PowerPoint® Lecture Presentations

CHAPTER 25

Microbial Infection and Pathogenesis

Microbiologie 2: Les 11

I. Human-Microbial Interactions

Schema Micro2

Les	Hoofdstuk	Paragraaf
1	7	7.1, 7.2, 7.3, 7.8
2	7	7.5, 7.6, 7.7
3	7	7.9, 7.10, 7.11
4	7	7.12, 7.13, 7.14, 7.15
5	5	5.1, 5.2, 5.3, 5.4, 5.5, 5.6
6	5 en 11	5.7, 5.8, 11.1, 11.2
7	11	11.6, 11.7, 11.8 (MS2 niet)
8	11	11.9, 11.11,
9	11	11.13, 11.15, 11.16
10	24	24.1, 24.2, 24.5
11	25	25.1, 25.2, 25.3, 25.5
12	25	25.6, 25.7, 25.8
13	28 en 8	28.5, 28.6, 28.7, 8.11
14	Oefententamen	Alles

NB: Hfdstnrs niet accuraat

I. Human-Microbial Interactions

- 25.1 Microbial Adherence
- 25.2 Colonization and Invasion
- 25.3 Pathogenicity, Virulence, and Attenuation

25.1 Microbial Adherence

- Infection
  - situation in which a microorganism is established and growing in a host, whether or not the host is harmed
- Pathogens
  - microbial parasites that cause disease, or tissue damage in a host
- Pathogenicity
  - the ability of a parasite to inflict damage on the host

25.1 Microbial Adherence

- Adherence is the enhanced ability of microbes to attach to host tissues. It is necessary for entry into the host, but not sufficient to start disease. (Figure 25.1)

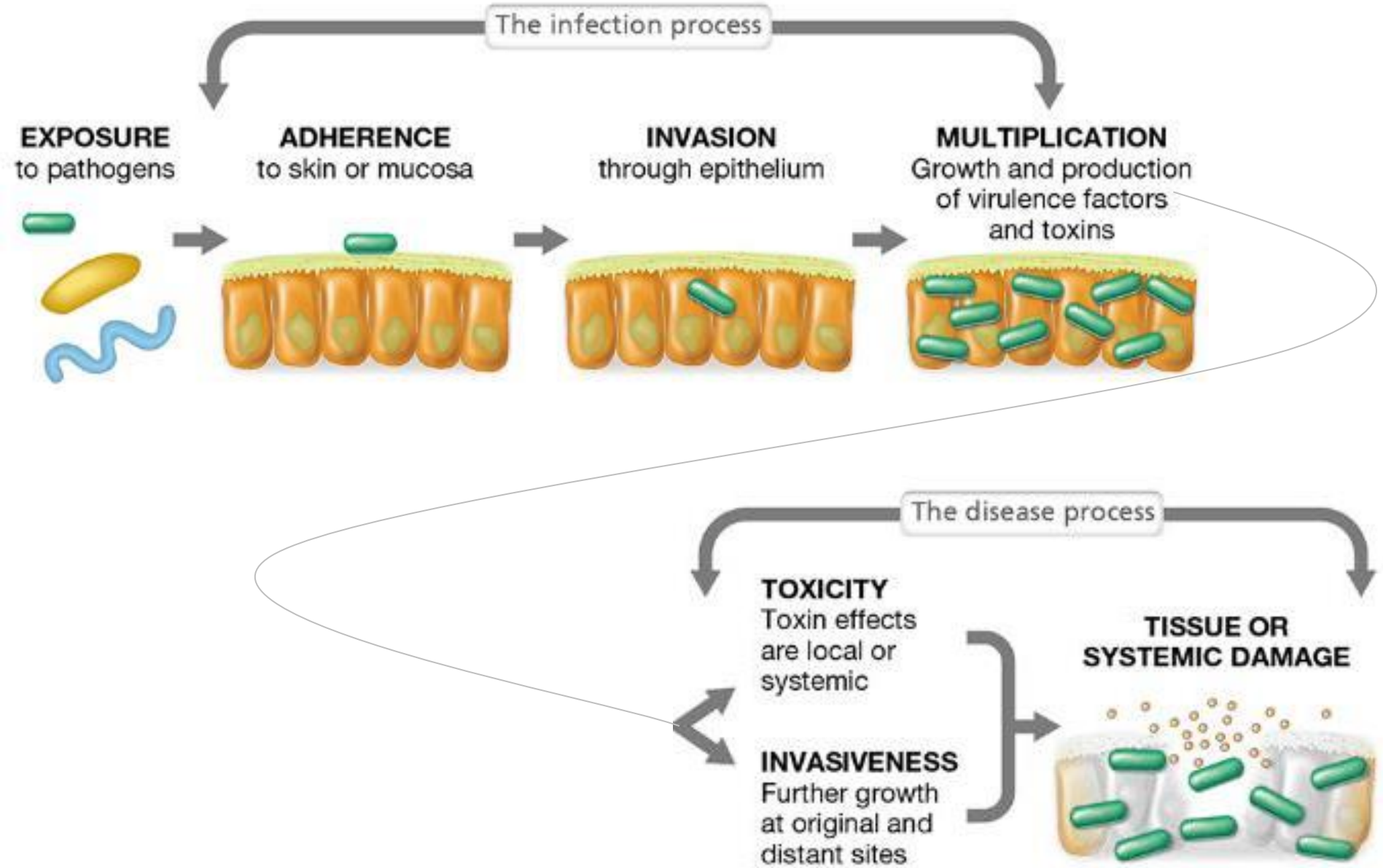


Figure 25.1

25.1 Microbial Adherence

- There are many different receptors coating both the pathogen and tissues where the bacteria or virus binds.

- *Adhesins* are glycoproteins or lipoproteins found on the pathogen's surface that enable it to bind to host cells. (Figure 25.2b)

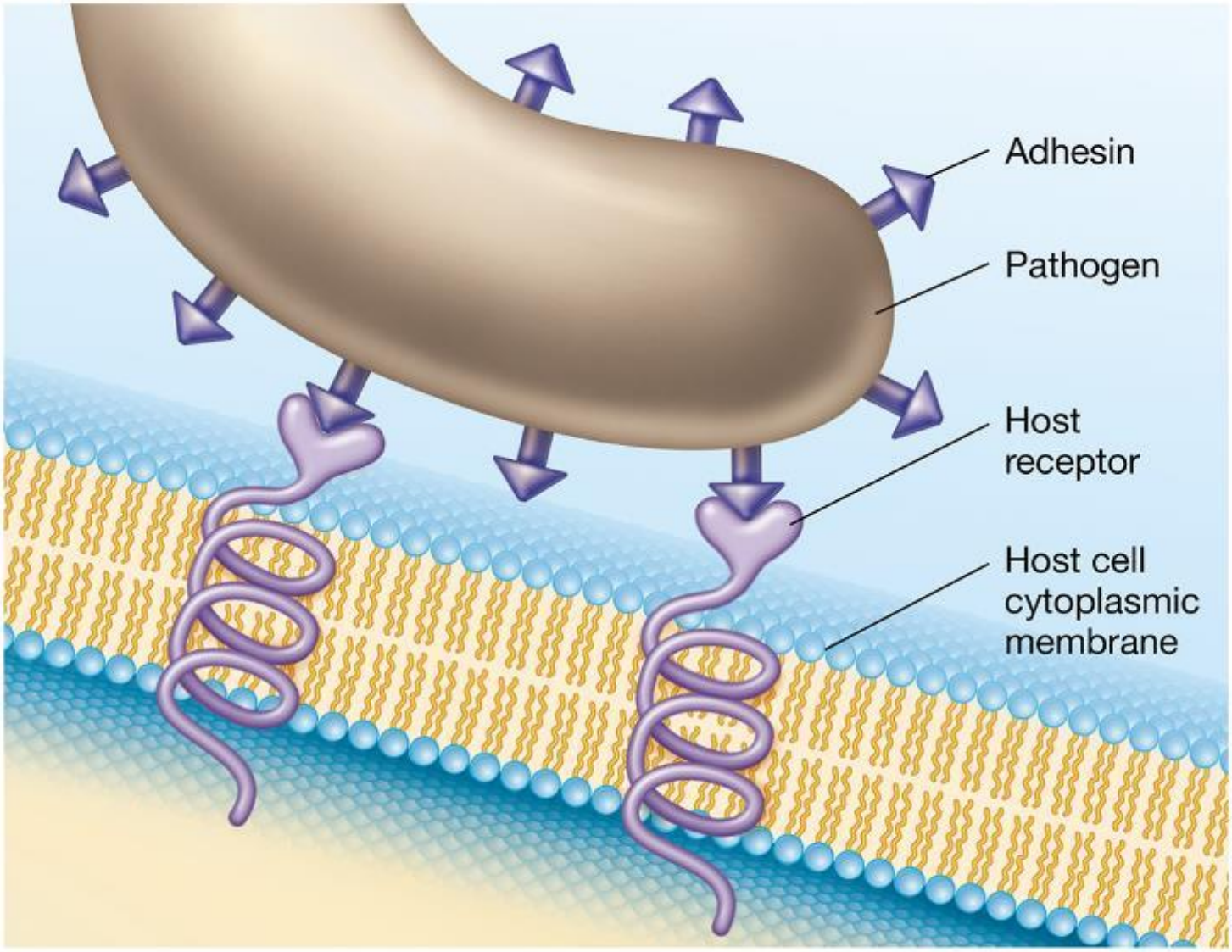


Figure 25.2b

25.1 Microbial Adherence

- Selective Adherence
  - Like viruses, bacteria may also adhere selectively to specific membrane proteins => tissue selective infection (e.g. Opa in *N. gonorrhoeae*)

25.1 Microbial Adherence

- Adherence Structures: Capsules

- The bacterial capsule forms a thick coating outside the plasma membrane and cell wall and serves two important functions in bacterial pathogenicity.
  - The capsule is both sticky and contains specific receptors to facilitate attachment on host tissues. (Figure 25.3b, c)
  - Capsules, such as those found in *Streptococcus pneumoniae*, protect the bacteria from ingestion by white blood cells. (Figure 25.4)

Biologie 3!

