Medical Microbiology

LD_{50} and Exotoxin types

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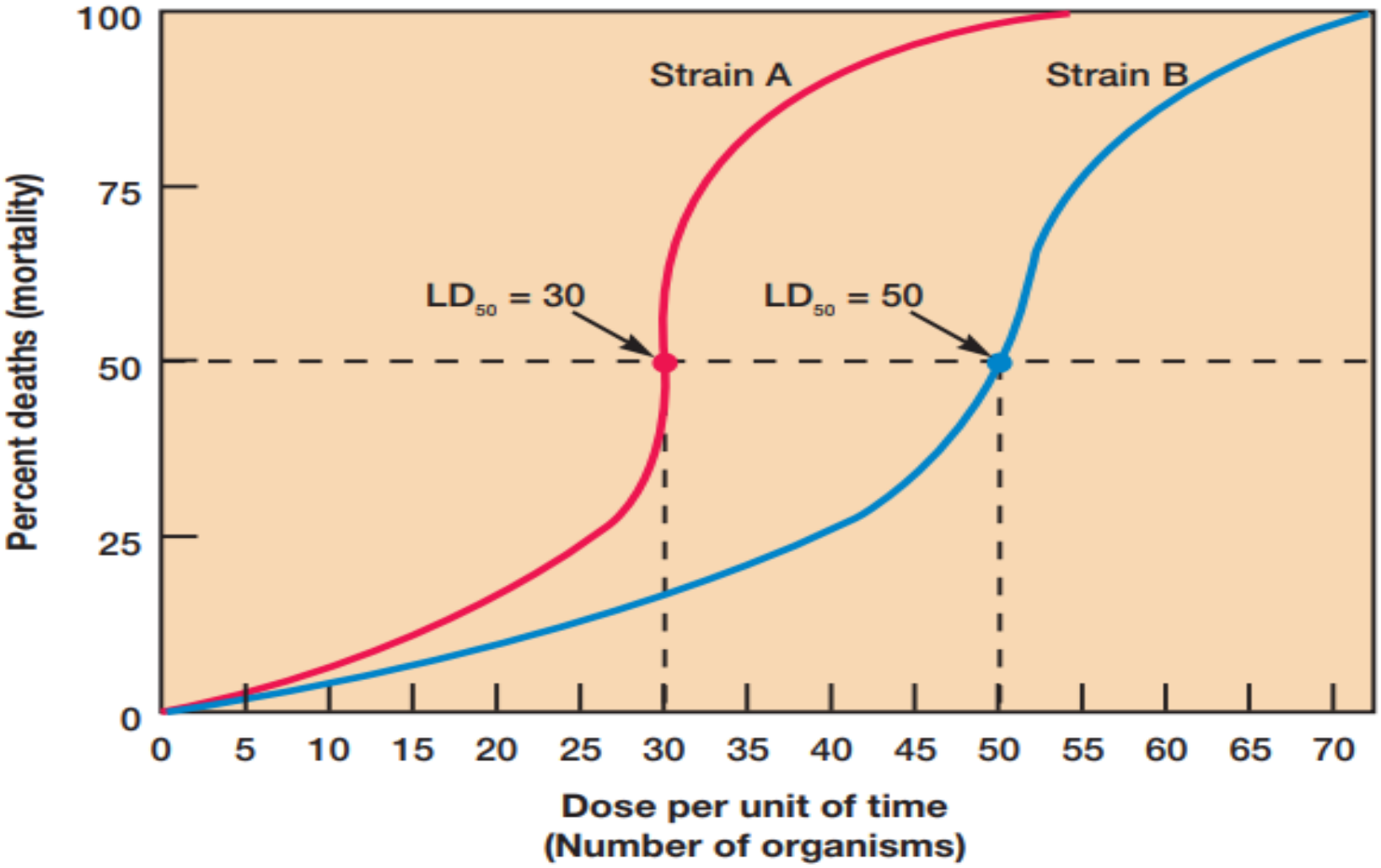
Determination of the LD50



Lethal dose 50 (LD50) or the infectious dose 50 (ID50)refer to the dose or number of pathogens that will either kill or infect 50% of an experimental group of hosts within a specified period.

