Lecture-10: Virulence Factors

Virulence is the relative ability of a microorganism to cause disease or the degree of pathogenicity. It is usually measured by the numbers of microorganisms necessary to cause infection in the host.

Organisms that can establish infection with a relatively low infective dose are considered more virulent than organisms that require high numbers for infection. For example, because *Shigella* spp. cause disease with a relatively low infective dose (100 organisms), Shigella is considered to be a highly virulent organism. This generalization is misleading because the severity of disease caused by different organisms varies from one to another.

If a microorganism requires a relatively high infective dose but the disease it causes is often fatal, we tend to think of the microorganism as highly virulent. A different organism may require a low infective dose but produces a relatively mild disease.

Microbial Virulence Factors

Infectious organisms have a wide variety of mechanisms or virulence factors that allow them to persist in a host and cause disease.

Some **virulence factors**, such as capsules and toxins, are used by many organisms. Other virulence factors tend to be **specialized and specific** to one particular organism, such as the tissue tropism of ***N. gonorrhoeae***. Virulence factors allow the pathogen to evade or overcome host defenses and cause disease and encompass functions such as **inhibiting phagocytosis**, **facilitating adhesion** to host cells or tissues, **enhancing intracellular survival** after phagocytosis, and **damaging tissue** through the production of toxins and extracellular enzymes.

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Many virulence factors are well defined, such as the ***diphtheria*** and ***cholera*** **toxins**, the **capsule** of ***S. pneumoniae***, and the **fimbriae** of ***N***. ***gonorrhoeae***.

Certain microorganisms produce extracellular factors that appear to aid in infection, but the exact role of these factors is unknown.

Ability to Resist Phagocytosis Phagocytes

Phagocytic cells, such as **macrophages** and **polymorphonuclear** cells, play a major role in defending the host from microbial invasion.

These cells ingest bacteria and destroy them. The lack of functioning phagocytic cells leaves the host important event in the life of an invading pathogen that invades the host is avoiding phagocytosis.

There are many ways by which microbial species evade phagocytosis:

1- The most common mechanism for evading phagocytosis that is used by many different microorganisms is that of having a polysaccharide capsule on the surface. Many of the microorganisms possessing a capsule are highly virulent until removal of the capsule, at which point virulence becomes extremely low.

2-Encapsulated strains of *S. pneumoniae* and *H. influenzae* are associated with highly invasive infections and are known to be more virulent than nonencapsulated strains.

3- The capsule is usually composed of polysaccharides but can also be made of proteins or a combination of protein and carbohydrate. The capsule inhibits phagocytosis primarily by masking the cell surface structures that are recognized by receptors on the surface of the phagocytic cell and in the same manner inhibits the activation of complement by masking structures to which complement proteins bind.

4- bacterial structure that protects organisms from phagocytosis is protein A. Protein A in the cell wall of ***S. aureus*** helps the organism avoid phagocytosis by interfering with the binding of the host's antibodies to the surface of the organism and preventing opsonization and phagocytosis by turning the antibody around on the surface.

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5- Some organisms evade phagocytic cell killing by releasing potent materials in tissues that kill phagocytes. ***Streptococci*** produce hemolysins that lyse red blood cells and induce toxic effects on white blood cells and macrophages.

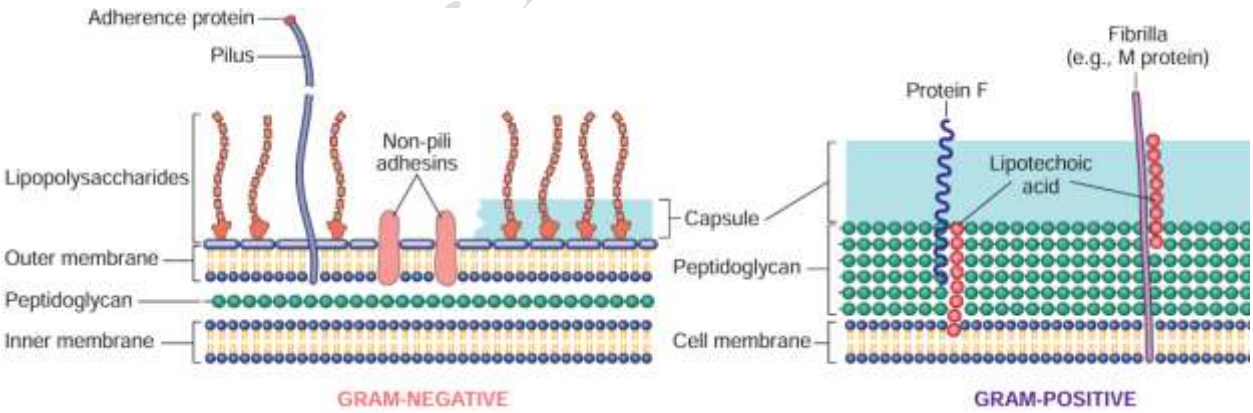
6- Pathogenic *staphylococci* release leukocidins that cause lysosomal discharge of white blood cells into the cytoplasm. A *staphylococcal* leukocidin, is lethal to leukocytes and contributes to the invasiveness of the organism.

