

Bacterial Toxins

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Toxin is a poisonous substance that is a specific product of the metabolic activities of a living organism and is usually very unstable, notably toxic when introduced into the tissues.

Toxin Production

- **Toxigenicity:** Ability of a microbe to produce toxins.
- **Toxemia:** Presence of toxins in the blood.
- **Toxin effects may include:**
 - fever
 - cardiovascular problems
 - diarrhea
 - shock
 - destruction of red blood cells and blood vessels
 - and nervous system disruptions.
 - Of 220 known bacterial toxins, 40% **damage eucaryotic cell membranes.**

How Bacterial Cells Damage Host Cells

Three mechanisms:

- 1- Direct Damage
- 2- Toxins*
- 3- Hypersensitivity Reactions

* Most bacterial damage is carried out by toxins.

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There are Two Types of Bacterial toxins

- 1- Endotoxins (Lipopolysaccharide) Gram negative only.
- 2- Exotoxins (Gram positive and some Gram negative) .

Bacterial Toxins

Endotoxin

Exotoxin

Enterotoxin

Neurotoxin

Cytotoxin

Adenylate
cyclase

Guanylate
Cyclase

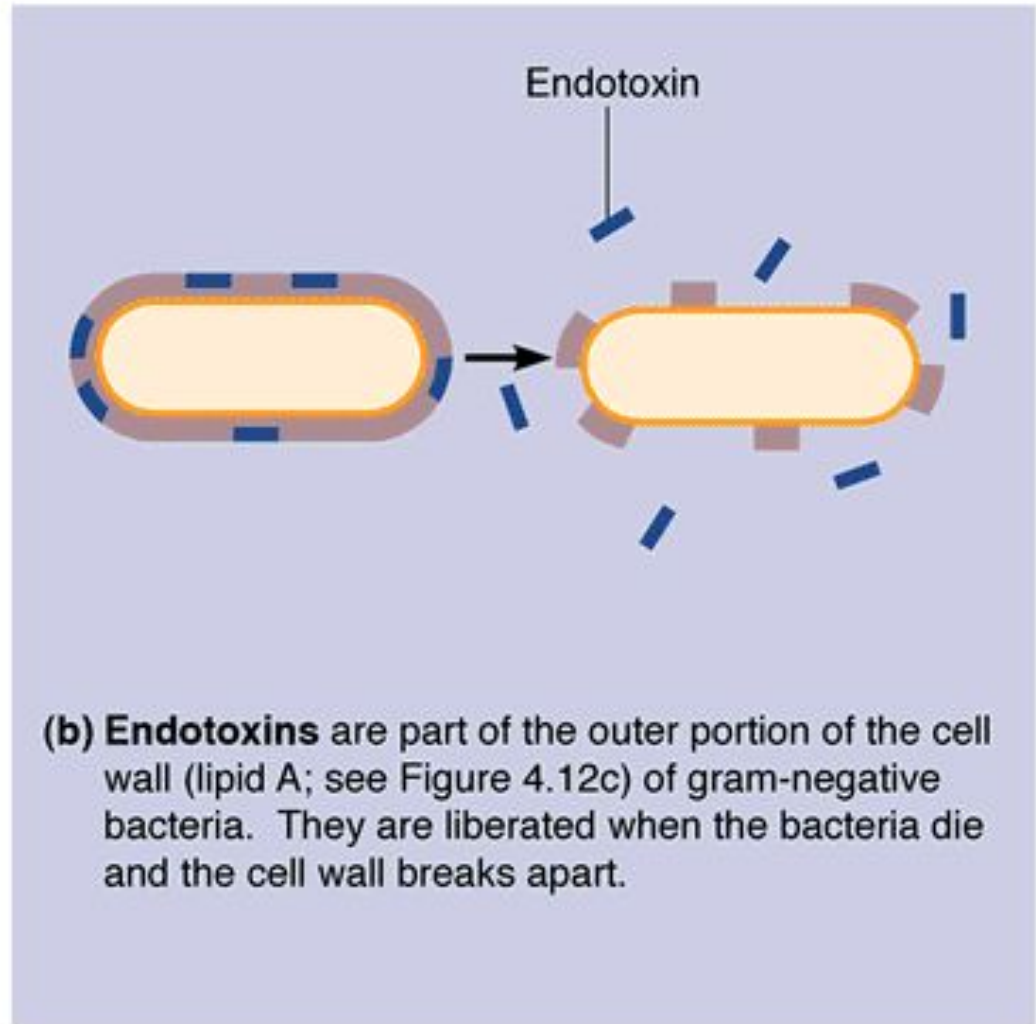
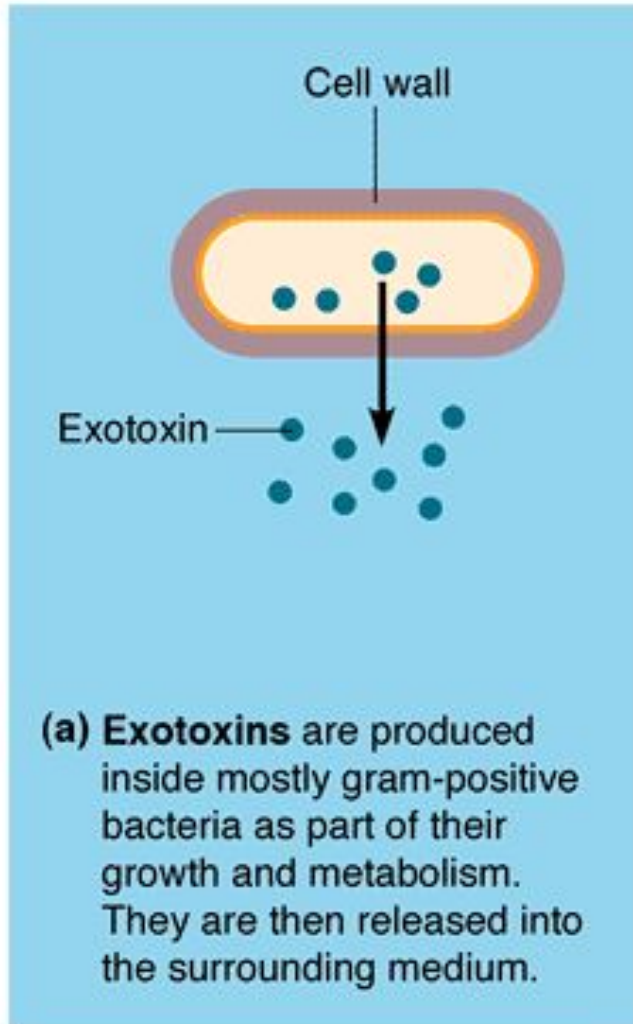
Food
Poisoning

