

# Chapter 7: Complement

- Heat labile Ptns → found in blood and tissue fluids → (# urine & CSF)
- Produced by liver
- Inactive  $\xrightarrow{\text{M.O.}}$  active → When activated → some factors are split
  - Small fragments (a) → by product
  - Large fragments (b) → continue the activation process
- They are activated in sequential manner one step after the other → the product of one reaction forms the enz. For the next
- This called **complement activation cascade**
- So called → because they are required to complement the bactericidal effect of Abs

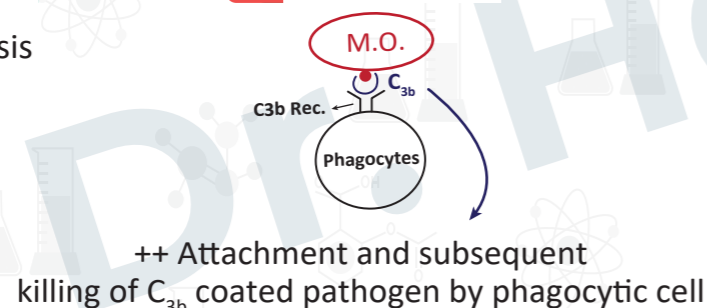
## Immunity (12)

### Functions of complements

#### 1 Direct cytotoxicity

MAC → osmotic lysis

#### 2 Opsonization

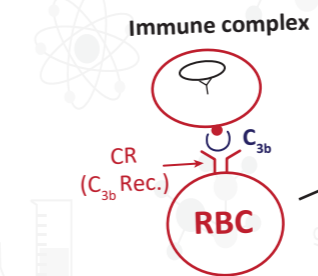


#### 3 Inflammatory response

$C_{3a}$  and  $C_{5a}$  are anaphylatoxins

- 1- Degranulation of mast cells and basophils → ++ histamine
- 2- Chemotaxis of phagocytic cells and ++ their phagocytic power and I.C. killing

#### 4 Immune complex clearance



- Transport immune complexes to organs rich in fixed phagocytes (liver and spleen)

Using their own  $C_{3b}$  Rec, these phagocytes remove immune complexes from RBCs

Clearance of immune complexes from circulation and -- development of immune. Complex dis.

### Regulation of complement system

#### 1 $C_1$ inhibitor

-- further cleavage of  $C_4$  &  $C_2$

#### 2 $C_3$ → spontaneous activation

(esp. by alternative pathway)

The activated complement can destroy any cell to which they bind

Host cells are protected from such damage by series of complement regulatory ptns

Some are associated with host cell surface

Others are plasma ptns

#### 3 Deficiency of regulatory ptns

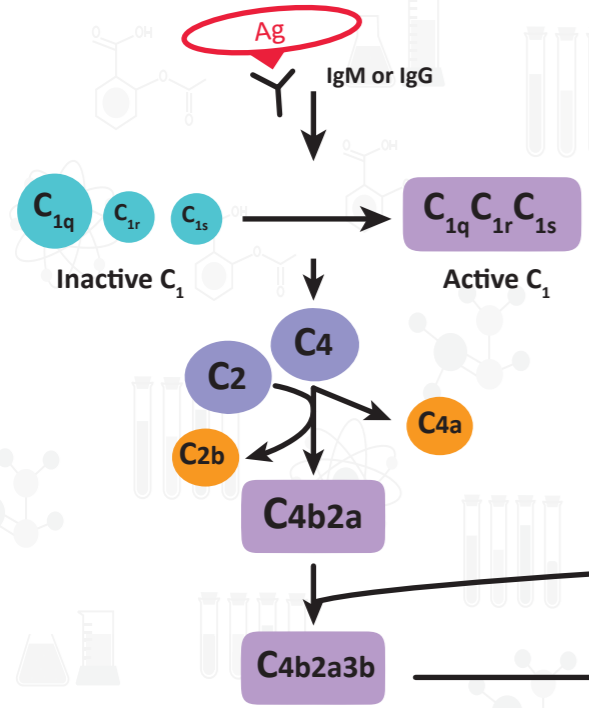
++ Comp. activation

++ Inflammation  
++ Tissue damage

# Complement Activation

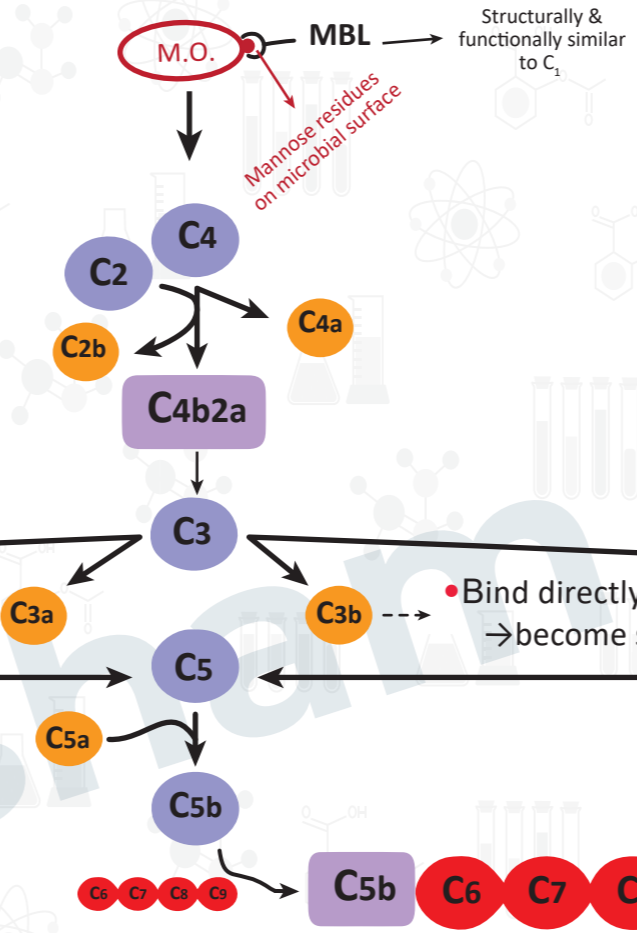
## 1 Classical pathway of complement activation

