

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

السلام عليكم ورحمة الله وبركاته

COMPLEMENT SYSTEM

1-structure

2-activation

3-function

Complement (C)

- Complement components are proteins or glycoprotein that are synthesized mainly in the liver hepatocytes monocytes, macrophages, epithelial cells.
- **Its function is to complete the action of antibodies to eliminate the pathogen.**
- Its present in the blood serum.
- Its designated by the numerals (C1-C2C9) **Numbered in order of discovered, not sequence of action** and letter symbols like D, B,
- ~ 15% of globulin fraction
- The complement destroyed by heating the serum at 56°C for 30 mins.

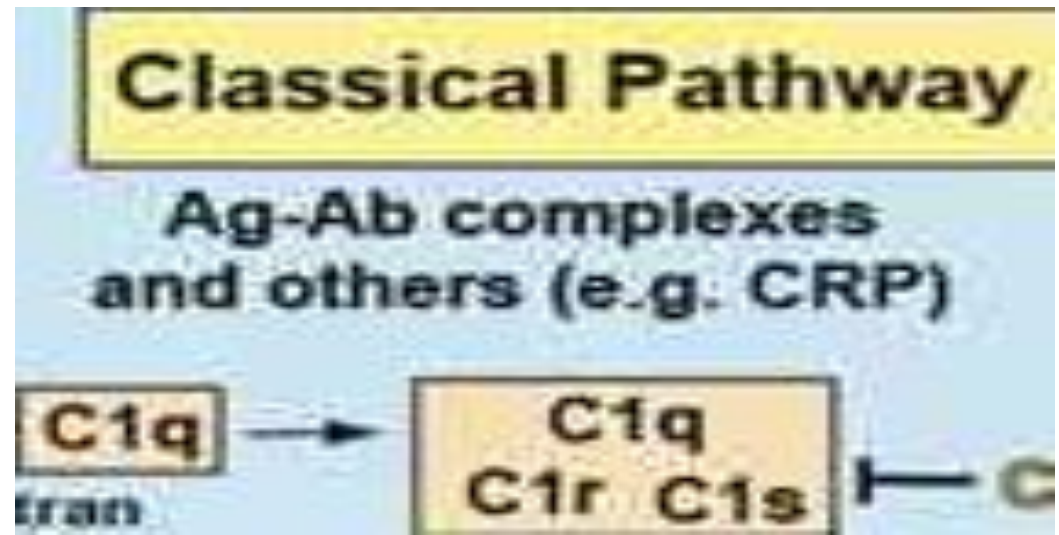
- circulate in **inactive state**
- once it is activated a peptide fragment will be formed and denoted by a small letters:
 - **small fragment designated ((a))**
 - **large fragment designated ((b))**

Complement activation

- Classical pathway.
- Alternative pathway.
- Lectin pathway.

Classical Pathway

- Adaptive immunity
- Ab(IgM, IgG3, IgG1, IgG2)+Ag called immune complex
- Fc portion of Ig recognized by C1
- C1q binds to Ag-Ab complex then C1r then C1s (C1qrs)



C1

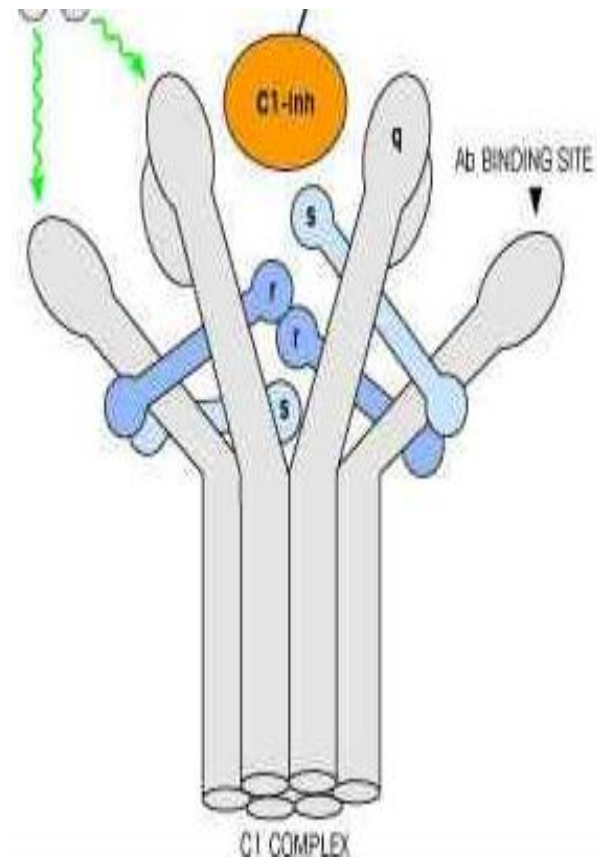
- is a macromolecule complex present in the serum . Consisting of 3 subunits

