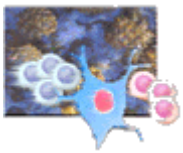
COMPLEMENT

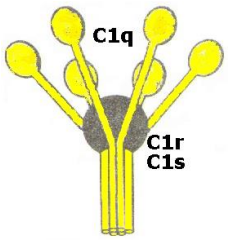


The **complement system** discovered by 1919 Nobel Laureate J. Bordet consists of

about 40 functionally linked serum and membrane-bound proteins, which are synthesized in the liver, small and large intestine. During fetal life complement proteins are made from the 6th week. Complement genes are located on many chromosomes, not only on *chromosome 6* (Class III HLA genes). The complement proteins are as follows:

(1) complement's components designated by letter C (C1-C9),
(2) subcomponents of the 1C (C1q, C1r, and C1s),
(3) fragments of activated complement such as C2a, C3a, C3b, etc,
(4) factors of alternative pathway (B, D and P),
(5) enzymes like convertases,
(6) membrane attack complex C5b6789...9 (MAC),
(7) complement inhibitors and inactivators, and
(8) complement receptors.

Concerning C2a and C2b, there are two approaches to their nomenclature. In the first case, the fragment that takes part in the formation of classical pathway C3 convertase is called C2a, whereas in the second case it is in contrast.



The complement can constitute protein cascades when each activated component catalyzes the activation of the next components. The consequences of complement cascade are the lysis of target cells, amplification of inflammation and phagocytosis, and the participation in completing soluble immune complexes, which include an antigen, antibody and complement fragment.

The complement typically exerts its activity locally, on the microbial membranes, and therefore must be well-controlled. There are several pathways of **complement activation**:

Classical pathway
– Lectin subpathway
– CRP subpathway
Alternative pathway

Fragments of activated complement exert activities, as follows:

Fragment	***Activity***
C2a	being kinin, it causes pain due to the irritation of nerve endings
C3a	exhibits *anaphylactic activity*; turns into acylation-stimulating protein, which upregulates synthesis adipocytes and skin fibroblasts
C3b	takes part in the opsonization to facilitate phagocytosis; recruits more factors B, D and P for the alternative pathway
C4a	exerts *anaphylactic activity*; causes edema
C5a	exhibits *anaphylactic activity*; has a potency to cell destruction
C5b	initiates the formation of MAC
Factor P (properdin)	stabilizes the C3bBb convertase; has a direct antibacterial effect
MAC	lyses target cells

There are some complement receptors: CR1 (CD35), CR2 (CD21), CR3 (CD11b/CD18), CR4 (CD11c/CD18), and C5aR (CD88). All complement receptors bind to C3 or fragments of C4 on the pathogen surface, but they have distinct functions. CR1 is expressed by erythrocytes, which carry immune complexes to the liver and spleen for degradation. Complement receptors CR1,

CR3 and CR4 take part in opsonization, and CR2 is a part of B-cell coreceptor and the receptor for *Epstein-Barr Virus (EBV).*

Clinical Significance. Deficiencies of the complement components are associated with high susceptibility to pyogenic infections, especially *Neisseria meningitidis.* Besides, defects of C1, C2, and C4-C8 may lead to autoimmune disorders like *Systemic Lupus Erythematosus (SLE).* Mutation in C1 inhibitor (C1NH) on 11q12.1 is a form of immunodeficiency (C1 inhibitor deficiency, *Hereditary angioedema*) characterized by progressive edema of deep tissues, especially dangerous in a case of laryngeal and intestinal edema.

If complement activation proceeds at the systemic level and is directed at self-cells, the *anaphylactoid shock* can develop.