The Complement system

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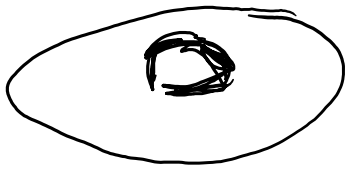
The complement system

- A defensive system consisting of over 30 proteins produced by the liver and found in circulating blood serum.
- Complement kills microbes in three different ways:
  - **1. opsonization**
  - **2. inflammation**
  - **3. membrane attack complex**



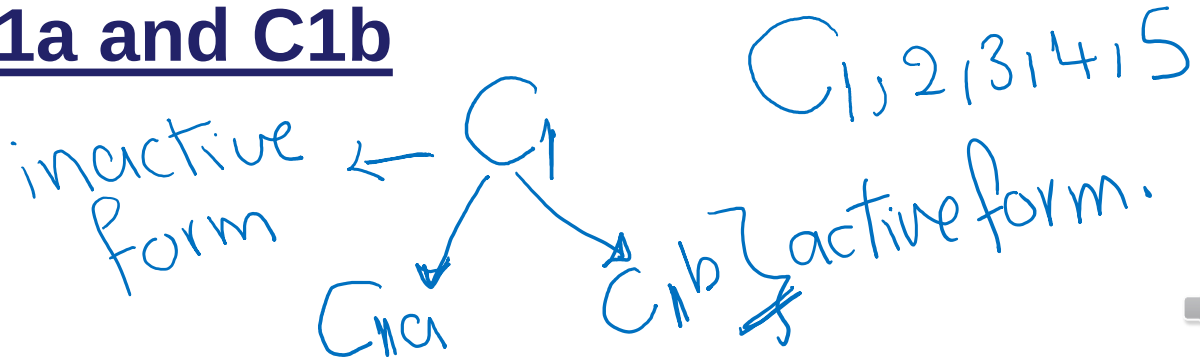
C is a group of plasma proteins, Made by liver, present in Blood, lymph & extracellular fluid

A Cascade system

- **The complement works as a cascade system.**
- **Complement protein don't actually activated that easily, because the complement proteins interact with each other ,induce a cascade of activation of complement protein activating another couple of protein and because of this , they are many complements**
  - **Cascade is when one reaction triggers another reaction which trigger others and so on. These types of systems can grow exponentially very fast.**

