Bacterial Virulence Factors

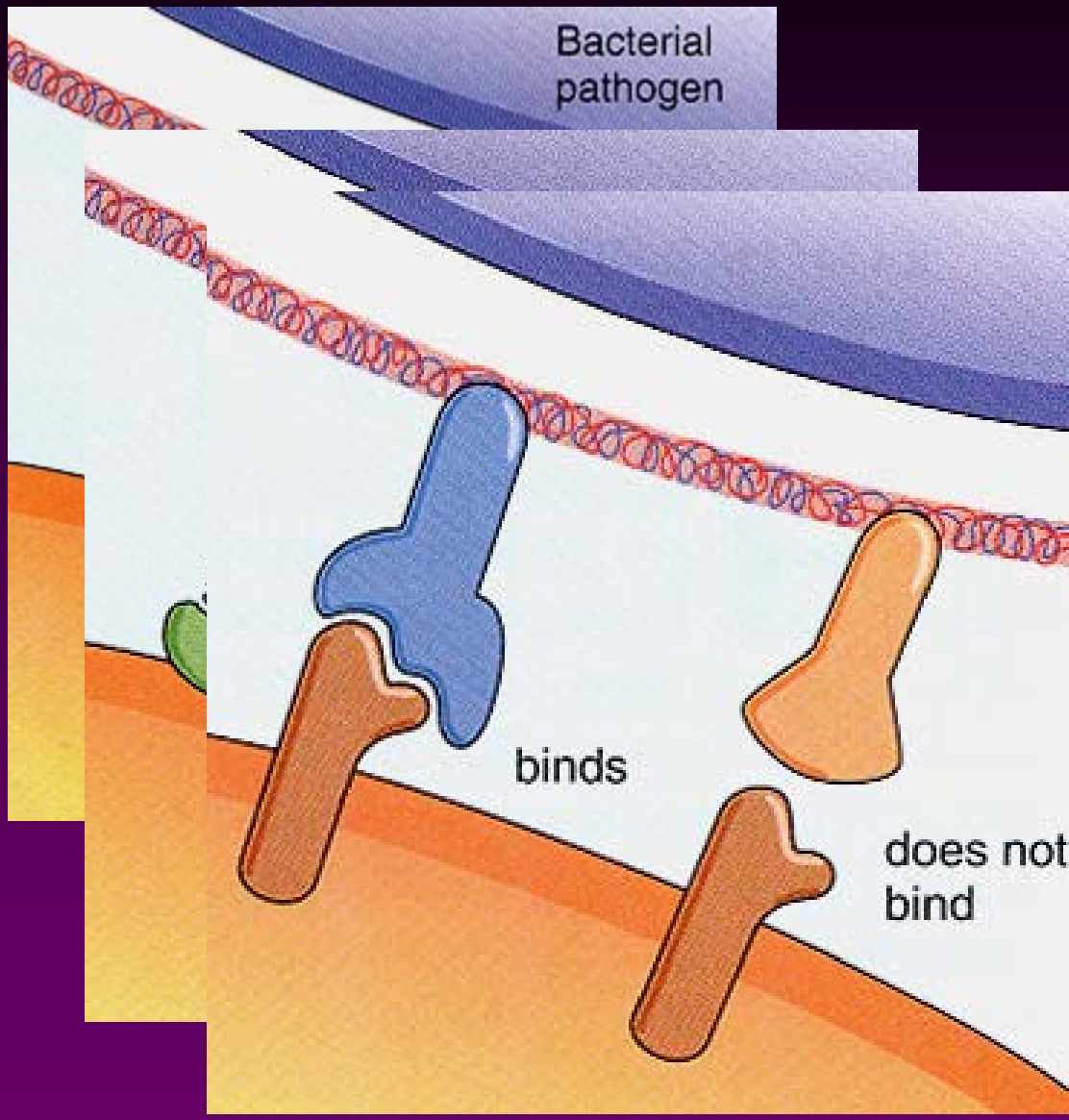
Bacteria cause disease by generating a bewildering array of factors that allow colonization, and promote bacterial growth at the expense of the host

General Aspects of toxins

- Promote colonization
  - adherence to cells or tissues
  - penetration into host
- Entry into cells (for some bacteria)
  - phagocytic & nonphagocytic cells
- Avoidance of host immune mechanisms
  - variety of mechanisms
- Families of Virulence Factors
  - contain conserved common regions
  - Often variations on a general theme