-C1q

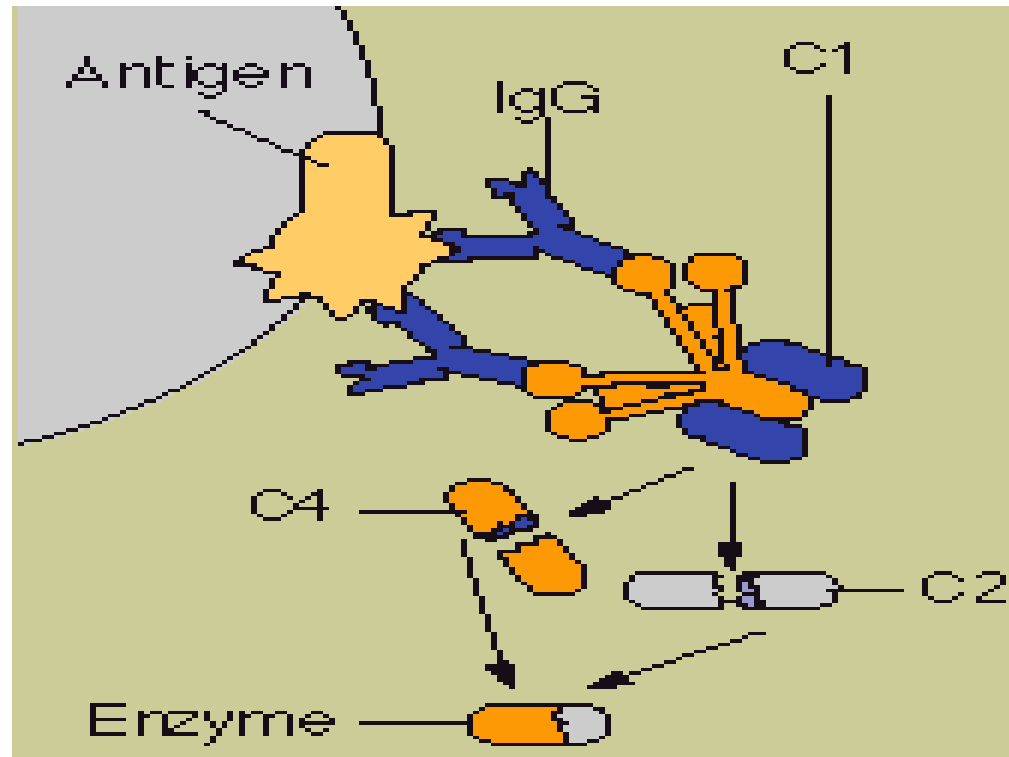
-C1r

-C1s

Connected to each other by Ca^{++} dependents bounds.

