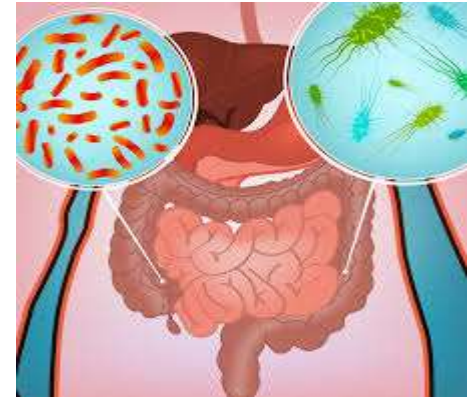




Oral and Gastrointestinal Diseases

Pharmaceutical Microbiology

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M.O of the GIT

- M.o entering the mouth are washed down into the GIT by the flow of saliva.
- About 8×10^{10} microbes are swallowed every day.
- Patterns of salivary flow vary from person to person; some are highly efficient at rinsing food and microbes away, while others are inefficient, accordingly tooth decay is greatly affected by the degree of efficiency.
- More than 400 species of m.o live in oral cavity.
- Esophagus does **not** have permanent normal microflora.
- The stomach's acid pH usually prevents colonization by microbes.
- The first two thirds of the small intestine contain very few microbes, mainly lactobacilli for passing through

M.O of the GIT

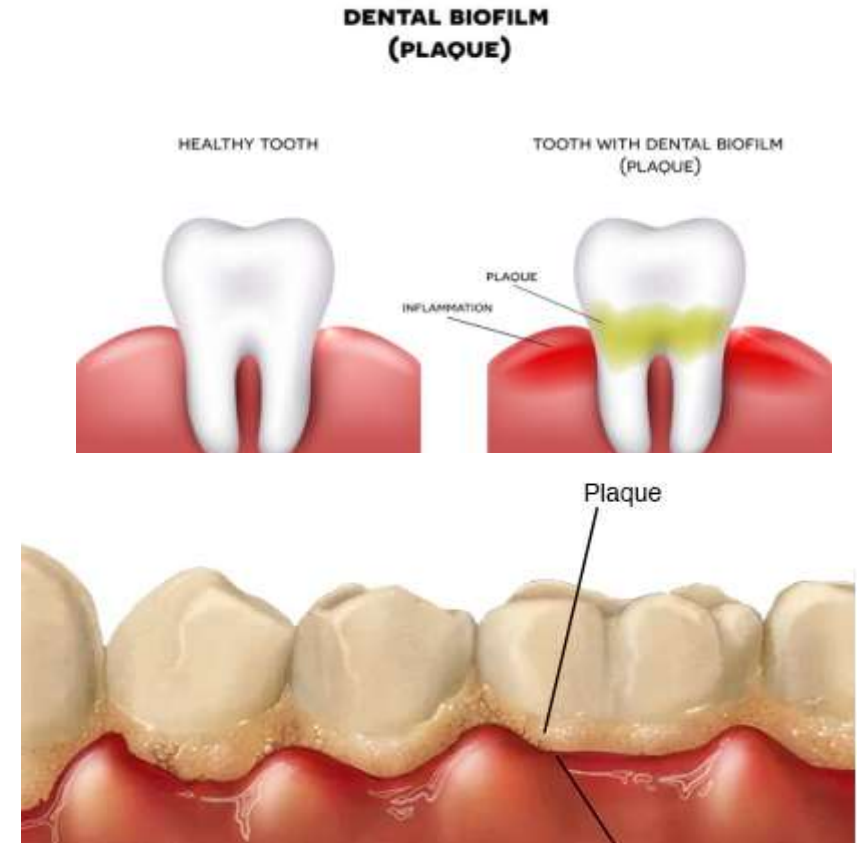
- the last third of the small **intestine**, motility of contents is slower, and some microbes are able to colonize its surfaces.
- These are mainly Gram-negative, facultatively anaerobic bacteria, Enterobacteriaceae (e.g., Escherichia coli), plus obligate anaerobes (e.g., Bacteroides and Clostridium).
- large intestine, food may remain as long as 60 hours, allowing m.o to colonize & replicate.
- The adult human gut holds hundreds to thousands of species and more than 100 trillion (100×10^{12}) individual bacteria.