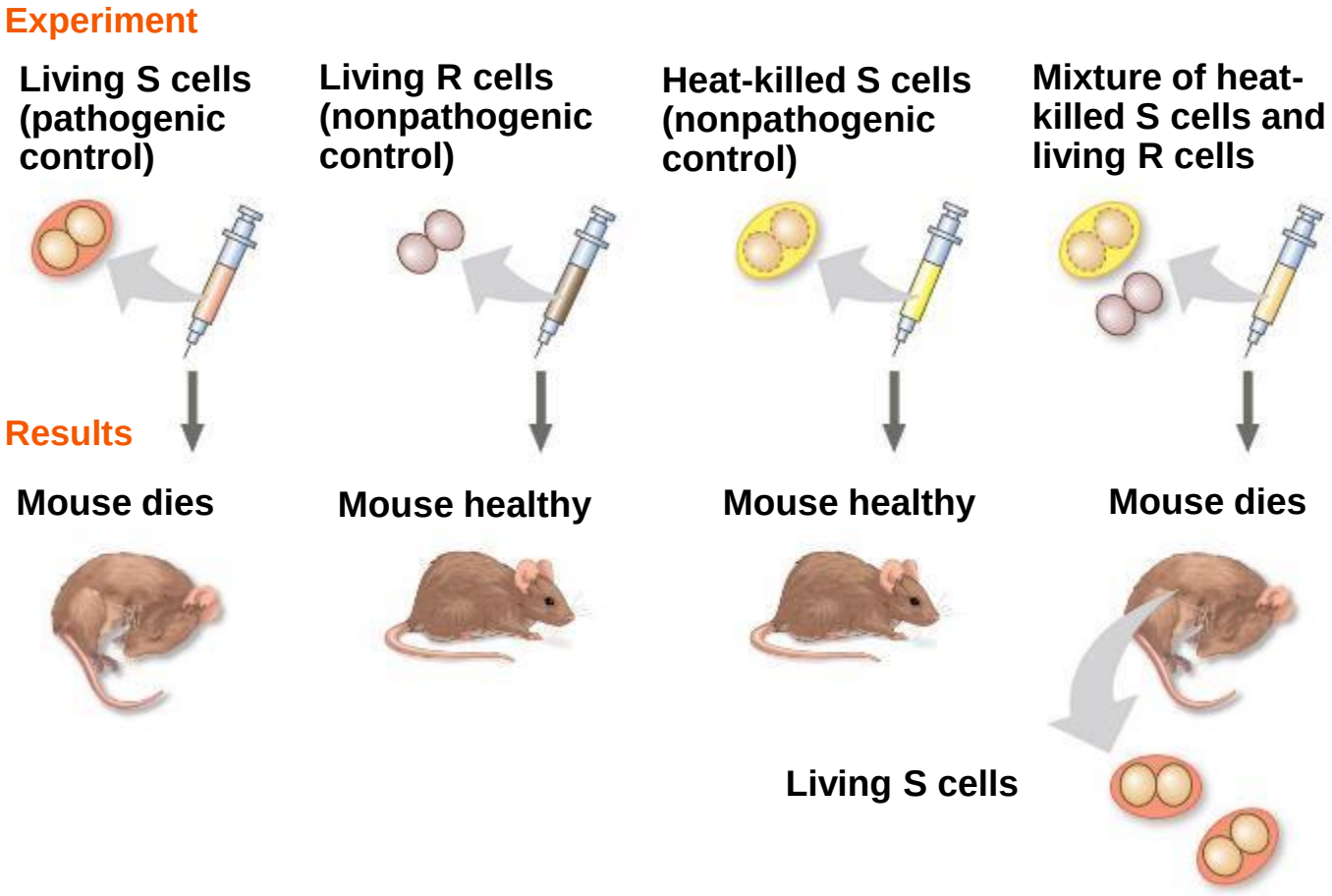
Overnemen van eigenschappen

Frederick Griffith in 1928

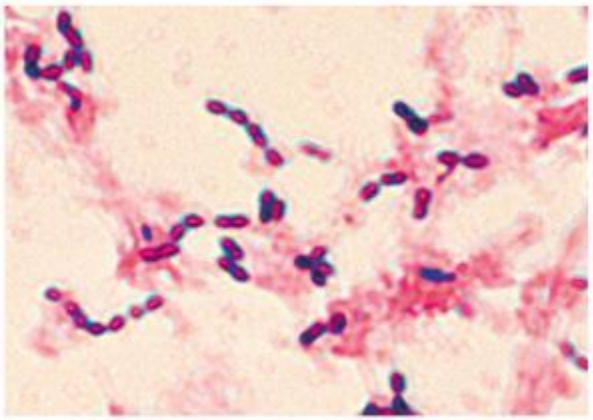
2 *Streptococcus pneumoniae* stammen:

S: pathogeen (=ziekmakend),

R: niet pathogeen

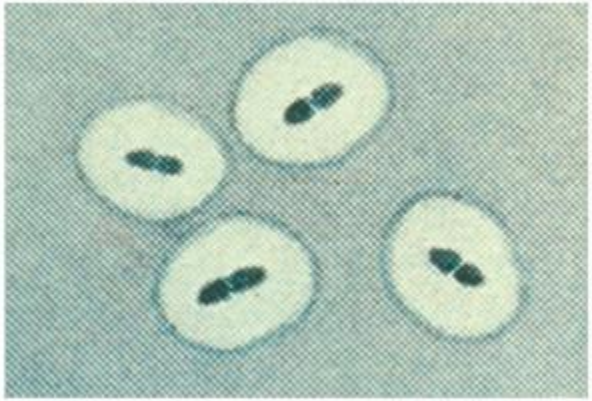


Strep. pneumoniae



CDC/PHIL, M. Miller

(a)



CDC/PHIL

(b)

CDC/PHIL, Dr. Richard Facklam

(c)

Figure 25.4

Athrax (b)

en

E. coli (c)

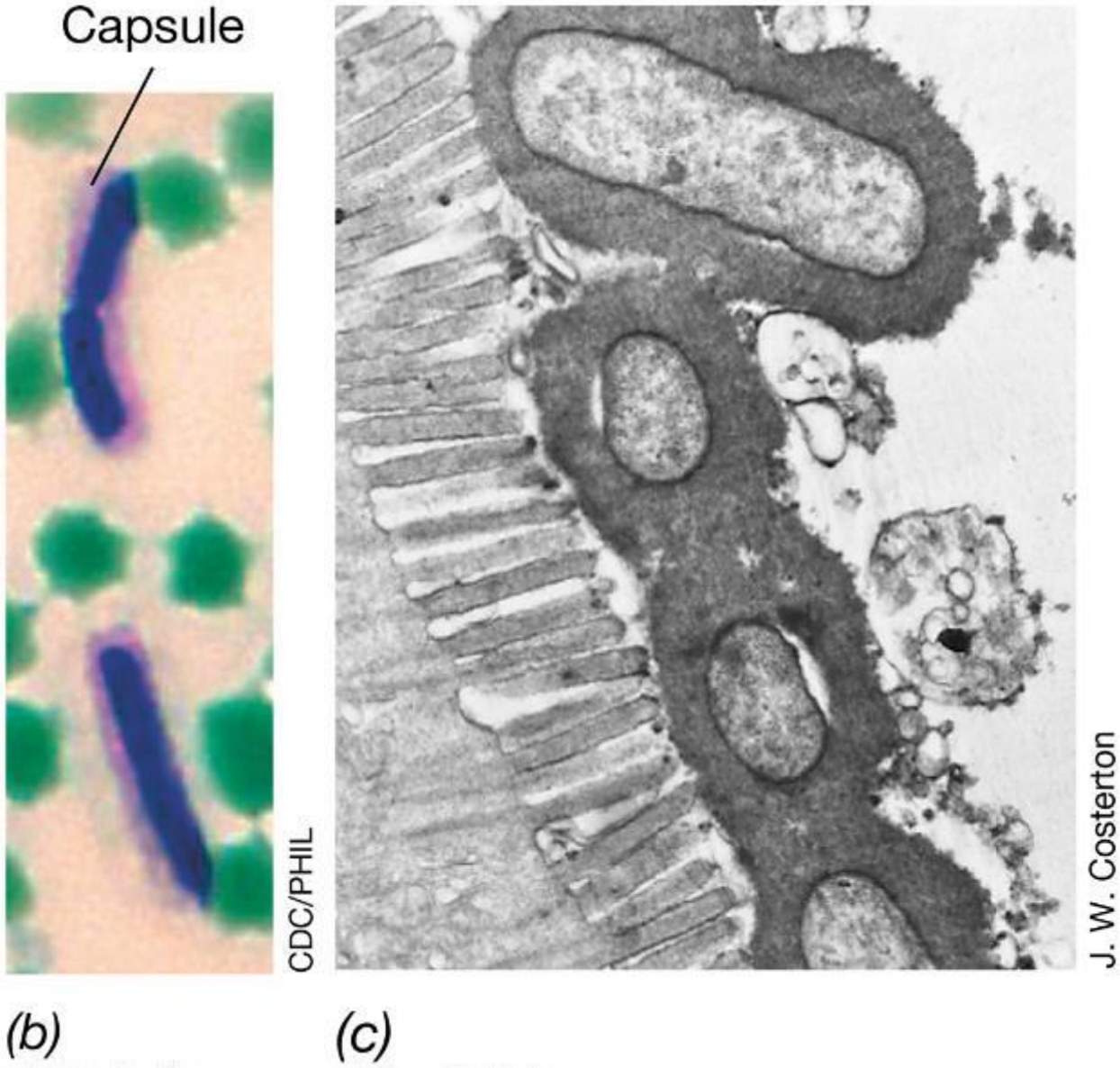


Figure 25.3b, c

25.1 Microbial Adherence

- Adherence Structures: Fimbriae, Pili, and Flagella
  - Fimbriae, Flagella, and pili are bacterial cell surface protein structures that function in attachment. (Figure 25.5)