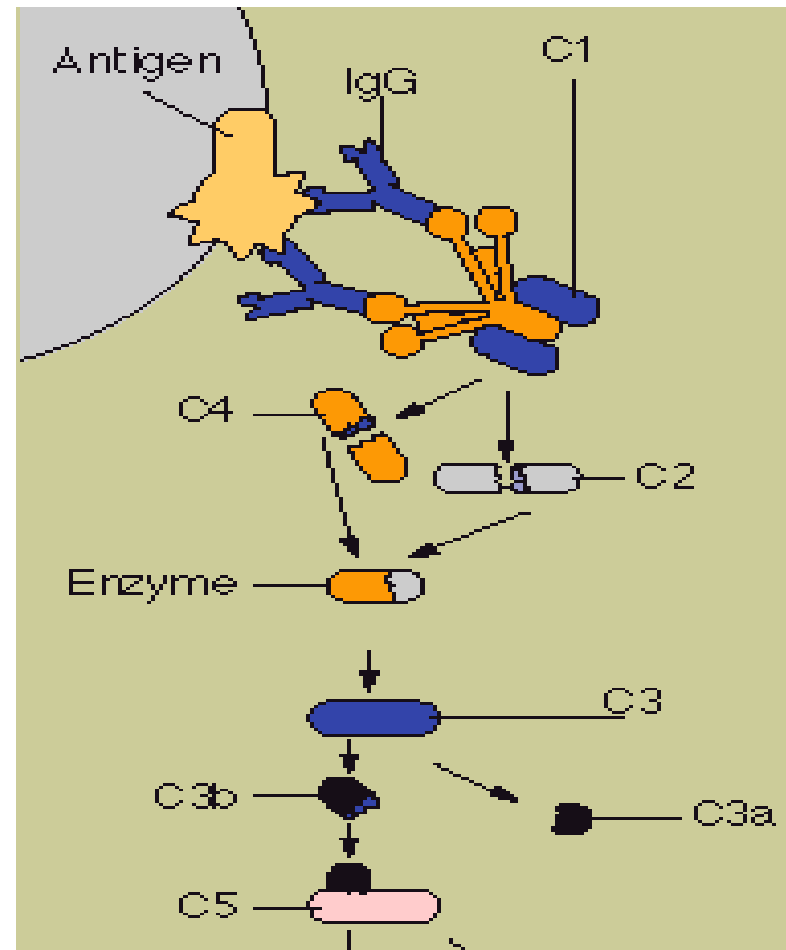


- *AgAb Activate C1q then C1r then C1s
- ***C1s** had enzymetic activity (estrase activity)
cleaves C4 into two fragments
- -C4a
- -C4b



C1s in the presence of C4b will split C2 into two fragments (C2a and C2b) and C2

Formation of **C3 convertase (C4b2a)** that Cleaved C3 into C3a and C3b forming a complex called **C5 convertase (C4b2a3b)**



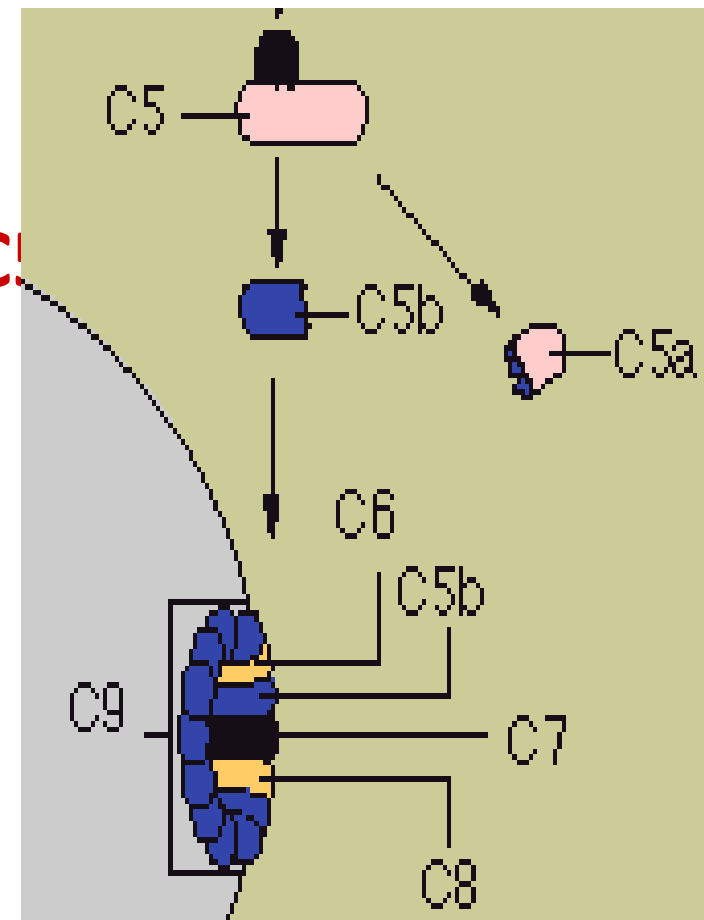
C5 is cleaved by C5 convertase which has enzymatic activity that cleaves C5 into:

