

PATHOPHYSIOLOGY – BP204T

UNIT : 1

CLASS: 6

TOPIC: Inflammation mediators

- Definition: Any messenger that acts on blood vessels, inflammatory cells, or other cells to contribute to an inflammatory response.

Classification

- Cell derived mediators
- Plasma derived mediators

1. Cell derived mediators

a) vasoactive amines (serotonin,histamine)

Histamine :-

- Stored in granuls of mast cells, basophiles and platelets.
- Released by the stimuli of various agents like Heat, Cold, Irradiation, Irritant chemicals, Anaphilatoxins, Interleukins,.. etc.
- Actions ; Vasodilation

Vascular permeability

Itching and pain

Serotonin/5-hydroxy tryptamine :-

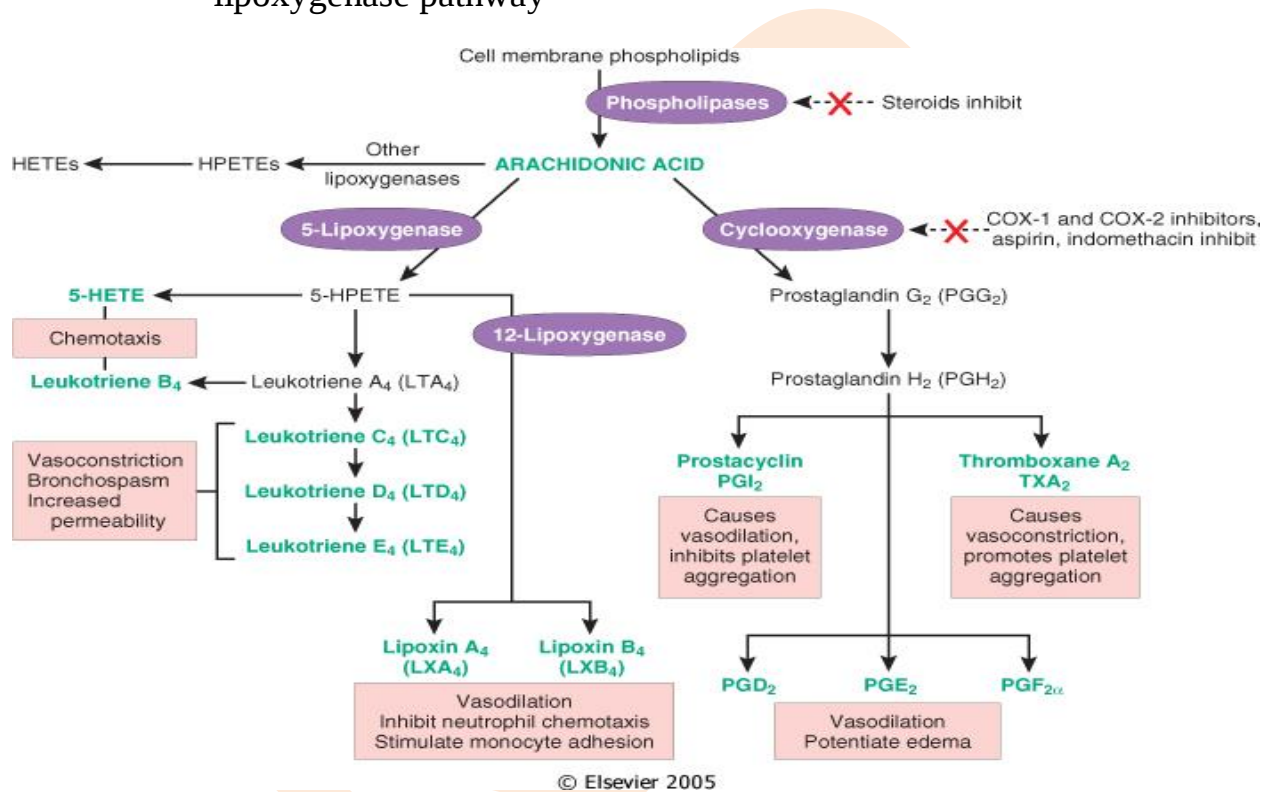
- Present in chromafin cells of GIT, Spleen, Nervous tissue, Mast cells, Platelets.
- Actions ; Similar to Histamine, but less potent