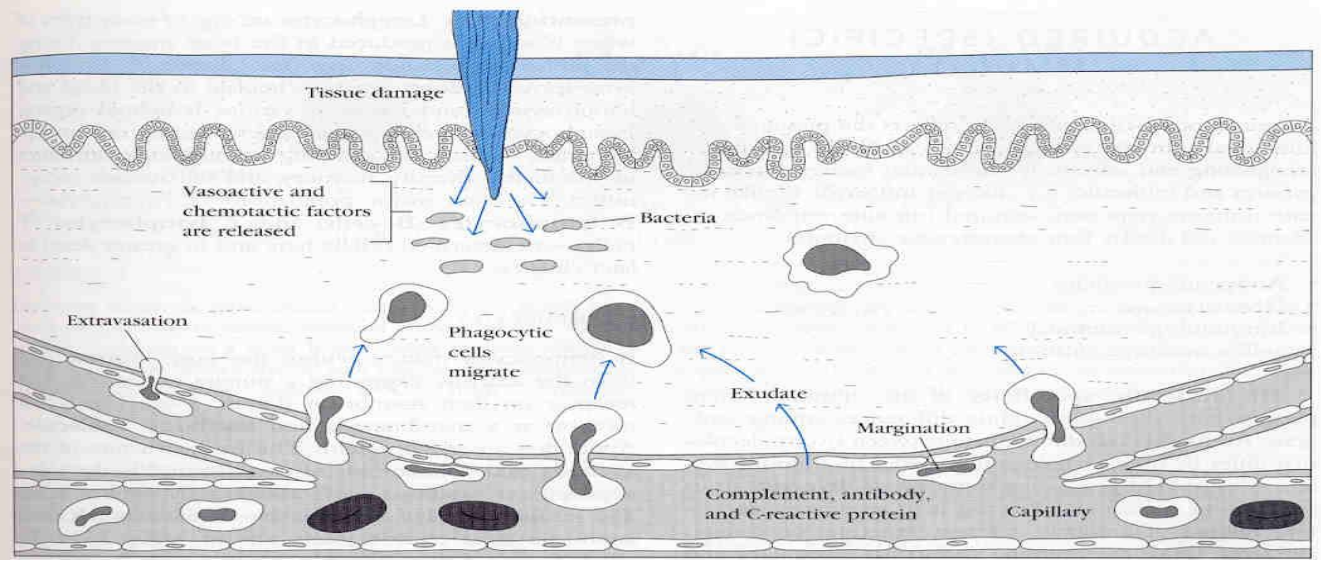
Cascade activation

- **Complement proteins are often designated by an uppercase letter C and are inactive until they are split into products.**
  - **Example: C1**
- **When the products are split, they become active. The active products are usually designated with a lower-case a or b.**
  - **Example: C1a and C1b**



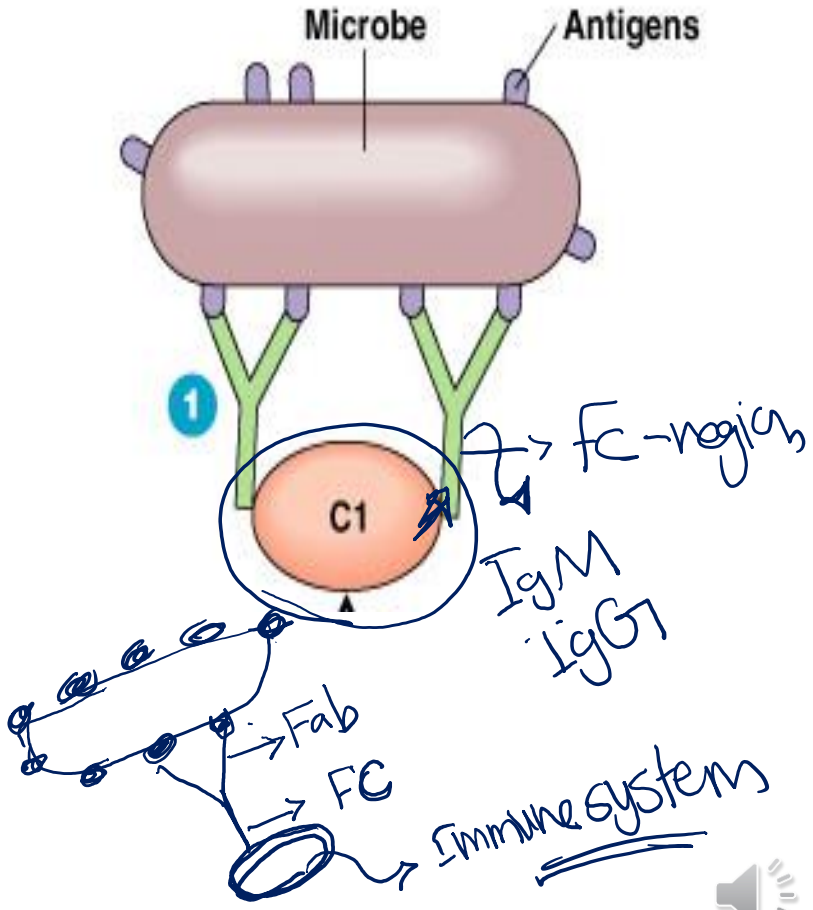
Three Pathways

- The complement pathway can be activated by either of three different pathways.
  - **Classical pathway (specific immune system)**
  - **alternative (non-specific immune system)**
  - **Lectin pathway**