GI infections

- Infections with a variety of agents can occur in any part of the gastrointestinal (GI) tract from the mouth to the anal canal.
- Infections can range in severity from self-limited to life-threatening.
- Infections are typically caused by the ingestion of exogenous pathogens in sufficient quantities to evade host defenses and then cause disease by multiplication, toxin production, or invasion

Bacterial diseases of oral cavity

- **Dental plaque**
- Is a continuous formed coating of m.o & organic matter on tooth surfaces, it is the 1st step in tooth decay & gum disease
- It is not removed by home cleaning methods, it is removed by professional cleaning (at dentists) but starts to build up few minutes after cleaning



Bacterial diseases of oral cavity

- **Periodontal disease**

- A combination of gum inflammation & the bone that supports teeth, occurs as a result of bacteria entrapment in gingival cavities which produce endotoxins & acids → inflammation initiated by plaque formation.
- its mildest form is gingivitis (affects only gums) which responds to Antibiotics.
- Advanced periodontal dis. Doesn't respond to AB & leads to chronic periodontitis → affects bone & tissues that support the teeth & gums.



Healthy Gums



Diseased Gums

Periodontal disease



(a)



(b)

- **Advanced periodontal disease.**
(a) Severe gum inflammation *this can* lead to **(b)** loss of bone (see arrows) surrounding roots of teeth, causing loosening and eventual loss of teeth. (*Phototake*)

Bacterial diseases of oral cavity

- Causative agent: various bacteria most important *Porphyromonas gingivalis* (G-ve anaerobe).
- Treatment of chronic Po: Antimicrobial mouth rinse, surgery & antibiotic therapy in unresponsive or rapidly progressing cases.
- Prevention: daily thorough cleaning & frequent professional removal of plaque from the pockets

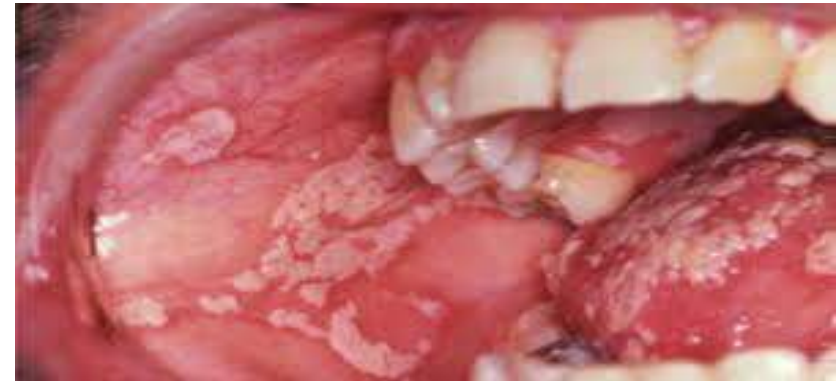
Fungal infection of the oral cavity

- **Oral thrush (oral candidiasis)**
- An infection of the lining of the mouth, caused by the yeast-like organism, *Candida albicans*
- Oral thrush in babies over the age of 4 months can usually be treated by the pharmacist.



Fungal infection of the oral cavity

- Oral thrush affects the surface of the tongue and the insides of the cheeks.
- White creamy or yellow raised spots on the mucous membrane of mouth often described as curd like appearance
- Spots can be scraped off, leaving a red tender area beneath, which can bleed



Fungal infection of the oral cavity

Treatment-Antifungal agents

Candida albicans is usually susceptible to all major agents

Most patients initially respond to topical therapy when treated with azole antifungal agents as **miconazole** or topical polyene (i.e., **nystatin** oral swishing retain as long as possible before swallowing),

Viral infection of the oral cavity

- **Mumps**
- Acute viral illness
 - Attacks large parotid salivary glands
- Causative agent
 - Mumps virus
 - Enveloped, -ssRNA *Rubulavirus* .
- Prevention
 - Prevention directed at immunization
 - Lifelong immunity



Infection of the stomach

- **Gastritis** refers to inflammation of the mucosa of the stomach. It may be erosive or nonerosive, depending on histologic and endoscopic findings.
- **Gastritis** can be mild (no signs & symptoms) or produce pain & indigestion. Severe gastritis may lead to ulceration
- **Peptic ulcers** are lesions of the mucous membranes lining the esophagus, stomach, or duodenum. The lesions are caused by the sloughing away of dead inflammatory tissue and exposure to acid.

