic acid metabolites



Arachidonic acids metabolites

- Thromboxane A2 - platelet aggregator and vasoconstrictor
- Prostacyclin - ↓ platelet aggregation and vasodilator.
- Prostaglandins:
  - dilation of vessels , ↑ vessels permeability
  - aggregation and adhesion of blood cells
  - fever, pain
- Leukotrienes :
  - ↑ smooth muscles tone (GIT, bronchi, blood vessels)
  - ↑ vessels permeability
  - chemotaxins for neutrophiles

Cellular mediators

- Active oxygen radicals:
  - endothelial cells damage (☐ vessels permeability)
  - other cells injury
- Platelet activating factor (PAF):
  - Platelet aggregation and release
  - ☐ smooth muscles tone (bronchi, vessels)
  - ☐ leukocyte adhesion to endothelium
  - ☐ leukocyte chemotaxis, degranulation and oxidative burst

Cellular mediators

- Lysosomal enzymes:
  - mediate tissue injury
  - activate bradykinine synthesis
  - mast cells degranulation
  - chemotaxis
- Nitric oxide:
  - vasodilation
  - cytotoxic effect
- Cytokines:
  - interleukins
  - TNF
  - interpherone

Plasma mediators

Bradykinin:	**Complement**
vasodilation and ↑ vascular permeability	
chemotaxis	
mast cells degranulation	opsonisation
activate AA cascade	

Clotting system

- mobilization of molecules of adherence
- activation of cyclooxygenase
- production of NO and PAF