Vasodilation

Vascular permeability

b) arachidonic acid metabolites

- cyclooxygenase pathway
- lipoxygenase pathway



c) Lysosomal components

- Source:- Neutrophils and monocytes
- Potent mediators
- Degredation of bacterial and extracellular components
- Chemotaxis
- Release of acid proteases, collagenase, elastase, plasminogen activator

d) Platelet activating factor

- Phospholipid derived mediator
- Released from :- Platelets, basophil, mast cells, neutrophils macrophages, endothelial cells
- Actions:-
 - Vascular permeability
 - Vasoconstriction
 - Vasodilatation
 - Bronchoconstriction
 - Adhesion of leukocytes to endothelium
 - Chemotaxis, degranulation

e) Cytokines (IL-1,TNF- α ,TNF- β ,IF- γ ,Chemokines)

“Cytokines are a diverse group of small protein molecules with potent biological activity whose main function is in the regulation of immune responses.”

Main Cytokines are :-

- Interleukins
- Interferons
- Tumor necrosis factor
- Chemokines
- Transforming growth factor-beta
- Adipokines- leptin & adiponectin

Actions :-

- Adhesion of leucocytes to endothelium
- Synthesis of Prostacyclin, which is a vasodilator and anti aggregator of platelets
- Synthesis of PAF and thrombogenic effect on endothelial surface

f) Nitric oxide and oxygen metabolites

- Endothelium derived relaxing factor
- Macrophages, endothelial cells, neurons

Actions :-

Vasodilation

Anti-platelet activating agent

Microbicidal action

- H_2O_2 , Superoxide, Toxic NO products produced by activated neutrophils and microphages

Actions :-

Endothelial cell damage, tissue damage and vascular permeability

2. Plasma derived mediators

a) The kinin system

b) The clotting system

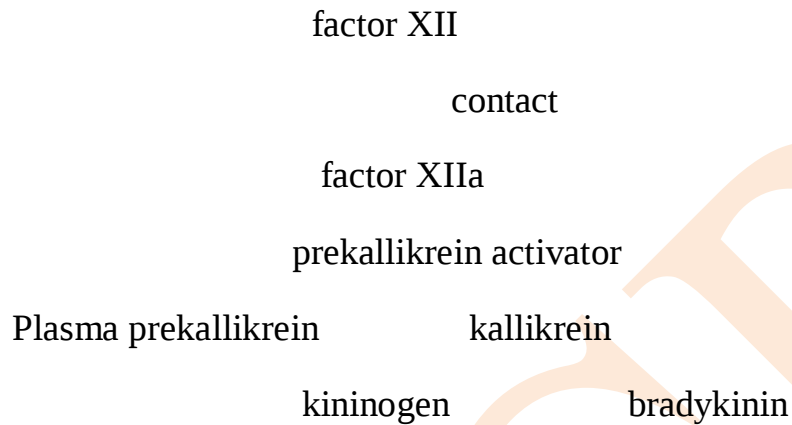
c) The fibrinolytic system

d) The complement system

- 4 interlinked systems
- Hageman factor(factor XII)

- End product of clotting ,fibrinolytic ,kinin system will activate complement system.

