

Complement

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Complement

- The Complement System Consists of :
- Approximately 20 proteins that are present in normal human serum
- Complement protein are synthesized in liver
- Complement is an important component of our innate defense
- Complement augment the effects of the component of the immune system e.g AB
- Complement is heat labile (i.e- Inactivated by heat) **56 degree centigrade for 30 minutes**

There are 3 main effects of complement

1. Lyses of cells such as bacteria allografts and tumor cells
2. generation of mediators which act inflammation and attract neutrophils
3. Opsonization enhancement and phagocytosis

Activation of Complement

- Activation of complement components occurs via one of the three pathways



cont

- All three pathways leads to the production of C_3b the central molecule of the complement decade.
 1. It combines with other complement component to generate C_5 (convertase enzyme) which lead to production to membrane attack complex
 2. It opsonize bacteria because phagocytes have receptors for C_3b on the surface

Regulation of the complement system

- In classic pathways only IgG and IgM fix complement antigen antibody complex activate **C₁**
- The complement binding site of complement on **FC** fragment of heavy chain is not available if antigen is not bound to antibodies
- This means that complement is not activated by IgM, IgG presented in blood if not attached with antigen

Several serum proteins regulate the complement system :

1. C₁ inhibitor regulate classic pathways
2. Alternattive pathway regulator
3. Decay accelerator factor in glycoprotien located on surface of human cell prevent formation of membrane attack complex

Biological affect of complement

1. Opsonization
2. Chemotaxis
3. Anaphylatoxin
4. Cytolysis
5. Enhancement of antibody production

Opsonization

- Microbes such as bacteria and virus are phagocytosed much better in presence of C_3b because C_3b receptor on surface of many phagocytes

Chemotaxis

- C_5a and $C_{5,6,7}$ complex attract neutrophils
- Also enhance the adhesion of neutrophil to the endothelium (inflammation)