The summary of inflammatory mediators' activity

Vasodilation

↑ of blood vessels permeability

Leukocyte adhesion

Chemotaxis

Fever

Tissue damage

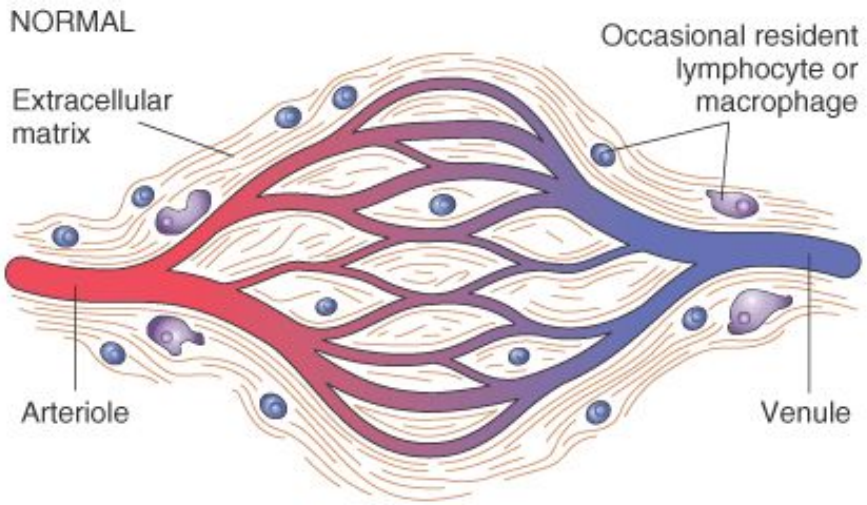
Pain

Changes in vascular flow

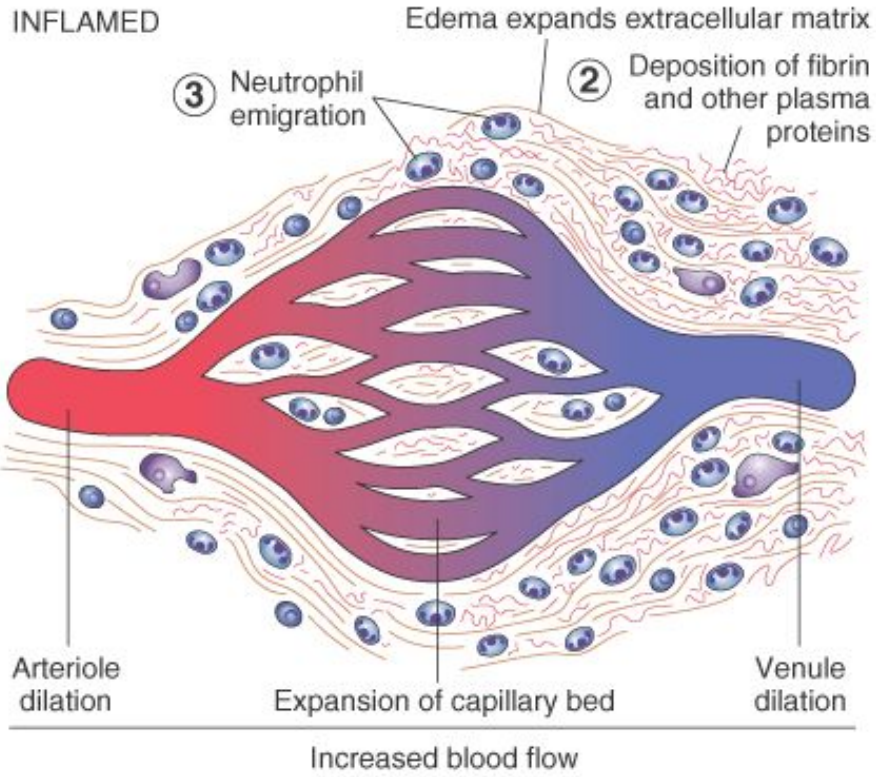
1. **Arterioles constriction** (activation of sympathetic nerves, mediators influence) -localization of injuring agent
2. **Arterial hyperemia** (dilatation of arterioles due to BAS) - increase the general rate of metabolism

Changes in vascular flow

3. **Venous hyperemia** and pre-stasis (dilation of venules and post-capillaries):
   - increased blood viscosity
   - swollen vessel walls
