

# **Chapter 19 – Pathogenic Gram-Positive Bacteria**

**NIMESH PATEL | HLSC 2400**

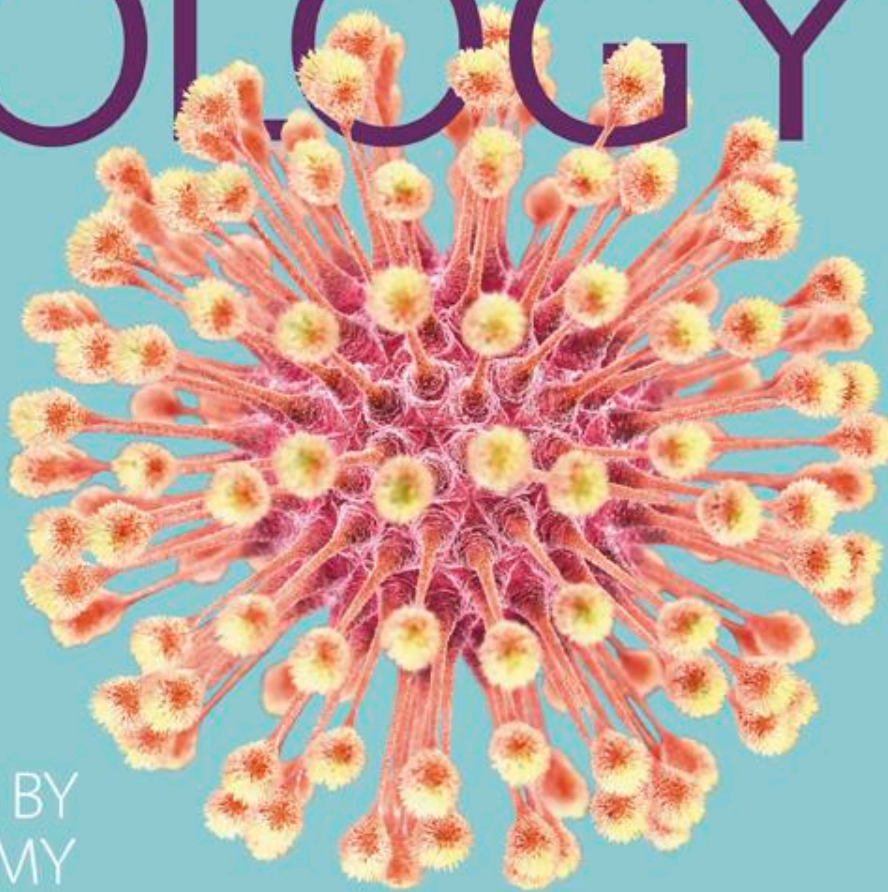
**OCTOBER 17, 2017**

# Oral Presentations

- Grading rubric & schedule: Available on Moodle
- Presentation should include the following topics:
  - Background about disease/organism, **why this is a public health concern**, etiology of a disease, sign and symptoms, management, mode of spread, prevention, surveillance, information about the first case ever diagnosed, any interesting fact about a disease/organism, etc.
- Length: 20 minutes (**including** 5 minutes of discussion)
- **First presentation: October 19**

# MICROBIOLOGY

5th Edition



WITH  
DISEASES BY  
TAXONOMY

ROBERT W. BAUMAN

PowerPoint® Lecture  
Presentations prepared by  
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University

## CHAPTER 19

### Pathogenic Gram-Positive Bacteria

# *Streptococcus*

- **Alpha-Hemolytic Streptococci: The Viridans Group**
  - Alpha-hemolysis = partial hemolysis
  - Lack group-specific carbohydrates
    - Cannot be grouped by Lancefield system
  - Many produce a green pigment when grown on blood media
  - Inhabit mouth, pharynx, GI tract, genital tract, and urinary tract
  - Opportunistic pathogens
  - One cause of dental caries and dental plaques
  - Can cause meningitis and endocarditis if it enters the blood

Figure 19.8 Dental caries.

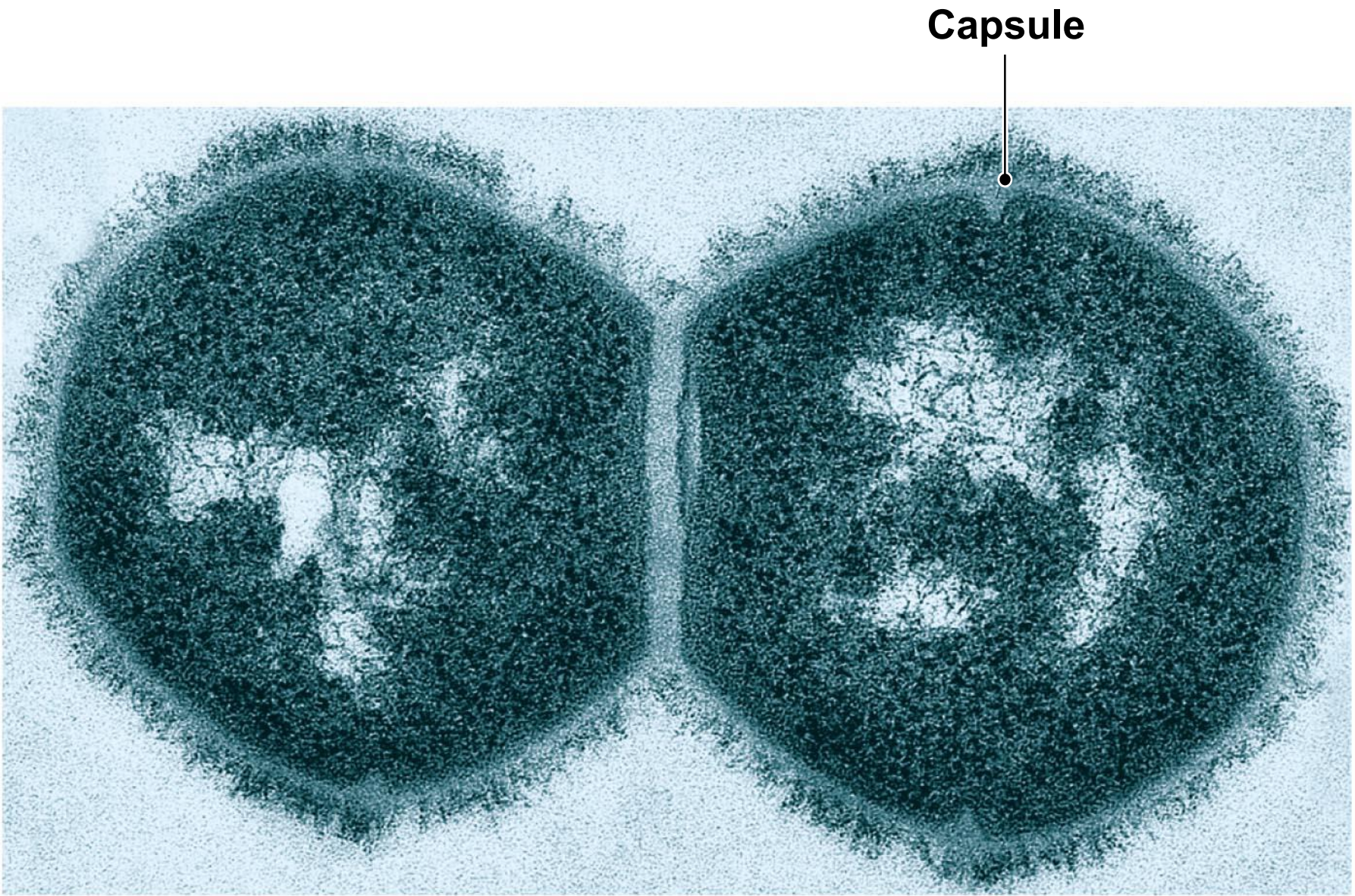


# Streptococcus

- ***Streptococcus pneumoniae***
  - Cocci that most commonly form pairs
  - Form unpigmented, alpha-hemolytic colonies on blood agar
  - Lacks Lancefield antigens



Figure 19.9 *Streptococcus pneumoniae*.



