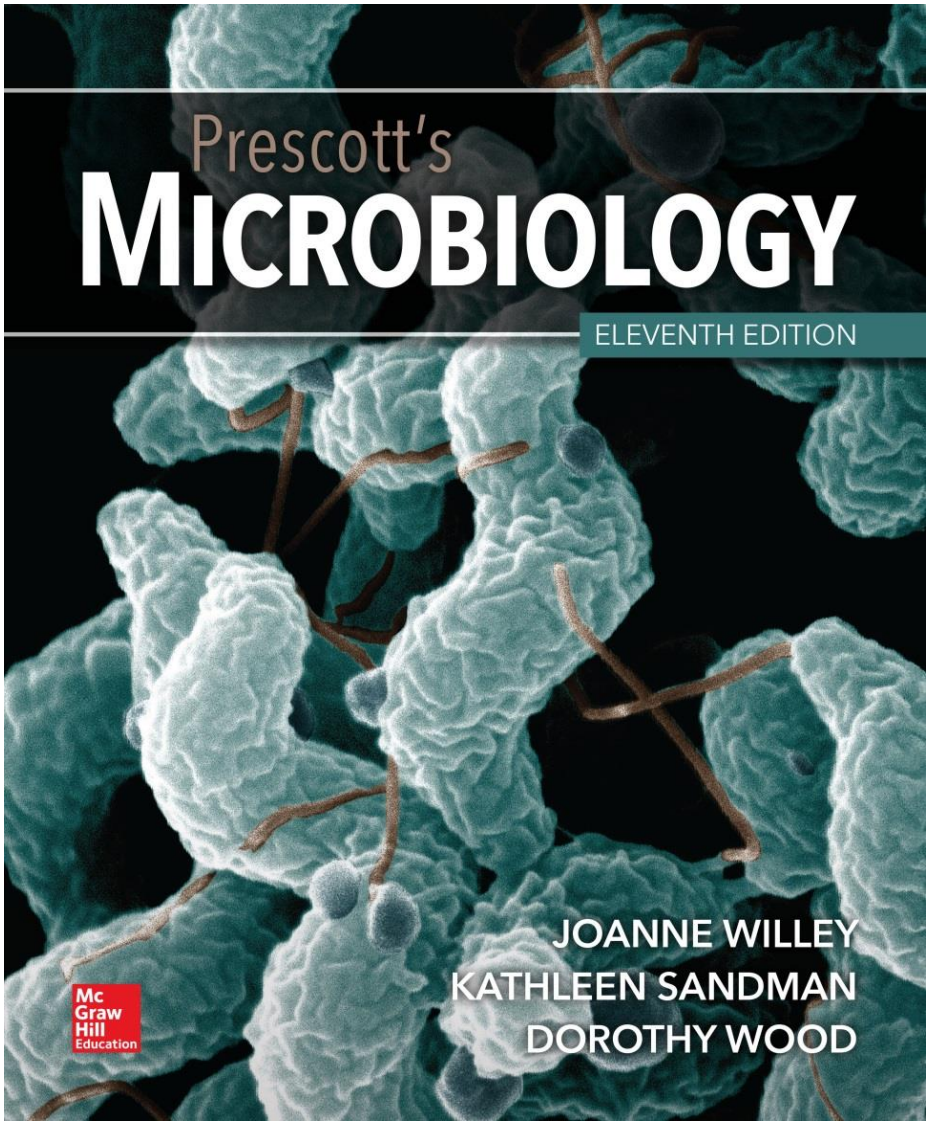

Prescott's MICROBIOLOGY

ELEVENTH EDITION

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Chapter 35

Infection and Pathogenicity

Extracellular vs. Intracellular Pathogens

A pathogen must contact a host AND survive within it to cause a disease.

Extracellular pathogens.

- Grow outside host cells in tissues and fluids.

Intracellular pathogens.

- Grow and multiply within host cells.
- **Facultative intracellular pathogens—reside** within the cells of the host or in the environment but can also be grown in pure culture without host cell support.
- **Obligate intracellular pathogens**—only grow when inside host cells.

Importance of Resources

The host provides the pathogen:

- **Protection.**
- **Nutrients.**
- **Energy to use.**

Infectious agents develop mechanisms to access and exploit hosts.

