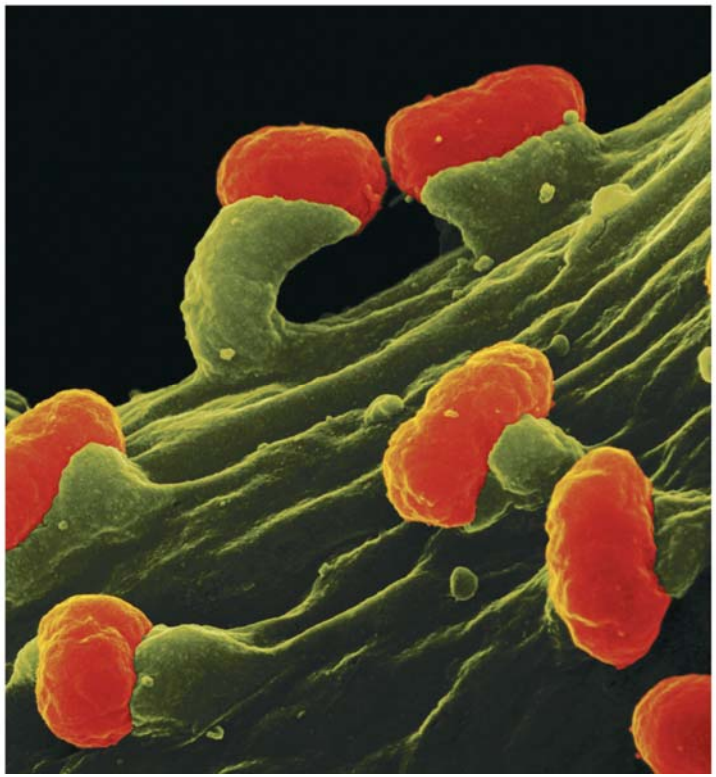
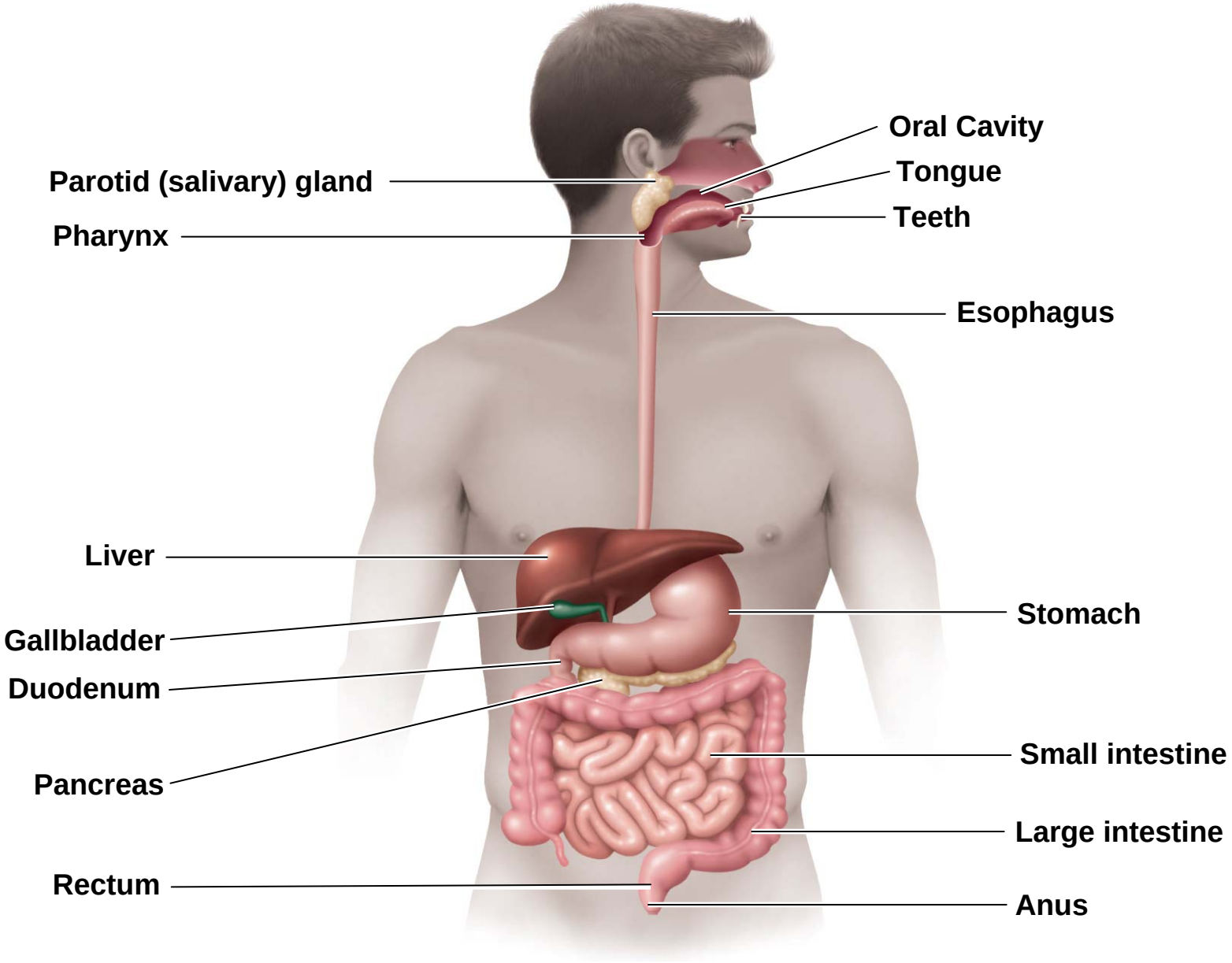
Chapter 25

Microbial Diseases of the Digestive System



The human digestive system.



Defenses

- Mucous membrane
- Lysozyme
- Stomach acidic
- Small intestine /// the Paneth cells
- IgA

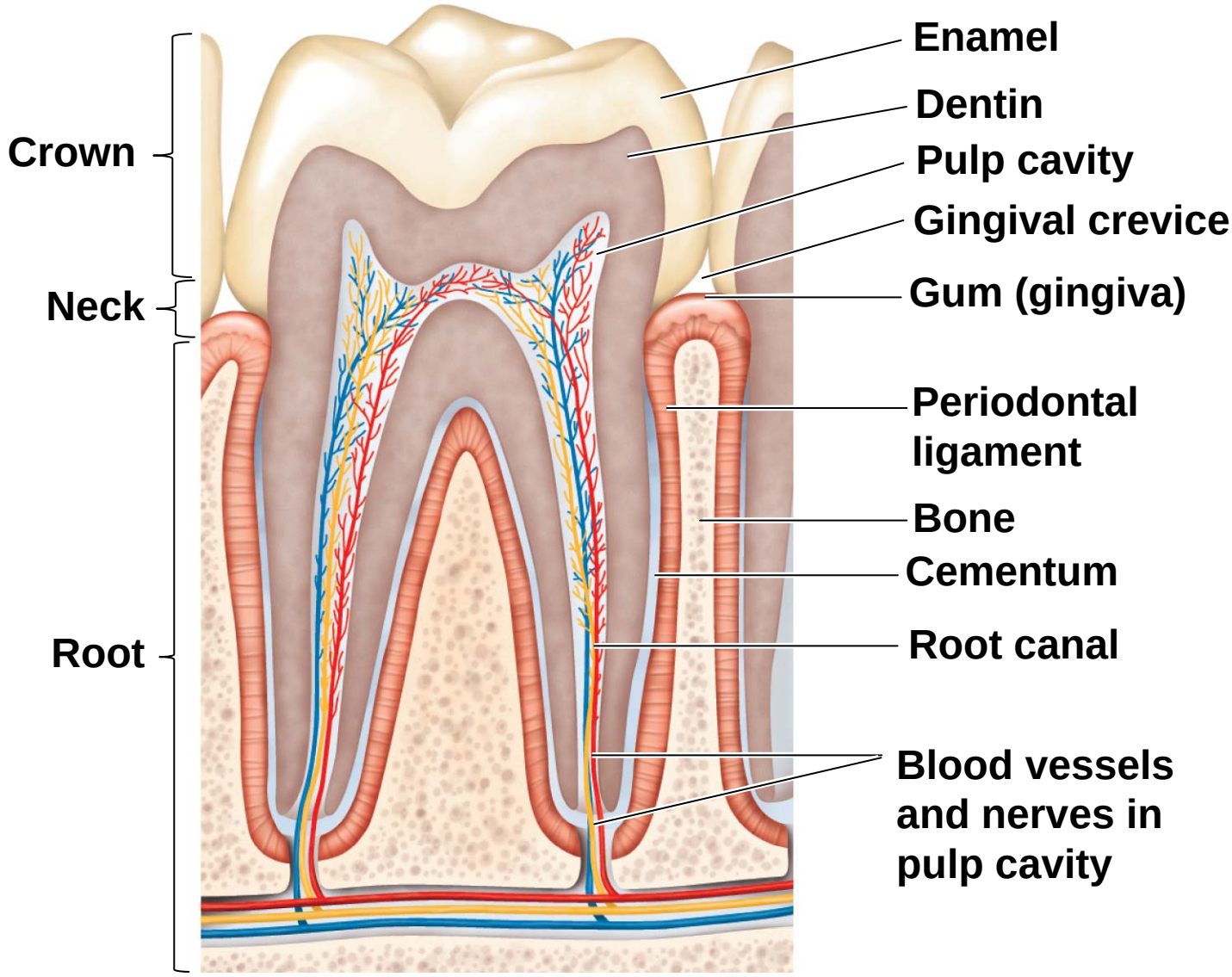
Normal Microbiota

- Millions of bacteria per ml of saliva
- Over 700 different species in oral cavity
- Evan larger numbers of bacteria in small and large intestines
- 100 billion bacteria per gram of feces

Dental Caries

- One of the more common disease today
- Few caries prior to 1700s / about 10% by examination of human remains
- Introduction of sucrose into diet correlates with increase in Western world caries

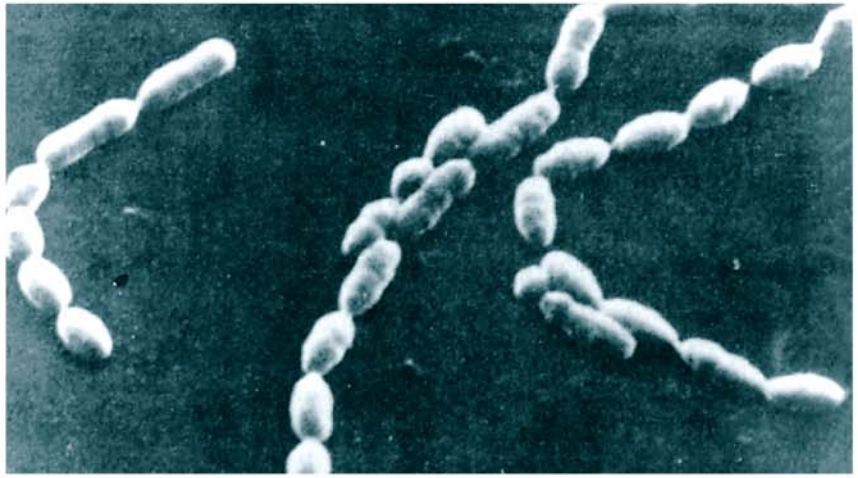
A healthy human tooth.



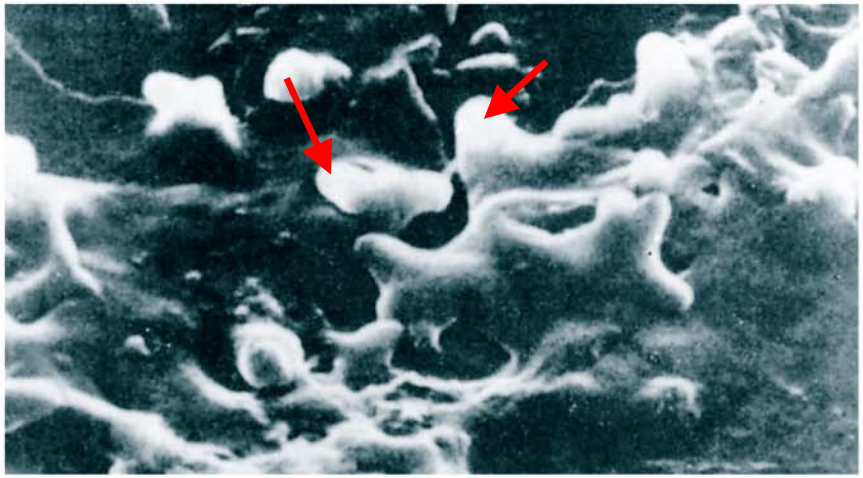
Dental Caries

- Dental plaque (biofilm) central role in formation of tooth decay
- Clean enamel surface resist attachment of Streptococcus mutans
- Saliva coats clean tooth within minutes with a protein film = pellicle
- Streptococcus mutans adheres to the pellicle film within hours // initiates formation of dental plaque

Dental Plaque = Biofilm



(a) ***S. mutans*** **growing in glucose broth**



(b) ***S. mutans*** **growing in sucrose broth; note the accumulations of dextran. Arrows point to** ***S. mutans*** **cells.**

The role of *Streptococcus mutans* and sucrose in dental caries.

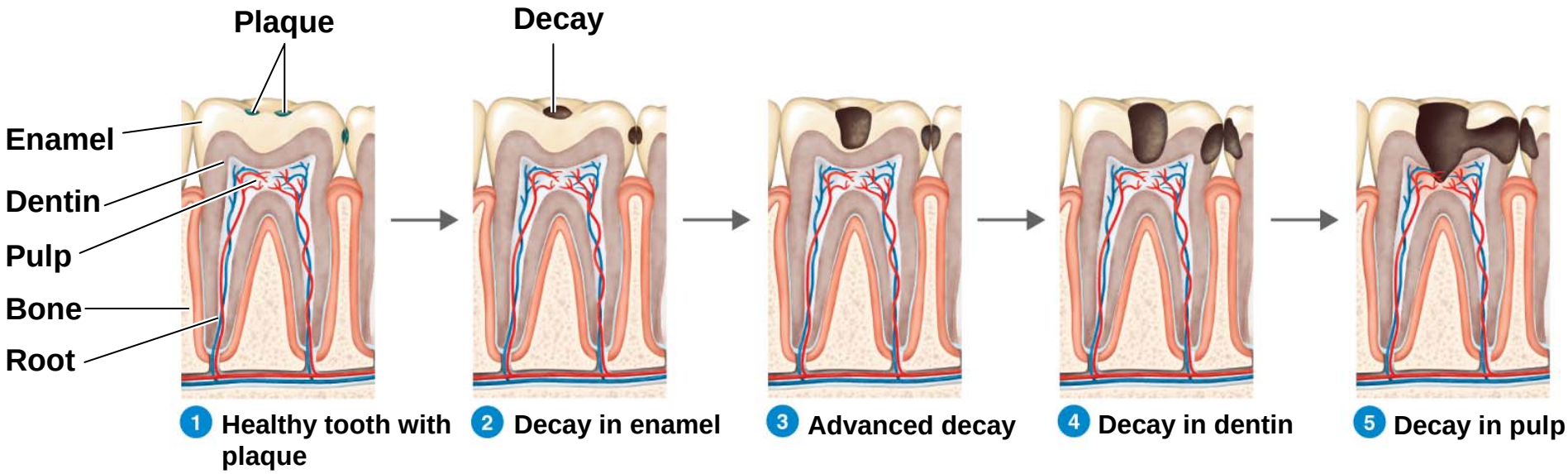
Dental Caries

- Streptococcus mutans metabolizes the disacharide sucrose into glucose and fructose
- S. mutans produces enzyme glucosyltransferase
- Enzyme converts glucose into dextran – gummy like molecule which sticks and build up on surface of tooth
- Dextrin is the matrix which allows the biofilm to assemble

Dental Caries

- Dental plaque may include up to 400 different species of bacterial // several hundred cells thick
- Fructose is fermented to lactic acid /// erodes the enamel surface
- Lactobacillus spp. - play central role in fermenting fructose – producing lactic acid
- Fluoride fills pours in enamel which hardens surface of tooth and helps resist dental caries

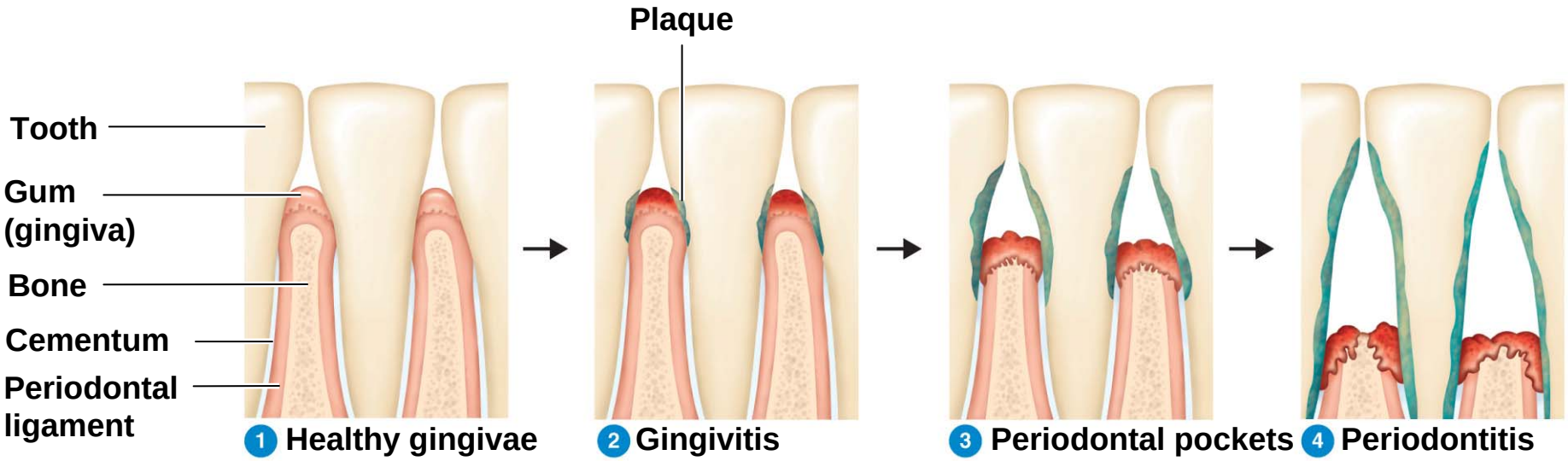
The stages of tooth decay.



After decay penetrates dentin and enters pulp // almost any bacteria of normal oral biota can be isolated in biofilm.

Direct passage into blood

The stages of periodontal disease.