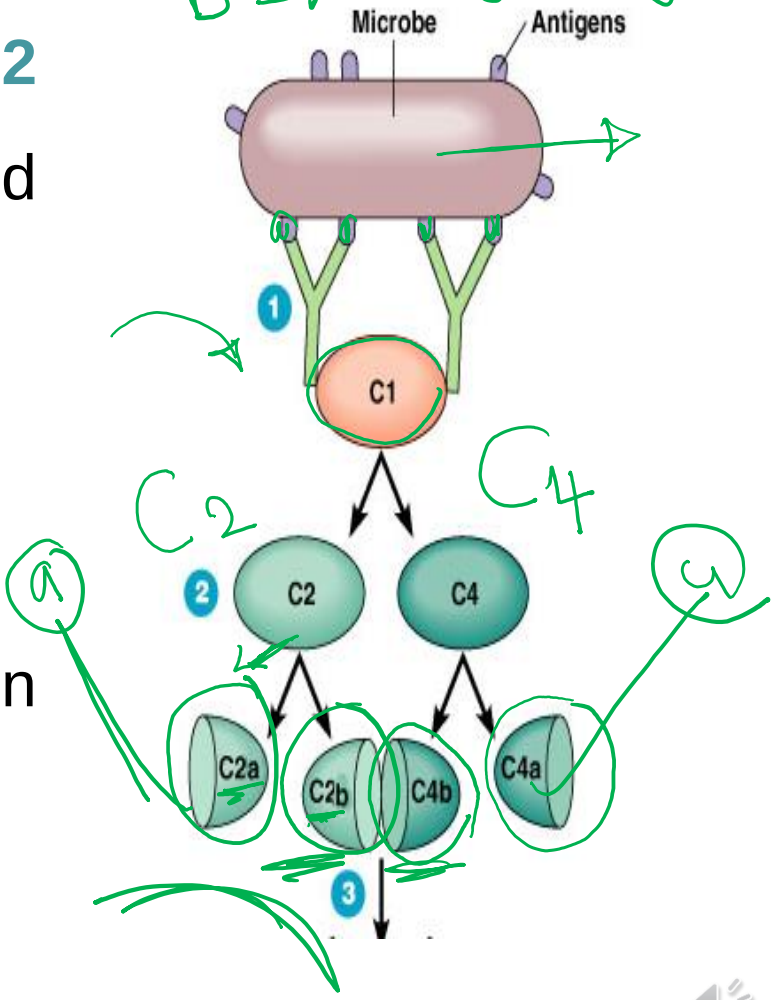
The Classical Pathway

- **The classical pathway is considered to be part of the specific immune response because it relies on antibodies to initiate it.**
- **Being to be discovered , the complement protein involved in the classical pathway C1q,S and r.**
- **C1 becomes activated when it binds to the ends of antibodies**



