

## Complement System

**The complement system is a collection of circulating and membrane-associated proteins that are important in defense against microbes.** The **alternative pathway** is triggered when some complement proteins are activated on microbial surfaces and cannot be controlled, because complement regulatory proteins are not present on microbes (but are present on host cells). The alternative pathway is a component of innate immunity. The **classical pathway** is most often triggered after antibodies bind to microbes or other antigens and is thus a component of the humoral arm of adaptive immunity. The **lectin pathway** is activated when a carbohydrate-binding plasma protein, mannose-binding lectin (MBL), binds to terminal mannose residues on the surface glycoproteins of microbes. This lectin activates proteins of the classical pathway, but because it is initiated by a microbial product in the absence of antibody, it is a component of innate immunity. **The complement system serves three functions in host defense. First,** C3b coats microbes and promotes the binding of these microbes to phagocytes, by virtue of receptors for C3b that are expressed on the phagocytes. Thus, microbes that are coated with complement proteins are rapidly ingested and destroyed by phagocytes. This process of coating a microbe with molecules that are recognized by receptors on phagocytes is called **opsonization. Second,** some proteolytic fragments of complement proteins, especially C5a and C3a, are chemoattractants for leukocytes (mainly neutrophils and monocytes), so they promote leukocyte recruitment (inflammation) at the site of complement activation. **Third,** complement activation culminates in the formation of a polymeric protein complex that inserts into the microbial cell membrane, disturbing the permeability barrier and causing either osmotic lysis or apoptosis of the microbe.

**B**

Protein	Serum conc. (ug/mL)	Function
C3	640-1660	C3b binds to the surface of microbes, where it functions as an opsonin and as a component of C3 and C5 convertases C3a stimulates inflammation
Factor B	200	Bb is a serine protease and the active enzyme of C3 and C5 convertases
Factor D	1-2	Plasma serine protease that cleaves Factor B when it is bound to C3b

**C**

Protein	Serum conc. (ug/mL)	Function
C1 (C1qr <sub>2</sub> s <sub>2</sub> )		Initiates the classical pathway; C1q binds to Fc portion of antibody; C1r and C1s are proteases that lead to C4 and C2 activation
C4	150-450	C4b covalently binds to surfaces of microbes or cells where antibody is bound and complement is activated C4b binds to C2 for cleavage by C1s C4a stimulates inflammation
C2	20	C2a is a serine protease functioning as an active enzyme of C3 and C5 convertases
Mannose binding lectin (MBL)	0.8-1	Initiates the lectin pathway; MBL binds to terminal mannose residues of microbial carbohydrates. A MBL-associated protease activates C4 and C2, as in the classical pathway.

## Biological Functions of Complement.