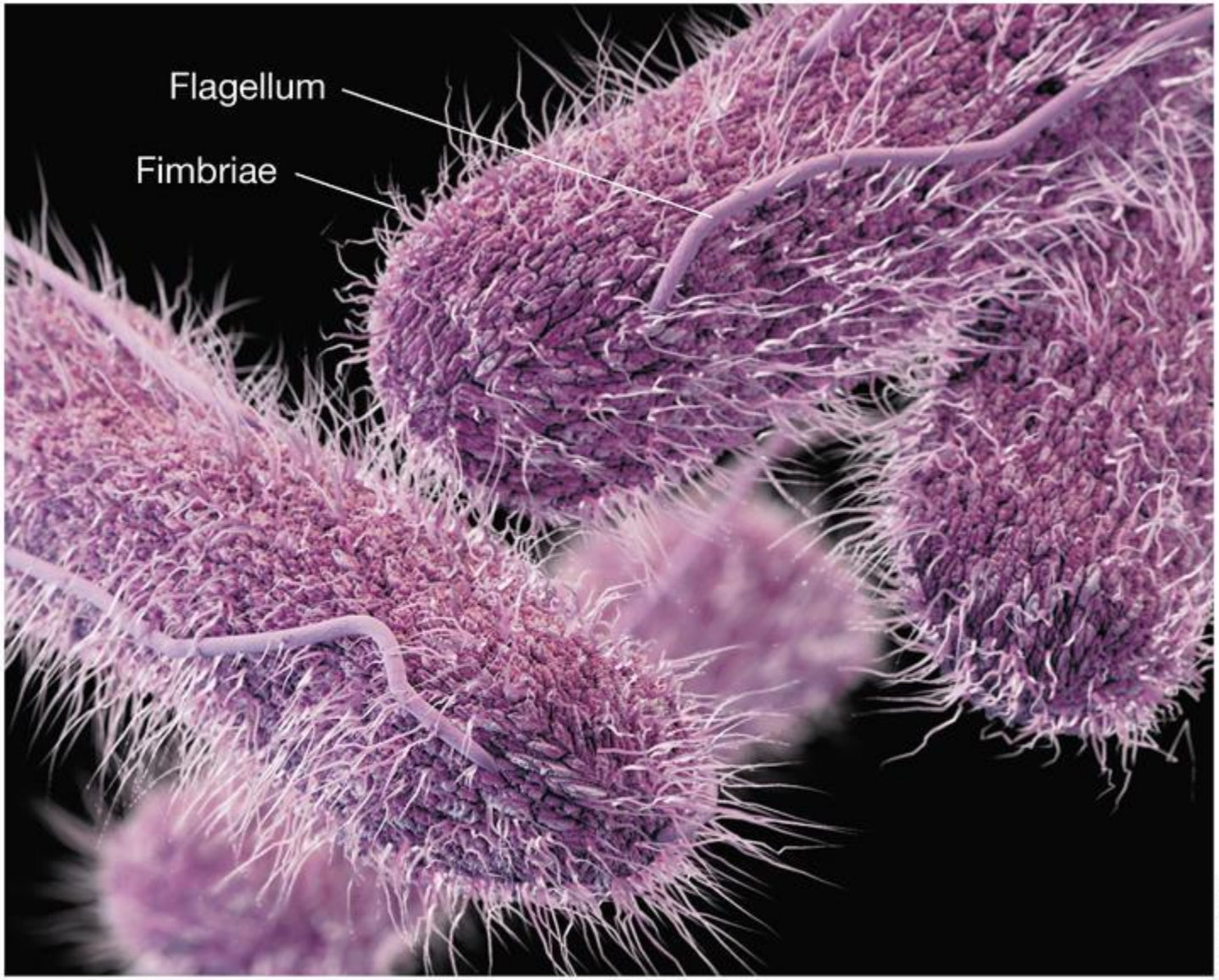


Figure 25.5

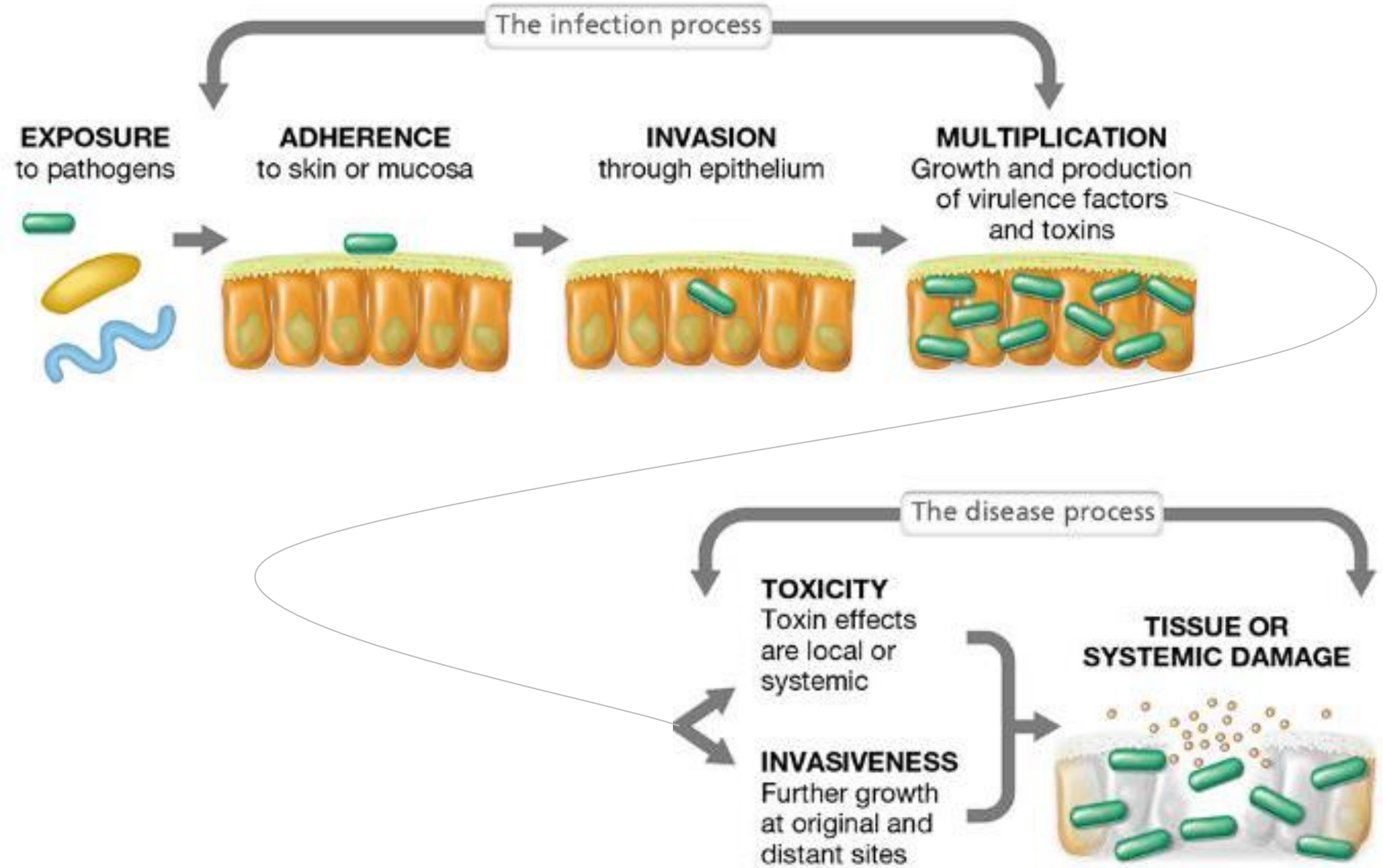


Figure 25.1

25.2 Colonization and Invasion

- Colonization is the growth of microorganisms after they've gained access to host tissues.
  - The process begins at birth.
- Typically starts with mucous membranes, or tightly packed epithelial cells coated in mucus, a thick liquid secretion of glycoproteins

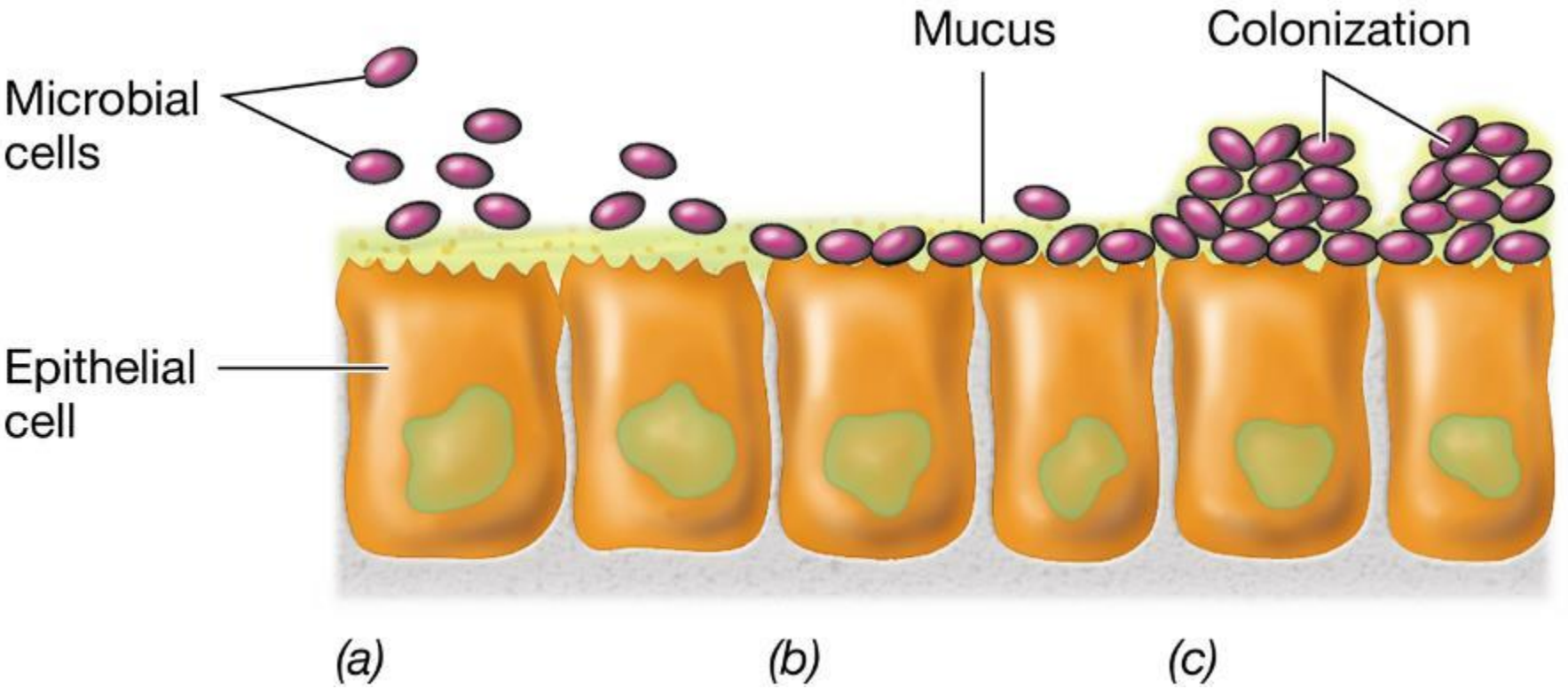


Figure 25.6

25.2 Colonization and Invasion

- Growth of the Microbial Community: An Example from Human Dental Caries
  - Dental caries, or cavities, are an oral microbial disease.
  - After initial contact, *Streptococcus sobrinus* and *Streptococcus mutans* attach and reproduce and form a biofilm called plaque. (Figure 25.7a, b).

Biofilm

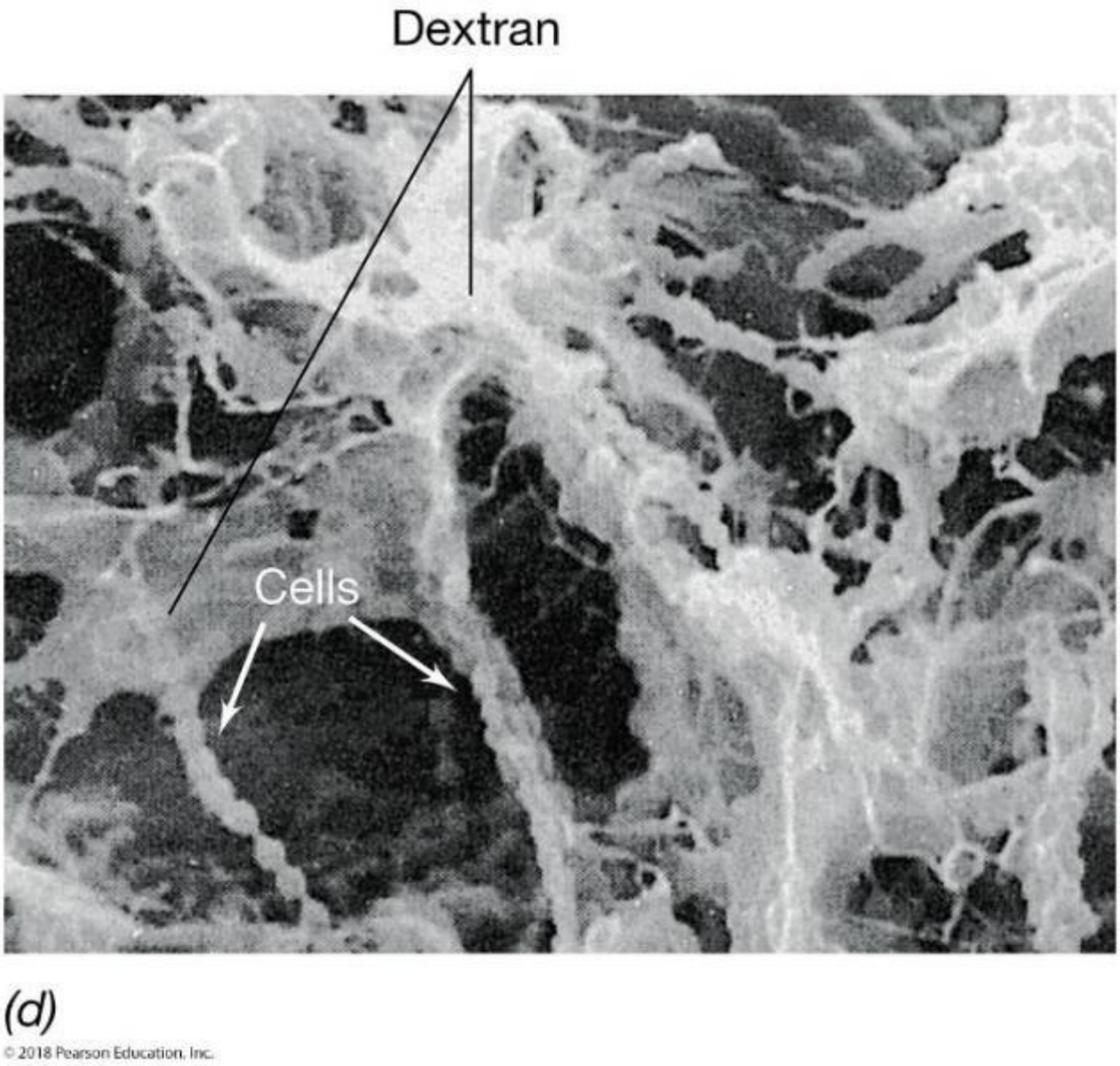


Figure 25.7d

25.2 Colonization and Invasion

- Invasion and Systemic Infection
  - Invasiveness
    - *ability* of a pathogen to grow in host tissue at densities that inhibit host function
  - Bacteremia: the presence of bacteria in the bloodstream
  - Septicemia (Bloedvergiftiging): bloodborne systemic infection
    - may lead to massive inflammation, septic shock, and death
  - Infection: any situation in which a microorganism (not a member of the local flora) *is established* and growing in a host

25.3 Pathogenicity, Virulence, and Attenuation

- Pathogens use various strategies to establish virulence.
  - *Virulence* is the relative ability of a pathogen to cause disease.