The building of a C3 activation complex

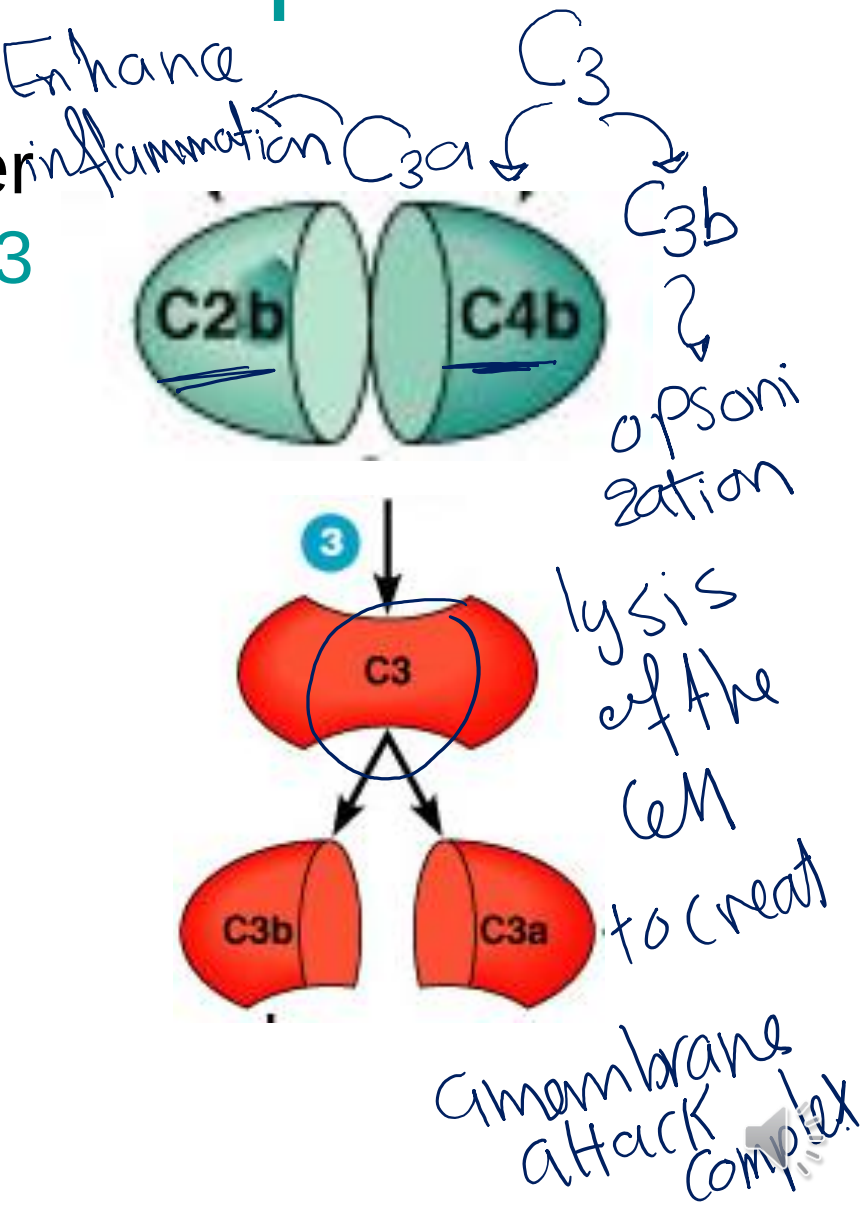
- Once **C1** is activated, it activates **2** other complement proteins, **C2** and **C4** by cutting them in half
- **C2** is cleaved into **C2a** and **C2b**
- **C4** is cleaved into **C4a** and **C4b**
- Both **C2b** and **C4b** bind together on the surface of the bacteria
- **C2a** and **C4a** diffuse away



C3 Activation complex

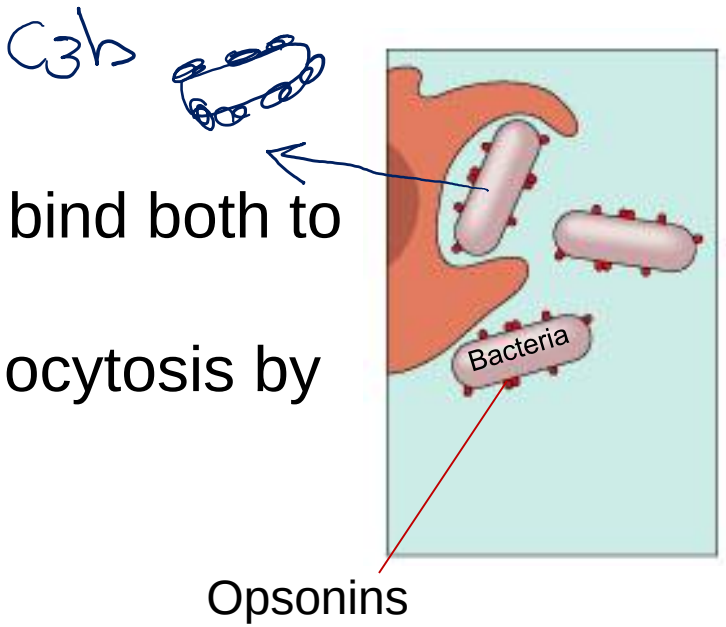
- **C2b** and **C4b** bind together on the surface to form a C3 activation complex

- The function of the **C3** activation complex is to activate **C3** proteins.
  - This is done by cleaving **C3** into **C3a** and **C3b**

