

Complement Disorders

Complement disorders encompass a variety of deficiencies in complement proteins. They can be separated by the complement proteins that are deficient. In early complement deficiency, C1-C4 proteins are at lower than normal levels. This is associated with an increased risk of pyogenic infections, autoimmune conditions e.g. lupus, and sinus infections. Terminal complement deficiency is an autosomal recessive condition in which complement proteins C5-C9 are deficient. This increases the risk of *Neisseria* infections because C5-C9 is involved in the membrane attack complex (MAC) that is used to destroy cells infected with *Neisseria*.



PLAY PICMONIC

Early Complement Deficiency

Protein-complimenting Early-Sun

Early complement deficiency (C1-C4) is rare, but because C1, C2, C3, and C4 complement proteins are involved in removing antigen-antibody complexes, individuals that lack any of these proteins can develop recurrent pyogenic infections, sinusitis, systemic lupus erythematosus, and renal failure.

Pyogenic Infections

Pus-pie

Deficiency of C3 results in recurrent pyogenic infections because C3 is a major opsonin. Opsonins facilitate removal of encapsulated bacteria, hence these patients are particularly susceptible to encapsulated organisms.

SLE

Loopy-butterfly

Deficiencies of early classical pathway components (C1, C2, C4) do not usually predispose individuals to severe infections (only C3 does). However, C1, C2, C4 deficiencies are associated with autoimmune disorders, especially systemic lupus erythematosus (SLE).

Sinus Infections

Sinner-with-big-nose

Sinus infections are common in these patients. Lack of C3 opsonin increases the risk of infections with encapsulated organisms such as *Streptococcus pneumoniae*.

Terminal Complement Deficiency

Protein-complimenting Terminator

Terminal complement deficiency is an autosomal recessive condition characterized by a deficiency of complement proteins C5-C9 (most commonly C5, C6, C8). This condition results in impaired opsonization and phagocytosis and is characterized by an increased risk of infections caused by *Neisseria*.

Autosomal Recessive

Recessive-chocolate

This condition is inherited in an autosomal recessive manner, which means that for the child to manifest the disease, he/she should inherit two abnormal alleles.

Neisseria Infections

Knife

Patients with terminal complement deficiency have an inability to form antigen-antibody complexes. This leads to defective opsonization and phagocytosis. The formation of the membrane attack complex (MAC) is also impaired. Hence these patients are at increased risk of infections, particularly from *Neisseria*.

C5-C9

Cat 5-Cat 9

Terminal complement proteins are C5b, C6, C7, C8, C9. Terminal complement proteins play a crucial role in the formation of membrane attack complex, which forms transmembrane channels and disrupts phospholipid bilayer of target cells leading to cell lysis. This division of immune system is particularly important for the prevention of neisserial infections; that's why patients who have a deficiency of terminal complement proteins are more susceptible to neisserial infections.

MAC (Membrane Attack Complex)

MAC-macaroni-gun

Activation of the terminal components of the complement system (C5-C9) results in the deposition of a membrane attack complex (MAC) onto the microbial cell membrane. This complex introduces large pores in the membrane, preventing it from maintaining the osmotic gradient, resulting in cell death. The formation of MAC is compromised in patients with terminal complement deficiencies.