25.3 Pathogenicity, Virulence, and Attenuation

- Measuring virulence
  - Virulence can be estimated from experimental studies of the LD_{50} (lethal $dose_{50}$).
    - the amount of an agent that kills 50 percent of the animals in a test group (Figure 25.10)
- Highly virulent pathogens show little difference in the number of cells required to kill 100 percent of the population as compared to 50 percent of the population.

NB: Denk ook terug aan quorum sensing-verhaal! (6.8)

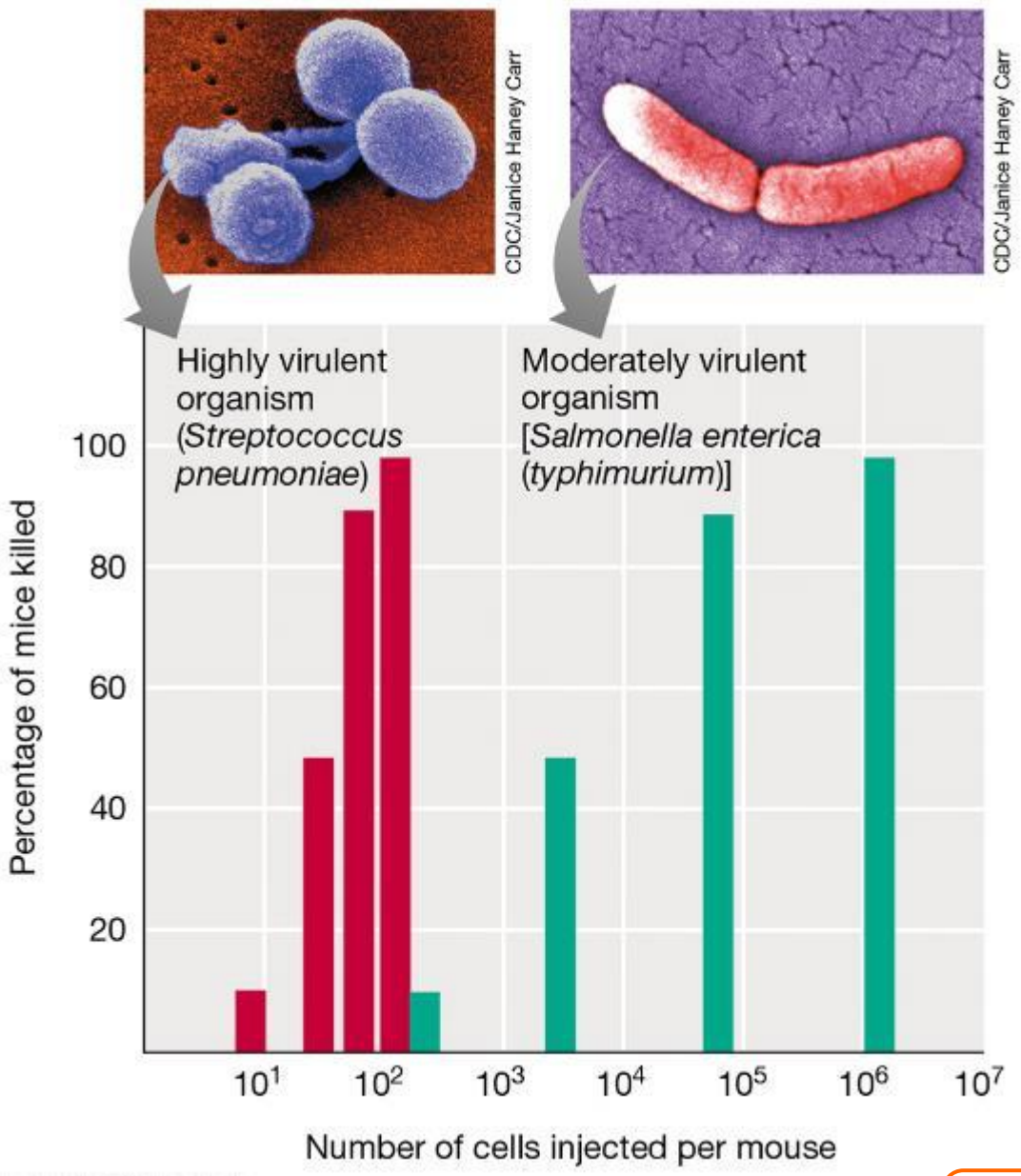


Figure 25.9

25.3 Pathogenicity, Virulence, and Attenuation

- Attenuation
  - the decrease or loss of virulence
- *Attenuated* strains of various pathogens are valuable to clinical medicine because they are often used for the production of viral vaccines.

Escherichia coli O157:H7

Go to:

Escherichia coli

Escherichia coli (*E. coli*) is a Gram-negative, rod-shaped, facultative anaerobic bacterium. This microorganism was first described by Theodor Escherich in 1885. Most *E. coli* strains harmlessly colonize the gastrointestinal tract of humans and animals as a normal flora. However, there are some strains that have evolved into pathogenic *E. coli* by acquiring virulence factors through plasmids, transposons, bacteriophages, and/or pathogenicity islands. These pathogenic *E. coli* can be categorized based on serogroups, pathogenicity mechanisms, clinical symptoms, or virulence factors [33, 47]. Among them, enterohemorrhagic *E. coli* (EHEC) is defined as pathogenic *E. coli* strains that produce Shiga toxins (Stxs) and cause hemorrhagic colitis (HC) and the life-threatening sequelae hemolytic uremic syndrome (HUS) in humans. Several serotypes in EHEC are frequently associated with human diseases such as O26:H11, O91:H21, O111:H8, O157:NM, and O157:H7 [44, 51]. *E. coli* O157:H7 is the most frequently isolated serotype of EHEC from ill persons in the United States, Japan, and the United Kingdom and it the focus of this review.

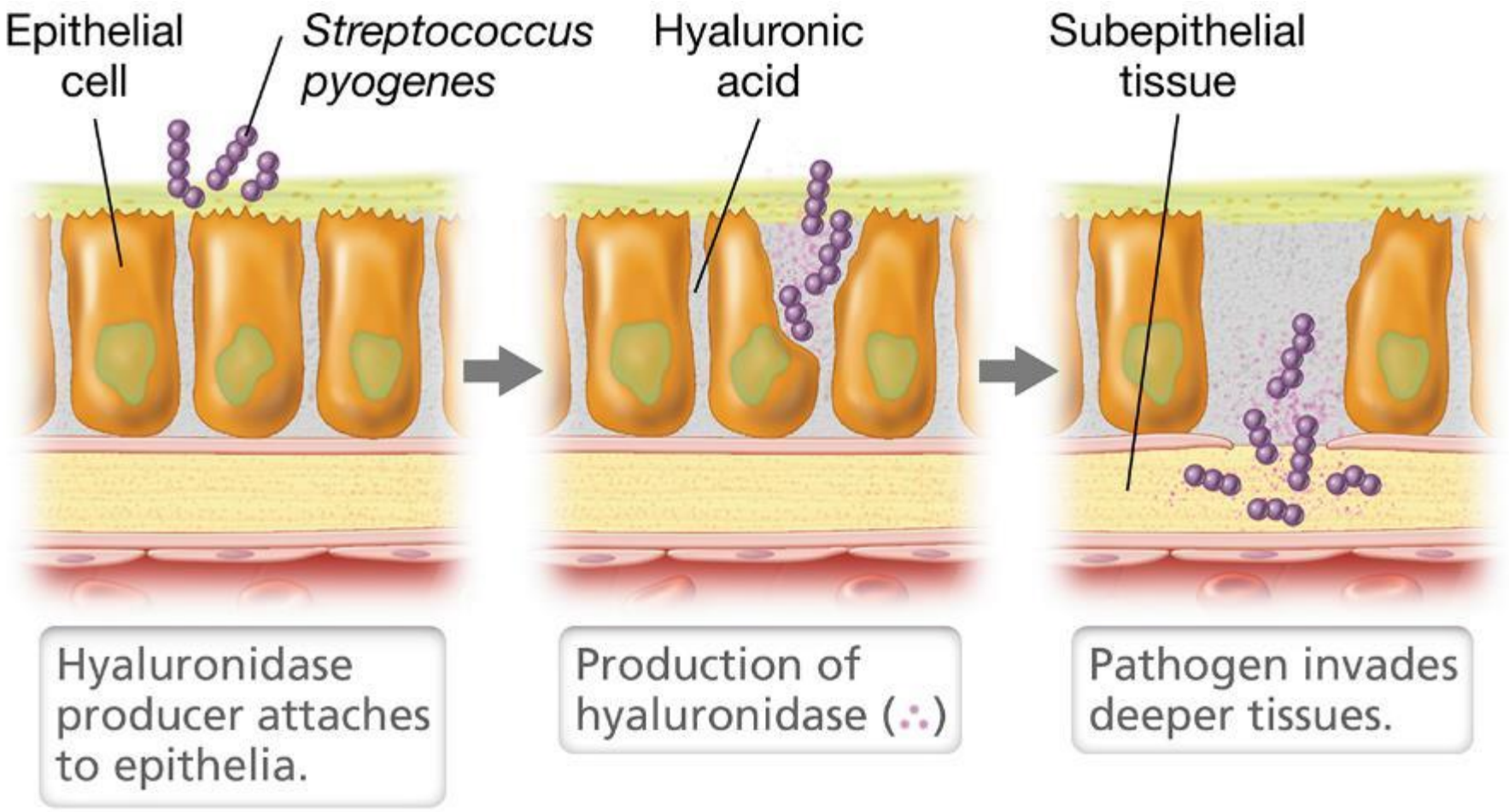
Experiment serial number	Reference	Host type	Agent strain	Route	# of doses	Dose units	Response	Best fit model	Optimized parameter(s)	LD_{50}/ID_{50}
213*	[8]	pig	EHEC O157:H7, strain 86-24	oral (in food)	3	CFU	shedding in feces	exponential	k=2.18E-04	3.18E+03
177	[6]	rabbit	EHEC UC741 (O157:H7)	intragastric (w. NaHCO3)	7	CFU	diarrhea	beta-Poisson	α = 4.87E-01 , N_{50} = 5.97E+05	5.97E+05

