Chemical Mediators of Acute Inflammation

M. Saranyaa

Perfusionist & lecturer

Chemical mediators

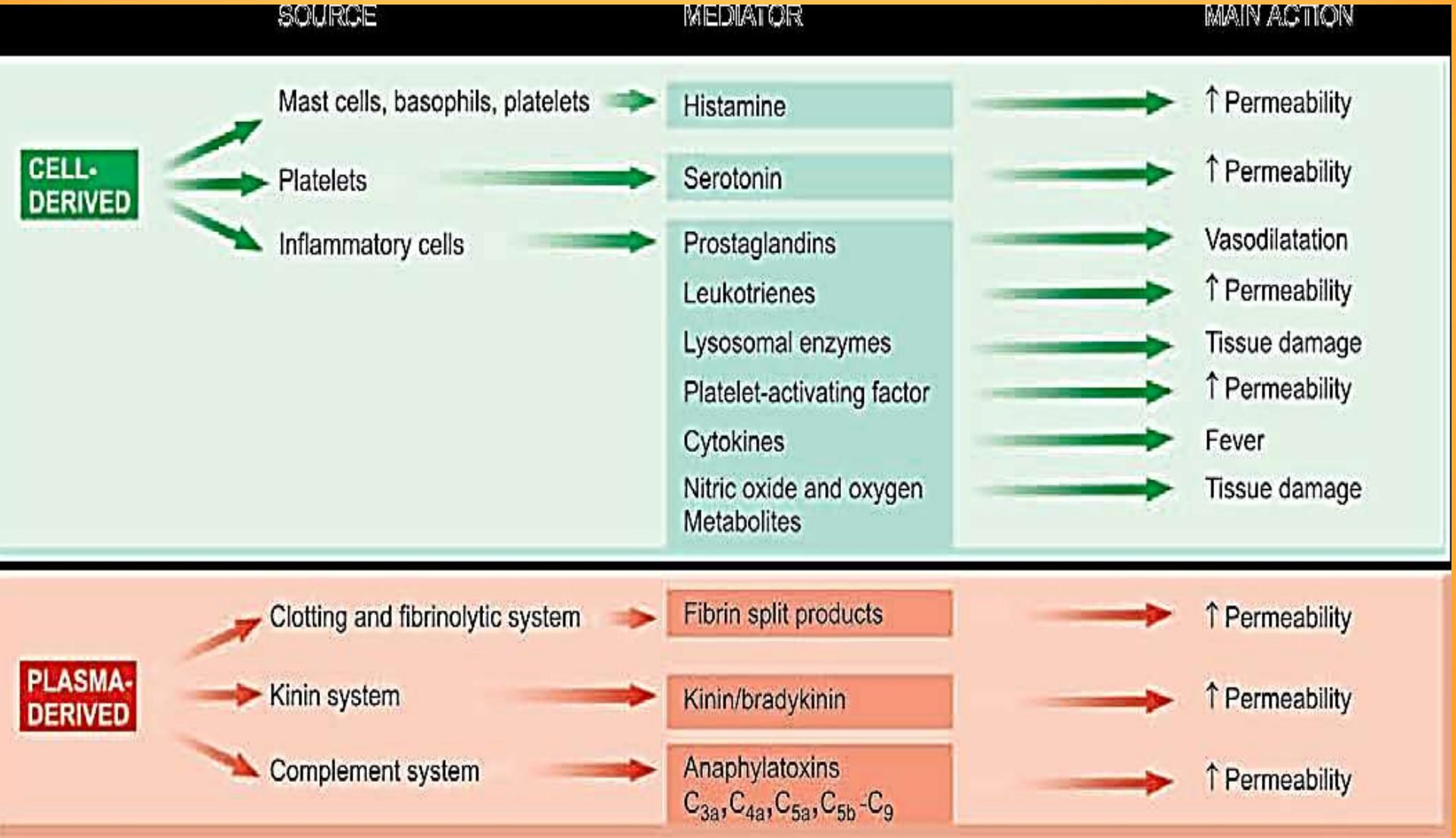
- It is also called as ***permeability mediators***
- ***Any messenger that acts on blood vessels, inflammatory cells or other cells to contribute to an inflammatory response***
- The chemical mediators have been identified which partake in other processes of acute inflammation as well e.g. vasodilatation, Chemotaxis, fever, pain and cause tissue damage.
- The substances acting as chemical mediators of inflammation may be released *from the* ***cells, the plasma, or damaged tissue***

Division of Mediators

They are broadly classified into 2 groups:

- ***mediators released by cells***
- ***mediators originating from plasma***

Sources and action of mediators



Cell derived mediators

- ***Vasoactive amines*** (Histamine, neuropeptides)
- ***Arachidonic acid metabolites*** (Eicosanoids)
- i. Metabolites via cyclo-oxygenase pathway (prostaglandins, thromboxane A2, prostacyclin)

