

**Complement System**  
**Lecture 4**  
**2024-2025**



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# Objectives

You should know the followings:

The **definition** of complement system

The **different pathways** associated with complement activation

**Why dose** complement system is activated?

**Complement system activation of** inflammatory response, lyses of foreign cells, and phagocytosis.

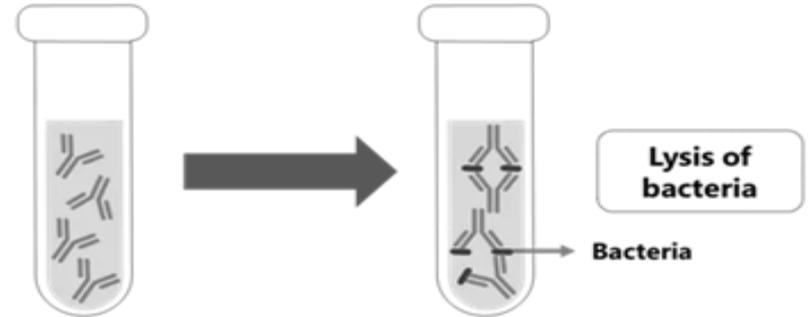
The **disorders** associated complement system

# History

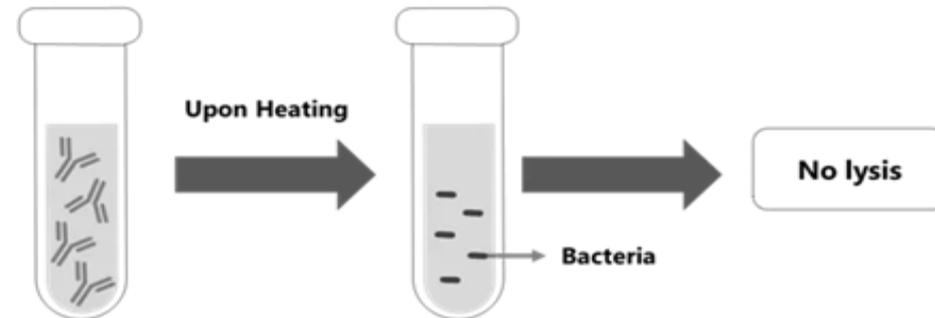
- Discovered in 1894 by Bordet
- It represents lytic activity of fresh serum
- Its lytic activity destroyed when heated at 56°C for 30 min



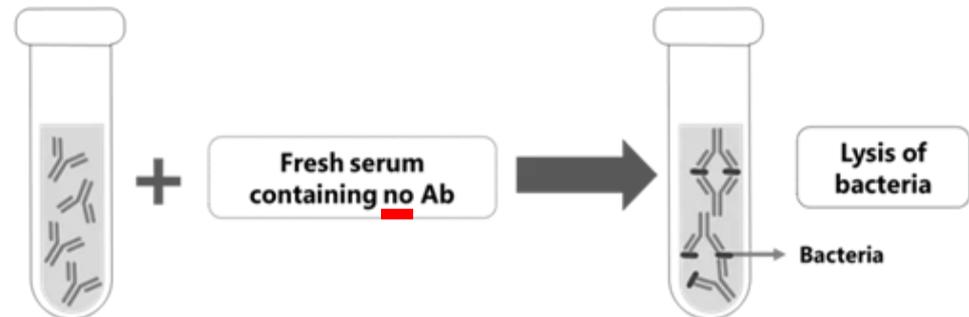
(a) Sheep antiserum containing antibacterial Ab



(b) Sheep antiserum containing antibacterial Ab



(c) Heated antiserum containing antibacterial Ab



# Innate immunity

**Third line defense**  
**Adaptive Immunity**

**Second line defense**

**First line defense**

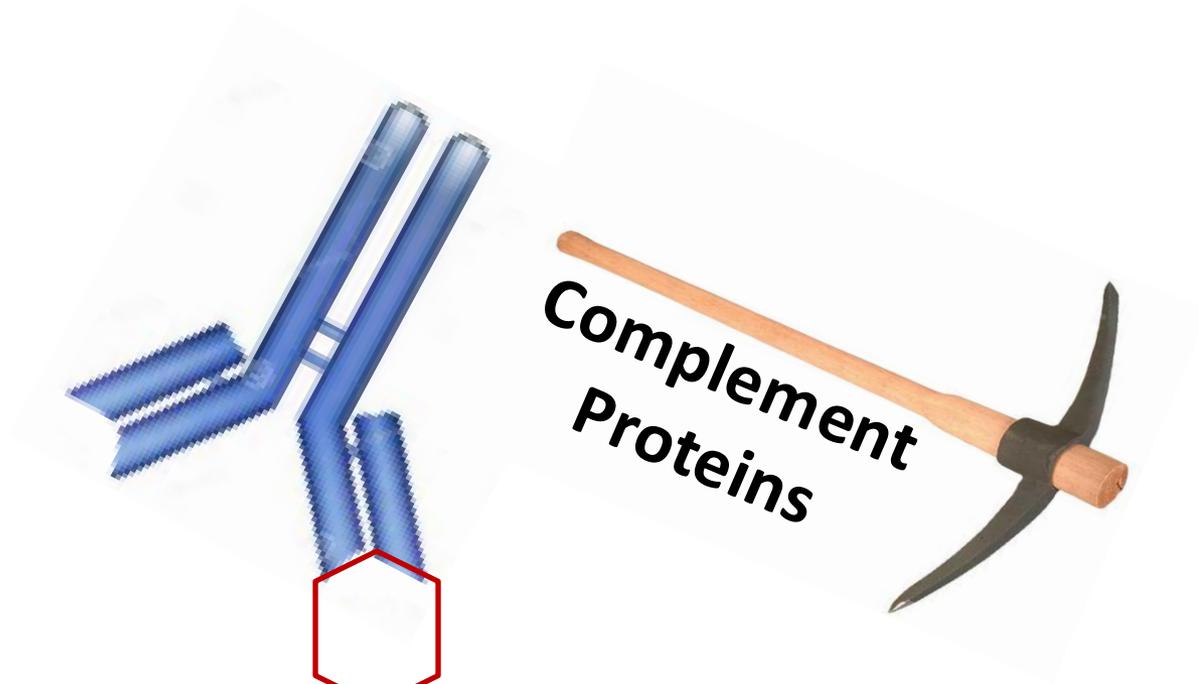
**Target**



**3- Classical complement pathway**

**1- Alternative complement pathway**

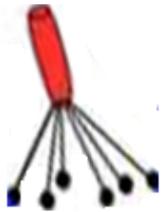
**2- Mannan binding lectin**



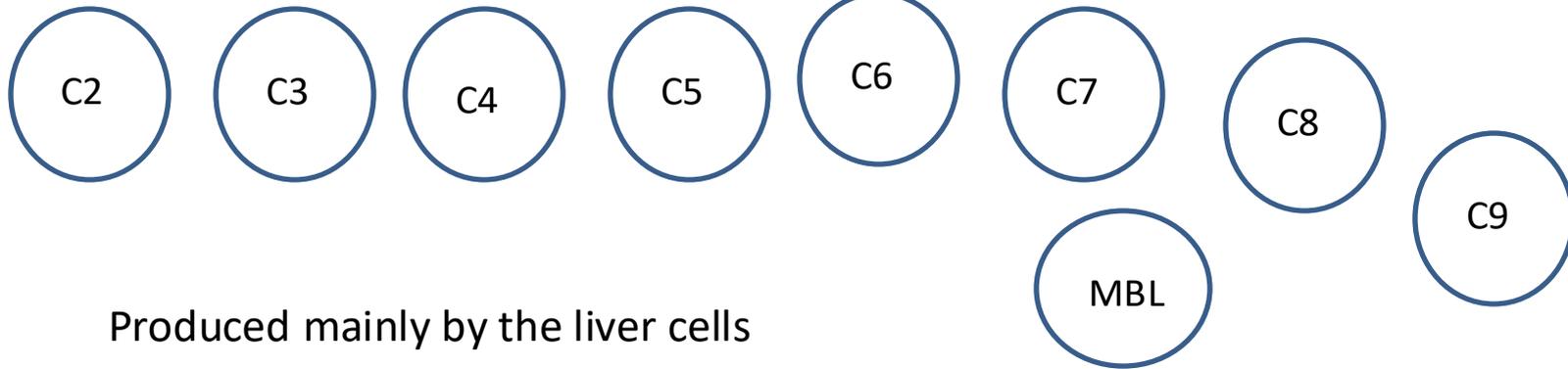
**Bacterium**

# The definition of complement system?

A set of over 20 different protein molecules always found in the blood



C1



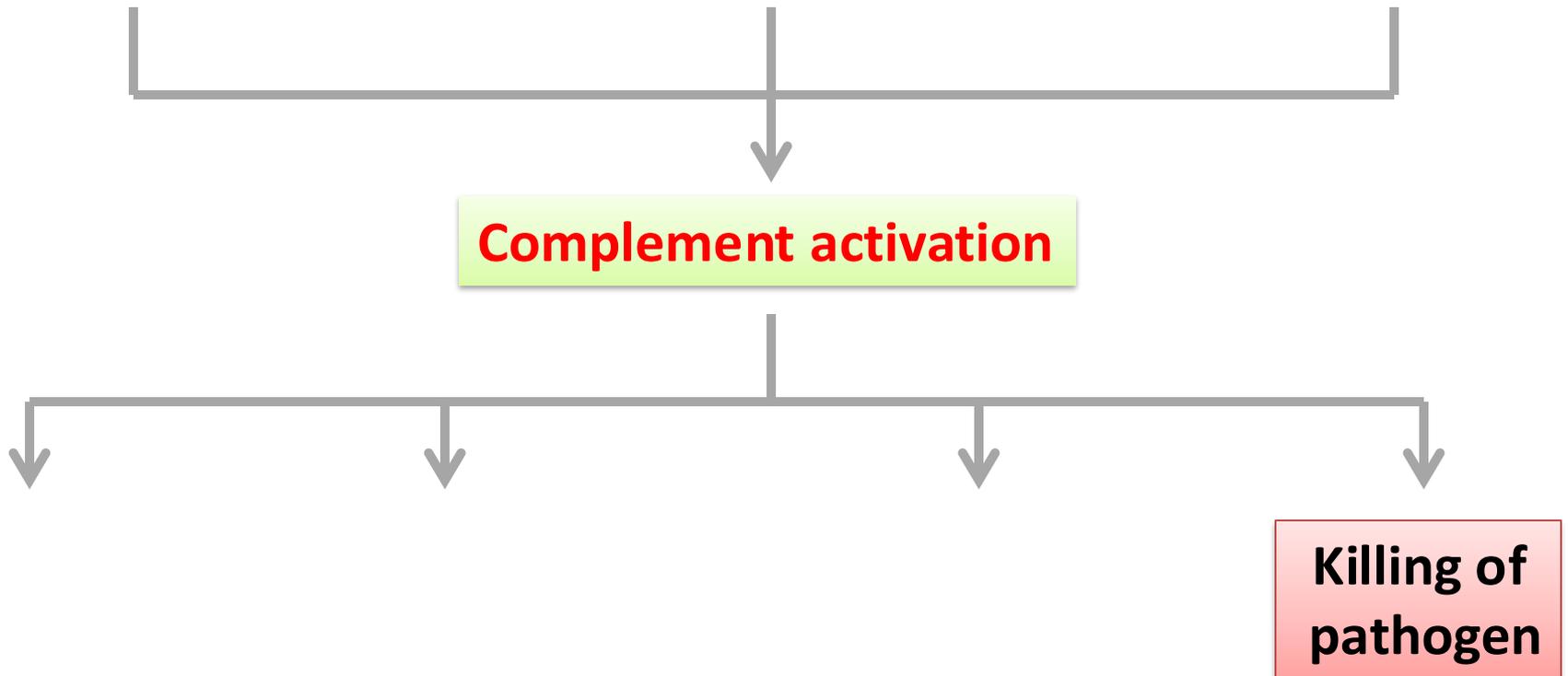
Produced mainly by the liver cells

Present in the blood as inactive enzymes called proenzymes

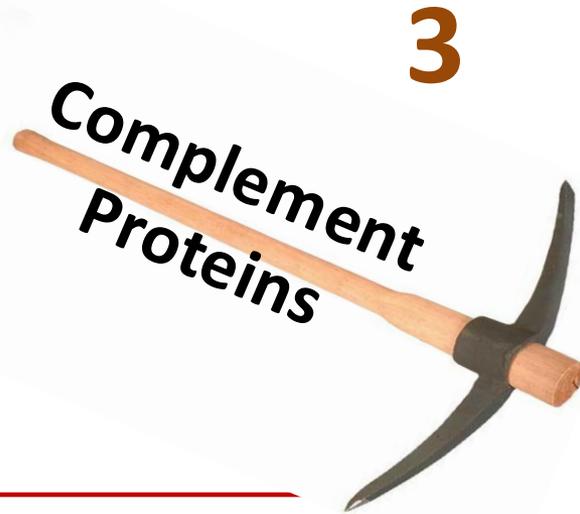
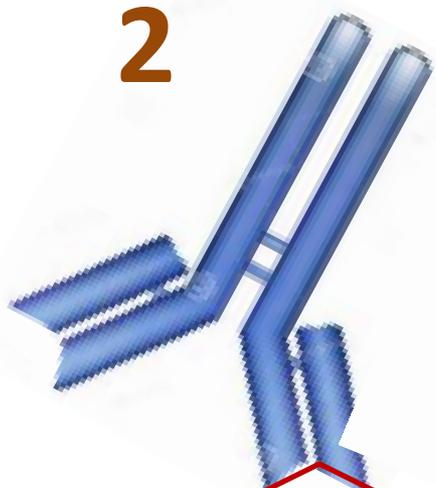
There are no cells in the system

