

Microbes as Agents of Infectious Disease

- Normal Flora
- Virulence and Pathogenicity
- Toxicity vs. Invasiveness

WE ARE NOT ALONE!

“We are outnumbered. The average human contains about 10 trillion cells. On that average human are about 10 times as many microorganisms, or 100 trillion cells...As long as they stay in balance and where they belong, [they] do us no harm...In fact, many of them provide some important services to us. [But] most are opportunists, who if given the opportunity of increasing growth or invading new territory, will cause infection.”

- Sullivan (1989)

Take Home Message:

Prokaryotic Cells $\sim 10^{14}$ cells/body

Eukaryotic Cells $\sim 10^{13}$ cells/body

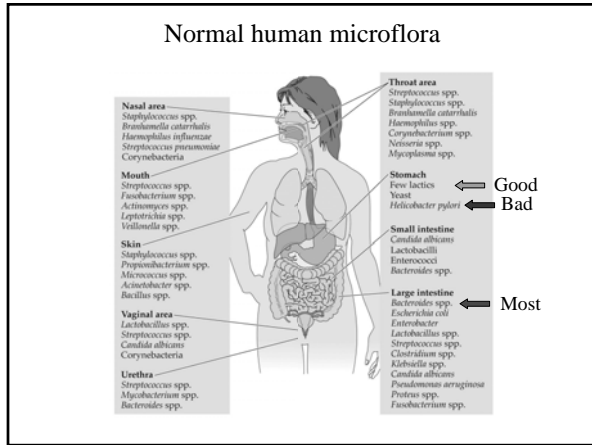
Normal Flora helps maintain our health

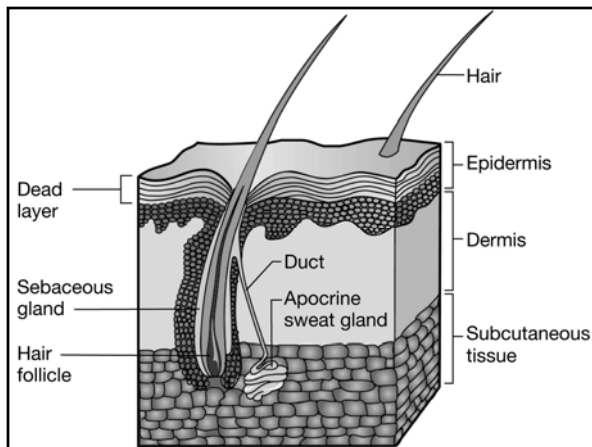
- Provides vitamins & nutrients
- Detoxify many compounds
- Prevent colonization of pathogens

TABLE 21.1 Representative genera of microorganisms in the normal flora of humans

| Anatomical site | Organism* |
|------------------------|---|
| Skin | <i>Staphylococcus</i> , <i>Corynebacterium</i> , <i>Acinetobacter</i> , <i>Pityrosporum</i> (yeast), <i>Propionibacterium</i> , <i>Micrococcus</i> |
| Mouth | <i>Streptococcus</i> , <i>Lactobacillus</i> , <i>Fusobacterium</i> , <i>Veillonella</i> , <i>Corynebacterium</i> , <i>Neisseria</i> , <i>Actinomyces</i> |
| Respiratory tract | <i>Streptococcus</i> , <i>Staphylococcus</i> , <i>Corynebacterium</i> , <i>Neisseria</i> |
| Gastrointestinal tract | <i>Lactobacillus</i> , <i>Streptococcus</i> , <i>Bacteroides</i> , <i>Bifidobacterium</i> , <i>Eubacterium</i> , <i>Peptococcus</i> , <i>Peptostreptococcus</i> , <i>Ruminococcus</i> , <i>Clostridium</i> , <i>Escherichia</i> , <i>Klebsiella</i> , <i>Proteus</i> , <i>Enterococcus</i> , <i>Staphylococcus</i> |
| Urogenital tract | <i>Escherichia</i> , <i>Klebsiella</i> , <i>Proteus</i> , <i>Neisseria</i> , <i>Lactobacillus</i> (vagina of mature females), <i>Corynebacterium</i> , <i>Staphylococcus</i> , <i>Candida</i> , <i>Prevotella</i> , <i>Clostridium</i> , <i>Peptostreptococcus</i> |

* This list is not meant to be exhaustive, and not all of these organisms are found in every individual. Most of these organisms can contribute to disease processes under certain conditions.