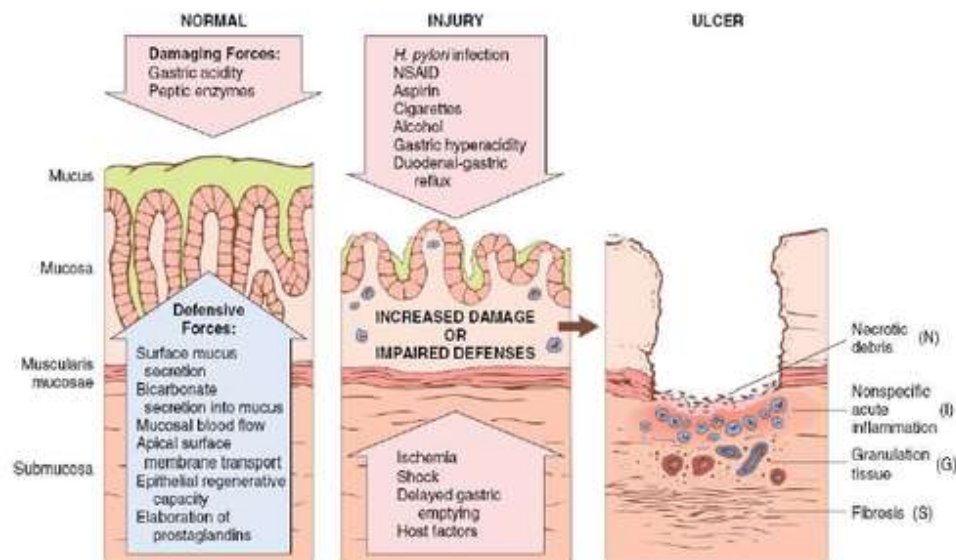
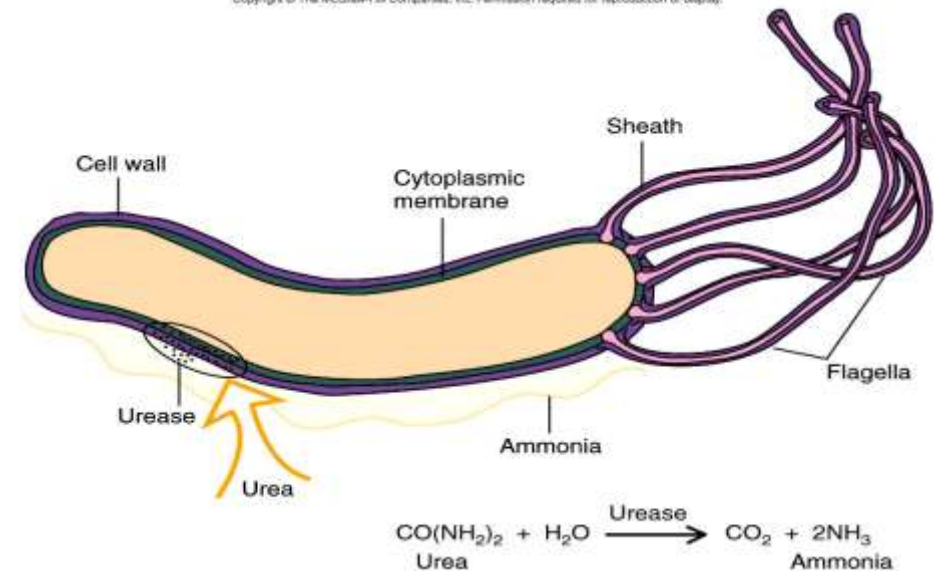


FIGURE 17-11 Mechanisms of gastric injury and protection. This diagram illustrates the progression from more mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrosis (N), inflammation (I), and granulation tissue (G), but a fibrotic scar (S), which takes time to develop, is only present in chronic lesions.

