

Topic :: Complement System, activation, functions & deficiencies

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Complement or the Complement System is so called since it complements or amplifies the action of antibody, is the principal means by which antibodies defend vertebrates against most bacterial infections. It consists of a system of serum proteins that can be activated by antibody-antigen complex or microorganisms to undergo a cascade of proteolytic reactions, whose end result is the assembly of membrane attack complexes. These complexes form holes in a microorganism and thereby destroy it. At the same time, proteolytic fragments released during the activation promote the defence response by dilating blood vessels and attracting phagocytic cells to the site of infection. Complement also amplifies the ability of phagocytic cells to bind, ingest and destroy the micro-organisms being attacked. Individual units

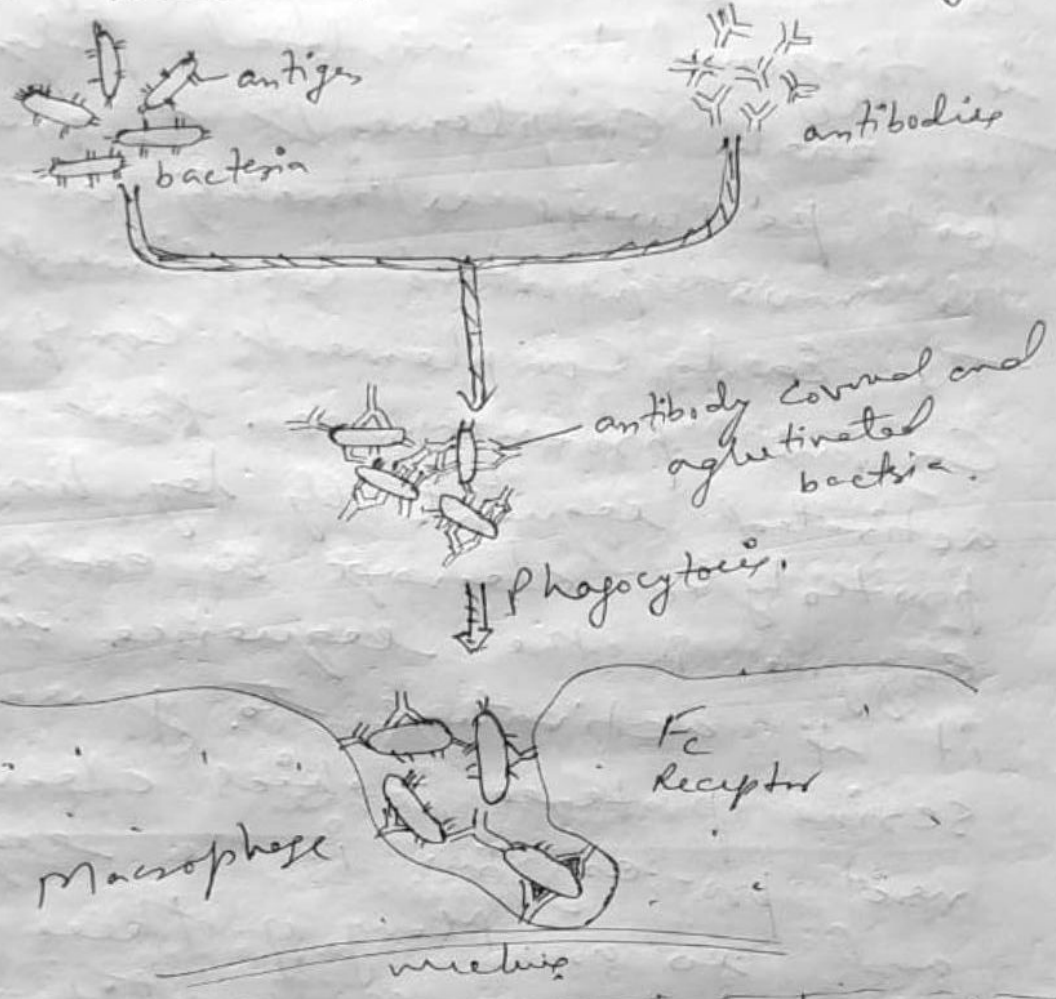
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a deficiency in one of the Central Component of Complement System, (e.g. C_3) are subject to repeated bacterial infections; just as an individual deficient in antibodies themselves. Complement deficient individuals may also suffer from immune complex diseases, in which antigen-antibody complexes precipitate in small blood vessels in skin; joints, kidney and brain where they cause inflammation and destroy of tissues. This suggest that Complement normally helps to solubilise immune complexes when they form during an immune response.

Mode of Complement Activation: -

Complement consists of about 20 interacting proteins of which seeding components are designated C_1 - C_9 factors and the rest are B and Factor D. and the rest comprising a variety of regulatory proteins. The Complement components are also soluble proteins. They are made mainly by the liver and circulate in the blood and extracellular fluid. Most are inactive unless they are triggered directly by an invading micro-organism or indirectly by an immune response. The ultimate result of complement

activation is the assembly of the Late Complement Components such as C5, C6, C7, C8 and C9. Into a large protein complex, the membrane attack complex, that mediates microbial cell lysis.



Agglutination by antibodies and phagocytosis by Macrophages

Because its function is to attack the plasma membrane of microbial cell, activation of Complement is focused on the microbial plasma membrane, where it is triggered either by antibody bound to the micro-organisms or by microbial envelope polyelectrolytes.

Both of these activate the early complement components. There are two early complement components belonging to this -

distinct pathways of Complement activation: (Pg. 4)

C_1 , C_2 and C_3 belongs to the classical pathway, which is triggered by antibody binding: ~~also~~ factor B and Factor D. belong to the alternative pathway, which is triggered by microbial polyelectrolytes.

The early Complement Components of both pathways ultimately act as C_3 , the most important complement component.

The Early Complement Components and C_3 are proenzymes, that are activated sequentially by limited proteolytic cleavage as each pro-enzyme in the sequence is cleaved, it is activated to generate a serine protease, which cleaves the next pro-enzyme in the sequence and so on. Many of these cleavages liberate a small peptide fragment and expose a membrane binding site on the large fragment. The larger fragment binds tightly to the target cell membrane by its newly exposed membrane binding site and to help to carry out the next reaction in the sequence. The smaller fragment often acts independently as a diffusible signal that promotes an inflammatory response.

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