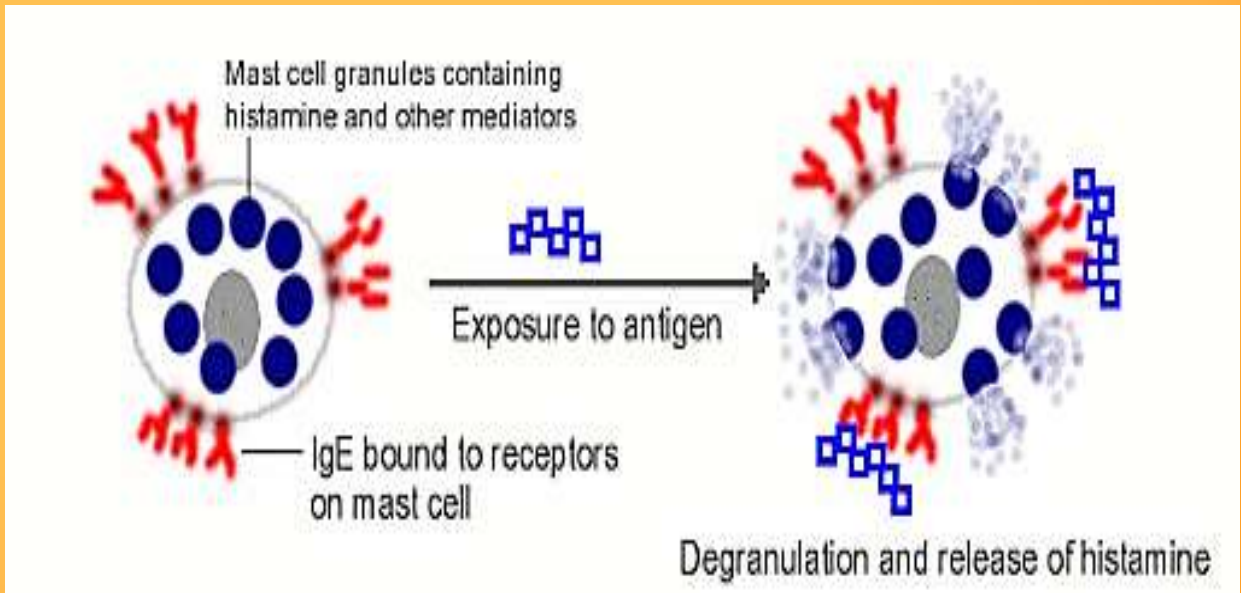
  ii. Metabolites via lipo-oxygenase pathway (leukotrienes, lipoxins)
- ***Lysosomal components*** (from PMNs, macrophages)
- ***Platelet activating factor***
- ***Cytokines*** (IL-1, TNF-α, TNF-β, IFN-γ, chemokines)
- ***Free radicals*** (Oxygen metabolites, nitric oxide)