TEM

200 nm

# Streptococcus

- ***Streptococcus pneumoniae***
  - Pathogenesis and Epidemiology
    - Polysaccharide capsule
    - Phosphorylcholine
      - Stimulates cells to phagocytize the bacteria
    - Protein adhesin
      - Mediates binding of cells to epithelial cells of pharynx
    - Secretory IgA protease
      - Destroys IgA
    - Pneumolysin
      - Lyses epithelial cells



# Streptococcus

- ***Streptococcus pneumoniae***
  - Pathogenesis and Epidemiology
    - Present in the mouths and pharynges of most humans
    - Causes disease when it travels to the lungs
    - Infections occur most often in children and the elderly

# Streptococcus

- ***Streptococcus pneumoniae***
  - Pneumococcal Diseases
    - Pneumococcal pneumonia
      - Most common disease caused by *S. pneumoniae*
    - Sinusitis and otitis media
      - Sometimes occur following viral infections
    - Bacteremia and endocarditis
      - *S. pneumoniae* can enter the blood through lacerations or tissue damage
    - Pneumococcal meningitis
      - Mortality rate higher than other causes of meningitis

# *Streptococcus*

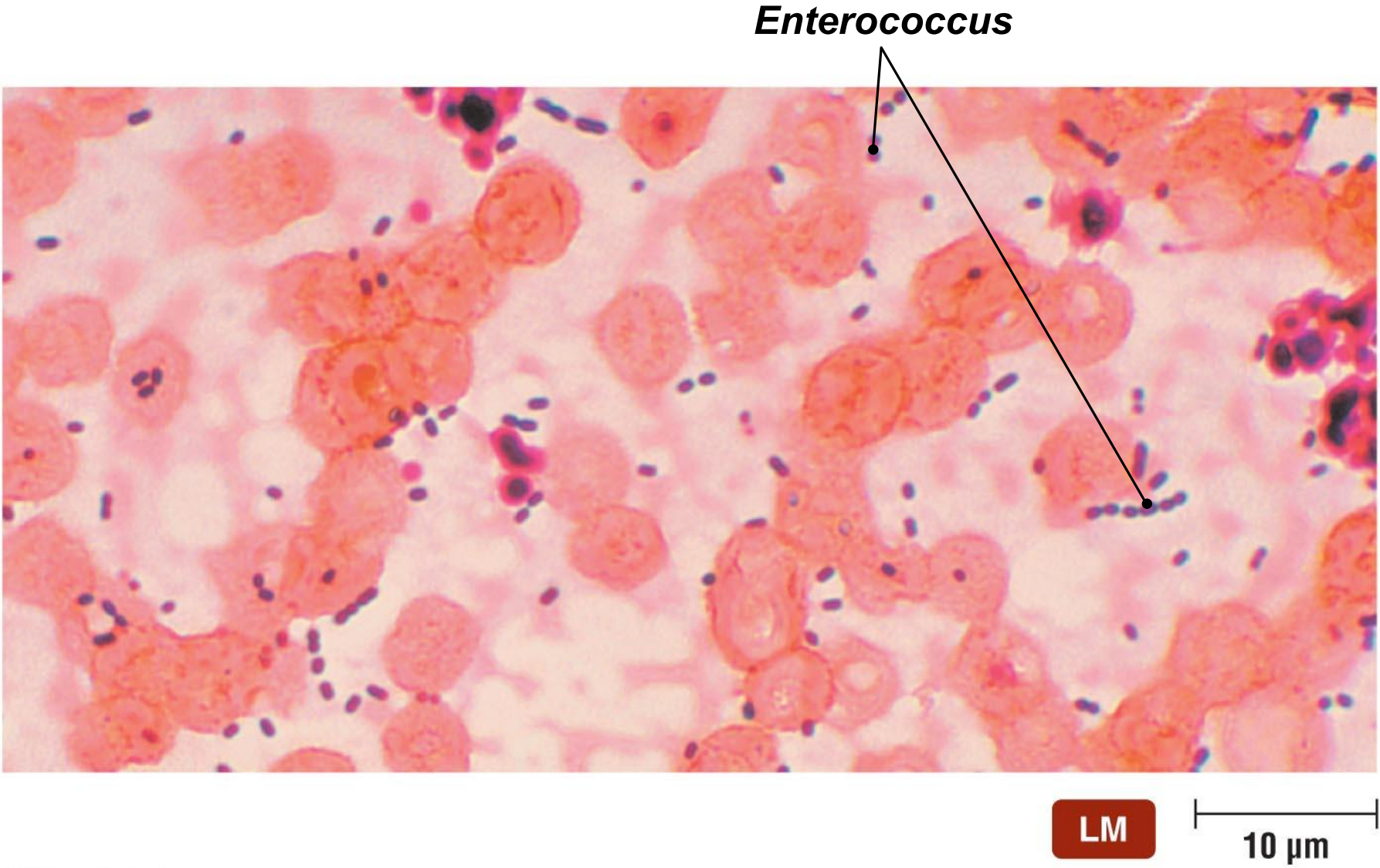
- ***Streptococcus pneumoniae***
  - Diagnosis, Treatment, and Prevention
    - Diagnosis
      - Gram stain of sputum smears
      - Confirmed with Quellung reaction
    - Treatment
      - Penicillin
        - Resistant strains have emerged
    - Prevention
      - Vaccine made from purified capsular material

# *Enterococcus*

- Previously classified with group D streptococci
- Reclassified as a separate genus
- All enterococci live in the intestinal tracts of animals



Figure 19.10 *Enterococcus faecalis* in lung tissue.



# Enterococcus

- **Structure and Physiology**

- Form short chains and pairs
- Lack a capsule, can grow at temperature up to 45C
- Two species cause disease in humans:
  - *E. faecalis*
  - *E. faecium*

- **Pathogenesis, Epidemiology, and Diseases**

- Found in the human colon
  - Rarely pathogenic at this site
- Can cause disease if introduced into other parts of the body
- Important cause of healthcare-associated infections

# Enterococcus

- **Diagnosis, Treatment, and Prevention**
  - Diagnosis
    - *Enterococcus* distinguished from *S. pneumoniae* by its sensitivity to bile
  - Treatment
    - Difficult to treat enterococcal infections
    - Enterococci often resistant to antimicrobials
  - Prevention
    - Prevention is difficult in health care setting
      - Patients often have weakened immune systems
    - Good hygiene and aseptic techniques minimize transmission

Table 19.2 Characteristics of Pathogenic Streptococci

TABLE 19.2 Characteristics of Pathogenic Streptococci

Lancefield Group	Scientific Name	Hemolytic Pattern	Significant Characteristics	Characteristic Diseases
A	<i>S. pyogenes</i>	Large zone of beta-hemolysis	1- to 2-mm white colonies on blood agar; bacitracin sensitive	Pharyngitis, rheumatic fever, scarlet fever, pyoderma, erysipelas, streptococcal toxic shock syndrome, necrotizing fasciitis, glomerulonephritis
B	<i>S. agalactiae</i>	Small zone of beta-hemolysis	2- to 3-mm butyry colonies on blood agar; bacitracin resistant	Puerperal fever, neonatal bacteremia, meningitis, pneumonia
C	<i>S. equisimilis</i>	Large zone of beta-hemolysis	1- to 2-mm white colonies on blood agar	Pharyngitis, glomerulonephritis
C, F, or G	<i>S. anginosus</i>	Small zone of beta-hemolysis	1- to 2-mm white colonies on blood agar	Purulent abscess
—	<i>S. mutans</i>	Alpha-hemolysis	Viridans group (produce green pigment when grown on blood agar)	Dental caries; rarely bacteremia, meningitis, endocarditis
—	<i>S. pneumoniae</i>	Alpha-hemolysis (aerobic); beta-hemolysis (anaerobic)	Diplococci; capsule required for pathogenicity; bile sensitive	Pneumonia, sinusitis, otitis media, bacteremia, endocarditis, meningitis
D	<i>Enterococcus faecalis</i> , <i>E. faecium</i>	None (gamma-hemolysis)	Diplococci; no capsule; bile insensitive	Urinary tract infections, bacteremia, endocarditis, wound infections