# Complement pathways activation

Classical Pathway



# Complement pathways activation

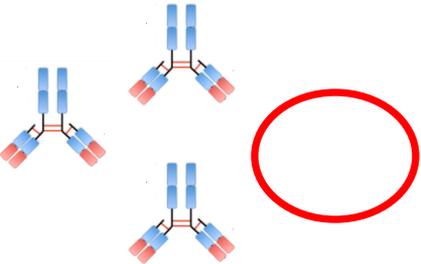
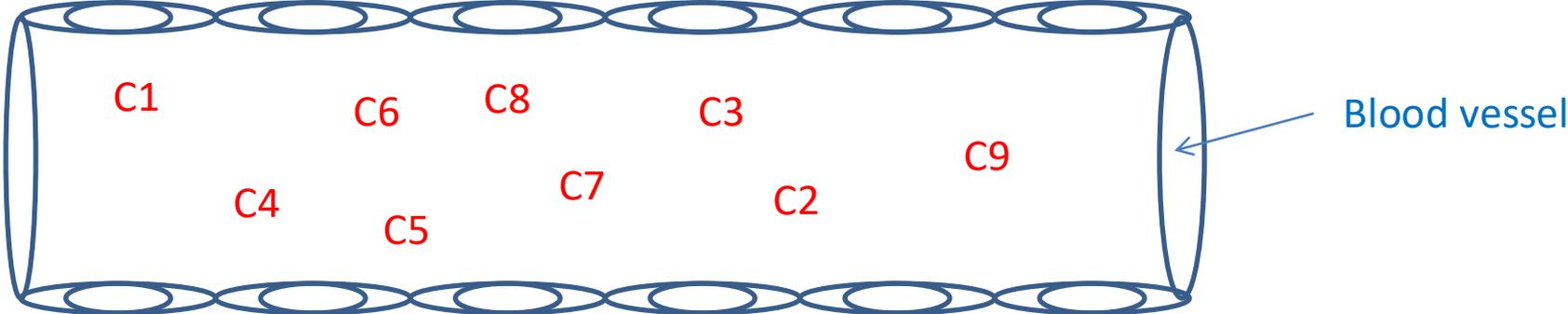


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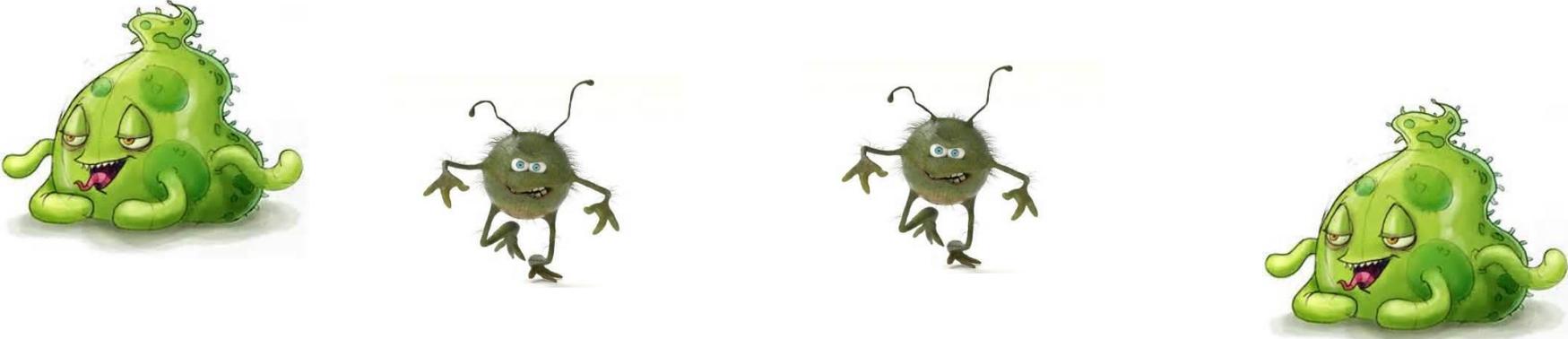
**Bacterium**