Exotoxins types

1. **AB toxin: The portion of the toxin (B) binds to a host cell receptor and is separate from the portion (A) that has the enzyme activity that causes the toxicity.**

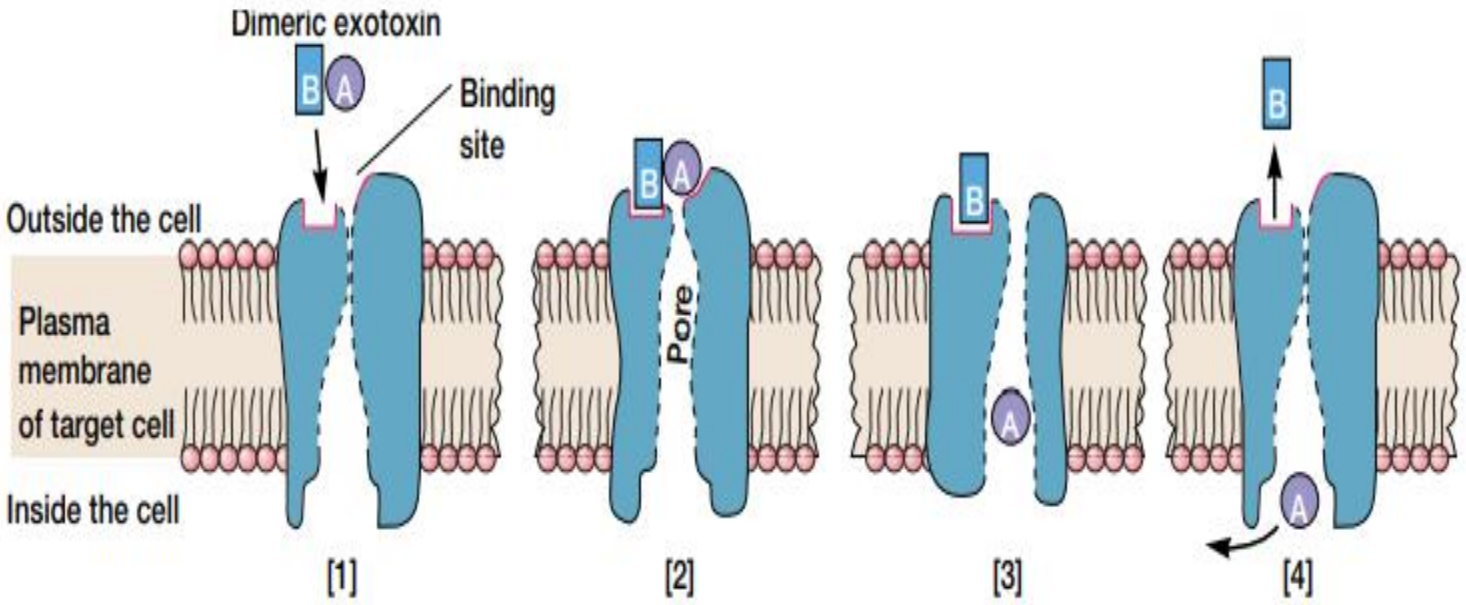
2. **A second type: an AB toxin, that affect a specific host site. Examples include nervous tissue (neurotoxins), the intestines (enterotoxins), general tissues (cytotoxins).**

3. **A third type does not have separable A and B portions and acts by disorganizing host cell membranes. Examples include the leukocidins, hemolysins, and phospholipases.**

4. **A fourth type is the superantigen that acts by stimulating T cells to release cytokines.**