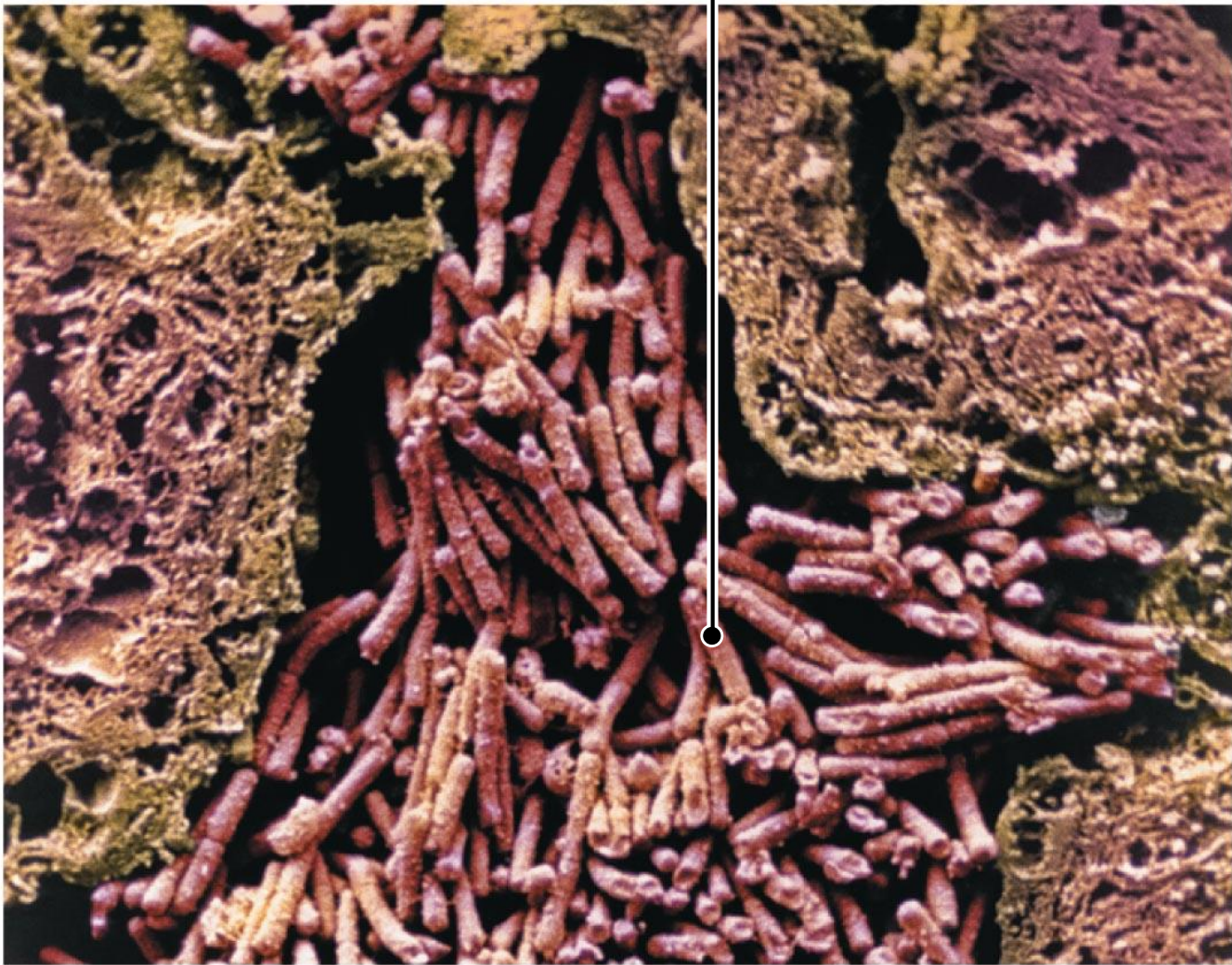


# *Bacillus*

- **Structure, Physiology, and Pathogenicity**
  - Facultative anaerobes
  - Bacilli that occur singly, in pairs, or in chains
  - **Form endospores**
  - Pathogenic strains produce anthrax toxins
- **Epidemiology**
  - Humans contract from infected animals
  - Transmission occurs via one of three routes:
    - Inhalation of spores
    - Inoculation of spores through break in the skin
    - Ingestion of spores

Figure 19.11 *Bacillus anthracis* as it appears in tissue.

*Bacillus anthracis*



SEM

10  $\mu$ m

# Bacillus

- **Disease**

- *Bacillus anthracis* only causes anthrax
- Three clinical manifestations:
  - Gastrointestinal anthrax
    - Rare in humans
  - Inhalation anthrax
    - Rare in humans
    - Requires inhalation of airborne endospores
    - High mortality rate
  - Cutaneous anthrax
    - Produces ulcer called an eschar
    - Fatal in 20% of untreated patients



Figure 19.12 Cutaneous anthrax.



Eschar



# Anthrax – Bioterrorism Threat

- *Bacillus anthracis*, the bacteria that causes anthrax, is one of the most likely agents to be used in a biological attack **(Tier 1 agent)**
  - Anthrax spores are easily found in nature, can be produced in a lab, and can last for a long time in the environment.
  - Anthrax makes a good weapon because it can be released quietly and without anyone knowing. The microscopic spores could be put into powders, sprays, food, and water. Because they are so small, you may not be able to see, smell, or taste them.
  - Anthrax has been used as a weapon before.

Source: <https://www.cdc.gov/anthrax/bioterrorism/threat.html>

# Anthrax – Bioterrorism Threat

- History

- In 2001, powdered anthrax spores were deliberately put into letters that were mailed through the U.S. postal system.
  - Twenty-two people, including 12 mail handlers, got anthrax, and five of these 22 people died



Source: <https://www.cdc.gov/anthrax/bioterrorism/threat.html>

# Anthrax – Bioterrorism Threat

## What Might an Anthrax Attack Look Like?

- In letters and mailed
- In food or water
- Could be released in air from a truck, building, or plane
- Only takes a small amount to infect a large number of people
- Inhalation anthrax is the most serious form and can kill quickly if not treated immediately

## What can you do to prepare?

# Bacillus

- **Diagnosis, Treatment, and Prevention**
  - Diagnosis
    - Large, nonmotile, Gram-positive bacilli in lung or skin samples
  - Treatment
    - Many antimicrobials are effective against *B. anthracis*
  - Prevention
    - Control of disease in animals
    - Effective vaccine available
      - Requires multiple doses and boosters



# *Clostridium*

- Anaerobic
  - Cannot use oxygen as terminal electron acceptor
- Endospore-forming bacillus
  - Function
    - Survival, not reproductive (1 bacterium -> 1 spore)
    - Resistance to chemicals, dessication, radiation, freezing, and heat
- Ubiquitous in soil, water, and gastrointestinal tracts of animals and humans
- Endospore-forming bacteria:
  - Bacillus and clostridium

# *Clostridium*

- Pathogenicity
  - Endospores
  - To the secretion by vegetative cells of potent histolytic toxins, enterotoxins, and neurotoxins

# *Clostridium*

- ***Clostridium perfringens***
  - Large, nonmotile bacillus, almost rectangular
  - *Clostridium* most frequently isolated from clinical specimens
  - Type-A is the most virulent subtype.

# *Clostridium*

- ***Clostridium perfringens***
  - Pathogenesis, Epidemiology, and Disease
    - Produces toxins that can cause irreversible damage to body
    - Grows in the digestive tracts of animals and humans

# *Clostridium*

- ***Clostridium perfringens***

- Diseases

- Food poisoning (Mild condition)
      - Abdominal cramps and watery diarrhea
    - Gas gangrene
      - Fatal in 40% of cases even with aggressive treatment
      - Trauma introduces endospores into body (bacteria are non-invasive)
      - Endospores germinate and cause necrosis
      - Produces hydrogen and CO<sub>2</sub> as a byproduct of its replication – results in characteristic gas production in tissues
      - Shock, kidney failure, and death may occur in a week



Figure 19.13 Gas gangrene, a life-threatening disease caused by *Clostridium perfringens*.



# *Clostridium*

- ***Clostridium perfringens***

- Diagnosis, Treatment, and Prevention
  - Diagnosis
    - Presence of minimum bacterial load in food or feces
    - Appearance of gas gangrene is usually diagnostic
  - Treatment
    - Food poisoning is self-limited
    - Gas gangrene requires removal of dead tissue and administration of antitoxin and penicillin
  - Prevention
    - Refrigeration of foods can reduce cases of food poisoning
    - Proper cleaning of wounds can prevent gas gangrene

# *Clostridium*

- ***Clostridium difficile***
  - Motile, anaerobic intestinal bacterium
  - Produces two toxins and the enzyme hyaluronidase

# *Clostridium*

- ***Clostridium difficile***

- Pathogenesis, Epidemiology, and Disease
  - Common member of the intestinal microbiota
  - Opportunistic pathogen in patients taking broad-spectrum antimicrobial drugs
  - Minor infections result in self-limiting explosive diarrhea
  - Serious cases can cause pseudomembranous colitis
    - Sections of the colon wall slough off, causing massive infection by fecal bacteria
    - Life-threatening condition

# *Clostridium*

- ***Clostridium difficile***

- Diagnosis, Treatment, and Prevention
  - Diagnosis
    - Isolation of organism from feces
    - Demonstrate the presence of toxins by immunoassay
  - Treatment
    - Discontinue causative antimicrobial drug to resolve minor infections
    - Serious cases treated with Metronidazole (DOC)
    - Vancomycin if metronidazole-resistant
  - Prevention
    - Proper hygiene to limit nosocomial infections



# *Clostridium*

- ***Clostridium botulinum***
  - Anaerobic, endospore-forming bacillus
  - Common in soil and water
  - Botulism results when the endospores germinate and produce botulism toxins