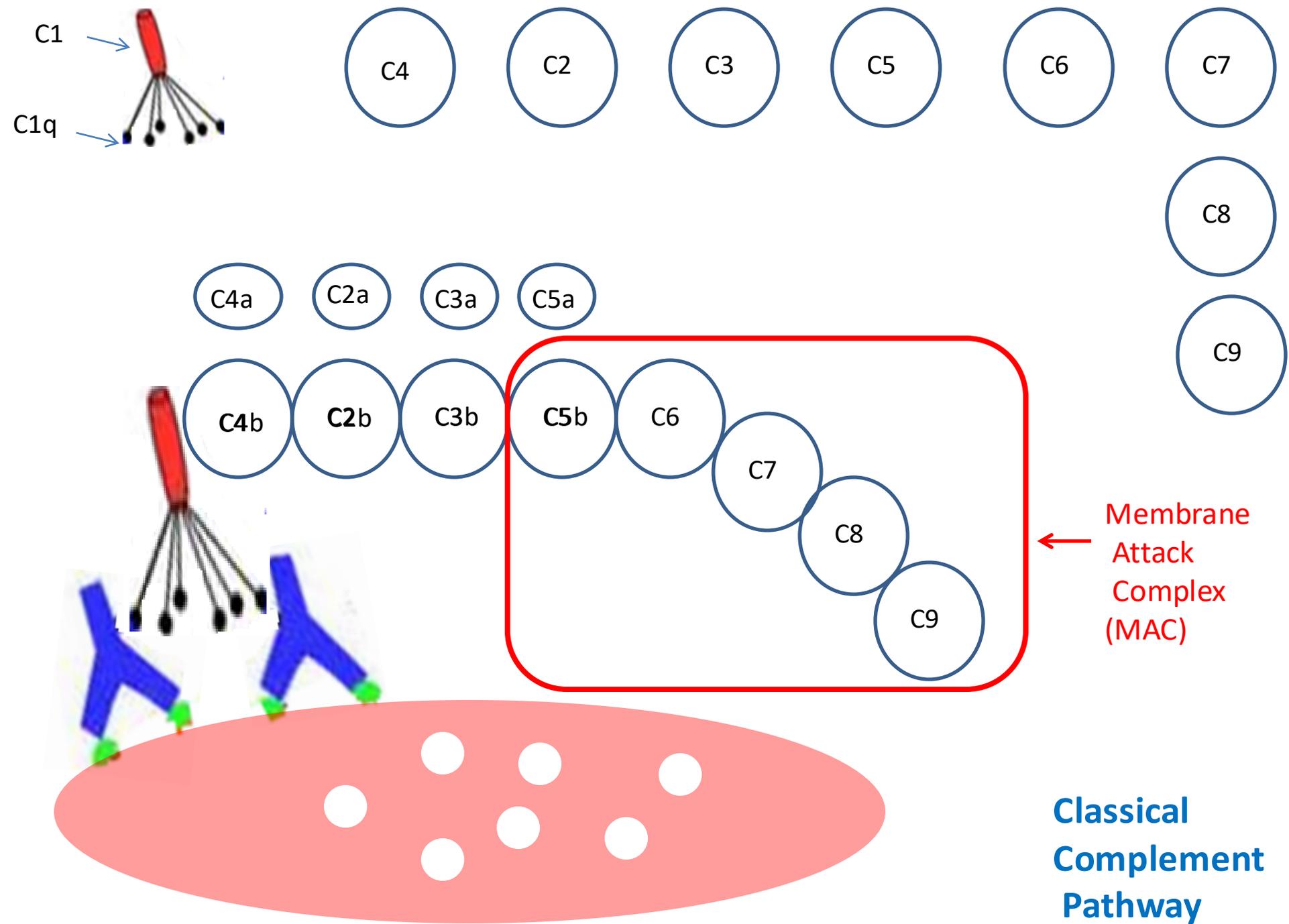
= Classical Complement Pathway

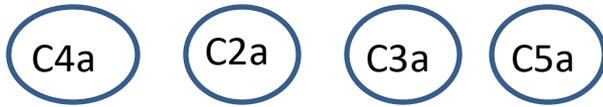
# Classical Complement Pathway



Inflammation

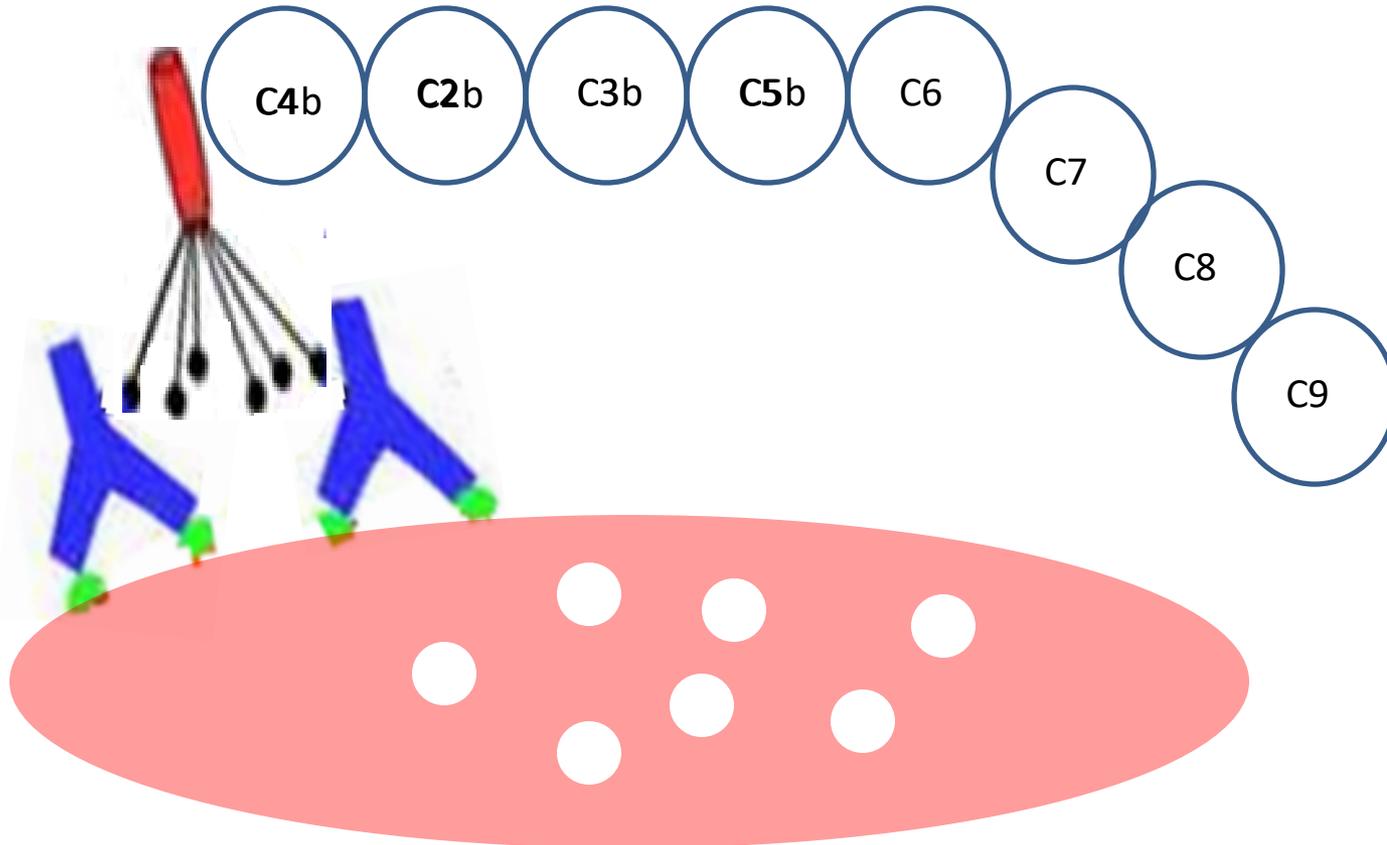






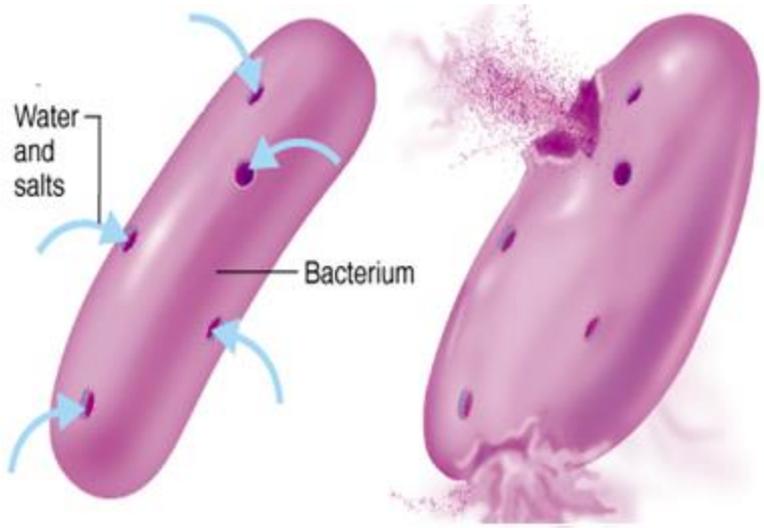
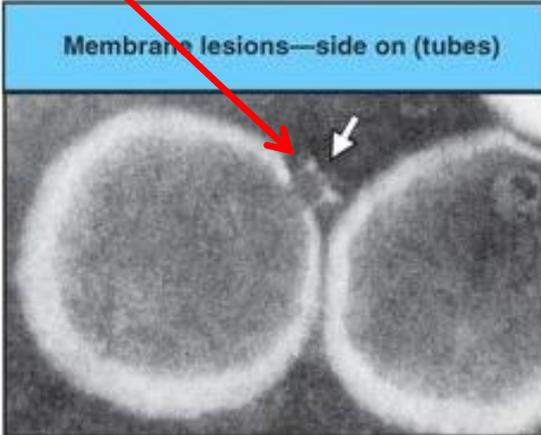
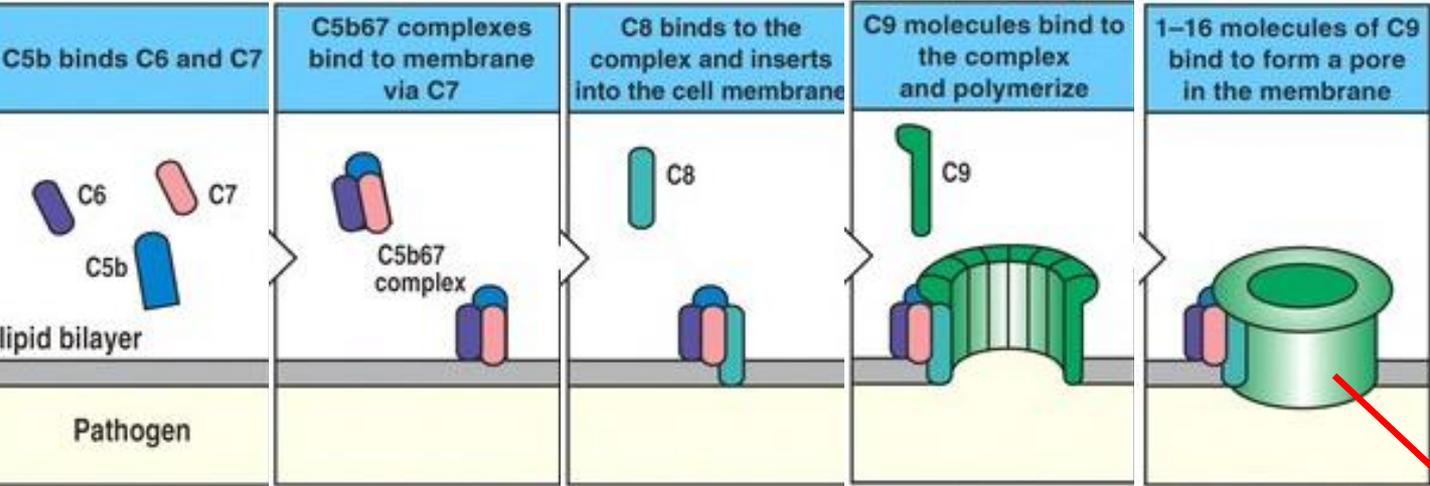
**C5 convertase**

**C3 convertase**

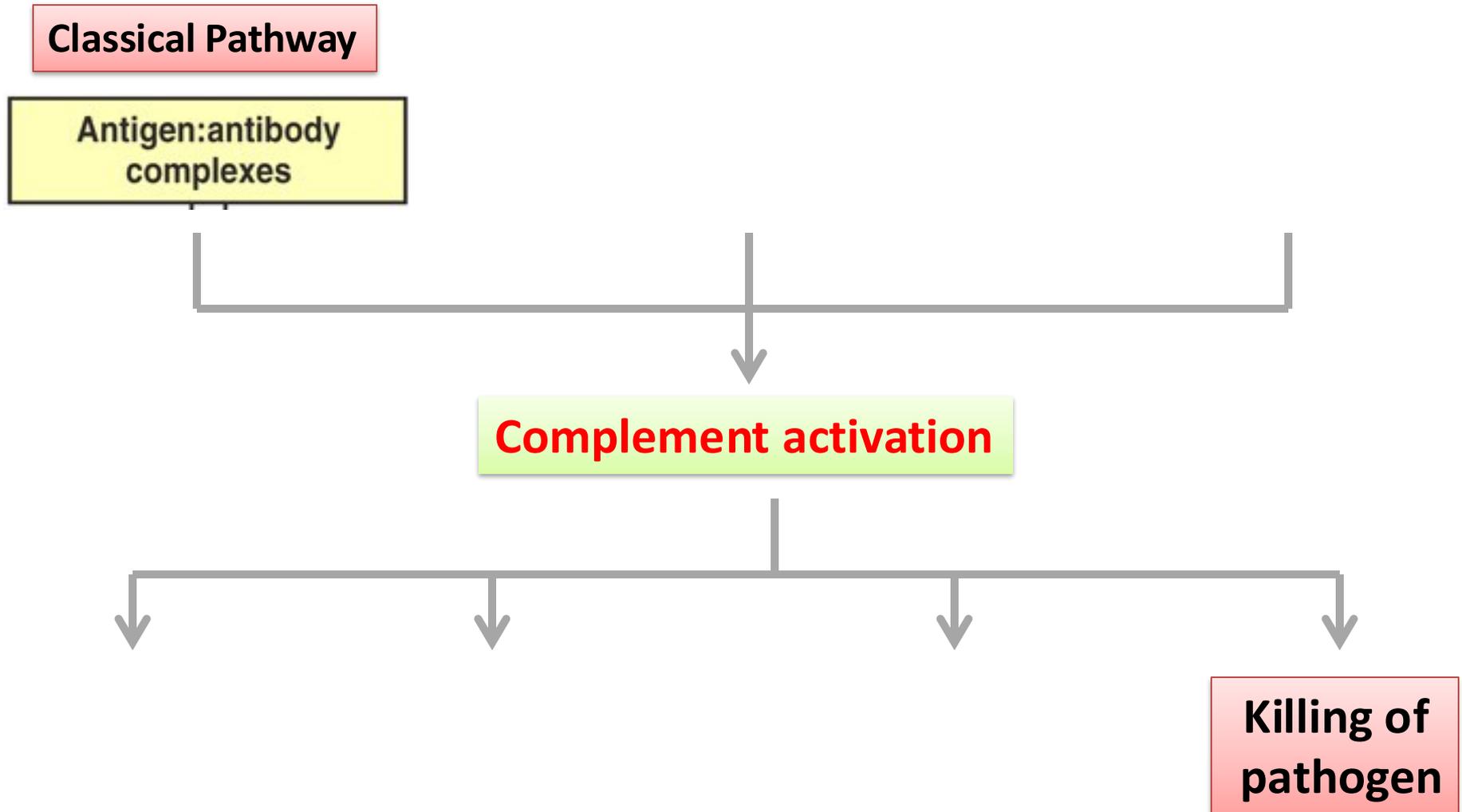


**Classical  
Complement  
Pathway**

# Classical Complement Pathway



# Complement pathways activation



# Complement pathways activation

Infection



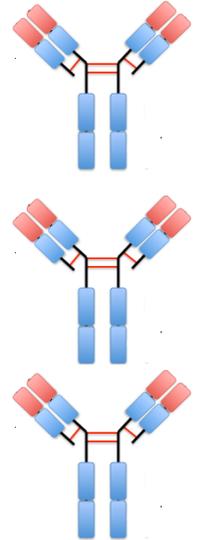
5-7 days



?