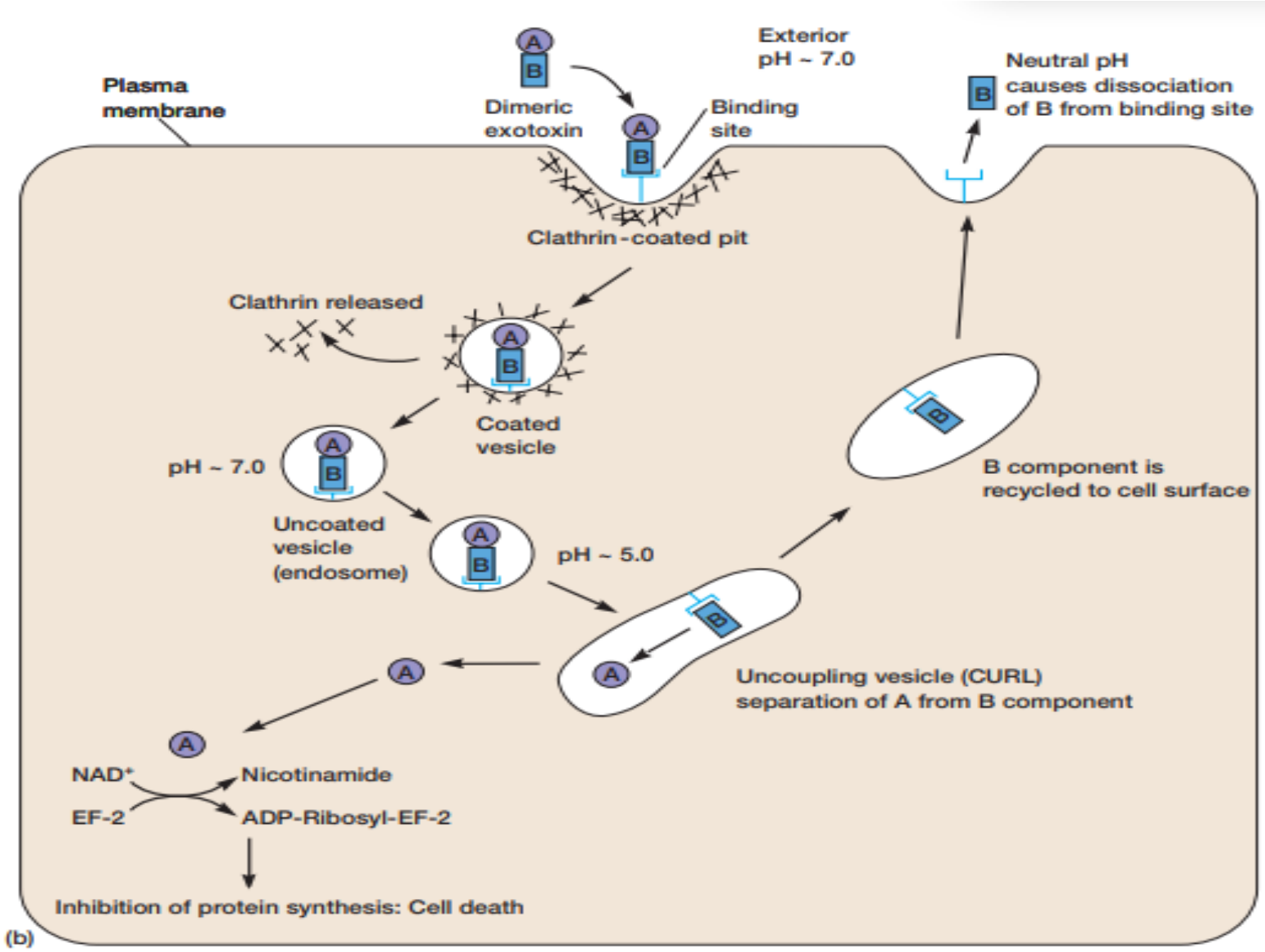
Exotoxin type-I

The B subunit interacts with specific receptors on the target cell or tissue such as the gangliosides GM1 for cholera toxin, GT1 and/or GD1 for tetanus toxin, and GD1 for botulinum toxin