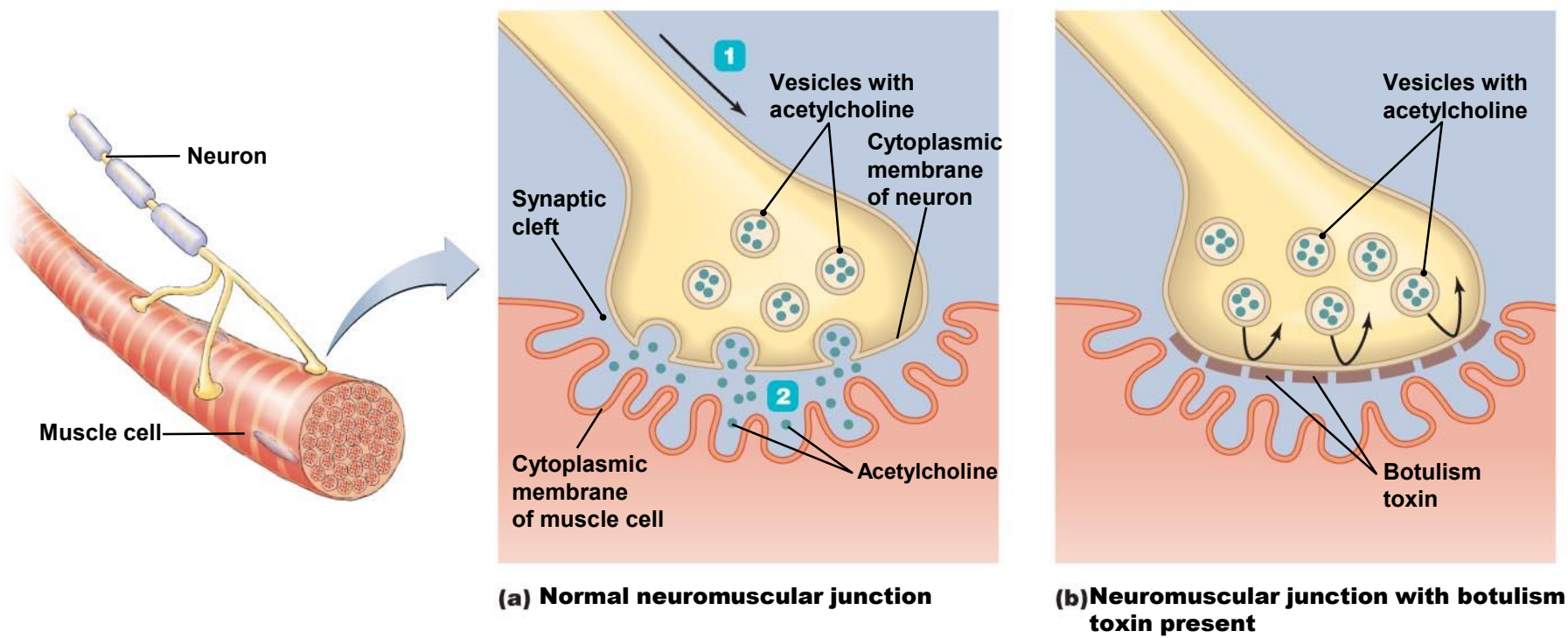
# *Clostridium*

- ***Clostridium botulinum***
  - Pathogenesis
    - Botulism toxins
      - *C. botulinum* strains produce seven distinct toxins
      - Among the deadliest known toxins
      - Bind neurons and prevent muscle contractions
      - 7 distinct forms of botulinum toxin, types A–G.
        - Four of these (types A, B, E and rarely F) cause human botulism.
        - Types C, D and E cause illness in other mammals, birds and fish.

# *Clostridium*

- ***Clostridium botulinum***
  - **Botulinum toxin**
  - A single gram of crystalline toxin, evenly dispersed and inhaled, can kill more than one million people
  - A major bioweapon threat because of its extreme potency and lethality; its ease of production, transport, and misuse; and the need for prolonged intensive care among affected persons
  - As a military or terrorist weapon, botulinum toxin could be disseminated via aerosol or by contamination of water or food supplies, causing widespread casualties
  - In the late 1980s, Canada approved use of the toxin to treat strabismus, in 2001 in the removal of facial wrinkles and in 2002, the FDA in the United States followed suit

Figure 19.14 How botulism toxin acts at a neuromuscular junction.



# Clostridium

- ***Clostridium botulinum***
  - Epidemiology and Diseases
    - Botulism is an intoxication with the following manifestations:
      - **Foodborne botulism**
        - Lightly preserved foods and in inadequately processed, home-canned, home-bottled foods, ready-to-eat foods in low oxygen-packaging.
        - Though spores of *C. botulinum* are heat-resistant, the toxin produced by bacteria growing out of the spores under anaerobic conditions is destroyed by boiling (for example, at internal temperature greater than 85C for 5 minutes or longer).
        - Combinations of low storage temperature and salt contents and/or pH are also used to prevent the growth of the bacteria or the formation of the toxin



# *Clostridium*

- ***Clostridium botulinum***
  - Epidemiology and Diseases
    - **Foodborne botulism**
      - Death can result from asphyxiation
      - Slow recovery from growth of new nerve cell endings
    - **Infant botulism**
      - Results from the ingestion of endospores
      - Paralysis and death are rare
    - **Wound botulism**
      - Contamination of a wound by endospores
      - Symptoms similar to foodborne botulism

# *Clostridium*

- Epidemiology and Diseases
  - Botulism is an intoxication with three manifestations:
    - **Inhalation botulism**
      - Rare, not natural, associated with accidental or international (bioterrorism) events
      - The median lethal dose for humans: 2 nanograms of botulinum toxin per kilogram of bodyweight, which is approximately 3 times greater than in foodborne cases
      - Onset of symptoms: 1–3 days
      - Symptoms: Muscular paralysis and respiratory failure.
      - The patient's clothing must be removed and stored in plastic bags until it can be washed thoroughly with soap and water. The patient should shower and be decontaminated immediately.

Source: <http://www.who.int/mediacentre/factsheets/fs270/en/>

# *Clostridium*

- ***Clostridium botulinum***
  - Diagnosis, Treatment, and Prevention
    - Diagnosis
      - Symptoms are diagnostic
    - Treatment
      - Wash intestinal tract to remove *Clostridium*
      - Administer neutralizing antibodies against botulism toxin
      - Administer antimicrobial drugs in infant and wound botulism cases
    - Prevention
      - Proper canning of food
      - Infants under 1 year should not consume honey

# Clostridium

- ***Clostridium botulinum***
  - Botulinum toxin uses
    - Medical
      - Strabismus
      - Achalasia cardia
      - Cervical dystonia (severe spasms in the neck muscles), muscle spasms in the arms and hands, and severe underarm sweating (hyperhidrosis)
    - Cosmetic
      - Wrinkle-free!



# *Clostridium botulinum*

## How much Botox will I need?



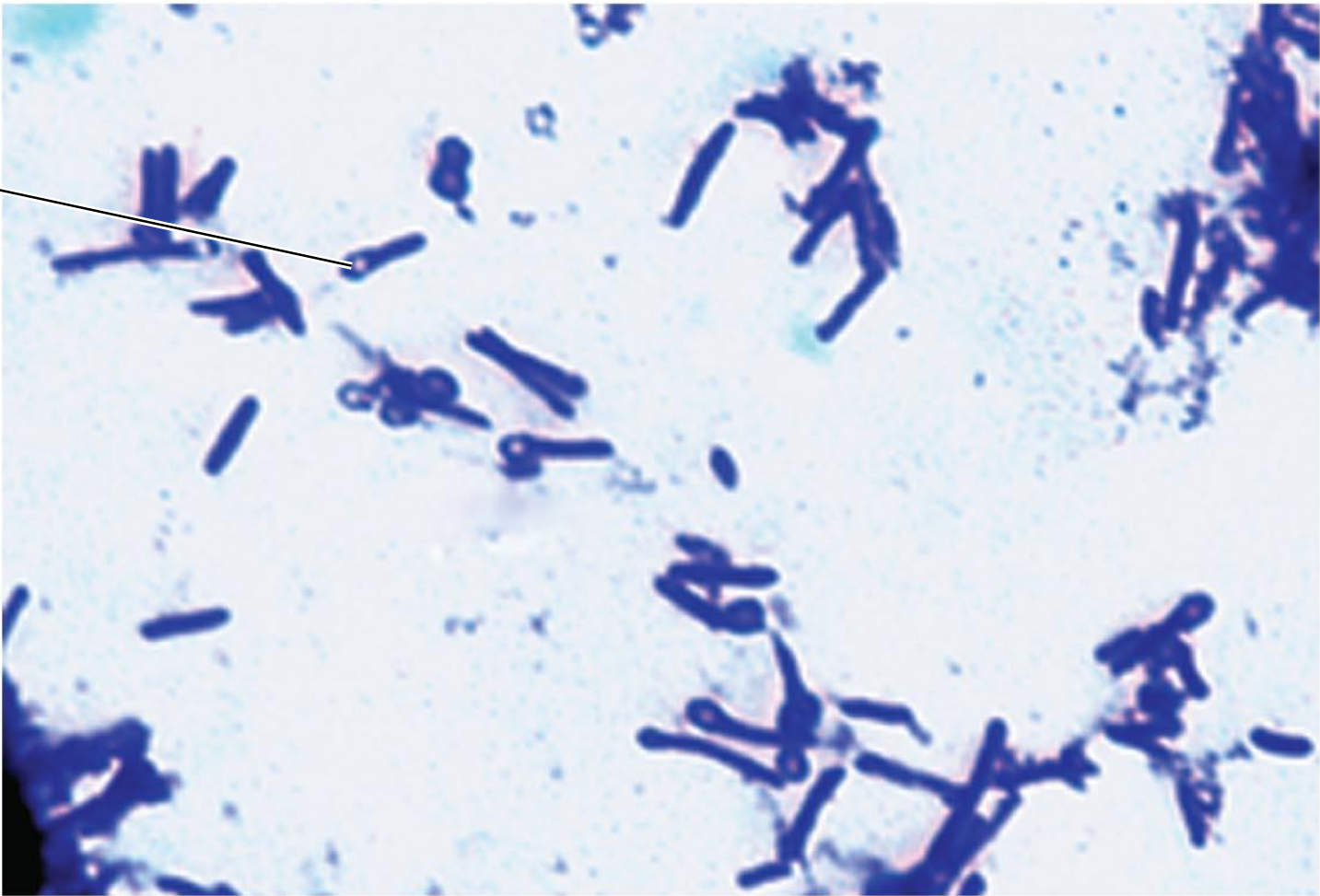


# *Clostridium*

- ***Clostridium tetani***
  - Motile, obligately anaerobic bacilli with a terminal endospore
  - Ubiquitous in soil, dust, and GI tract of animals and humans
  - Tetanus results when endospores germinate and produce tetanus toxin

Figure 19.15 Cells of *Clostridium tetani*, with terminal endospores.