- To survive, must also devise methods to move on to a new location or host when necessary.

Events in Infection and Disease

Transmission from previous host or reservoir to new host.

- **Virulence of organism, number of invading organisms, and presence of adhesion and invasion factors will affect success.**

Organism outcompetes the resident microbiota for resources and survives host defense mechanisms.

Disease occurs **when organism produces molecules that directly damage host cells** OR **stimulates host immune cells to destroy infected tissue** OR **alters the host cell genome affecting normal function.**

Sources of Pathogens

Can be **animate** (other humans or animals).

- Infections passed from animal to human are termed zoonoses.

Can be **inanimate** (water, food).

Reservoir.

- Natural environmental location in which the pathogen normally resides.

Vector.

- Organism that spreads disease from one host to another.
- For example, mosquitoes, ticks, fleas, mites, or biting flies.

Pathogen Transmission

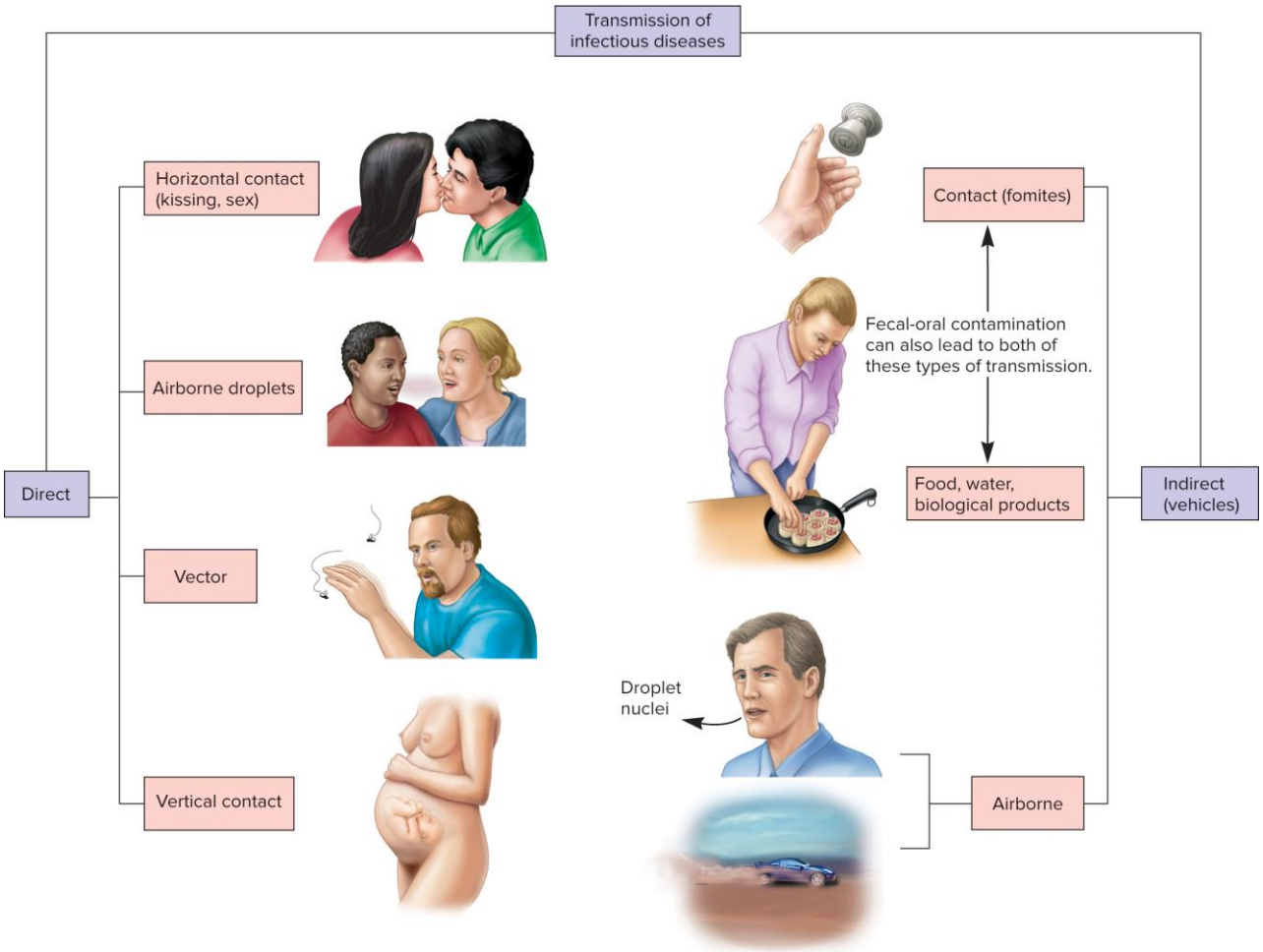
Occurs either directly or indirectly.

