Complement System

- Forms part of innate immune system
  - Non specific
  - Nil memory formation
- present as inactive forms C1-C9
- activated to become proteases that cleave each other in an amplifying cascade
- key step = activation of C3
- C3 & C5 are most impt mediators
  ↳ can also be activated by proteolytic enzymes within exudate eg plasmin & lysosomal enzyme from neutrophils

Activation

- pathways to activate C3:
  - Classical: C1 fixes to antigen-antibody complexes ⇒ C3 convertase
  - Alternative: triggered by microbial surface molecules (eg endotoxin) & complex polysaccharides
  - Lectin: plasma mannose binding lectin binds to microbe carbohydratye ⇒ activates C1

Effector Functions

- Cell lysis of bacteria (MAC):
  - C5b binds components of C6-9 ⇒ membrane attack complex (MAC)
- Inflamatory functions (C3a, C5a):
  - Degranulation of mast cells ⇒ histamine release ⇒ VD & ↑permeability
  - Neutrophil aggregation
  - Stim arachidonate metabolism
  - Chemotaxis
- Opsonisation (C3b): opsonin = binding enhancer for phagocytosis ⇒ ↑phagocytosis

Regulation

- Complement activation regulated by
  - Cell associated proteins eg DAF (decay accelerating factor)
    ↳ defect ⇒ paroxysmal nocturnal haemoglobinuria (=rbc lysis & anaemia)
  - Circulating proteins eg C1 inhibitor
    ↳ deficiency ⇒ hereditary angioneurotic oedema (=episodic oedema)