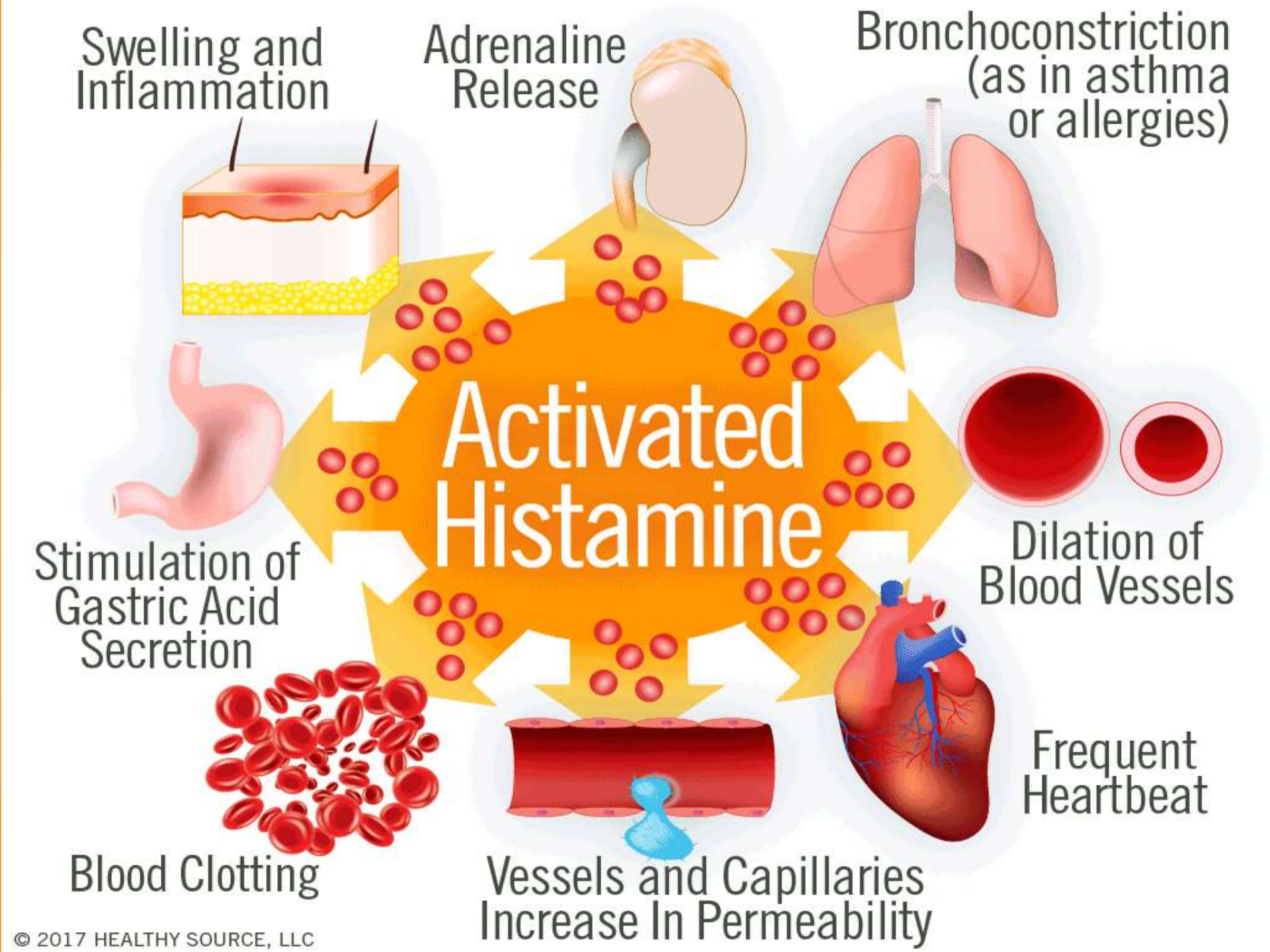
Vasoactive amines

- **Histamine =** stored in the granules of ***mast cells, basophils and platelets***
- Histamine is released because of Stimuli or substances inducing acute inflammation e.g. heat, cold, irradiation, trauma, irritant chemicals, immunologic reactions.

The main ***actions*** of histamine are:

- ***vasodilatation,***
- ***increased vascular permeability,***
- ***itching***
- ***pain.***



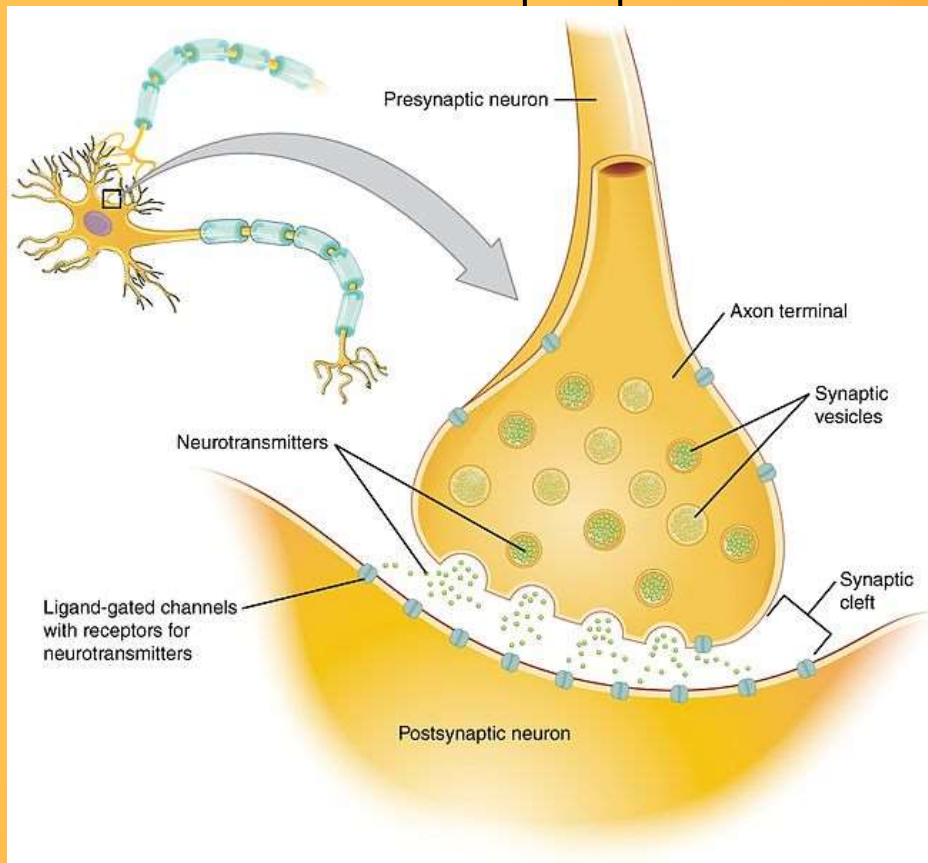


Neuropeptides

- The neuropeptides are also called as substance P , vasoactive intestinal polypeptide (VIP) and Somatostatin
- These small peptides are produced in the central and peripheral nervous systems