A: AB Exotoxin Transport Mechanisms

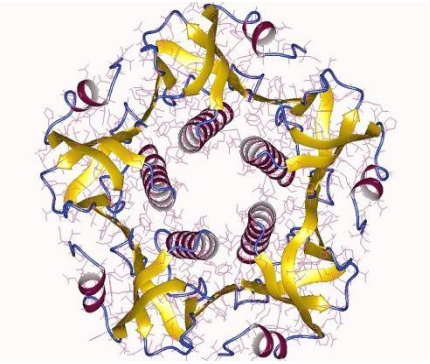
B: AB Exotoxin Transport Mechanisms



NAD + EF2 → ADP-ribosyl-EF2 + nicotinamide

Host Site Specific Exotoxins

Exotoxin type-II

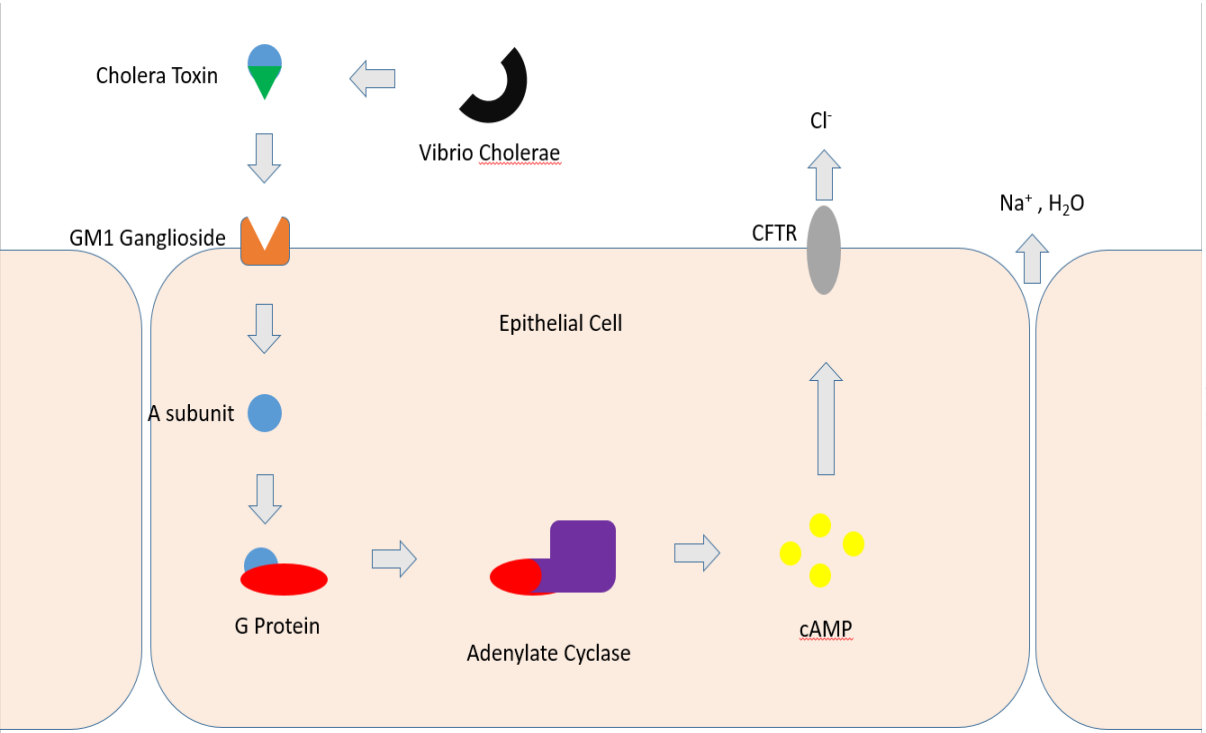


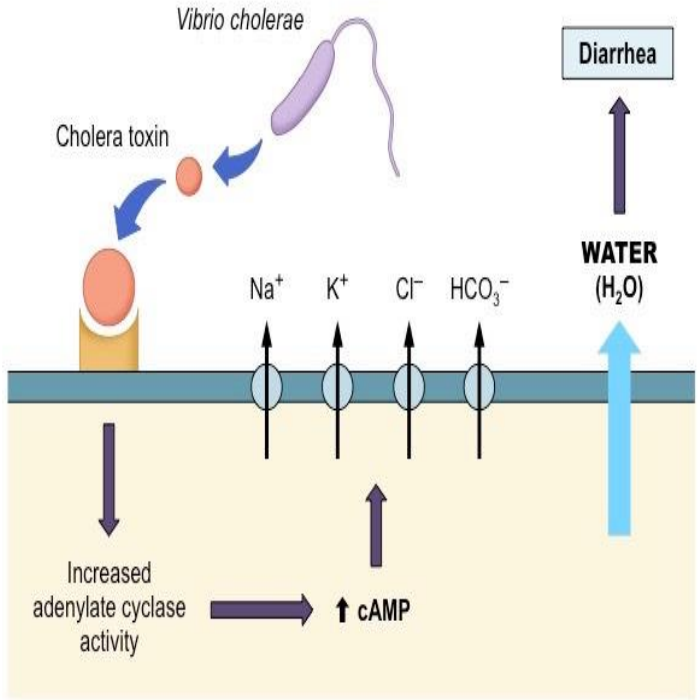
Neurotoxins* (botulinum toxin and tetanus toxin), enterotoxins (cholera toxin, *E. coli* heatlabile toxins), and cytoxins (diphtheria toxin, Shiga toxin).

The A subunit activates tissue adenylate cyclase to increase intestinal cyclic AMP (cAMP) concentrations. Examples include nephrotoxin (kidney), hepatotoxin (liver), and cardiotoxin (heart).

A subunit which is 28 kDa B subunit which is 11 kDax5

$=AB_5$





(1 February 1915 – 15 April 1985)

Cholera toxin was discovered in 1959 by Indian microbiologist

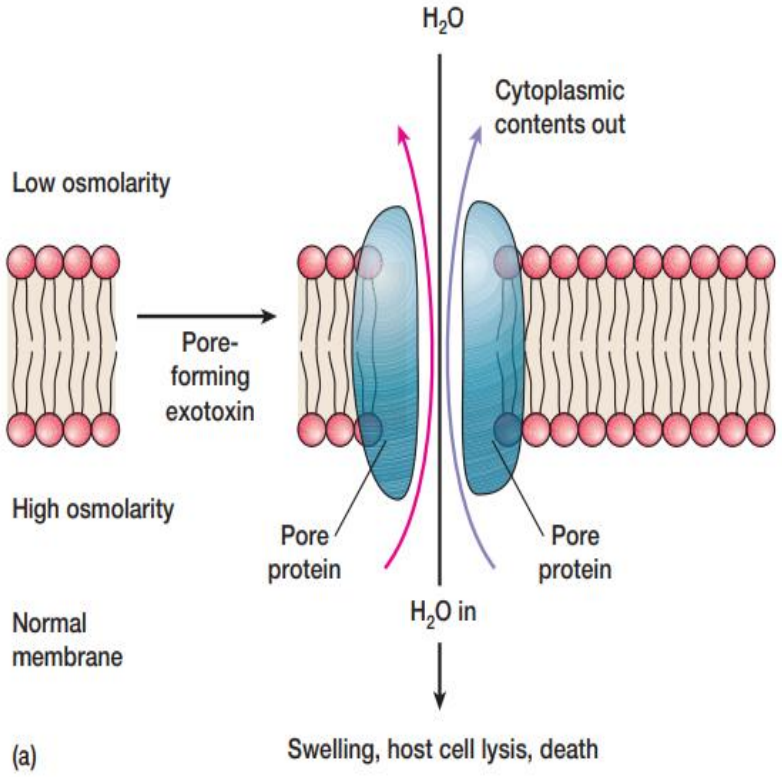
Sambhu Nath De

Another classification of exotoxins

1. **Superantigens (Type I toxins)**
2. **Exotoxins that damage host cell membranes (Type II toxins)**
3. **A-B toxins and other toxin that interfere with host cell function (Type III toxins).**