Skin:

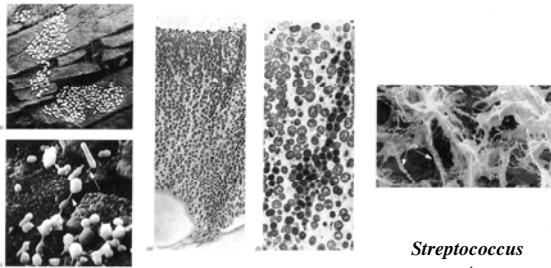
Resident Microbes:

- Most are Gram +
Staphylococcus
Micrococcus
- Few G - & fungi

Environmental Conditions: Hostle

- o High Salt
- o Low pH
- o Dry

Dental Plaque Bacteria



Tooth Colonies

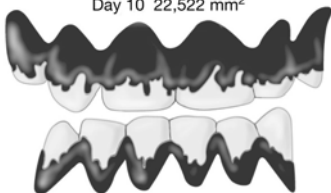
Plaque Cross Section

Streptococcus mutans

Day 1 1436 mm²



Day 10 22,522 mm²



Mouth:

Resident Microbes:

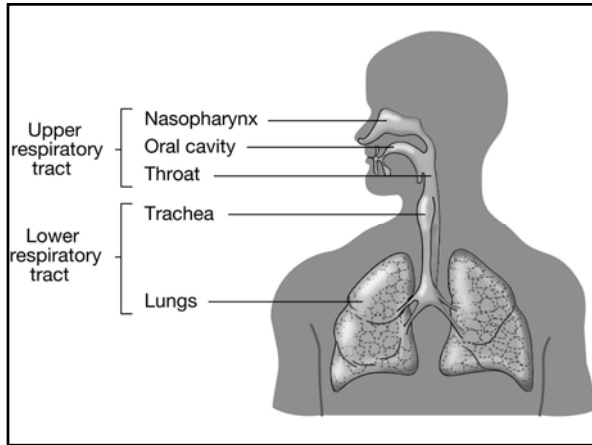
Gram +: *Streptococcus & Lactobacilli*

Gram - : obligate anaerobes

Spirochetes: *Borrelia*

Environmental Conditions: More Favorable

- o Moist, though contains lysozyme
- o Lots of polysaccharides
- o Lots of amylase & protease



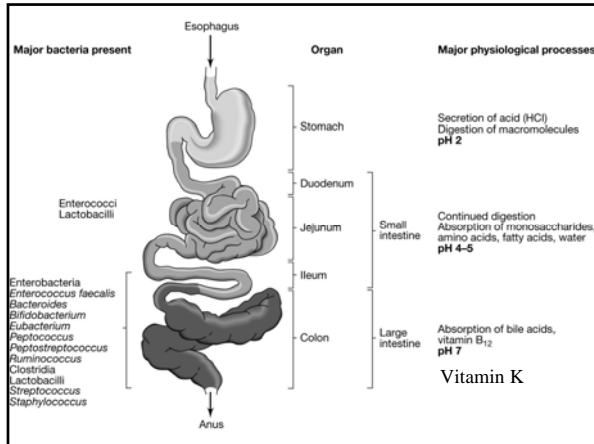
Respiratory Tract:

Resident Microbes: Upper Only

Gram +: *Streptococcus & Staphylococcus*

Environmental Conditions:

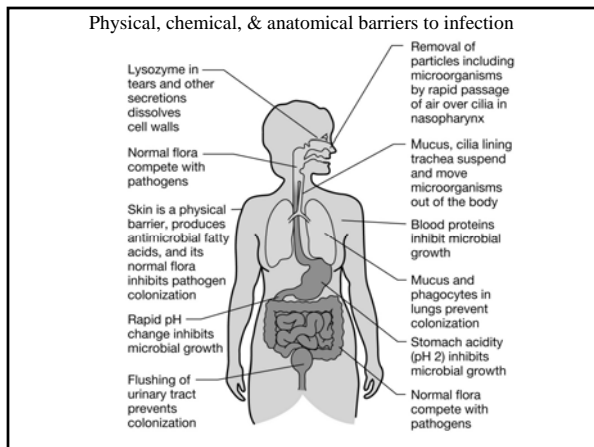
- o Mucous membranes
- o Others compete with potential pathogens



G.I. Tract:
Stomach: Hostile, pH ~2
 Gram +: *Lactobacilli* & *Streptococcus*
 Gram - : *Helicobacter pylori*

Small Intestine: Gradient in pH
 low pH: *Lactobacilli*
 neutral: *Enterococcus*

Large Intestine: Moist and pH ~7
 10¹¹ to 10¹² bacteria/g wet wt feces
 #1 is *Bacteroides vulgatus* at ~15%
E. coli is only ~0.03%



Virulence and Pathogenicity

Pathogen: A parasitic organism that causes damage to, or disease in its host.

Pathogenicity: The ability to cause disease.

Virulence: The relative degree or intensity of pathogenicity.

Virulence is determined by the five following characteristics of the pathogen →

Invasiveness: The ability of the organism to spread to adjacent tissues or other tissues.

Toxigenicity: The ability of the organism to produce toxic products that cause disease and/or damage in the host.

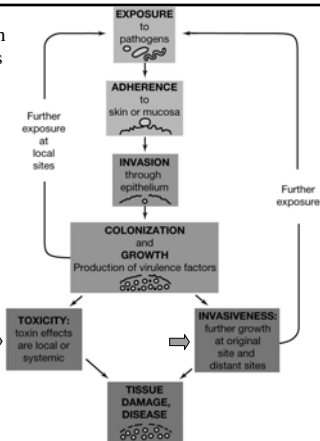
Infectivity: The ability of the organism to establish a focal point of infection through growth.

Pathogenic potential: The degree that the pathogen causes morbid symptoms.

Hypersensitivity: Host's innate sensitivity to pathogen.

The presence or even growth of microbes on the host does not always lead to disease.

These two are key factors to the success or failure of a potential pathogen to cause disease!

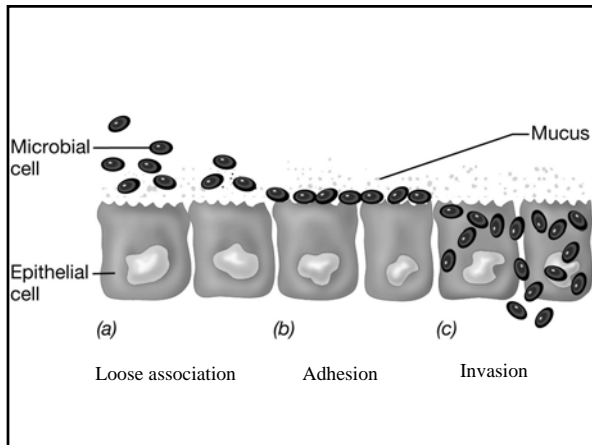


Determinants of Infectious Disease

To produce an infectious disease, a pathogen must be able to:

1. initially be transported to the host
2. adhere to, colonize or invade the host
3. grow, multiply, or complete its life cycle in the host
4. initially evade host defense mechanisms
5. damage the host by mechanical and/or chemical means

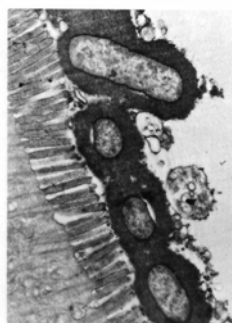
In the end it is – Numbers (of bacteria) that make you sick!



