Game Plan

Lecture

Disease pathogenesis
Portals of entry
Mechanisms of pathogenicity
Toxins

Lab

Staph, Strep and Enteric Unknowns

Next Class: Lab Exam

Bacterial strategies for pathogenicity and virulence

1. Portals of entry
2. Infectious dose
3. Adherence
4. Penetration, evasion and damage
5. Portals of exit

1. Portals of entry

TABLE 15.1 Portals of Entry for the Pathogens of Some Common Diseases

Portal of Entry	Pathogen*	Disease	Incubation Period
Mucous Membranes			
Respiratory tract	*Streptococcus pneumoniae*	Pneumococcal pneumonia	Variable
	Mycobacterium tuberculosis†	Tuberculosis	Variable
	Bordetella pertussis	Whooping cough (pertussis)	12–20 days
	Influenza virus	Influenza	18–36 hours
	Measles virus *(Morbillivirus)*	Measles (rubeola)	11–14 days
	Rubella virus *(Rubivirus)*	German measles (rubella)	2–3 weeks
	Epstein-Barr virus *(Lymphocryptovirus)*	Infectious mononucleosis	2–6 weeks
	Varicella-zoster virus *(Varicellovirus)*	Chickenpox (varicella) (primary infection)	14–16 days
	Histoplasma capsulatum (fungus)	Histoplasmosis	5–18 days
Gastrointestinal tract	*Shigella* spp.	Bacillary dysentery (shigellosis)	1–2 days
	Brucella spp.	Brucellosis (undulant fever)	6–14 days
	Vibrio cholerae	Cholera	1–3 days
	Salmonella enterica	Salmonellosis	7–22 hours
	Salmonella typhi	Typhoid fever	14 days
	Hepatitis A virus *(Hepatovirus)*	Hepatitis A	15–50 days
	Mumps virus *(Rubulavirus)*	Mumps	2–3 weeks
	Trichinella spiralis (helminth)	Trichinosis	2–28 days

*All pathogens are bacteria, unless indicated otherwise. For viruses, the viral species and/or genus name is given.
†These pathogens can also cause disease after entering the body via the gastrointestinal tract.
‡These pathogens can also cause disease after entering the body via the parenteral route.

1. Portals of entry

TABLE 15.1 **Portals of Entry for the Pathogens of Some Common Diseases** *(continued)*

Portal of Entry	Pathogen*	Disease	Incubation Period
Mucous Membranes			
Genitourinary tract	*Neisseria gonorrhoeae*	Gonorrhea	3–8 days
	Treponema pallidum	Syphilis	9–90 days
	Chlamydia trachomatis	Nongonococcal urethritis	1–3 weeks
	Herpes simplex virus type 2	Herpes virus infections	4–10 days
	Human immunodeficiency virus (HIV)‡	AIDS	10 years
	Candida albicans (fungus)‡	Candidiasis	2–5 days
Skin or Parenteral Route	*Clostridium perfringens*	Gas gangrene	1–5 days
	Clostridium tetani	Tetanus	3–21 days
	Rickettsia rickettsii	Rocky Mountain spotted fever	3–12 days
	Hepatitis B virus *(Hepadnavirus)*†	Hepatitis B	6 weeks–6 months
	Rabiesvirus *(Lyssavirus)*	Rabies	10 days–1 year
	Plasmodium spp. (protozoan)	Malaria	2 weeks

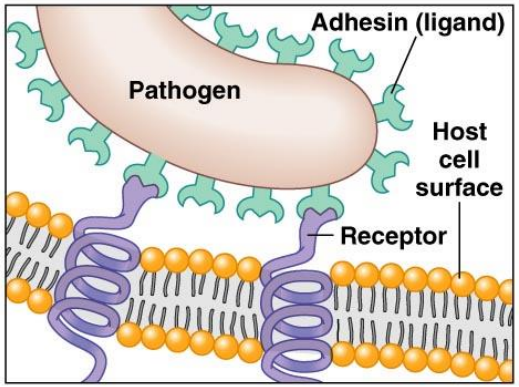
*All pathogens are bacteria, unless indicated otherwise. For viruses, the viral species and/or genus name is given.
†These pathogens can also cause disease after entering the body via the gastrointestinal tract.
‡These pathogens can also cause disease after entering the body via the parenteral route.

2. Infectious Dose- ID_{50}

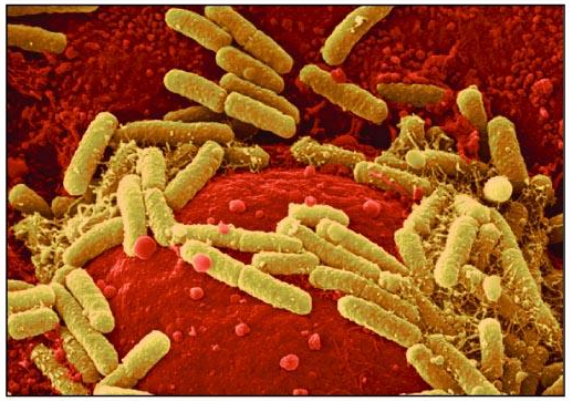
Portal of entry	ID_{50} for *B. anthracis*
Skin	10-50 endospores
Inhalation	10,000-20,000 endospores
Ingestion	250,000-1,000,000 endospores

Organism	ID_{50}
Ebola virus	1-10 particles (non-human primates)
Influenza virus	100- 1000 particles (humans)

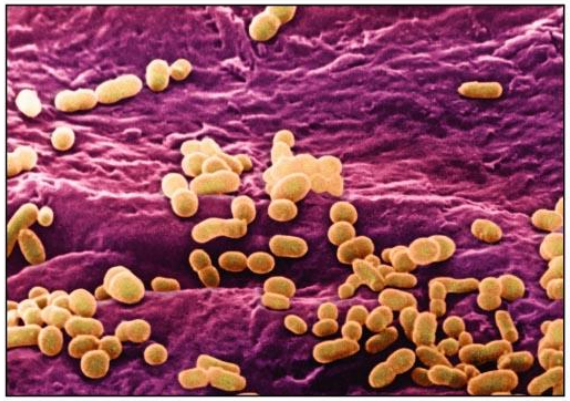
3. Adherence



(a) Surface molecules on a pathogen, called adhesins or ligands, bind specifically to complementary surface receptors on cells of certain host tissues.



