Pathogenicity and Microbial Virulence Factors

A microbe capable of causing disease is referred to as **a pathogen**.

Pathogenicity is the ability of a microorganism to cause disease in another organism, namely the host.

Pathogens vary in their ability to produce disease.

The measurement of pathogenicity is called **virulence**, with highly virulent pathogens being more likely to cause disease in a host.

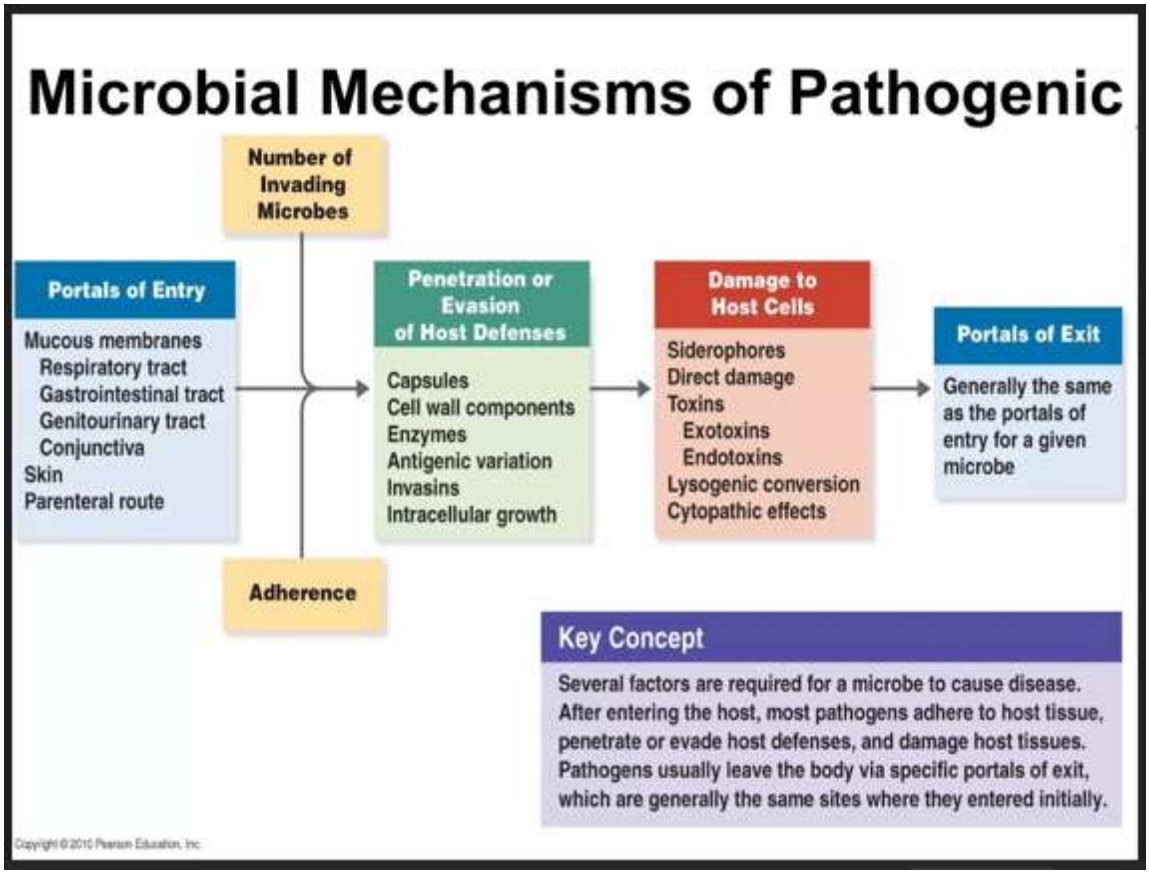
"**Virulence"** is a quantitative measure of the pathogenicity of a micro-organism that may be expressed by the ratio of the number of individuals developing clinical illness to the number of individuals exposed to the microorganism, or in a comparative manner, by the number of individuals that develop clinical disease if the same dose of different microorganisms is applied to each of them.