II. Enzymes and Toxins of Pathogenesis

- 25.5 Enzymes as Virulence Factors
- 25.6 AB-Type Exotoxins
- 25.7 Cytolytic and Superantigen Exotoxins
- 25.8 Endotoxins

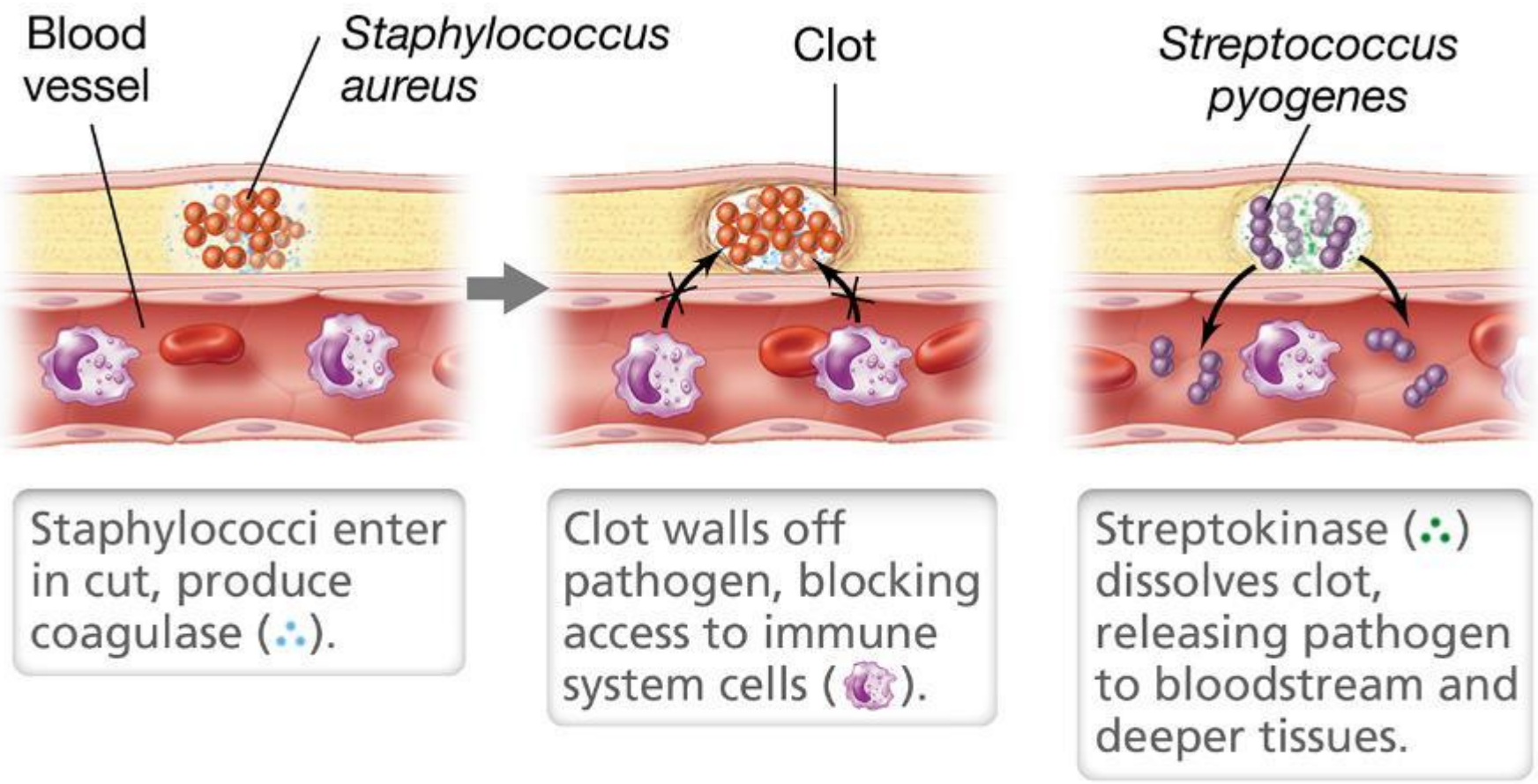
25.5 Enzymes as Virulence Factors

- Invasiveness requires a pathogen break down host tissues. This is often done with *enzymes* that attack host cells.
- Tissue-Destroying Enzymes
  - *Hyaluronidase* breaks down host *extracellular matrix* which can cause tissue damage. (Figure 25.12a)
  - *Coagulase* and *streptokinase* manipulate clotting. Coagulase forms clots, while streptokinase breaks them down. (Figure 25.12b and 25.12c)



(a) **Hyaluronidase**

Figure 25.12a



(b) **Coagulase and streptokinase**

Figure 25.12b

Human defenses

- Secretion of e.g. IgA antibodies and lysozyme (enzyme that breaks down bacterial cell walls)

EINDE LES 11

Microbiologie 2: Les 12
II. Enzymes and Toxins of Pathogenesis

Schema Micro2

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II. Enzymes and Toxins of Pathogenesis

- 25.5 Enzymes as Virulence Factors
- 25.6 AB-Type Exotoxins
- 25.7 Cytolytic and Superantigen Exotoxins
- 25.8 Endotoxins

25.6 AB-Type Exotoxins

- Toxicity is the ability of an organism to cause disease by means of a toxin that inhibits host cell function or kills host cells.
- Exotoxins (Table 25.2)
  - proteins released from the pathogen cell as it grows
  - three categories
    - *AB toxins*
    - *cytolytic toxins*
    - *Superantigen toxins*

25.6 AB-Type Exotoxins

- Diphtheria Exotoxin: Blockage of Protein Synthesis
- AB toxin that is made up of an Active (A) domain and a binding (B) domain
  - The A domain adds an ADP-ribosyl group to EF-2, which prevents its function in translation. (Figure 25.13)
  - 1 molecule sufficient to kill a cell…
- NB: the *tox* gene is encoded in the genome of lysogenic phage β (*phage conversion*)

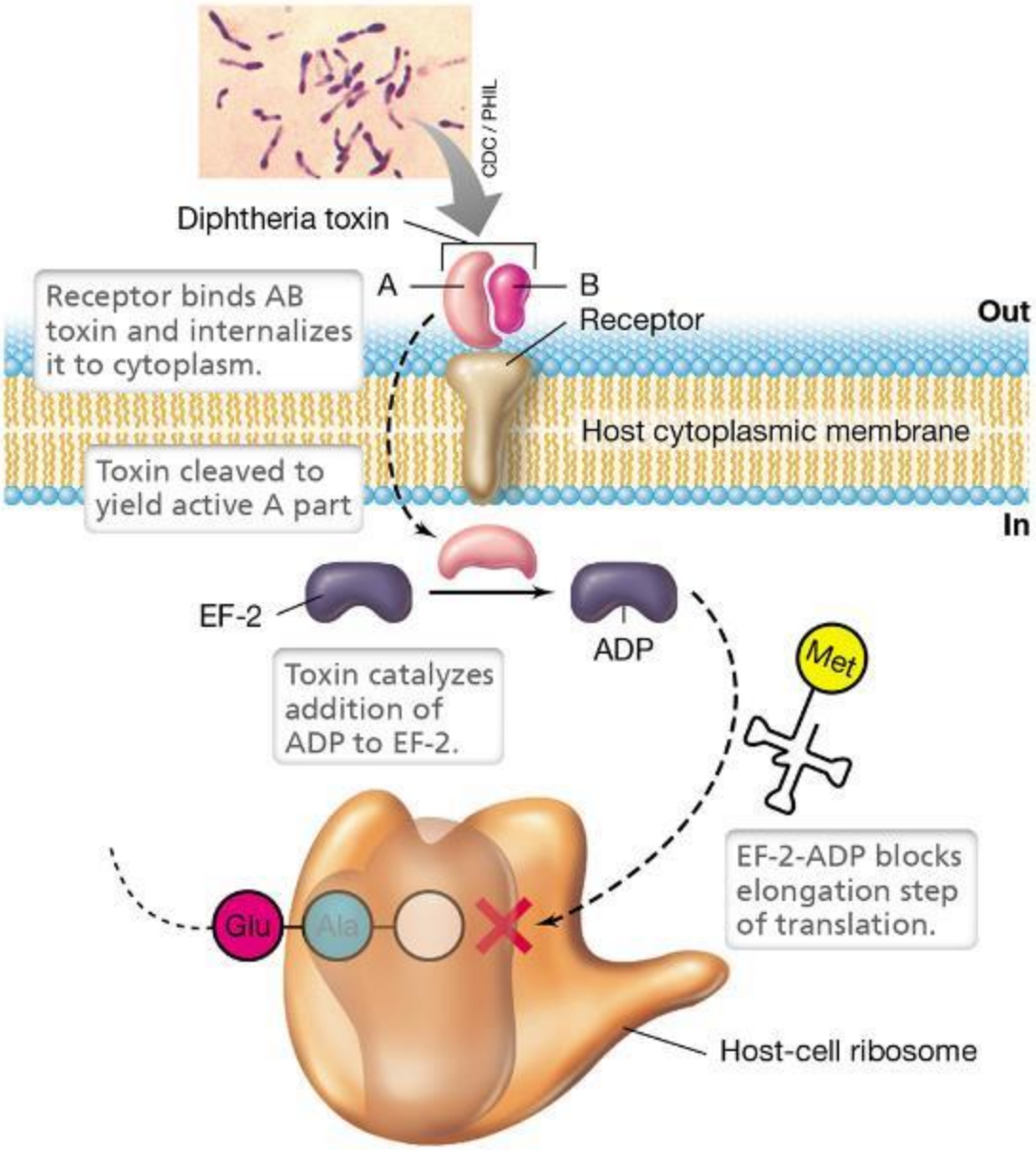

Figure 25.13

25.6 AB-Type Exotoxins

- *Clostridium tetani* and *Clostridium botulinum* produce potent Neurological Exotoxins.
  - Botulinum toxin (*Botox*) consists of several related AB toxins that are the most potent biological toxins known. (Figure 25.14)
  - Tetanospasmin is also an AB protein neurotoxin.(Figure 25.15)

