☑ Complement Activation :→

Complement is normally present in the body in an inactive form but when its activity is induced by antigen-antibody combination or others stimuli, Complement components react in a specific sequence as a cascade.

Basically, the complement cascade is a series of reactions in which the preceding components act as enzymes on the succeeding components, cleaving them into dissimilar fragments. The larger fragments usually join the cascade. The smaller fragments which are released often possess biological effects which contribute to defence mechanisms by various basic effector mechanisms including ——

- Lysis of cells and bacteria.
- Promoting virus neutralisation.
- Opsonisation, which promotes phagocytosis of particulate antigens.
- Immune clearance, which removes immune complexes from circulations and deposits them in the spleen and livers.

6. Amplifying the inflammatory process, increasing vascular permeability, inducing smooth muscle contraction and effecting the release of histamine from mast cells.

PATHWAYS

The complement cascade can be triggered off by three parallel but independent mechanisms or pathways which differ only in the initial steps. Once C3 activation occurs, the subsequent steps are common to all pathways; this is called the classical complement pathways, alternative or properdin pathway and lectin pathway.

The classical pathway is so called because it was the first one identified. It is a more recently evolved mechanism of specific active immunity, while the alternative pathway and lectin pathway represent a more primitive system of non-specific innate immunity.

☒ Classical Complement pathway ☒

The chain of events in which complement components react in a specific sequence following activation of C1qrs and typically culminate in immune cytolysis is known as the classical pathway.

Steps :-

1. The first step is the binding of C1 to the antigen - antibody complex (traditionally represented as EA). The recognition unit of C1 is C1q, which reacts with the F_c piece of bound IgM or IgG.

C1q has six combining sites. Effective activation occurs only when C1q is attached to immunoglobulins by at least two of its binding sites. One molecule of IgM or two molecules of IgG can therefore initiate the process. C1q binding in the presence of calcium ions leads to sequential activation of C1r and C1s.

2. $\overline{C1s}$ is an esterase ($\overline{C1s}$ esterase), one molecule of which can cleave several molecules of C4, an instance of amplification. C4 is split into C4a, which is an anaphylatoxin, and C4b, which binds to cell membranes along with C1.

3. $\overline{C4b}$ in the presence of magnesium ions cleaves C2 into C2a, which remains linked to cell-bound $\overline{C4b}$, and C2b, which is released into the fluid phase. $\overline{C4b2a}$ has enzymatic activity and is referred to as the classical pathway C3 convertase.

4. C3 convertase splits C3 into two fragments: C3a, which is an anaphylatoxin and C3b which remains cell-bound along with $\overline{C4b2a}$ to form a trimolecular complex $\overline{C4b2a3b}$ which has enzymatic activity and is called C5 convertase.

5. The membrane attack phase of complement activity begins at this stage, with C5 convertase cleaving C5 into C5a, an anaphylatoxin which is released into the medium, and C5b

which continues with the cascade. C6 and C7 then join together.

. A heat stable trimolecular complex C567 is formed, part of which binds to the cell membrane and prepares it for lysis by C8 and C9 which join the reaction subsequently.

☑ The classical pathway is generally activated by the antigen-antibody complex or aggregated immunoglobulin, activation may also be due to other stimuli, such as DNA, complement reactive protein, trypsin-like enzymes or some retroviruses.

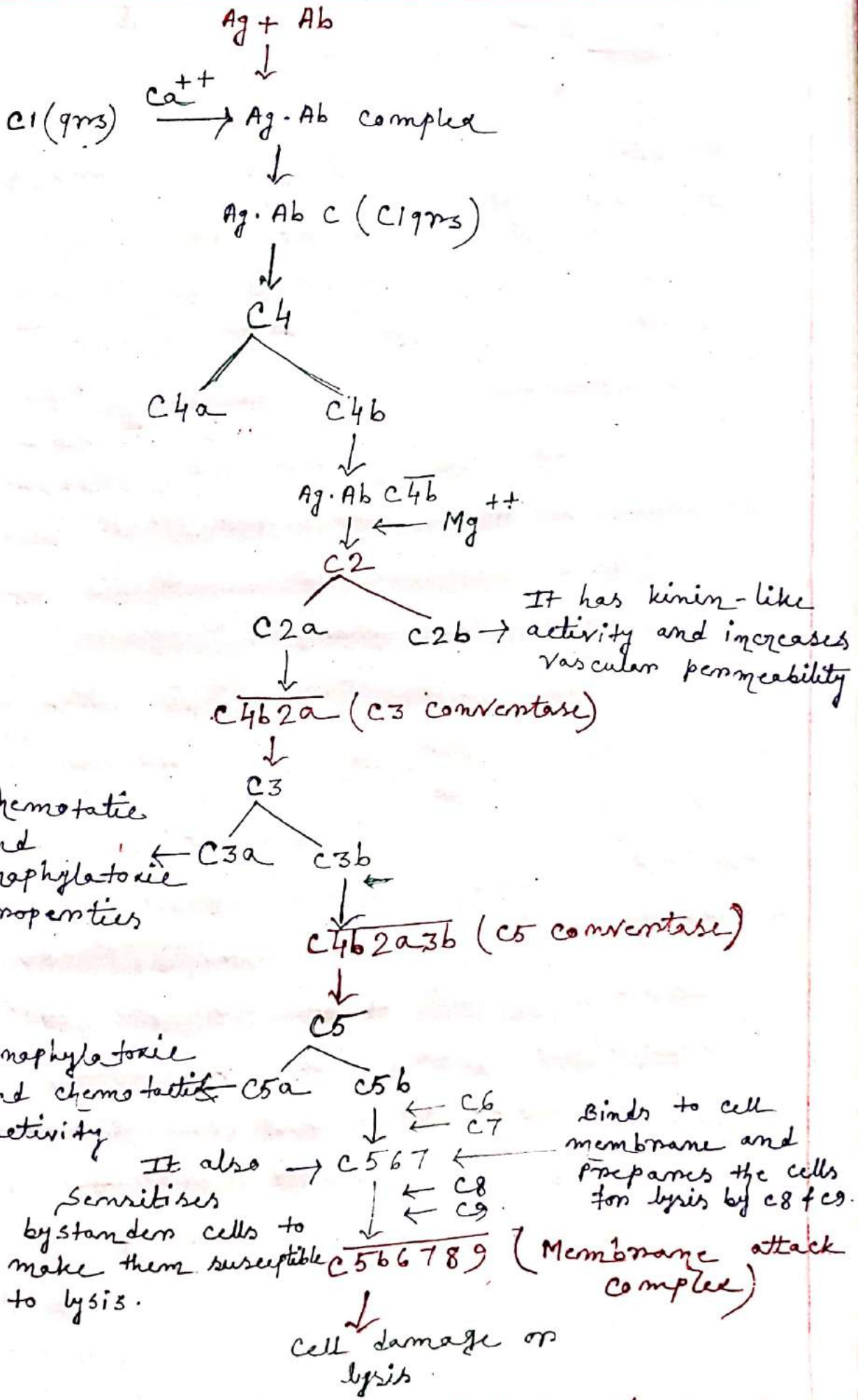

Fig :- The classical Pathway of complement.