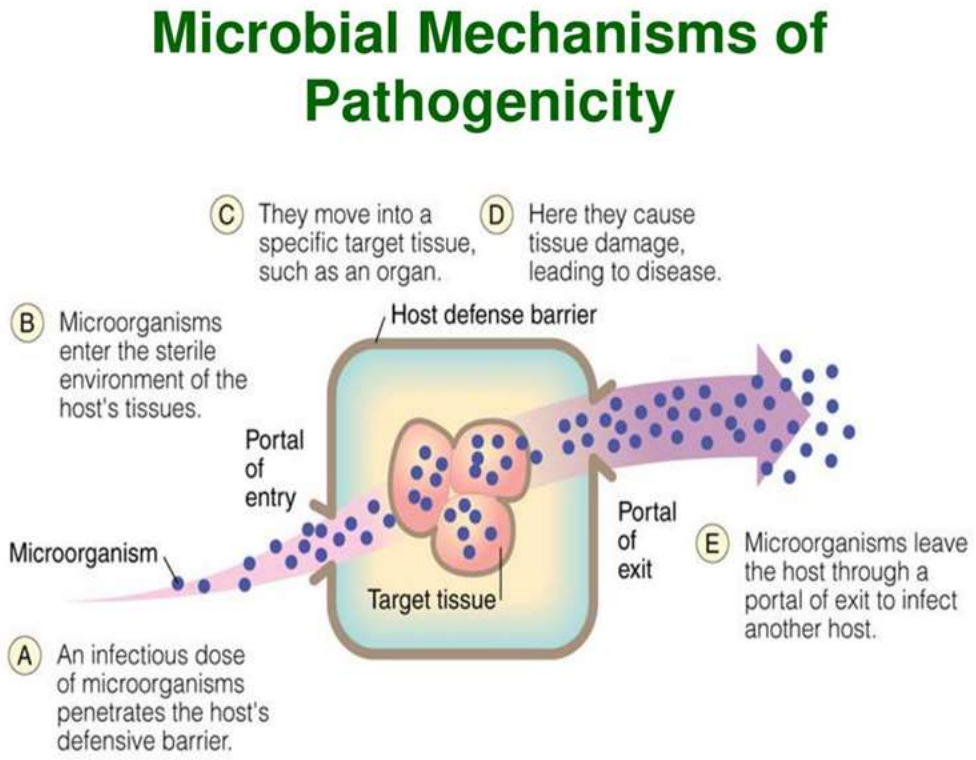
Determinants of Pathogenesis

1. Transmission
2. Adherence and invasion
3. Enzymes
4. Toxin production
5. Immunopathogenesis

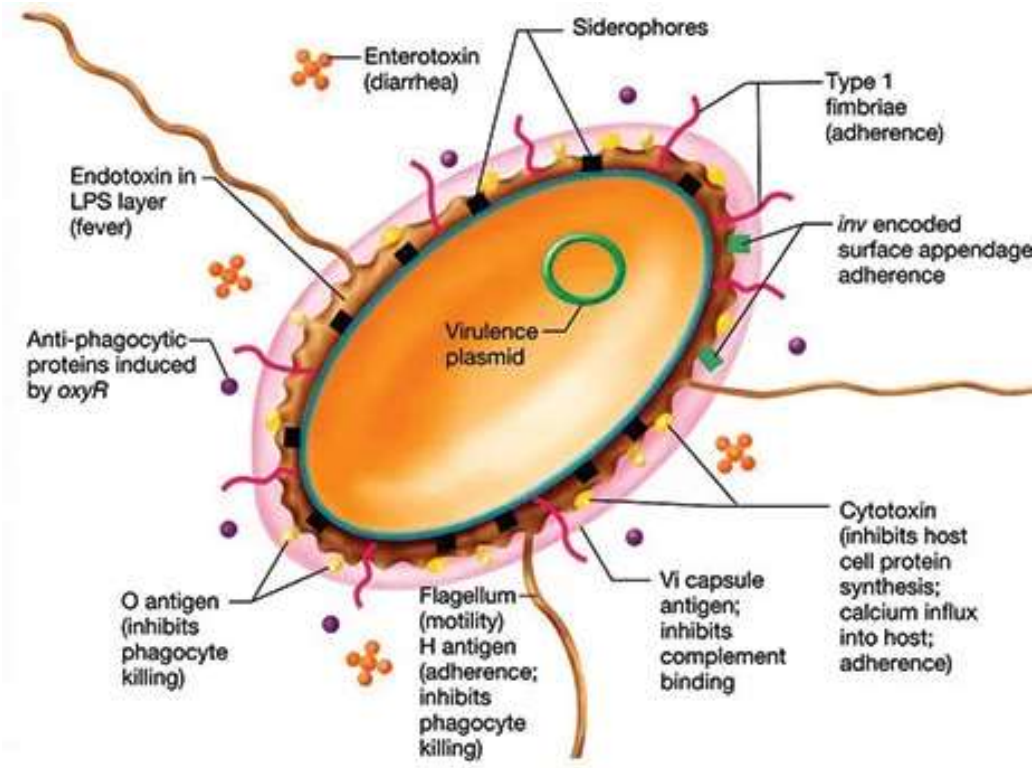
How Pathogens Damage Host Cells

1. Use the host's nutrients
2. Cause direct damage
3. Produce toxins
4. Induce hypersensitivity reaction


Microbial Mechanisms of Pathogenic
Number of Invading Microbes
Portals of Entry
Mucous membranes
Respiratory tract
Gastrointestinal tract
Genitourinary tract
Conjunctiva
Skin
Parenteral route
Penetration or Evasion of Host Defenses
Capsules
Cell wall components
Enzymes
Antigenic variation
Invasins
Intracellular growth
Damage to Host Cells
Siderophores
Direct damage
Toxins
Exotoxins
Endotoxins
Lysogenic conversion
Cytopathic effects
Portals of Exit
Generally the same as the portals of entry for a given microbe
Adherence
Key Concept
Several factors are required for a microbe to cause disease. After entering the host, most pathogens adhere to host tissue, penetrate or evade host defenses, and damage host tissues. Pathogens usually leave the body via specific portals of exit, which are generally the same sites where they entered initially.
Copyright © 2010 Pearson Education, Inc.


Microbial Mechanisms of Pathogenicity
C They move into a specific target tissue, such as an organ.
D Here they cause tissue damage, leading to disease.
B Microorganisms enter the sterile environment of the host's tissues.
Host defense barrier
Portal of entry
Microorganism
Target tissue
Portal of exit