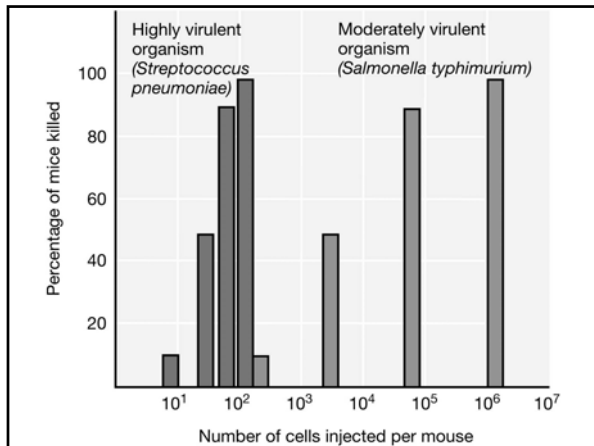
Adherence of microorganisms

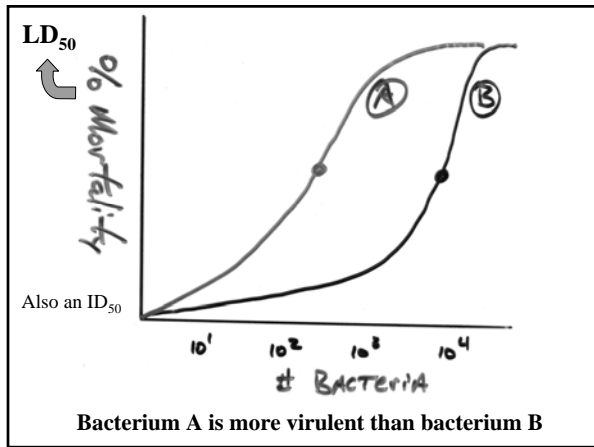


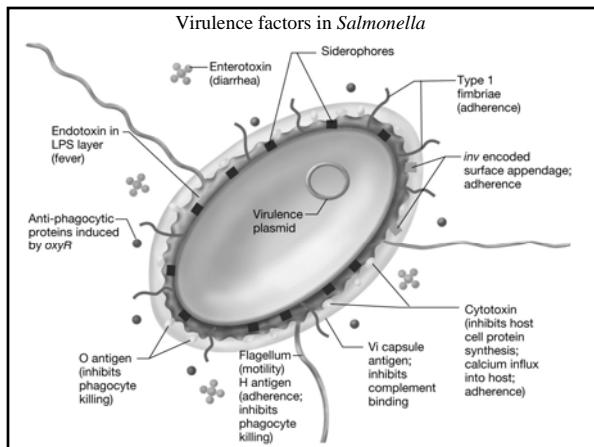
(a) Entero-toxic *Vibrio cholerae*



(b) Entero-invasive *E. coli*







Adherence Factors:

Table 26.2 Adherence factors involved in attachment of organisms to host cells

| Adherence Factor | Example |
|--------------------------------------|--|
| Fimbriae (adhesion proteins) | <i>Proteus mirabilis</i> —urinary tract infections <i>Neisseria gonorrhoeae</i> —attach to urinary epithelia <i>Salmonella</i> —attach to intestinal epithelia <i>Streptococcus pyogenes</i> —M protein attaches to epithelia |
| Capsule (glycocalyx) | <i>Streptococcus mutans</i> —dextrans attach to teeth <i>Streptococcus salivarius</i> and <i>S. sanguis</i> —attach to tongue epithelia |
| Teichoic acids Lipoteichoic acids | <i>Staphylococcus aureus</i> —attach to nasal epithelia |

Virulent Factors: Invasiveness

Table 26.3 Some enzymes produced by pathogenic bacteria that promote invasion of the host

| Enzyme | Organism | Function |
|-----------------|---|--|
| Collagenase | <i>Clostridia</i> | Breaks down collagen in connective tissue |
| Coagulase | <i>Staphylococcus aureus</i> | Clot formation around point of entry protects from host defenses |
| ⇒ Elastase | <i>Pseudomonas aeruginosa</i> | Disrupts membranes |
| ⇒ Hyaluronidase | <i>Streptococcus</i> <i>Staphylococcus</i> <i>Clostridium</i> | Hydrolyzes hyaluronic acid—intercellular cement |
| ⇒ Lecithinase | <i>Clostridia</i> | Disrupts phosphatidylcholine in membranes |
| Streptokinase | <i>Staphylococcus</i> <i>Streptococcus</i> | Digests fibrin clots |

⇒ Also considered cytolytic toxins!