Root of tooth protected by cementum // gums recede with age or overly aggressive brushing

Gums may become infected (gingivitis)

Plaque form on lateral surface of tooth / periodontitis = *Porphyromonas* spp

Bacterial Diseases of the Mouth

Disease	**Pathogen**
Dental caries	*Streptococcus mutans*
Periodontal disease	*Porphyromonas* spp.
Acute necrotizing gingivitis	*Prevotella intermedia*

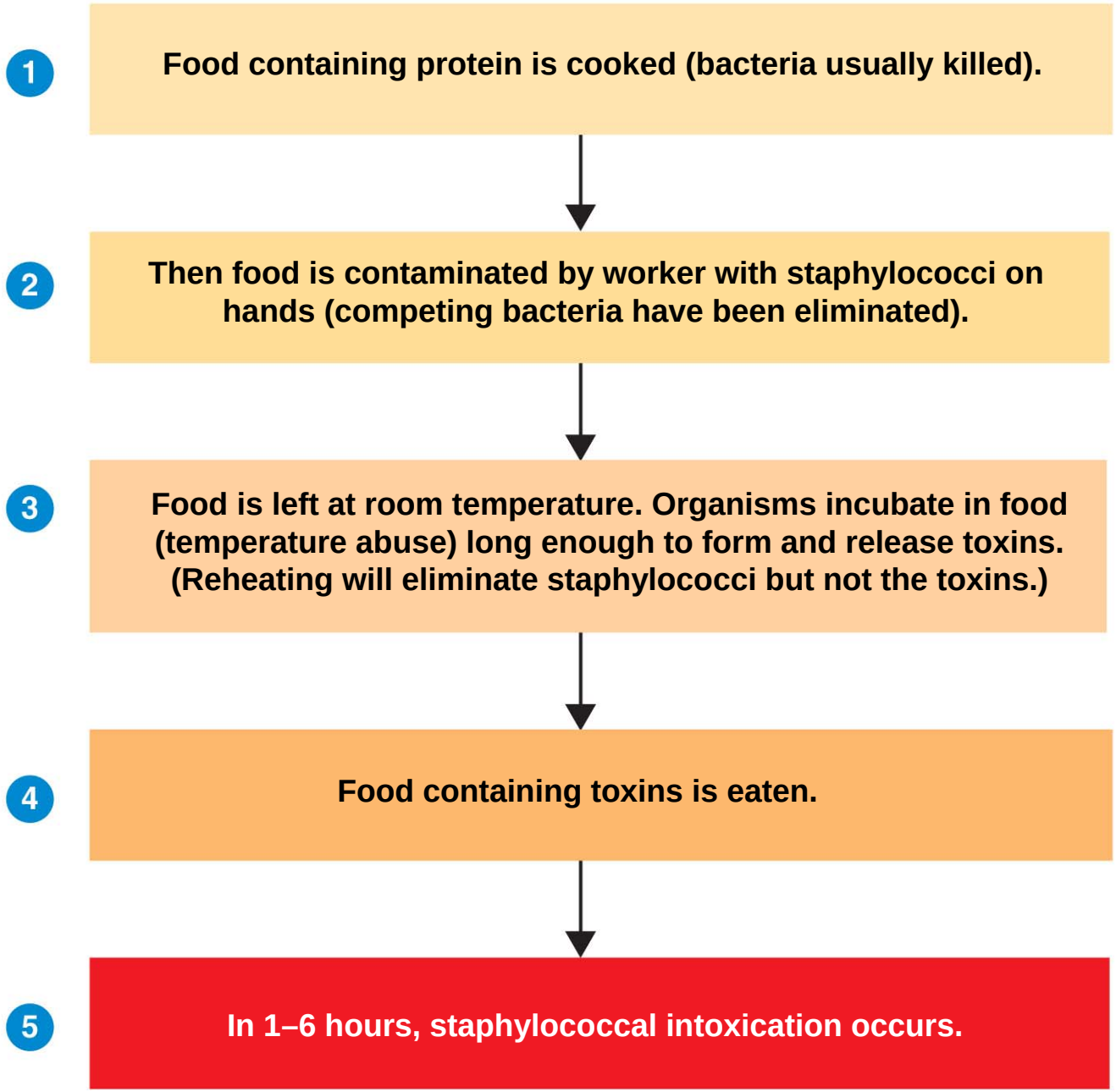
Diseases of Lower Digestive System

- **Infection**: Incubation is from 12 hours to 2 weeks /// generation time for some only 20 minutes // Fever common
- **Intoxication**: in some cases bacteria produce exotoxin (toxin) // ingestion of toxin causes disease condition // some intoxication less than 20 min others symptoms appear 1 to 48 hours after ingestion
- **Gastroenteritis**: diarrhea vs dysentery
- **Treatment**: oral rehydration therapy

Bacterial Diseases of Lower Digestive System

- Staphylococcal Enterotoxicosis
- Shigellosis (Bacillry Dysentery)
- Salmonellosis (Salmonella Gastroenteritis)
- Typhoid Fever
- Cholera
- Noncholera Vibrios
- Esherichia coli Gastroenteritis
- Campylobacter Gastroenteritis
- Helicobacter Peptic Ulcer Disease
- Yersinia Gastroenteritis
- Clostridium perfringens Gastroenteritis
- Clostridium difficile Associated Diarrhea
- Bacillus cereus Gastroenteritis

The sequence of events in a typical outbreak of staphylococcal food poisoning.

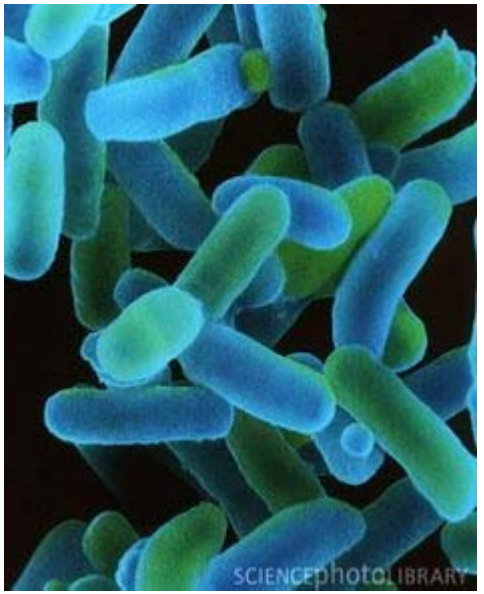


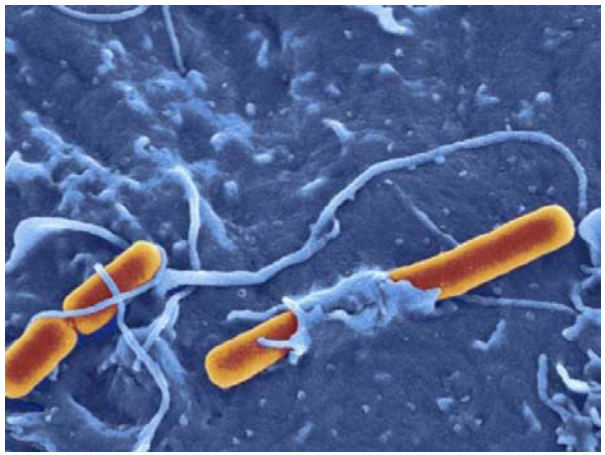
Staphylococcal Food Poisoning

Pathogen	*Staphylococcus aureus*
Symptoms	Nausea, vomiting, and diarrhea
Intoxication/Infection	Intoxication Enterotoxin (superantigen)
Diagnosis	Phage typing
Treatment	None

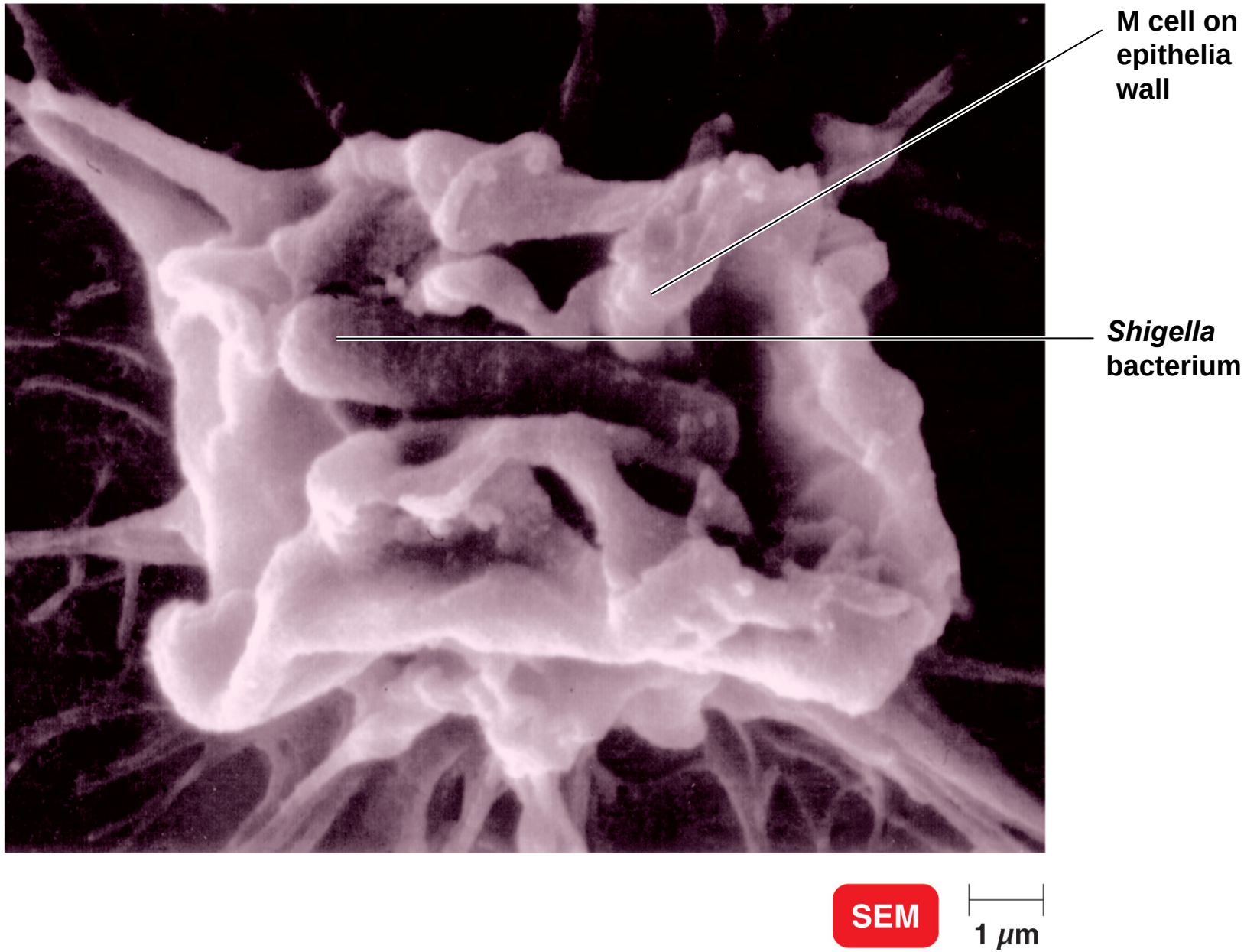
Shigelosis (Bacillary Dysentery)

- Shigella ssp. / facultative anaerobic gram-negative
- Resident in intestine of humans
- Traveler's diarrhea / mild form of shegelosis
- Toxin responsible for more virulent forms = Shiga toxin / S. dysenteriae
- Shiga toxin destroys tissue
- Shigella ssp. Live and multiply in phagocytes // bacteria actually kills the phagocytes!
- Shigella infection can result in as many as 20 bowel movements per day

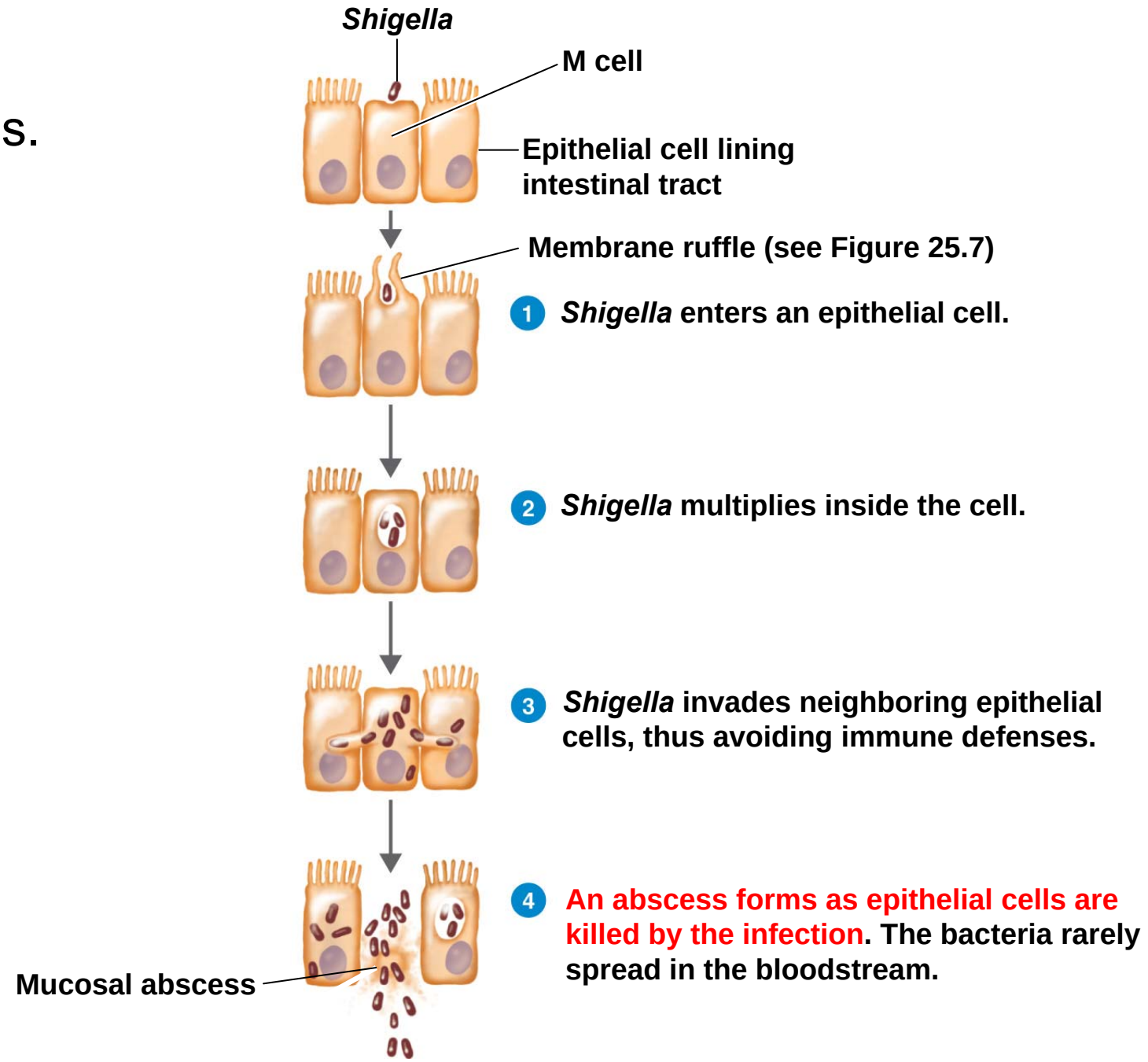




Invasion of intestinal wall by *Shigella* bacterium.



Shigellosis.



Shigellosis (Bacillary Dysentery)

Pathogen	*Shigella* spp.
Symptoms	Tissue damage and dysentery
Intoxication/Infection	Infection Endotoxin and Shiga exotoxin
Diagnosis	Isolation of bacteria
Treatment	Fluoroquinolones

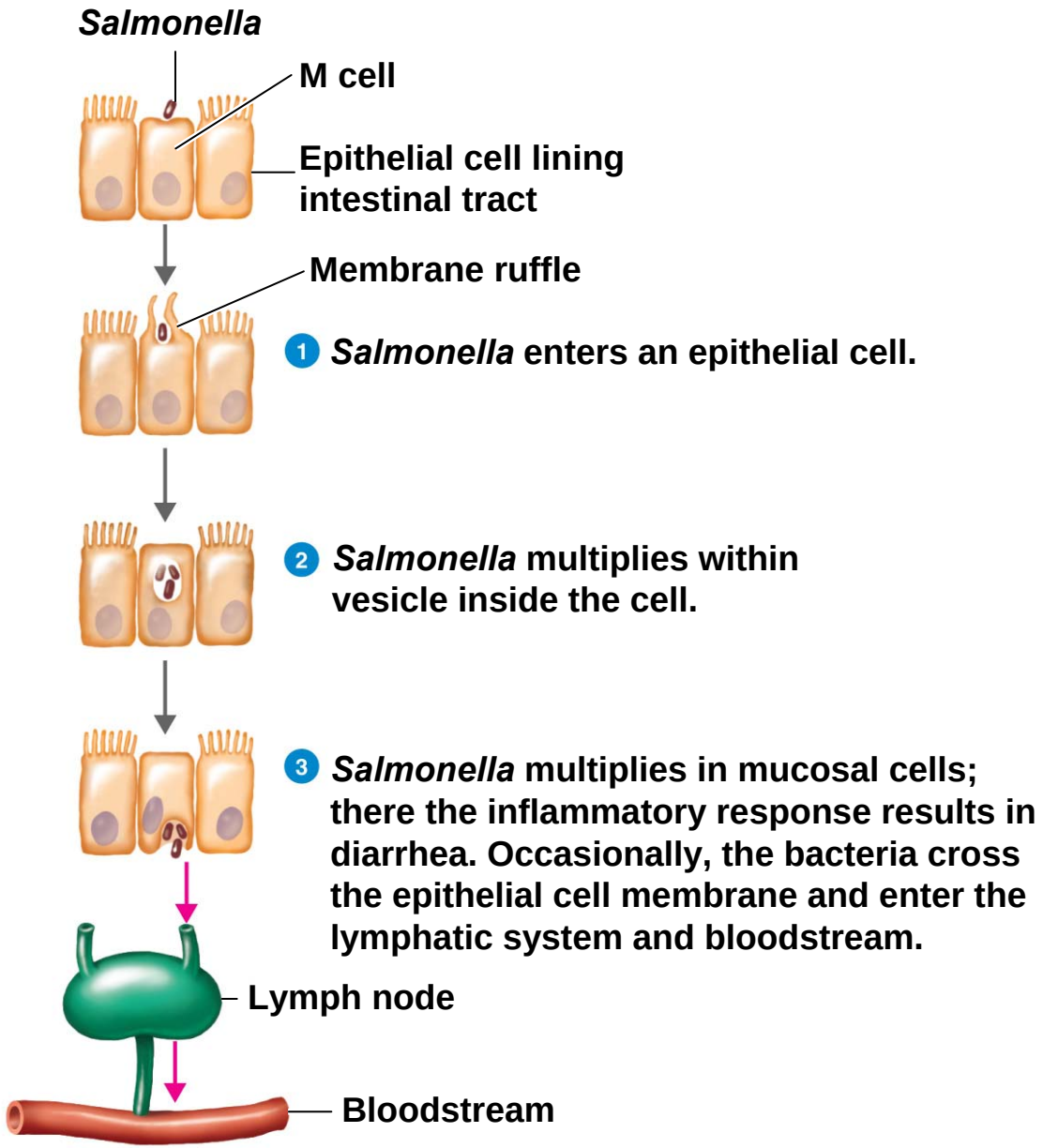
Salmonellosis (Salmonella Gastroenteritis)

- Salmonella ssp. // gram negative facultatively anaerobic
- Normal habitat = intestinal tracts of humans and many other animals
- All species considered pathogenic // causes salmonellosis
- Small turtles have carriage rate up to 90% - why FDA prohibited sale as pets to children

Salmonellosis (Salmonella Gastroenteritis)

- Typhoidal salmonellae (more serious disease) vs non-typhoidal = salmonellae (milder disease)
- *Salmonella enterica VS Salmonella typhi*
- Salmonellosis mortality rate very low (less than 1%) // higher for infants and very old
- Recovery in few days /
- May continue to shed bacteria for up to 6 months.