The functions are;

- Increased vascular permeability.
- Transmission of pain stimuli.
- Mast cell degranulation



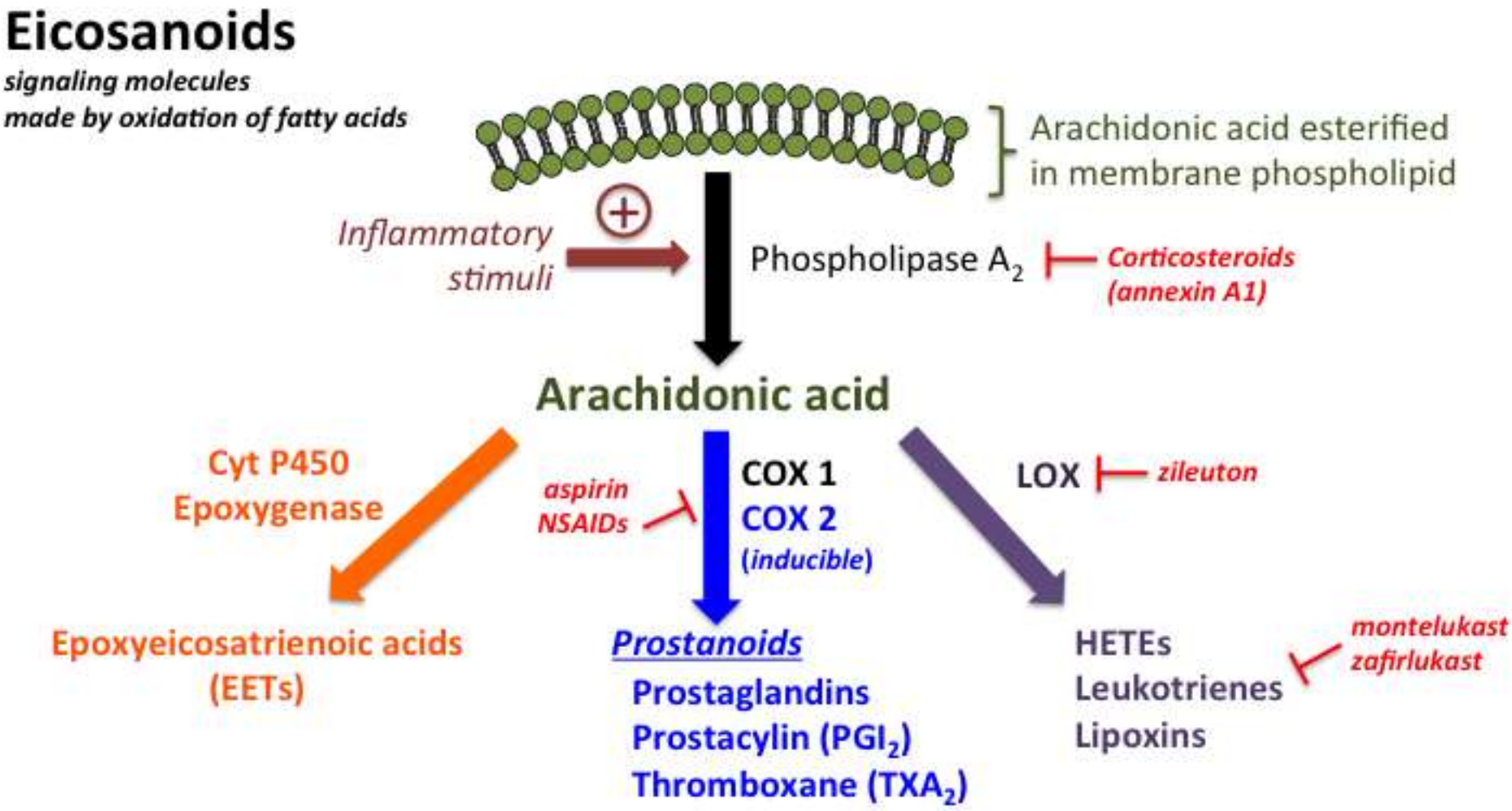
Arachidonic Acid Metabolites

- Arachidonic acid metabolites or eicosanoids are the ***most potent mediators of inflammation***
- Arachidonic acid is a constituent of the ***phospholipid cell membrane.***

The two important pathways:

- ***cyclooxygenase (COX)***
- ***lipoxygenase***
- It is produced by endothelial cells, leukocytes and platelets
- It act locally on smooth muscle, endothelium and platelets.