(b) *E. coli* bacteria (yellow-green) on human bladder cells. SEM 1 μm



(c) Bacteria (yellow) adhering to human skin. SEM 1 μm

1. Capsules

2. Pili and fimbriae

3. Biofilms

3. Other adhesins
   - Glycoproteins
   - Lipoproteins

Figure 15.1 - Overview

4. Penetration, evasion and damage- exoenzymes and other substances

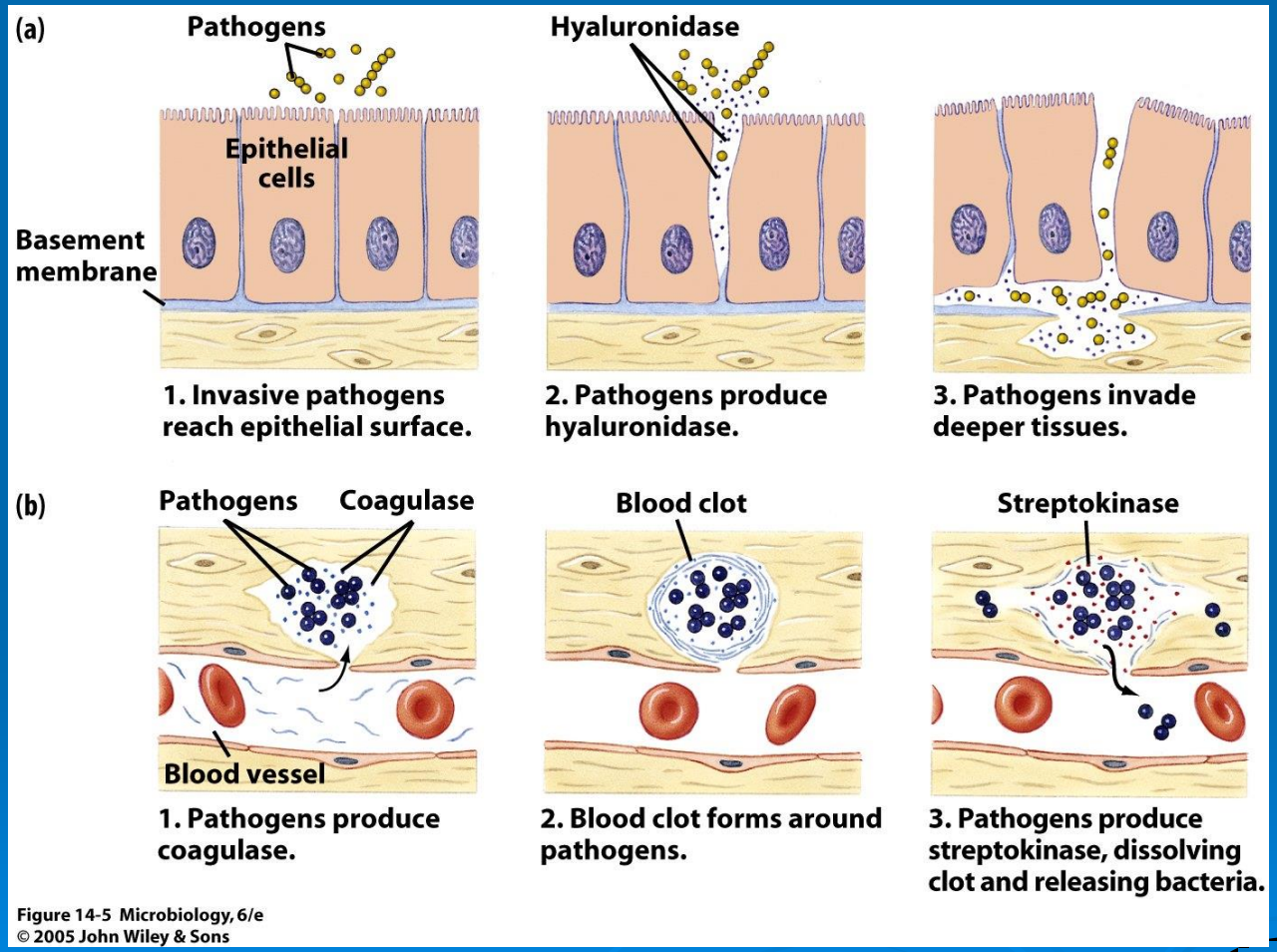
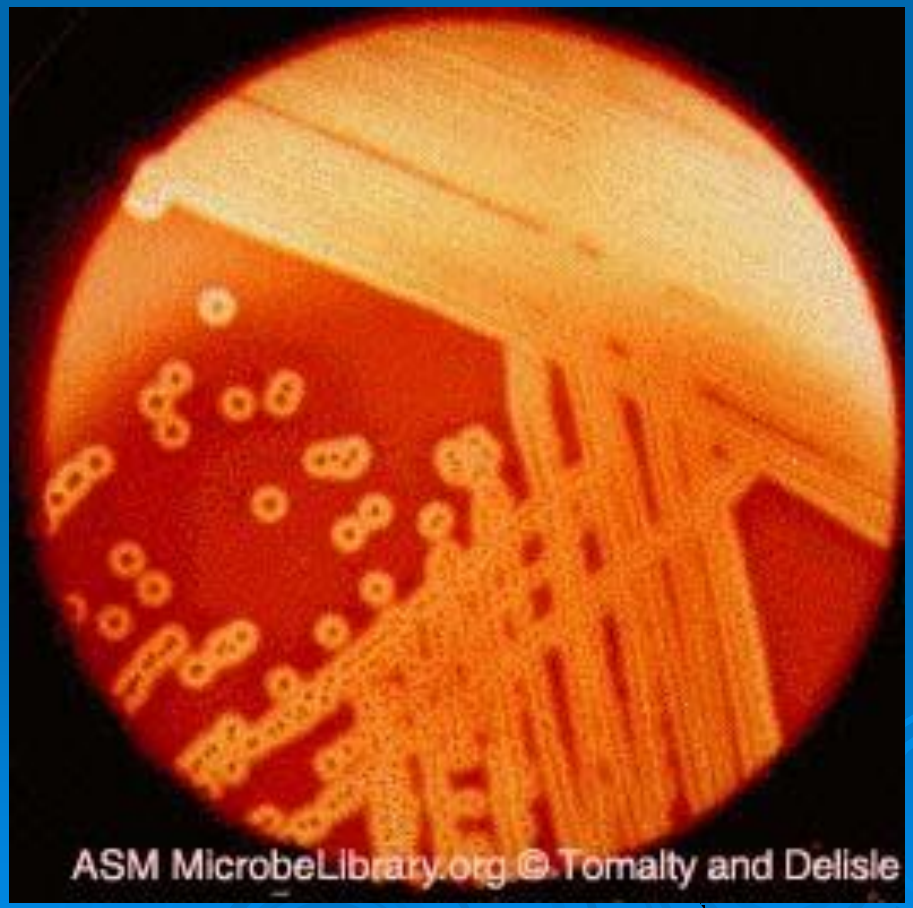