Membrane-Disrupting Exotoxins

First sub-type



Leukocidins are produced by Pneumonococci, Streptococci, and Staphylococci

Hemolysins form pores in the plasma membrane of erythrocytes

Streptolysin-O (SLO) *Streptococcus pyogenes* **β**
Streptolysin-S (SLO) *Streptococcus pyogenes* **β**

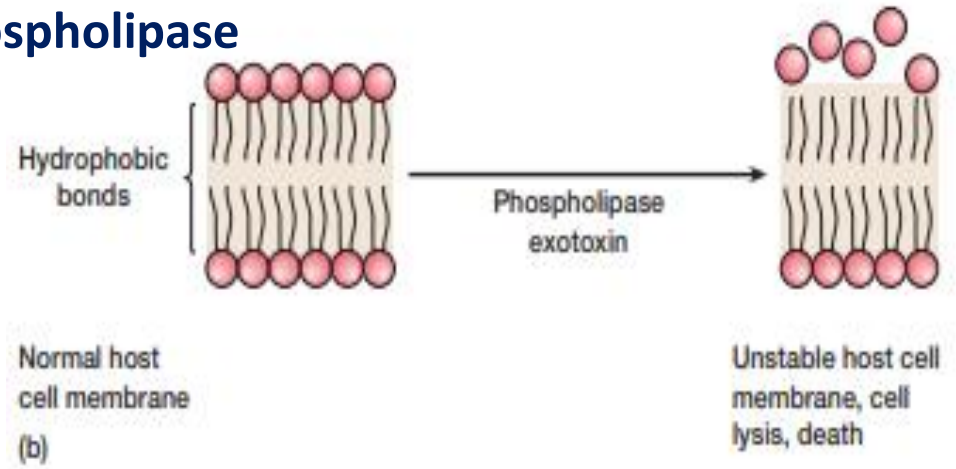
β-hemolysis: Beta-hemolysin breaks down the red blood cells and hemoglobin completely.

α-hemolysis: Alpha-hemolysin partially breaks down the red blood cells and leaves a greenish color because of biliverdin

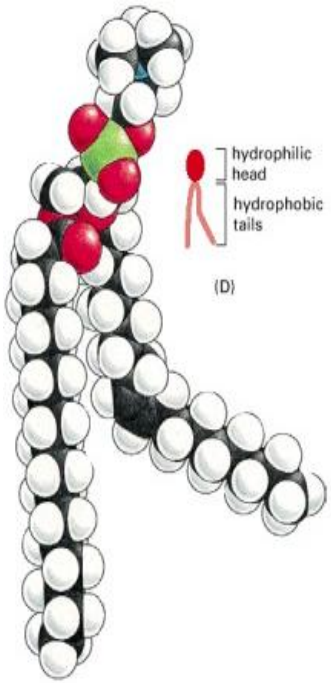
γ-hemolysis: If the organism does not produce hemolysins and does not break down the blood cells, no clearing will occur.

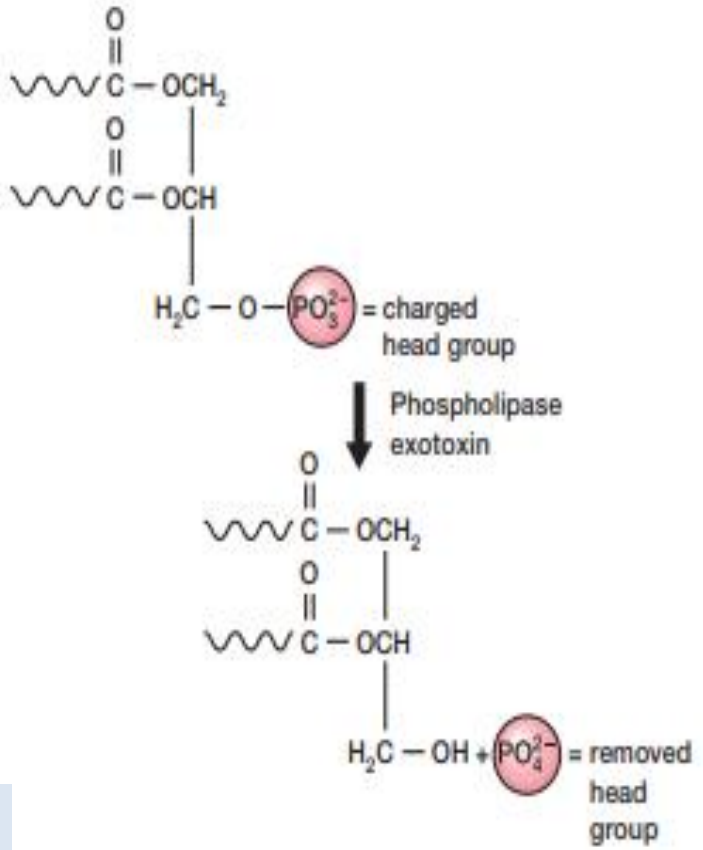
The second sub-type of membrane-disrupting toxins are the phospholipase