Arachidonic Acid Metabolites



Lysosomal components

- The inflammatory cells— ***neutrophils and monocytes***, contain lysosomal granules

- ***Lysosomes will break down unwanted microbes***

- ***Myeloperoxidase*** causes oxidative lysis by generation of oxygen free radicals, acid hydrolases act within the cell to cause destruction of bacteria in ***phagolysosome*** while proteases attack on the extracellular constituents such as basement membrane, collagen, elastin, cartilage.

Platelet activating factor

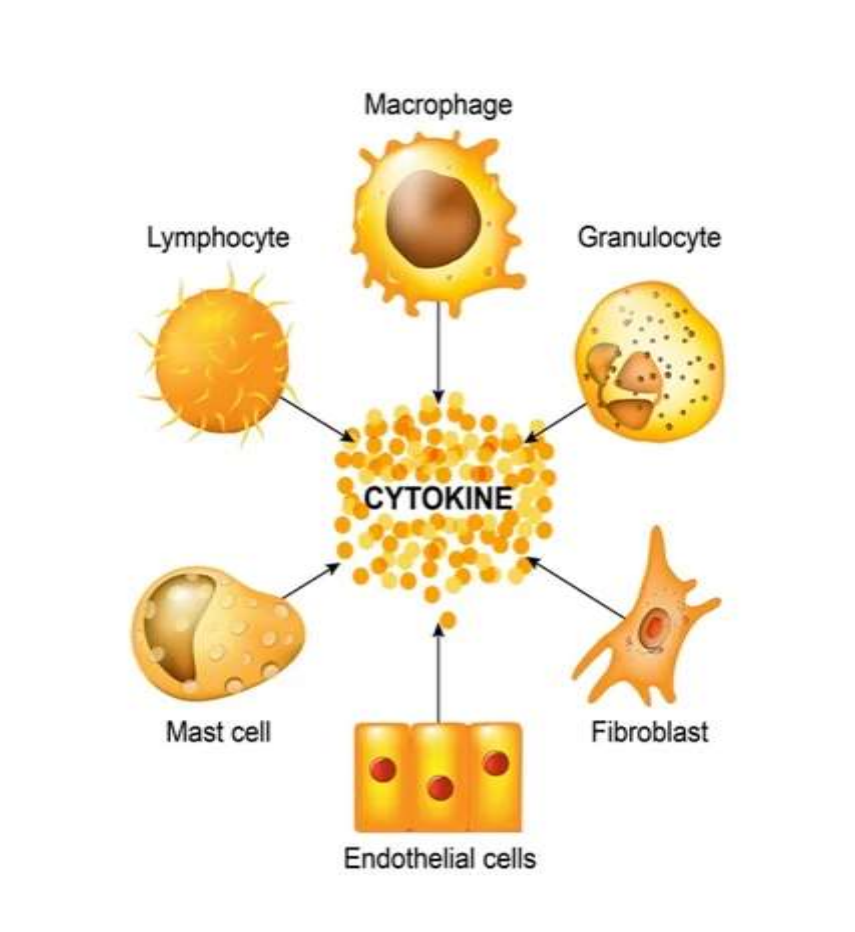
- It is produced by platelets, endothelial cells, leukocytes

Functions:

- platelet aggregation and release
- bronchoconstriction & vasoconstriction [high]
- vasodilation and vascular permeability [low]
- increases leukocyte adhesion & chemotaxis
- increases leukocyte degradation