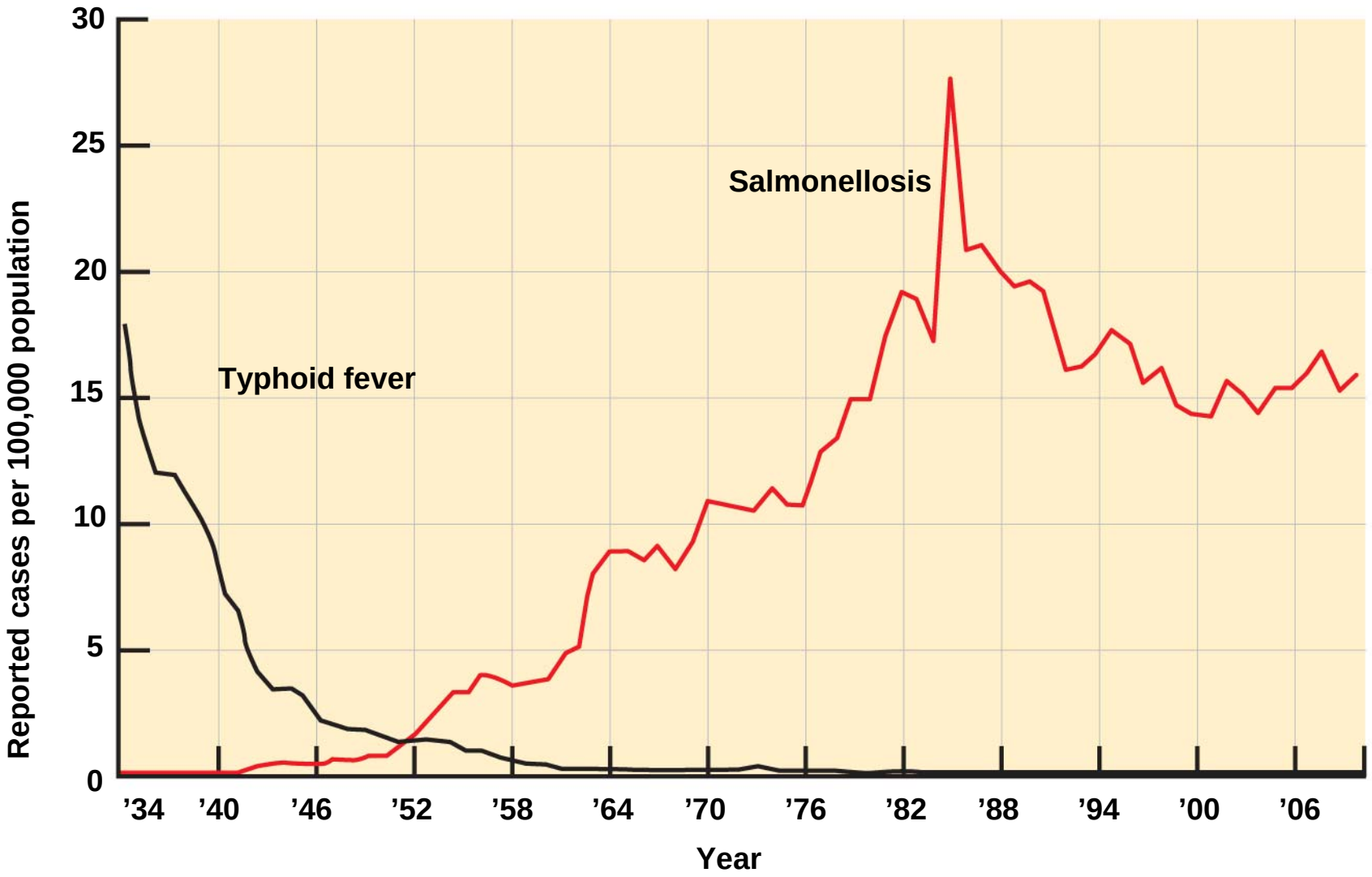
Salmonellosis



Typhoid Fever (Salmonella typhi)

- *Only found in human feces*
- Bacteria spread throughout body in phagocytes // spread into other tissues // primarily spleen and liver
- Incubation period 2 – 3 weeks // high fever and diarrhea results after 2nd week
- 1–3% of recovered patients become **chronic carriers** ***//*** pathogen in Gall bladder – Typhoid Mary
- Recovery confers lifelong immunity

The incidence of salmonellosis and typhoid fever.



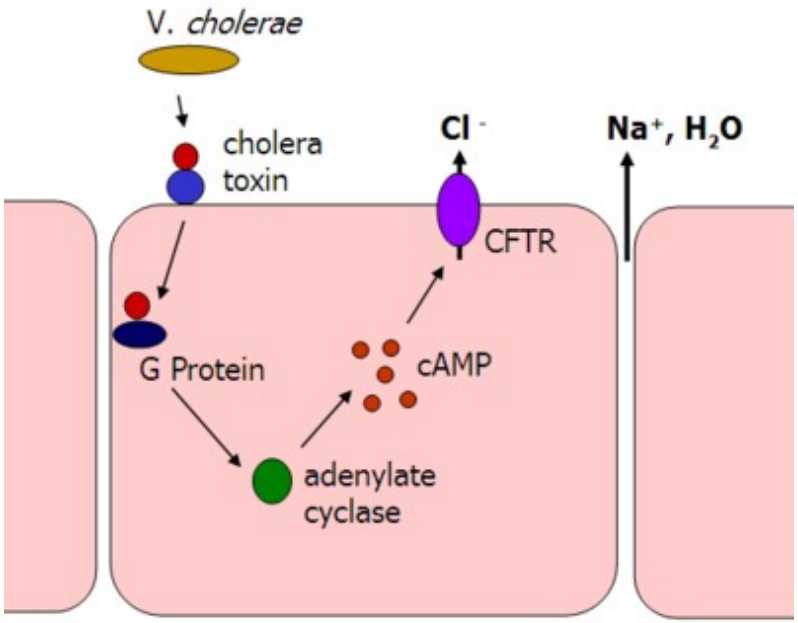
Disease	**Salmonellosis**	**Typhoid Fever**
Pathogen	*Salmonella enterica*	*S. typhi*
Symptoms	Nausea and diarrhea	High fever, significant mortality
Intoxication/ Infection	Infection Endotoxin	Infection Endotoxin
Diagnosis	Isolation of bacteria; serotyping	Isolation of bacteria; serotyping
Treatment	Oral rehydration	Quinolones; cephalosporins

Vibrio cholera (Cholera)

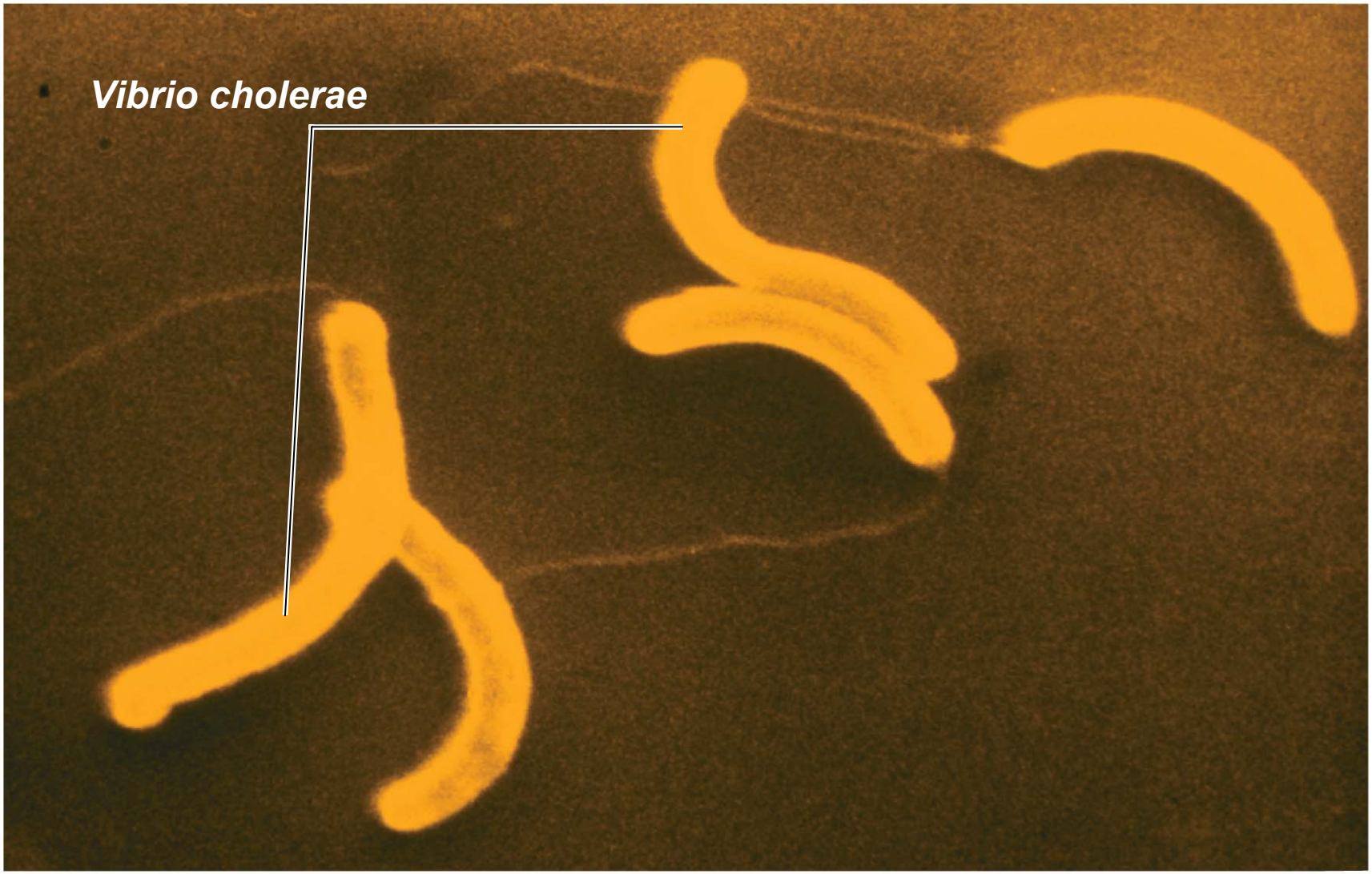
- *Gram negative rod*
- *Effective dose 100 million bacteria*
- Recovery – effective immunity but only to causative serotype
- Not invasive // not associated with fever
- Associated with brackish waters but also able to survive in fresh water
- Flagella virulence factor // successive generations able to turn gene on and off as needed

Vibrio cholera

- Grow in intestine and produce exotoxin = cholera toxin
- Toxin enters small intestine epithelial cells // Toxin causes host cells to secrete Cl^-, HCO^-, and water // second messenger mechanism
- Diarrhea called rice water stools
- Up to 5 gallons per day with violent vomiting
- Untreated mortality rate 50% +

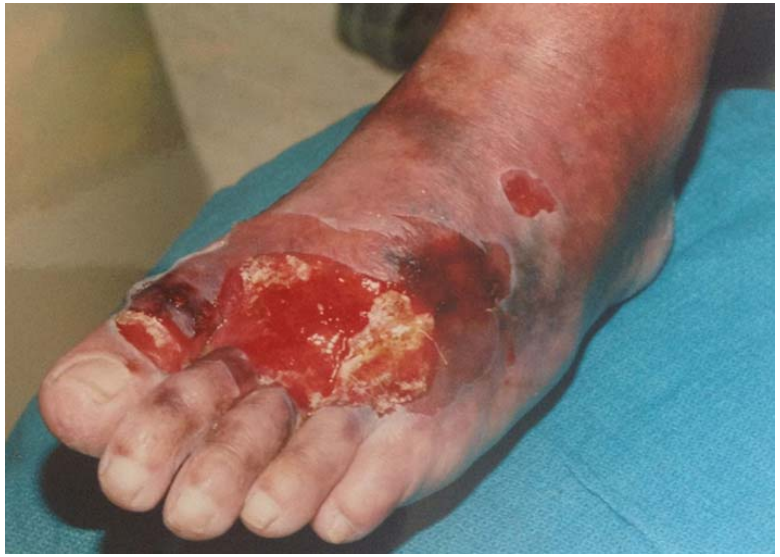


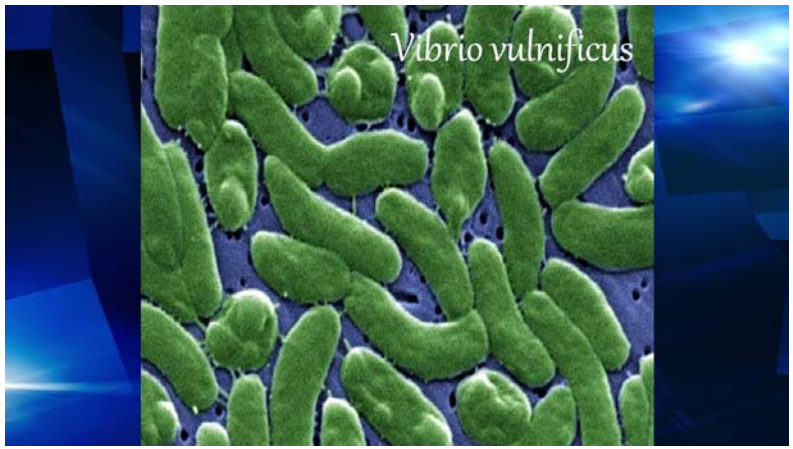
Vibrio cholerae, the cause of cholera.



Non-cholera vibrios

- *V. parahaemolyticus & V. vulnificus*
- Usually from contaminated crustaceans or mollusks
- Walking in costal salt water with skin lesion portal of entry for V. vulnificus
- V. vulnificus invasion of the bloodstream // if sepsis occurs – fatality rate 25%
- Rapid destruction of tissue // may necessitate limb amputations

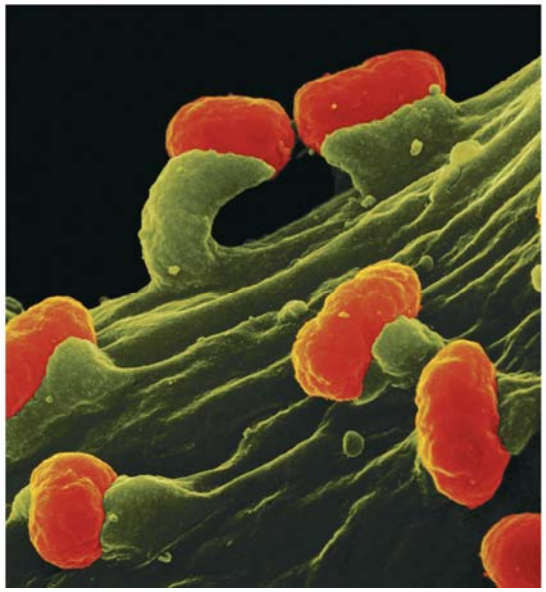




Disease	**Cholera**	**Noncholera Vibrios**	
Pathogen	*Vibrio cholerae* O:1 and O:139	*V. parahaemolyticus*	*V. vulnificus*
Symptoms	Diarrhea with large water loss	Cholera-like diarrhea, but generally milder	Rapidly spreading tissue destruction
Intoxication/ Infection	Cholera toxin (exotoxin)	Infection, enterotoxin	Infection, siderophores
Diagnosis	Isolation of bacteria	Isolation of bacteria	Isolation of bacteria
Treatment	Rehydration; doxycycline	Rehydration; antibiotics	Antibiotics

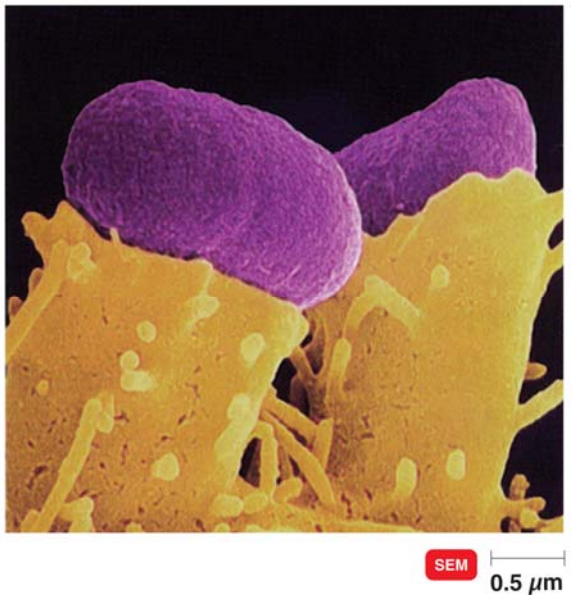
Escherichia coli Gastroenteritis

- E. coli common intestinal bacteria in many animals
- Most studied bacterial – considered a “lab pet”
- Most species of E. coli are harmless // some strains are pathogenic
- Pathogenic E. coli do not infect cattle
- Cattle cell’s lack receptors so E. coli can not attach to host cells // cattle reservoir – 2-3% cattle carry STEC
- Meat contaminated with pathogenic E. coli able to attach and infect humans
- Oral rehydration recommended for all diarrhea

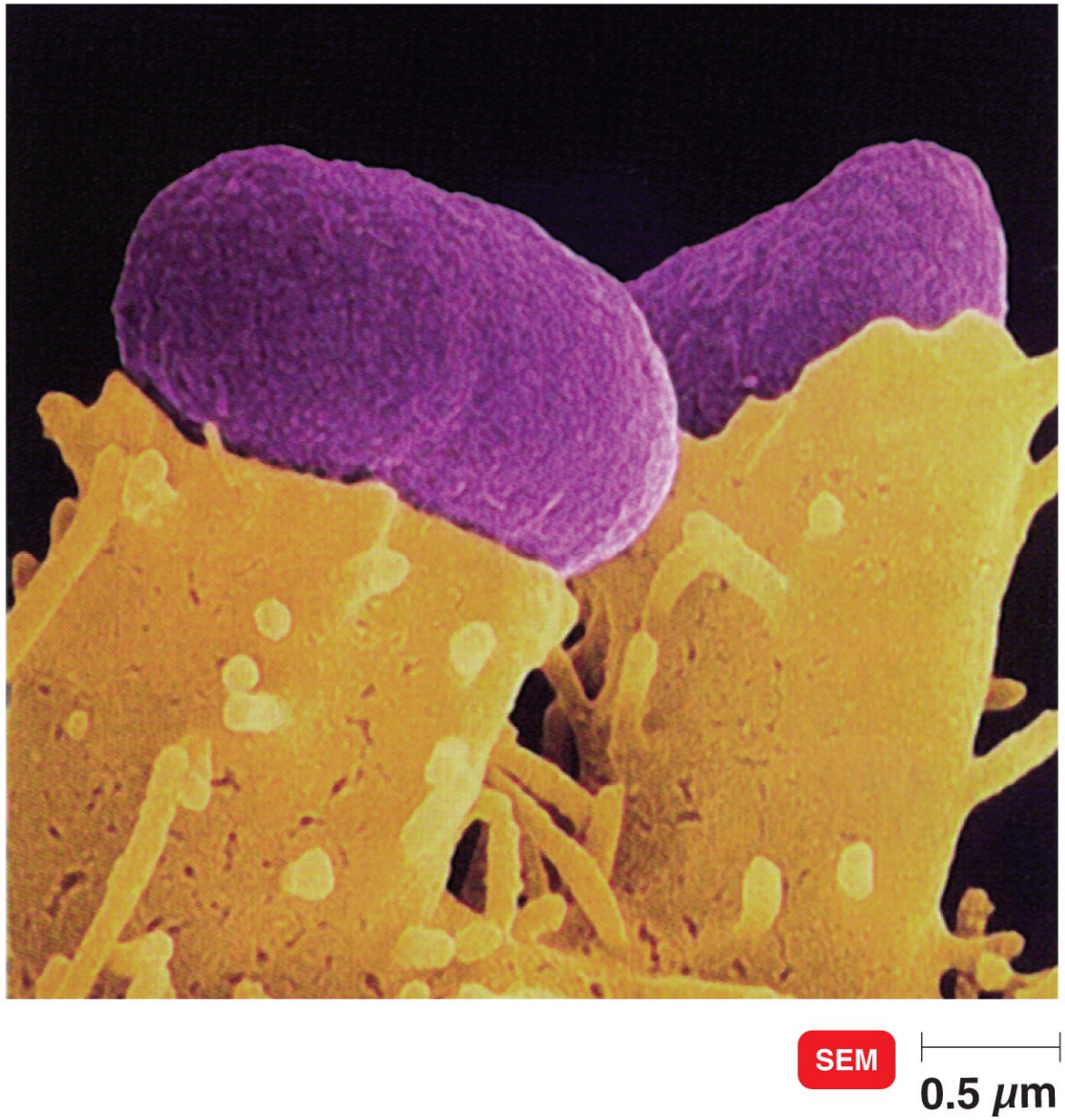


Escherichia coli Gastroenteritis

- Enteropathogenic E. coli
  - major cause of diarrhea in developing countries
  - fatal to infants
  - bacteria eliminates microvilli
  - stimulates host cell's actin to form pedestal
  - bacteria secrete effector proteins – contribute to diarrhea



Pedestal formation by Enterohemorrhagic *E. coli* (EHEC) O157:H7.