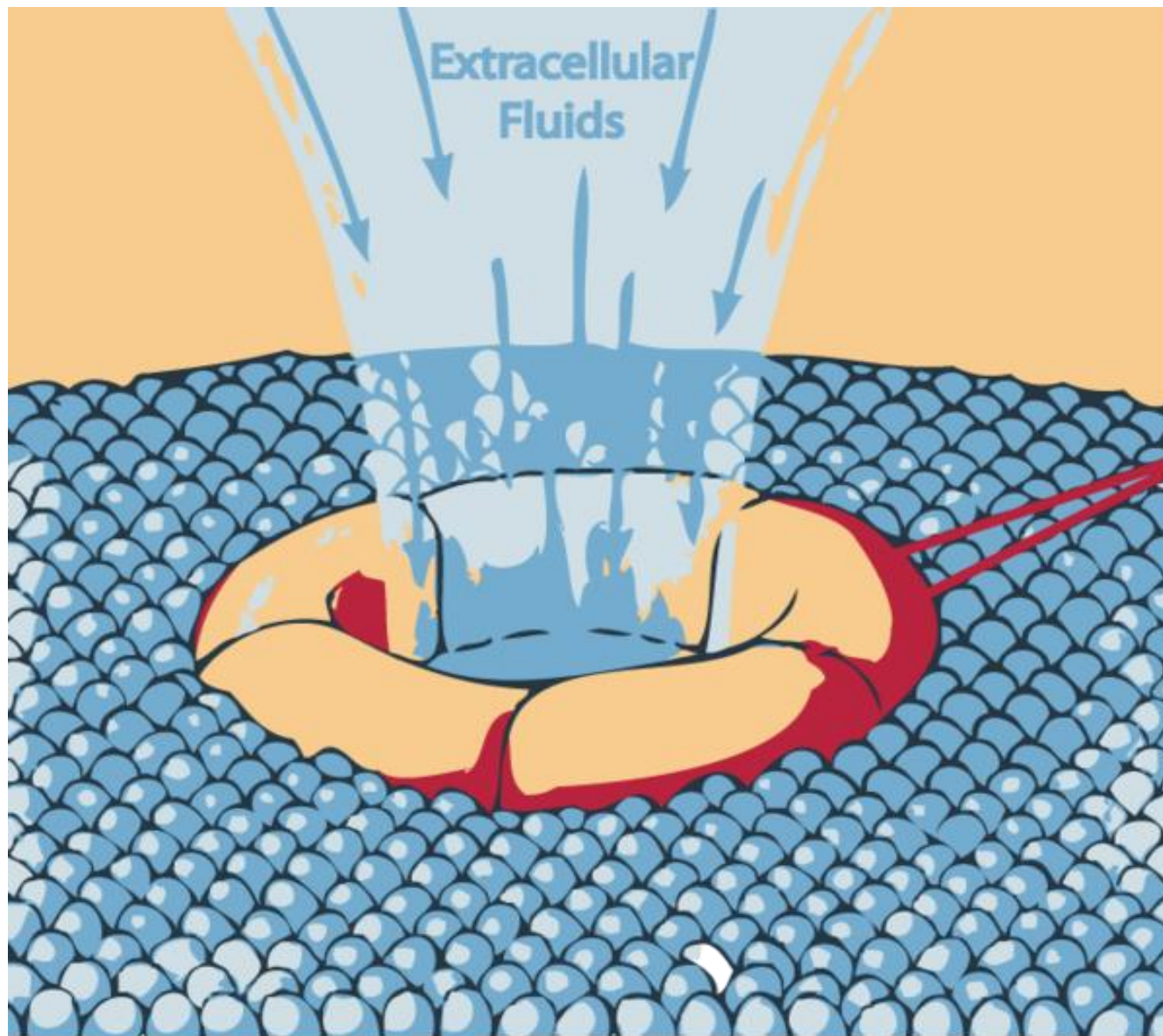
C5a and C5b

-C5b attached to cell membrane to form

C4b2a3b5b act as a **receptor** to
C6 then C7 then C8 and C9

to form a complex called
membrane attack complex (**MAC**) (C5b-6-7-8-9)
causing a pore on the
cell surface → influx of
Na⁺ and water → lysis of the cell.