Four main routes:

- Airborne.
- Contact.
- Vehicle.
- Vector-borne.

Pregnant women can also pass a pathogen to their unborn child via vertical transmission.

Transmission of Infectious Diseases



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Course of Infectious Disease

Incubation period.

- Period after pathogen entry, before signs and symptoms.

Prodromal stage.

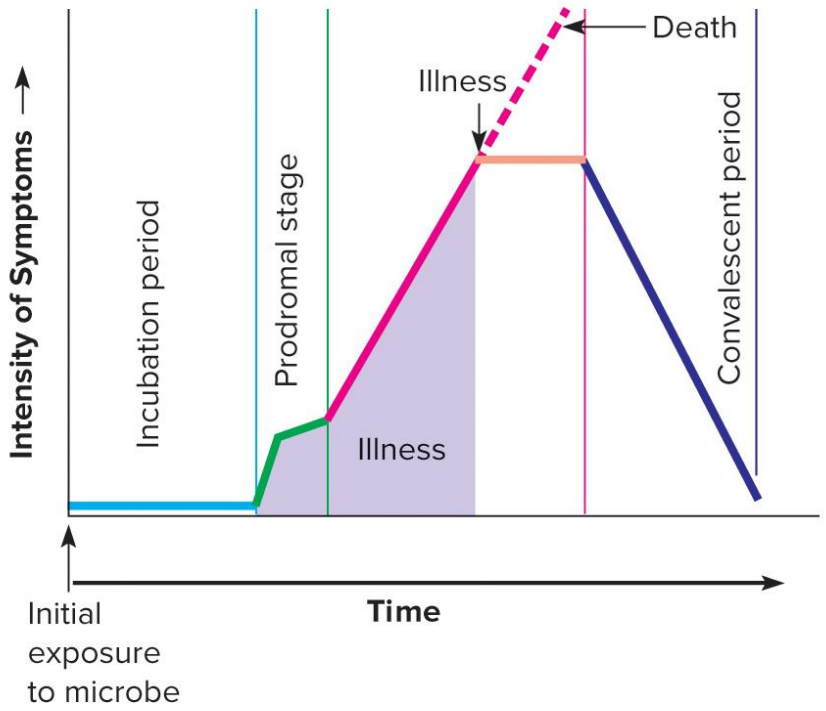
- Onset of signs and symptoms.
- Not clear enough for diagnosis.

Illness period.

- Disease is most severe, signs and symptoms.

Convalescence.

- Signs and symptoms begin to disappear.