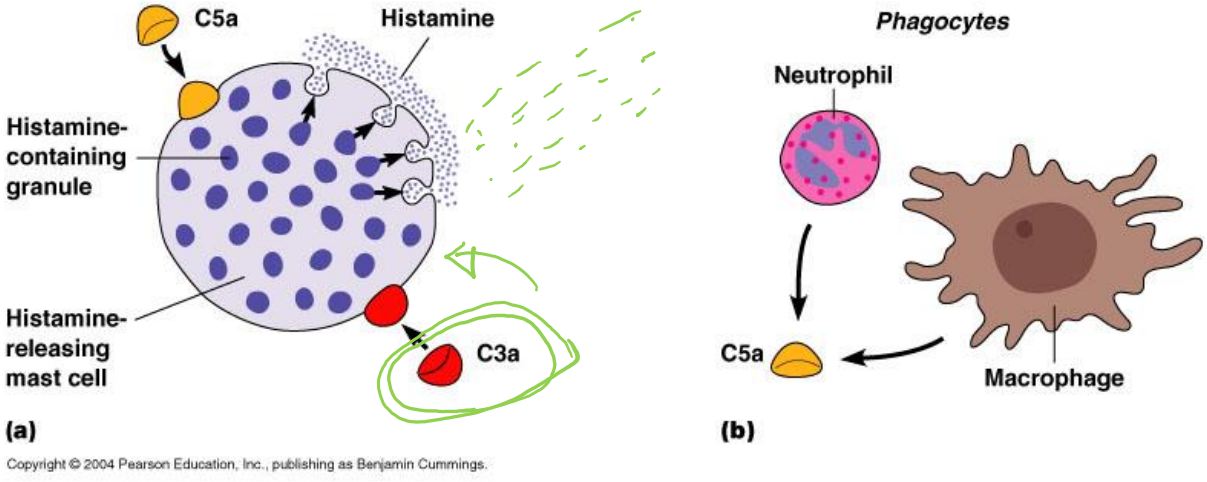


C3b

- Many **C3b** molecules are produced by the **C3** activation complex.
- The **C3b** bind to and coat the surface of the bacteria.
- **C3b** is an opsonin
  - Opsonins are molecules that bind both to bacteria and phagocytes
  - Opsonization increases phagocytosis by **1,000** fold.

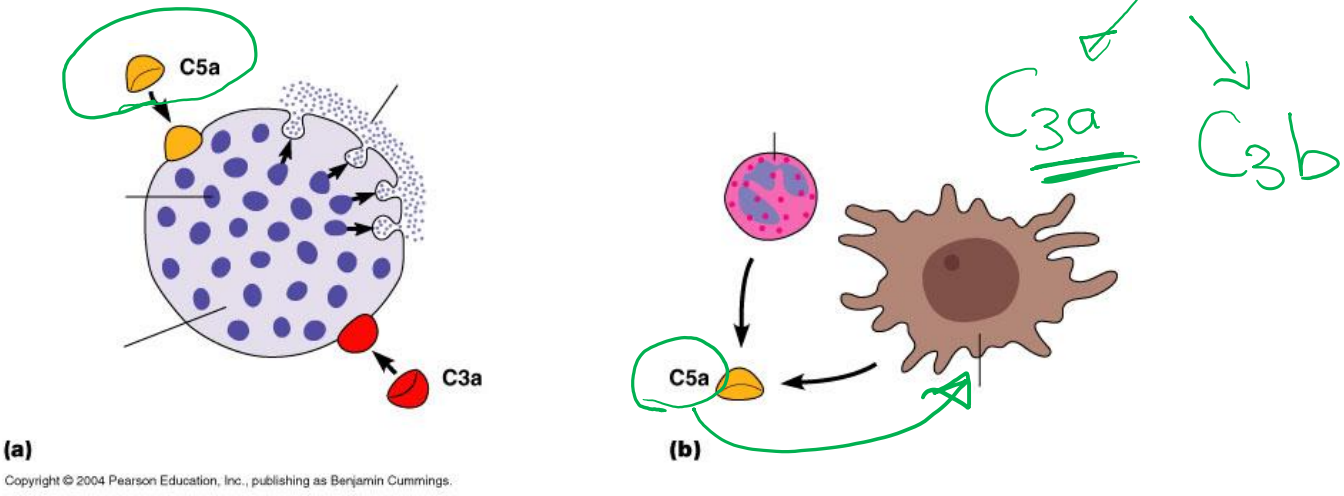


C3a



C3a increases the inflammatory response by binding to mast cells and causing them to release histamine