Microbial Adherence

- Bacterial Colonization
  - a necessary step
- Adhesion Mechanisms
  - Pili adhesion
    - Pilus tip specificity
    - given cell or tissue tropism
    - Type IV, no tip
  - Non-pilus adhesion
    - bind extracellular
      - tissue colonization
    - collagen, fibronectin
    - Gm+ pathogens (Staph & Strep)



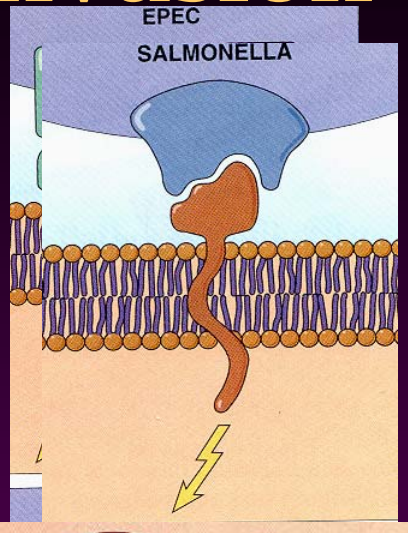
Non-pilus binding

Bacterial cell-invasion

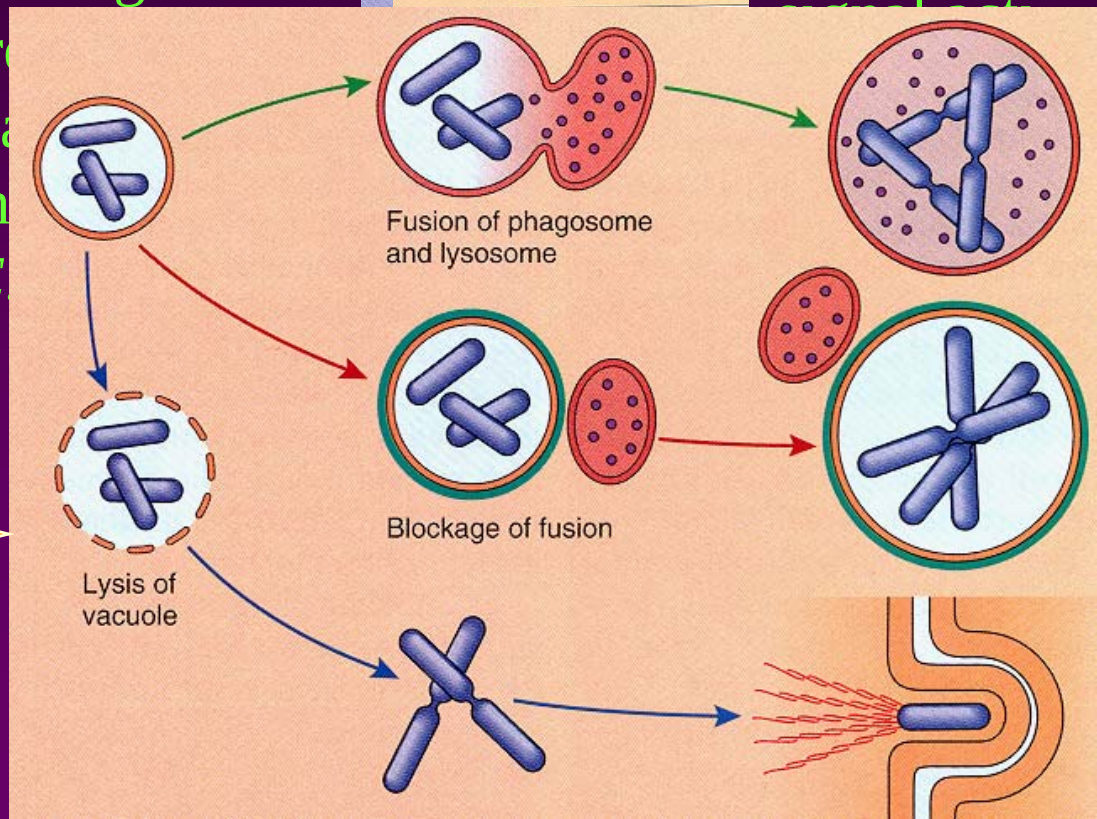
- **Many intracellular pathogens**
  - *Salmonella, Listeria, Rickettsia, Shigella*
- **Invasion into non-phagocytes**
  - Invasins, direct components of cytoskeleton
    - actin filaments & microtubules
- **Avoidance of digestion**
  - no lysosome fusion
  - lack of needed ATPase