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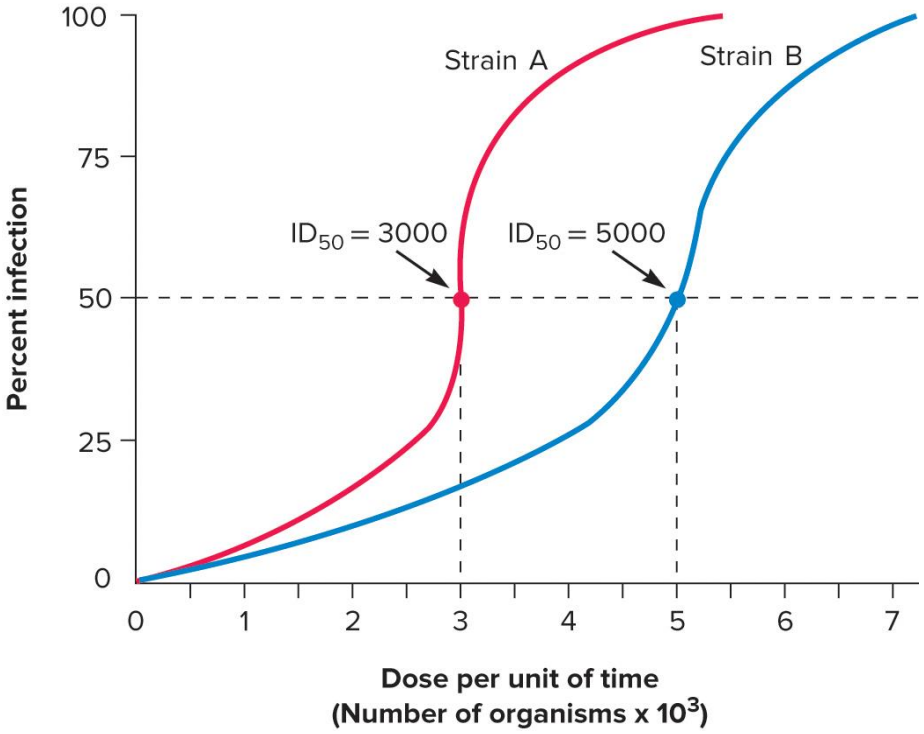
Infectious Dose

Infectious dose 50 (ID_{50}).

- Number of pathogens that will infect 50% of inoculated hosts.
- Varies with pathogen.

Hand washing reduces number of pathogens.



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Lethal Dose

Lethal dose 50 (LD_{50}).

- Dose that kills 50% of experimental animals within a specified period.

Cytopathology—cellular changes.

- Can be used to observe cells in tissue culture for death rates rather than entire organisms.

Examining virulence factors and their release.

Adherence and Colonization

First steps in disease are entry and attachment

Portal of entry.

- Skin, respiratory, gastrointestinal, urogenital systems, or conjunctiva of eye.

Adherence.

- Mediated by special molecules called *adhesins.*

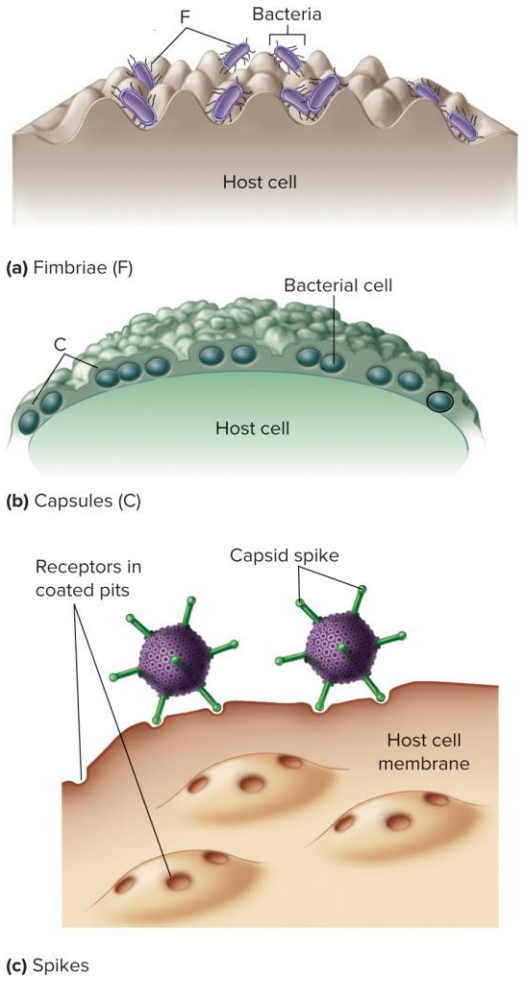
Colonization.

- A site of microbial replication on or within host.
- Does not necessarily result in tissue invasion or damage.

Microbial Adherence Mechanisms

Adherence structures bind complementary receptor sites on host cell surface; classified as virulence factors.

- Pili.
- Fimbriae.
- Membrane and capsular materials.
- Specialized adhesion molecules on bacterium's cell surface.



Invasion Disseminates Pathogens

Infectivity—ability to create a discrete point of infection

Invasiveness—ability to spread to adjacent tissues.