Escherichia coli Gastroenteritis

- Enteroinvasive E. Coli
  - bacteria receives genetic code to make Shiga toxin
  - same disease mechanism as Shigella like dysentery // essentially synonymous with Shigella
  - Invade submucosa via M cells
  - Shigella-like dysentery

Escherichia coli Gastroenteritis

- Enteroaggregative E. coli
  - Found only in humans
  - “Stacked-brick” configuration when grown on tissue cultures
  - Not invasive
  - Produce toxins which cause watery diarrhea

Escherichia coli Gastroenteritis

- Enterohemmorrhagic E. coli
  - Caused serious disease outbreaks in US // associated with hamburger meat recalls
  - Pedestal formation as EPEC // but slightly different mechanism
  - Produce “Shiga toxin” // sometimes referred to as Shiga-toxin producing E. coli (STEC)
  - Toxin released when bacteria lysis // antibiotic therapy can worsen the attack
  - Secondary complication // Hemolytic uremic syndrome (HUS) – Shiga toxin affects kidneys // blood in urine // leads to kidney failure – accounts for up to 500 deaths annually

Escherichia coli Gastroenteritis

- Enterotoxigenic E. coli (ETEC)
  - Not invasive
  - Secretes enterotoxin to cause diarrhea // frequent fatal to children
  - Toxin similar to function of Cholera toxin
  - Most likely cause of “traveler’s diarrhea” // travel broadens the mind and loosens the bowels

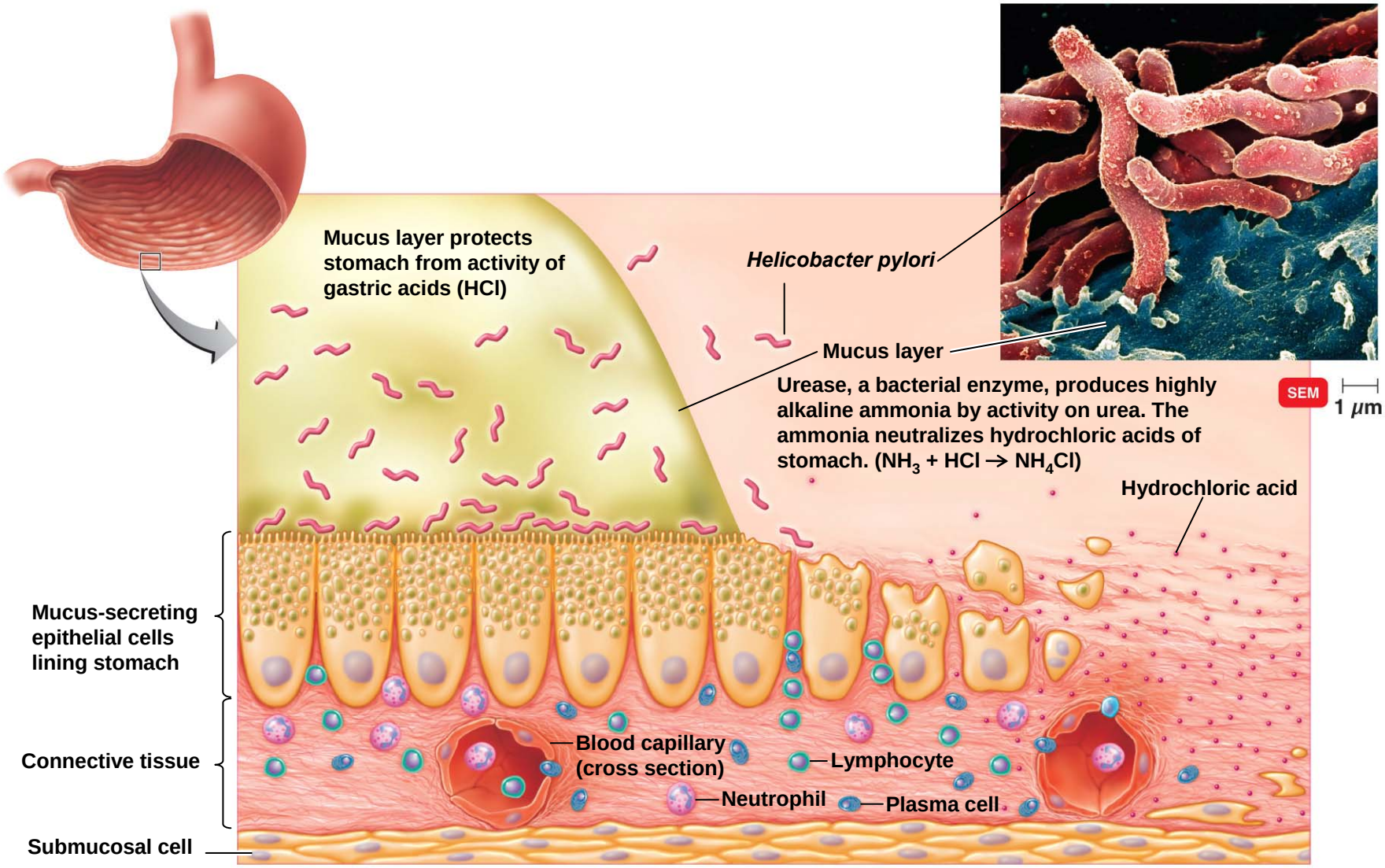
Escherichia coli Gastroenteritis

EPEC	Stimulate host-cell actin to form pedestals beneath attachment site
EIEC	Access intestinal submucosa through M cells
EAEC	Not invasive; enterotoxin causing a watery diarrhea
EHEC (STEC)	Phage-encoded Shiga toxin

Helicobacter pylori

- Responsible for peptic ulcer disease // ulceration in stomach and duodenum
- 50% people test H. pylori positive but only 15% develop ulcers // blood type O increase odds
- H. pylori produce enzyme that metabolizes urea to form ammonia a strong base // neutralizes low pH
- Changing pH associated with breakdown of mucous // Causes gastritis // resulting inflammation results in ulceration
- Antibiotics that eliminate H. pylori reverses ulcerations

Helicobacter pylori infection, leading to ulceration of the stomach wall.

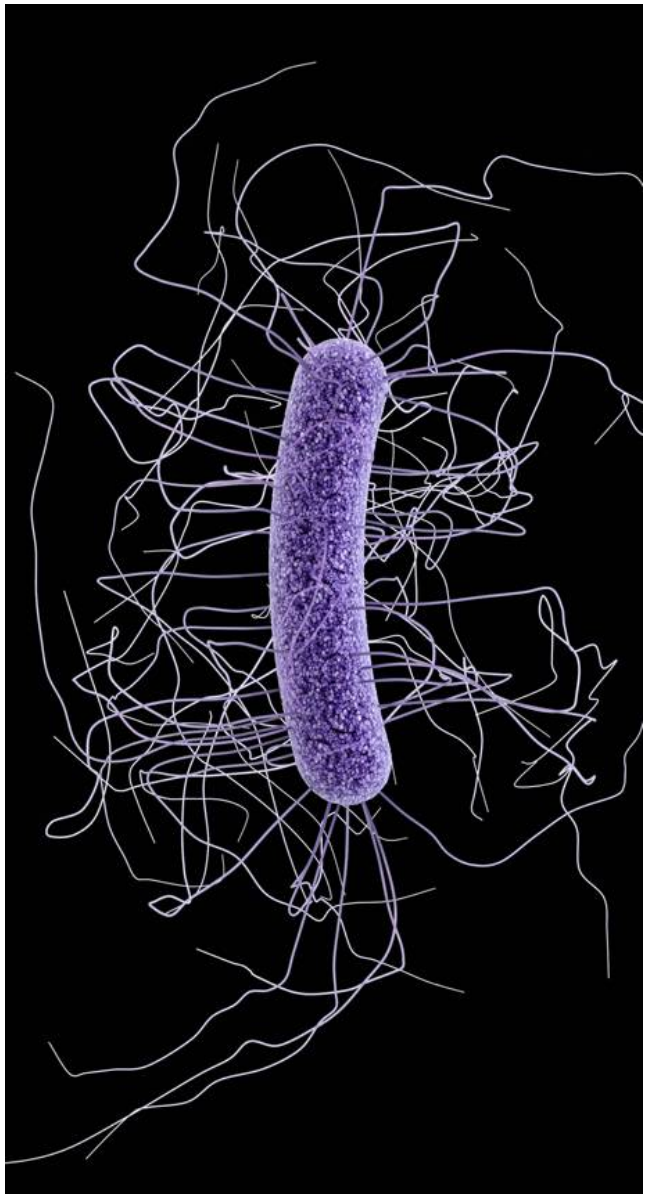


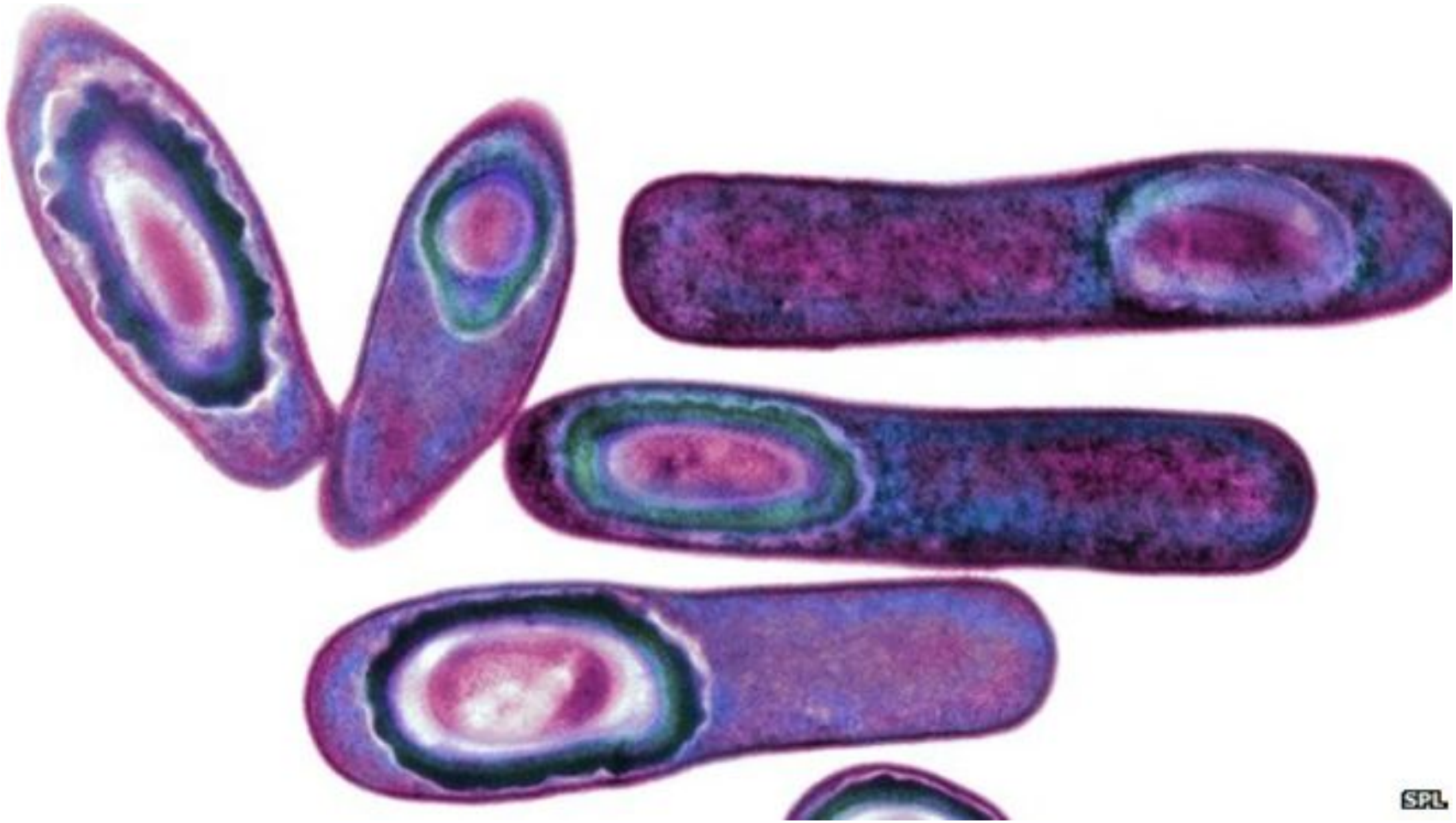
Helicobacter Peptic Ulcer Disease

Pathogen	*Helicobacter pylori*
Symptoms	Peptic ulcers
Intoxication/Infection	Infection
Diagnosis	Urea breath, bacterial culture
Treatment	Antimicrobial drugs

Clostridium difficile

- Serious nosocomial infection // antibiotic resistant
- Gram positive endospore forming anaerobe
- Exotoxin symptoms range from mild diarrhea to life-threatening colitis – with ulceration and sepsis into abdominal cavity
- Responsible for more deaths than all other intestinal infections
- Now seen more as community disease

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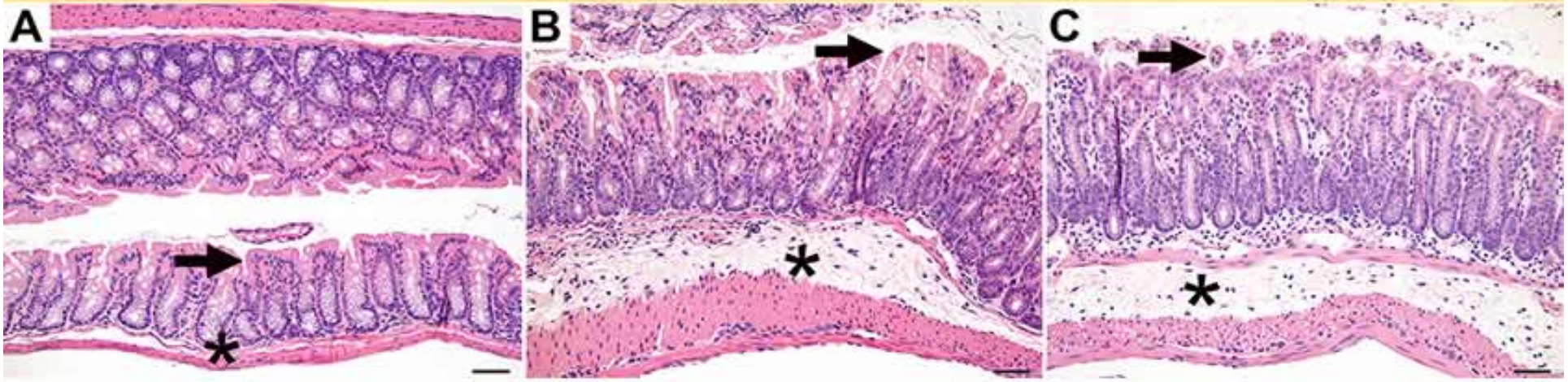
What does *C. difficile* do to the gut?



24 hours after exposure:
Cells of colon lining are normal

30 hours after exposure:
C. difficile toxin has started to damage cells, triggering inflammation & fluid buildup

36 hours after exposure:
Inflamed cells burst & die. *C. difficile* spores leave colon via diarrhea & await next host.

MEDICAL SCHOOL

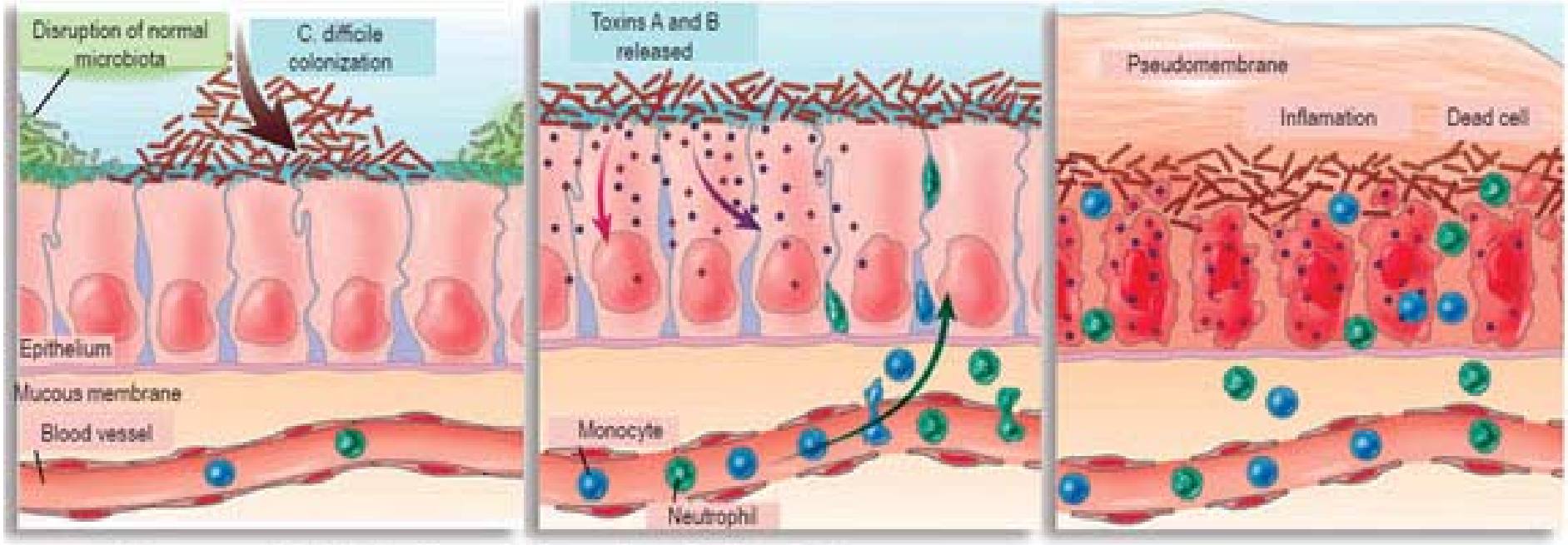
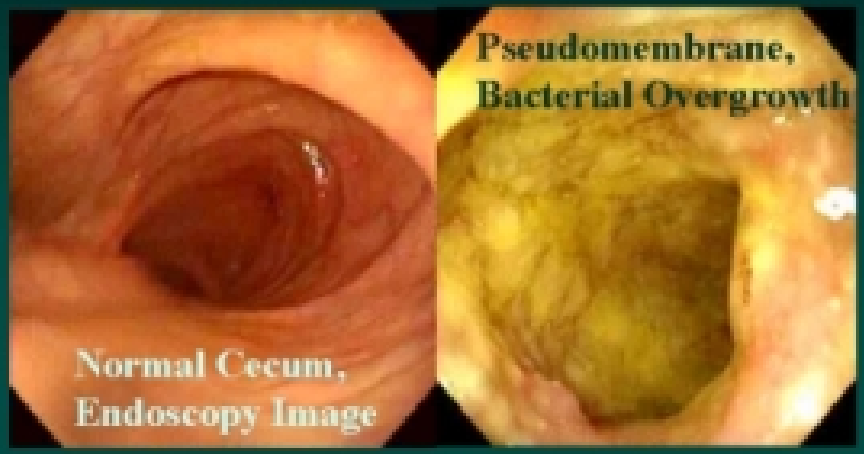
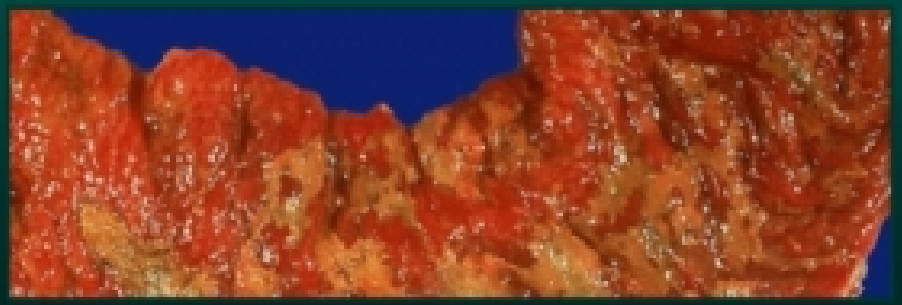


Figure 1. Pathogenesis of C. difficile infections. Taken and modified from Reference 2.