The function of C5a

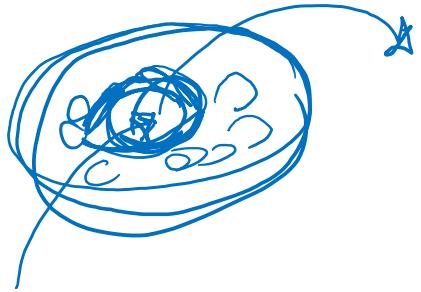


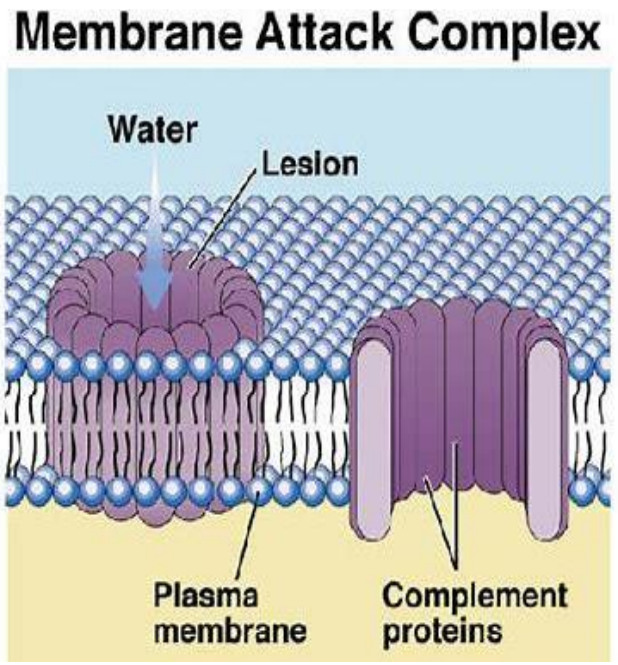
- **C5a** disperses away from the bacteria.
  - Binds to mast cells and increases inflammation.
  - Most powerful chemotactic factor known for leukocytes

Membrane Attack complex

- The MAC causes Cytolysis.
  - Couple of proteins can also make a membrane attack complex , it is essentially when a group of complement proteins makes a hole in a pathogen which in rushing fluids on creating a disk balanced in osmolarity which the pathogen to lyse to be destroyed.

The circular membrane attack complex acts as a channel in which cytoplasm can rush out of and water rushes in.