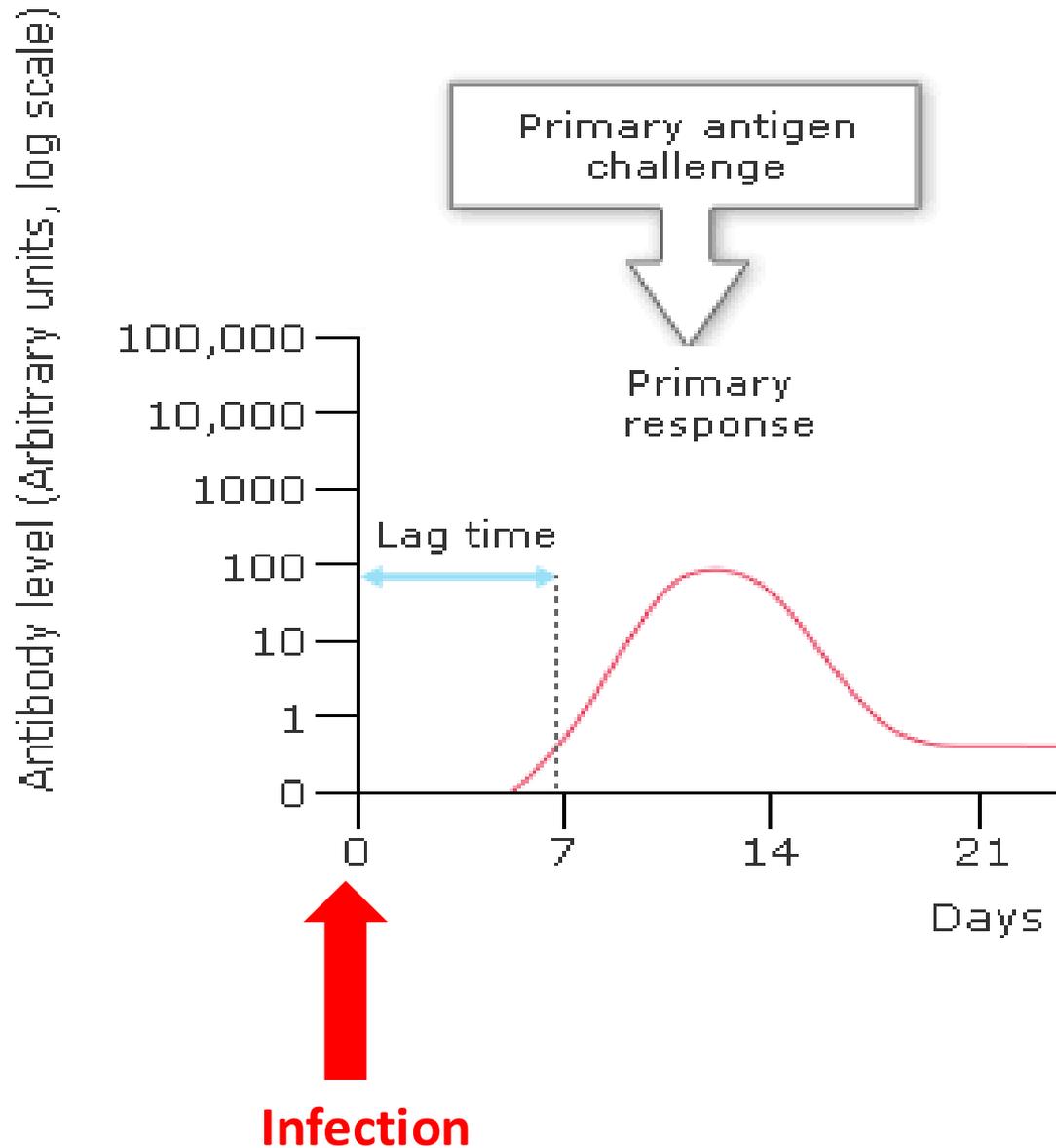
Alternative Pathways

Mannan Binding Lectin Pathway

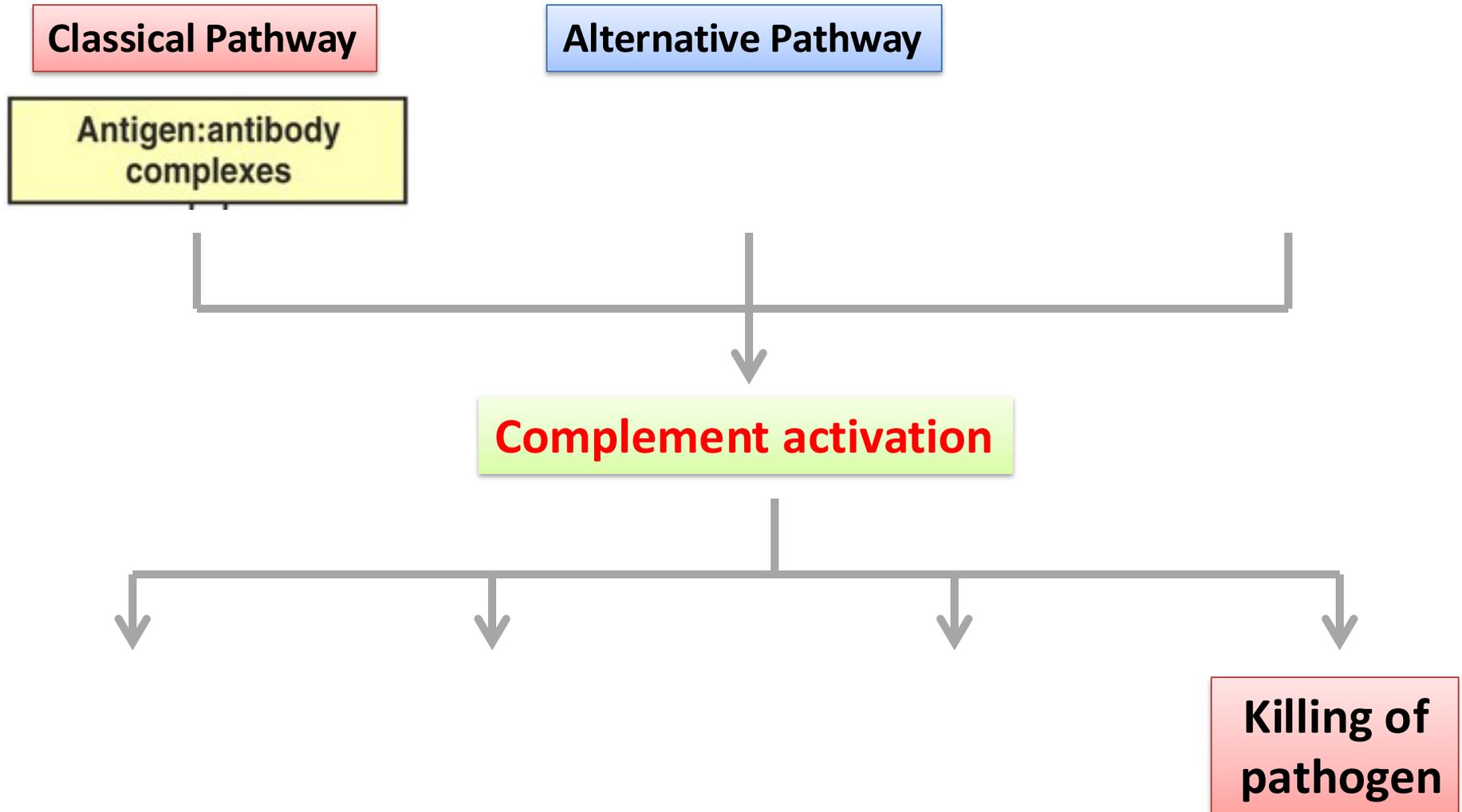


Classical pathway

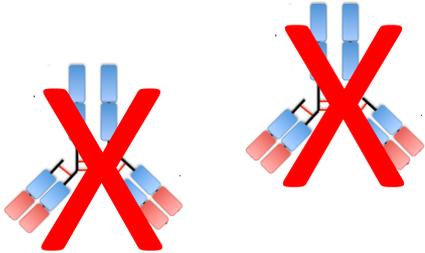
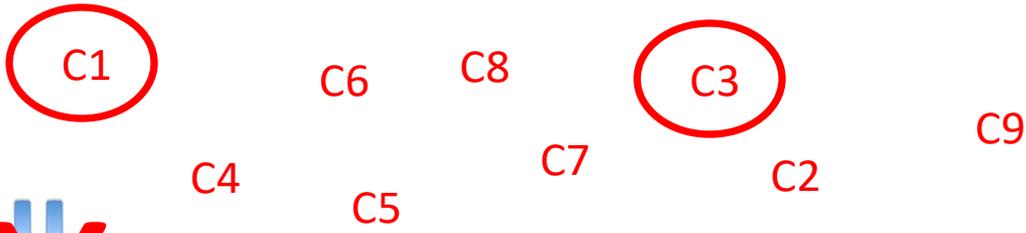
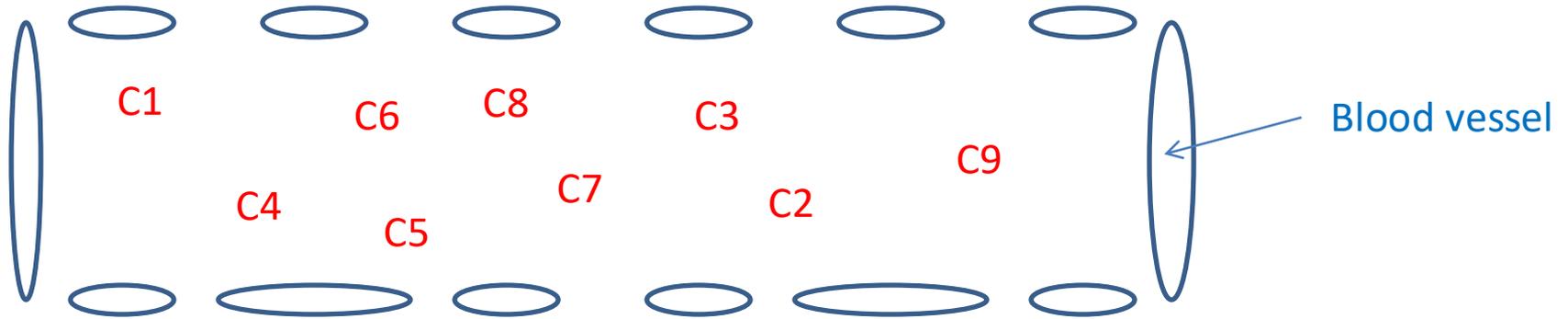
# Time required for antibody production after first exposure to an antigen