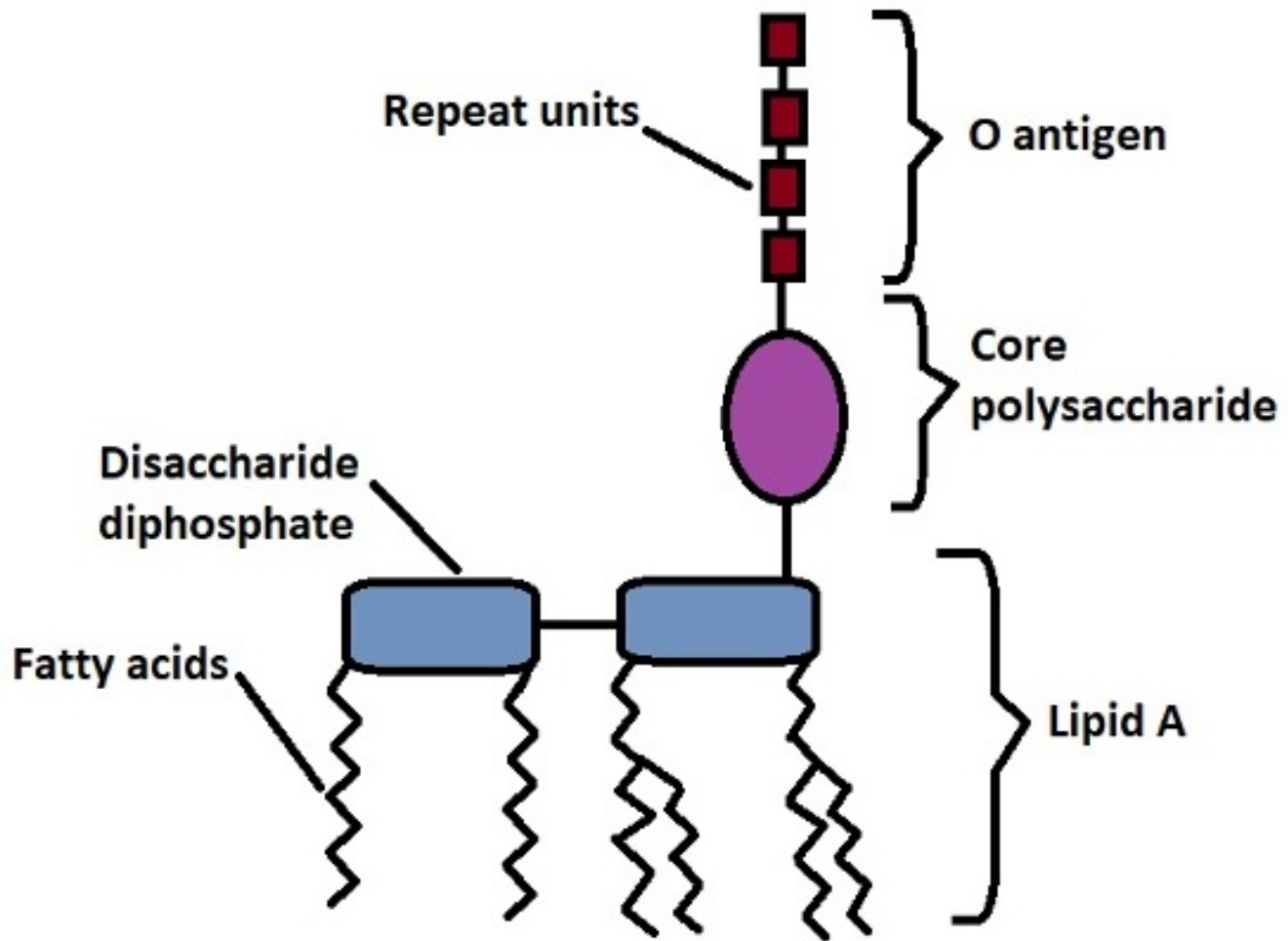
Macrophage
cytotoxin

Vacuolation

Thiol-
activated

Exotoxins versus Endotoxins





Structure of endotoxins

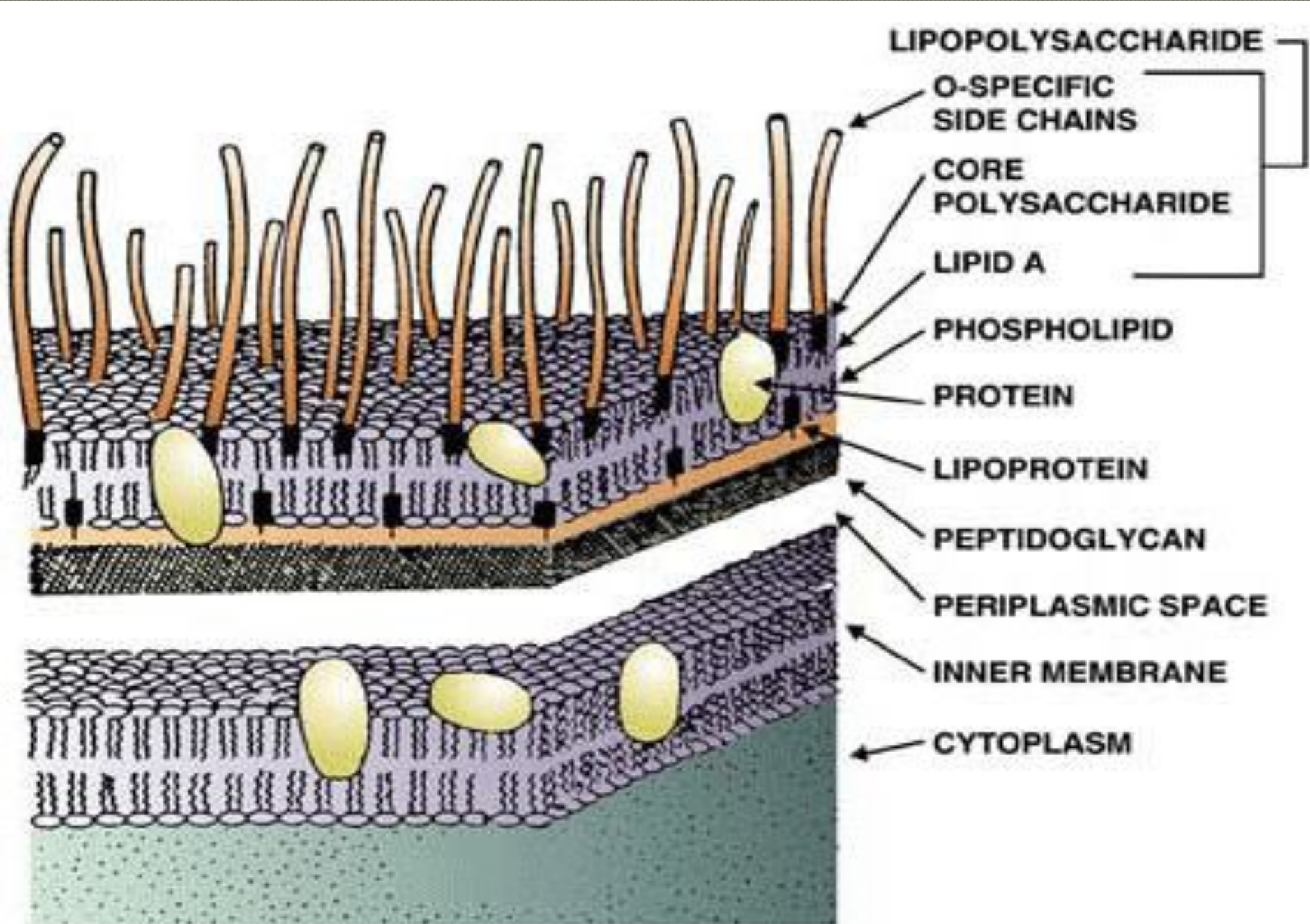


DIAGRAM OF A GRAM-NEGATIVE CELL MEMBRANE

A. Exotoxin criteria

- **1- Proteins:** Enzymes that carry out specific reactions.