Phospholipases remove the charged head group from the lipid portion of the phospholipids in the host-cell plasma membrane



In the disease gas gangrene, the *Clostridium perfringens* alpha-toxin almost totally destroys the local population of white blood cells





Phospholipid molecule

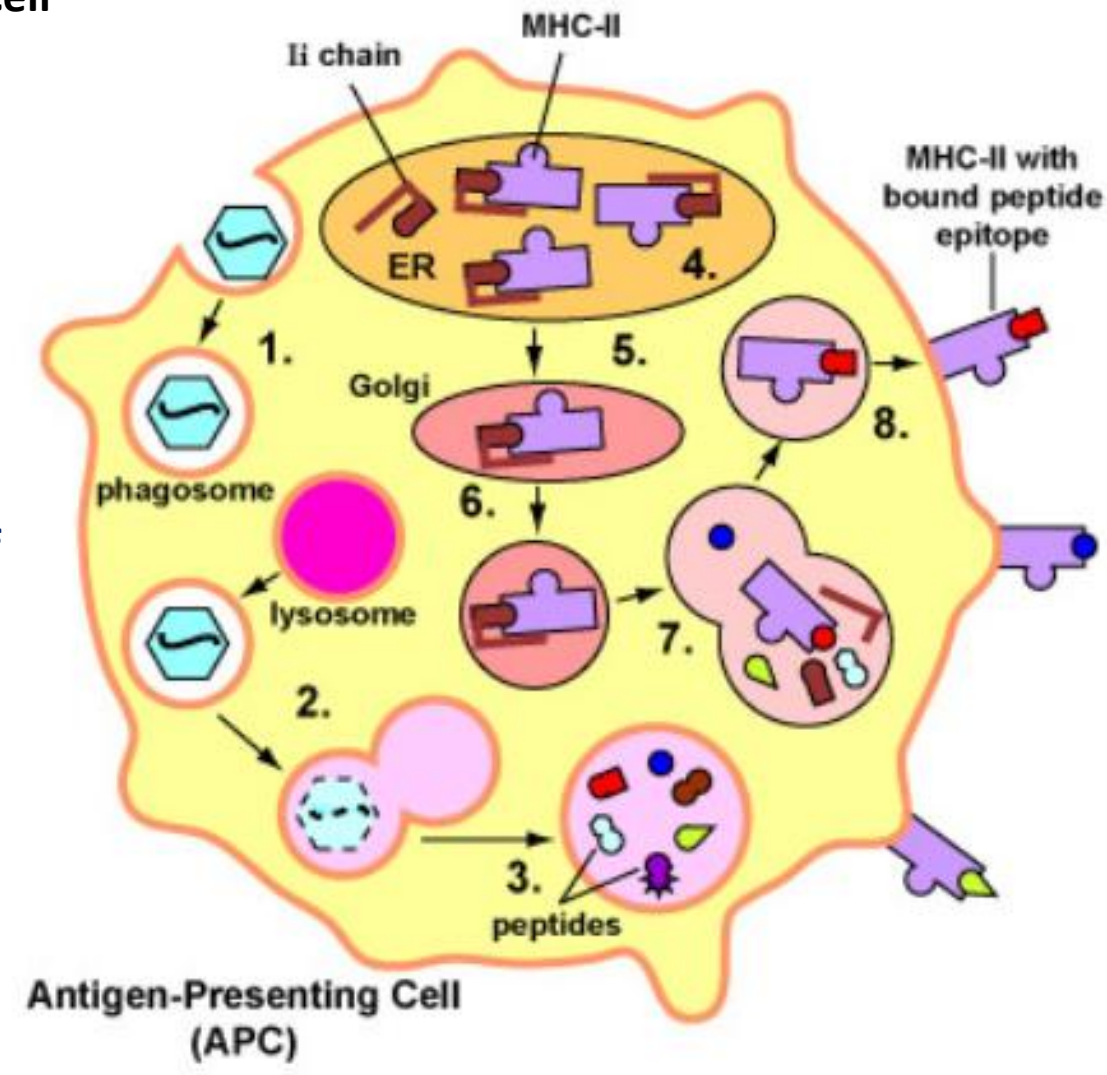
Superantigens

They bind to the surface of the target cell but do not enter the cell.