E Microorganisms leave the host through a portal of exit to infect another host.
A An infectious dose of microorganisms penetrates the host's defensive barrier.

Virulence factors : are molecules produced by pathogens (bacteria, viruses, fungi and protozoa) that contribute to the pathogenicity of the organism, and enable them to achieve colonization and attachment, immunoevasion and inhibition of the host's immune response, entry into and exit out of cells, and acquire nutrition from the host cell.



Bacterial virulence factors

- Specific pathogens possess a wide group of virulence factors. Some are chromosomally encoded and basic to the bacteria (e.g. capsules and endotoxin), whereas others are obtained from mobile genetic elements like plasmids and bacteriophage (e.g. some exotoxins).

- Gram-positive bacteria secrete a variety of virulence factors at the host pathogenic interface, via membrane vesicles operating like bacterial outer membranes for invasion, nutrition, and other cell-cell communications.

-Bacterial virulence factors have different routes used to help them survive and grow: These factors include adhesins, invasins, and antifagocytic factors. ex: toxins (hemolysin and proteases, bring damage to the host).

Types of virulence factors:

1- Adherence Factors: Many pathogenic bacteria colonize mucosal sites by using pili (fimbriae) to adhere to cells.

2- Invasion Factors: Surface components that allow the bacterium to invade host cells that can be encoded on plasmids, but more often are on the chromosome.