a) The kinin system

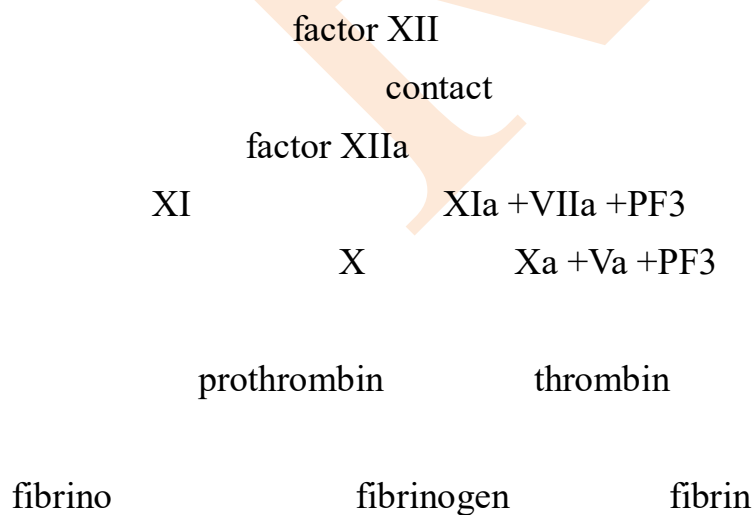


Actions :-

- ❖ Smooth muscle contraction
- ❖ Vasodilation
- ❖ vascular permeability

pain

b) Clotting system

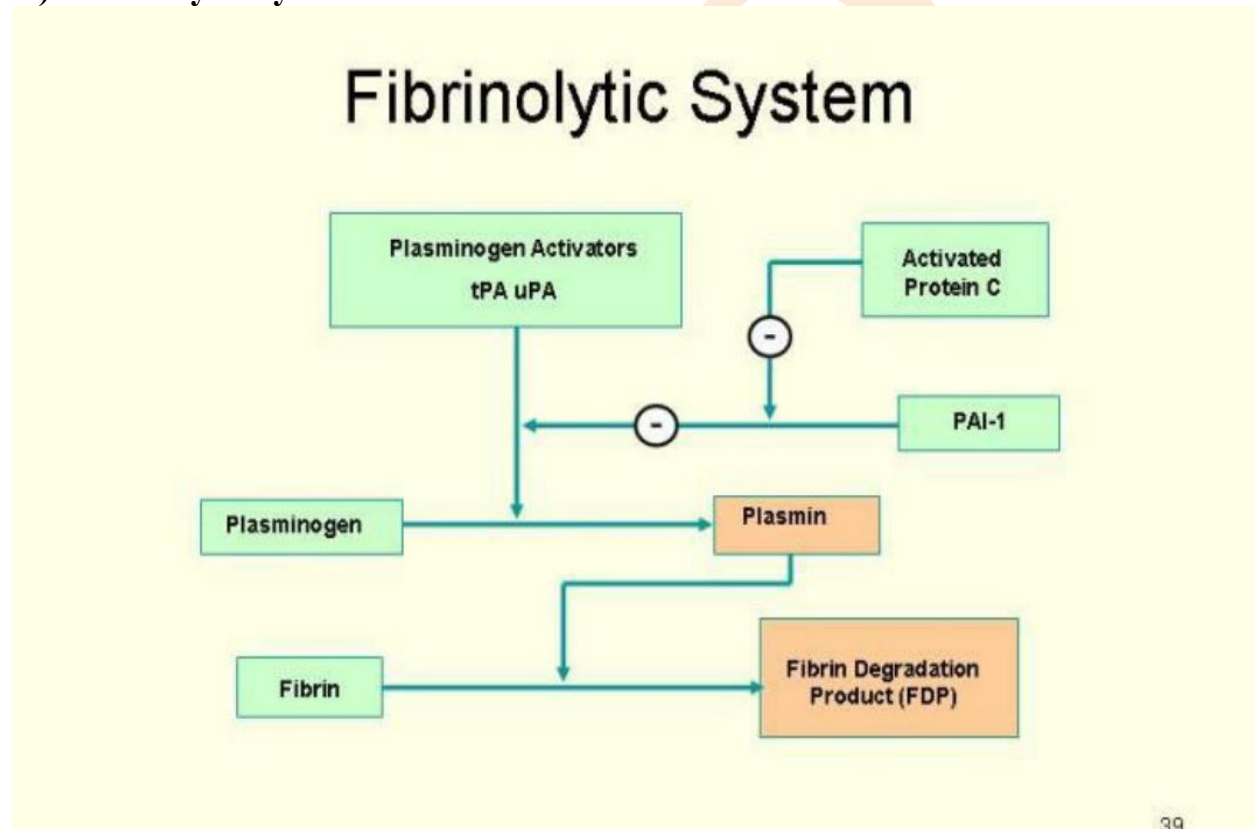


Peptides plasmin

Actions :-

- ☐ Increase vascular permeability
- ☐ Chemotaxis for leucocytes
- ☐ Anticoagulant activity

C) Fibrinolytic system



Actions :-

- Activation of factor XII to form prekallikrein activator that stimulates kinin system to generate bradykinin
- Splits off complement c3 to form c3a, which is permeability factor
- Degrades fibrin to split products, they increase vascular permeability

Complement system

- Product of complement system is anaphylatoxins c3a and c5a.
 - Potency is $c3a > c5a > c4a$
 - Actions:- release histamine from mast cells and basophils
 - C5a is chemotactic for leucocytes.
 - Membrane attack complex cause pores in cell of invading microbes.