Penetration can **be active or passive:**

- **Active** occurs through **lytic substances that alter host tissue by (1) attacking the extracellular matrix and basement membranes of integuments and intestinal linings**, **(2) degrading carbohydrate-protein complexes between cells or on the cell surface,** or **(3) disrupting the host cell surface.**
- **Passive**—not related to the pathogen itself (For example, skin lesions, insect bites, wounds).

Invasion—Specific Examples

Once in circulatory system, bacteria have access to all organs and systems.

- **Bacteremia**—presence of viable bacteria in the blood.
- **Septicemia**—bacterial or fungal toxins in the blood.

Varies among pathogens.

- For example, ***Clostridium tetani*** **(tetanus) produces a number of virulence factors but is noninvasive.**
- For example, ***Bacillus anthracis*** **(anthrax) and** ***Yersinia pestis*** **(plague) also produce many virulence factors and are highly invasive.**
- For example, ***Streptococcus*** **spp. span the spectrum of virulence factors and invasiveness.**

Overcoming Host Defenses

Most microbes eliminated before they can cause disease due to immune system.

Successful pathogens **overcome the competition** and elude initial host responses as well as the adaptive immune system:

- Produce Type VI secretion system.
- Find shelter to avoid recognition by defense cells.
- Survive and replicate inside host cells.
- Squeeze between host cells.
- Make capsules to avoid phagocytosis.
- Burrow under mucus.
- Secrete exopolysaccharides to form communal shelters within biofilms.
- Produce enzymes that inactivate innate resistance mechanisms.
- Excrete specialized proteins to selectively kill host cells.

(282) How Pathogens Evade the Immune System - YouTube

Strategies to Evade Host Immune Response

Production of decoy proteins to bind available neutralizing antibodies.

Change cell surface proteins **by mutation or recombination or downregulate the level of expression of cell surface proteins.**

Produce capsules that resemble host tissue components.

- Some bacterial capsules prevent deposition of host complement, protecting the pathogen from host defenses.

Phage variation to alter pili protein sequence and expression.

Produce proteases that degrade host proteins.

Produce special proteins that interfere with the host's ability to detect and remove them.

Forms biofilms.

Suppressing Host Immune Response

Infect cells of the immune system and diminish their function while ensuring their own survival.

Bacteria such as *Streptococcus pneumoniae, Neisseria meningitidis,* and *Haemophilus influenzae* **produce a slippery mucoid capsule that prevents the host immune cells from effectively capturing the bacterium**.

Eliminate O-antigen on lipopolysaccharide to diminish immune response and clearance.

Pathogenicity Islands

Large segments (10 to 200 kilobases) of bacterial chromosomal and plasmid DNA found to encode virulence factors.

- Increase bacterial virulence.
- Absent in nonpathogenic members of same genus or species.
- Can be spread through horizontal transfer of virulence genes to bacteria.

Toxigenicity

Some microbes possess toxigenicity.

- Ability to produce toxins.

Toxin.

- Specific substance that damages host.

Intoxications.

- Diseases that result from entry of a specific preformed toxin into host.

Exotoxins

Soluble, heat-labile proteins.

Secreted into surroundings as pathogen metabolizes.

Often travel from site of infection to other tissues or cells where they exert their effects.

Usually synthesized by specific bacteria that have **toxin genes in their plasmids or prophage DNA.**

Among the most lethal substances known.

Types of Exotoxins

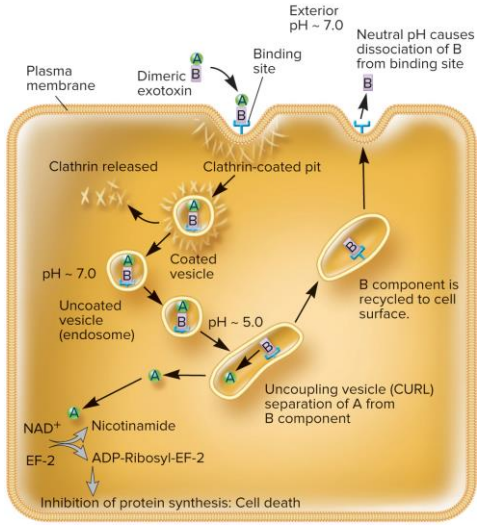
AB toxins.