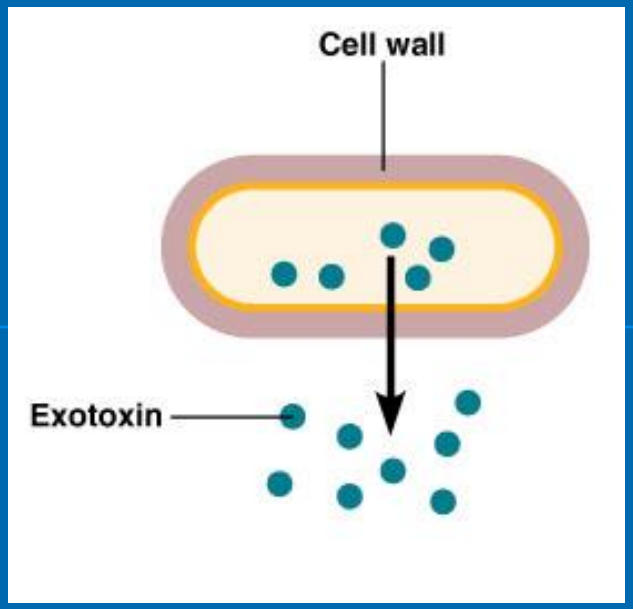
Figure 14-5 Microbiology, 6/e

1. Hyaluronidase
2. Coagulase
3. Kinase
4. IgA protease
5. Siderophores

4. Penetration, evasion and damage- TOXINS



Exotoxins

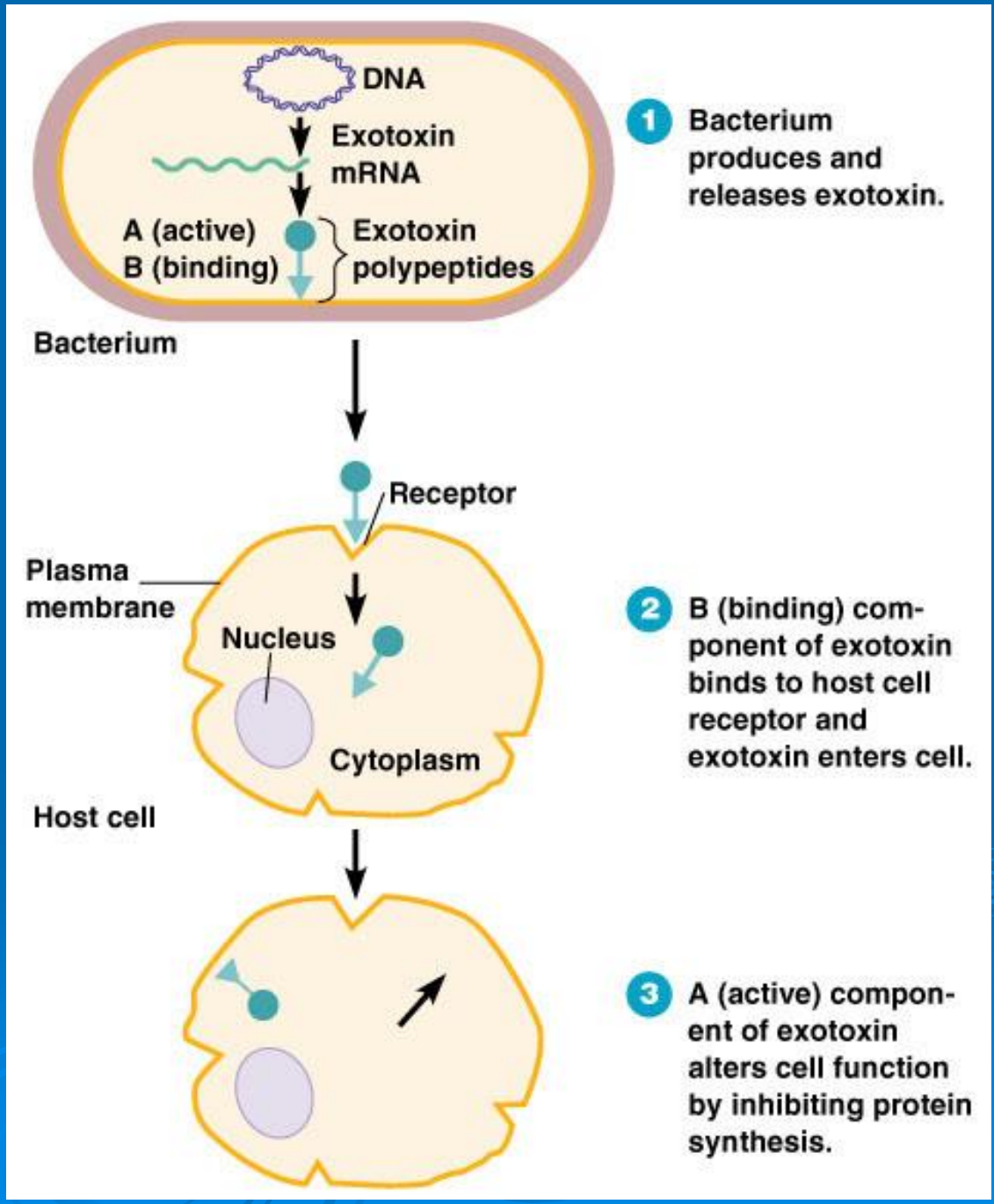


Exotoxin	
Source	Mostly Gram + (can be Gram -)