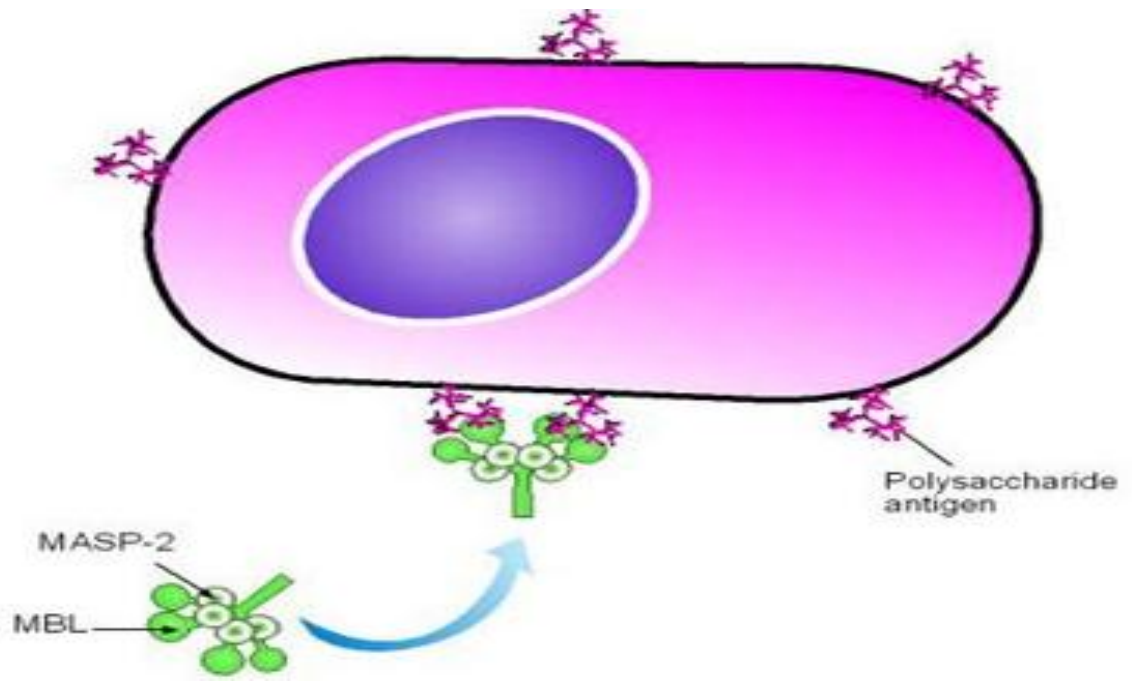




- C3a, C4a = act as a mediator of anaphylaxis and chemotactic substance.
- C3b = immune adherence in opsonization

Mannose Binding Lectin (MBL) pathway

- MBL: is a serum protein that binds to mannose in microbial cell wall
- Is part of Innate immunity
- This complex had a function as **C1qrs**
- This complex cleaves C4 and C2C9



Alternative Pathway

Can be initiated by three distinct ways:

1-Tickover pathway

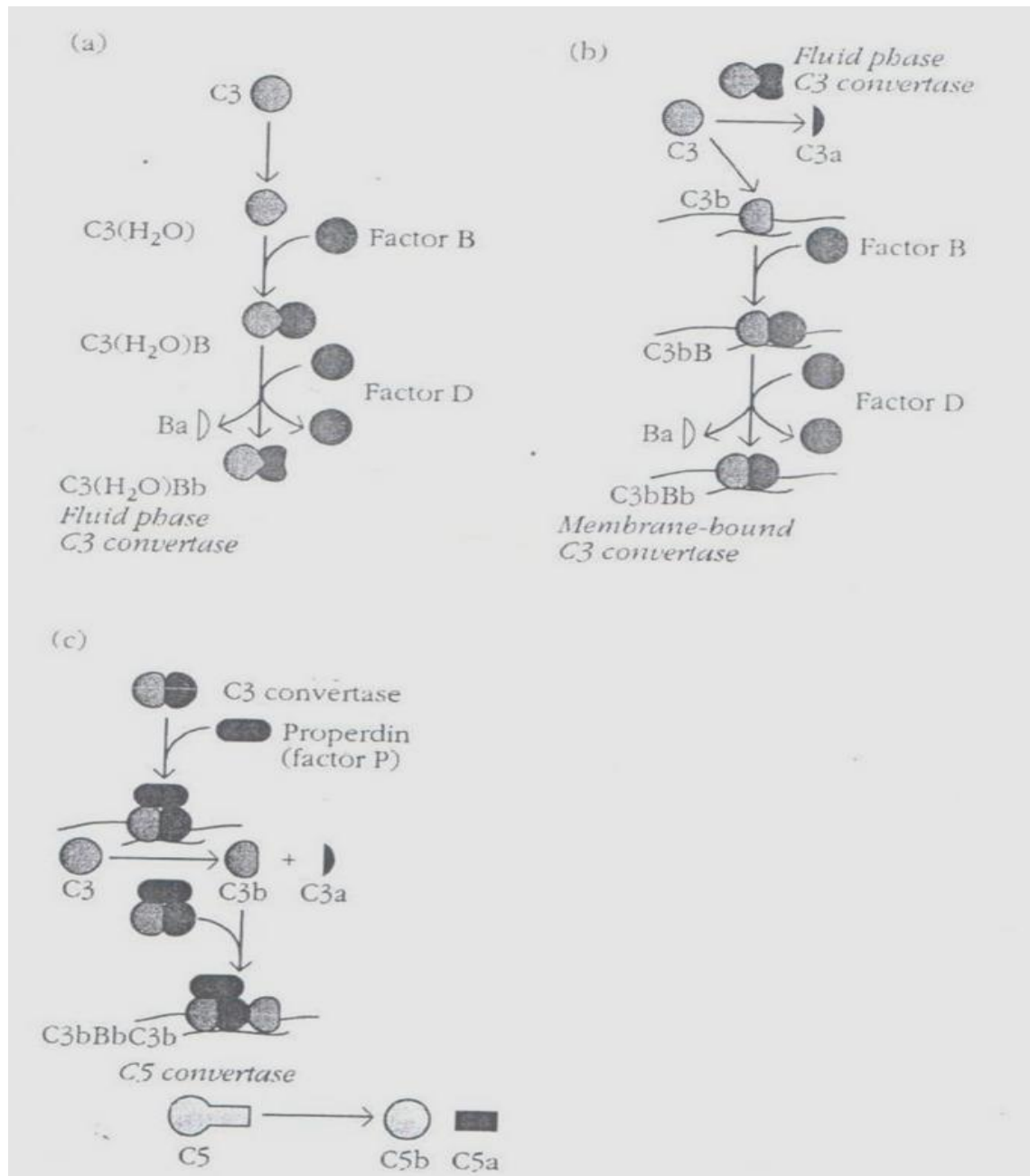


FIGURE 6-8 The initiation of the alternative tickover pathway of complement. (a) Spontaneous hydrolysis of soluble

Alternative Pathway

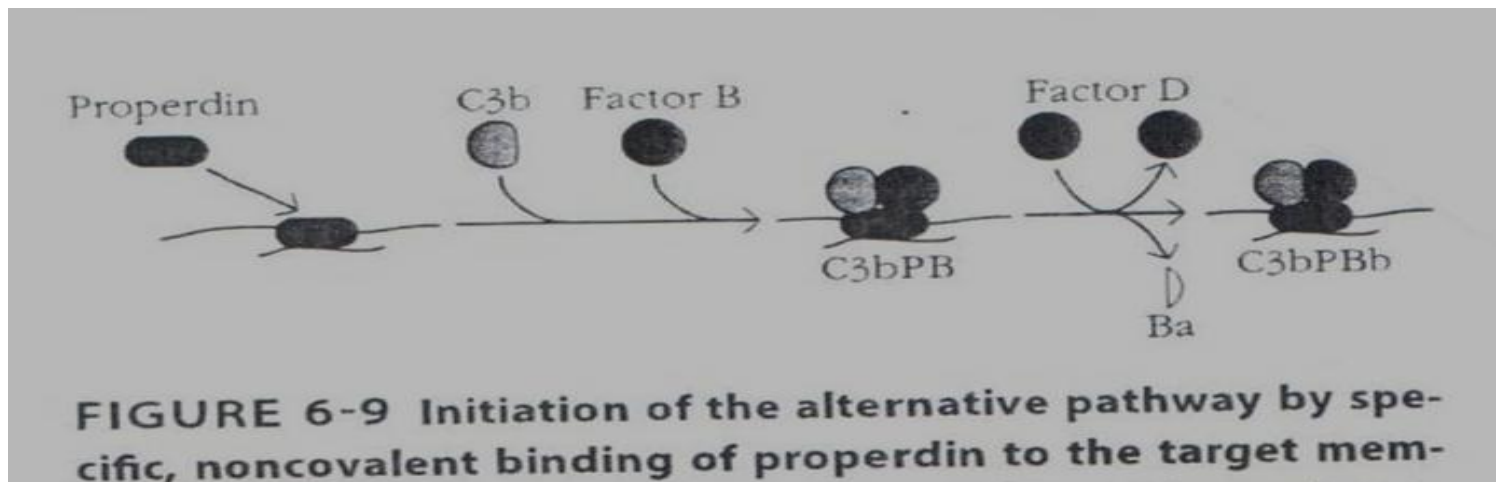
- Can be initiated by three distinct ways:

- 1-Tickover pathway: by spontaneous hydrolysis of C3 yielding C3(H₂O) that bind to factor B in the presence of factor D will be cleaved into :
C3(H₂O)Bb called C3 convertase(fluid phase) and Ba
- this initiate more breaking down of C3 into C3a and C3b
- This C3b bound to microbial surface and bind to factor B that cleaves into Ba and Bb in the presence of factor D lead to formation C3bBb called C3 convertase (Membrane bound) and Ba.