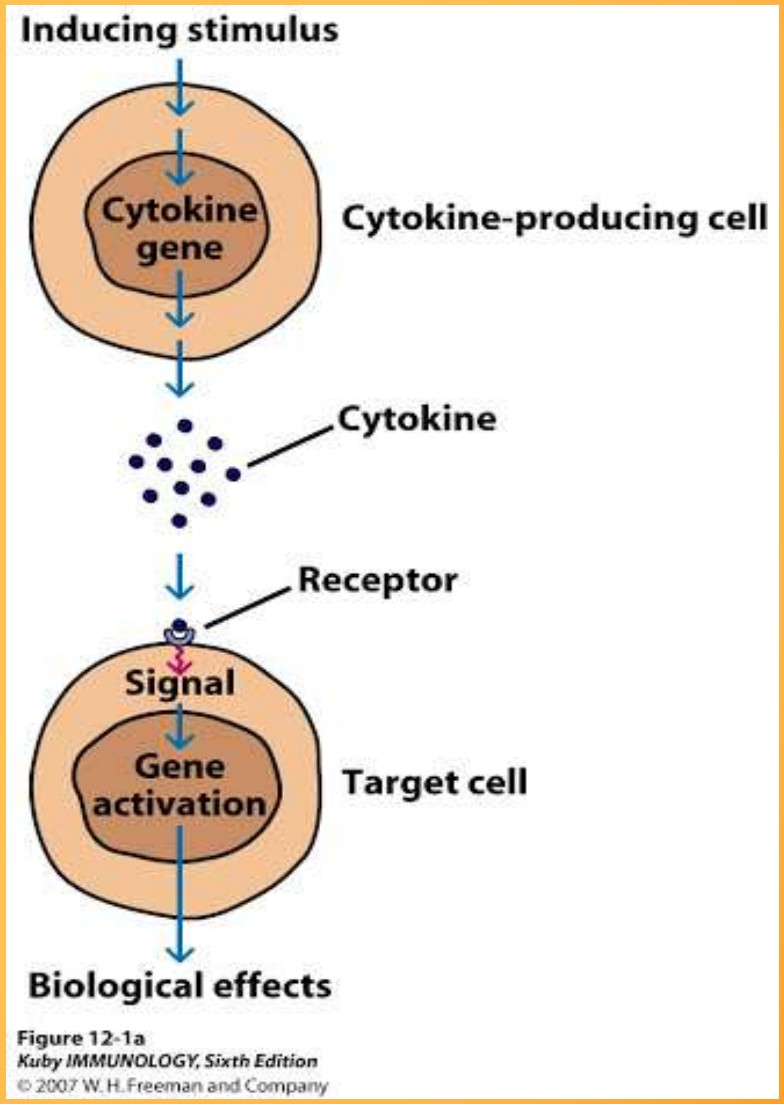
Cytokines

- Cytokines are polypeptide substances produced by activated lymphocytes and activated monocytes
- Major cytokines are interleukin-1 (IL-1), tumour necrosis factor (TNF)-α and β, interferon (IFN)-γ, and chemokines (IL-8, PF-4)



Cytokines function

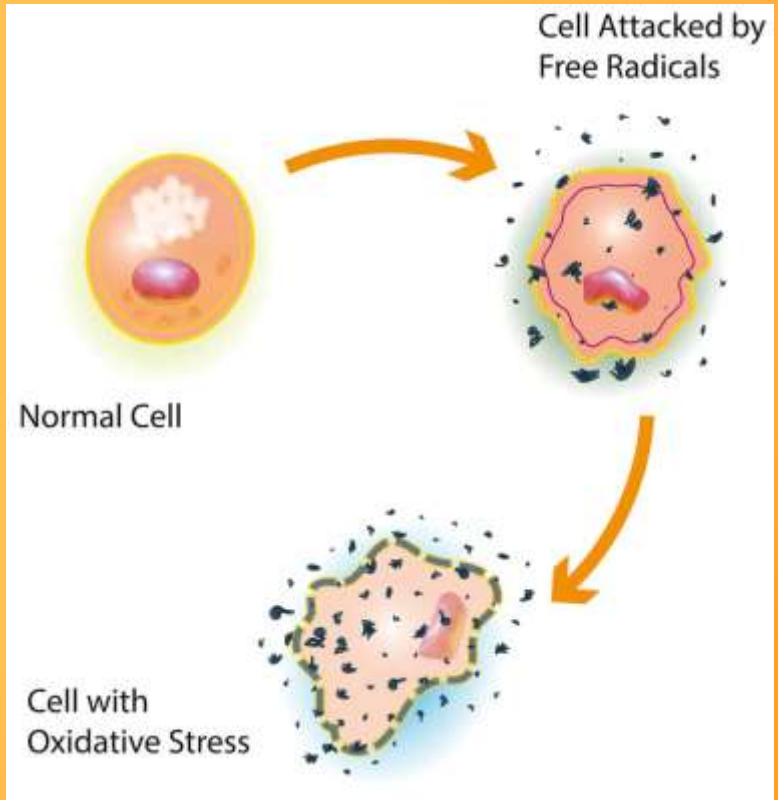
- Increased leucocyte adherence
- thrombogenicity
- elaboration of other cytokines
- fibroblastic proliferation and
- acute phase reactions