Virulent Factors: Plasmids

Table 26.4 Virulence factors that are generally encoded in plasmids

| Organism | Factor | Disease |
|----------------------------------|-----------------------|---------------------------------------|
| <i>Escherichia coli</i> | Enterotoxin | Diarrhea |
| <i>Clostridium tetani</i> | Neurotoxin | Tetanus |
| <i>Staphylococcus aureus</i> | Coagulase enterotoxin | Boils/skin infections, food poisoning |
| <i>Streptococcus mutans</i> | Dextranucrase | Tooth decay |
| <i>Agrobacterium tumefaciens</i> | Tumor | Crown gall |
| <i>Staphylococcus</i> spp. | Antibiotic resistance | Various |

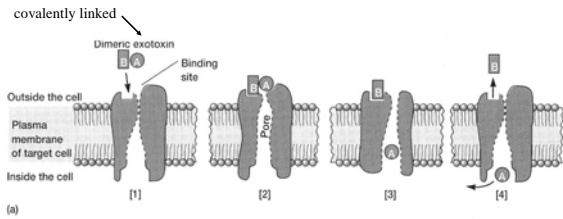
Virulent Factors: Antiphagocytic

Table 26.5 Antiphagocytic factors produced by bacteria and their mode of action

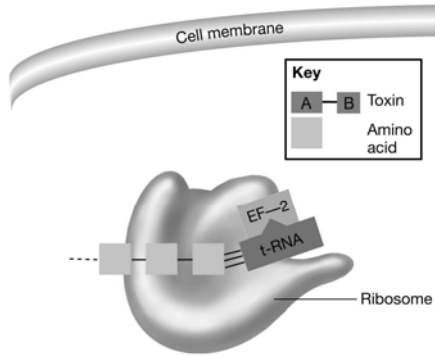
| Factor | Action |
|-----------------------|--|
| ⇒ Leukocidins | Specific lytic agent for leukocytes including phagocytes |
| ⇒ Hemolysins | Form pores in host cells including macrophages. Streptolysin O affects sterols in membranes. Streptolysin S is a phospholipase |
| Capsules (glycocalyx) | Long polymers of carbohydrate—physically prevents engulfment |
| Fimbriae | (1) Bind to surface components of phagocytes, prevent close contact, and phagocytosis may not occur (2) Phase variation—a change in the antigenic composition |

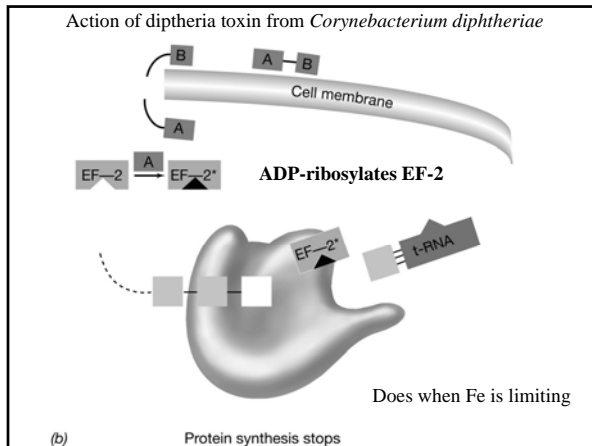
⇒ Also considered cytolytic toxins!