- Formation of **C3 convertase (C3bBb)** requires properdin (Factor P) that Breaks more C3 . This is called positive feedback loop.
- This leads to formation **C5 convertase (C3bBbC3b)** that act on C5 cleaves it into C5a and C5b and continue the same reaction as classsical pathway (C6789)→cell lysis.

2- Alternative Properdine –activated pathway:

- Properdine may also serve to initiate complement
- Proberdine binds to components of microbial membranes and stabilizes the binding of C3b to Bb complex resulting C3bPBb complex that act as C3 convertase



3- Alternative Protease –activated pathway

- Proteins factors involved in blood clotting such as thrombin and plasmin are capable of generating both C3a and C5a
- C5b binds to microbial cell wall and stabilized by C6

Classical pathway

**Antigen-antibody
immune complexes**

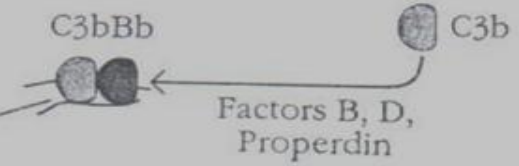
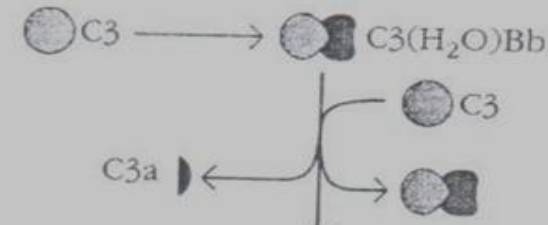
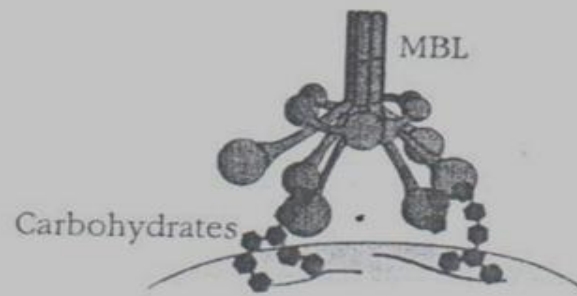
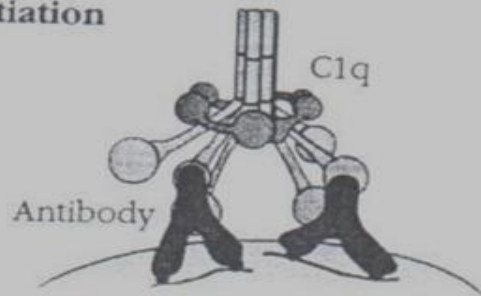
Lectin pathway