- Composed of two subunits: A subunit (responsible for toxic effect) and B subunit (binds to specific target cell).

Specific host site exotoxins.

Membrane-disrupting exotoxins.

Superantigens.



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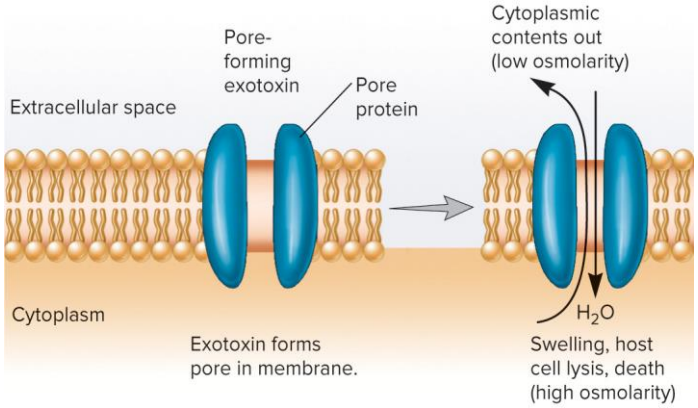

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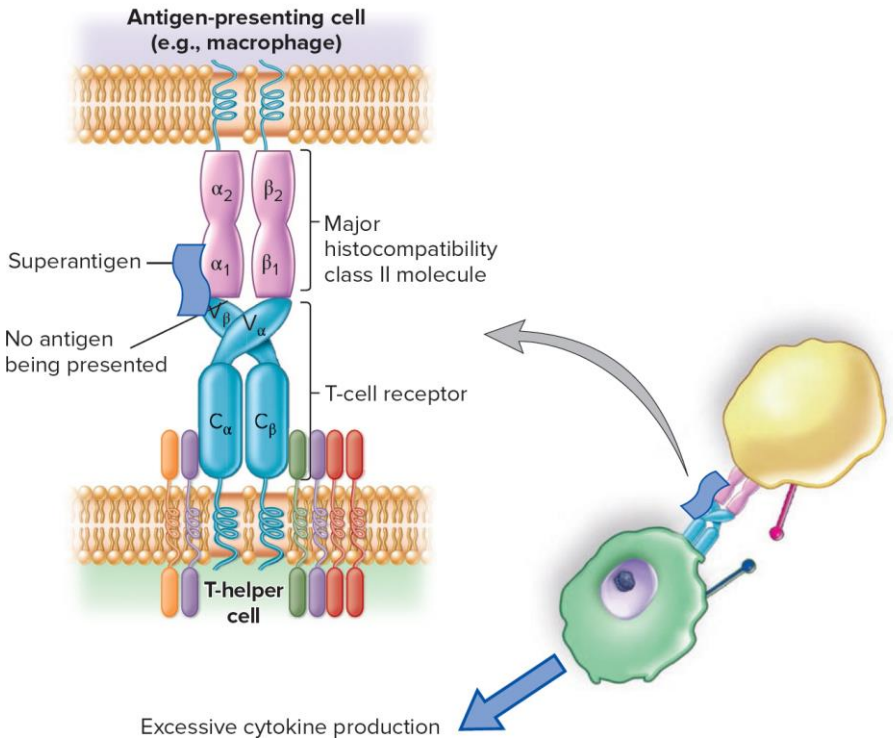
Superantigens



Stimulate about 30% of T cells of the immune system.

- Causes the T cells to overexpress and release pro-inflammatory cytokines.
- Results in failure of multiple host organs allowing time for the microbe to disseminate.