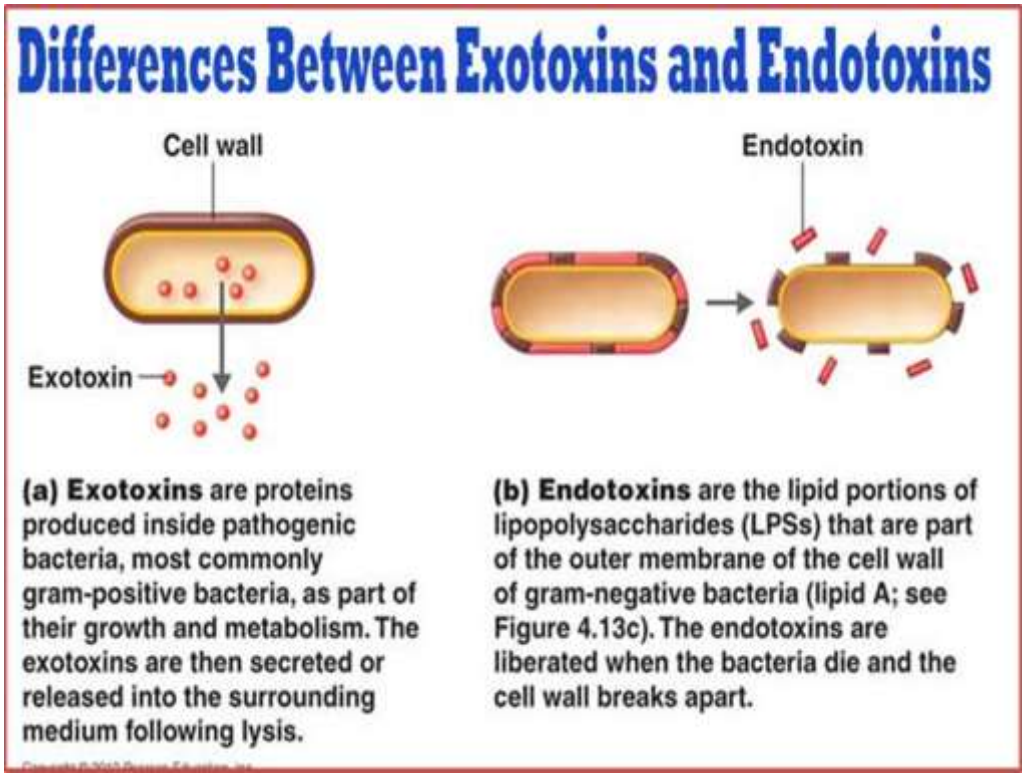
3- Capsules: Many bacteria are surrounded by capsules that protect them from opsonisation and phagocytosis.

4- Endotoxins: The lipopolysaccharide endotoxins on Gram-negative bacteria cause fever, changes in blood pressure, inflammation, lethal shock, and many other toxic events.

