Complement System

Complement!

Similar fashion to our → Clotting factors! [illegible]

Always present in Circulation – In their inactive state!

Major effector system → Humoral branch of Immunity.

Antibodies secreted by B-cells.
↓
Conjugate with their Antigen Molecules
↓
[Antigen - Antibody] → Complex.

once [Ag-Ab] complex formed, now the the imp. role of Complement system

Composed of [illegible] in serum and Membrane bound Proteins

Research on Complement System
1890s – Jules Bordet
at Pasteur Institute.
(Paris)

Showed that – Sheep's antiserum to the bacteria Vibrio cholerae (causes Cholera) caused lysis of the bacteria

↳ Heated Antiserum → destroyed the bacteriolytic property!

↳ Ability to lyse the bacteria was restored to the heated serum by adding fresh serum that contained no Antibodies directed against the bacterium. (Vibrio cholerae)

Jules Bordet reasoned that bacteriolytic activity requires two different substances–

(i) The specific antibacterial Ab. which survive the heating process

(ii) Heat sensitive Complement responsible for lytic activity.

"Alexins" → Cause hemolysis to Ab-Coated RBCs.

Ehrlich → defined Complement -

The activity of blood serum that completes the action of Antibody (Ab & Proteins)

Complement is the result of the interaction of a large and Complex group of protein

Proenzymes or Zymogens.

A Chain of a.a. to be removed! → become

Zymogen granules (Inactive)
↓ Released!

Zymogens → Active Enzymes!!!

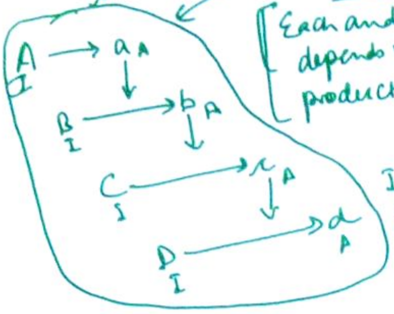
Trypsinogen (Inactive) → Trypsin (Active)
↳ A Chain of a.a. to be removed!

Similarly → Complement protein (In

[illegible] fragment

Active Complement protein
↓
Cascade process

Small p of Protein/
Polypeptide
Chain
is removed!



[Each and every successive step depends upon the availability of product from previous / penultimate reaction]

I - Inactive form
A - Active form

Complement system pathways - Cascade pathways!

I ↳ Classical pathway → Essential Component ↳ [Ag-Ab] ← complex.

II ↳ Lectin pathway → Lectin must Present ↳ Microbial cell wall.

III ↳ Alternative pathway → Microbial cell surface

Basic purpose of all the pathways → FORM ↳ MAC. → Membrane Attack complex.

Complement proteins → Secreted from ↓ Liver

C1 [C1q ×1, C1r ×2, C1s ×2] → Complex formation ↳ $C1qr_2s_2$

C2
C3
C4
C5
C6
C7
C8
} All of them - Released in their Inactive form.
C9
B-factor.

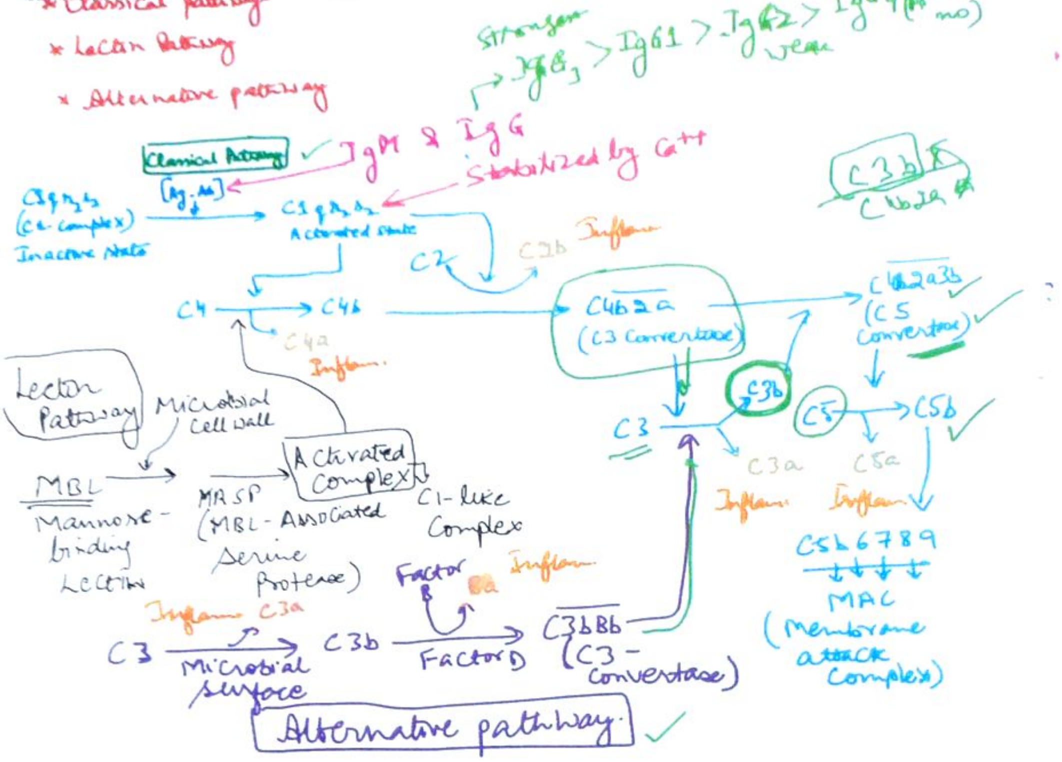
Complements proteins - In order to activate they get Clipped off into two fragments!