- **2- Soluble** in body fluids, **rapidly transported** throughout body in blood or lymph.
- **3- Produced mainly by Gram-positive bacteria.**
- **4- Most genes for toxins are carried on plasmids or phages.**
- **5- Produced inside bacteria and released into host tissue.**

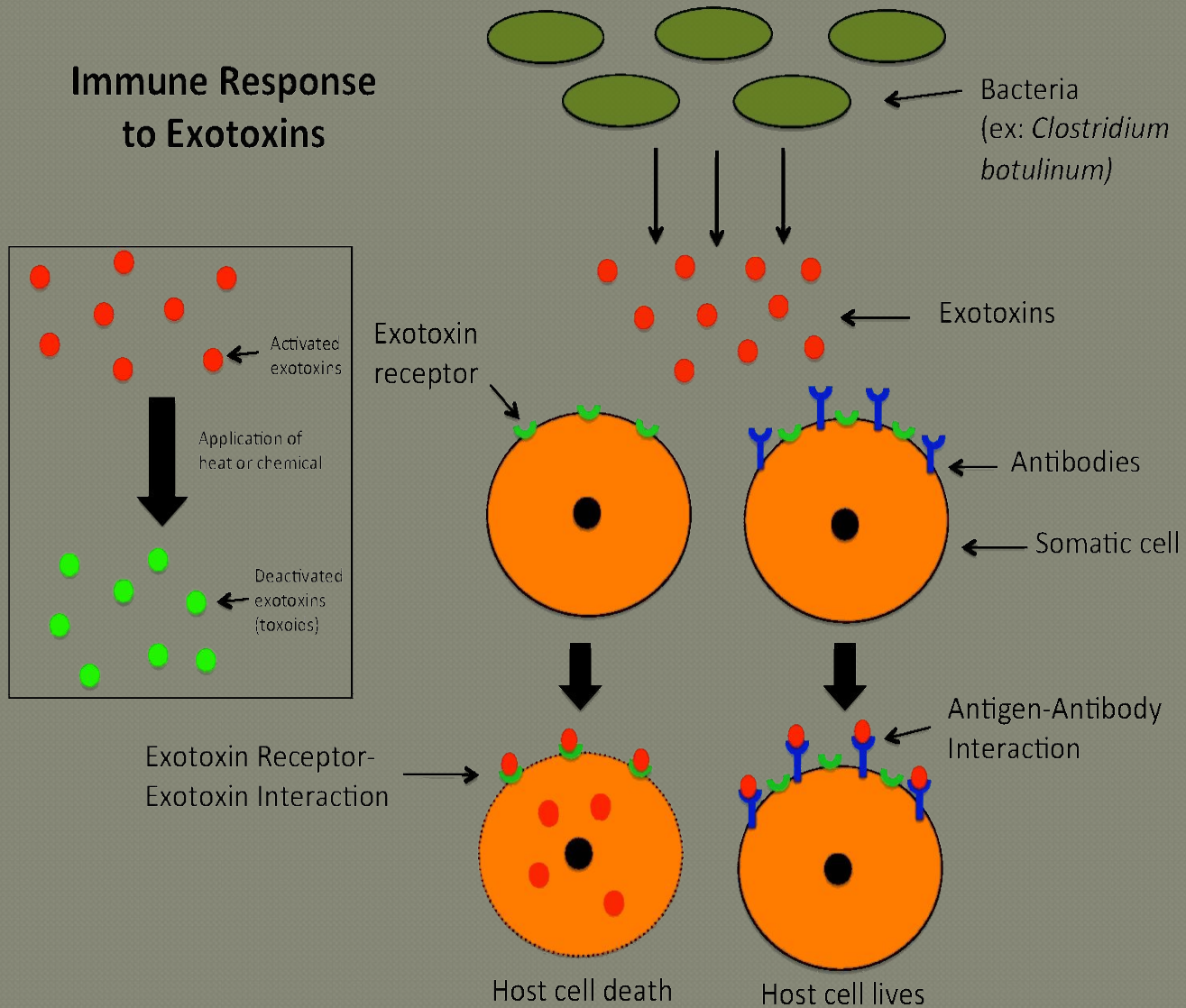
- **6- Responsible for disease symptoms and/or death, like**
 - **A- Cytotoxins:** Kill or damage host cells.
 - **B- Neurotoxins:** Interfere with nerve impulses.
 - **C- Enterotoxins:** Affect lining of gastrointestinal tract.
- Antibodies called **antitoxins** provide immunity.
- **7- Toxoids:** Toxins that have been altered by heat or chemicals. Used as vaccines for diphtheria and tetanus.