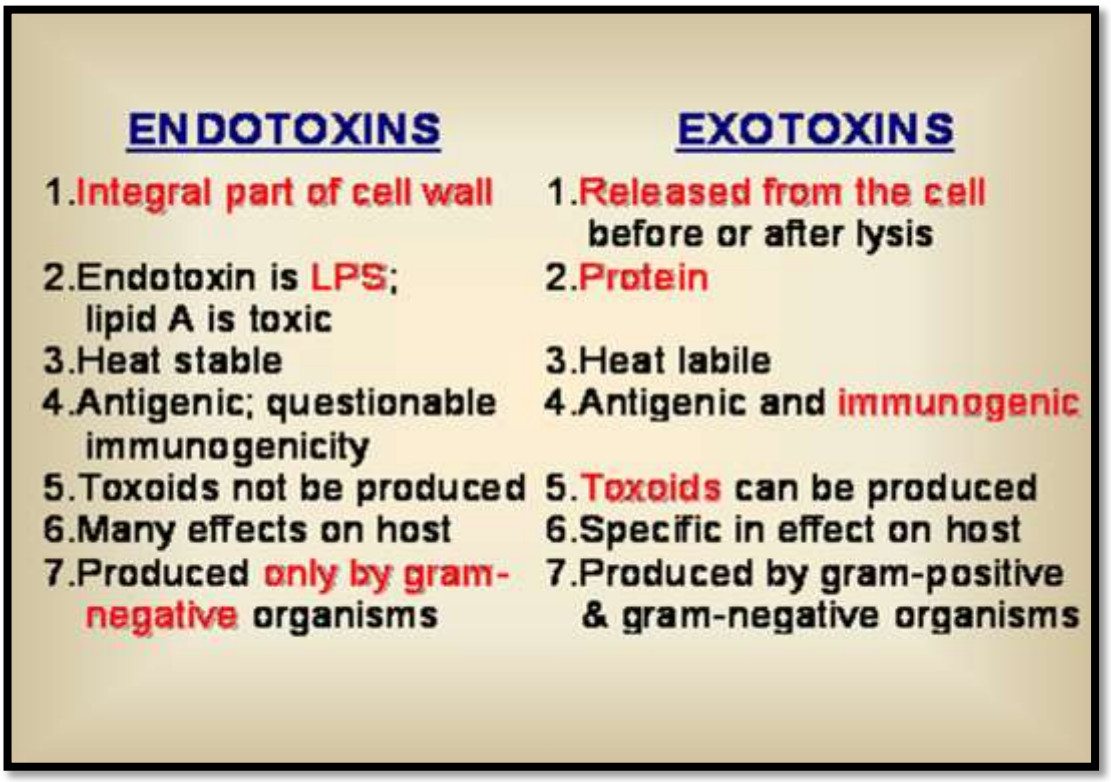
5- Exotoxins: include several types of protein toxins and enzymes produced and/or secreted from pathogenic bacteria. Major categories include cytotoxins, neurotoxins, and enterotoxins. The toxin is the major factor in determining virulence, e.g. strains of *E. coli* without the exotoxins are low/non-virulent.

The toxins can remain toxic even at very low concentrations. Exotoxins are typically named descriptively to show where the toxin acts, for example; neurotoxin, leukotoxin, enterotoxin and haemolysin.

6- Siderophores: Siderophores are iron-binding factors that allow some bacteria to compete with the host for iron, which is bound to haemoglobin, transferrin, and lactoferrin.



Comparison of Exotoxin and Endotoxin



Mechanism of exotoxins

Damage to cell membranes – For example, *Clostridium perfringens* α-toxin has phospholipase C activity which causes degradation of the cell membrane. *Staphylococcus aureus* α-toxin causes the formation of a pore in the membrane of target cells. This pore alters ion influx/efflux and can lead to swelling/lysis of the cell.

Inhibition of protein synthesis – Toxins which inhibit protein synthesis target the elongation factors and ribosomal RNA which are associated with protein synthesis. By targeting these factors, the cell is prevented from synthesising protein and the cell dies. An example of such a toxin is the diphtheria toxin.

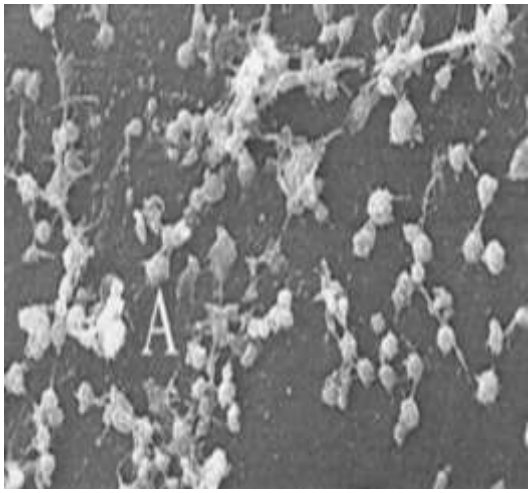
Interfere with cell signalling – These toxins target the proteins associated with signal transduction, either blocking or altering the signalling pathways. Such alteration of these pathways disrupts cellular function. For example *E. coli* cytotoxic necrotising factors modify RHO GTP-binding proteins, their modification disrupts the cell cyctoskeleton and thus the cell membrane.