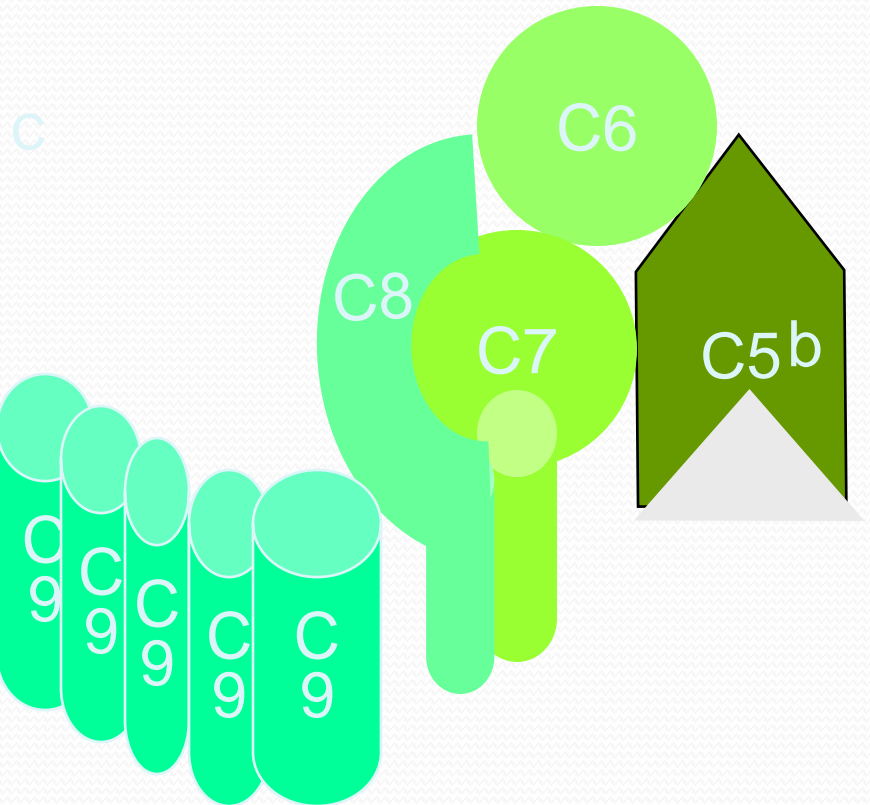
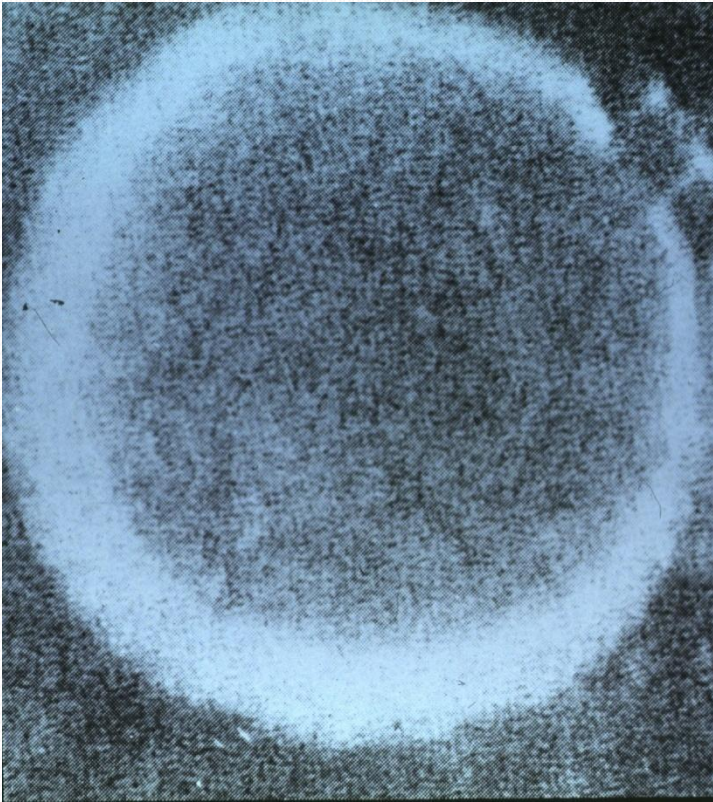
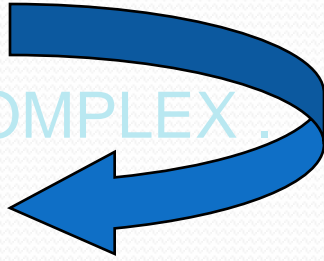
Anaphylatoxin

- C_{3a}, C_{4a} C_{5a} cause degranulation of mast cells with release of mediators
- E.g histamine → ↑ vascular permeability and smooth muscle contraction (bronchospasm)

Cytolysis

- C_{5b,6,7,8,9} complex into the cell membrane
- ↑ Killing (lysis of many cells including erythrocytes ,bacteria and tumor cells)

MEMBRANE ATTACK COMPLEX



Enhancement of antibody production

- B cells have receptors for C_3b so binding C_3b with its receptor on a B cell will activate production of antibodies. Therefore, people with C_3B deficiency have much less antibody production.

Clinical Aspects of complement

- Inheritance or acquired deficiency of some complement component can greatly enhance susceptibility to infection with *NEISSERIA*
- Deficiency of C1 esterase inhibitor → ↑ anaphylatoxin which cause capillary permeability → oedema (angioedema)
- In blood transfusion mistake classic pathway complex well activated → red cell hemolysis
- Immune complex bind complement e.g (acute glomerulonephritis and systemic lupus erythematosus → attracts polymorphonuclear leukocytes which release enzymes that damage tissues
- Patients with severe liver disease e.g alcoholic cirrhosis or chronic hepatitis B will have significant ↓ ↓ complement → ↑ pyogenic bacterial infection



Thank you