Important Exotoxins

- **Botulinum Toxins:** Produced by *Clostridium botulinum*. **Neurotoxin** that inhibits release of neurotransmitter acetylcholine and **prevents transmission of nerve impulses to muscles**, causing flaccid paralysis. Extremely potent toxins.
- **Tetanus Toxin:** Produced by *Clostridium tetani*. A **neurotoxin** that **blocks relaxation of skeletal muscles**, causing uncontrollable muscle spasms (lockjaw) and convulsions.

- **Vibrio Enterotoxin:** Produced by *Vibrio cholerae*. Two polypeptides: A (active) and B (binding). The A subunit of **enterotoxin** causes epithelial cells to discharge large amounts of fluids and electrolytes.
- **Staphylococcal Enterotoxin:** *Staphylococcus aureus* produces an **enterotoxin** similar to cholera toxin.

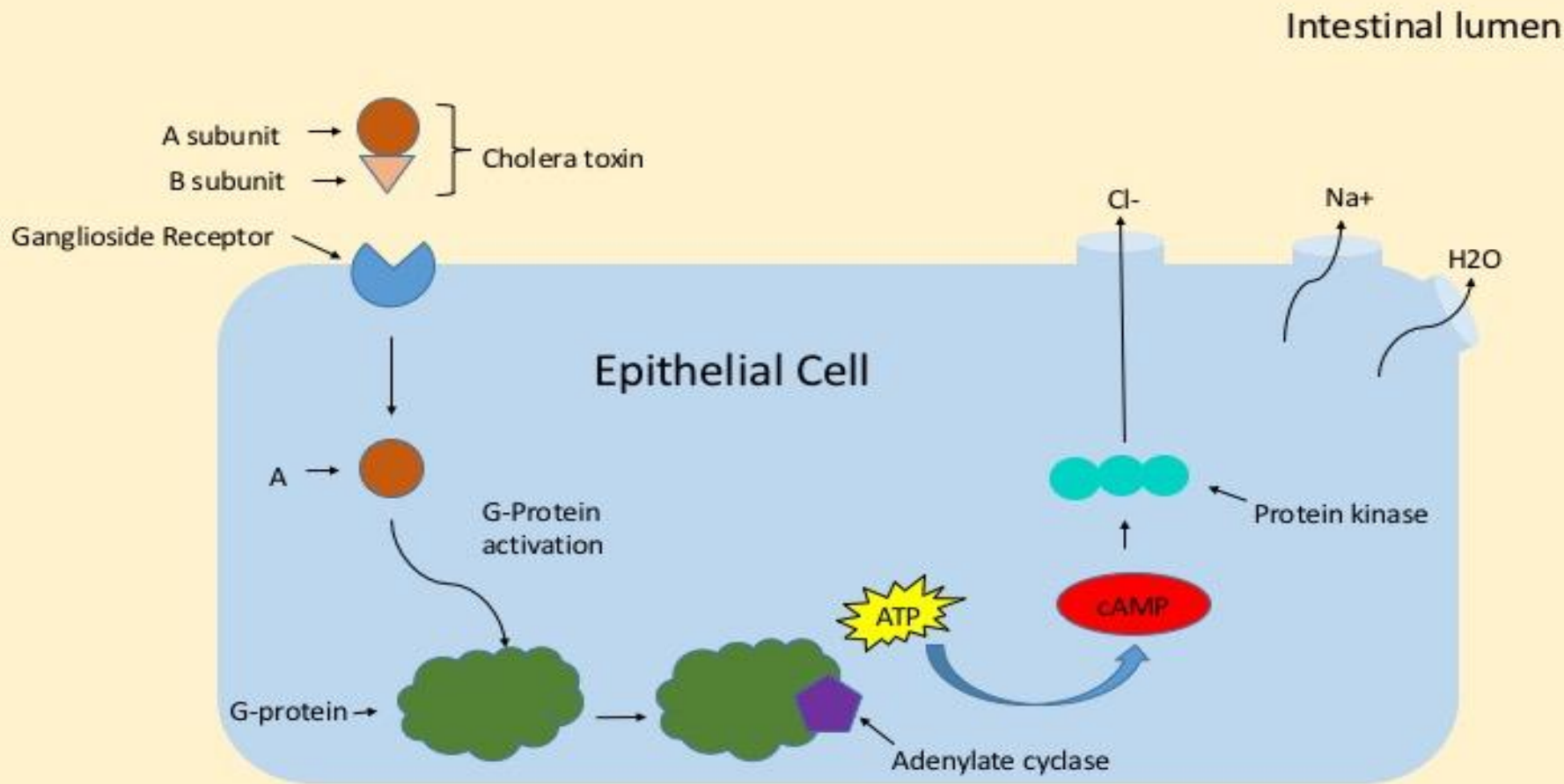
Immune Response to Exotoxins



Exotoxins

They usually have two general functions, which can often be uncoupled: the ability to bind to a host cell receptor, and enzymatic activity. For example, **cholera toxin**, labile toxin, and many others have **five binding (B) subunits** coupled to the **active enzymatic subunit (A)**. Several vaccines are made from the B subunits without the catalytic subunit, ensuring no toxin activity.

The B subunits bind to host cell molecules such as carbohydrates (for example, cholera binds the GM1 ganglioside, a glycolipid on the intestinal surfaces). Following binding, the A subunit then enters the cell, which is facilitated by the B subunits.



Mechanism of action of cholera toxin

Properties of bacterial toxin

Exotoxin	Endotoxin
Secreted outside cell by both Gram positive and Gram negative bacteria	Released after lysis of Gram negative cellwall
Protein	Lipopolysaccharide
Heat labile (except- enterotoxin of S.aureus)	Heat stable (upto 250°C)
Highly antigenic	Less antigenic
Highly toxic in minute dose (microgram is fatal to animals)	Moderately toxic
Filterable	not so (obtained only by cell lysis)
Can be converted to toxoid	cannot
Often enzymatic action	no