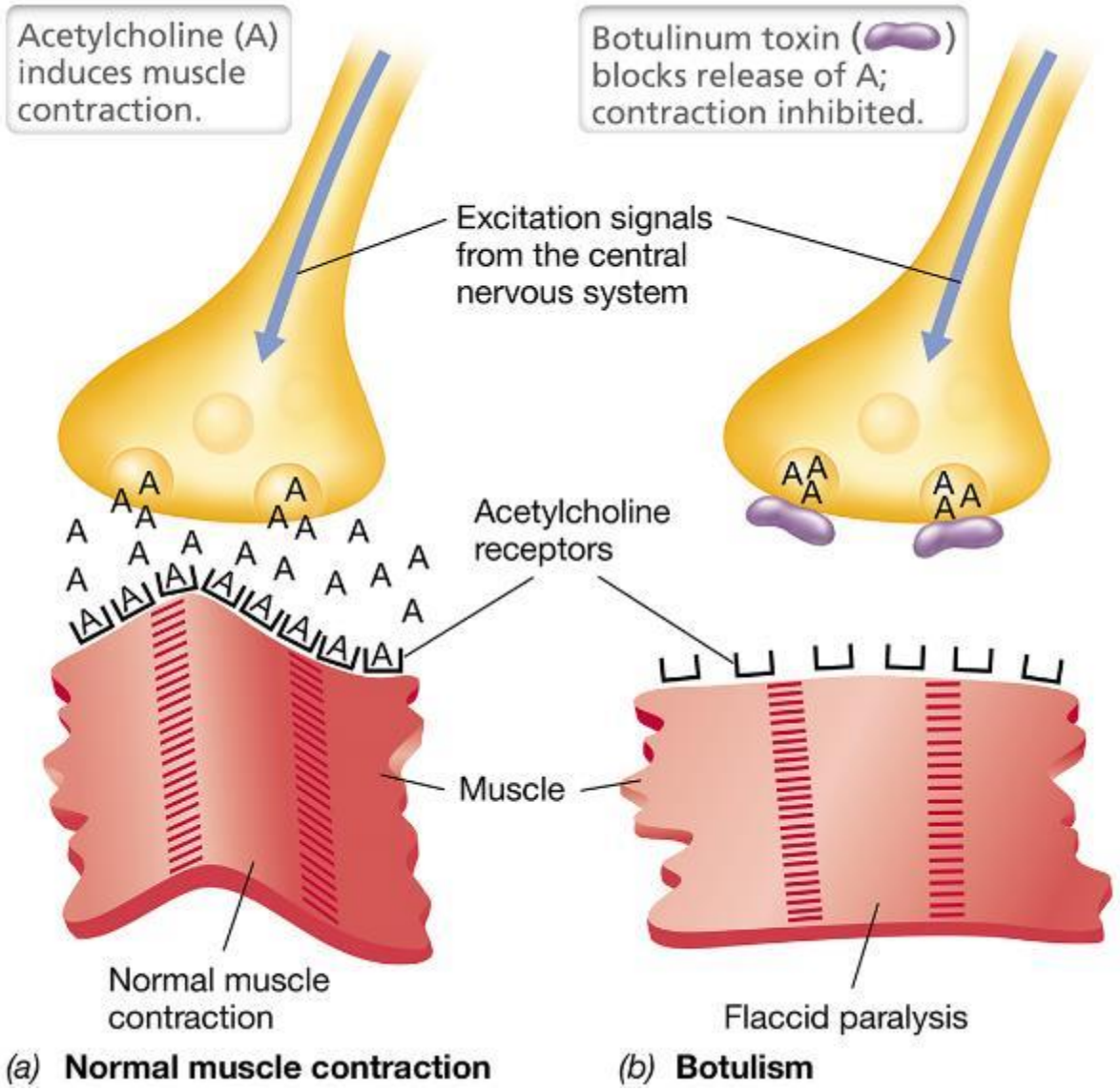

Figure 25.14

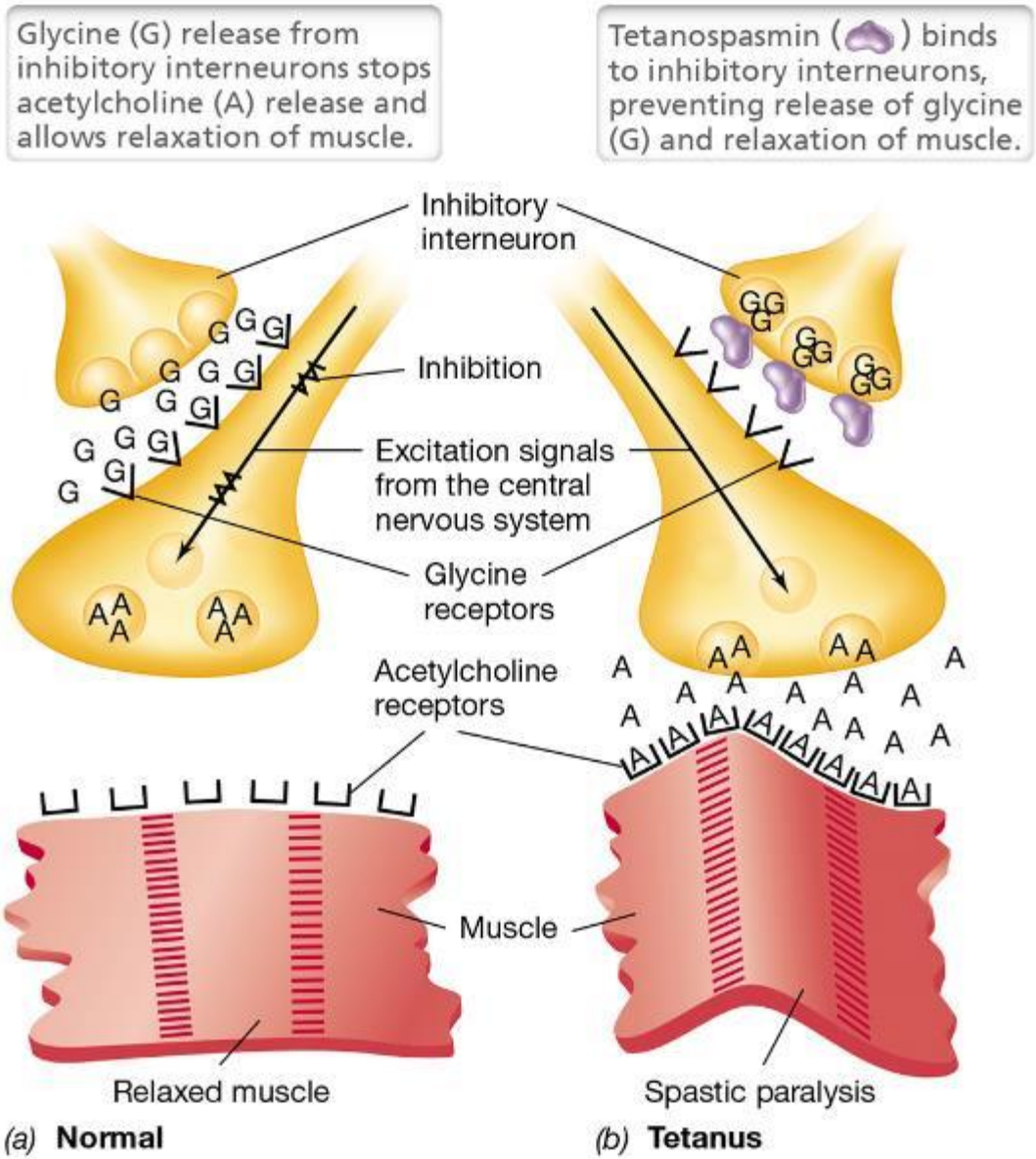

Figure 25.15

25.6 AB-Type Exotoxins

- Enterotoxins
  - exotoxins whose activity affects the small intestine
  - generally cause massive secretion of fluid into the intestinal lumen, resulting in vomiting and diarrhea
  - example: cholera toxin (Figure 25.16)

Cholera

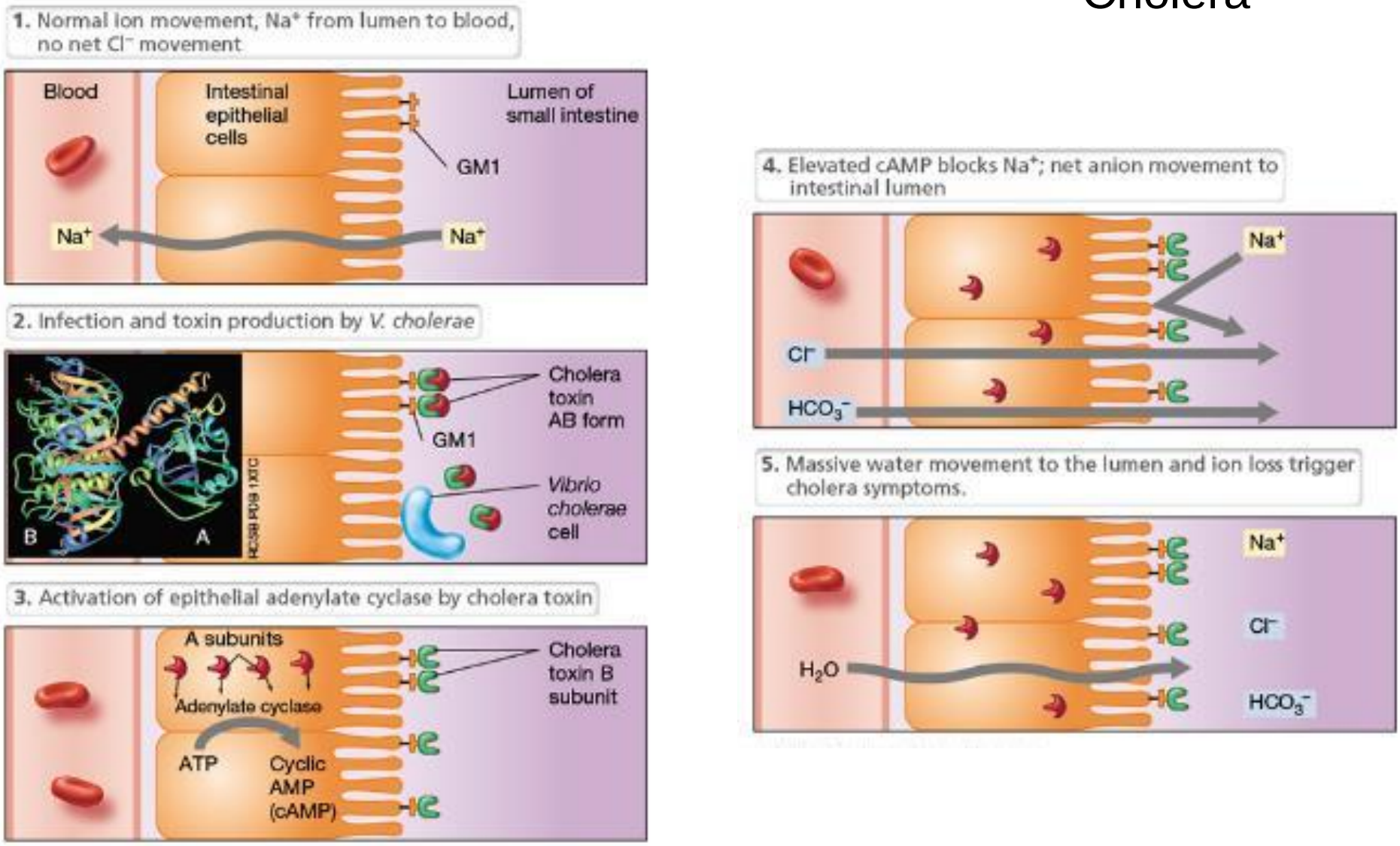

Figure 25.16

Escherichia coli O157:H7

Go to:

Escherichia coli

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TABLE 25.2 Some classic exotoxins and cytotoxins produced by human bacterial pathogens