   - squeezing with inflammatory exudates
   - leukocytes margination along the vessels walls
4. **Stasis** - complete stop of blood flow.



Venous hyperemia and stasis prevent the spreading of the damage to surrounding tissues.

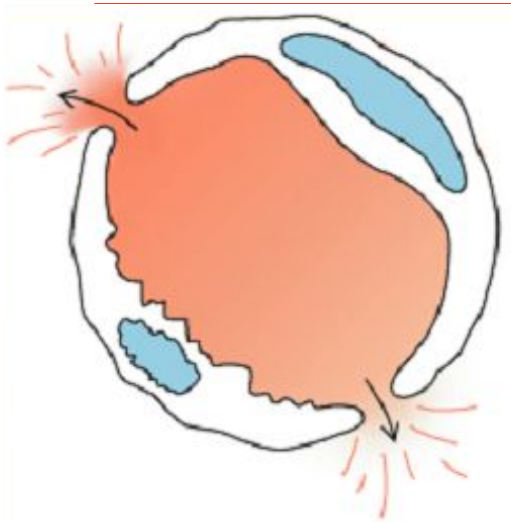


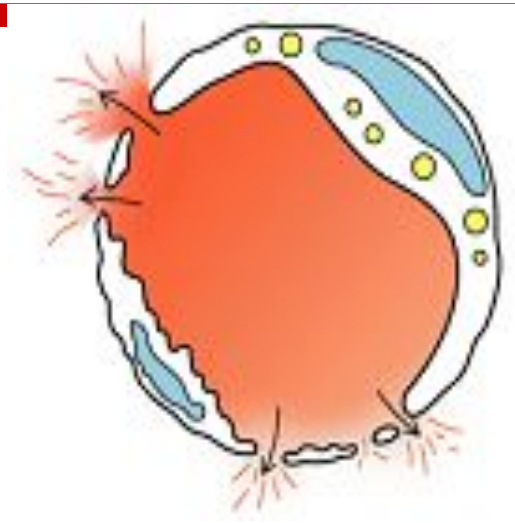
Arterial and venous hyperemia result in the increase of vessels permeability and promote exudate formation.

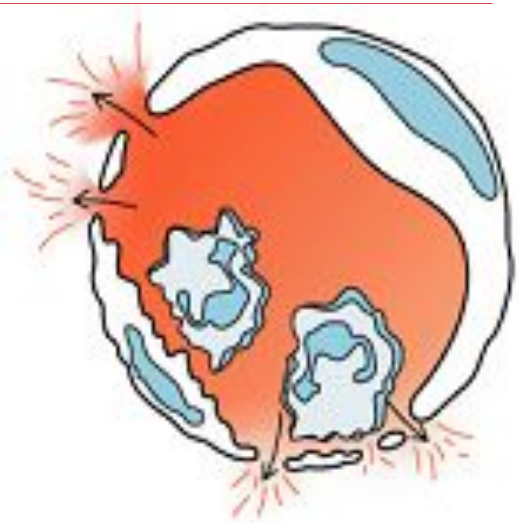
Mechanisms of exudation

- ↑ vascular permeability (vascular leakage).
- ↑ intravascular hydrostatic pressure
- ↑ osmotic and oncotic pressure of interstitial fluid