Inhibition of neurotransmitters – These toxins target proteins of the synaptic cleft. They prevent the release of neurotransmitters from the presynaptic membrane. For example *Clostridium botulinum* neurotoxin or the *Clostridium tetani* tetanus toxin.

Affecting immune response – One example of altering the immune response is the super antigen TSS-1 released by *Staphylococcus aureus* which causes Toxic shock syndrome. The toxin interacts with T-cells of the host immune system in an abnormal manner and provokes the release of enormous amounts of inflammatory cytokines, which are harmful to the host.

Biofilm formation: is a process whereby microorganisms irreversibly attach to and grow on a surface and produce extracellular polymers that facilitate attachment and matrix formation.

- Matrix composed of DNA, proteins and fiber of polysaccharides of the cell's glycocalyces.
- The matrix adheres cells to one another, sticks the biofilm to the substrate, forms microenvironments within the biofilm, restores nutrients, and may protect individuals in the biofilm from environmental stresses, including UV, antimicrobial drugs and changes in pH, ….etc



Staphylococcal biofilm

Scanning electron micrograph for a developed biofilm

Biofilm formation begins when planktonic cells adhere to a weak, reversible, non-specific surface and excrete EPS. This is the first in a series of five main stages of biofilm formation that include:

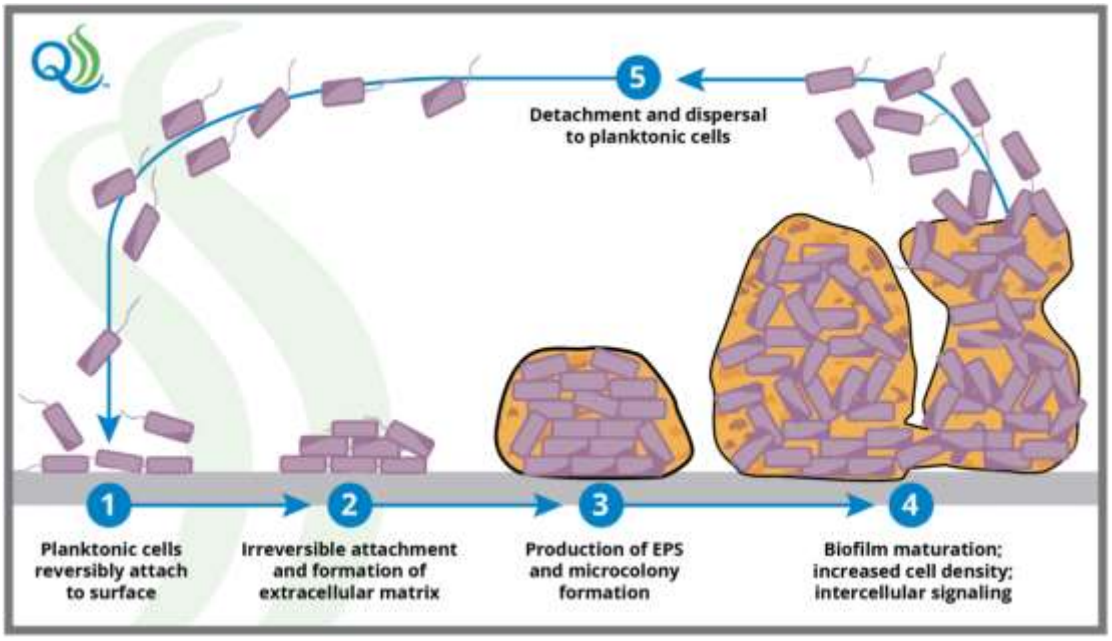
(i) The reversible attachment phase

(ii) the irreversible attachment phase, where interaction between surfaces and lipopolysaccharides found on hair-like bacterial appendages (pili or fimbriae) form tight ionic attachments;

(iii) production of EPS phase by the cells forming the biofilm.

(iv) biofilm maturation phase, during which cells grow, cell density increases, and cells synthesize and release signaling molecules allowing them to sense and communicate with each other; and

(v) dispersal or detachment phase, where the cells depart in large numbers to become planktonic cells again.



Five main stages of biofilm formation