28/9 MEDIATORS OF ACUTE INFLAMMATION

Inflamation is a response of vascularised tissues to infections and damaged tissues that brings

Mediators of Inflamation
substances that initiate & regulate inflamatory r^ns.
Therapeutic targets to limit inflamation

Mediators of acute inflamation
1. Vasoactive amine - histamine, seedonin
2. Lipid product - prostaglandins (PGs) and leukotrienes (LT)
3. cytokines - TNF, IL1, IL6, chemokines.
4. Complement system

Vasoactive Amine (Histamine, serotonin)
Stored as preformed granules
- released during inflammation
- Mast cells, basophils, platelets
Function: dilation of arterioles and permeability of venules.

Mediators → cell derived
→ Plasma derived. (complement syst)

Histamine act on H1 receptors (microvascular endothelial cells)
Anti histamine drugs - Cetirizine
Secretion: platelets, neuroendocrine cells (GI tract)
primary fn - neurotransmitter in GI tract.

Arachidonic acid metabolites
Cell membrane - phospholipids - arachidonic acid - PGs, LTs.

cell membrane phospholipids
↓ phospholipases
Arachidonic acid → lipoxygenase → HPETES → HETES
Arachidonic acid → cyclooxygenase → PG, TX
Lipoxygenase → LT, Lipoxins

Prostaglandins
Most impt. PGs in inflamation.
PGE2, PGD2, PGF2α, PGI2 (prostacyclin) and TxA2 (Thromboxane A2).

Prostaglandin.
PGI_2 → vasodilation
↓ platelet aggregation.

Thromboxane A2
↳ vasoconstriction
promote platelet aggregation

·PGD2
PGE2 → vasodilation, ↑
vascular permeability.

PGF2a
↓
~~Leuko~~ cont. of uterine
and bronchial smooth
muscle & small
arteriol

PGD2 → chemoattractant
X PGE2 → fever, hyperalgesia

Leukotrienes.
produced by leukocytes and
mast cells
LTB4 → chemotactic agent,
activates of neutrophils.

LTC4, D4, E4.
vaso constriction -
Bronchospasm.
↑ permeability of venules.

Lipoxins.
Lipoxin A2, B4.
Inhibition of inflammation.

Pharmacologic Inhibitors (PGs PGs)
(COX 1&2)
cox Inhibitors

↑Lipoxygenase Inhibitors
↓Zileuton

→ Corticosteroids : broad
spectrum anti-inflammatory
agents

Leukotriene receptor antagonist
drug → Montelukast
modify intake.

Cytokines and chemokine
produced by infl. cell
mediate & regulate ...

→ In A/c. Inflammation.
TNF, IL-1, IL-6,
Chemokines, IL-17.

→ chronic inflammation
IL-12.
IF
IL-17.

① Endothelial activation
(TNF & IL7.
↑ expression of endothelial
adhesion molecules
↑ production of other cytokines
and chemokines.
↑ procoagulant activity.

2. Activation of cell

TNF → augments neutrophil response
macrophage activity

IL-1 → activate fibroblast.
Stimulate TH 17 response.

③ Systemic acute phase response
→ fever.
→ regulate energy balance (promote lipid and protein metabolism).

Chemokines
Family of proteins - chemo attractants for specific type of leukocytes.

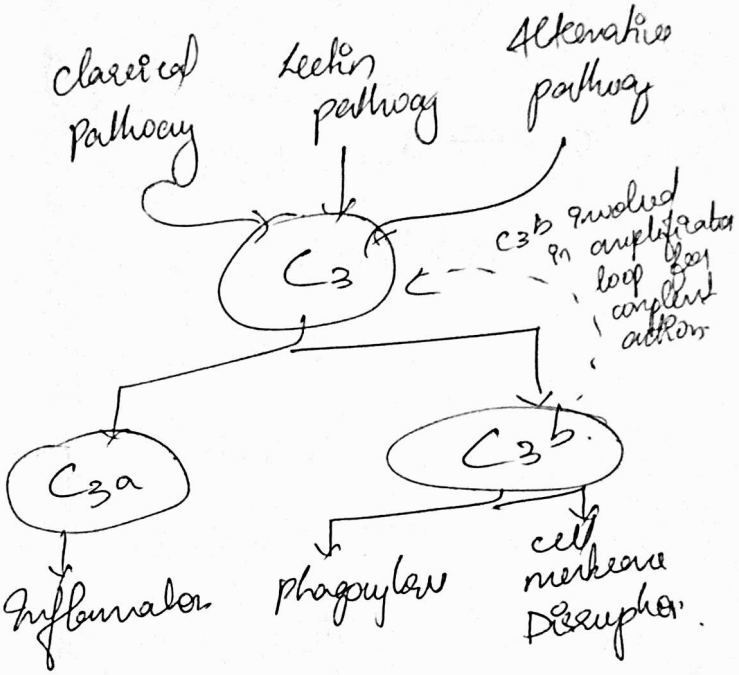
→ C-X-C chemokines
IL8
neutrophils

→ C-C chemokines
MCP-1, eotaxin,
monocytes, eosinophils basophils & lymphocytes.

→ C - chemokines.
lymphotactin
lymphocytes

→ CX3C chemokines
Fractalkine
monocytes & T cells.

Complement system
Function: host defense against microbes, inflammatory rx.
consists of 20 proteins (produced by liver, marker forms in the plasma).



C3A, C5A → anaphylatoxins
C3B - opsonin.

Regulatory proteins of complement system
① C1 inhibitor → blocks C1 action.
② Decay accelerating factor (DAF) and CD59:
DAF → prevent formation of C3 convertase

CD59 → inhibits formation of MA

paroxysmal nocturnal hemoglobinu

Morphological patterns of inflammation