Increase of vascular permeability







Endothelial cells contraction

- histamine, bradykinin
- occurs rapidly after exposure to mediator
- reversible

Direct endothelial injury

- severe non-specific injuries (burns or bacterial infection)
- leakage lasts until vessels are thrombosed or repaired

Leukocyte-dependent endothelial injury

- toxic oxygen radicals and proteolytic enzymes

Mechanisms of exudation

- ↑ hydrostatic pressure - ↑ filtration of fluid from capillaries.
  - Ultrafiltrate of blood plasma with protein less then 2 % - transudate.
  - Inflammatory - more then 2 % protein.
- ↑ osmotic and oncotic pressure
  - Inflow of protein rich fluid from plasma to the site of inflammation.
  - Destruction of molecules by the enzymes

The role of exudation

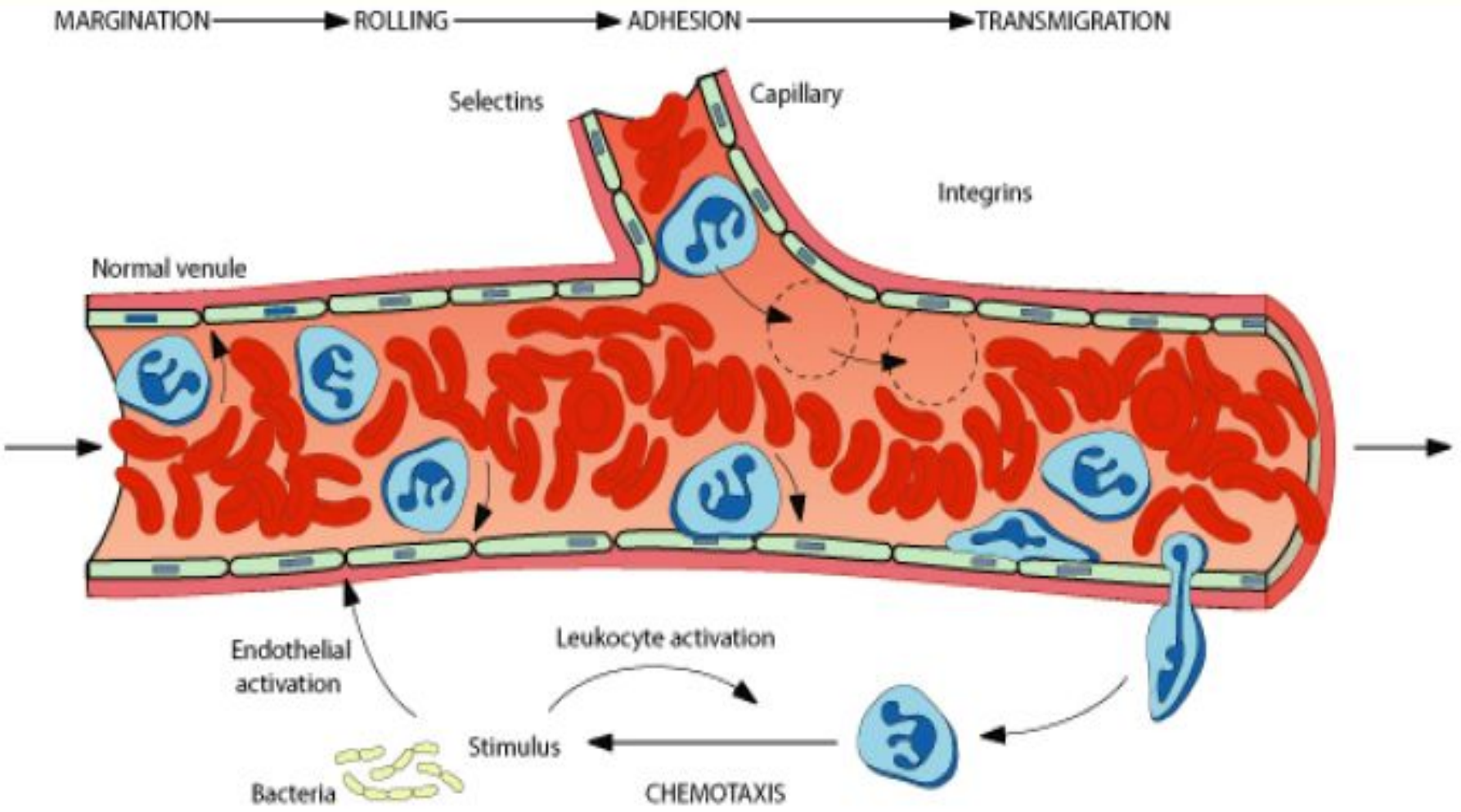
Negative

- squeezing of tissues and organs
- exudate outflow to body cavities and big vessels
- abscess and phlegmon formation

Positive

- transport of antibodies, inflammatory mediators
- elimination of toxins and metabolites from inflammatory site
- localization of the inflammatory agents

Extravasation of leukocytes



Leukocytes migration

- Move pseudopods into the junctions between the endothelial cells
- Squeeze through interendothelial junctions
- Release proteolytic lysosomal enzymes making gaps in vessels walls
- Order of migration: neutrophiles, monocytes, lymphocytes

Chemotaxis

Chemotactic agents:

- bacterial membrane lipopolysaccharides
- components of the complement (3b, 5a,5b,6,7
- leukotrienes
- products of tissue decay