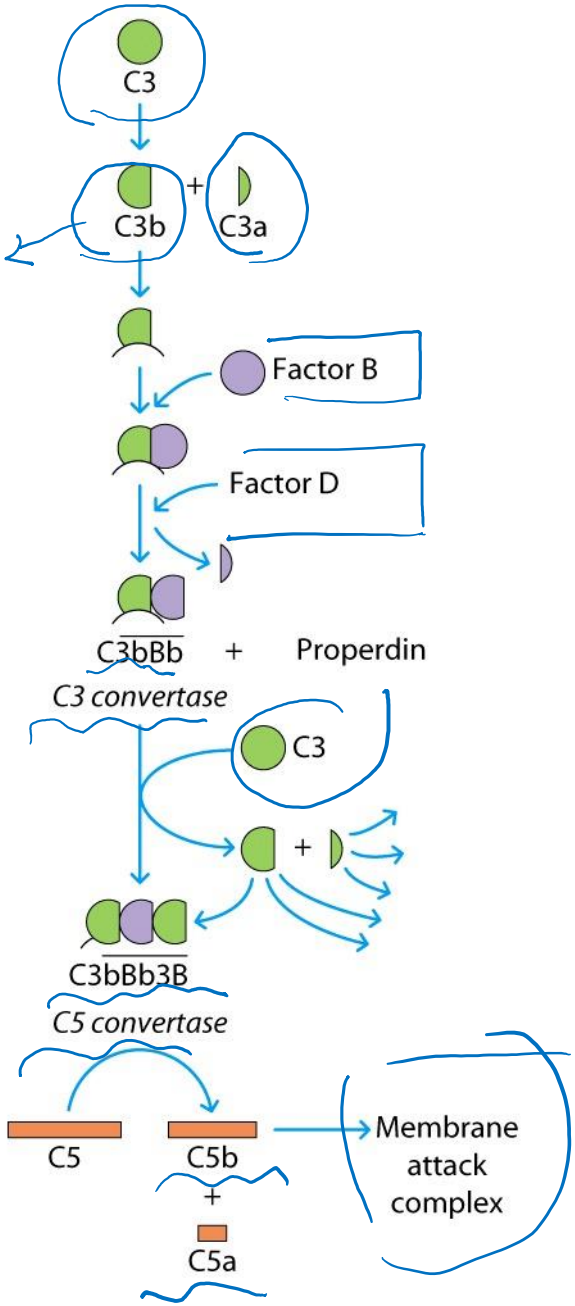


The alternative pathway

- The alternative pathway is part of the non-specific defense because it does not need antibodies to initiate the pathway.

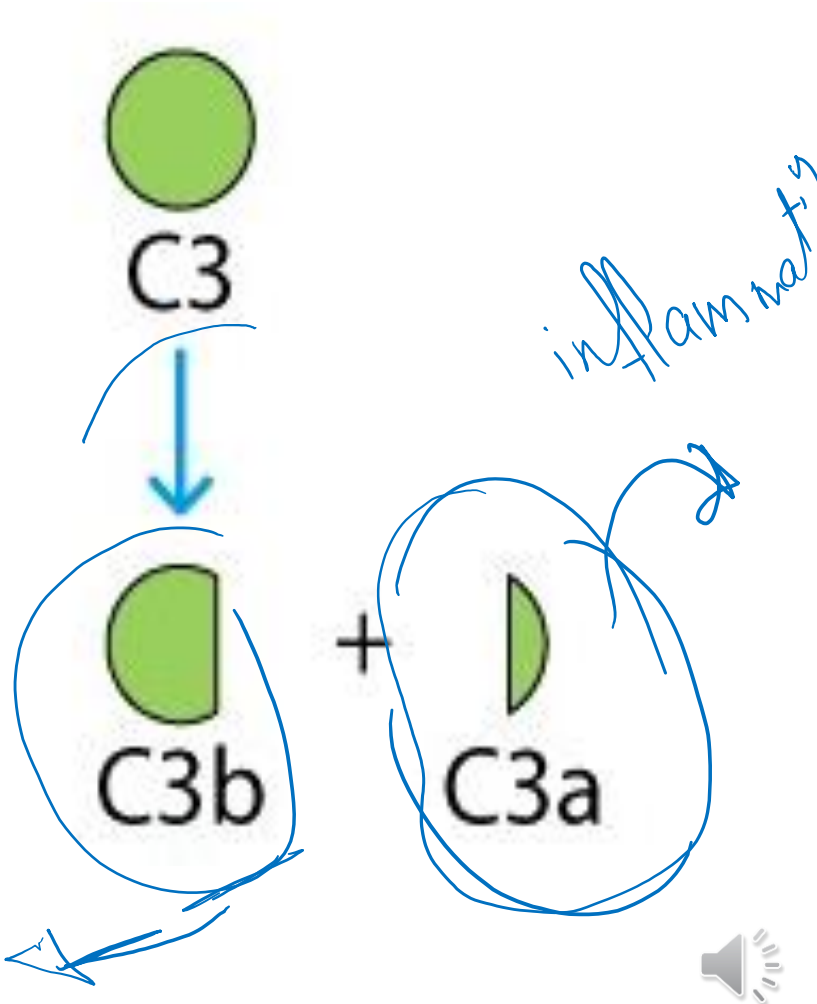
- The alternative pathway is slower than the Classical pathway

The Alternative complement pathway



Initiation of The Alternative pathway

- The pathway essentially help in splitting or activating **C3** to make up **C3a** and **C3b**.
- C3a enhances inflammation together with other proteins and **C3b** which is initiates opsonization and lysis of cell to create a membrane attack complex.
- The **C3b** is able to bind to foreign surface antigens.