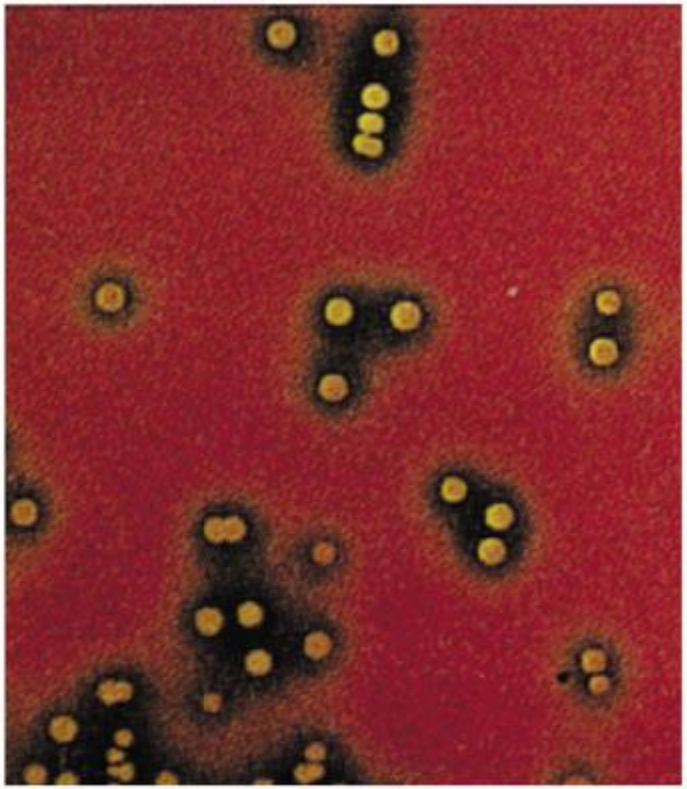
Organism	Disease	Toxin[a]	Activity[b]
Bacillus anthracis	Anthrax	Lethal factor Edema factor Protective antigen (AB)	Combine to cause cell death
Bordetella pertussis	Whooping cough	Pertussis toxin (AB)	Blocks G protein function; kills cells
Clostridium botulinum	Botulism	Botulinum toxin (AB)	Causes flaccid paralysis
Clostridium tetani	Tetanus	Tetanospasmin (AB)	Causes rigid paralysis
Clostridium perfringens	Gas gangrene Food poisoning	a, b, g, d toxins (AB) Enterotoxin (CT)	Hemolysis, lecithin destruction Alters intestinal tract permeability
Corynebacterium diphtheriae	Diphtheria	Diphtheria toxin (AB)	Inhibits eukaryotic protein synthesis
Escherichia coli (enterotoxigenic strains only)	Gastroenteritis	Shiga-like (*E. coli*) (AB)	Inhibits protein synthesis, induces bloody diarrhea
Pseudomonas aeruginosa	Burn and certain wound and ear infections; cystic fibrosis lung infections	Exotoxin A (AB)	Inhibits eukaryotic protein synthesis
Salmonella sp.	Gastroenteritis	Enterotoxin (AB) Cytotoxin (CT)	Lyses cells; inhibits protein synthesis Induces fluid loss from intestine
Shigella dysenteriae	Gastroenteritis	Shiga toxin (AB)	Bloody diarrhea and hemolytic uremic syndrome
Staphylococcus aureus	Pyogenic (pus-forming) wounds; food poisoning, toxic shock	a, b, g, d toxins (CT) Toxic shock toxin (SA) Enterotoxins A–E (SA)	Hemolysis, leukolysis, cell death Systemic shock Vomiting, diarrhea, systemic shock
Streptococcus pyogenes	Pyogenic infections; strep throat; scarlet fever	Streptolysis O, S (CT) Erythrogenic toxin (SA)	Hemolysis Causes scarlet fever
Vibrio cholerae	Cholera	Cholera (AB)	Induces fluid loss from intestine

[a]AB, AB toxin; CT, cytotoxin; SA, superantigen.
[b]See Figures 25.11–25.16 for the mode of action of some of these toxins.

Table 25.3

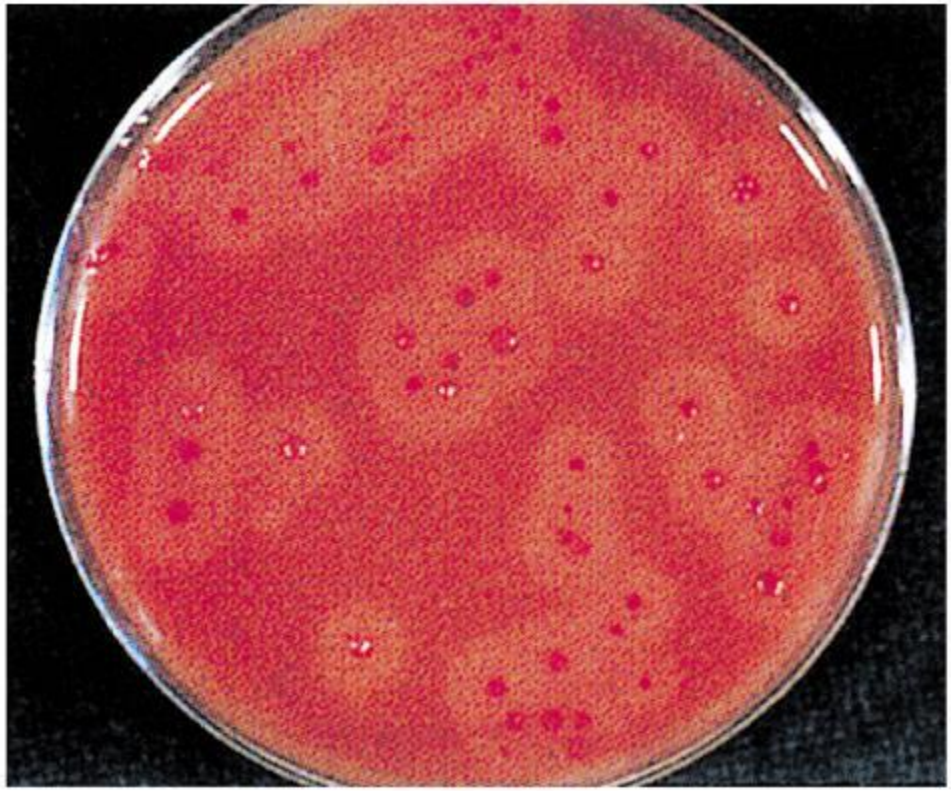
25.7 Cytolytic and Superantigen Exotoxins

- Cytolytic Exotoxins
  - work by degrading cytoplasmic membrane integrity, causing cell lysis and death
    - Toxins that lyse red blood cells are called *hemolysins.* (Figure 25.17) e.g. phospholipase
  - *Staphylococcal α-toxin* kills nucleated cells and lyses erythrocytes. (Figure 25.18)



T. D. Brock

(a)



Leon J. LeBeau

(b)

Figure 25.17

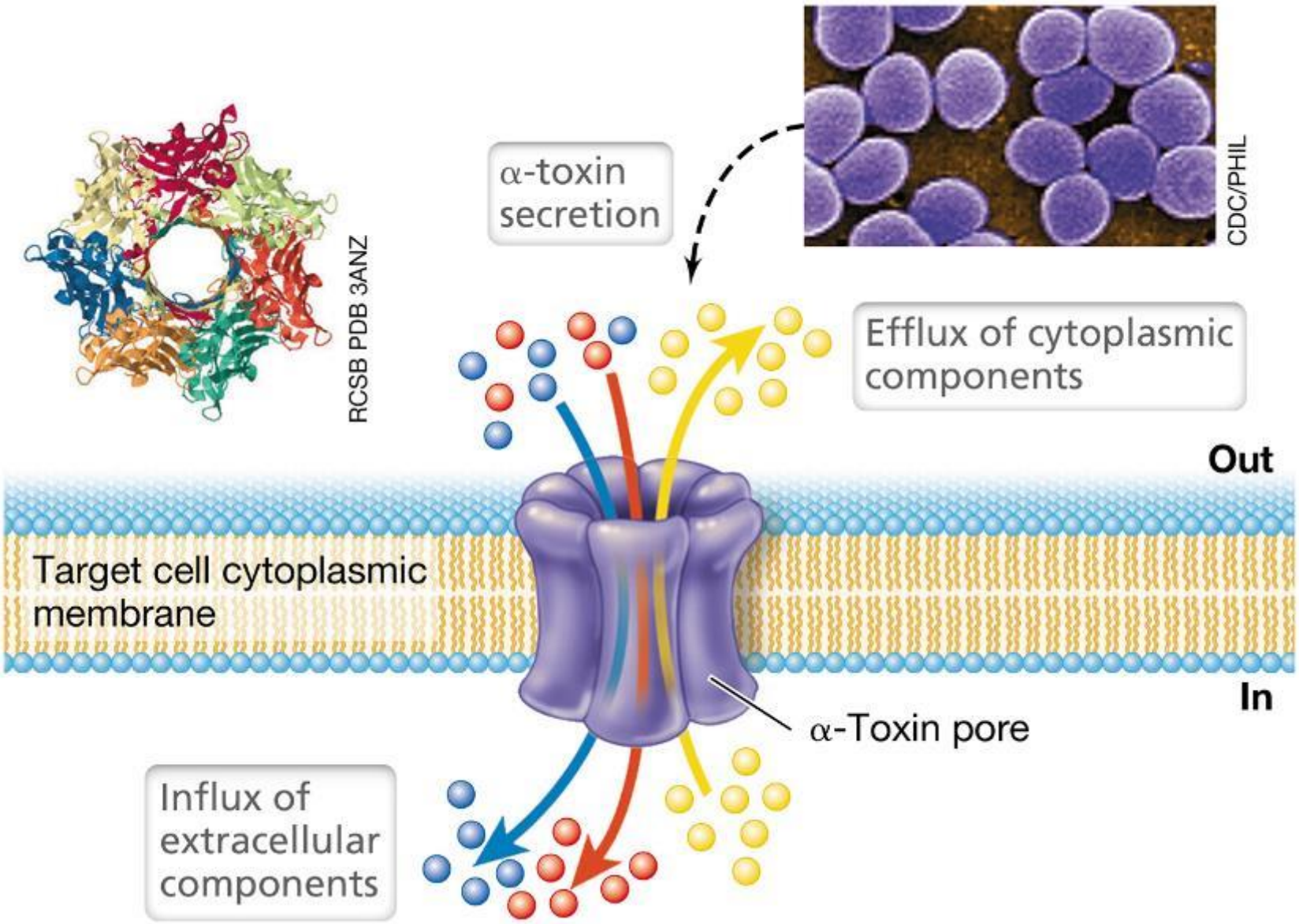
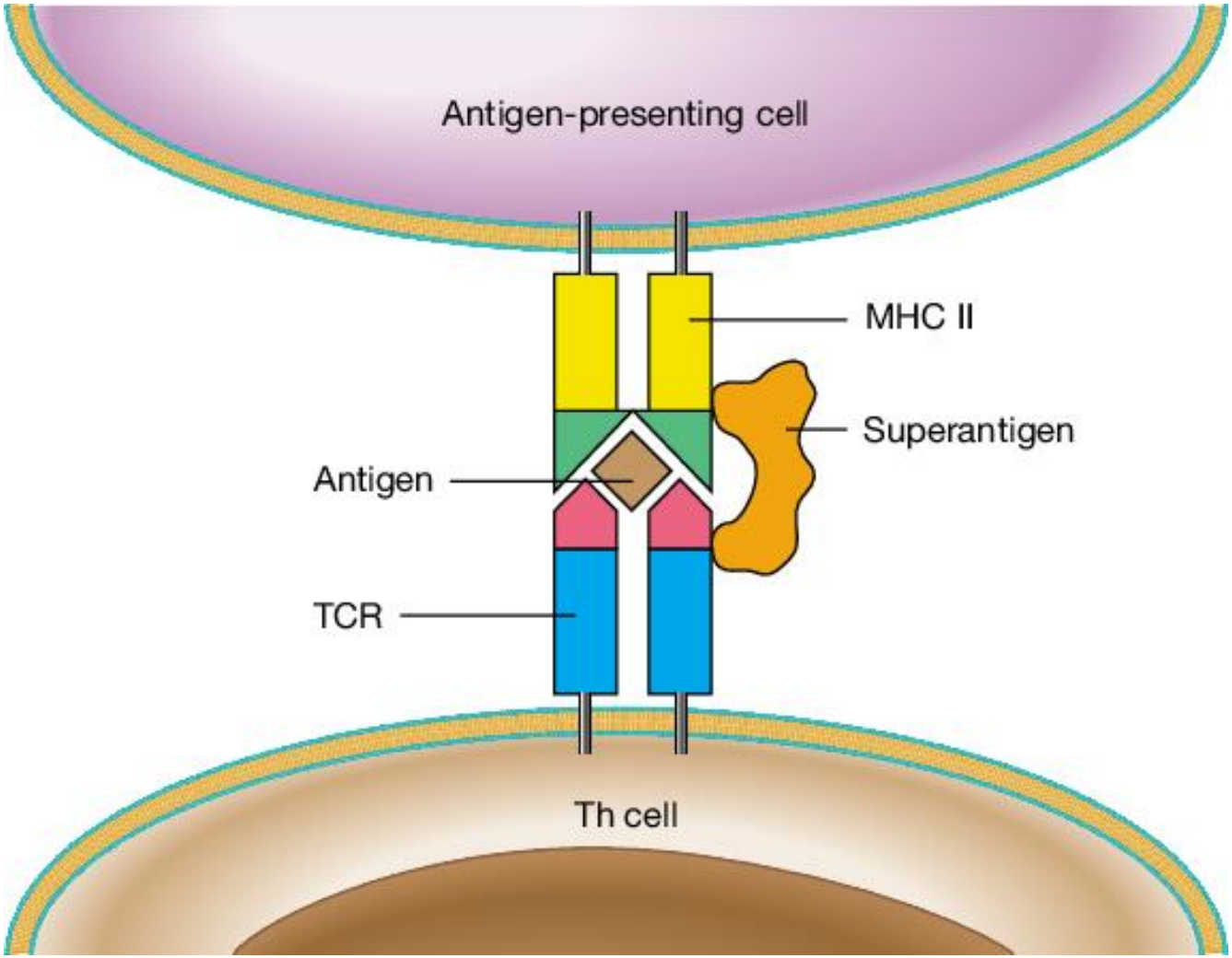