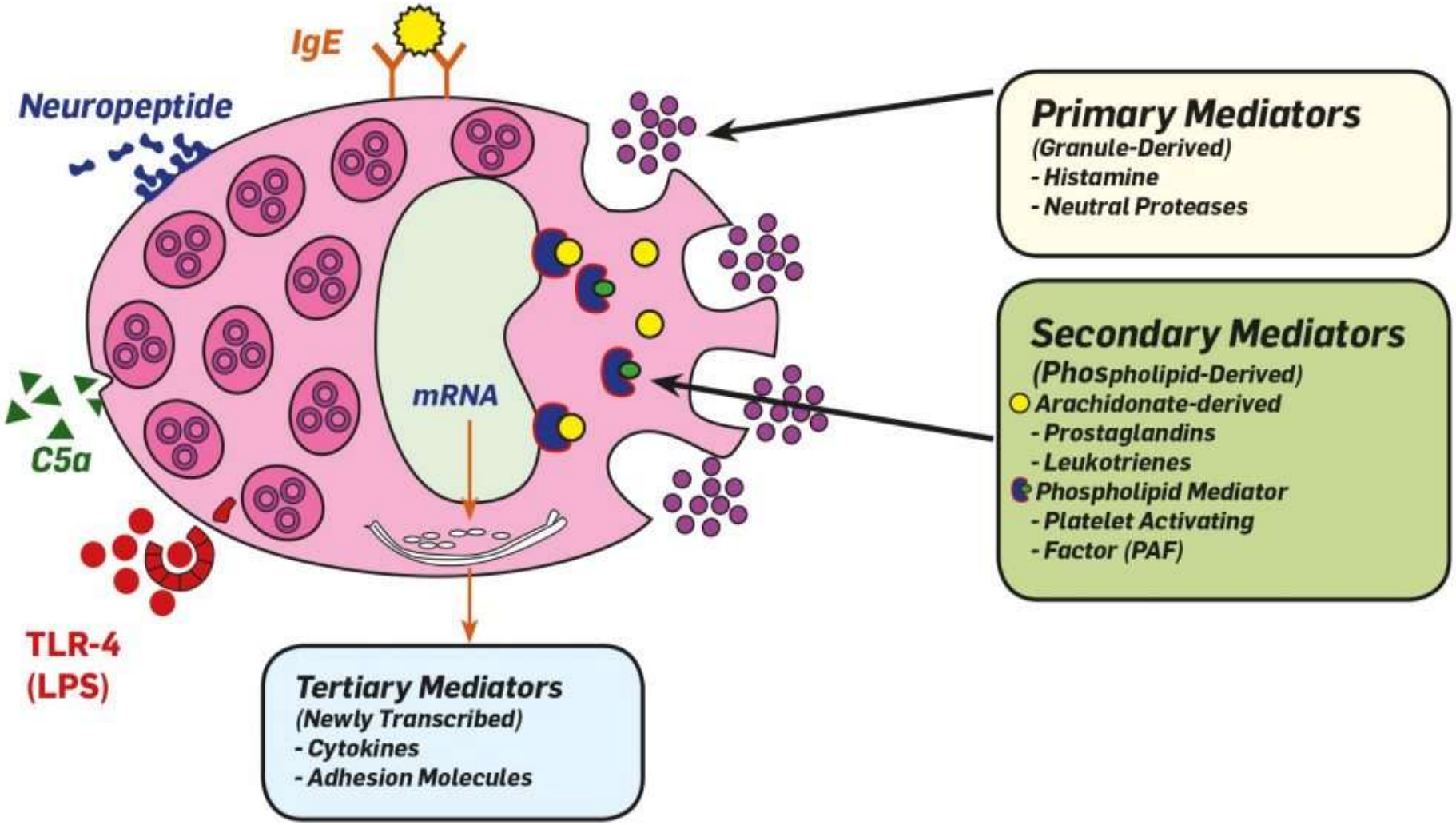
Free Radicals

- Free radicals act as potent mediator of inflammation
- Oxygen-derived metabolites are released from activated neutrophils and macrophages and include superoxide oxygen (O'2), H2O2, and toxic NO products
- This causes increased