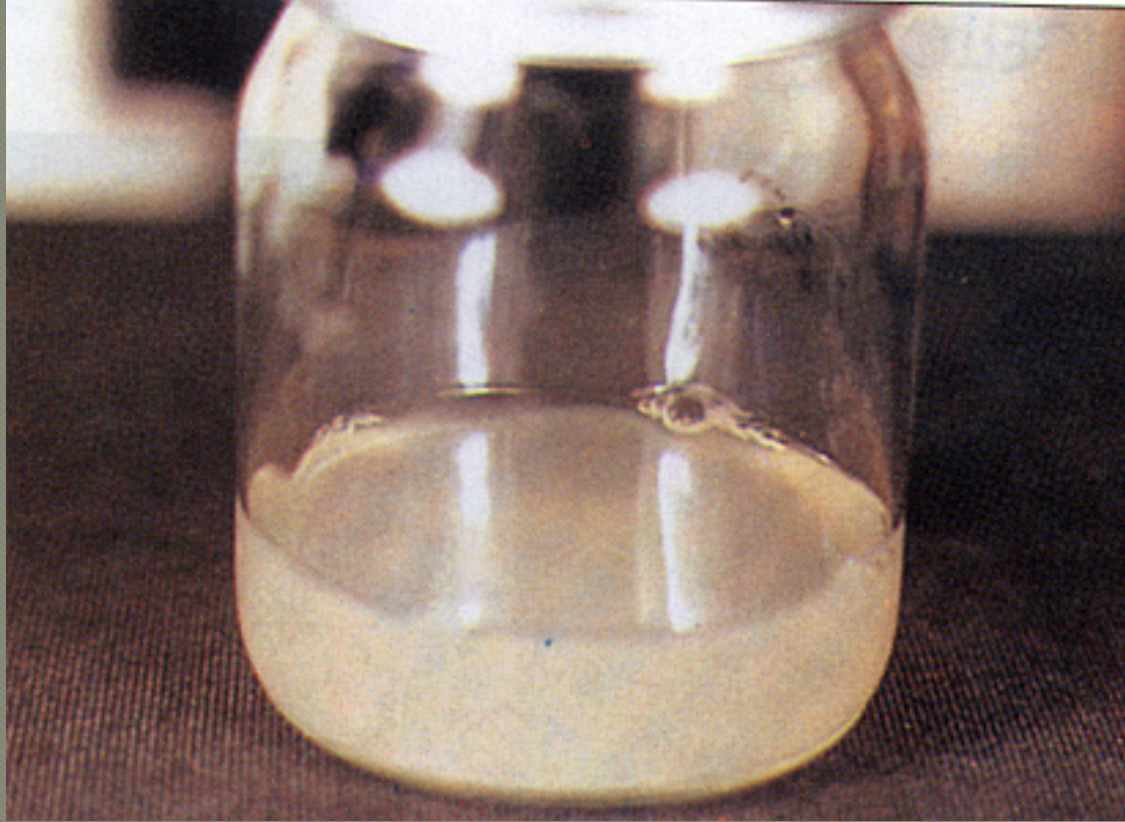
Muscle Spasms of Tetanus are Caused by Neurotoxin of *Clostridium tetani*



Neonatal Tetanus (Wrinkled brow and risus sardonius)

Source: Color Guide to Infectious Diseases, 1992

Vibrio Enterotoxin Causes Profuse Watery Diarrhea



Rice-water stool of cholera. The A subunit of **enterotoxin** causes epithelial cells to discharge large amounts of fluids and electrolytes.

Source: Tropical Medicine and Parasitology, 1995

Diseases Caused by Staphylococcal Toxins



Scalded Skin Syndrome



Toxic Shock Syndrome

B- Endotoxin criteria

1- Part of outer membrane surrounding gram-negative bacteria (LPS).

- 2- Endotoxin is lipid portion of lipopolysaccharides (LPS), called **lipid A**.
- 3- Effect exerted when gram-negative cells die and cell walls undergo lysis, liberating endotoxin.
- 4- **All produce the same signs and symptoms:**
 - Chills, fever, weakness, general aches, blood clotting and tissue death, shock, and even death. Can also induce miscarriage.

- **5- Fever:** Pyrogenic response is caused by endotoxins.
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6- Endotoxins do not promote the formation of effective antibodies.

- **7- Organisms that produce endotoxins include:**
 - *A- Salmonella typhi.*
 - *B- Pseudomonas spp.*
- ***Limulus* amoebocyte assay (LAL) is a test used to detect tiny amounts of endotoxin.**

The mode of actions of bacterial toxins

consists of:

- 1- Toxin Disrupting the membrane integrity..
- 2- Toxin tagging chemicals, affecting cytoskeleton.
- 3- Toxin cause pore formation.
- 4- Toxin effect delivery of proteins to cells and interfering with cell signaling.
- 5- Toxin damaging DNA.
- 6- Toxin with enzymatic activity.

Toxins as a therapeutic agent

- 1- The botulinum toxin (neurotoxin) used in tiny amount for pharmacological insights (Botox) .
- 2- Some bacterial toxins used in cancer therapy.
- 3- Some bacterial toxins have antimicrobial effects on the bacteria like **Bacteriocin** and **Colicin**.