Adherence, then calcium release reorganization of actin,

Resulting in reor… surf… arch… in *E*…

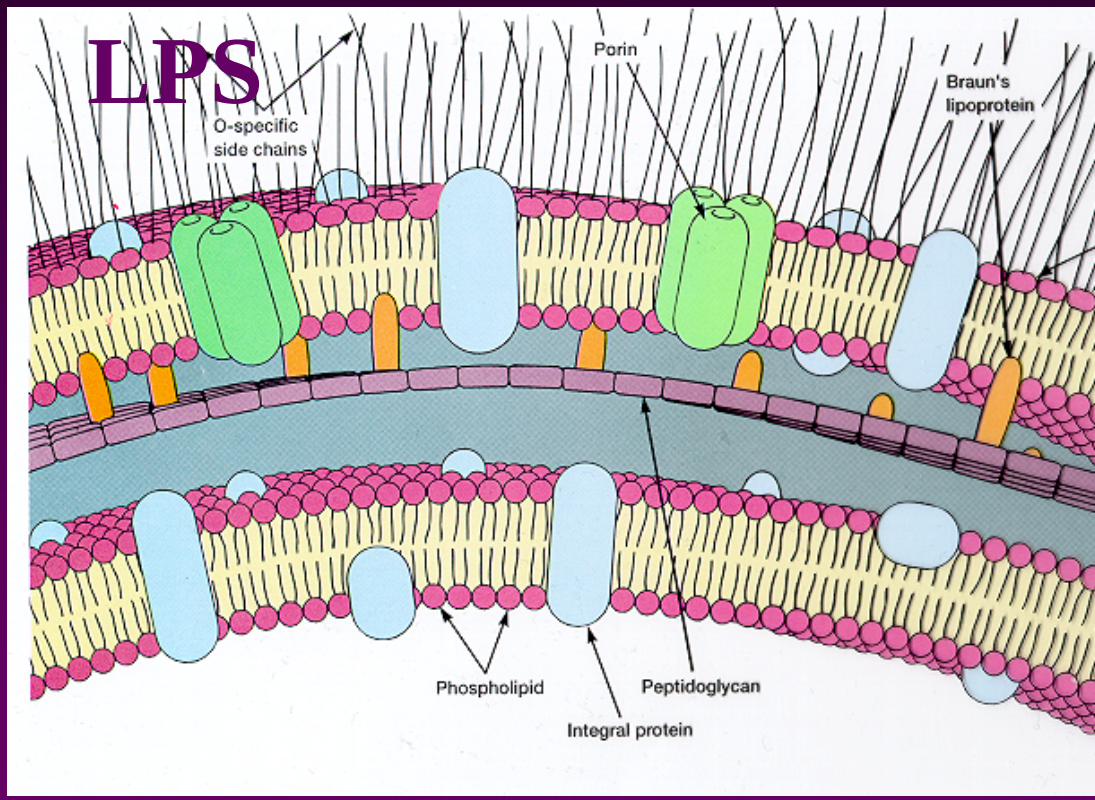


Salmonella -adhesion



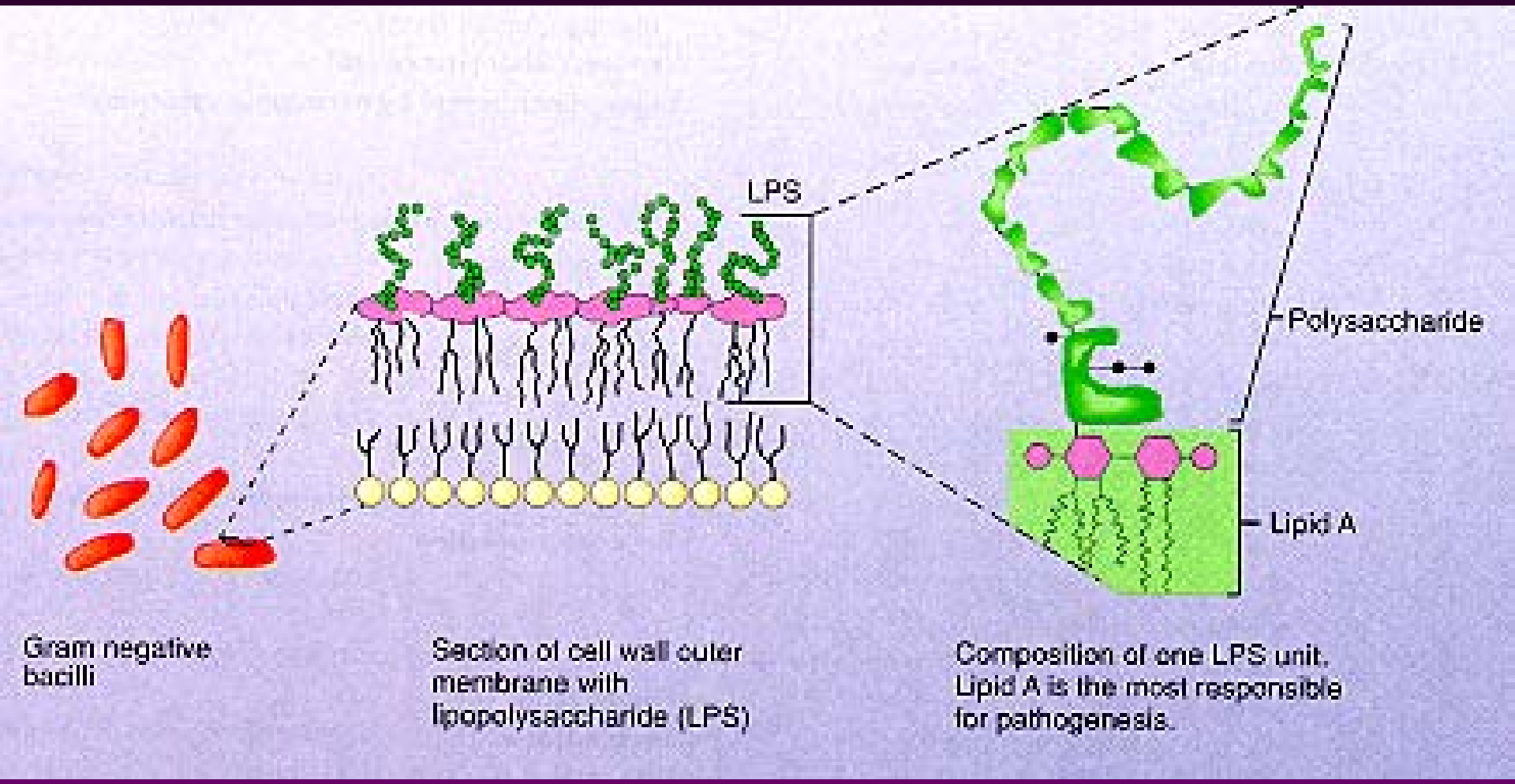
Endotoxin

- Gram--Surface component
  - Lipopolysaccharide (LPS)
  - Lipid A
  - Must be released--cell lysis, cell division
  - binds to macrophages
    - Il-1, TNF
    - fevers, malaise, myalgia, rigors, shock
  - Heat resistant
  - Medical supplies must be free of LPS