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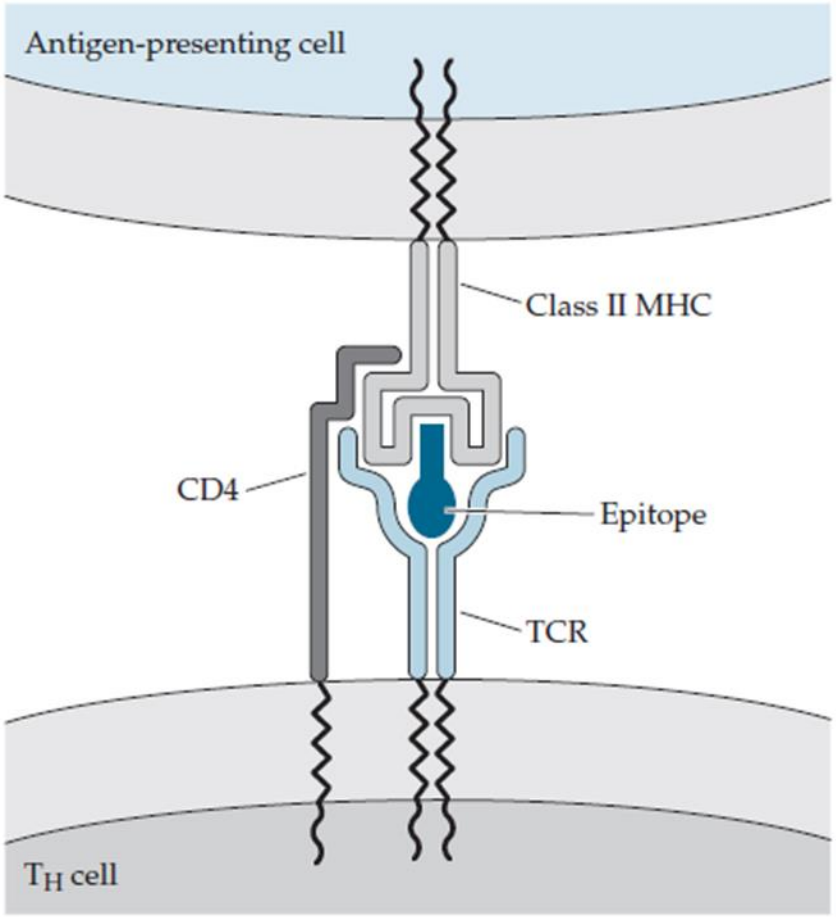
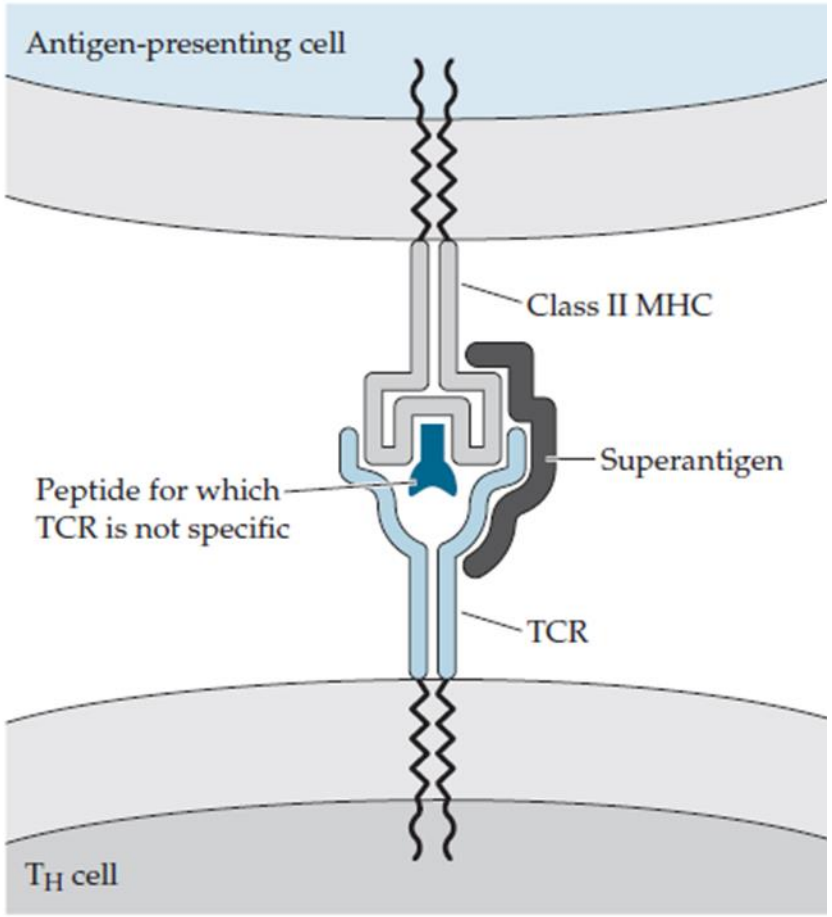




Endotoxin—Lipopolysaccharide

Lipopolysaccharide (LPS) in Gram-negative cell wall can be toxic to specific hosts.