Figure 25.18

25.7 Cytolytic and Superantigen Exotoxins

- Superantigens
  - cause an overstimulation of the immune system
  - can lead to shock and death
  - generally due to a localized infection, but with systemic effects

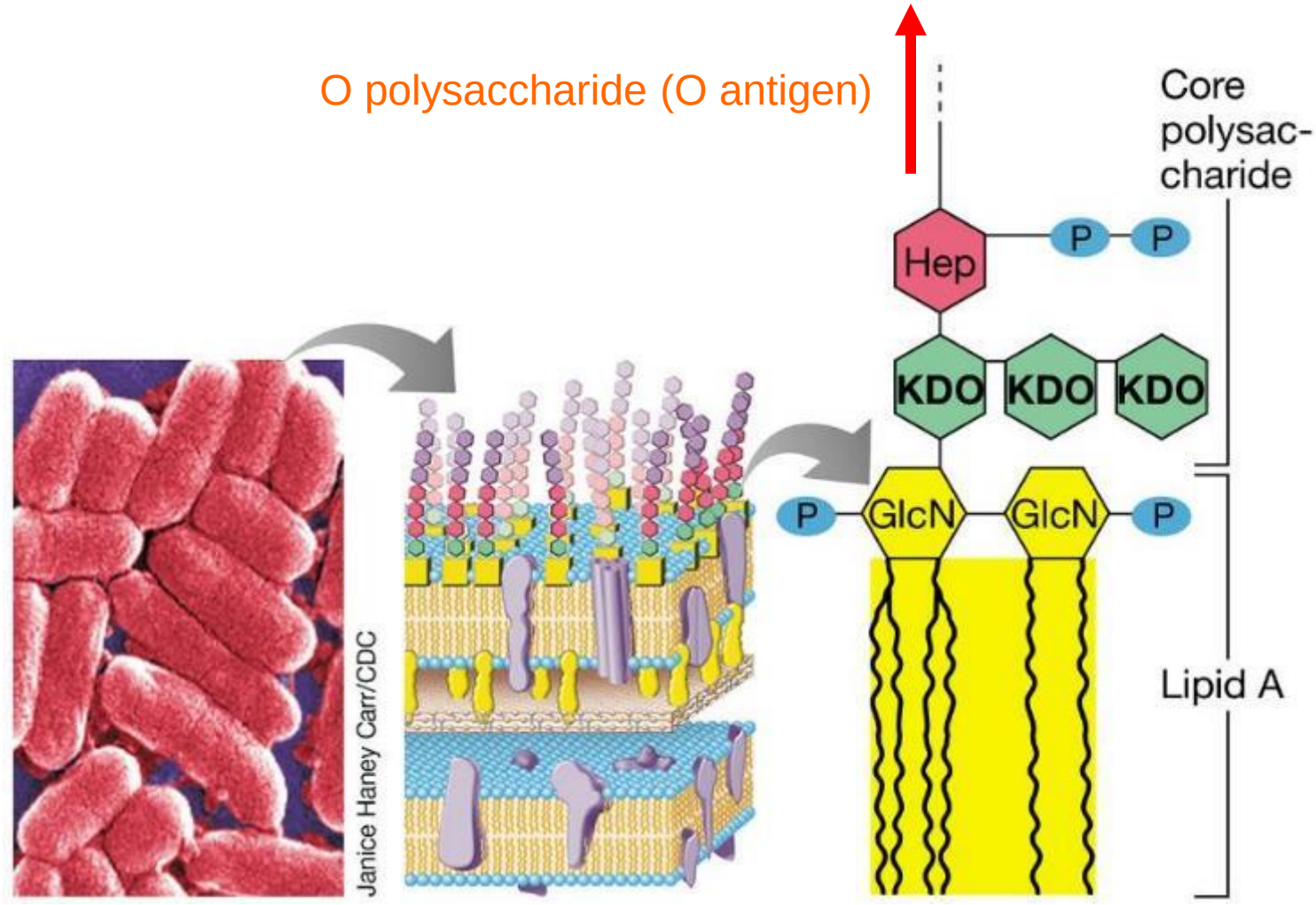


https://www.youtube.com/watch?v=qSams9-onRs

Figure 28.6

25.8 Endotoxins

- Endotoxin Structure and Biology
  - the lipopolysaccharide (LPS) portion of the cell envelope of certain **gram-negative** *Bacteria*, is a toxin when solubilized (Figure 25.18)
  - generally less toxic than exotoxins
  - Lipid A portion is a very potent stimulant of the immune system.
  - At high concentrations it may cause shock and death by an "out of control" excessive immune reaction (after bacterial lysis, e.g.)



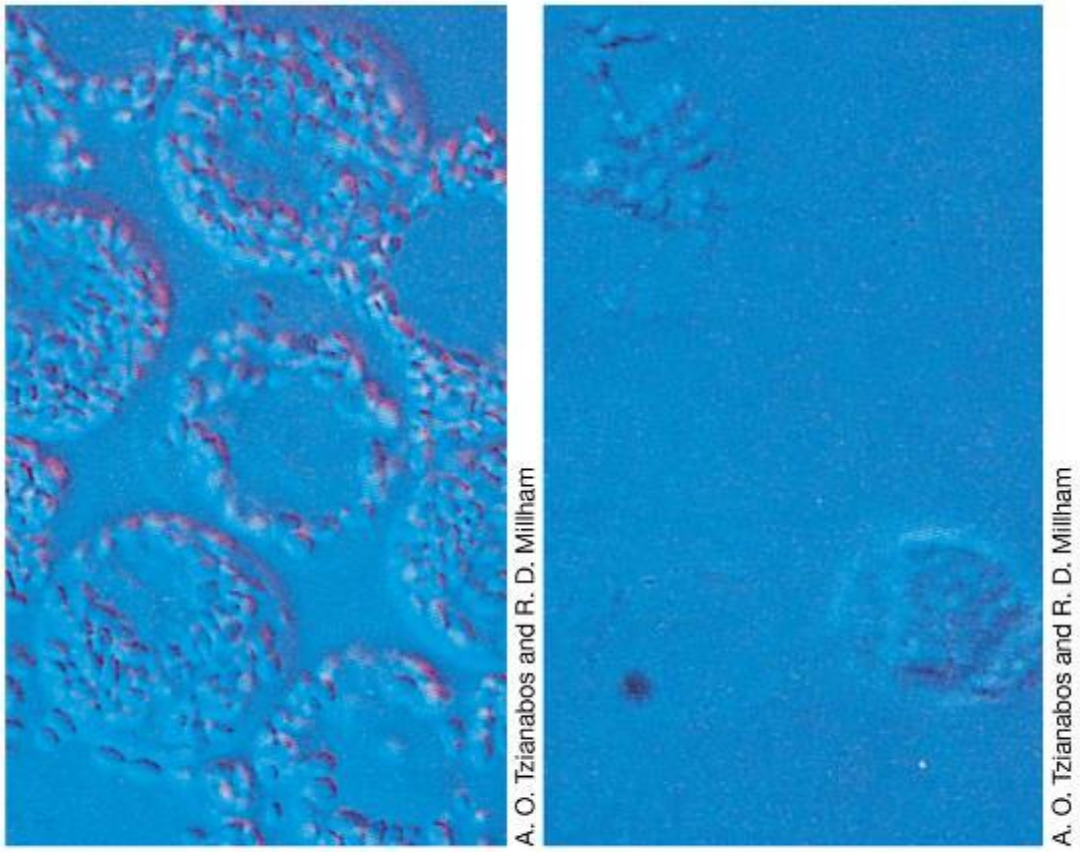
- Core: heptose and KDO (keto-deoxyoctulosonate)
- Lipid A: phosphorylated glucosamine disaccharide decorated with multiple fatty acids.

Figure 25.19

25.8 Endotoxins

- Endotoxin Structure and Biology
  - the lipopolysaccharide (LPS) portion of the cell envelope of certain gram-negative *Bacteria*, is a toxin when solubilized (Figure 25.19)
  - generally less toxic than exotoxins
- *Limulus* amoebocyte lysate (LAL)
  - Presence of endotoxin can be detected by the *Limulus* amoebocyte lysate (LAL) assay. (Figure 25.20)
  - Overharvesting of horseshoe crabs is a concern, as their blood is used in this assay.

LAL assay



- Amoebocytes lyse in presence endotoxin

=> Solution becomes more turbid and viscous.

- 10 picogram LPS per ml detectable

25.8 Endotoxins

- Endotoxins are very different from Exotoxins

TABLE 25.3 Properties of exotoxins and endotoxins

Property	*Exotoxins*	*Endotoxins*
Chemistry	Proteins, secreted by certain gram-positive or gram-negative *Bacteria;* generally heat-labile	Lipopolysaccharide–lipoprotein complexes, released on cell lysis as part of the outer membrane of gram-negative *Bacteria;* extremely heat-stable
Mode of action; symptoms	Specific; usually binds to specific cell receptors or structures; either cytotoxin, enterotoxin, or neurotoxin with defined, specific action on cells or tissues	General; fever, diarrhea, vomiting
Toxicity	Often highly toxic in picogram to microgram quantities, sometimes fatal	Moderately toxic in tens to hundreds of microgram amounts, rarely fatal
Immune response	Highly immunogenic; stimulate the production of neutralizing antibody (antitoxin)	Relatively poor immunogen; immune response not sufficient to neutralize toxin
Toxoid potential[a]	Heat or chemical treatment may destroy toxicity, but treated toxin (toxoid) remains immunogenic	None
Fever potential	Nonpyrogenic; does not produce fever in the host	Pyrogenic; often induces fever in the host
Genetic origin	Often encoded on extrachromosomal elements or lysogenic bacteriophages	Encoded by chromosomal genes

[a]A toxoid is a modified toxin that is no longer toxic but can still elicit an immune response against the toxin (Section 28.9).

Table 25.3

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