**PAMP recognition
by lectins**

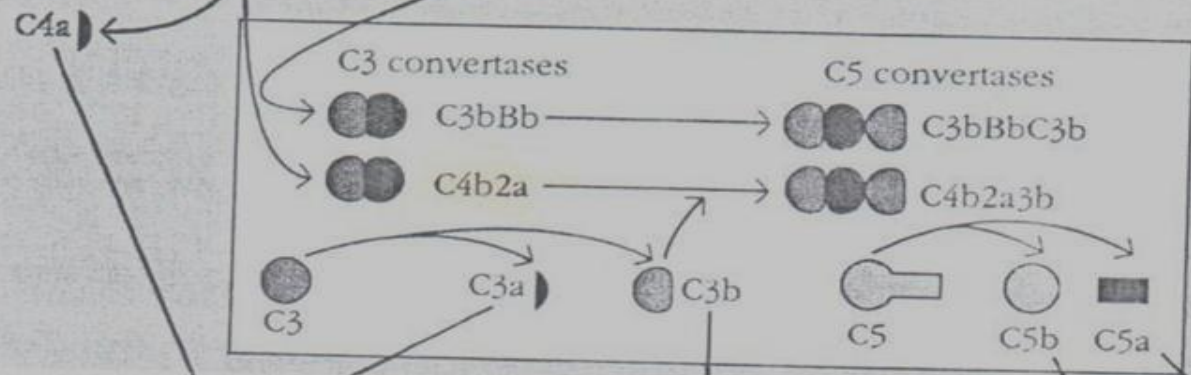
Alternative pathway

**Spontaneous hydrolysis
or pathogenic surfaces**

Initiation



Amplification



Termination

Inflammation

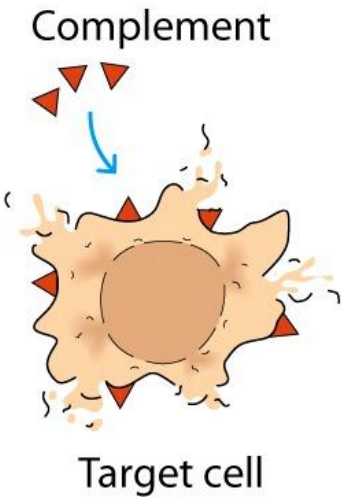
Opsonization

Lysis

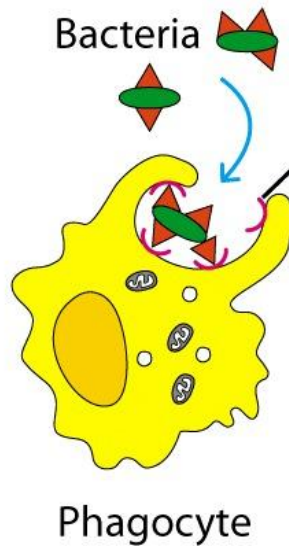
Inflammation

Biological Effects of Complement Activation

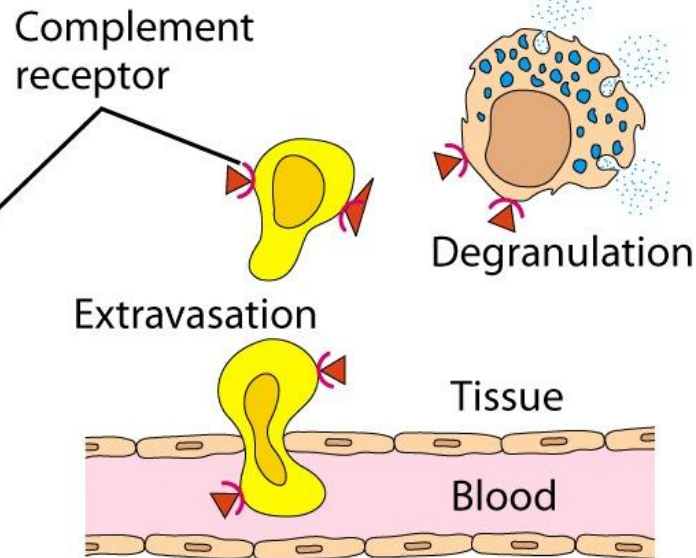
LYSIS



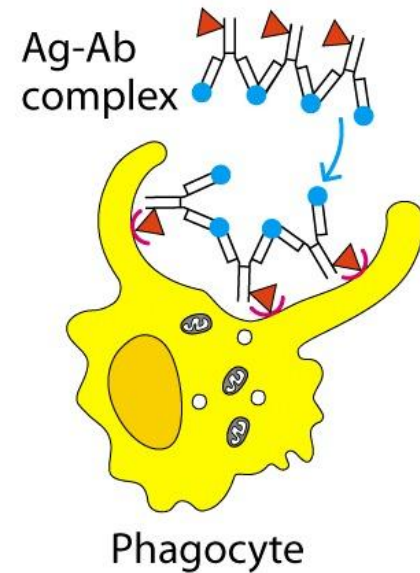
OPSONIZATION



ACTIVATION OF INFLAMMATORY RESPONSE



CLEARANCE OF IMMUNE COMPLEXES



Cell Receptors for Complement

- CR1(complement receptor 1)(CD35)
 - Present on Macrophages, neutrophils
 - Binds C3b
 - clearance of immune complexes and enhancement of phagocytosis
- CR3(complement receptor 3)
 - present on Macrophages, neutrophils
 - Binding to adhesion molecules facilitates extravasation

Regulation of Complement activity

1. C1 inhibitor promotes dissociation of C1 components.
2. Decay accelerating factor promotes decay of C3 convertase
3. Protein S prevents insertion of C3b67 into host cell membrane

Complement Deficiencies

- C3 deficiency leads to recurrent bacterial infection
- C9 Deficiency leads to increase Neisseria infection (Gonococcal and Meningococcal)
- C1 inhibitor Deficiency leads to Hereditary angioneurotic edema.

Thank you