Pseudomembranous Ulcerative Colitis





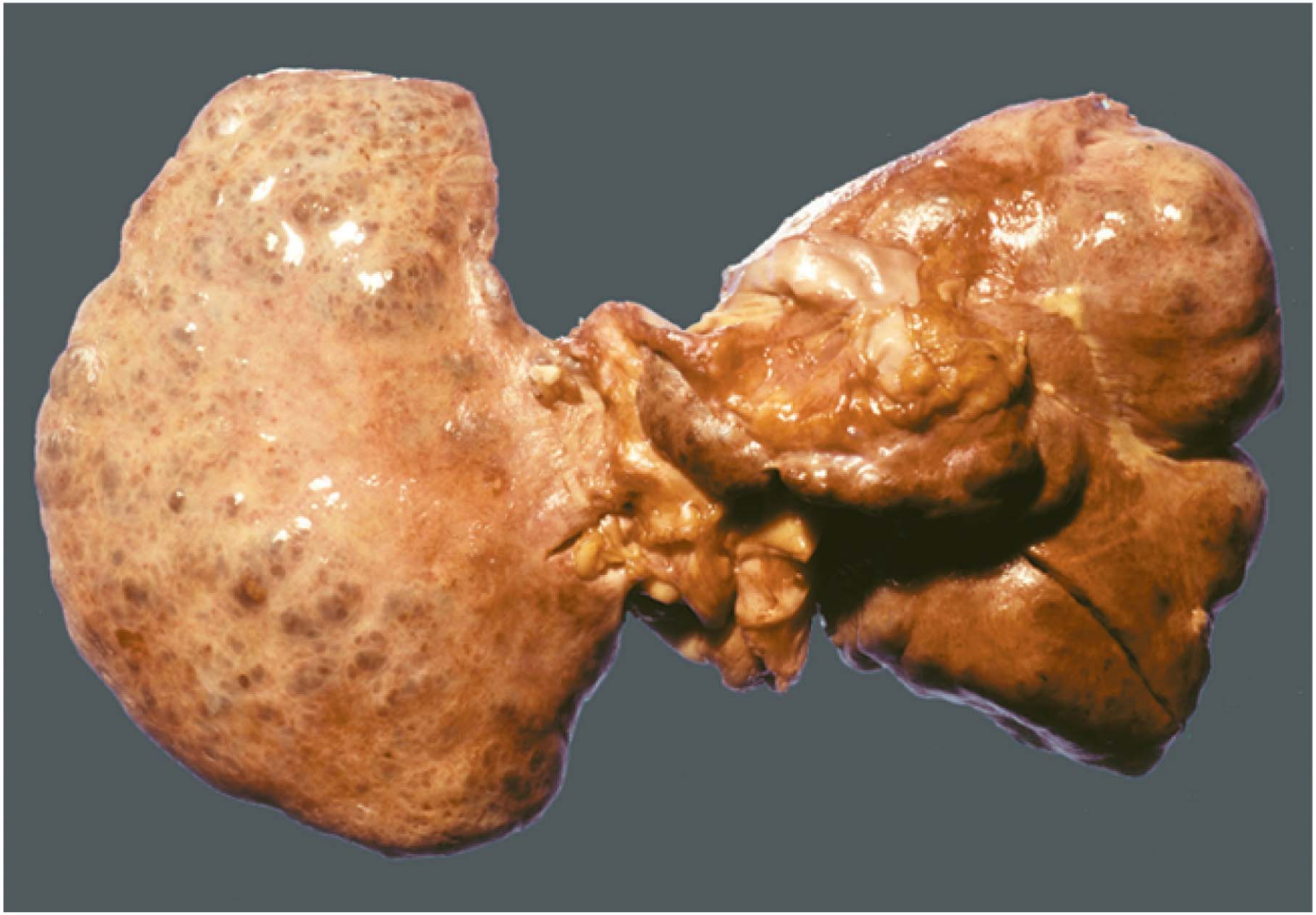
C. difficile overgrowth

Hepatitis

- An inflammation of the liver
- May result from drug or chemical toxicity, virus, or the hepatitis viruses

Characteristics of Viral Hepatitis

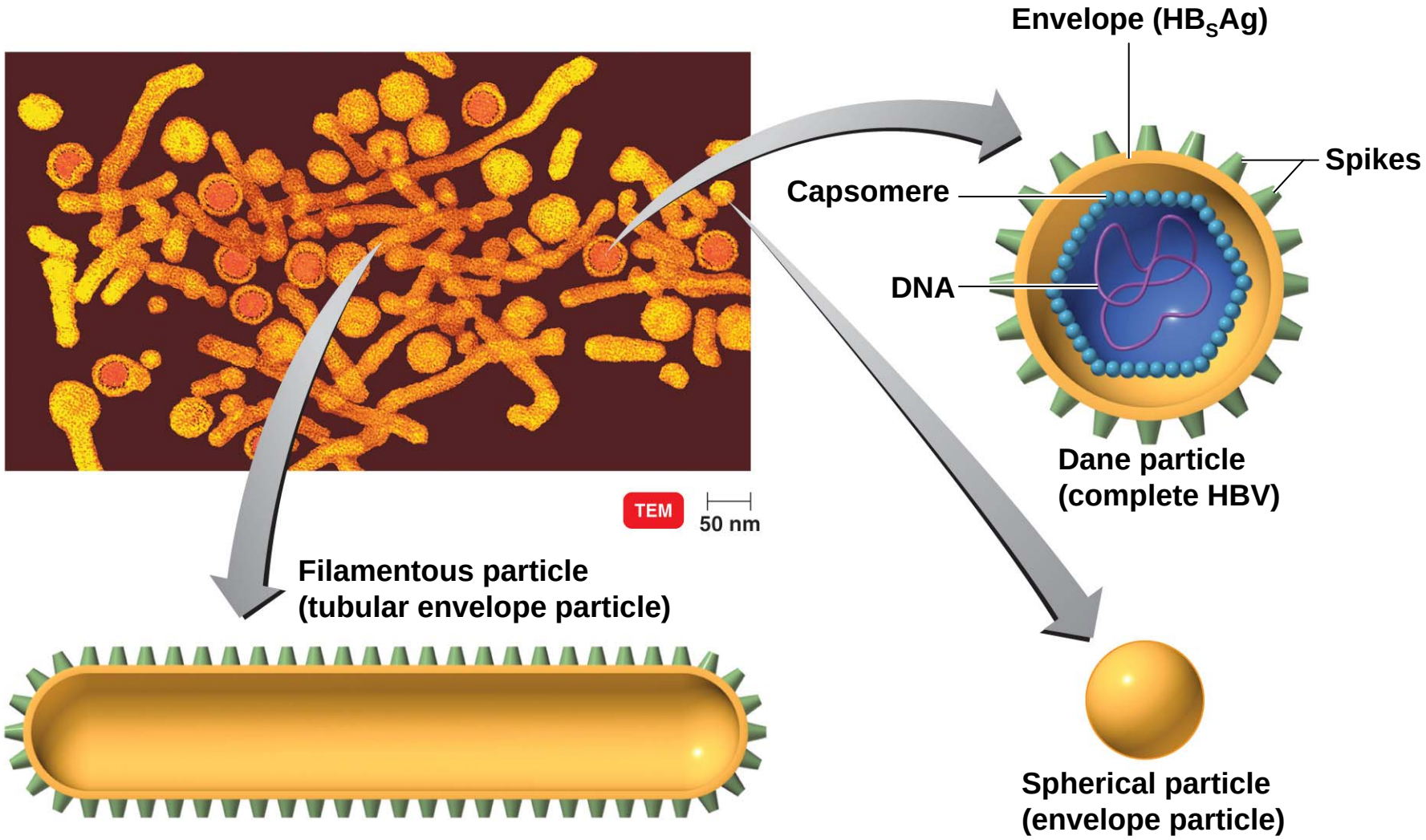
Characteristics of Viral Hepatitis



Hepatitis Viruses

Disease	Transmission	Pathogen	Chronic Liver Disease?	Vaccine?
Hepatitis A	Fecal-oral	Picornaviridae	No	Inactivated virus
Hepatitis B	Parenteral, STI	Hepadnaviridae	Yes	Recombinant
Hepatitis C	Parenteral	Filoviridae	Yes	None
Hepatitis D	Parenteral, HBV coinfection	Deltaviridae	Yes	HBV vaccine
Hepatitis E	Fecal-oral	Caliciviridae	No	HAV vaccine

Hepatitis B virus (HBV).



Viral Gastroenteritis

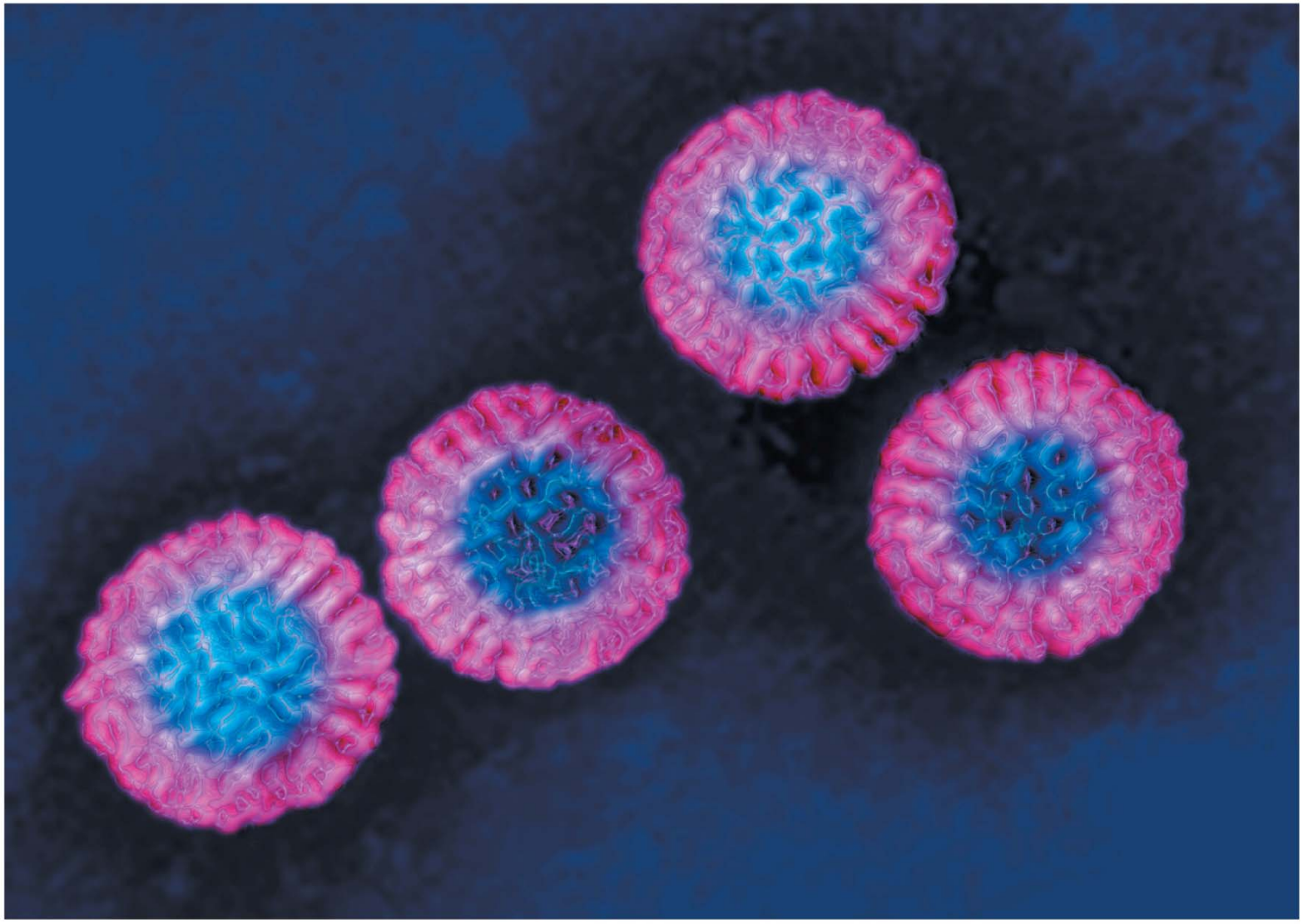
- Rotovairus / most common cause of viral gastroenteritis // 2 – 3 day incubation period with low grade fever and diarrhea for about a week

- Acquired immunity prevents most secondary infection // some strains able to cause second infections

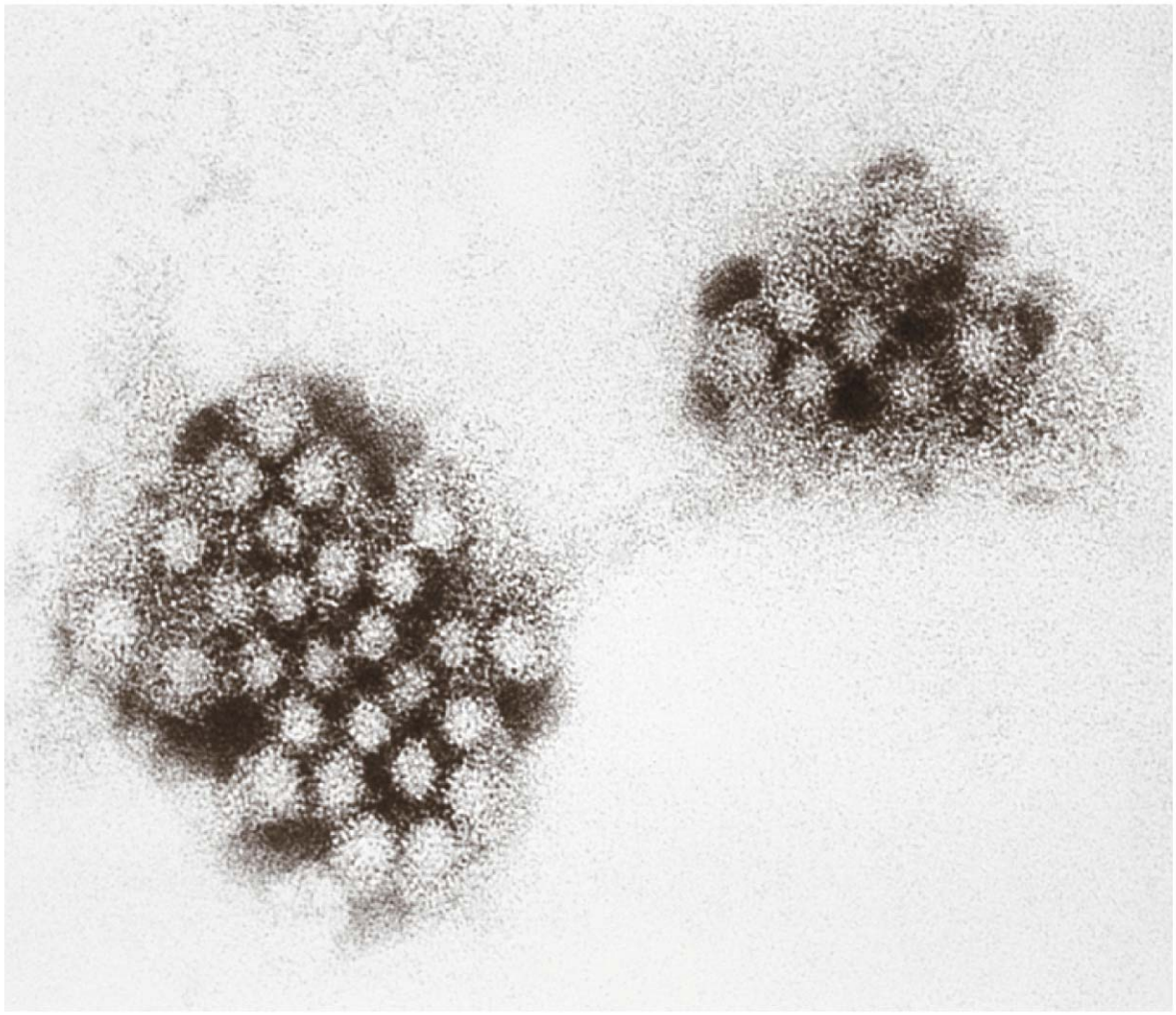
Viral Gastroenteritis

- Norovirus // identified in 1972
- Infected by fecal oral transmission
- Incubation period of 18 – 48 hours / suffer from vomiting and diarrhea for 2 – 3 days

Rotavirus.



Viral Diseases of the Digestive System



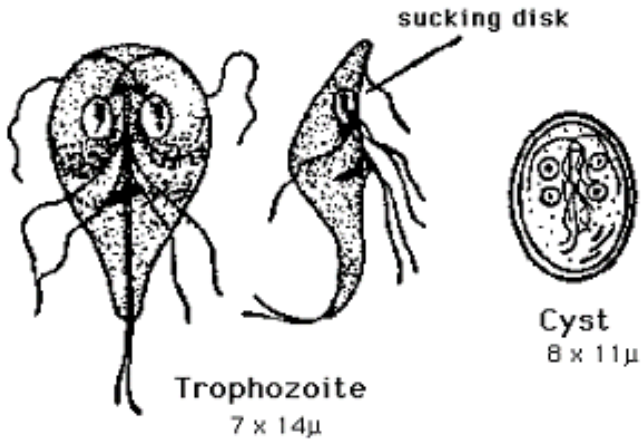
Norovirus

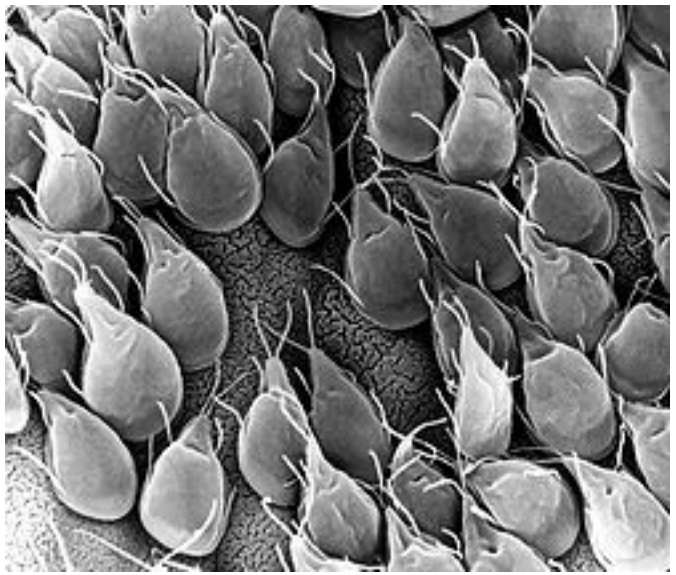
Viral Gastroenteritis

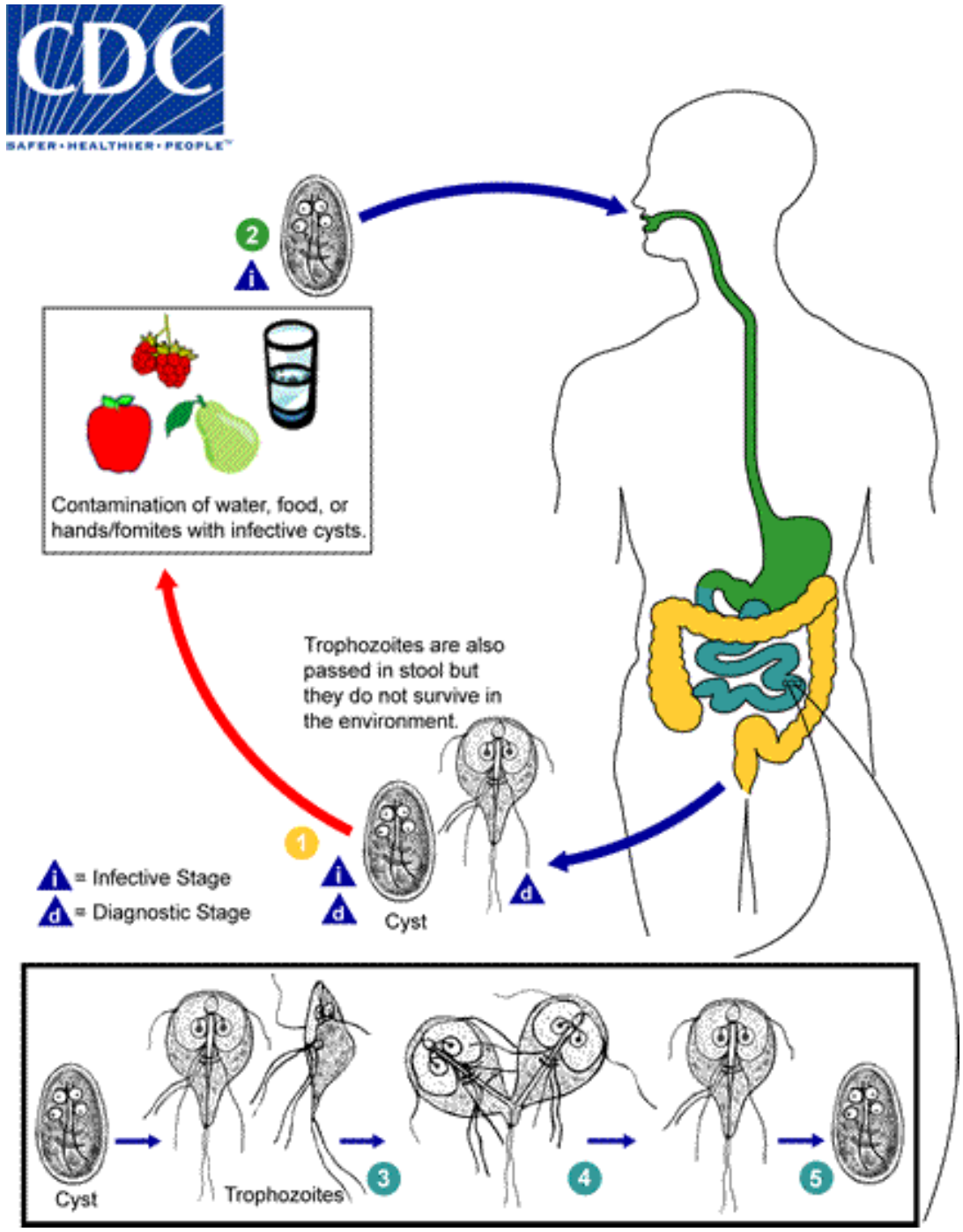
Pathogen	Rotavirus	Norovirus
Symptoms	Vomiting, diarrhea; 1 week	Vomiting, diarrhea; 2–3 days
Incubation period	1–3 days	18–48 hours
Diagnostic test	EIA	PCR
Treatment	Oral rehydration	