Endospore



LM

10  $\mu$ m

# *Clostridium*

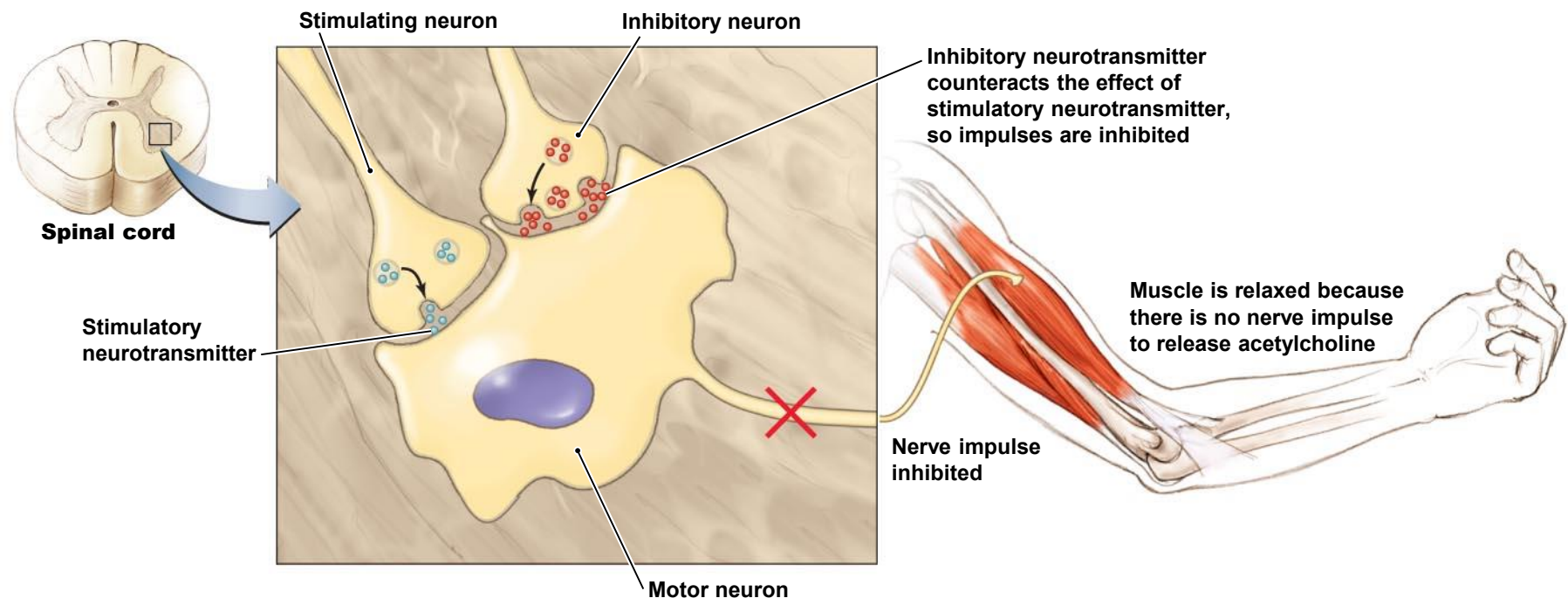
- ***Clostridium tetani***

- Pathogenesis

- **Tetanus toxin** (tetanus toxin)

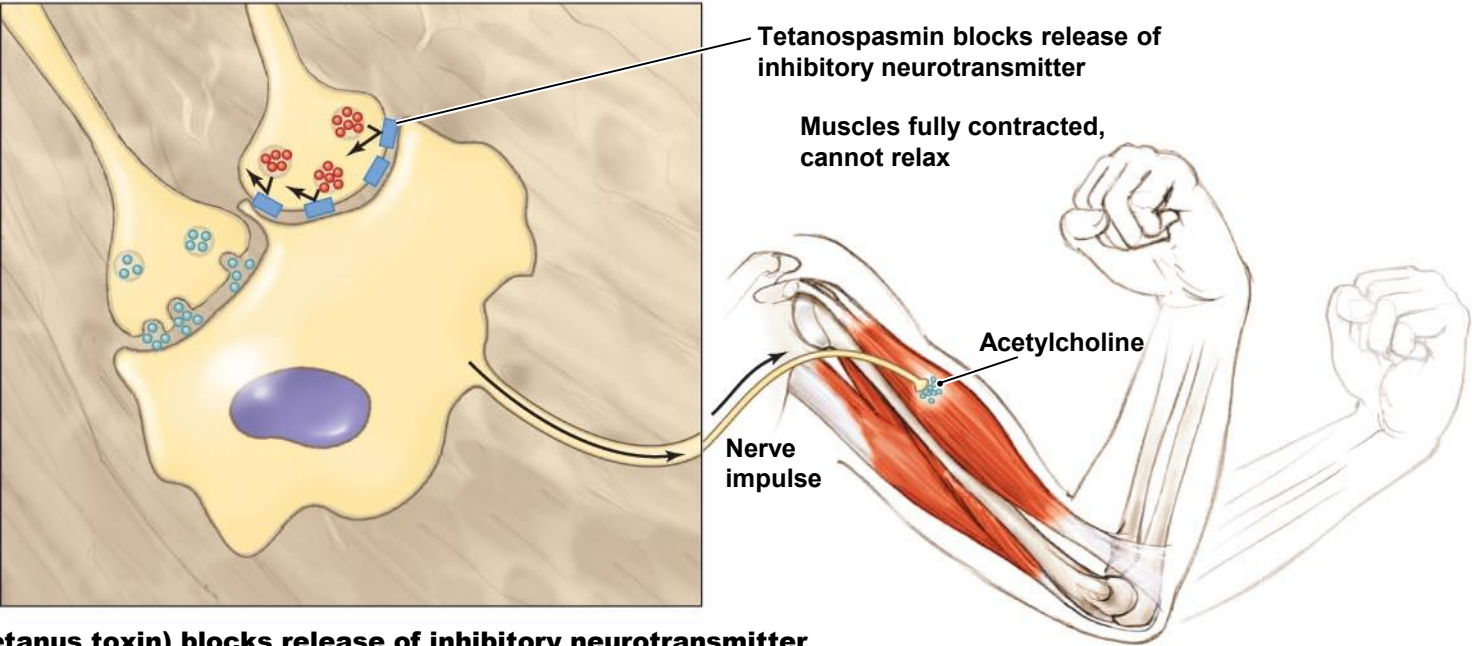
- Released by *C. tetani* cells when they die
      - Potent neurotoxin
      - Causes continuous muscle contractions, which can in severe cases break bones

**Figure 19.16a** The action of tetanospasmin (tetanus toxin) on a pair of antagonistic muscles.



**(a) Normal action of inhibitory neurotransmitter**

**Figure 19.16b** The action of tetanospasmin (tetanus toxin) on a pair of antagonistic muscles.



**(b) Tetanospasmin (tetanus toxin) blocks release of inhibitory neurotransmitter**

# *Clostridium*

- ***Clostridium tetani***

- Epidemiology and Disease
  - Initial tightening of the jaw and neck muscles
    - Commonly called **lockjaw**
  - Spasms and contractions can spread to other muscles
  - Unrelenting contraction of the diaphragm can cause death
  - Most cases occur in less-developed countries
    - Due to inadequate medical care and lack of vaccination
  - Recovery requires growth of new neuronal terminals
  - **Mortality rate about 50%**



Figure 19.17 A patient with tetanus.



# *Clostridium*

- ***Clostridium tetani***

- Diagnosis, Treatment, and Prevention
  - Diagnosis
    - Characteristic muscular contraction
  - Treatment
    - Cleansing of wounds to remove endospores
    - Administer immunoglobulin against tetanus toxin
    - Administer antimicrobial drugs
    - Active immunization with tetanus toxoid
  - Prevention
    - Immunization with tetanus toxoid

# Listeria

- ***Listeria monocytogenes***
  - Non-endospore-forming bacillus
  - Cold-tolerant
  - Found in soil, water, and animals
  - Enters body via contaminated food and drink

# Listeria

- **Pathogenesis, Epidemiology, and Disease**

- *L. monocytogenes* is an intracellular pathogen
  - Grows in phagocytes often in the gallbladder
- Listeriolysin O helps *Listeria* avoid digestion by the host cell
- Virulence directly related to *Listeria*'s ability to live within cells
- Can cause meningitis in certain at-risk groups
- Pregnant women can transmit *Listeria* to their fetus
  - Cause premature delivery, miscarriage, stillbirth, or meningitis in the newborn

DISEASE  
IN DEPTH

# LISTERIOSIS

*Listeria monocytogenes*  
with actin "tails"



## ONE WAY *LISTERIA* AVOIDS HOST'S IMMUNE SYSTEM WHILE INFECTING NEW CELLS

1 *Listeria* enters the body, usually through contaminated drink or food.

