

Sepsis results from septicemia, infections of the blood, in particular those involving gram-negative bacteria such as salmonella and e.coli. The major cause of sepsis from gram negative bacteria is the cell wall component LPS (endotoxin). LPS is a highly potent inducer of innate immune mediators, including; the proinflammatory cytokines TNF-alpha, IL-1beta, and IL-6; chemokines; and antimicrobial compounds. Systemic infections activate PRRs on monocytes, neutrophils vascular endothelial cells, inducing them to produce cytokines, chemokines, adhesion molecules, and clotting factors that amplify the inflammatory response. Enzymes and reactive oxidative species released by activated neutrophils and increased vascular permeability, results in fluid loss into the tissues that lowers blood pressure. TNF also stimulates the release of clotting factors by vascular endothelial cells, systemically this results in blood clotting in capillaries. These effects are damaging to the lungs and kidneys. High TNF-alpha, and IL-1 beta adversely affect the heart.

Toxic shock syndrome

Toxic shock syndrome is an extreme, acute inflammatory response, itself caused by the release of exotoxins from pathogens.

Superantigens

Superantigens are viral or bacterial proteins that bind simultaneously to specific V beta regions of T cell receptors and to the alpha chain of MHC class II molecules. V beta regions are encoded by over 65 different V beta genes in humans. Each superantigen displays a specificity for one of these V beta versions, which can be expressed by up to 5% of T cells, regardless of their antigen specificity. This connection mimics a strong TCR-MHC interaction and induces activation, bypassing the need for TCR antigen specificity. Superantigen binding however, does not bypass the need for costimulation. Professional antigen presenting cells are still required for full T cell activation by these microbial proteins. Because superantigens bind outside the TCR antigen-binding cleft, any T cell expressing that particular V beta sequence will be activated by a corresponding superantigen. Hence the activation is polyclonal and can result in a massive T cell activation, resulting in overproduction of the cell cytokines and systemic toxicity. Disorders caused by superantigen-induced cytokine overproduction include; food poisoning induced by staphylococcal enterotoxins SEA, SEB, SEC1, SEC2, SEC3, SED and SEE, and toxic shock induced by toxic shock syndrome toxin.

Immune system response to viral infection

Innate response elements commonly engaged by encounter with viral PAMPs, such as secretion of type 1 interferons, inflammasomes, and NK cell activation, as well as IL-2 production, can help eliminate the virus but also provide crucial instructions for the adaptive response that will follow. Recognition of PAMPs by PRRs expressed by phagocytic cells induces expression of IFN-alpha and beta. When IFN- alpha and beta bind to their receptors, the JAK-STAT pathway is activated and results in the production of new transcripts, one of which encodes an enzyme that leads to viral DNA degradation. IFN- alpha and beta binding also induces dsRNA-dependent protein kinase, which leads to inactivation of protein synthesis, thus blocking viral replication in neighbouring infected cells. Neutralising antibodies, especially those at the sites of infection, as well as circulating antibodies that foster opsonization, complement activation and phagocytosis, protect the host by blocking or