Giardiasis

- Giardia lamblia // protozoan disease
- Parasite that attaches to lining of small intestine
- Persisting for weeks
- Malaise, nausea, intestinal gas / weakness, weight loss, abdominal cramps
- Trophozoites become so dense they can slow down intestinal absorption






CDC
SAFER·HEALTHIER·PEOPLE™
2
i
Contamination of water, food, or hands/fomites with infective cysts.
Trophozoites are also passed in stool but they do not survive in the environment.
1
i
d
Cyst
i = Infective Stage
d = Diagnostic Stage
Cyst
Trophozoites
3
4
5

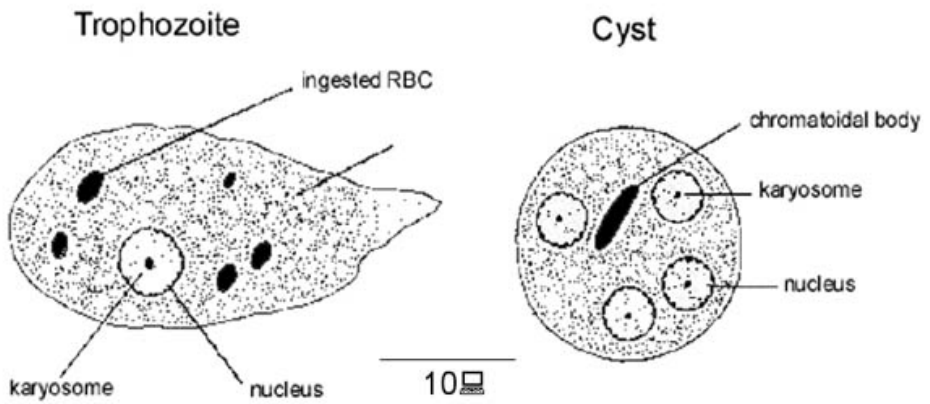
The trophozoite form of *Giardia lamblia*, the flagellated protozoan that causes giardiasis.

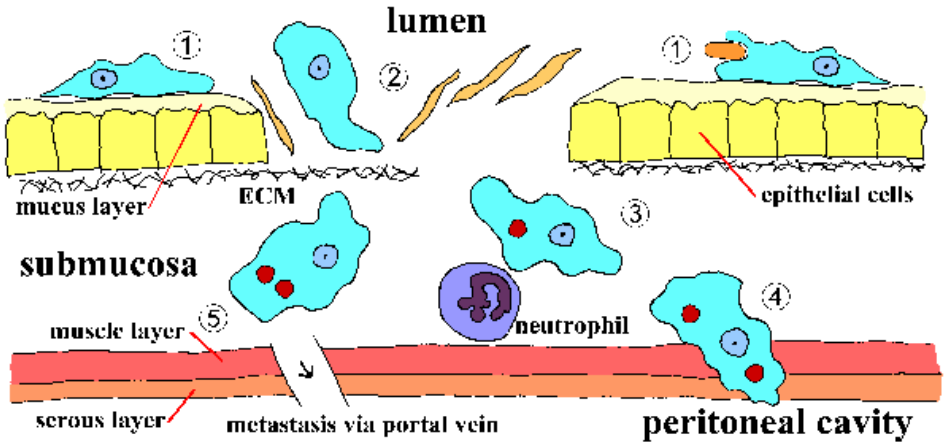
Giardiasis

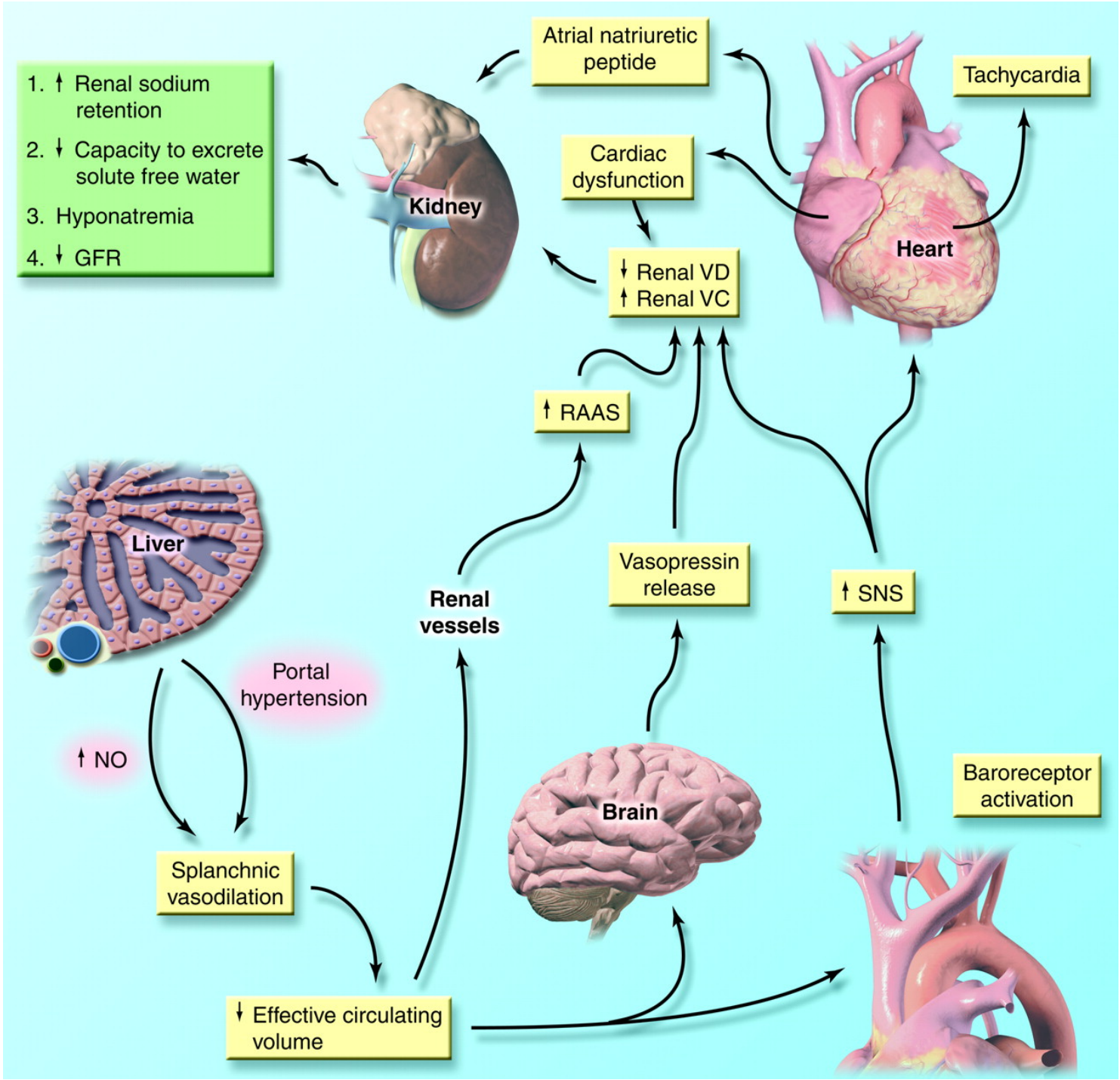
Pathogen	*Giardia lamblia*
Symptoms	Protozoan adheres to intestinal wall, leading to diarrhea
Reservoir	Water or mammals
Diagnosis	FA test
Treatment	Metronidazole; quinacrine

Amebic Dysentery (amebiasis)

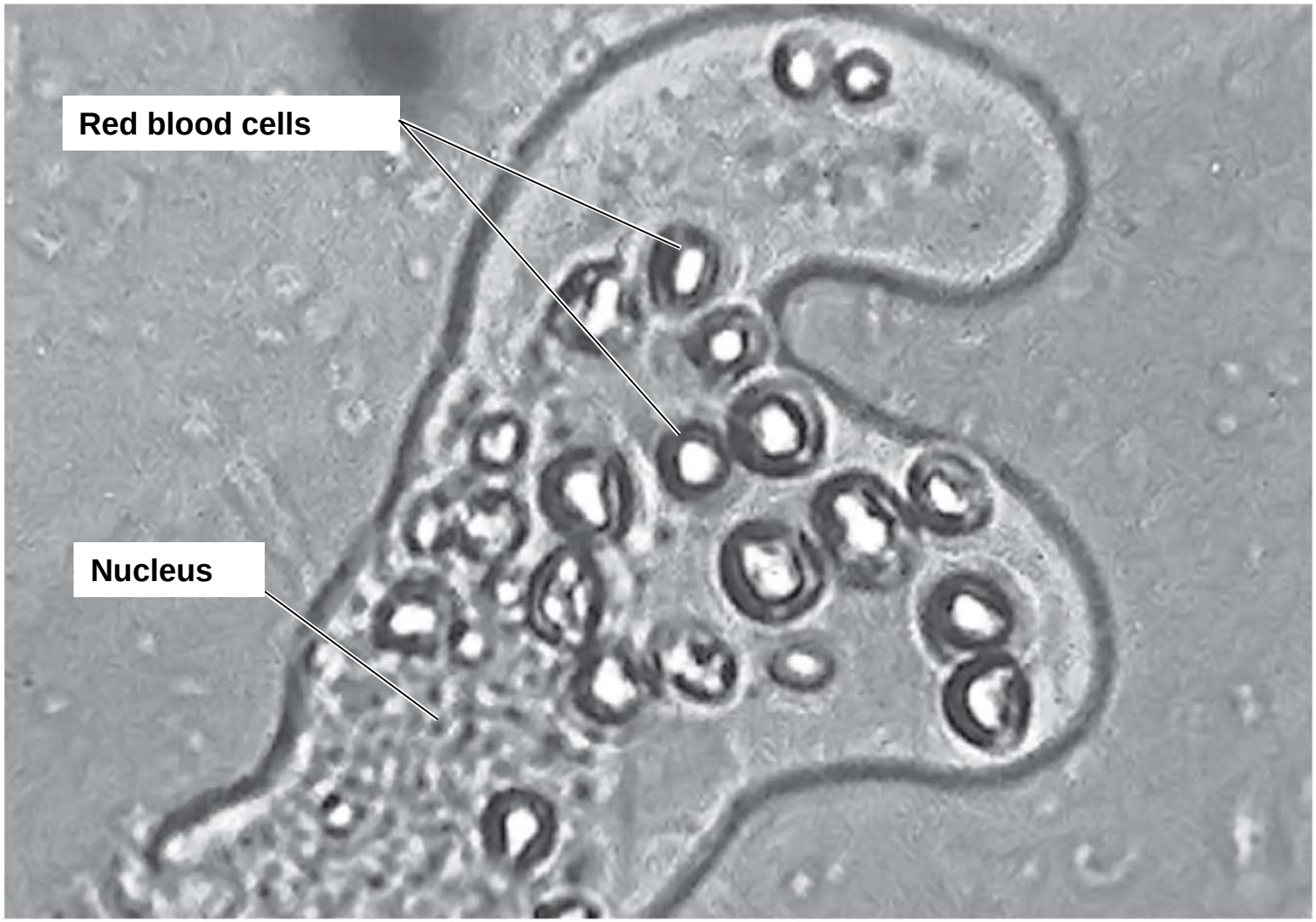
- Entamoeba histolytica // cysts of protozoa spread into humans by food and water
- Stomach acid able to kill trophozoites but not cysts
- Trophozoites feed on gastrointestinal tract
- Cause severe dysentery with perforation of intestinal wall



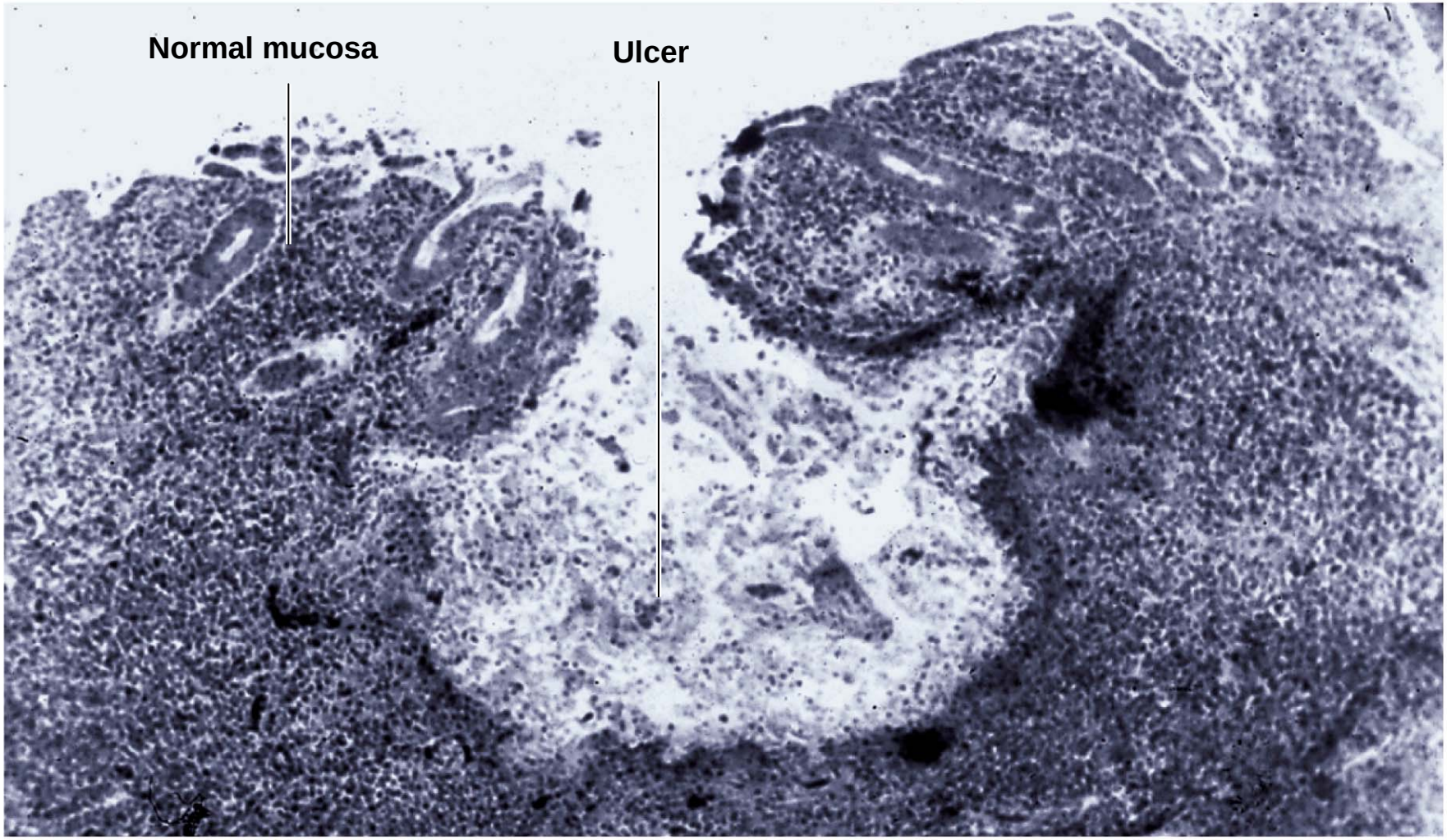



1. ↑ Renal sodium retention
2. ↓ Capacity to excrete solute free water
3. Hyponatremia
4. ↓ GFR
Atrial natriuretic peptide
Kidney
Cardiac dysfunction
Tachycardia
Heart
↓ Renal VD
↑ Renal VC
↑ RAAS
Liver
Renal vessels
Vasopressin release
↑ SNS
Portal hypertension
↑ NO
Brain
Baroreceptor activation
Splanchnic vasodilation
↓ Effective circulating volume

Amebae.



Section of intestinal wall showing a typical flask-shaped ulcer caused by *Entamoeba histolytica*.

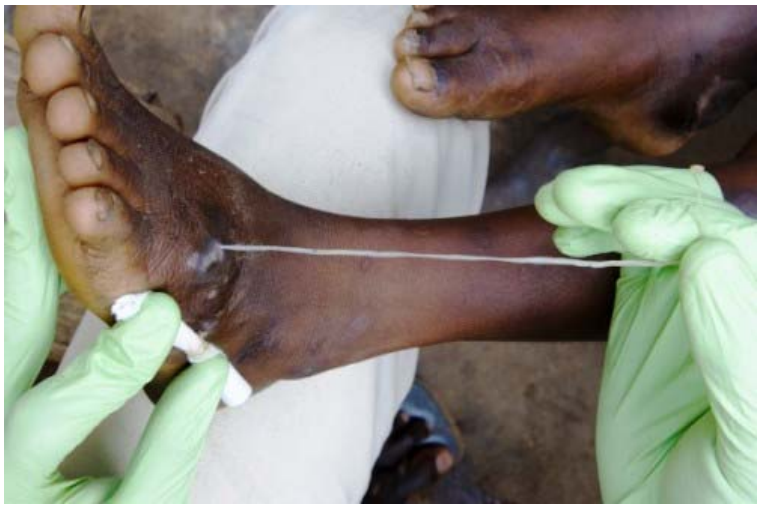


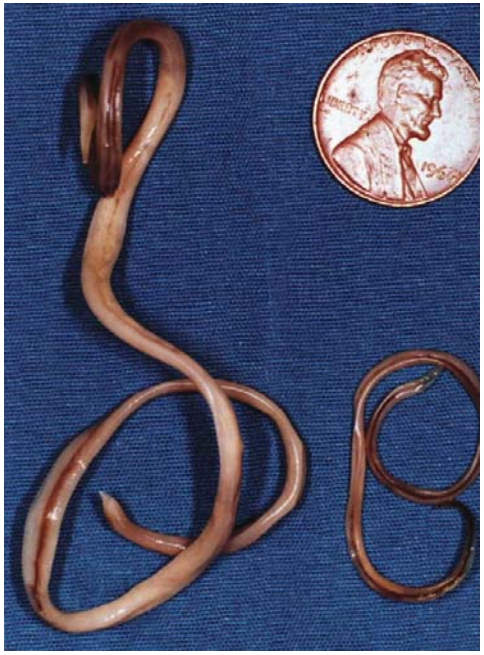
Amebic Dysentery

Pathogen	*Entamoeba histolytica*
Symptoms	Abscesses; significant mortality rate
Reservoir	Humans
Diagnosis	Microscopy; serology
Treatment	Metronidazole