vascular permeability



Chemical Mediators



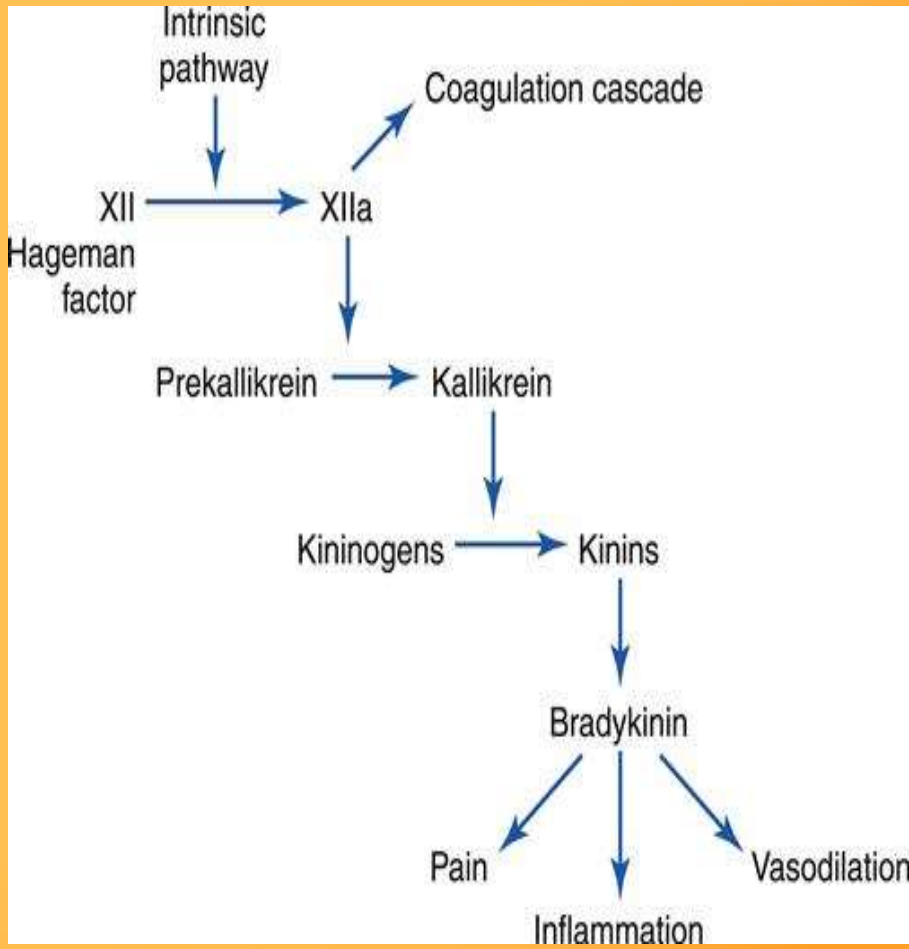
Plasma-derived mediators

- The kinin system
- The clotting system
- The fibrinolytic system
- The complement system

The kinin System

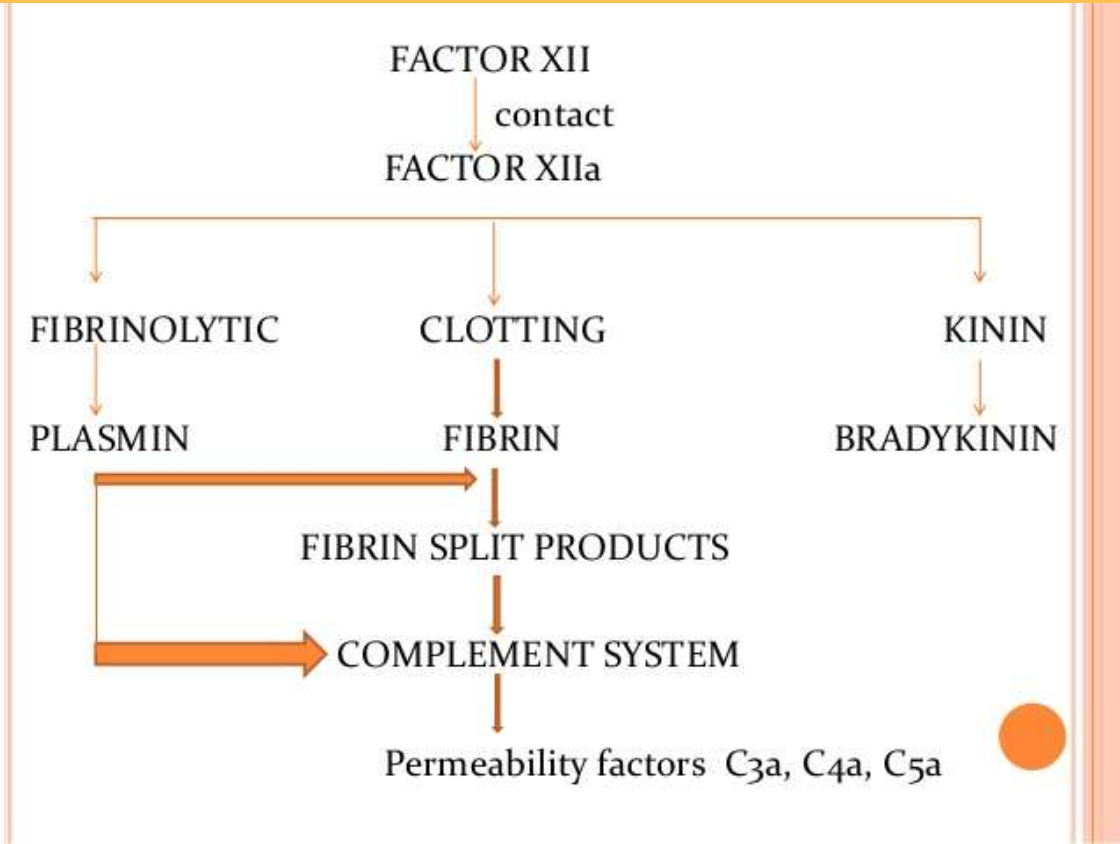
Bradykinin acts in the early stage of inflammation and its effects include:

- smooth muscle contraction;
- vasodilatation;
- increased vascular permeability;
- pain.



The clotting system & Fibrinolytic system

- Factor Xlla initiates the cascade of the clotting system resulting in formation of fibrinogen which is acted upon by thrombin to form fibrin and fibrinopeptides



Complement Activation system

- The actions of activated complement system in inflammation are as under:
- C3a, C5a, C4a (anaphylatoxins) activate mast cells and basophils to release of histamine, cause increased vascular permeability causing oedema in tissues, augments phagocytosis.
- C3b is an opsonin.
- C5a is chemotactic for leucocytes.
- Membrane attack complex (MAC) (C5b-C9) is a lipid dissolving agent and causes holes in the phospholipid membrane of the cell.

THANK YOU