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Infection of the stomach

- **Helicobacter pylori** is gram negative bacteria which is known to cause peptic ulcer, chronic gastritis & a cofactor of stomach cancer. It is isolated from 95% of duodenal ulcers & 70% of gastric ulcers
- For *H. pylori*, treatment:
combination therapy with two antibiotics, such as ampicillin amoxicillin, or clarithromycin or metronidazole , plus a proton pump inhibitor. such as omeprazole is used with varying success



Bacterial Diseases of the GIT

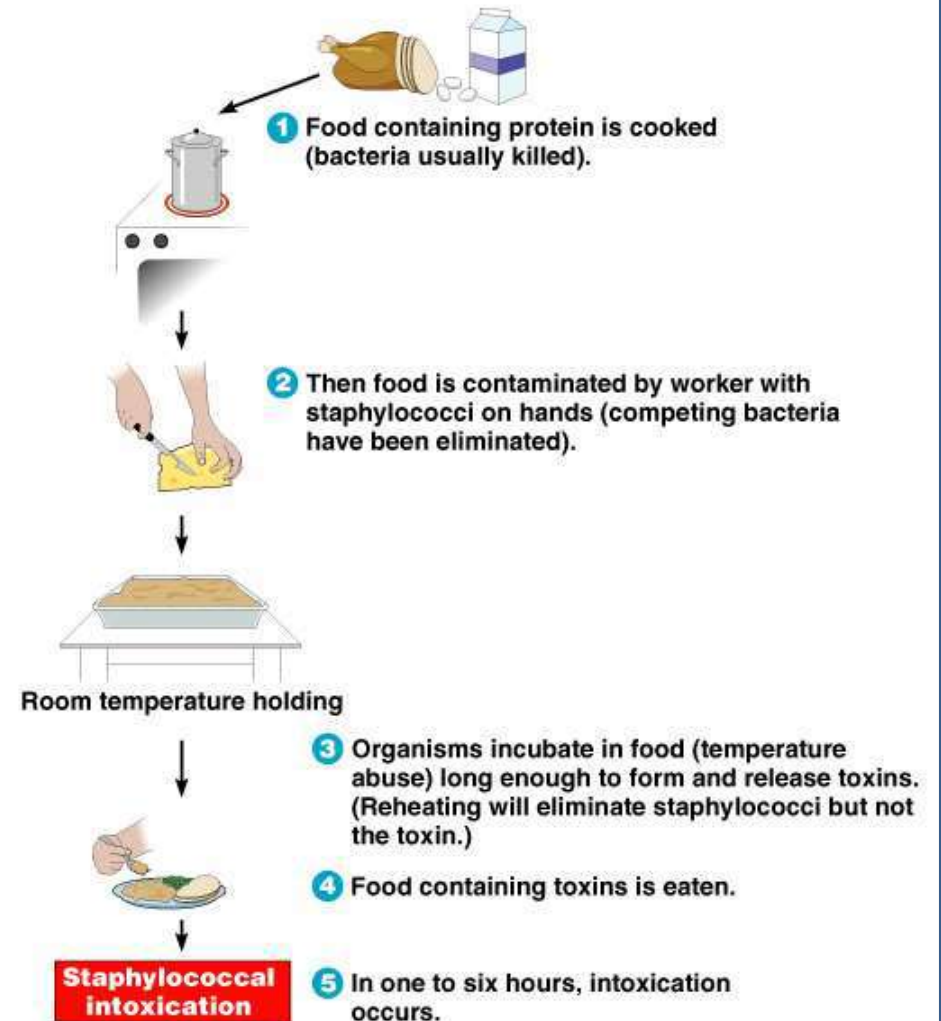
- **Bacterial Food Poisoning**

- Food poisoning is caused by ingesting food contaminated with preformed toxins.