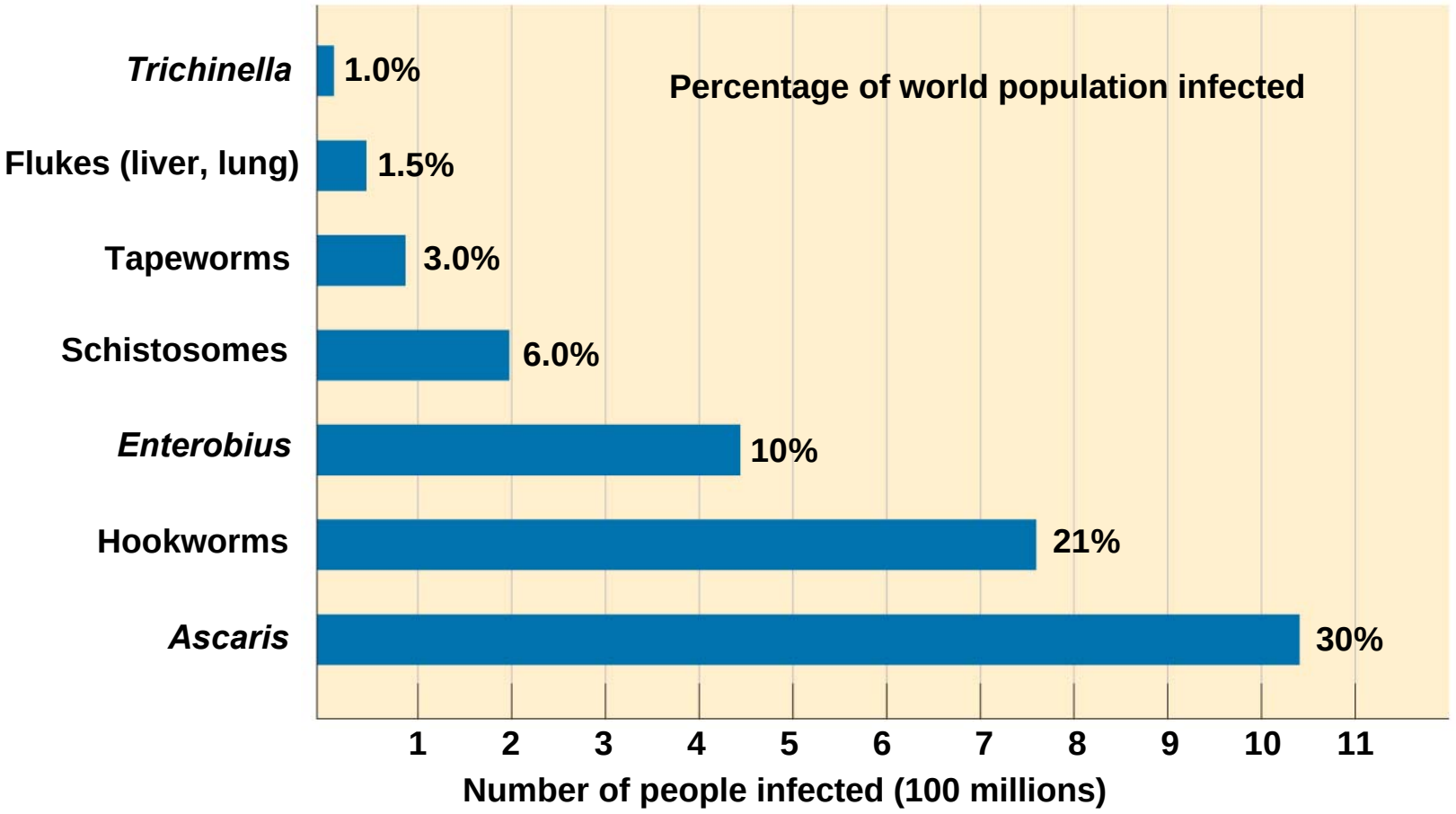
Helminthic Diseases of Digestive Tract

- Common parasite of human intestinal tract
- Often produce few symptoms // well adapted to life in human's intestinal tract
- Helminths include tape worms, nematodes (pinworms), roundworms, hookworms, flukes
- Worm load // use resources of host

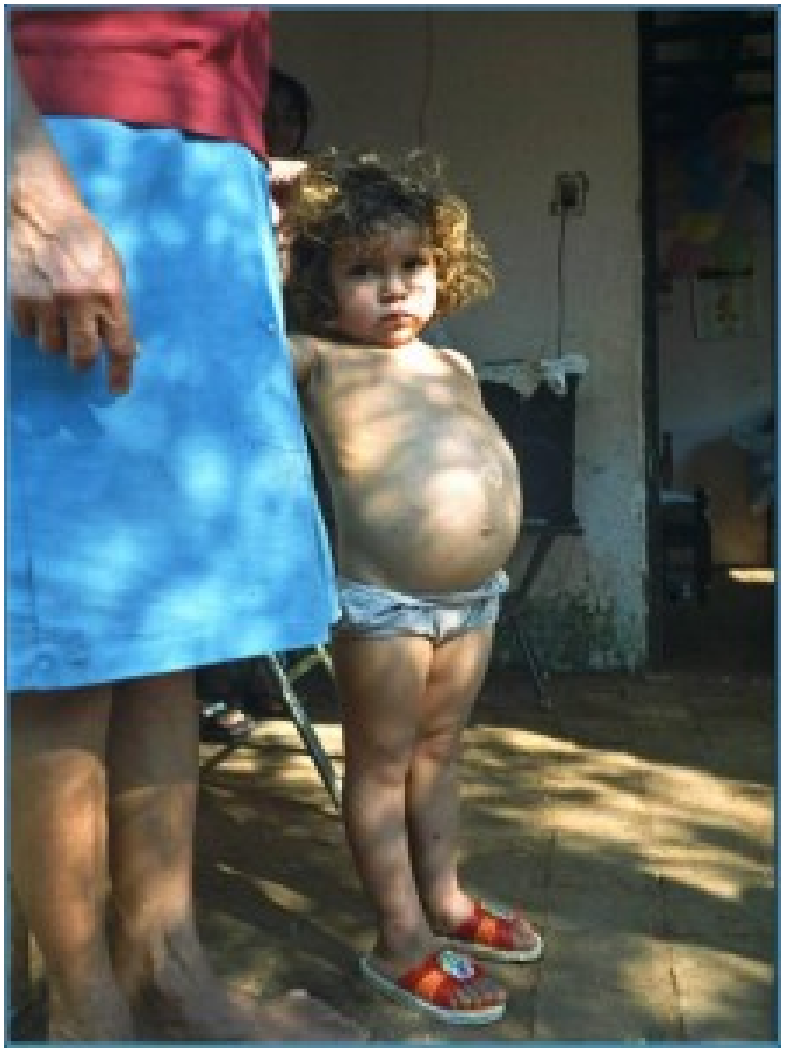


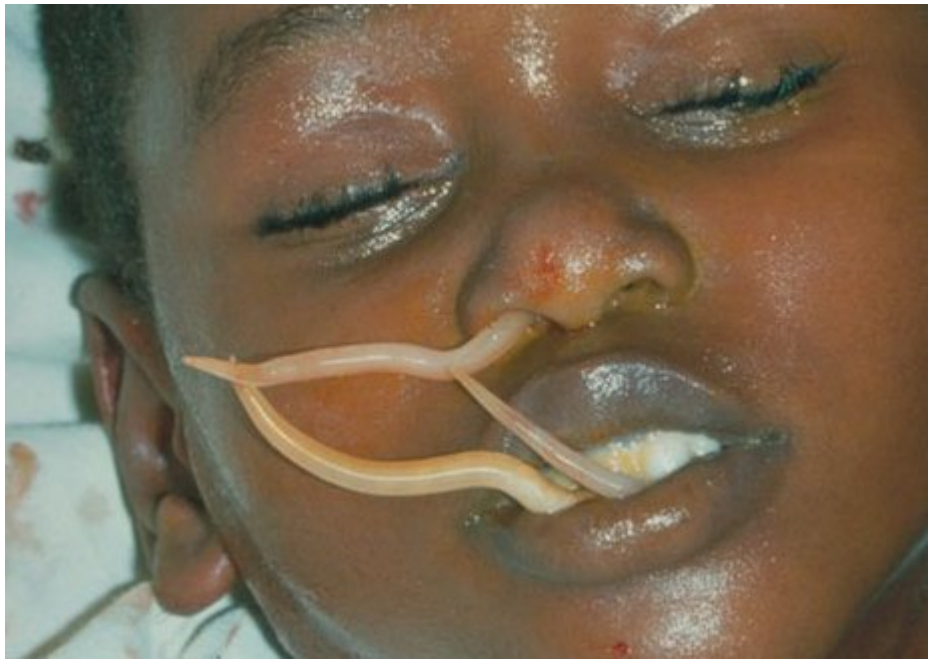


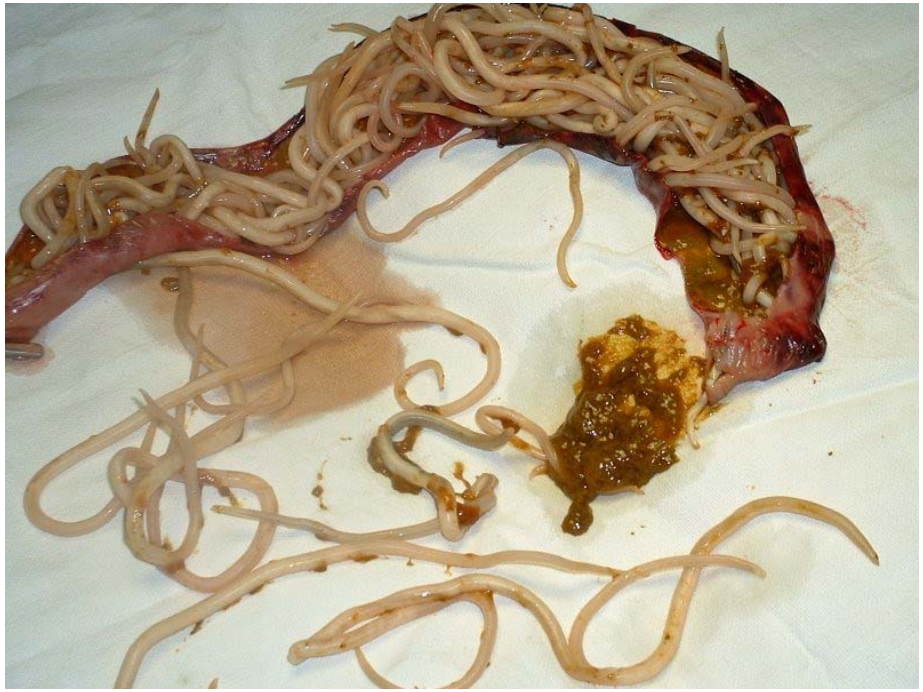
The woldwide prevalence of human infections with selected intestinal helminths.

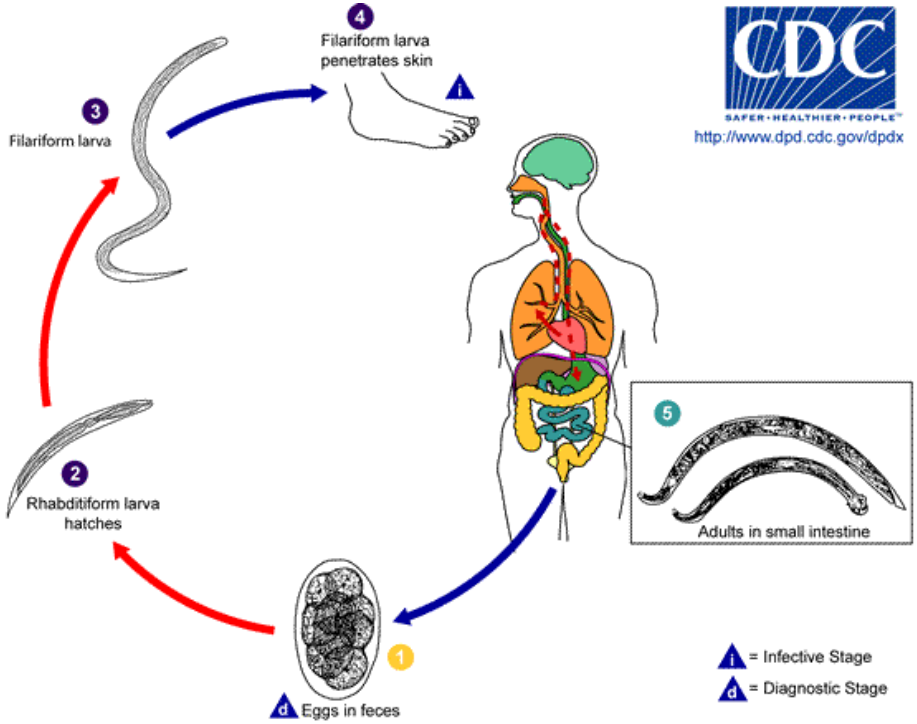


Ascaris lumbricoides, the cause of ascariasis.








4
Filariform larva
penetrates skin
i
3
Filariform larva
2
Rhabditiform larva
hatches
5
Adults in small intestine
1
d
Eggs in feces
i = Infective Stage
d = Diagnostic Stage
CDC
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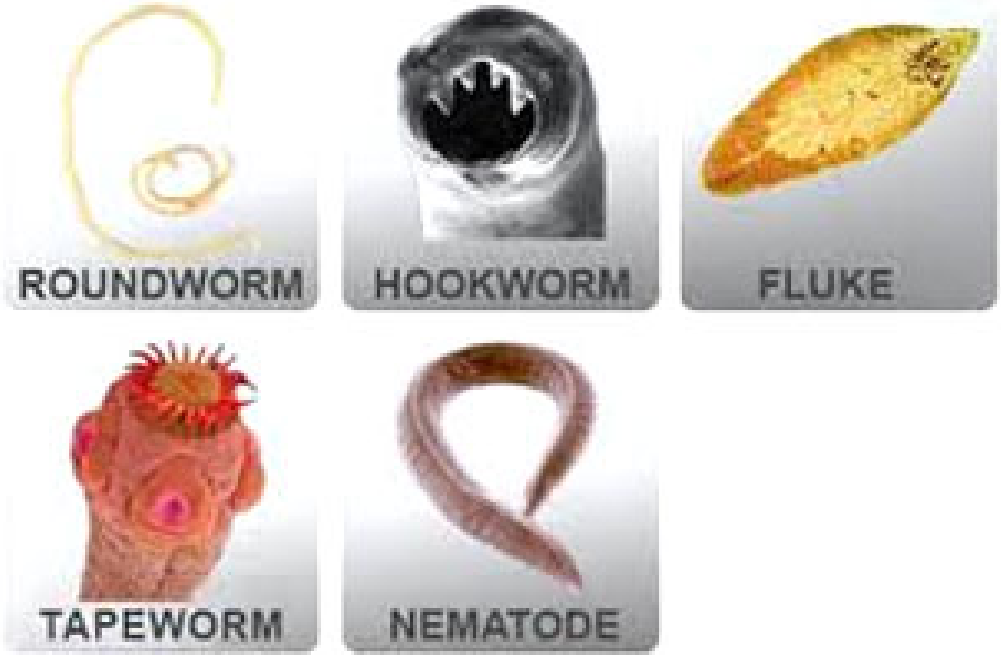
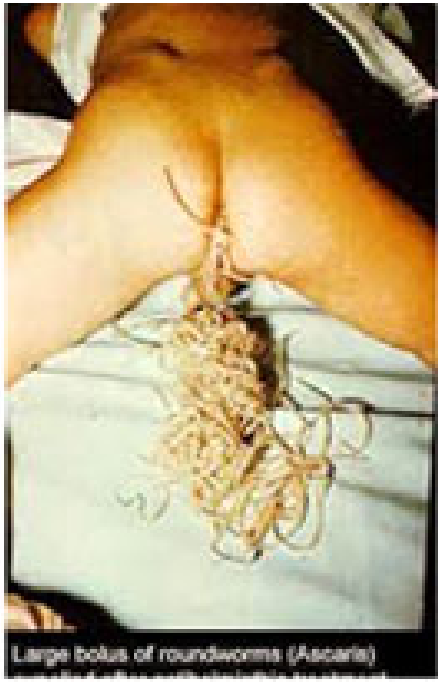
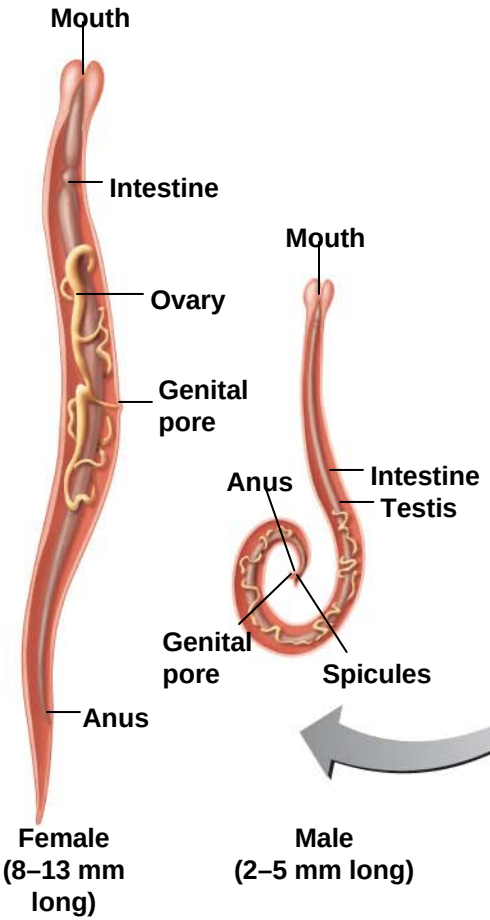
http://www.dpd.cdc.gov/dpdx

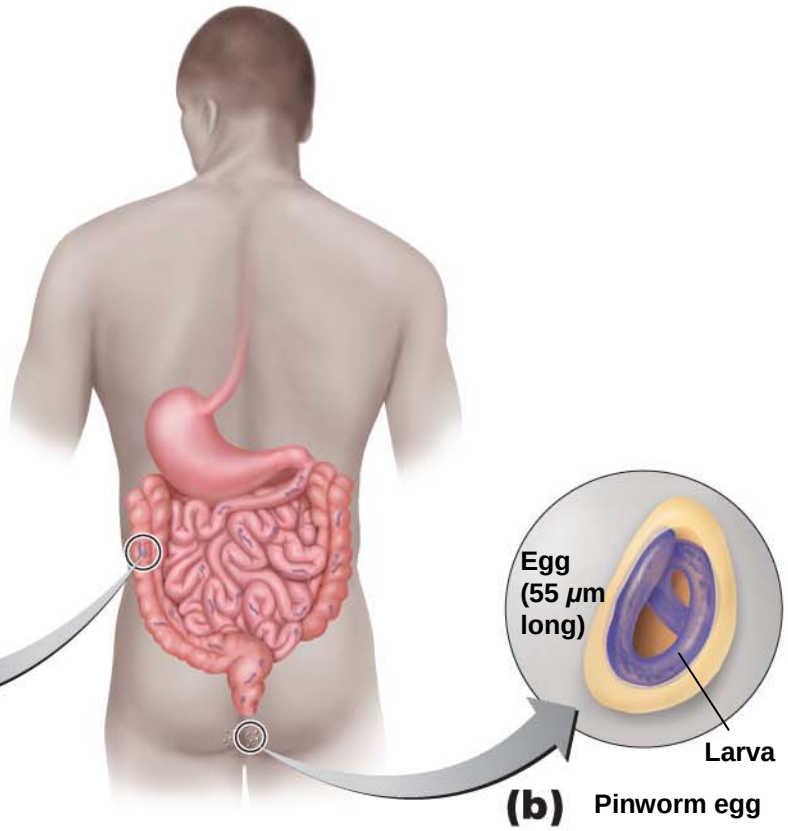

ROUNDWORM
HOOKWORM
FLUKE
TAPEWORM
NEMATODE


Large bolus of roundworms (Ascaris)

The pinworm *Enterobius vermicularis*.