7- Other organisms inhibit chemotaxis, which is the movement of white blood cells to sites of tissue damage, and the host is less able to direct polymorphonuclear neutrophils (PMNs) and macrophages into the site of infection.

Surface Structures That Promote Adhesion to Host Cells and Tissues

Most infectious agents must attach to host cells before infection occurs. In some diseases caused by **exotoxins** (e.g., botulism, staphylococcal food poisoning).

The microbial surface structures that mediate attachment are called adhesins. Host cells must possess the necessary receptors for the adhesins. If the host or the infectious agent undergoes a mutation that changes the structure of the adhesin or the host receptor, adherence is not likely to take place.



surface bacterial structures that are involved in the pathogenesis of disease

The main **adhesins** in **bacteria** are fimbriae (**pili**) and **surface polysaccharides**. Fimbriae enable bacteria to adhere to host cell surfaces, increasing the organism's colonizing ability, and providing resistance to phagocytosis, For example, the

strains of E. coli that cause traveler's diarrhea use their fimbriae to adhere to cells of the small intestine, where they secrete a toxin that causes the disease symptoms.

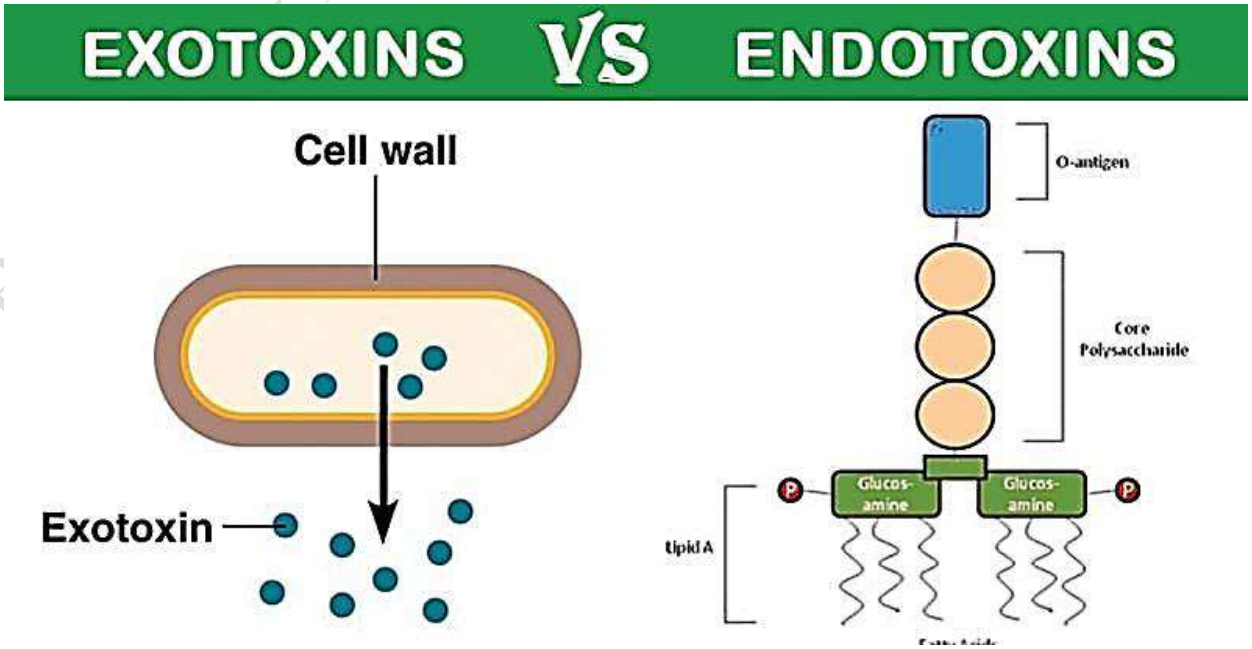
Some organisms prevent fusion of phagosomes and lysosomes, others have a resistance to the effects of the lysosomal contents, and still others escape from the phagosome into the cytoplasm.

Some species not only are able to survive inside the macrophages, but protected from the host's other immune defenses, they are able to multiply intracellularly, this process is called **invasion**.

Ability to Produce Extracellular Toxins and Enzymes

The ability of organisms to produce exotoxins and extracellular enzymes is another major factor that contributes to the virulence and invasiveness of organisms.

Exotoxins are produced by both gram-negative and gram-positive bacteria and are secreted by the organism into the extracellular environment, or they are released on lysis of the organism. Exotoxins can mediate direct spread of the microorganisms through the matrix of connective tissues and can cause cell and tissue damage. **Some organisms produce soluble substances, such as proteases and hyaluronidases that liquefy the hyaluronic acid** of the connective tissue matrix, helping bacteria to spread in tissues, promoting the dissemination of infection.



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Endotoxins are a constituent, the lipopolysaccharide (LPS), of the outer cell membrane of gram-negative bacteria exclusively. Endotoxins, in contrast to exotoxins, do not have enzyme activity, are secreted in only very small amounts, do not have specificity in their activity on host cells, are not very potent, and are not destroyed by heating.

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