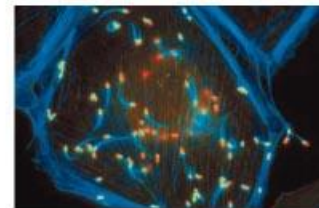


2 *Listeria* triggers its own phagocytosis by a host cell, typically in the gallbladder.

*Listeria*

3 The intracellular bacterium escapes the phagosome.

4 The bacterium reproduces within the phagocyte. Some of the mRNA in a *Listeria* cell activate at 37°C, so the bacterium reproduces more rapidly inside human cells.

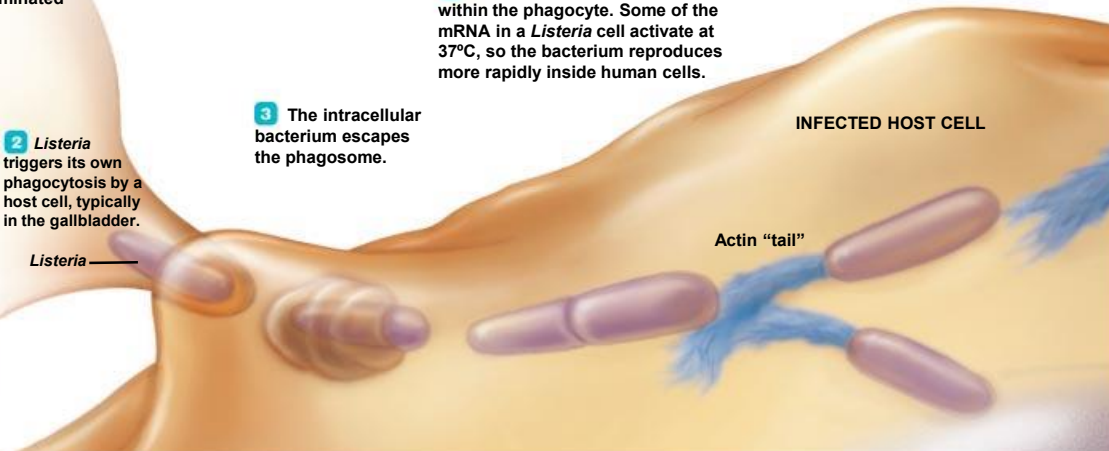


Photomicrograph of *Listeria* showing blue-stained actin "tails" LM 10 μm

5 The bacterium polymerizes the host cell's actin filaments into a "tail."

INFECTED HOST CELL

Actin "tail"



DISEASE  
IN DEPTH

LISTERIOSIS

*Listeria monocytogenes*  
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ONE WAY *LISTERIA* AVOIDS HOST'S IMMUNE  
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DISEASE  
IN DEPTH

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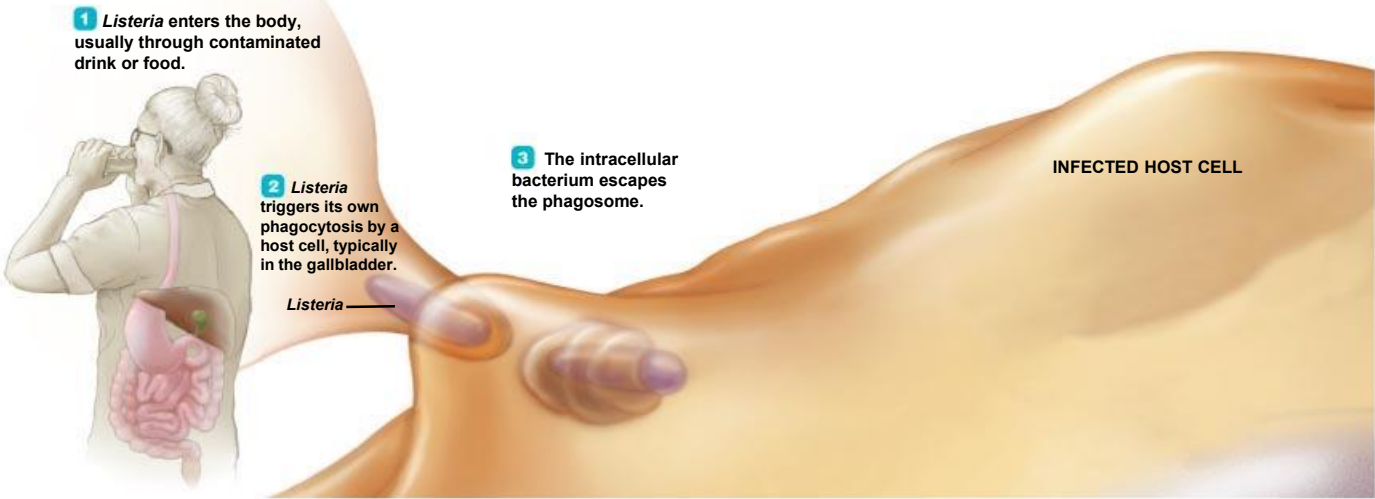
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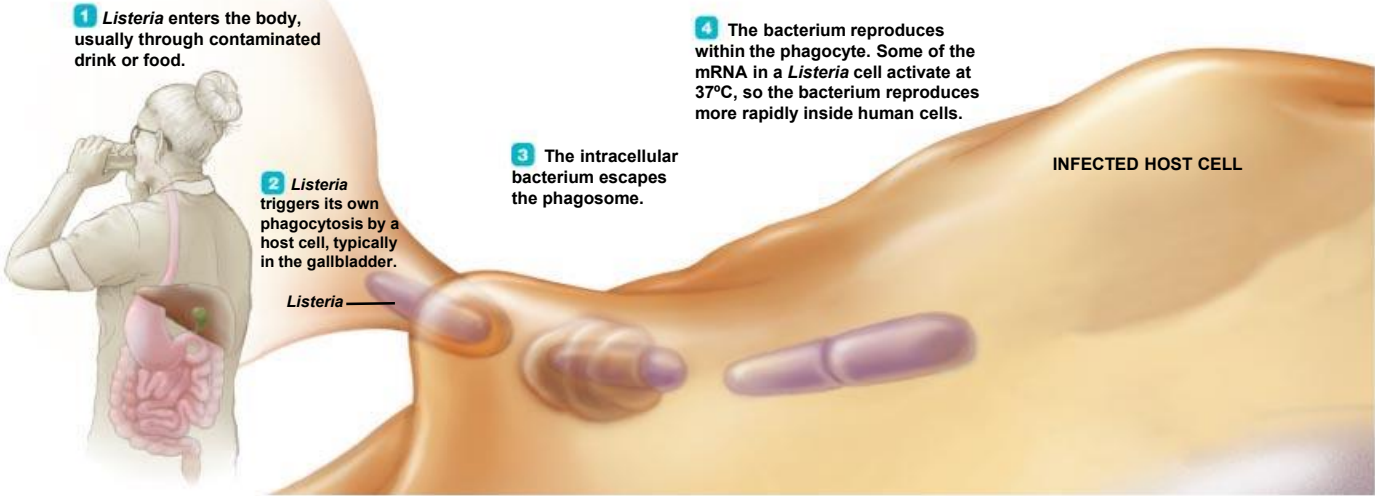
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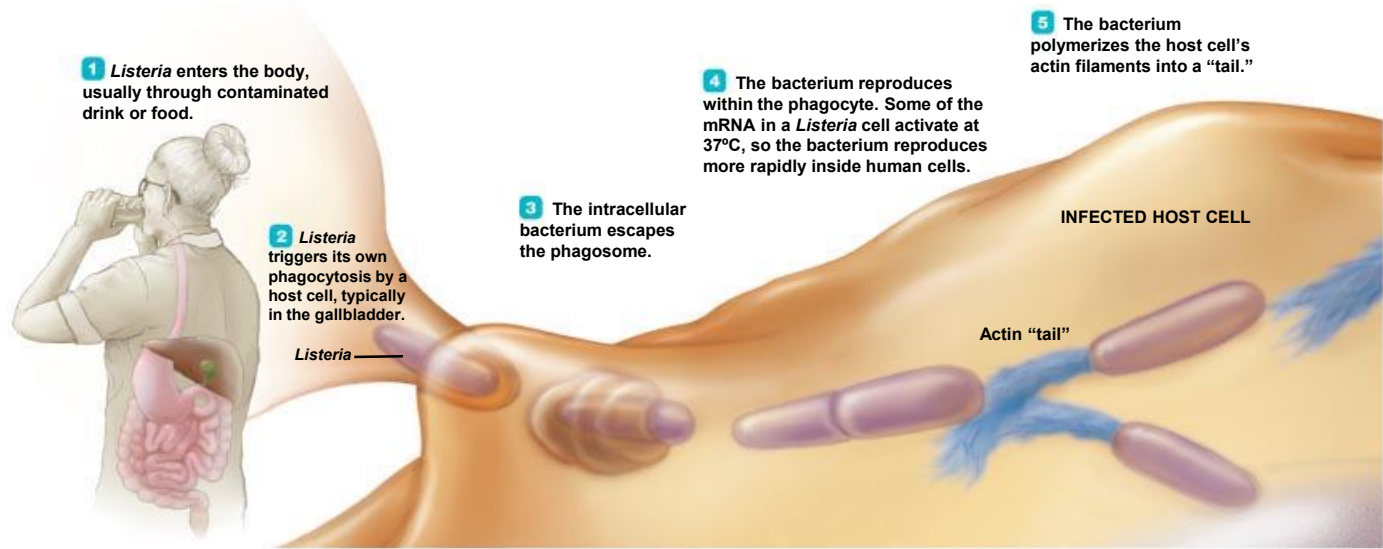
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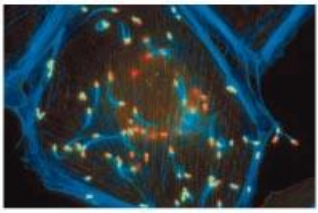
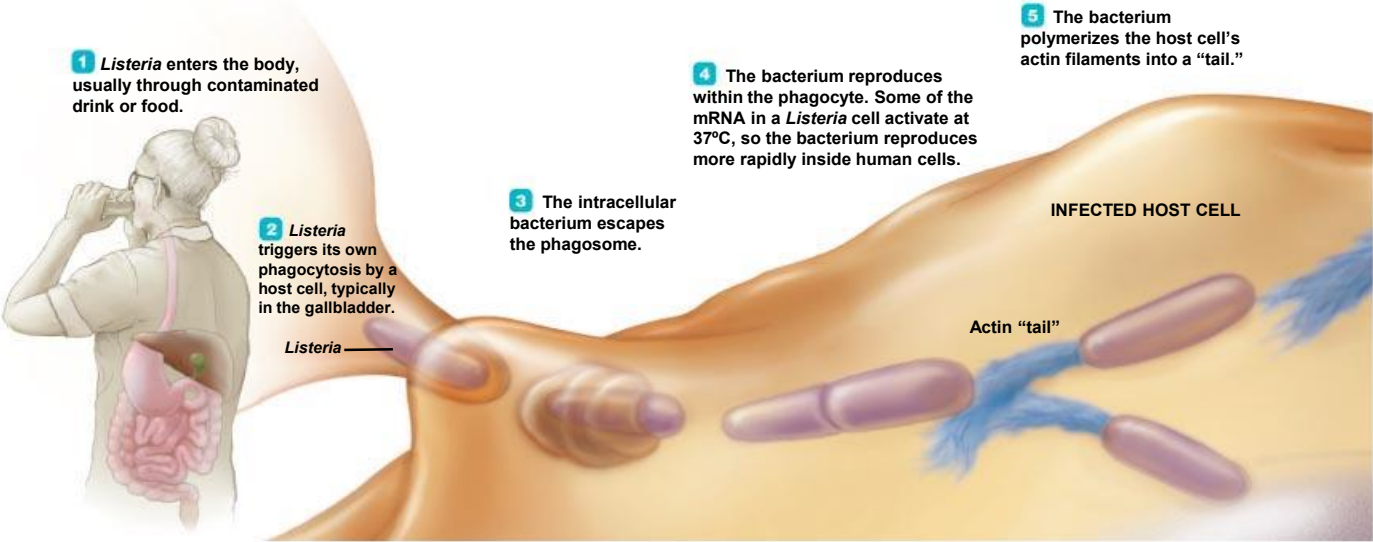
DISEASE  
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LISTERIOSIS