# Complement pathways activation



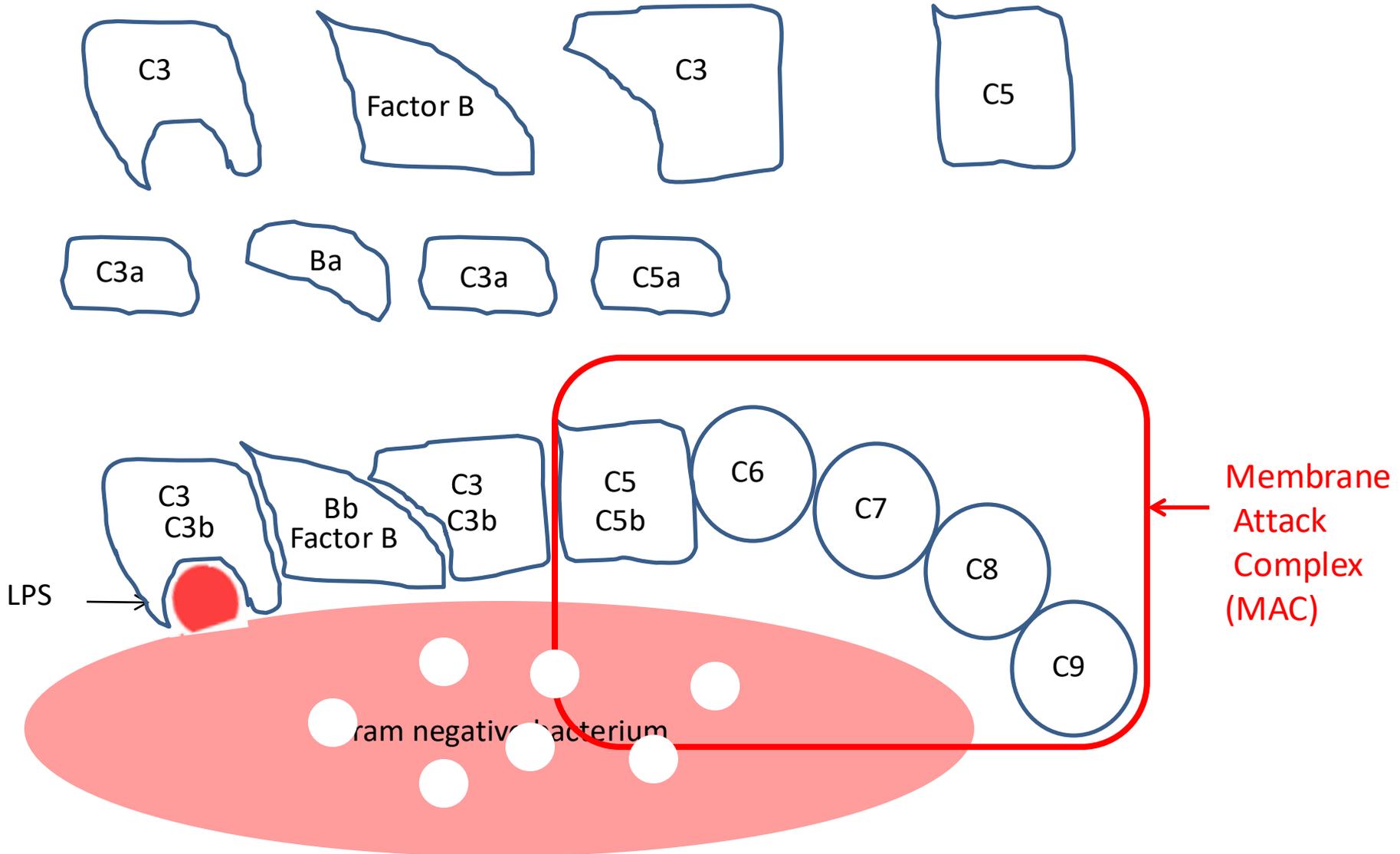
# Alternative Complement Pathway



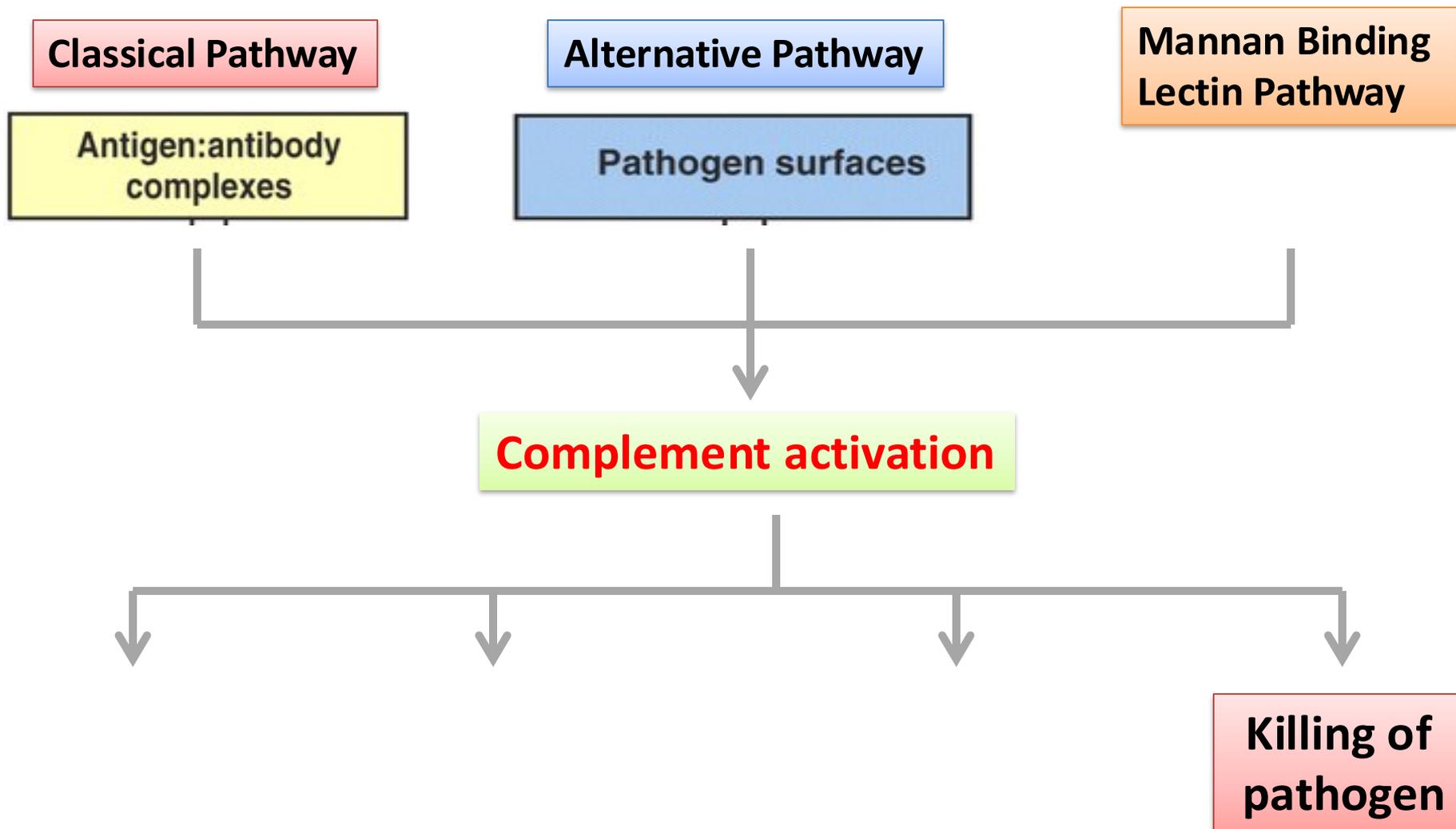
Inflammation



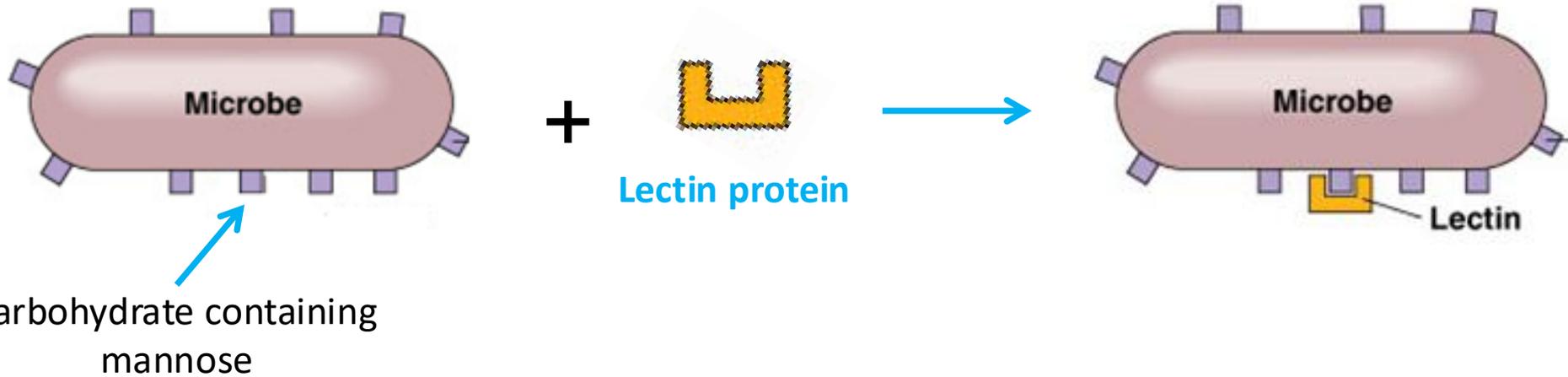
# Alternative Complement Pathway



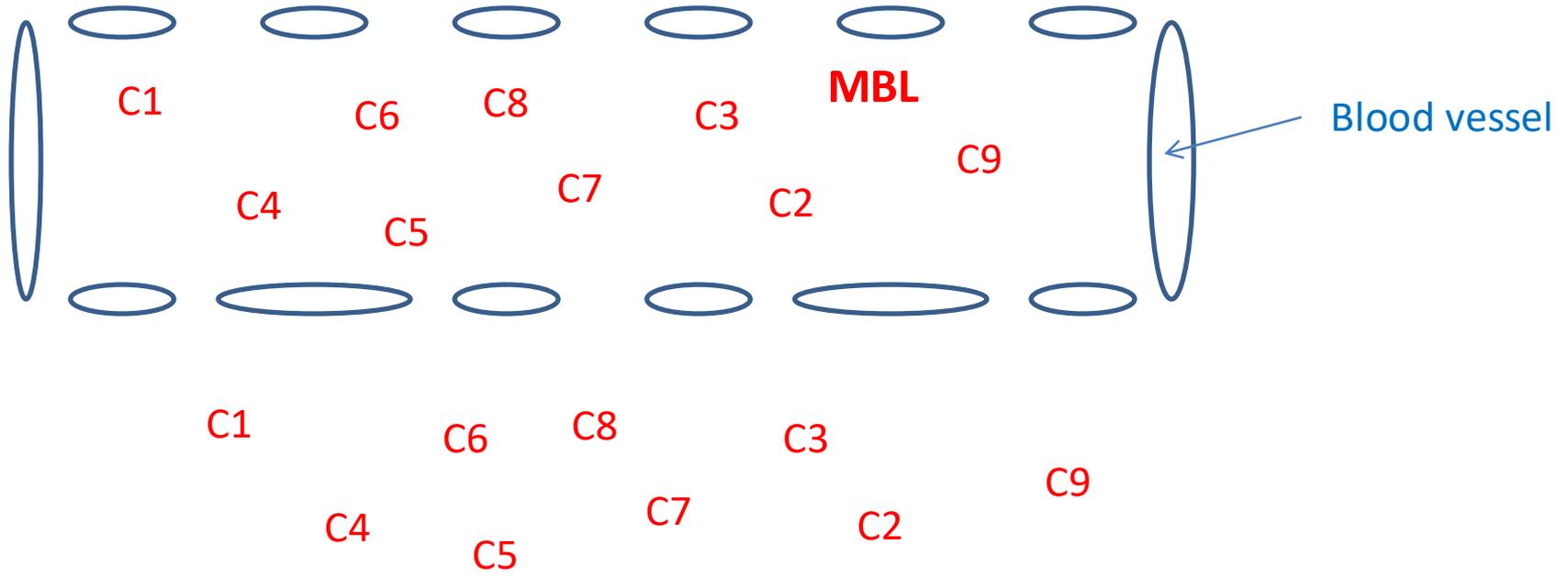
# Complement pathways activation



# Mannan Binding Lectin Pathway



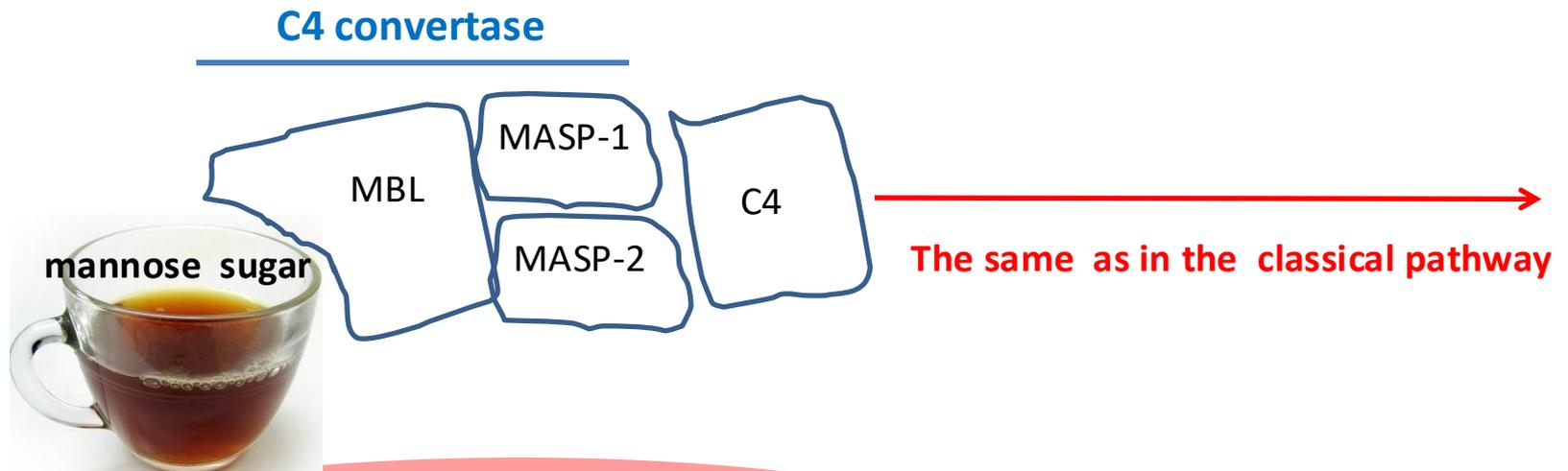
# Mannan Binding Lectin Pathway



Inflammation

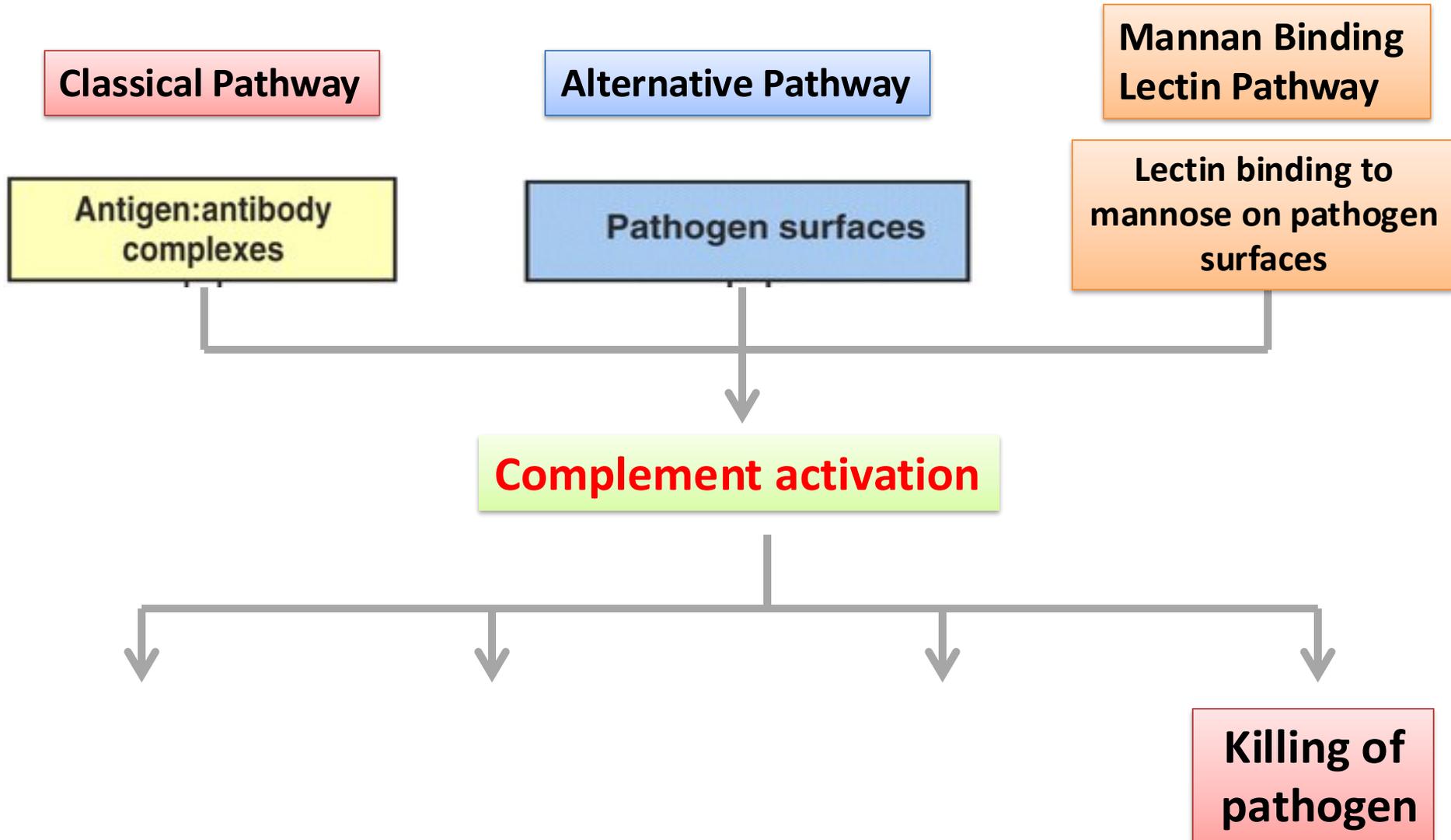


# Mannan Binding Lectin Pathway



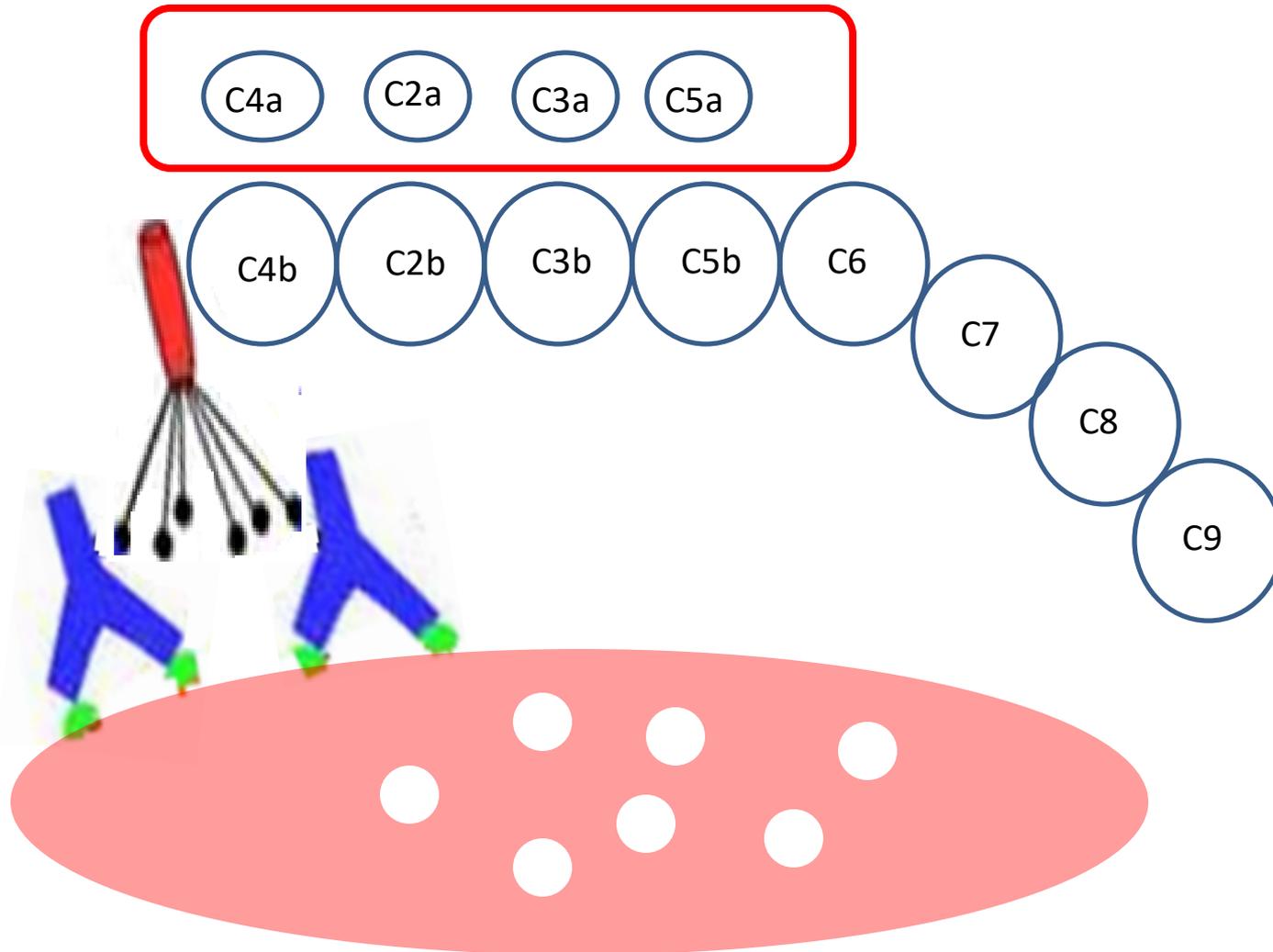
mannose residues on the surface of a large number of pathogens including bacteria, viruses, protozoa and fungi.