Gram-negative surface components

Endotoxin and Gram-- bacteria

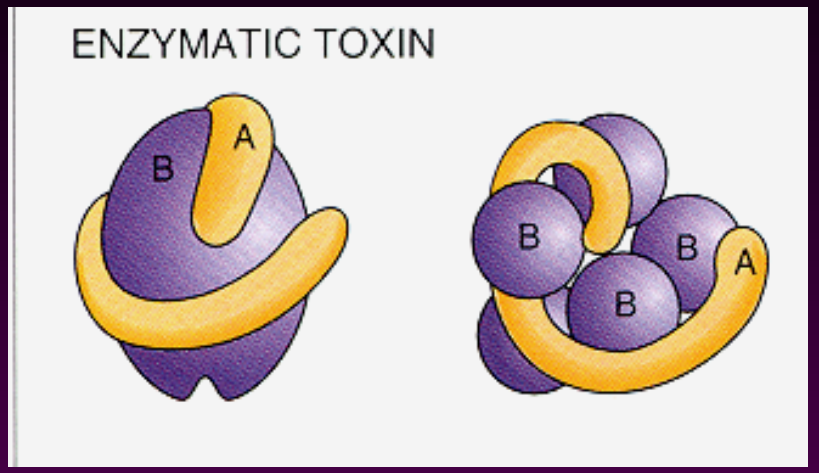


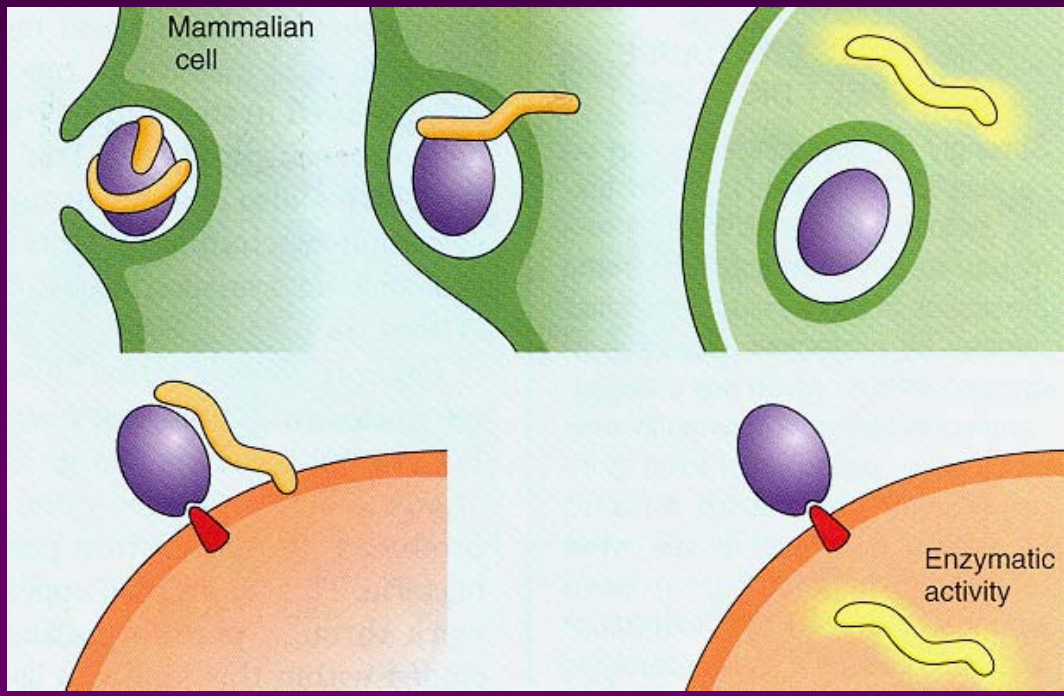
Exotoxins

- Secreted free from the bacteria
  - Many cause disease without bacteria present
  - bacteremia versus toxemia
- Generally are enzymes or pores
  - promote bacterial colonization or reproduction by providing nutrients
  - allow penetration into cells or tissues
  - some of unknown natural function
- Specific in changing or killing cells
  - enterotoxins, neurotoxins, cytotoxins, etc.
- May potentate other virulence factors