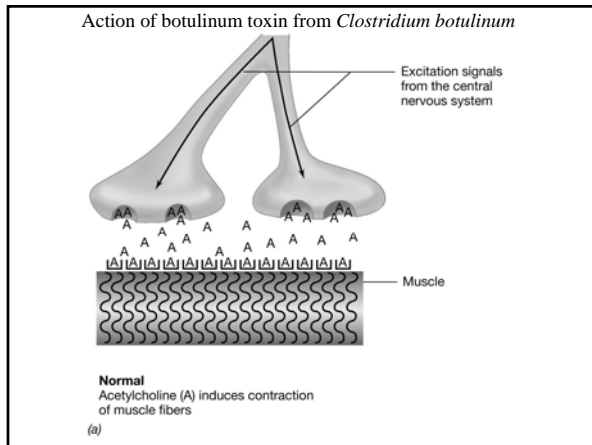
A-B exotoxins and their cellular entry

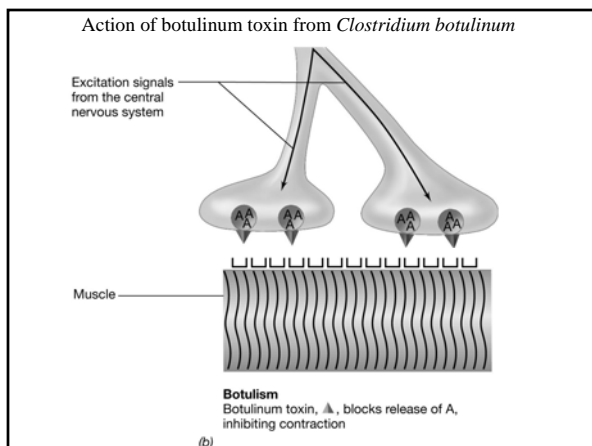


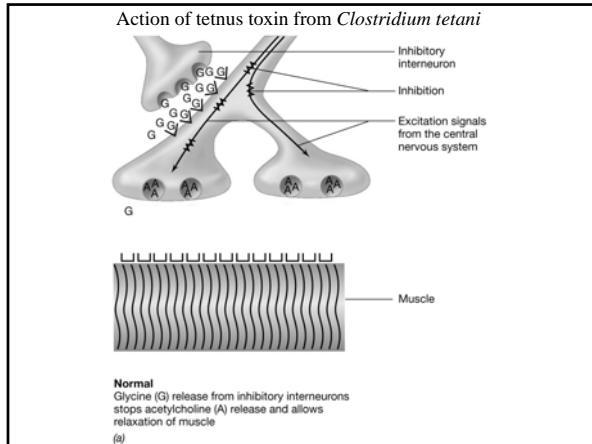
Action of diphtheria toxin from *Corynebacterium diphtheriae*