# Complement pathways activation

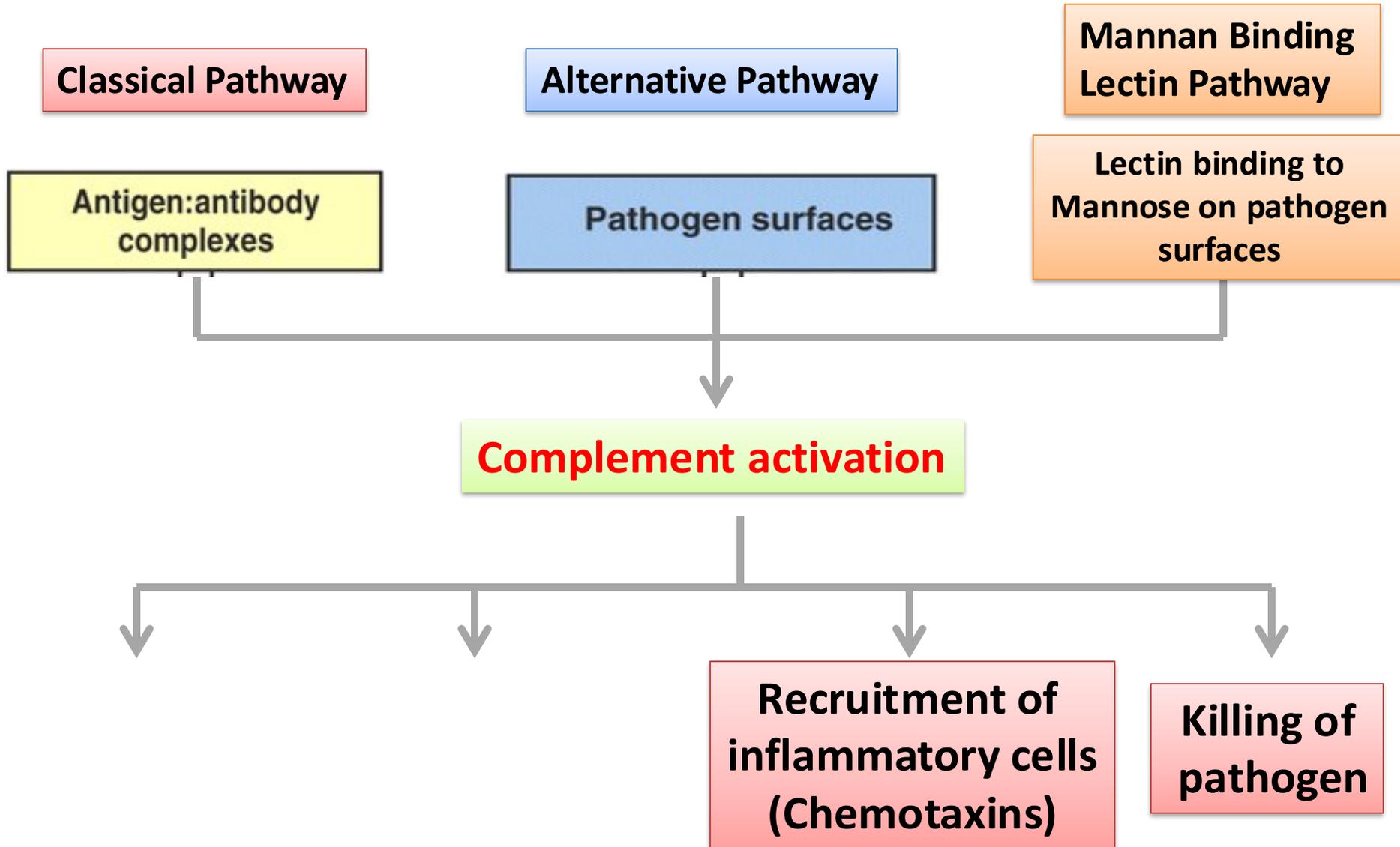


## **Biological activities of complement components**

# Biological activities of complement components



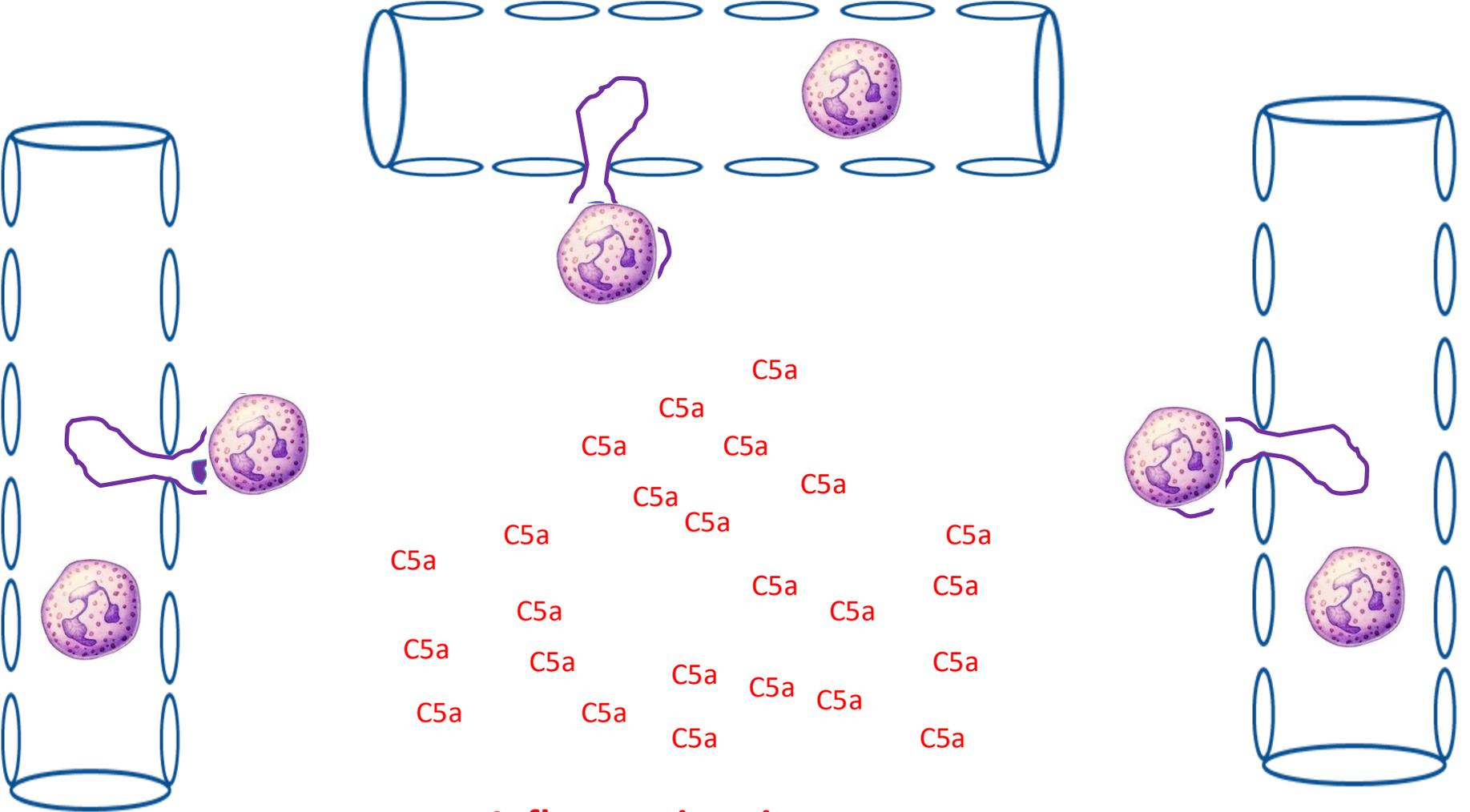
# Complement pathways activation



# Biological activities of complement components

Recruitment of Inflammatory cells  $\longrightarrow$  Chemotaxis

C3a, C5a



Inflammation site

# Biological activities of complement components

Recruitment of Inflammatory cells → Chemotaxis

C3a, C5a

Step 1: stationary cell



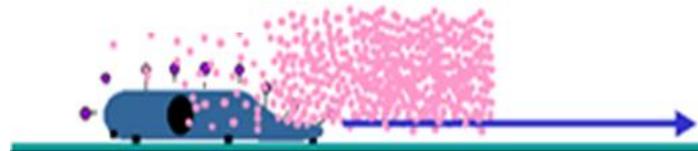
Step 2: Gradient sensing



Step 3: Pseudopod extension

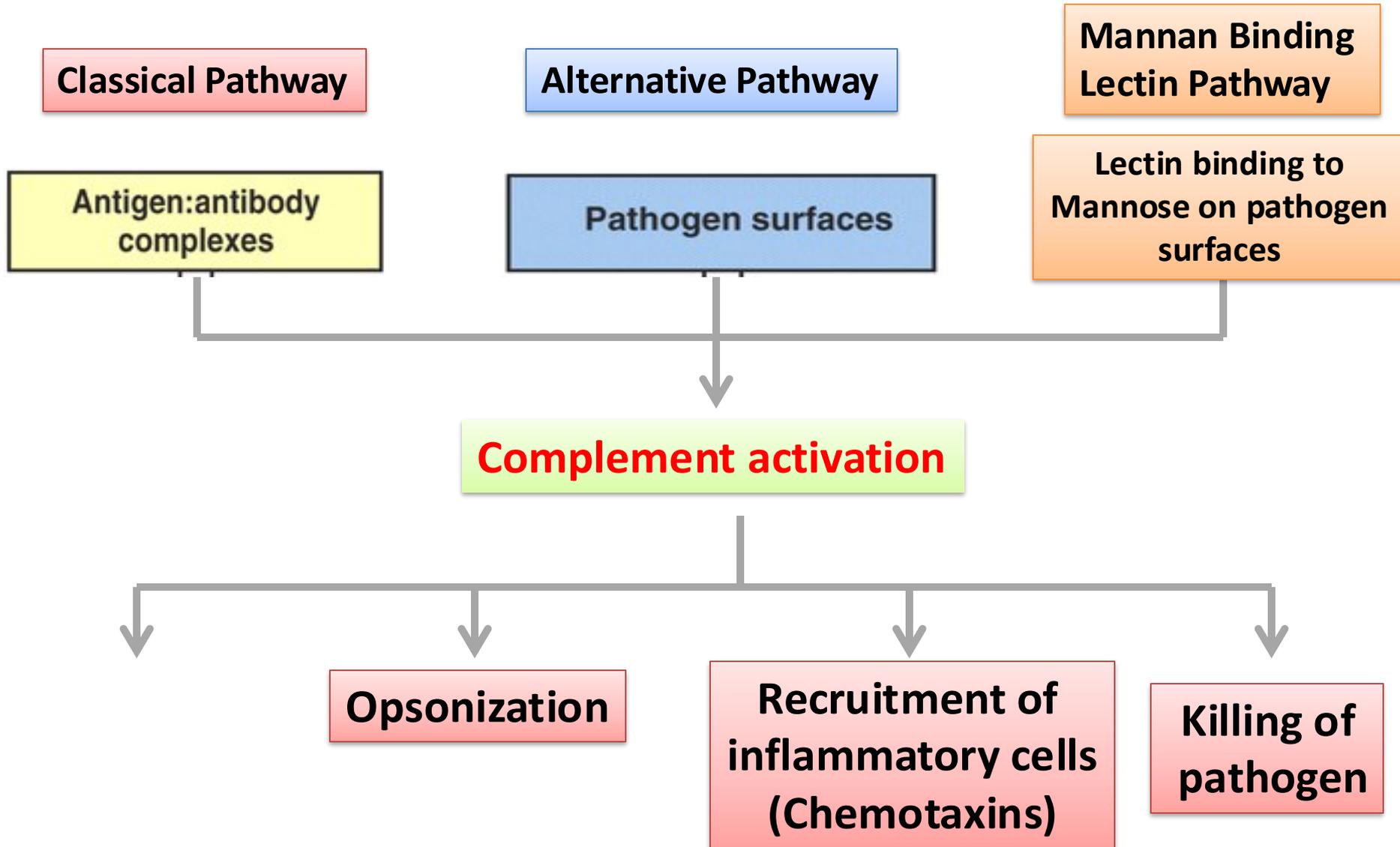


Step 4: Direction of motility



Chemotaxins are substances that attract phagocytic cells and cause their migration from the an area of lesser concentrations to an area of higher concentrations