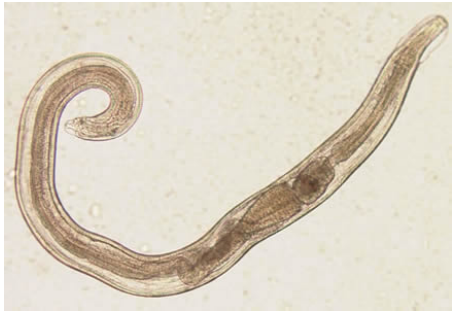
(a) Adult pinworm

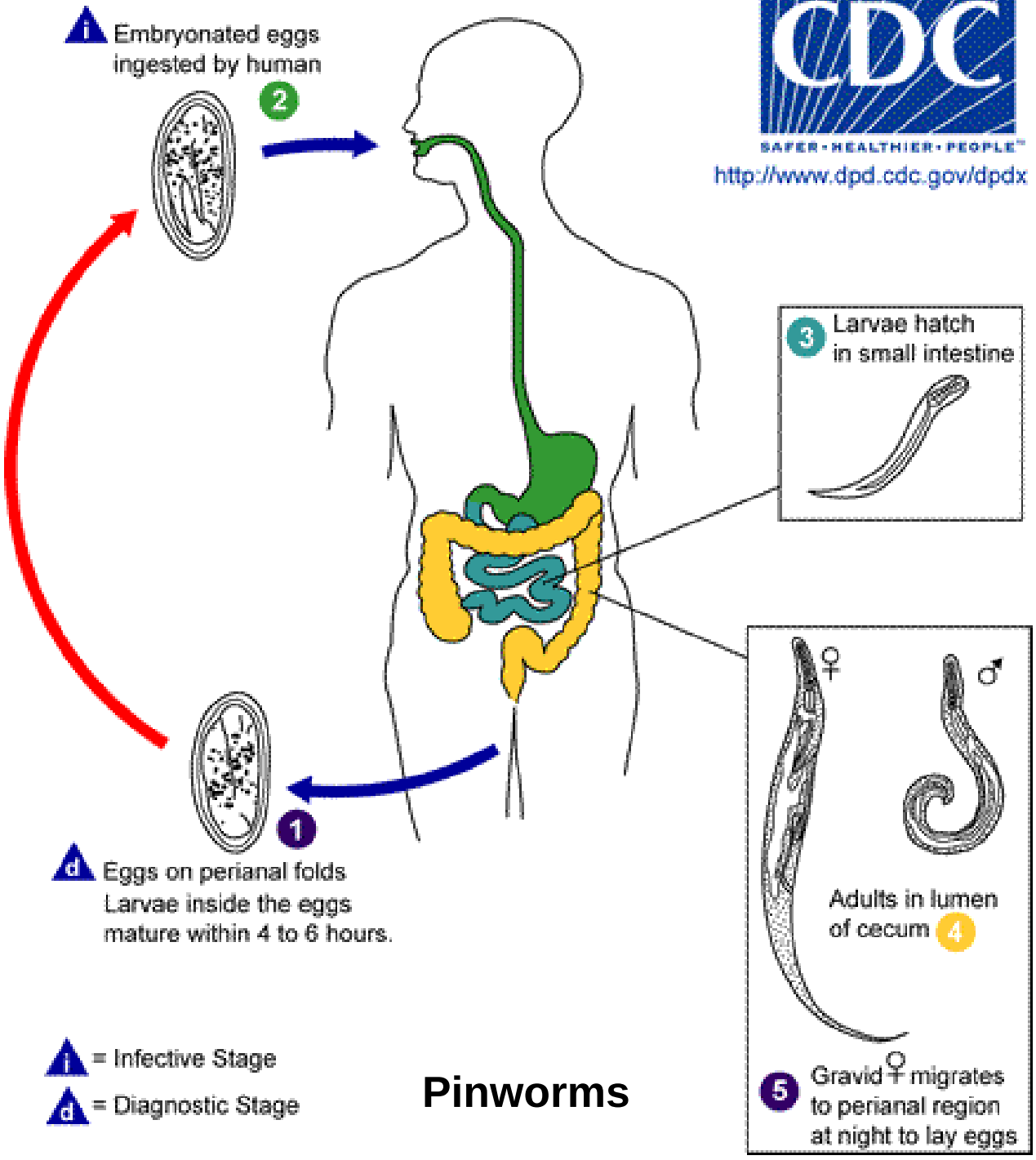




Pinworms


3
4
5

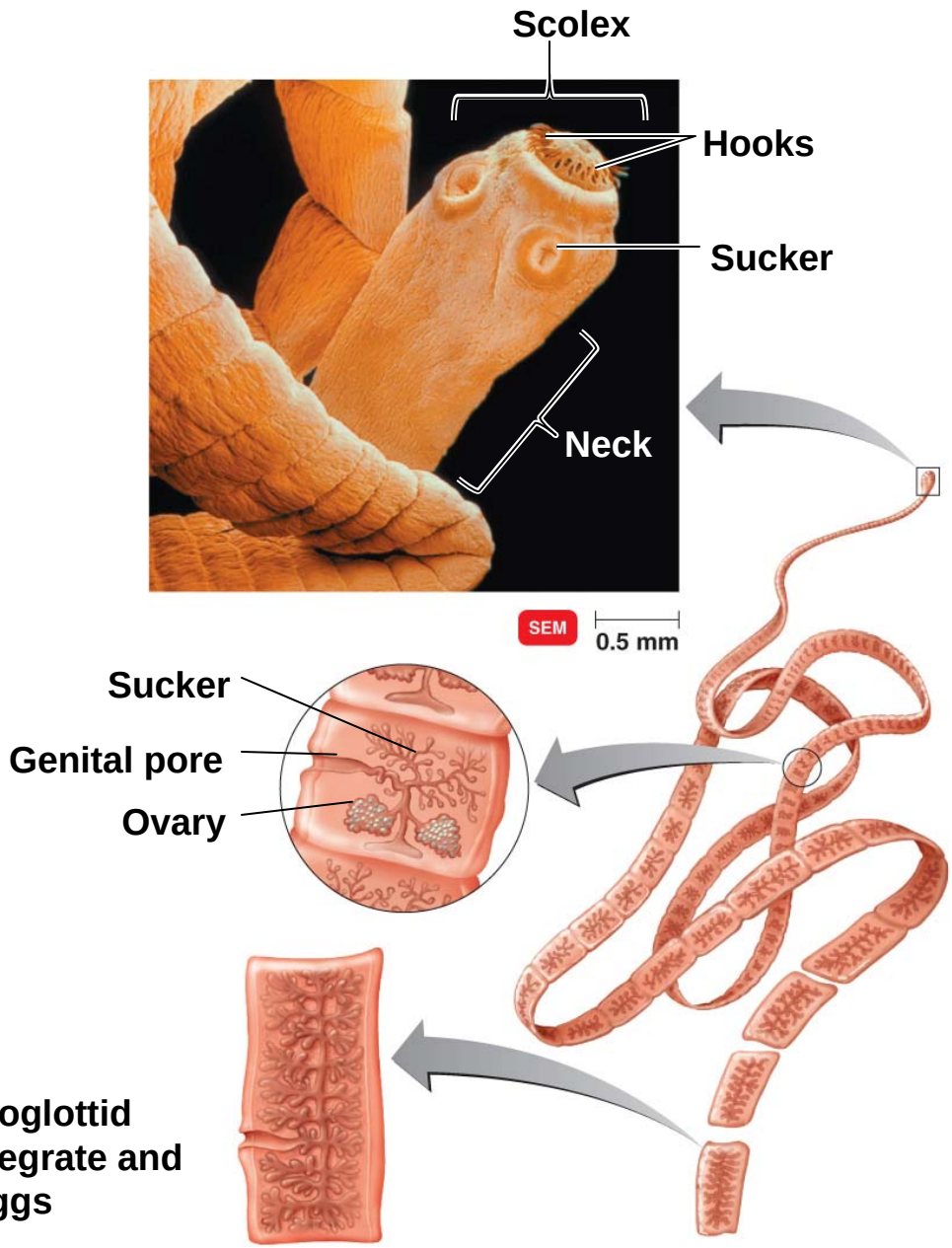



Embryonated eggs ingested by human
2
CDC
SAFER·HEALTHIER·PEOPLE™
http://www.dpd.cdc.gov/dpdx
3 Larvae hatch in small intestine
1
Eggs on perianal folds
Larvae inside the eggs mature within 4 to 6 hours.
Adults in lumen of cecum 4
♀
♂
5 Gravid ♀ migrates to perianal region at night to lay eggs
= Infective Stage
= Diagnostic Stage
Pinworms

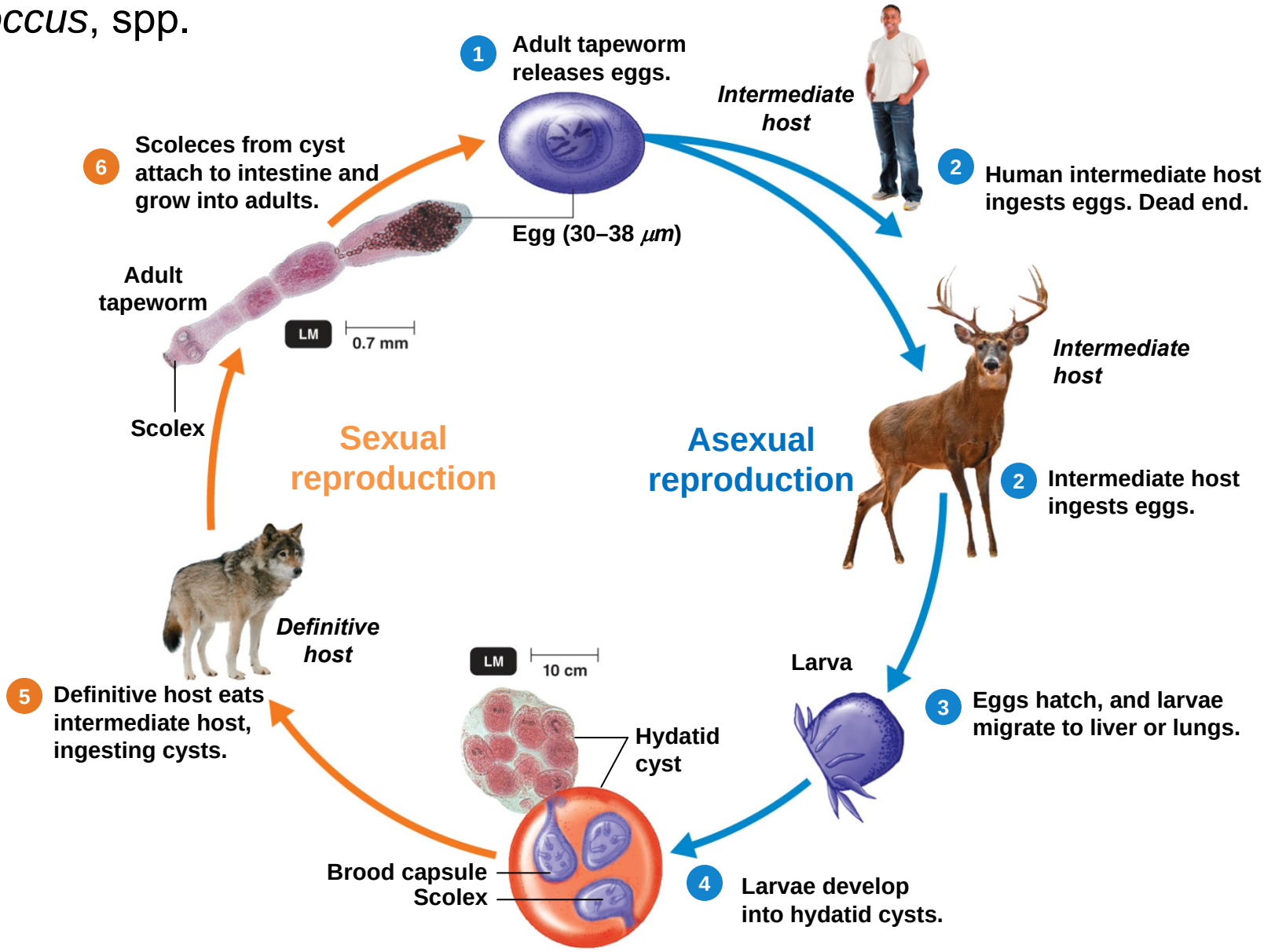
Pinworms

Pathogen	*Enterobius vermicularis*
Symptoms	Itching around anus
Intermediate host	Humans
Definitive host	Humans
Diagnosis	Microscopy
Treatment	Pyrantel pamoate

General anatomy of an adult tapeworm



The life cycle of the tapeworm, *Echinococcus*, spp.



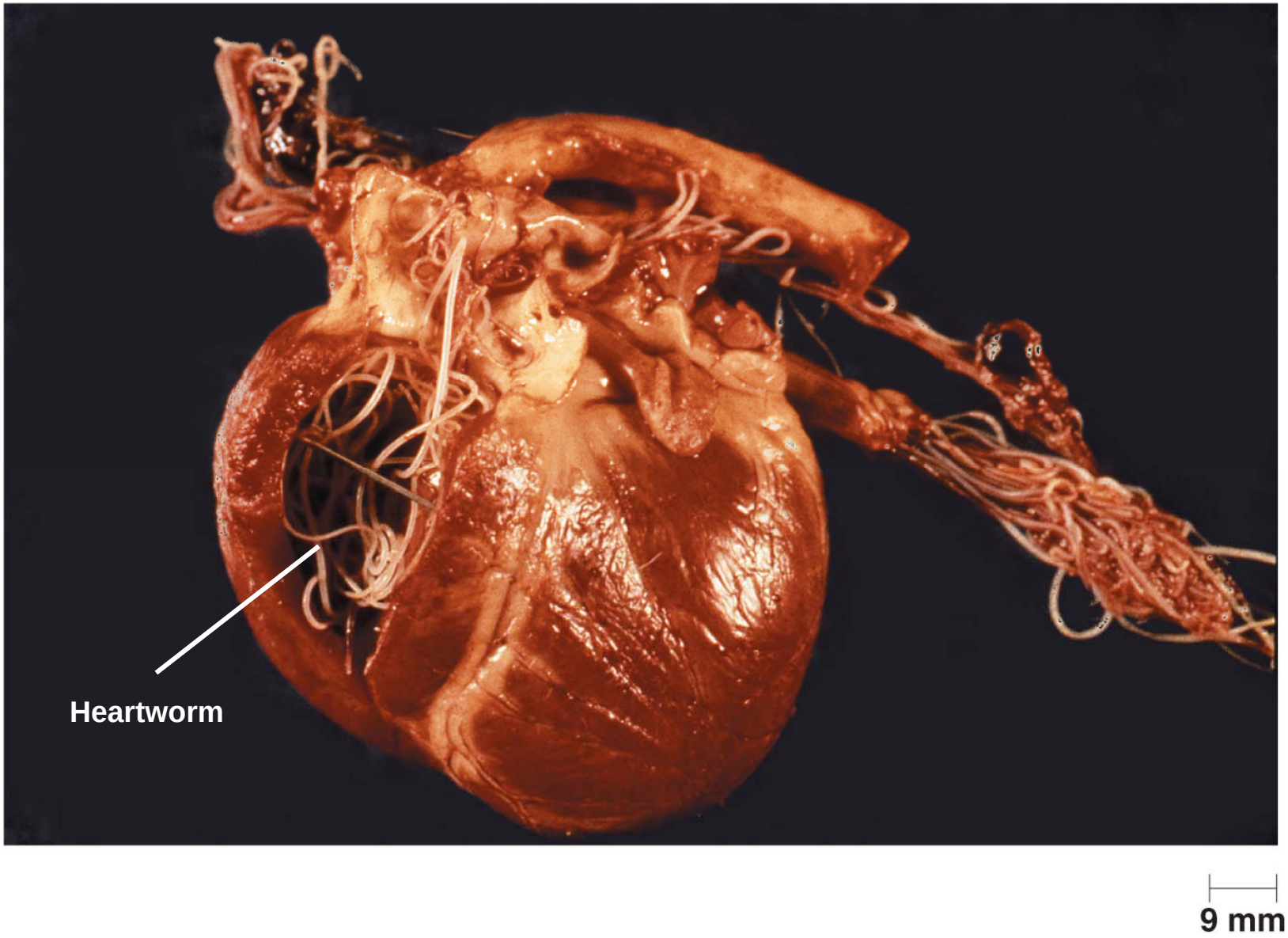
Tapeworms and Hydatid Disease

Disease	Tapeworm	Hydatid Disease
Pathogen	*Taenia saginata, T. solium, Diphyllobothrium latum*	*Echinococcus granulosus*
Symptoms	Neurocysticercosis	Tissue damage
Intermediate Host	Cattle, pigs, fish	Humans
Definitive Host	Humans	Dogs

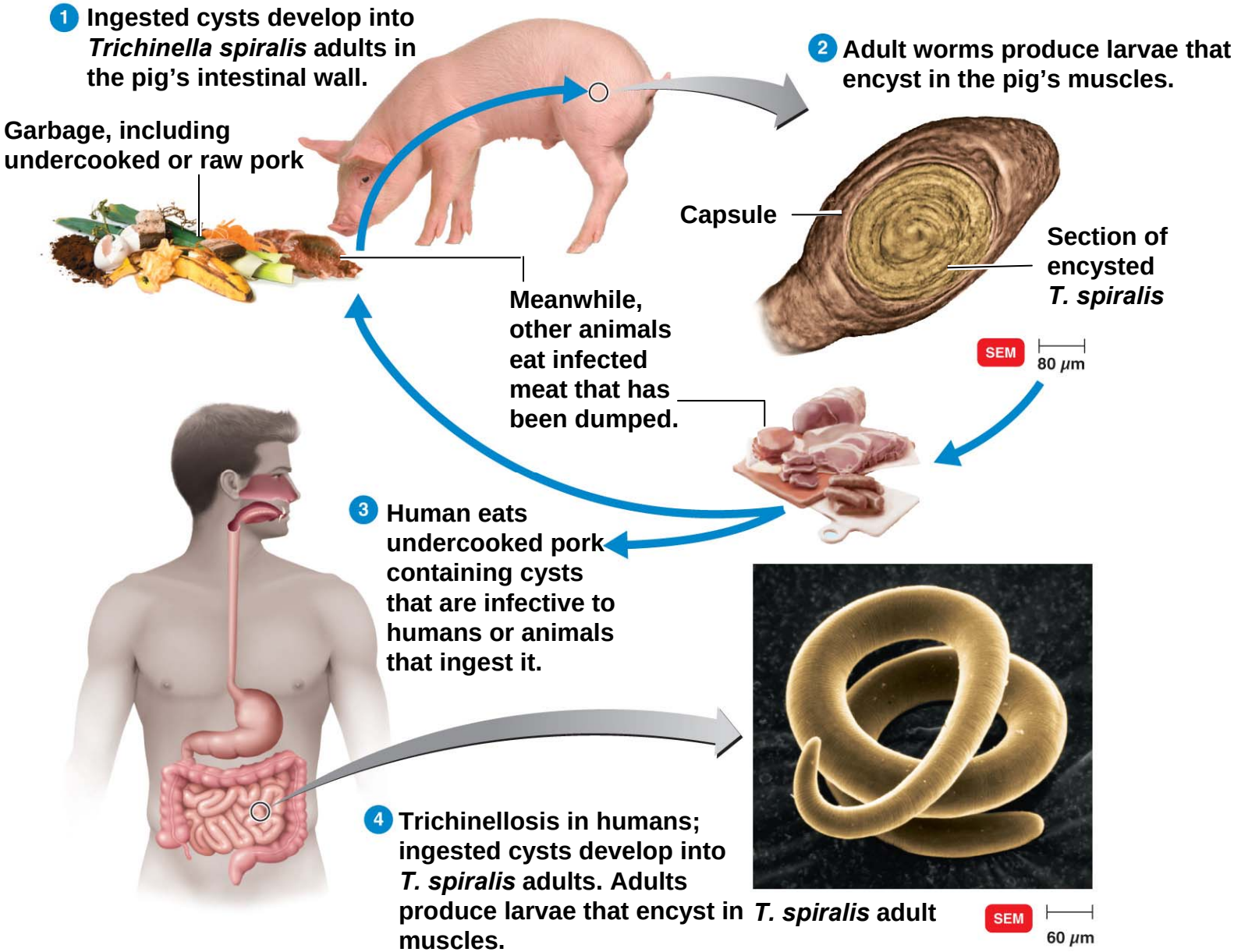
Tapeworms and Hydatid Disease

Disease	Tapeworm	Hydatid Disease
Diagnosis	Microscopic exam of feces	Praziquantel; albendazole
Treatment	Serology; X-ray exam	Surgical removal; albendazole

The heartworm *Dirofilaria immitis*.



The life cycle of *Trichinella spiralis*, the causative agent of trichinellosis.



An *Ancylostoma* hookworm attached to intestinal mucosa.