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ONE WAY *LISTERIA* AVOIDS HOST'S IMMUNE  
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Photomicrograph of *Listeria*  
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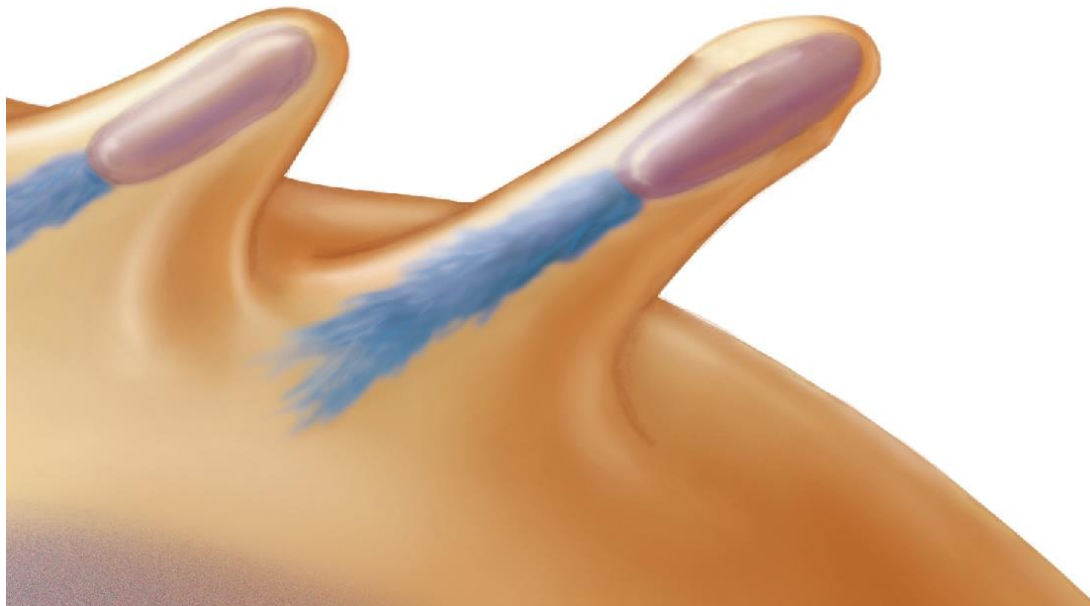
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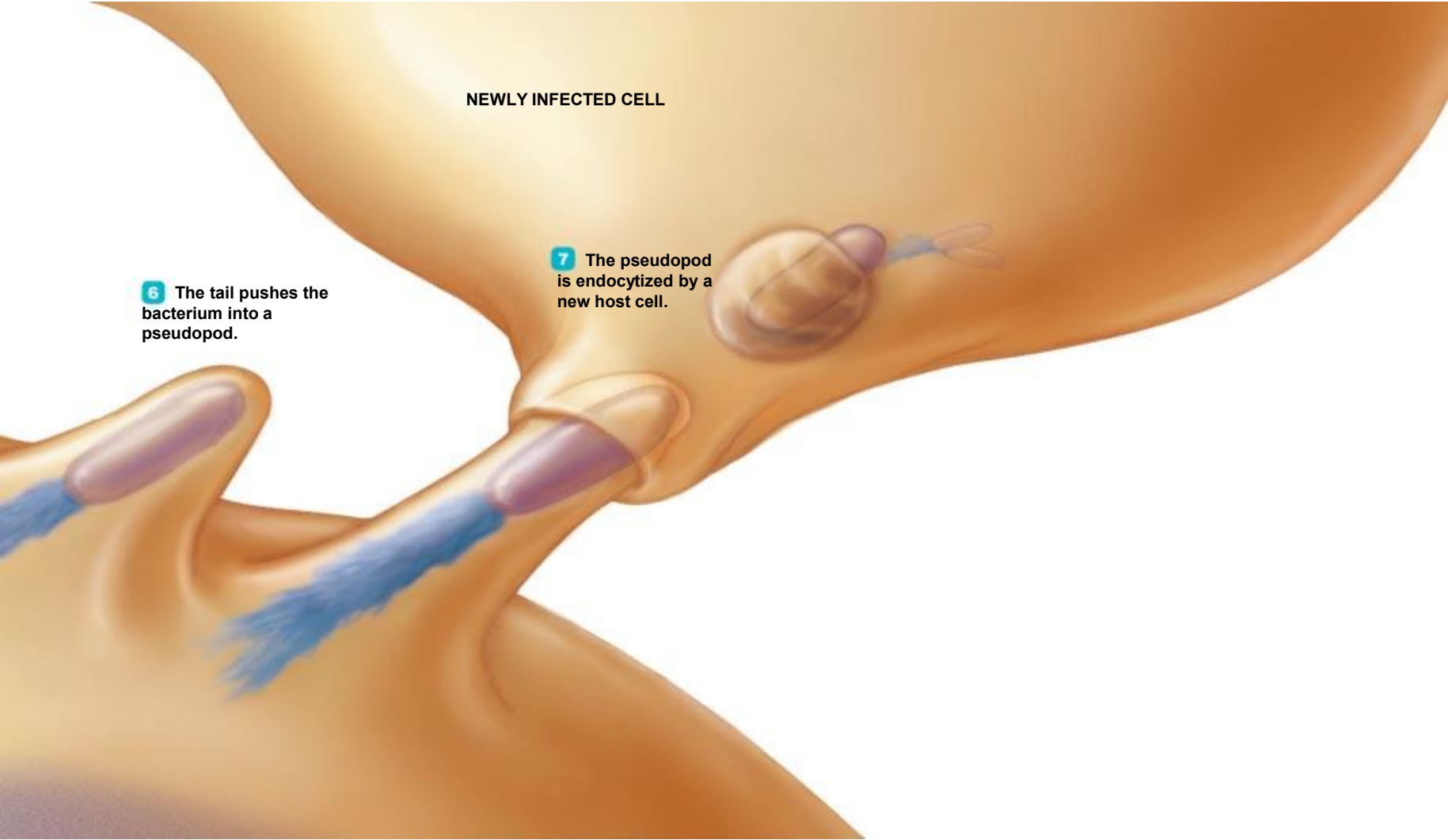
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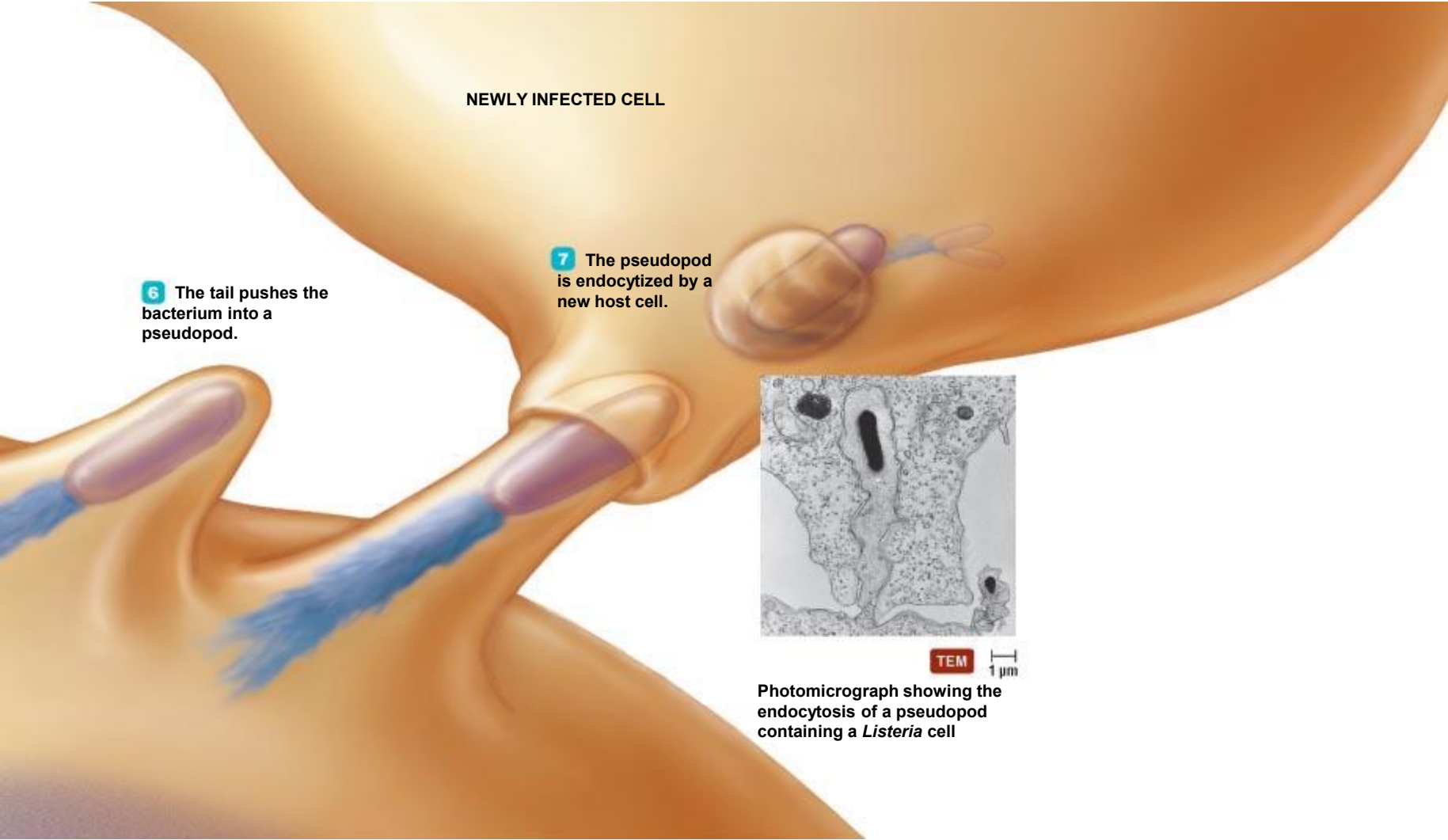
5 The bacterium  
polymerizes the host cell's  
actin filaments into a "tail."