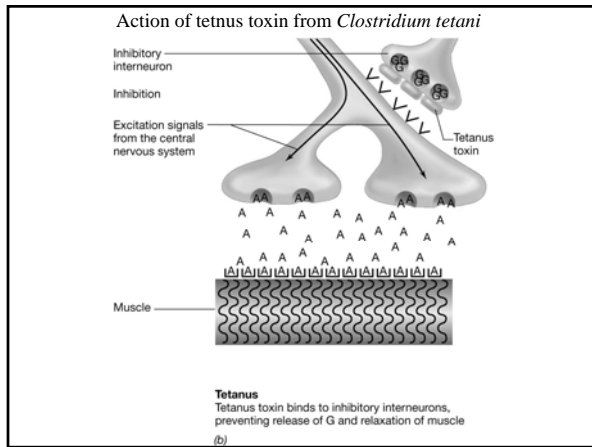


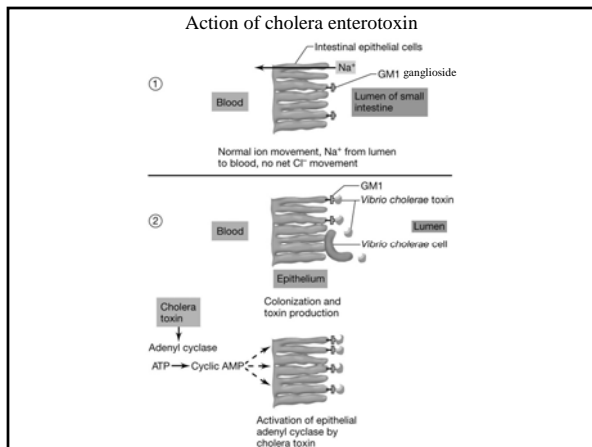












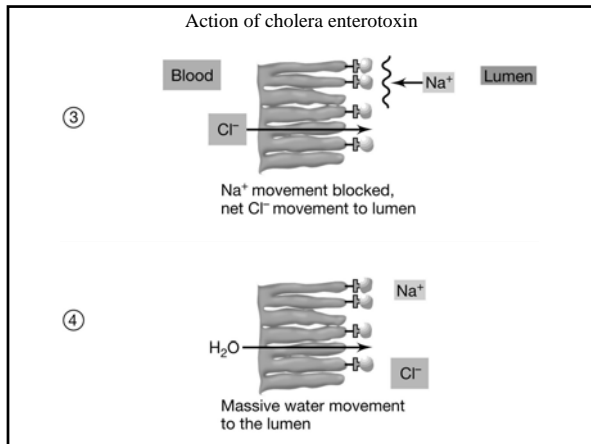


Table 26.6 Characteristics of exotoxins and endotoxins

| Exotoxins | Endotoxins |
|---|--|
| Heat labile 60°C to 80°C | Heat stable |
| Immunogenic | Weakly immunogenic |
| Cause no fever | Cause fever |
| Can be lethal at low concentrations | Toxic at high doses |
| Different genera produce different toxins | Similar regardless of source |
| Released by live bacterium | Released on lysis of bacterium |
| Inactivated by chemicals that affect proteins | Not generally harmed by chemicals that affect proteins |

Rem: Lipid A region of LPS

Table 26.7 Some exotoxins produced by bacteria (Part 1)

| Exotoxin | Producing Organism | Disease | Effect |
|--------------------|------------------------------------|----------------------|--|
| Diphtheria toxin | <i>Corynebacterium diphtheriae</i> | Diphtheria | Inhibits protein synthesis; affects heart, nerve tissue, liver |
| Botulism toxin | <i>Clostridium botulinum</i> | Botulism | Neurotoxin; flaccid paralysis |
| Perfringens toxin | <i>Clostridium perfringens</i> | Gas gangrene | Hemolysin, collagenase, phospholipase |
| Erythrogenic toxin | <i>Streptococcus pyogenes</i> | Scarlet fever | Capillary destruction |
| Pyrogenic toxin | <i>Staphylococcus aureus</i> | Toxic shock syndrome | Fever, shock |
| Exfoliative toxin | <i>Staphylococcus aureus</i> | Scalded skin | Massive skin peeling |
| Exotoxin A | <i>Pseudomonas aeruginosa</i> | — (~ Diphtheria) | Inhibits protein synthesis |

Table 26.7 Some exotoxins produced by bacteria (Part 2)

| Exotoxin | Producing Organism | Disease | Effect |
|-----------------|--------------------------------|------------------------|--------------------------------------|
| Pertussis toxin | <i>Bordetella pertussis</i> | Whooping cough | Stimulates adenylyl cyclase |
| Anthrax toxin | <i>Bacillus anthracis</i> | Anthrax | Pustules; blood poisoning |
| Enterotoxin | <i>Escherichia coli</i> | Diarrhea | Water and electrolyte loss |
| Enterotoxin | <i>Vibrio cholerae</i> | Cholera | Water and electrolyte loss |
| Enterotoxin | <i>Staphylococcus aureus</i> | “Staph” food poisoning | Diarrhea, nausea |
| Enterotoxin | <i>Clostridium perfringens</i> | Food poisoning | Permeability of intestinal epithelia |
| Neurotoxin | <i>Clostridium tetani</i> | Tetanus | Rigid paralysis |