Metabolic product	By-products of growing cell
Chemistry	Protein, water soluble, heat labile
Fever?	No
Neutralized by antitoxin	Yes
LD_{50}	Small - Very potent 1 mg of *Clostridium botulinum* toxin can kill 1 million guinea pigs

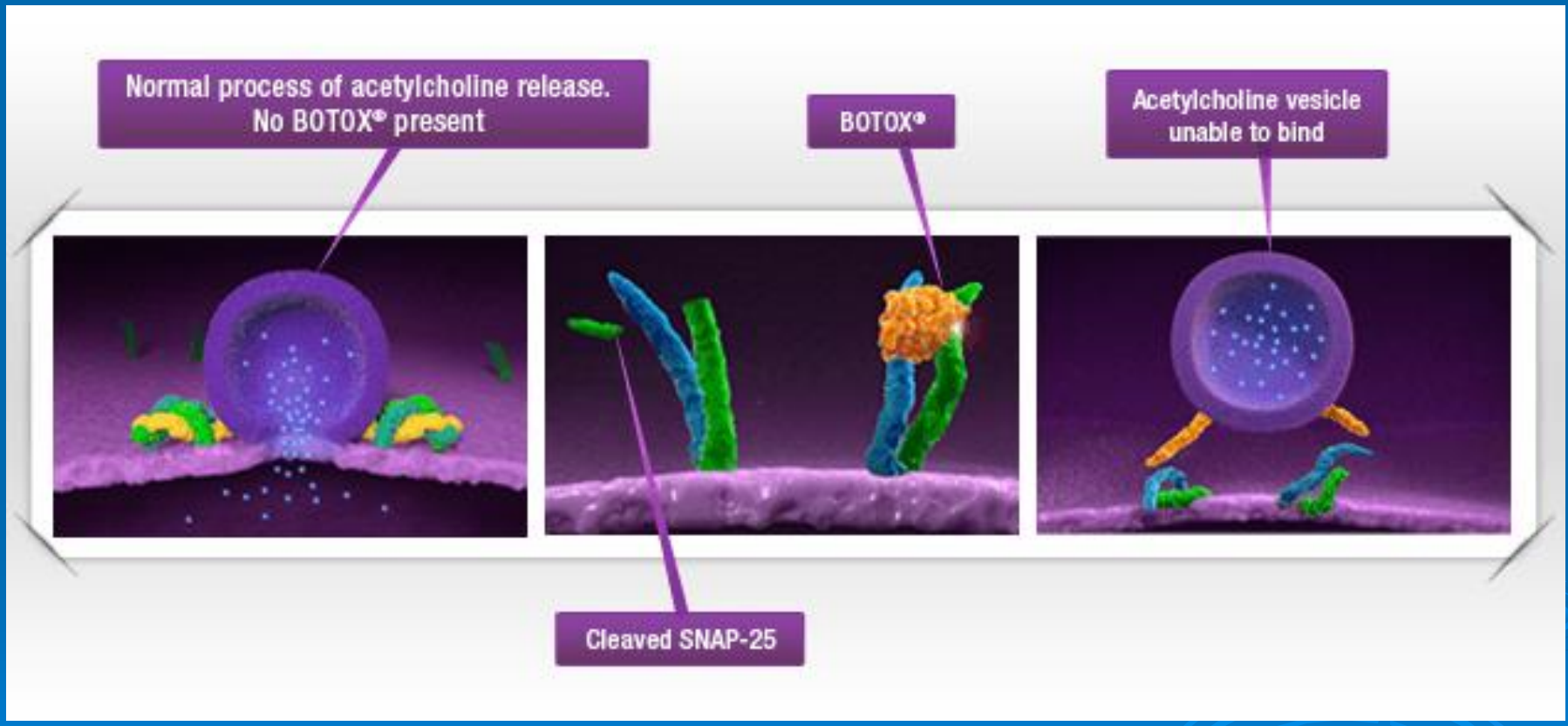
Types of Exotoxins:

1. A-B toxins

Ex. *Clostridium botulinum* toxin

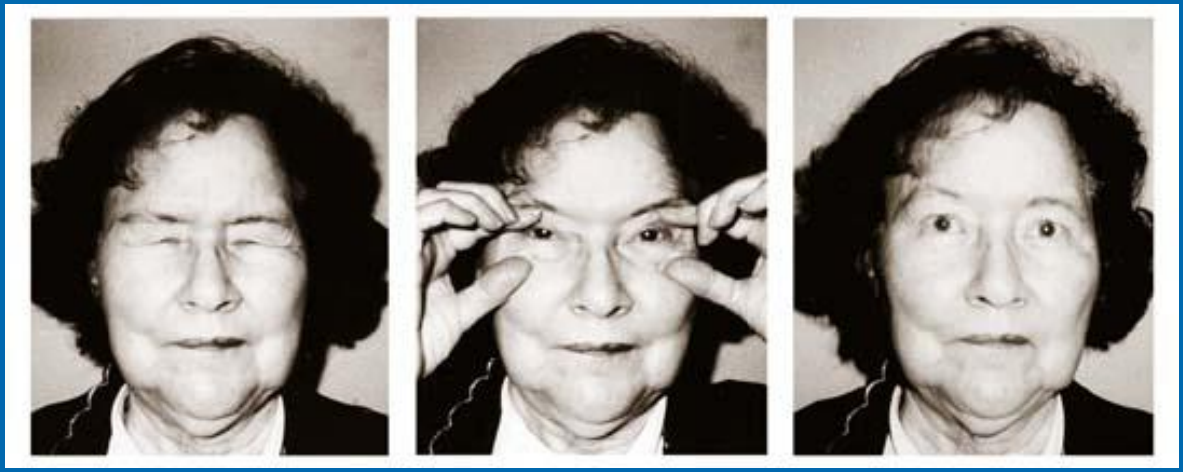


Botulinum toxin (BOTOX) prevents acetylcholine release at neuromuscular junction



http://www.botoxmedical.com/Blepharospasm/MechanismOfAction

BOTOX:
medical applications



Joseph Jankovic, M.D., professor of neurology, Baylor College of Medicine, Houston, Texas

Blepharospasm

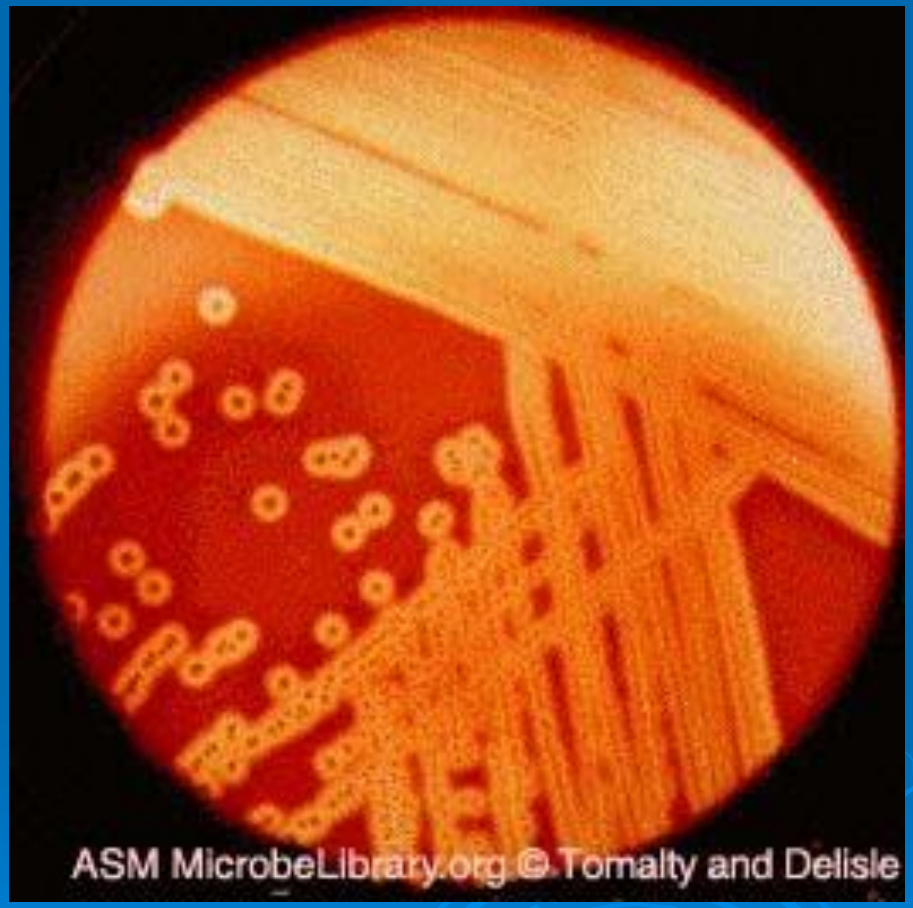
Hyperhidrosis

BOTOX:
cosmetic applications

Types of Exotoxins:

2. Membrane disrupting or cytolytic toxins

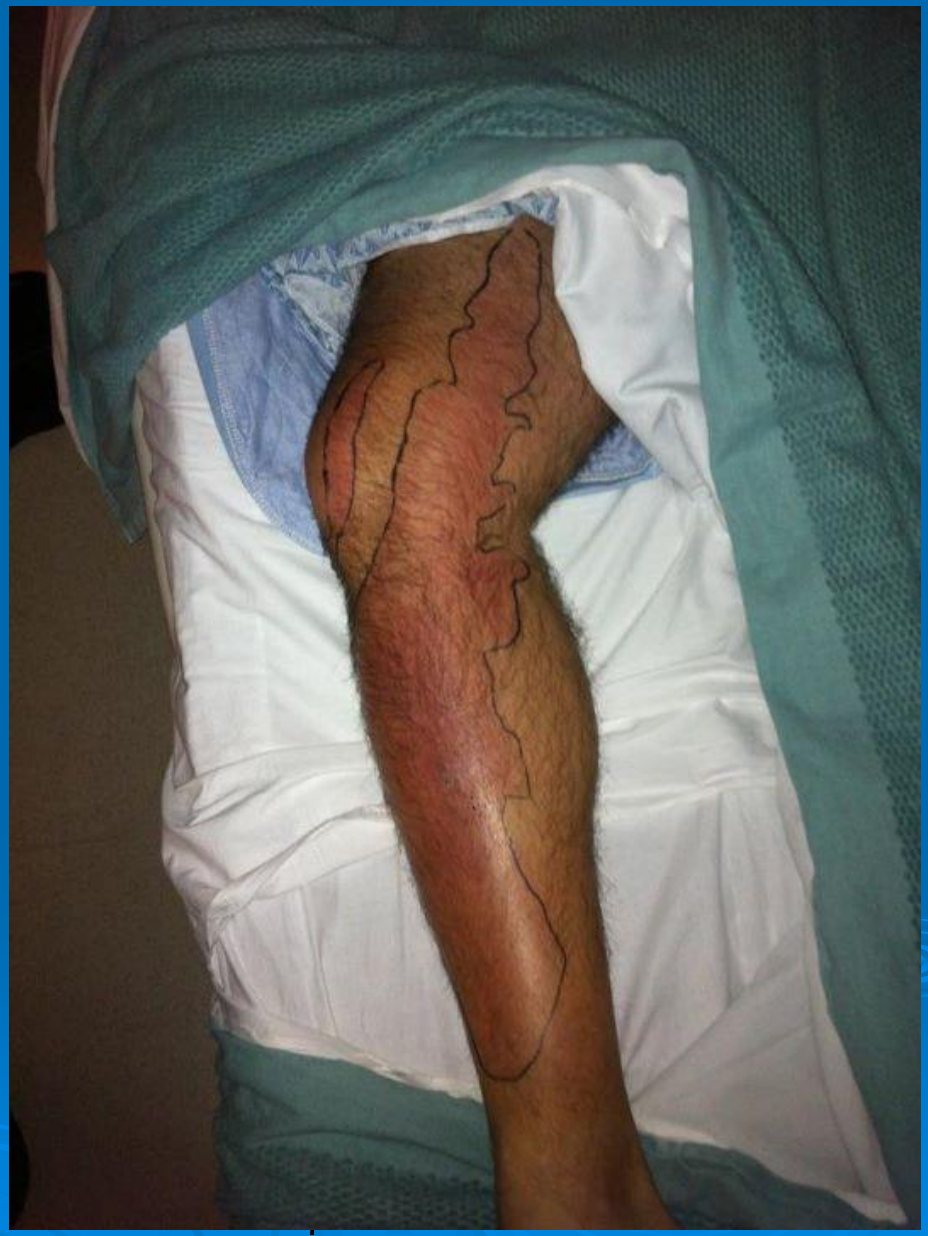
Ex. Hemolysins and leukocidins



Types of Exotoxins:

3. Superantigens

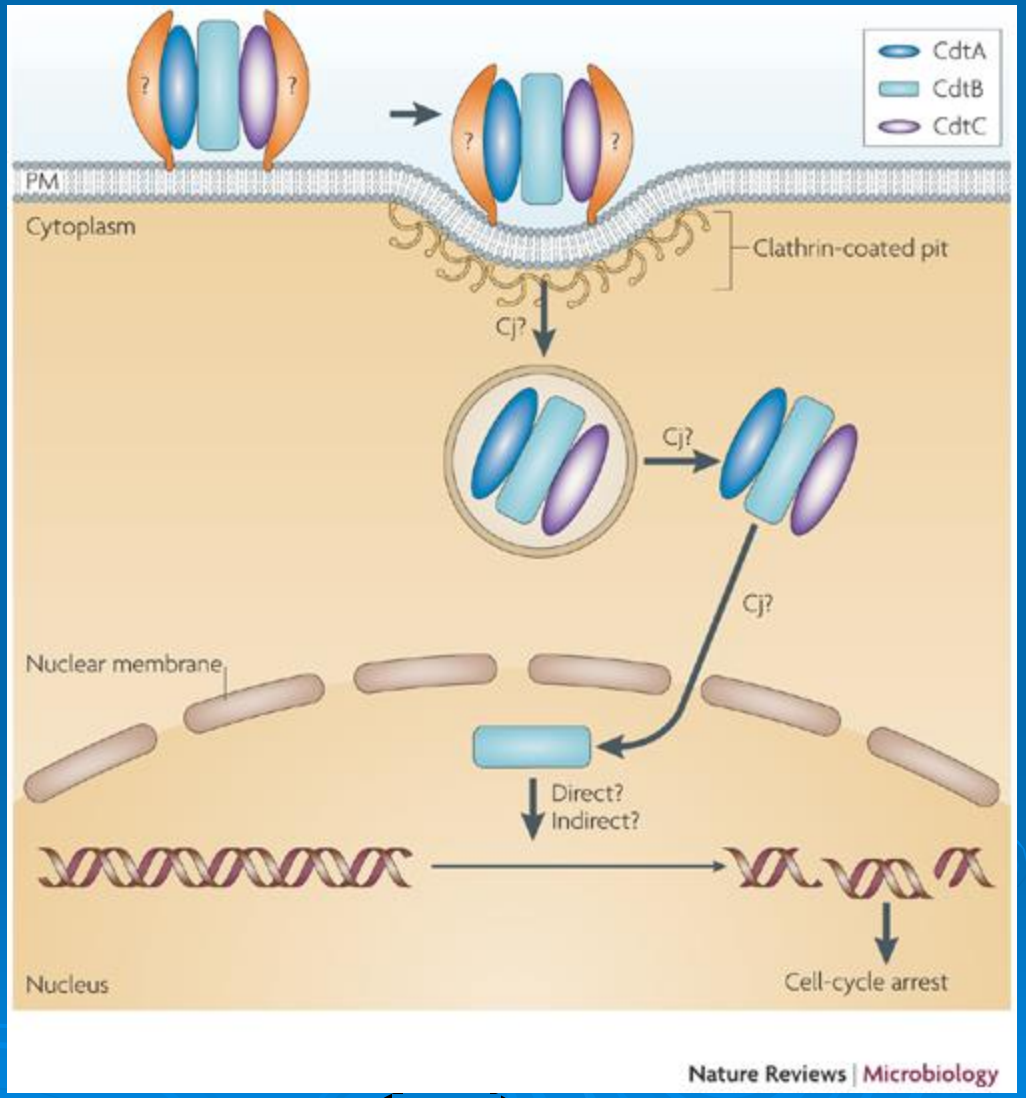
Ex. Staphylococcal and Streptococcal toxins that cause toxic shock syndrome