**6** The tail pushes the bacterium into a pseudopod.

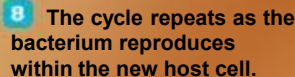


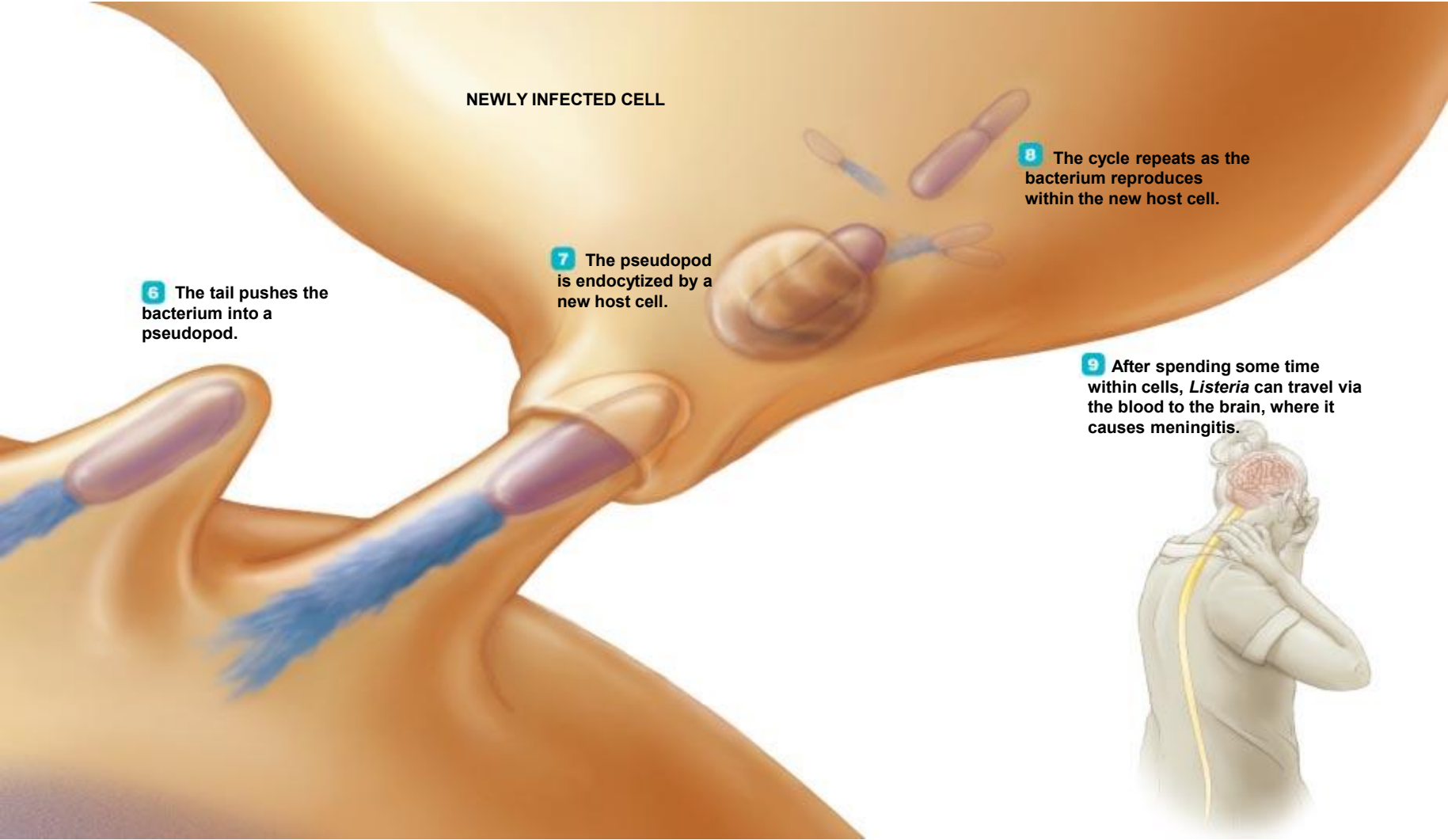












# *Listeria*

- **Diagnosis, Treatment, and Prevention**
  - Diagnosis
    - Presence of bacteria in the cerebrospinal fluid of individuals with meningitis
    - Rarely seen in Gram-stained preparations
  - Treatment
    - Ampicillin
    - Other antibiotics used for patients allergic to penicillins
  - Prevention
    - At-risk individuals should avoid certain foods