Classical A/B toxins

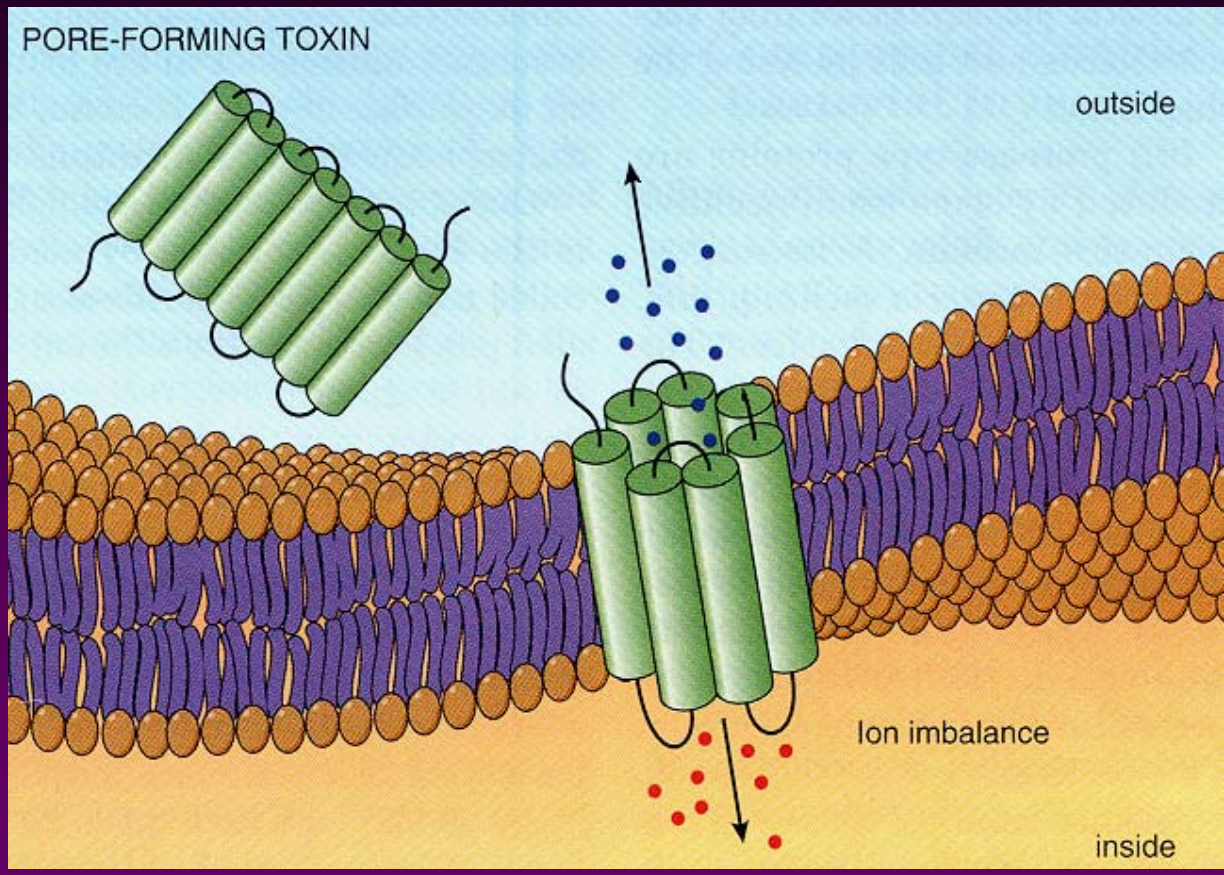
- **B-domain**:
  - "binding site"
  - responsible for cell specificity
- **A-domain:**
  - "active portion"
  - alters cell functions
  - Cholera & Diphtheria toxin modify host proteins
- Tetanus vrs Botulinum
  - B-domain
  - A-domain