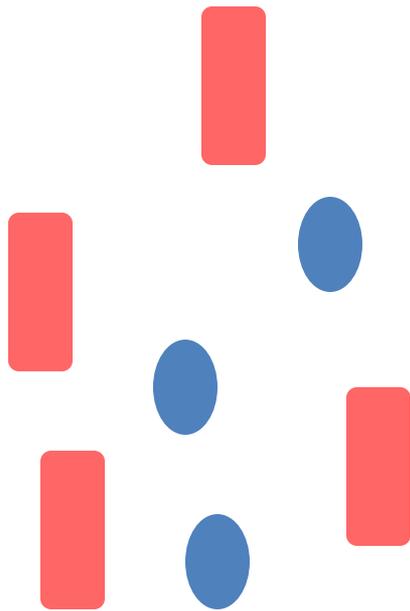
# Complement pathways activation



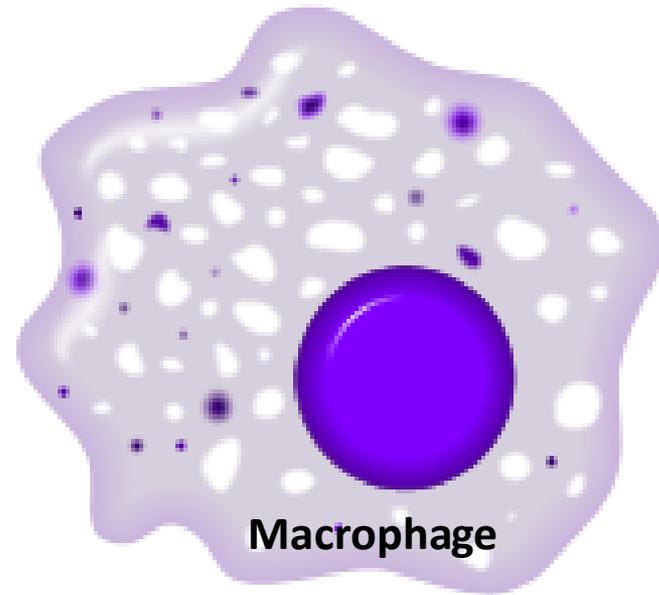
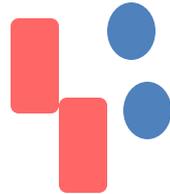
# Biological activities of complement components

Opsonization

C3b



**Bacteria**



**Macrophage**

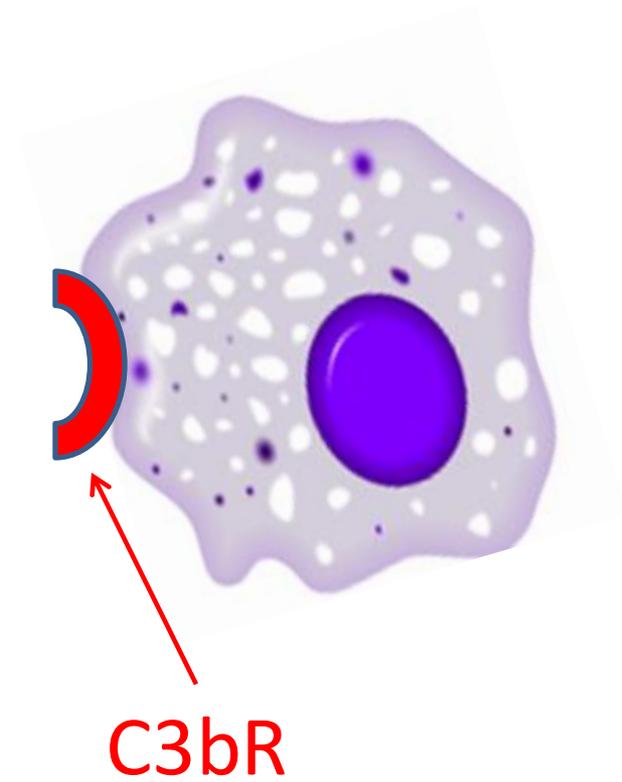
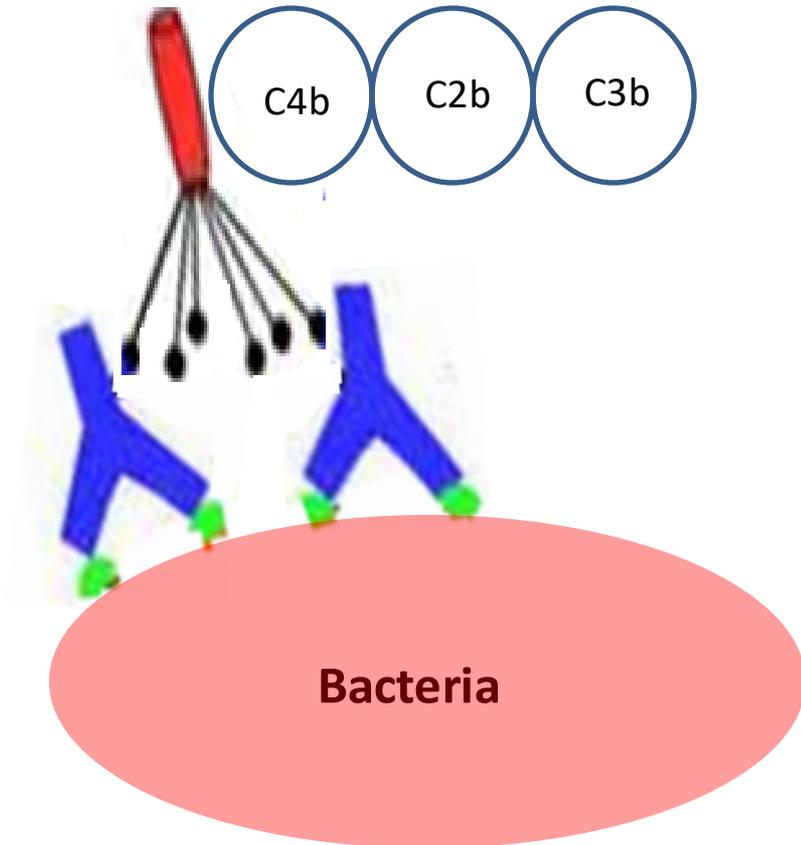
Macrophage requires more time to phagocytize this number of bacteria

# Biological activities of complement components

## Opsonization

Opsonin: to prepare for eating

C3b



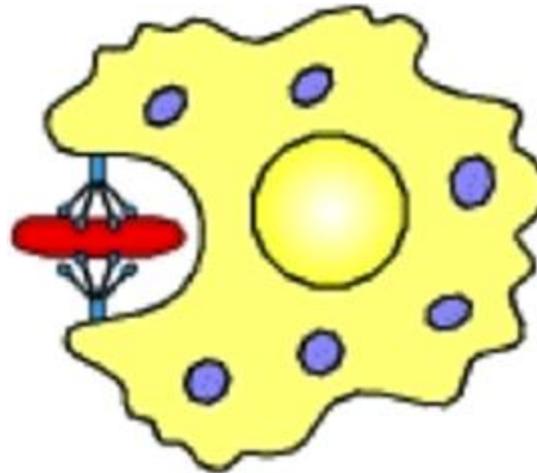
C3b act as opsonin which makes phagocytosis easier and faster

# Biological activities of complement components

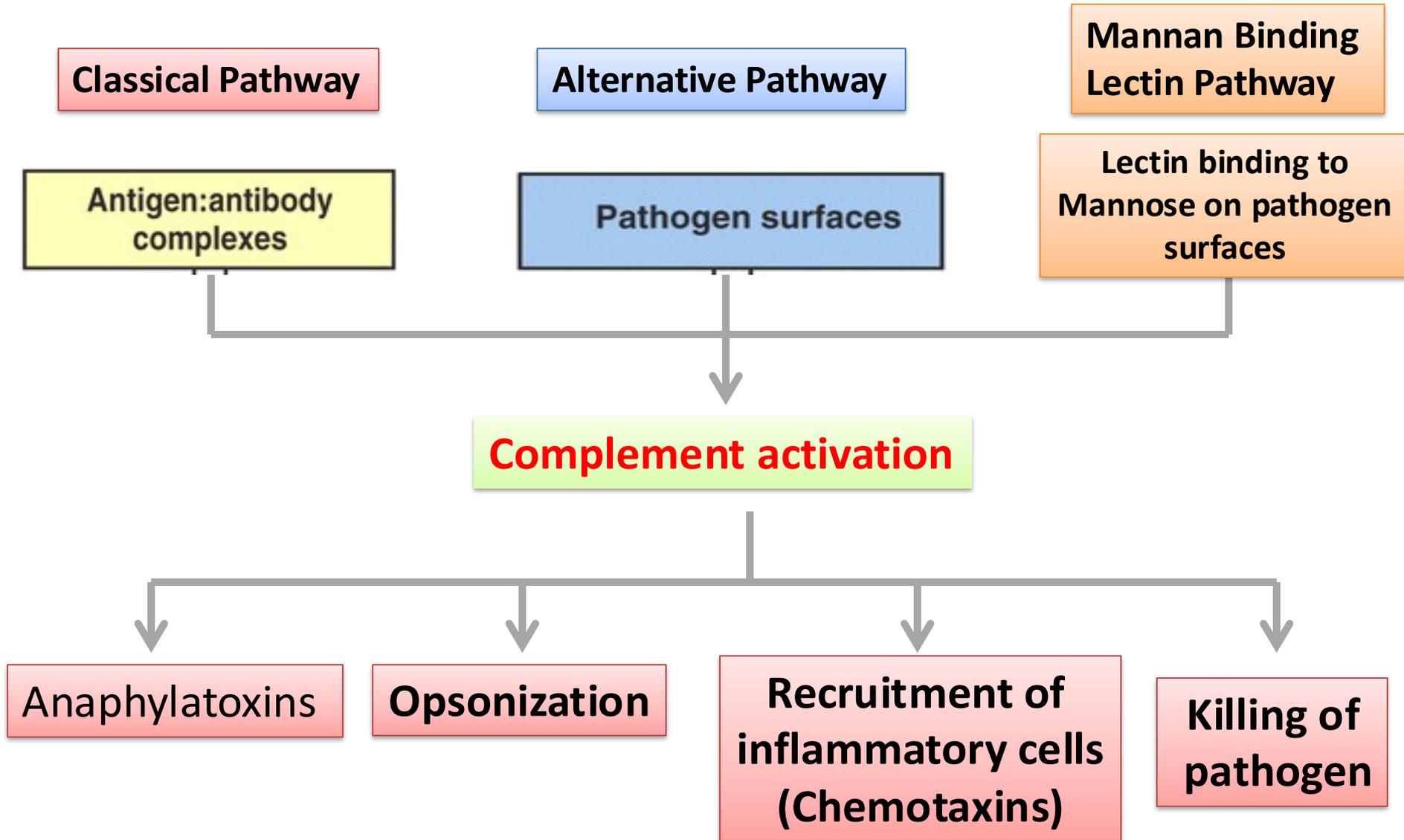
Opsonization

MBL

MBL act as opsonin



# Complement pathways activation

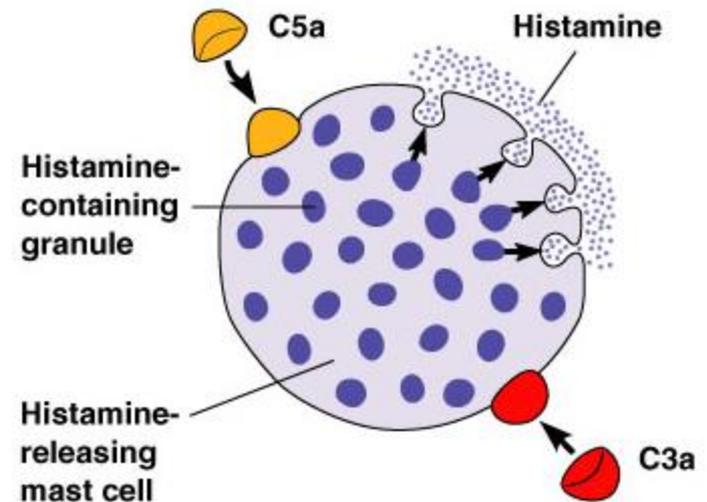


# Biological activities of complement components

## Anaphylatoxins

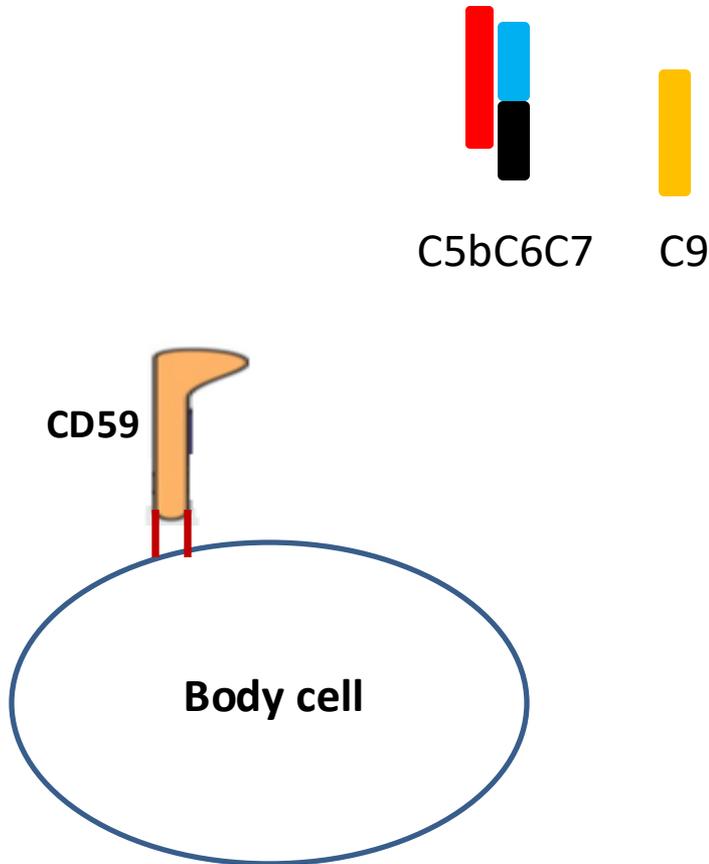
An anaphylatoxin is a substance that induces the degranulation of mast cells and/or basophils causing the release of histamine. Histamine stimulates vasodilatation and endothelial cells retraction which allows the reaching of more complement proteins and inflammatory cells from the blood circulation to the infected site to amplify the immune response.

