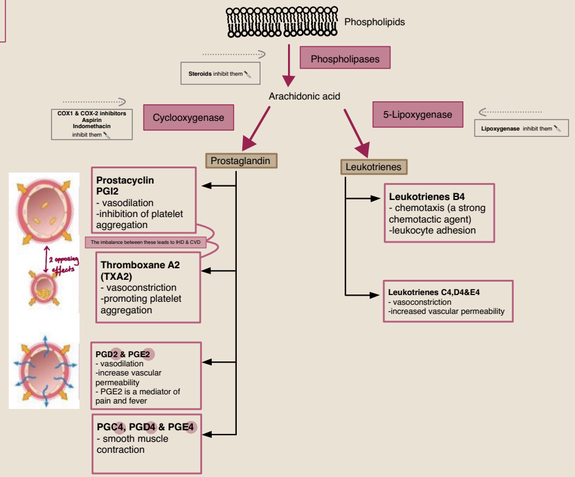
Mediators of inflammation

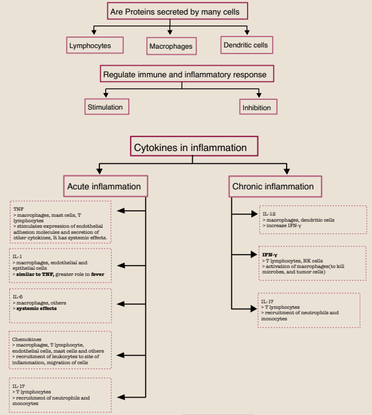
Vasoactive amines

Mainly **Histamine**
-Vasodilation
- increased vascular permeability

Arachidonic acid metabolites (Eicosanoids)



Cytokines



Chemokines

- small family protein of the big cytokines family, they are strong chemoattractants
- They are G-protein coupled receptors
- 40 different groups with 20 receptors for them
- there are four groups:-
C-X-C / C-C / C / CX3-C
- functions:- inflammation && maintains tissue architecture

Complement system

➢ soluble proteins (circulating in blood stream),produced by liver
➢ it's inactive (needs activation)
➢ There are more than 20 (the most important are C1-C9)
➢ **C3** is most abundant (it's the main gate when it is a stimulated or other C S are stimulated (stimulating/activating/stimulating agents) , and it's used to measure activity inflammation)
➢ innate & adaptive immunity

Extra ⬇

➢ functions:-
- vascular permeability
- chemotaxis
- opsonization(recall…it's marking pathogens for phagocytosis)

There are 3 major mechanisms to fix(activate) the complement via activating C3 [classical,alternative and lectin pathways]
Functions of C S:-

Inflammation:- C3a,C5a anphylatoxins(strongest chemotactic agents.

Opsonization&phagocytosis:- C3b enhancement of phagocytosis

Cell lysis:- MAC (membrane attack complex), C9 multiples making small holes in thin membranes of microbial walls

Regulatory proteins of C S:-
1) **C1** inhibitor (if it's deficient it leads to <u>hereditary angioedema</u>)
2) Decay accelerating factor (DAF) , inhibits formation of **C3 convertases**
3) CD59 inhibits membrane attack complex (**MAC**)
- deficiency in DAF and CD59(abnormalities)lead to paroxysmal Nocturnal Hemoglobinuria (<u>PNH</u>)
3) factor H :- promoting the proteolysis of C3 convertase (if it is deficient, it leads to <u>hemolytic uremic syndrome</u>)
4) complement system protein deficiencies (deficiencies in compliment proteins can lead to increase susceptibility to infections since the immune systems ability to eliminate pathogens is compromised)

Platelet activating factor (PAF)

Platelet aggregation and other functions

Protease activating receptors(PAR)

Platelet aggregation

Kinins

group of vasoactive peptides(amino acids that affect the diameter of blood vessels)that play an essential role in inflammation and blood vessel regulation. The most well-known kinin is **bradykinin**, which is the active form in many inflammatory responses:-
-VD
- increases vascular permeability
- smooth muscle contraction
- pain

Neuropeptides

Substance P and neurokinin A
—> small protein-like molecules used by neurons to communicate with each other.

Summary…