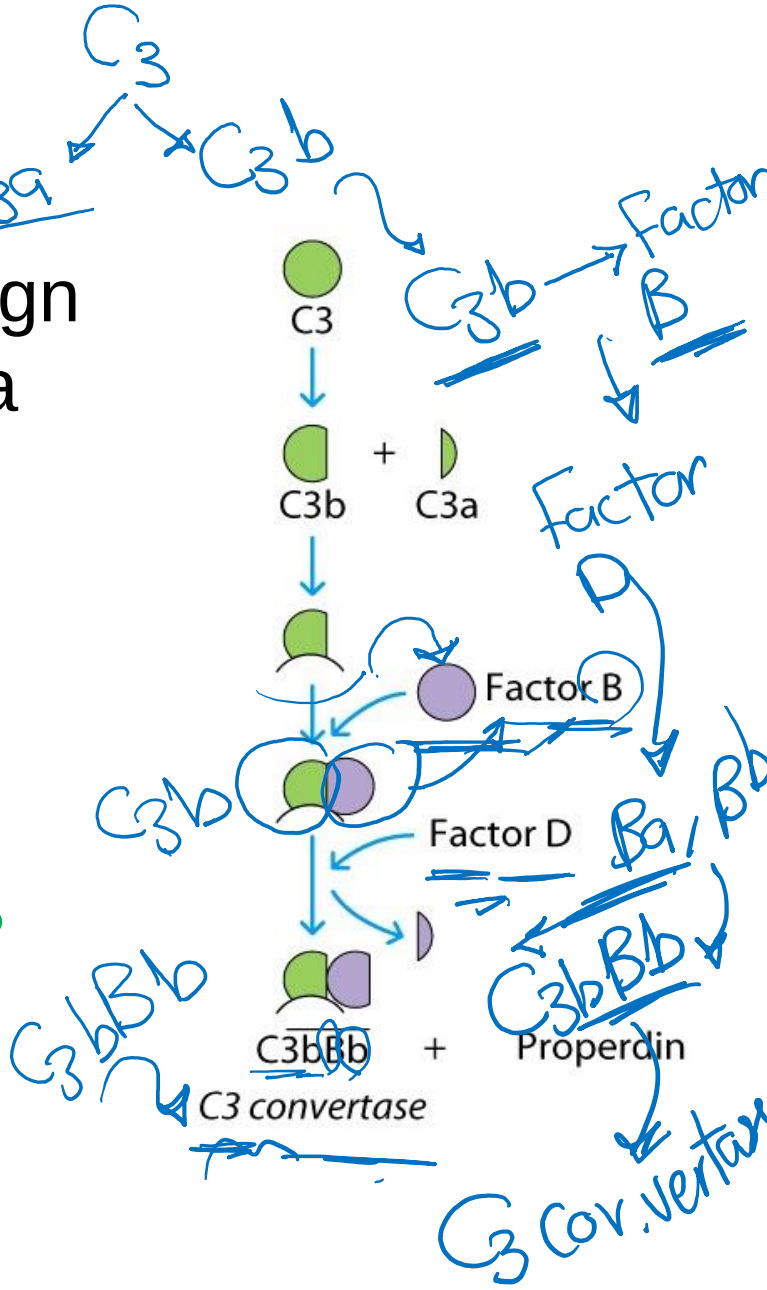


Factor B

- **C3b** on the surface of a foreign cells binds to another plasma protein called **factor B**

Factor D

The binding of **C3b** to **Factor B** allows a protein enzyme called **Factor D** to cleave **Factor B** to **Ba** and **Bb**.



C5 activation complex

- When an additional **C3b** binds to the **C3** activation complex it converts it into a **C5** activation complex.
- The **C5** activation complex cleaves **C5** into **C5a** and **C5b.**
- **C5b** begins the production of the **MAC.**