Exotoxins as Pores

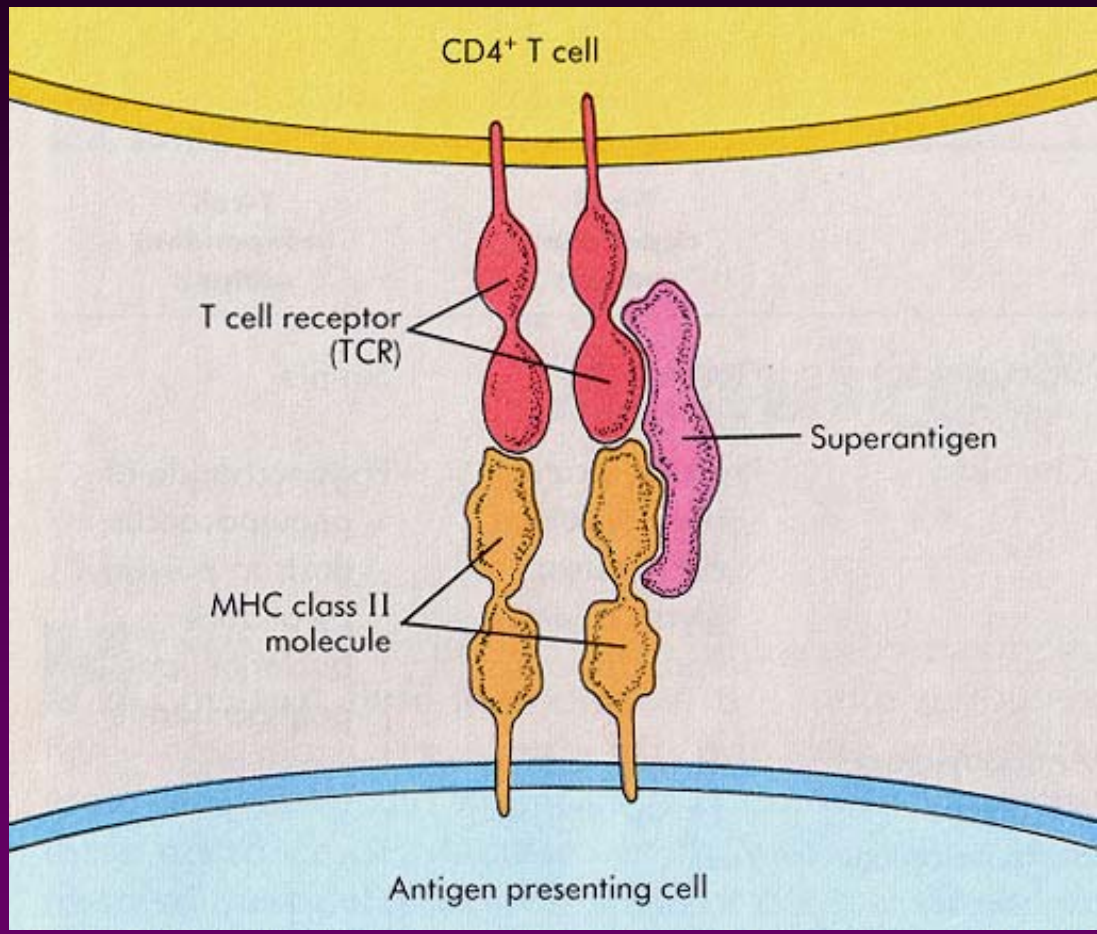
- **Cytotoxins**
  - **similar in AA structure**
  - **different families**
  - **differ in host-cell specificity**
    - Hemolysins
    - Leukolysins
    - Neurotoxins
    - Enterotoxins
    - Cytolysins
- Basic structure is conserved among many bacteria spp