Types of Exotoxins:

4. Genotoxins (usually A-B)

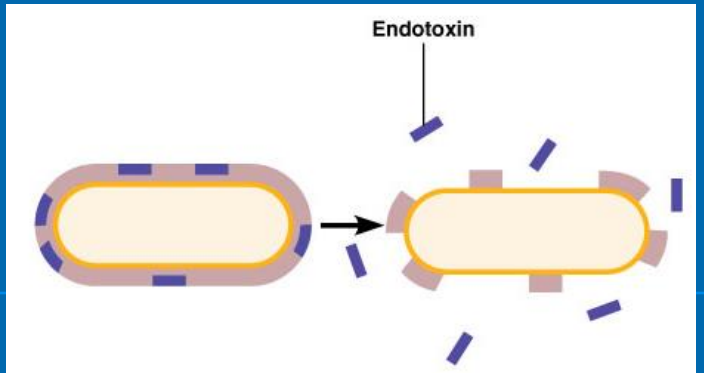
Ex. Cytolethal Distending Toxin (CDT) that causes mutations, disrupts cell division and may lead to cancer



TOXINS	Description	Lysogenic conversion
• *Streptococcus pyogenes- Erythrogenic toxin*	Membrane-disrupting superantigens. Erythrogenic.	+
• *Clostridium botulinum- Botulinum toxin*	A-B toxin. Neurotoxin - flaccid paralysis Botox	+
• *Vibrio cholerae- Vibrio Enterotoxin*	A-B toxin. Enterotoxin. Stimulates cAMP to cause severe diarrhea	+
• *Staphylococcus aureus- Enterotoxin*	Superantigen. Enterotoxin.	