1. Staphylococcal Enterotoxigenesis

Staphylococcus releases certain enterotoxins (**exotoxins**) that inflame the intestinal lining and inhibit water adsorption from the intestine (diarrhea), and also cause neural stimulation of the vomiting center of the brain (vomiting).

- Source: food contaminated with M.O from food handlers or environment.



Bacterial Diseases of the GIT

- Nearly any food can be contaminated with *S. aureus*, but Cream pies, dairy products, poultry products, and picnic foods such as potato salad are common
- Contamination is difficult to detect as appearance, odor, taste are not changed.
- Unlike most exotoxins, the toxin is heat-stable and withstands boiling for 30 minutes. Hence cooking foods can kill the organisms but does not destroy the toxin.
- Treatment: **No** treatment is required because the disease is self-limiting.

The best way of preventing food poisoning by *S. aureus* is to use sanitary food-handling procedures.

Bacterial Diseases of the GIT

Bacterial Food Poisoning

2. Clostridium perfringens .

The enterotoxin which is released only during sporulation, is produced under anaerobic conditions, as when undercooked meats and gravies are kept warm for a while.

- The main symptom is diarrhea. However, It, too, is self-limiting and can be prevented by sanitary food handling.

Bacterial Food Poisoning

Botulism, which is caused by a neurotoxin produced by *Clostridium botulinum*, is acquired when toxin-contaminated food is eaten.

Although it is a kind of food poisoning, it has little effect on the digestive system. Its effects on the nervous system

Bacterial Enteritis and Enteric Fevers

- Enteritis is an inflammation of the intestine. Bacterial enteritis is an intestinal infection, not an intoxication as is food poisoning.
- The causative bacteria actually invade and damage the intestinal mucosa or deeper tissues. Enteritis which affects chiefly the small intestine usually causes diarrhea.
- When the large intestine is affected, the result is often called **dysentery, a severe diarrhea that** often contains large quantities of mucus and sometimes blood or even pus.

Organisms That Cause Watery Diarrhea	Organisms That Cause Bloody Diarrhea
Enterotoxigenic <i>Escherichia coli</i> (ETEC)	Shigatoxin-producing <i>Escherichia coli</i> (STEC)
<i>Vibrio cholerae</i>	<i>Shigella</i> species
<i>Staphylococcus aureus</i>	<i>Salmonella enterica</i>
<i>Bacillus cereus</i>	<i>Campylobacter jejuni</i>
<i>Listeria monocytogenes</i>	<i>Clostridium difficile</i>
Norovirus	<i>Yersinia enterocolitica</i>
Rotavirus	<i>Entamoeba histolytica</i>
<i>Giardia lamblia</i>	
<i>Cryptosporidium hominis</i>	

Bacterial Enteritis and Enteric Fevers

- **Salmonellosis (sal"mo-nel-o'sis) is a common enteritis** caused by some members of the genus *Salmonella*.
- *Salmonella* species other than *S. typhi*, the cause of typhoid fever.
- *Salmonella* infection is generally associated with the ingestion of improperly prepared, previously contaminated food.
- Meat and dairy products and uncooked eggs are most likely candidates.
- Signs and symptoms of salmonellosis include abdominal pain, fever, and diarrhea with blood and mucus.
- Disease is self limiting. Antibiotics usually not given to healthy patients as they tend to induce resistant strains