(Part of acquired immunity → due to presence of Abs)  
(Involve 9 complement)



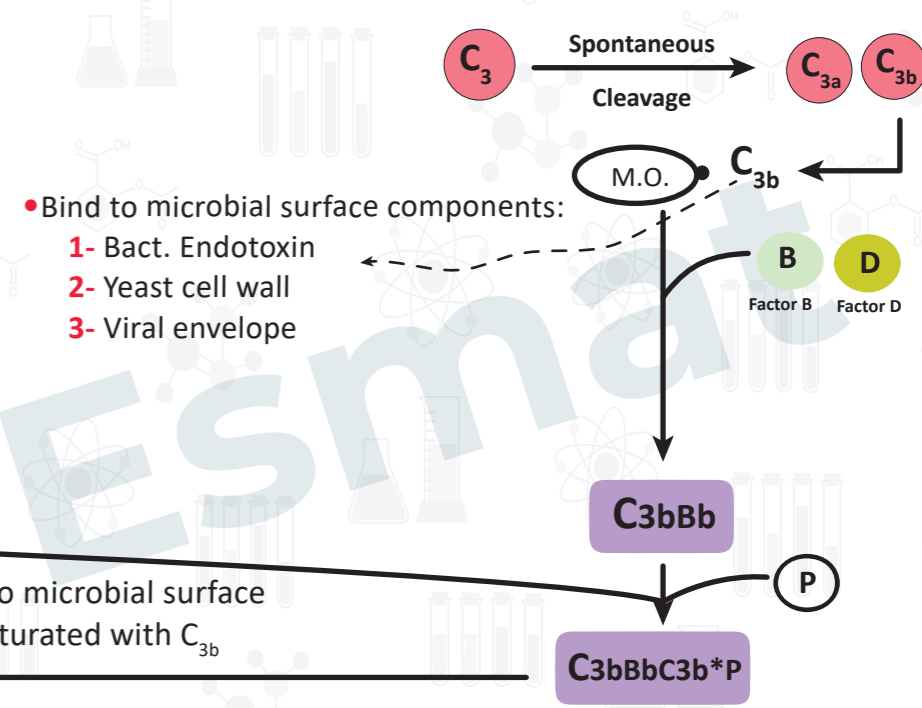
## 2 Lectin pathway of complement activation

(No Ab) → part of innate immunity  
Involve 8 complement (All # C<sub>1</sub>)



## 3 Alternative pathway of complement activation

(Part of innate imm.)  
6 complement → (all # C<sub>1</sub>, C<sub>4</sub>, C<sub>2</sub>)



Early steps of Complement activation

Late steps of Complement activation

- Bind to microbial surface components:
  - 1- Bact. Endotoxin
  - 2- Yeast cell wall
  - 3- Viral envelope

- Bind directly to microbial surface → become saturated with C<sub>3b</sub>

- Form hollow cylinder that becomes interested into target cells memb. → entry of H<sub>2</sub>O and solutes across the membrane → cell death (osmotic lysis)

Immunity (13)

## Comparison between the 3 pathways of complement activation:

	Classical pathway	Lectin pathway	Alternative pathway
Type of immunity	Acquired (specific)	Innate (non-specific)	Innate (non-specific)
Initiation	Antigen-antibody complex	Lectin binding to pathogen surface	Deposition of C <sub>3b</sub> on microbial surface
Role of antibodies	Needed for initiation (activation of C <sub>1</sub> )	Have no role	Have no role
Role of factors B, D & P	Have no role	Have no role	Have a role
Role of MBL	Has no role	Has a role	Has no role
The involved components	C <sub>1</sub> , C <sub>4</sub> , C <sub>2</sub> , C <sub>3</sub> , C <sub>5</sub> , C <sub>6</sub> , C <sub>7</sub> , C <sub>8</sub> & C <sub>9</sub>	C <sub>4</sub> , C <sub>2</sub> , C <sub>3</sub> , C <sub>5</sub> , C <sub>6</sub> , C <sub>7</sub> , C <sub>8</sub> & C <sub>9</sub>	C <sub>3</sub> , C <sub>5</sub> , C <sub>6</sub> , C <sub>7</sub> , C <sub>8</sub> & C <sub>9</sub>

**N.B**

- If C<sub>3b</sub> → deposited on host cell surface → prevented from binding stably by several regulatory Ptns present on host cells and absent from microbes → complement activation on host cells is prevented