Mechanism

Binding to receptors□

calcium mobilisation□

contraction of microfilaments□

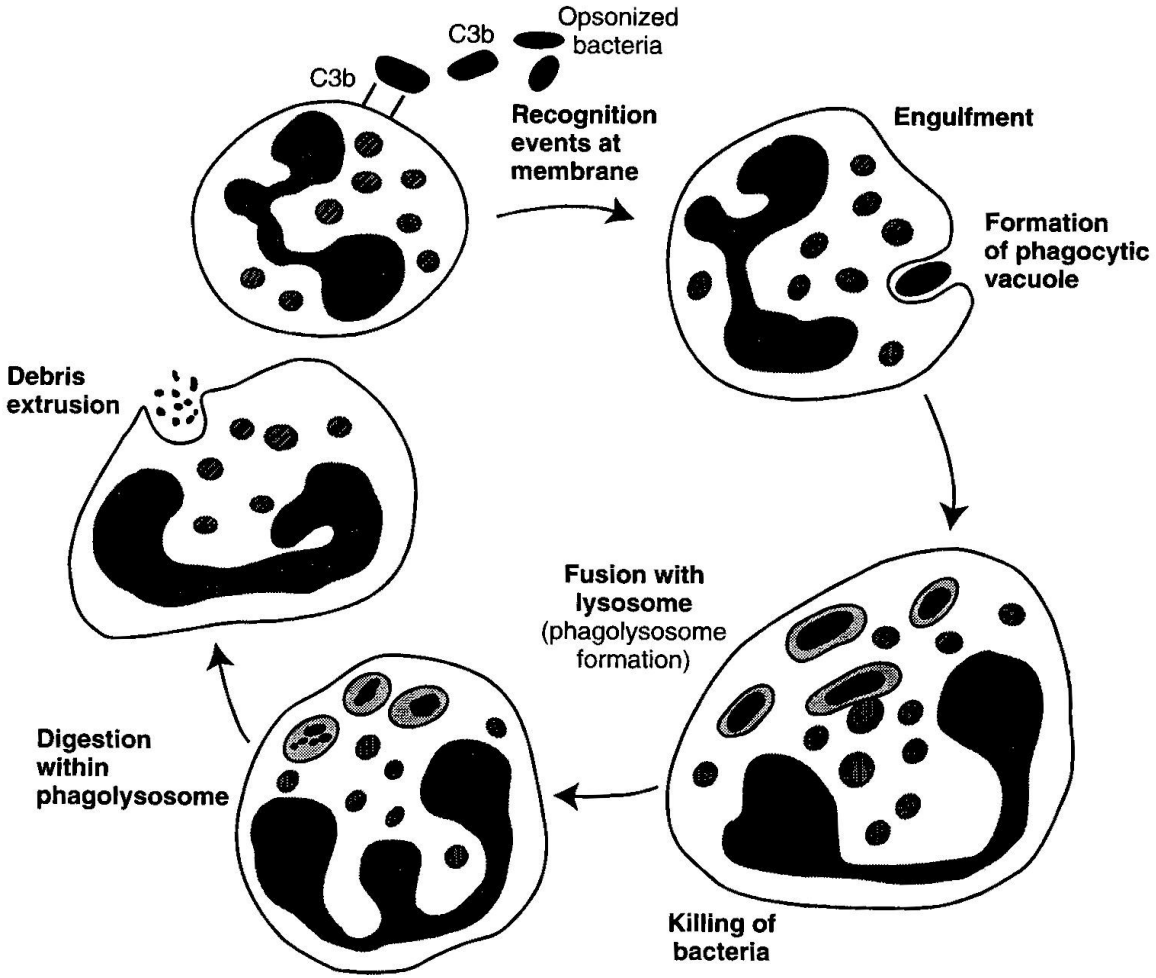
movement

Leukocytes role in inflammation

- Protective function – phagocytosis.
- Synthesis and secretion of inflammatory mediators.
- Processing and presentation of foreign agents for the immune systems.
- Tissue damage with :
  - Lysosomal enzymes
  - Active oxygen radicals
  - Products of AA metabolism (prostaglandins and leukotrienes)

Stages of phagocytosis

1. **Chemotaxis**
2. **Adherence (opsonins - IgM, IgG, C3b)**
3. **Phagosome formation**
4. **Killing or degradation of the ingested material**



Two mechanisms of bacterial killing

- **Oxygen-dependent mechanism** reactive oxygen species – superoxide anion, hydroxyl ion, hydroperoxide
- **Oxygen Independent Mechanisms** – using the content of granules (lysozyme, proteins influencing bacterial cell wall)

Proliferation in inflammation

- Regeneration - replacement of dead cells with new ones; the function is restored.
- Repair - replacement with fibrous connective tissue cells and fibers; the functions is not restored.

The steps of repair

- Phagocytosis
- Proliferation of endothelial cells and fibroblasts in the damaged area.
- The growth of new vessels to establish blood circulation in the healing area
- Fibroblasts produce collagen.
- Mature scar is produced.

Factors influencing proliferation

Local:

- Persisting infection, foreign material
- Inadequate blood supply
- Excessive movement
- Irradiation

Systemic:

- Age
- Nutritional deficiencies
- Metabolic diseases
- Catabolic state associated with malignancies

Substances:

Growth factors, TNF – activation

Chalones, glucocorticoids - inhibition

Classification of inflammation

Classification based on the cause of inflammation:

- *Infectious:* non-specific (cocci) and specific (tuberculosis, syphilis)
- *Non-infectious* (aseptic) – caused by infarctions, hemorrhages, salt deposition

Classification of inflammation

Classification based on the prevailing mechanism:

- *Alterative* –prevailing alteration develops in parenchymal organs (myocardium, liver, kidneys).
- *Exudative* - prevailing exudate formation.
- *Proliferative* (productive) - prevalence of reparative process; proceeds chronically

Types of exudative inflammation

- *Serous inflammation* - 3-8% of protein, single neutrophiles in exudate.
- *Catarrhal inflammation* presence of mucus in exudates.
- *Fibrinous inflammation* presence of fibrin in exudate
  - *Croupous inflammation* - fibrinous pericarditis (hairy heart), croupous pneumonia.
  - *Diphtheritic* – throat, pharynx, tonsils

Types of exudative inflammation

- *Purulent (suppurative) inflammation* production of pus - pyogenic bacteria (staphylococci).
  - **Abscesses** are localized collections of pus.
  - **Phlegmon** and **empyema** are diffuse pus infiltrations.
- *Putrefactive inflammation* - a result of putrefactive bacteria injury.
- *Haemorrhagic inflammation* - presence of erythrocytes in exudates. (anthrax, plague, influenza).

Neural and hormonal control of inflammation

- Pro-inflammatory hormones - growth hormone, mineralocorticoids
- Glucocorticoids, catecholamines - anti-inflammatory effect
- Violation of peripheral innervation leads to chronic inflammation development

Inflammation outcomes

- Complete resolution - the injury is limited
- Healing by scarring – impossibility of regeneration or s abundant fibrin exudation.
- Abscess formation - pyogenic microorganisms.
- Progression to chronic inflammation

Chronic inflammation

- follow acute inflammation
- chronic from the onset due to:
  - disturbances of phagocytosis
  - high level of glucocorticoids and catecholamines
  - persistent infections or intoxications.
  - prolonged exposure to nondegradable material (silica particles – silicosis)
  - autoimmune diseases.