Superantigens bind non-specifically and directly to the outside of MHC-II molecules that interact with exceedingly large numbers of T4-lymphocytes

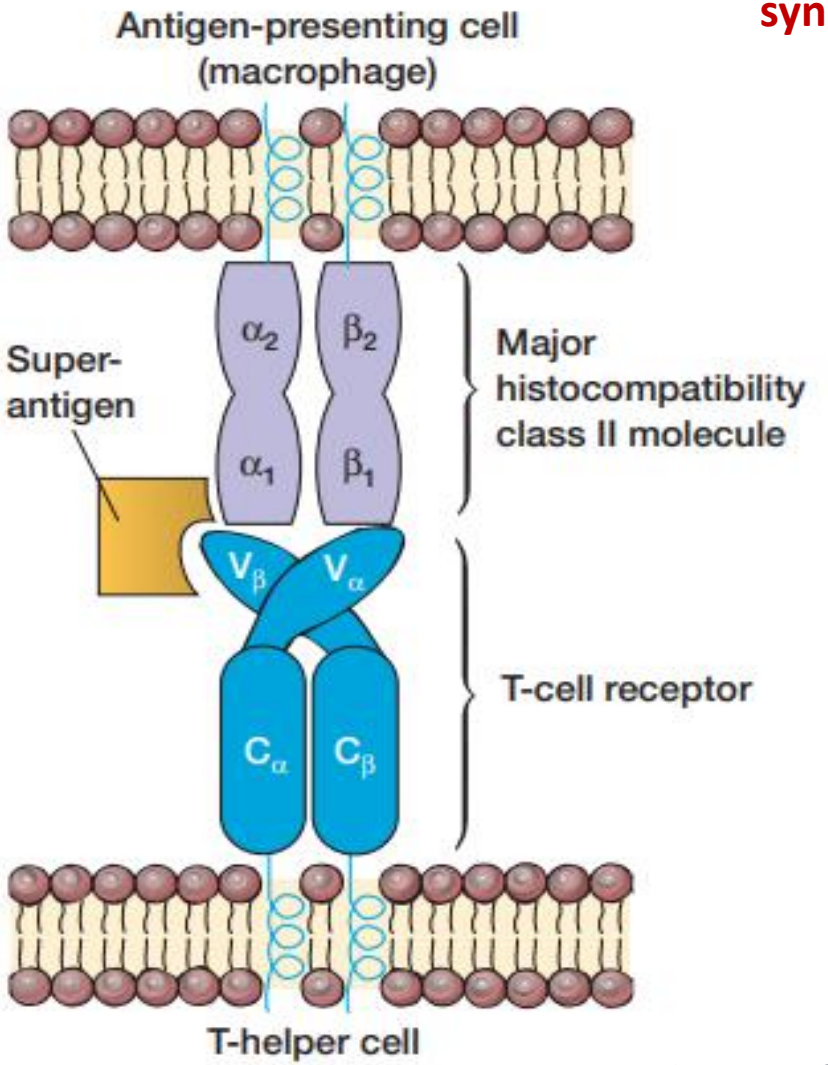
Activate of very large numbers of T4-lymphocytes results in the secretion of excessive amounts of a cytokine called interleukin-2 (IL-2)

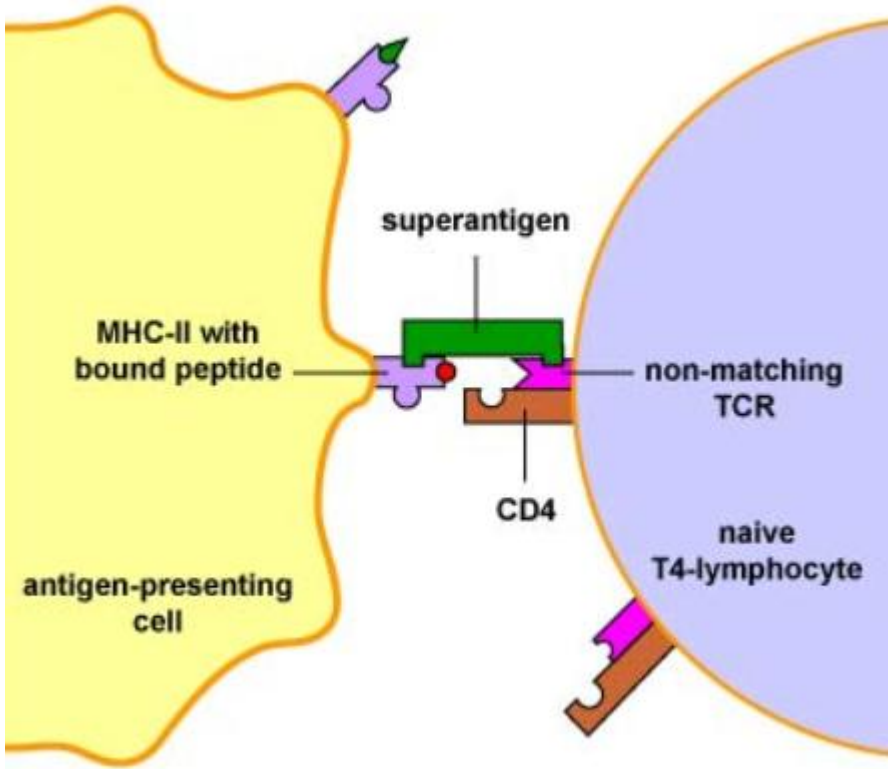
Staphylococcal enterotoxins (SE) cause staphylococcal food poisoning. Excessive Il-2 production results in fever, nausea, vomiting,and diarrhea. ETEC enterotoxin causing traveler's diarrhea.