C3a, C4a, C5a



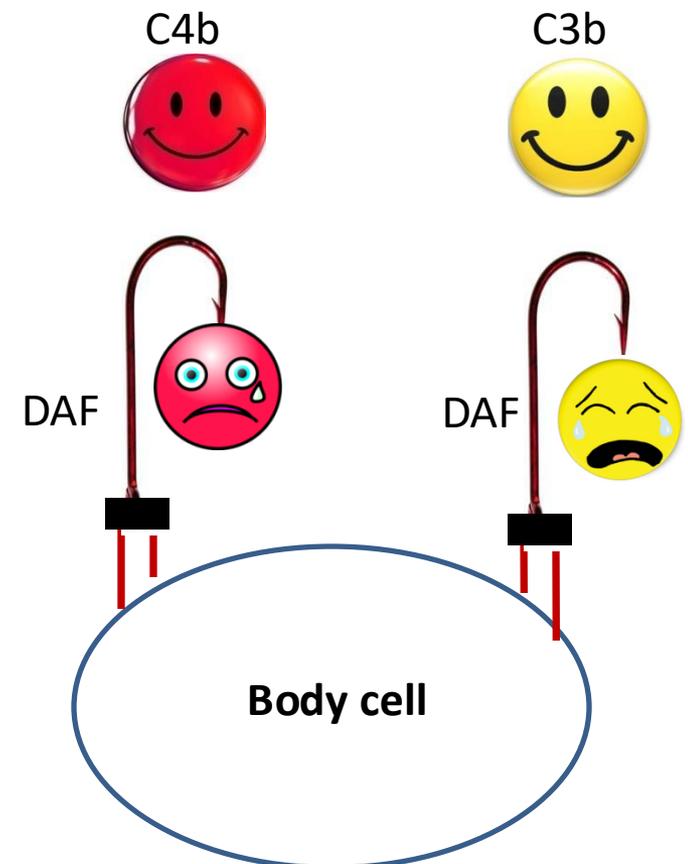
# What protect our cells from complement system?

## 1. MAC-inhibitory protein (CD59)



CD59 inhibits the recruitment of C9 which inhibits the formation of MAC

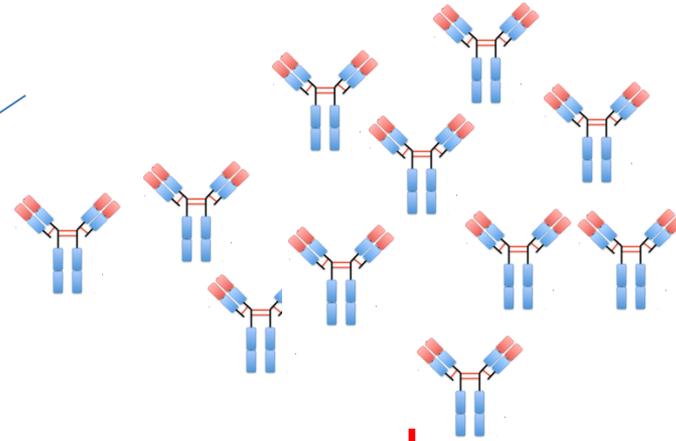
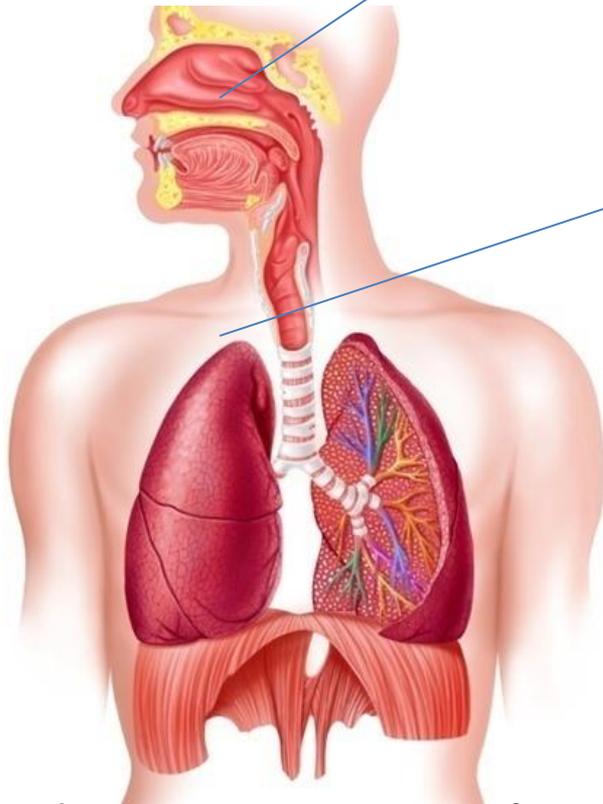
## 2. Decay-Accelerating Factor (DAF)



C4b and C3b interaction with DAF inhibits the stimulation of complement on the surface of body cells

# Diseases associated with complement system

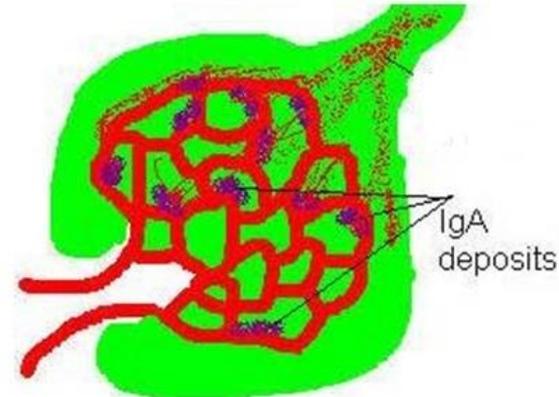
## IgA nephropathy (Berger disease)



Polymerization



Deposition in the glomerular mesangium



Patient with respiratory tract infection

# Diseases associated with complement system

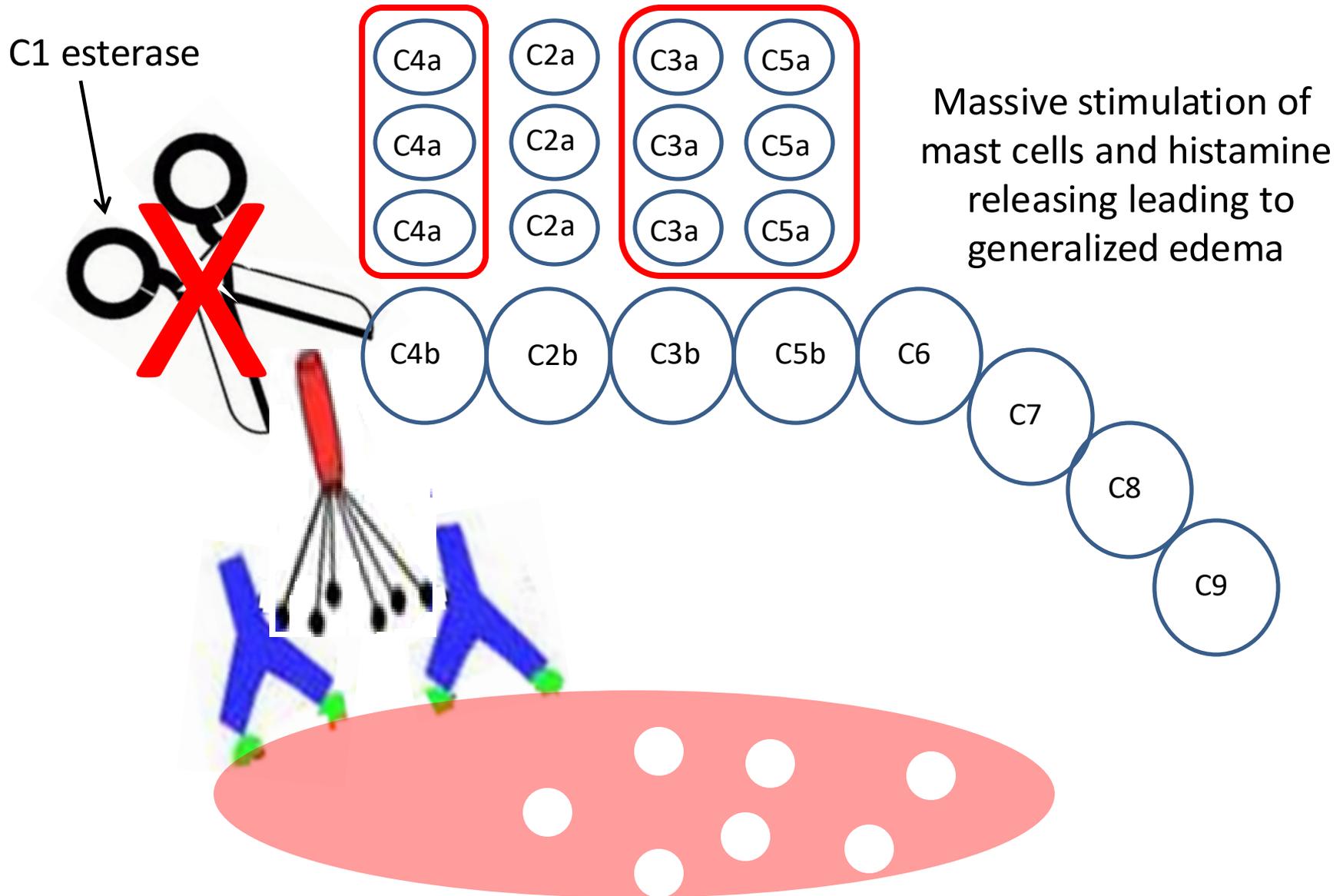
## Henoch-Schönlein purpura (HSP)



HSP is a small-vessel vasculitis in which complexes of IgA and complement component are deposited on arterioles, capillaries, and venules. HSP involves the skin and connective tissues, scrotum, joints, gastrointestinal tract and kidneys

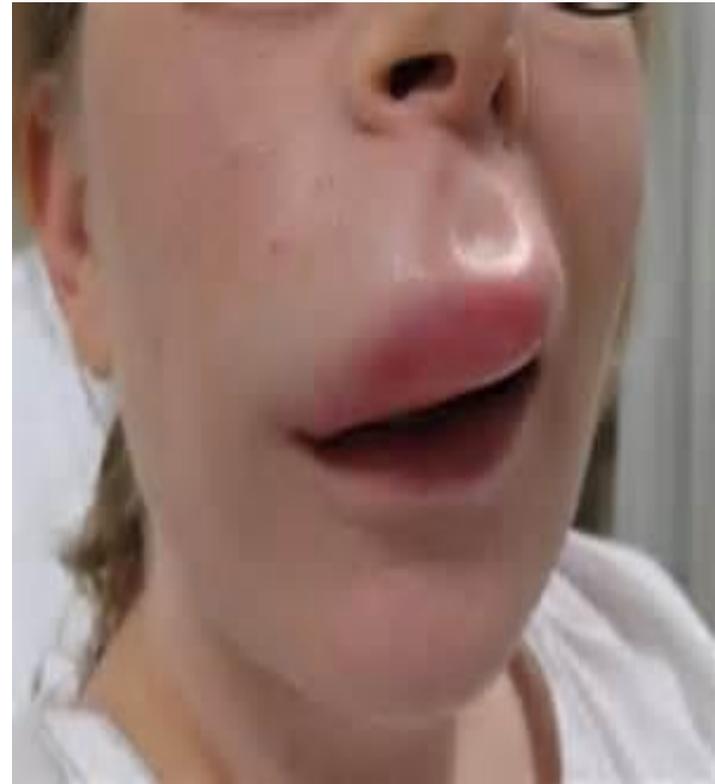
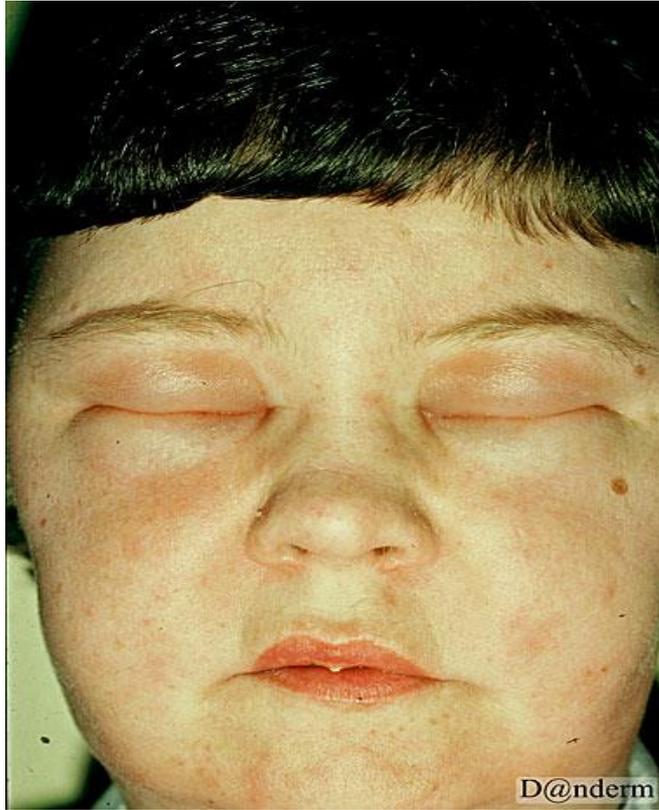
# Diseases associated with complement system

## Angioedema



# Diseases associated with complement system

## Angioedema



# Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Is a complement-induced intravascular hemolytic anemia (anemia due to destruction of red blood cells in the bloodstream).
- This disease is associated with a defect in the cell membrane protein that anchors the decay accelerating factor (DAF).
- Therefore, cells lack DAF will be exposed to complement destruction.