Table 15.2

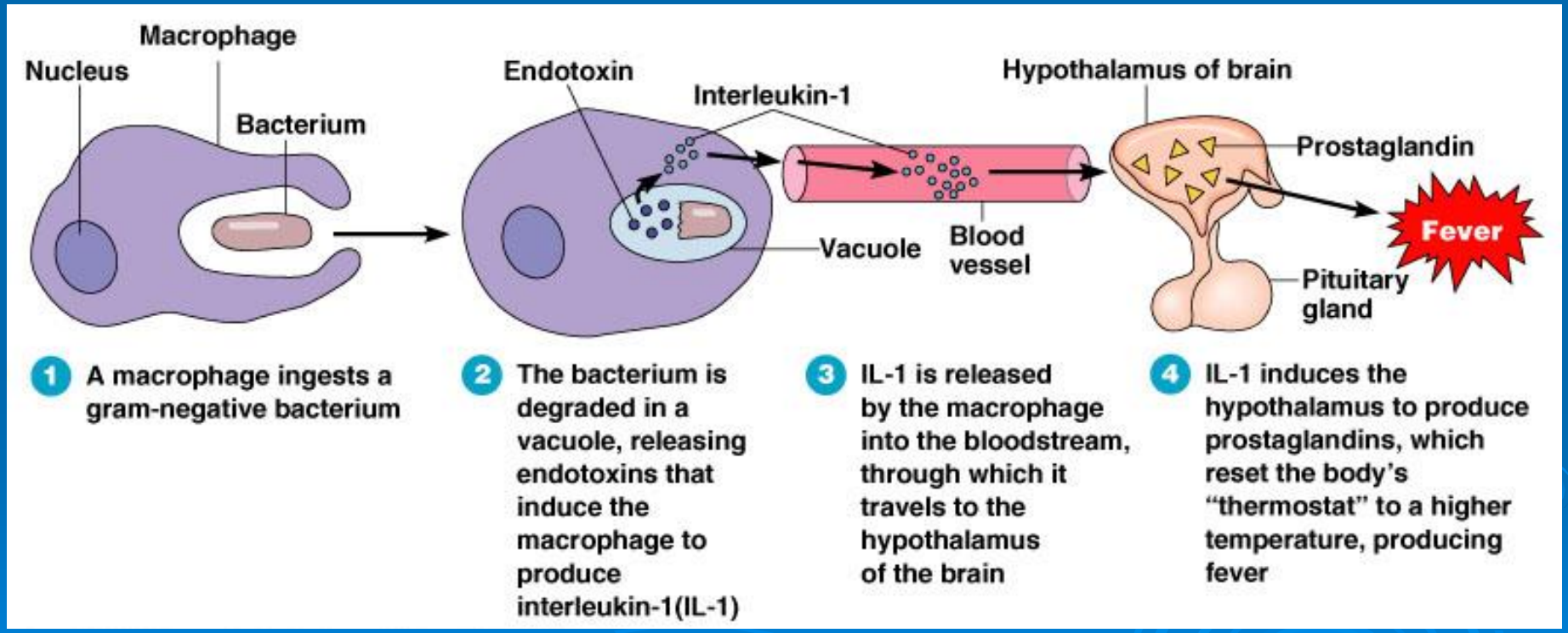
Endotoxins



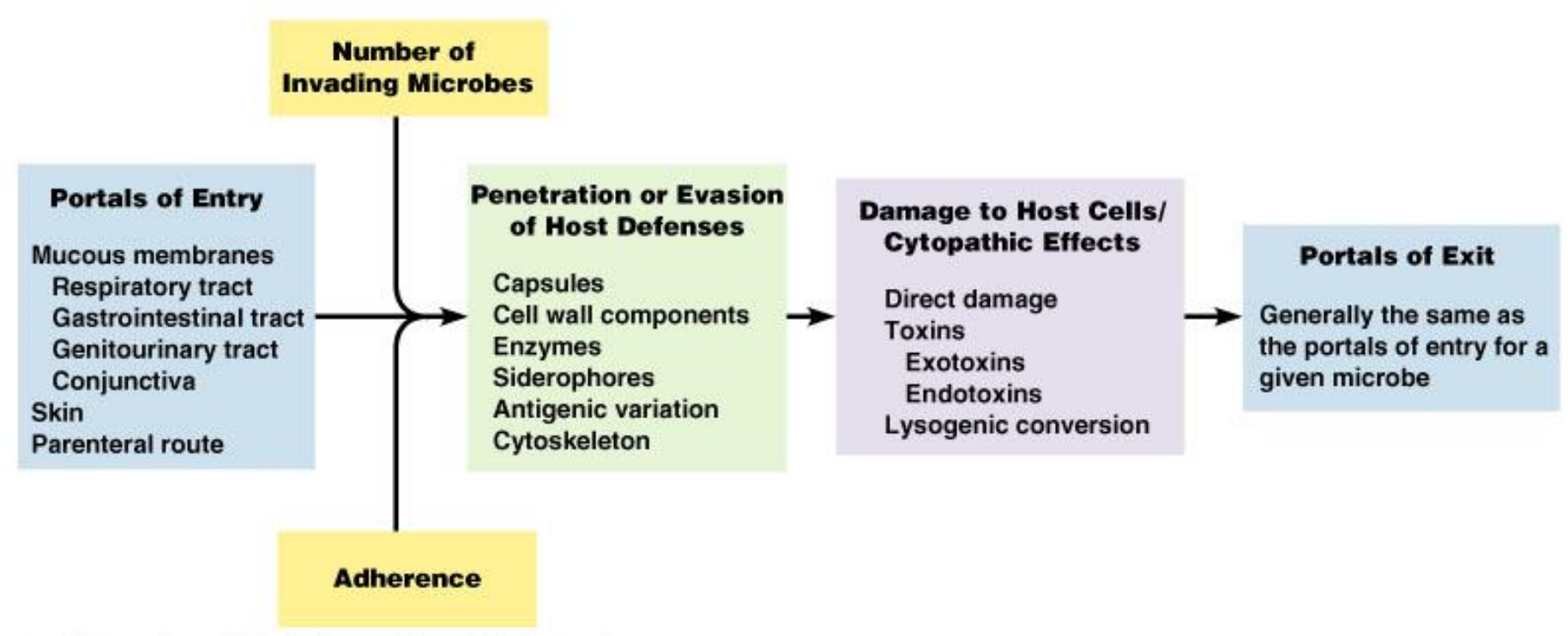
(b) **Endotoxins** are part of the outer portion of the cell wall (lipid A; see Figure 4.12c) of gram-negative bacteria. They are liberated when the bacteria die and the cell wall breaks apart.

Source	Gram –
Metabolic product	Present in LPS of outer membrane
Chemistry	Lipid, heat stable
Fever?	Yes
Neutralized by antitoxin	No
LD_{50}	Relatively large- 10 million times greater than LD_{50} for botulinum toxin

Endotoxins


Macrophage
Nucleus
Bacterium
Endotoxin
Interleukin-1
Vacuole
Blood vessel
Hypothalamus of brain
Prostaglandin
Fever
Pituitary gland
1 A macrophage ingests a gram-negative bacterium
2 The bacterium is degraded in a vacuole, releasing endotoxins that induce the macrophage to produce interleukin-1(IL-1)
3 IL-1 is released by the macrophage into the bloodstream, through which it travels to the hypothalamus of the brain
4 IL-1 induces the hypothalamus to produce prostaglandins, which reset the body's "thermostat" to a higher temperature, producing fever

Mechanisms of pathogenicity



Independent Study

Microbes and you- who will win the war?
Feel free to modify word doc so that you have room to write out answers. **TYPED APO-5 is due on the day of Exam 3.**

APO-5 will encompass several lectures and includes Chapters 15-18. It is due the day of Exam 3.

Mechanisms of Virulence

For each virulence factor below, describe whether it contributes to increased virulence by being invasive or toxic or both, and how it helps the pathogen to overcome a host defense mechanism.

1. *Neisseria gonorrhea* produces pili and adhesins specific to the human urogenital epithelium.

2. The pilin genes in *Neisseria gonorrhea* periodically recombine.

3. Many *Streptococcus* strains coat themselves in a slimy glycocalyx.

4. *Staphylococcus aureus* can synthesize hemolysins.

5. *Chlamydia* infects a host phagocyte and prevents lysosome fusion.

Etc.