Binding of Peptide Epitopes from Exogenous Antigens to MHC-II Molecules

Associated with rheumatic fever, arthritis, Kawasaki syndrome, atopic dermatitis, and one type of psoriasis.





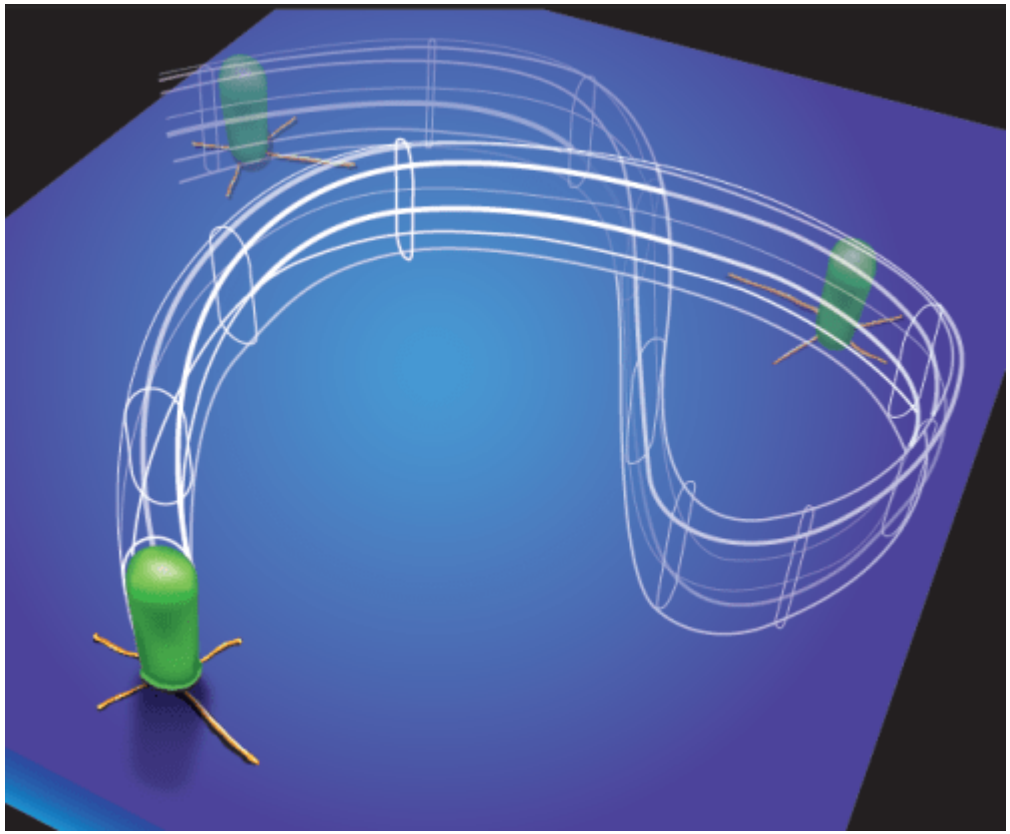
Binding of Superantigens

Compared to a conventional antigen-induced T-cell response where 0.0001-0.001% of the body's T-cells are activated, these are capable of activating up to 20% of the body's T-cells

Bacteria Use Type IV Pili to Walk Upright and Detach from Surfaces

Maxsim L. Gibiansky,[1]* Jacinta C. Conrad,[2]* Fan Jin,[1] Vernita D. Gordon,[1] Dominick A. Motto,[4] Margie A. Mathewson,[3] Wiktor G. Stopka,[3] Daria C. Zelasko,[3] Joshua D. Shrout,[4] Gerard C. L. Wong[1,3]†

division site by detaching, walking, or crawling. TFP governed this motility; TFP-deficient bacteria did not move apart after division. By using our search engine to locate all detachment events, we observed that detaching bacteria were overwhelmingly oriented out of plane (Fig. 1C). We found that TFP facilitated detachment by tilting from horizontal to vertical orientations; the influence of prevailing conditions was weak. TFP-deficient Δ*pilA* bacteria were defective in making this transition. This suggests a physical onset of



Walking Bacteria