- Called endotoxin because it is an endogenous , bound to the bacterium and released when the microorganism lyses; some is also released during multiplication.
- Toxic component is the lipid portion, lipid A.

Endotoxins—General Features

Heat stable.

Toxic (nanogram amounts).

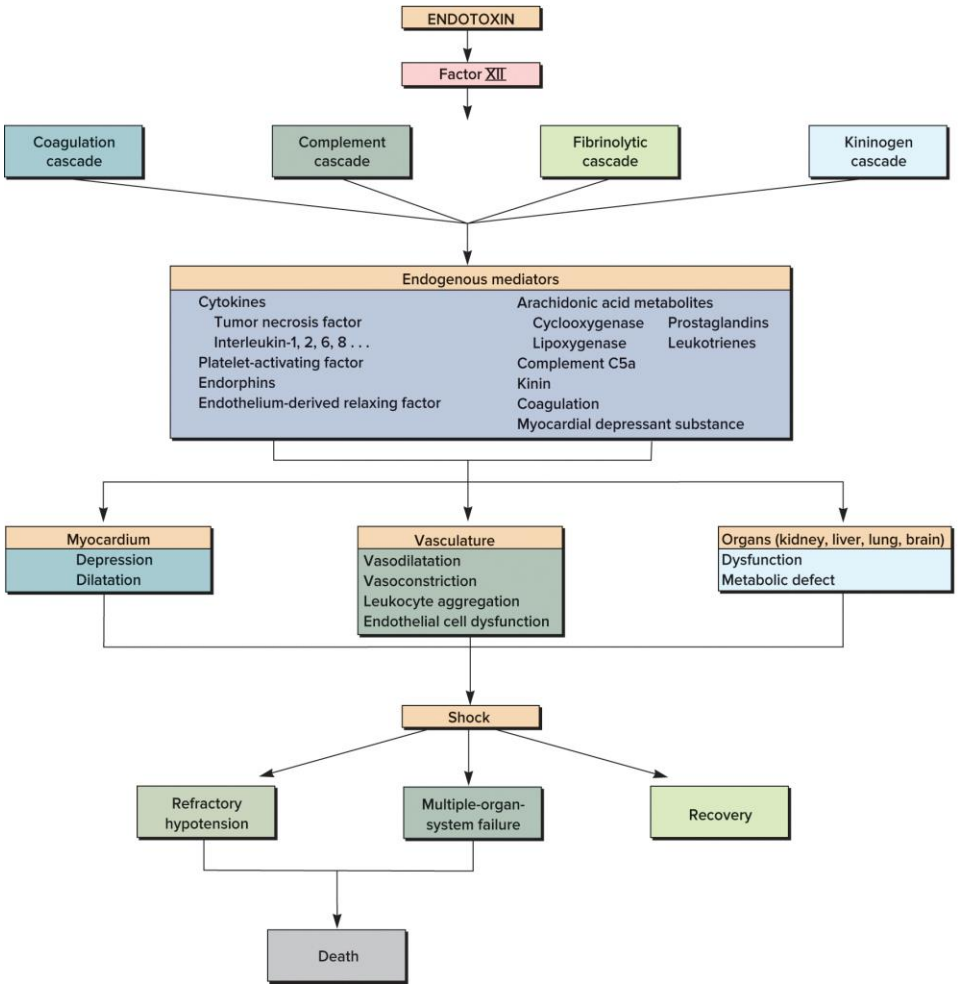
Weakly immunogenic.

Generally similar, despite source.

Cause general system effects:

- Fever, shock, damage to the lining of blood vessels, weakness, diarrhea, inflammation, intestinal hemorrhage, and fibrinolysis.

The Septic Shock Cascade



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