Pathogen	Clinical Presentation	Diagnosis	Treatment	Comments
1. Acute noninflammatory diarrhea (watery, nonbloody stools; usually no fever)				
A. Bacteria				
<i>Staphylococcus aureus</i>	Vomiting, epigastric pain, diarrhea (mild)	Clinical. Food and stool can be tested for toxin	Supportive care (e.g., fluids, electrolytes)	Usually within 6 hours of consumption of infected food (dairy products, mayonnaise, meat products); recovery in 1–2 days
<i>Bacillus cereus</i>	Vomiting, epigastric pain, diarrhea	Clinical. Food and stool can be tested for toxin	Supportive care (e.g., fluids, electrolytes)	Usually within 6 hours of consumption of infected food (reheated rice)
Enterotoxigenic <i>Escherichia coli</i> (ETEC)	Afebrile, watery diarrhea	Clinical. Reference laboratory can perform DNA probe for LT or ST toxins	Ciprofloxacin	"Traveler's diarrhea"
<i>Listeria monocytogenes</i>	Often febrile, vomiting, diarrhea	Suspect <i>Listeria</i> when routine stool cultures do not show a pathogen, particularly in an outbreak setting	Supportive care (e.g., fluids, electrolytes)	Acquired by ingestion of unpasteurized soft cheese, deli meats and raw vegetables. Can grow at refrigerator temperature
<i>Vibrio cholerae</i>	Severe, watery diarrhea with rapid fluid and volume loss. Vomiting in early disease	Clinical. Can be confirmed by stool culture	Supportive care (e.g., aggressive fluid repletion, electrolytes). Antibiotics (e.g., ciprofloxacin) in severe disease	Suspect cholera if watery diarrhea associated with rapid and severe volume loss, or in an outbreak setting
B. Viruses				
Norovirus	Afebrile, vomiting, headaches, diarrhea	Clinical. Stool PCR available	Supportive care (e.g., fluids, electrolytes)	Cruise ship and nursing home outbreaks
Rotavirus	Fever and vomiting prodrome, then diarrhea	Clinical. Rapid antigen test. Stool PCR available	Supportive care (e.g., fluids, electrolytes)	Common in children
C. Protozoa				
<i>Giardia lamblia</i>	Abdominal cramps, flatulence, diarrhea (acute or chronic); stools are fatty, foul-smelling, and may float	Stool ova and parasite analysis may reveal cysts or trophozoites. Stool antigen test increasingly used	Metronidazole or tinidazole	Diarrhea may persist for weeks
<i>Cryptosporidium hominis</i>	Abdominal pain and cramps, watery diarrhea	See cysts in acid-fast stain of stool	Nitazoxanide for severe diarrhea. Antiretroviral therapy to restore immune system in AIDS patients	Cause of large communitywide outbreaks from contaminated water supply; important cause of diarrhea in AIDS patients

Clinical Presentation, Diagnosis, and Treatment of Diarrhea Caused by Important Gastrointestinal Tract Pathogens

Pathogen	Clinical Presentation	Diagnosis	Treatment	Comments
2. Acute Inflammatory diarrhea (stools can be bloody; can be febrile)				
A. Bacteria				
Shiga toxin-producing <i>E. coli</i> (STEC), esp. <i>E. coli</i> O157:H7	Bloody diarrhea, abdominal pain, usually afebrile	Stool culture grows <i>E. coli</i> that does not ferment sorbitol. Need special test to identify toxin-producing strains	None. Antibiotics may increase risk of hemolytic-uremic syndrome, especially in children	Acquired by ingestion of undercooked ground beef, fruits and vegetables contaminated with cattle manure
<i>Clostridium difficile</i>	Bloody diarrhea, fever	Stool test for toxin production. Colonoscopy may reveal characteristic yellowish plaques	Oral (or intravenous) metronidazole, or oral vancomycin	Traditionally associated with antimicrobial drug use; increasingly, community-acquired cases in patients without traditional risk factors
<i>Shigella</i>	Diarrhea with blood or pus usually; abdominal cramps; can be febrile	Stool culture	Ciprofloxacin	Person-to-person spread can occur; humans are the reservoir; not found in animals
<i>Salmonella</i>	Syndrome is called bacillary dysentery Diarrhea can be bloody; low-grade fevers	Stool culture	Ciprofloxacin (if severe illness); supportive care (if mild illness)	Acquired by ingestion of undercooked eggs, unpasteurized dairy products, raw vegetables, or undercooked poultry. Also by exposure to pet snakes and turtles
<i>Campylobacter jejuni</i>	Fever, diarrhea	Stool culture on special medium	Azithromycin or ciprofloxacin	Acquired by ingestion of unpasteurized dairy products, or undercooked poultry. Associated with Guillain-Barré syndrome
<i>Yersinia enterocolitica</i>	Fever, diarrhea	Stool culture on special medium	Ciprofloxacin (if severe illness)	Causes mesenteric adenitis that can mimic appendicitis
B. Protozoa				
<i>Entamoeba histolytica</i>	Bloody diarrhea, fever, and abdominal pain. Syndrome is called amebic dysentery	Stool ova and parasite analysis may reveal cysts or trophozoites; serology	Metronidazole or tinidazole to eliminate tissue trophozoites, plus a luminal agent such as paromomycin	Can also cause hepatic abscesses