a (Smaller) → Major Function ↓ Inflammation
} Fragment
b (Larger) ↳ It becomes a part of enzyme system which Plays an Imp. role in Complement system activation)
↓
Involved in the actual Cascade pathway.

Generally - - -> "NOT ALWAYS"

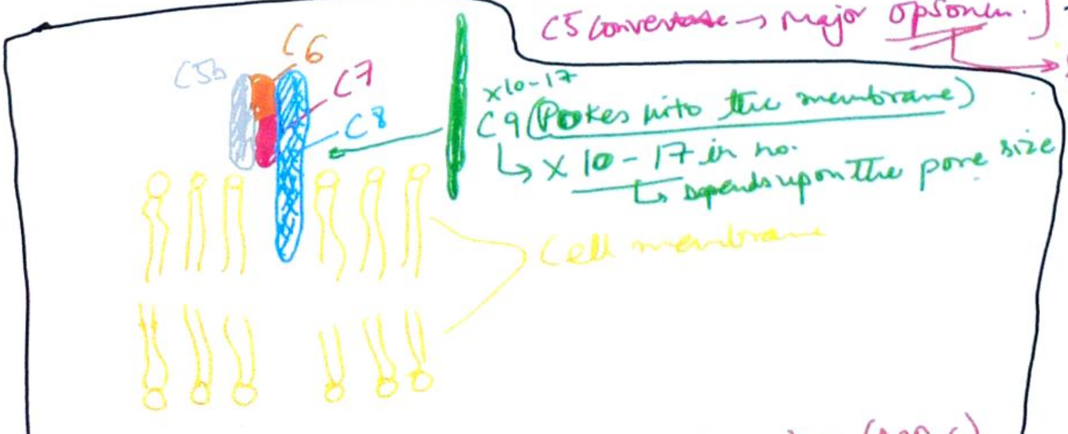
[illegible]

- Classical pathway
- Lectin Pathway
- Alternative pathway



Components	Active / Split protein	Immunological functions
C1	C1q,	→ Binds to F_c region of IgM & IgG
	C1r	→ Serine protease – Enzymatically activates C1s
	C1s	→ Serine protease – enzymatically activates C4 and C2
C4	C4a	Peptide mediator of Inflammation (Anaphylatoxin)
	C4b	Binds to C2 forming a Complex yields $C\overline{4b2a}$
C2	C2a	Serine protease – $C\overline{4b2a}$ acts as C3 Convertase
	C2b	→ unknown function.
C3	C3a	→ Peptide mediator of Inflammation
	C3b	→ Binds to $C\overline{4b2a}$ to form C5 convertase → major opsonin.

→ Solubilization & Clearance of [Ag-Ab]
→ Neutralization of Invading pathogens.
→ Phagocytosis by Neutrophils & Macrophages



Assemblage of Membrane Attack Complex (MAC)

Lysis of the membrane results due to C9 assemblage
+
Any change in pressure difference outside & inside the cell

Inflammatory
↓
C5a + C3a → Chemotaxis – Bind to mast cells
↓
Acts on Basophils + Macrophages.

↓
Degranulation & Release of histamines!
↓
Leads to Vascular Permeability
+
Smooth muscles Contraction.
+
Activation of neutrophils & Macrophages augmenting Phagocytosis and the acute phase Response!
+
Increases adhesion molecules expression on endothelial cells adding movements of phagocytic cells into the site of infection!