Cytolysins are pores inserted into cells

Superantigens

- Poly T-cell stimulation
  - Cross links MHC--II to CD4+ heterodimer
  - Cytokine cascade
    - Il-1, TNF-*a*, *et al.*
    - local & systemic
      - circulatory collapse
      - respiratory collapse
      - Shock & death
    - Ex. Staph TSST-1



No specific antigen involved

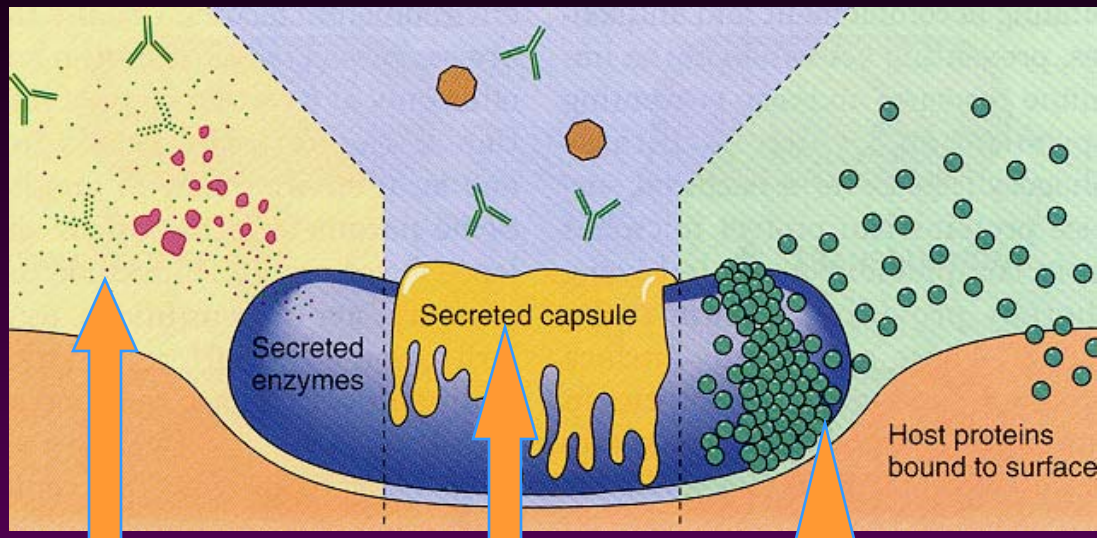
Immune Avoidance

- **Cloaking devises**
  - collecting a surface coat: fibronectin, albumin, etc.
- **Capsules:** protect from: --Complement, Antibody, phagocytosis

Anti-immunity factors

- IgAase,
- Protein A,
- Complement degradation

- **Antigenic variation**
  - *Neisseria* >50 pilus genes
  - genetic switching of surface components



Degradation of complement or antibodies

Secreted surface capsules

Binding of host proteins such as fibronectin