Clinical Presentation, Diagnosis, and Treatment of Diarrhea Caused by Important Gastrointestinal Tract Pathogens

Bacterial Enteritis and Enteric Fevers

- **Traveler's Diarrhea:**
- The most common causes of traveler's diarrhea are pathogenic strains of *Escherichia coli*, which account for 40 to 70% of all cases.
- Other causes of traveler's diarrhea include bacteria such as *Shigella*, *Salmonella*, *Campylobacter*, *rotaviruses*, and protozoa such as *Giardia* and *Entamoeba*.
- Symptoms of traveler's diarrhea vary from mild to severe and include nausea, vomiting, diarrhea, bloating, malaise, and abdominal pain.
- The disease is especially hazardous in infants, who are subject to severe dehydration.
- It is usually self-limiting but can have complications

Viral Diseases of the GIT

- **Viral enteritis**

1. **Rotavirus**: major cause of viral enteritis in infants & young children, has high morbidity & mortality rate.

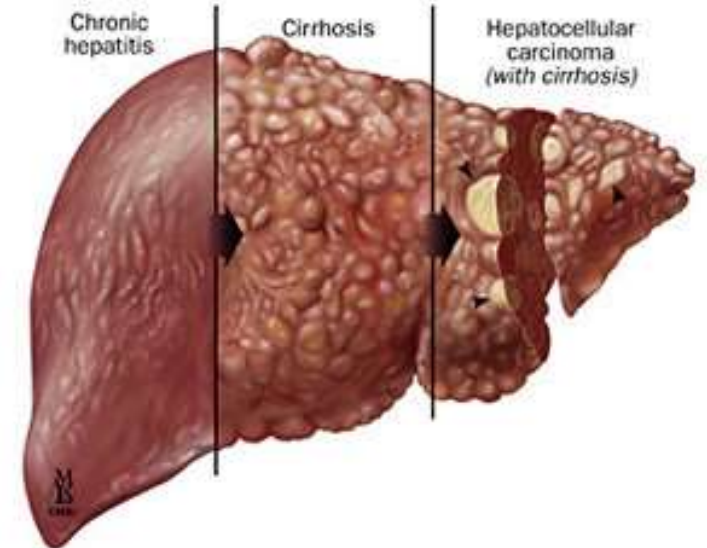
2. ***Norovirus***

Symptoms: vomiting, diarrhea for 2-3 days

Treatment: restoring fluids & electrolytes.

Viral Hepatitis

- The hepatitis viruses thus far identified (A, B, C, D, and E) each have a pathogenesis specifically involving replication in and destruction of hepatocytes.
- Of this group, hepatitis B (DNA virus) and hepatitis C (RNA virus) are the most common causes of chronic hepatitis, cirrhosis, and hepatocellular carcinoma



Prevention

- There is no vaccine to protect against hepatitis C. The only way to prevent this disease is to avoid the risk factors.
- The hepatitis B vaccine is typically given as three or four injections over six months. You can't get hepatitis B from the vaccine.

Anti-hepatitis treatment

- Hepatitis A is a common infection caused by oral ingestion of the virus (fecal-oral), but it doesn't cause chronic disease.
- Chronic hepatitis B may be treated with peginterferon- α -2a.
- Oral therapy for chronic hepatitis B includes lamivudine.
- The preferred treatment for chronic hepatitis C is the combination of peginterferon- α -2a plus ribavirin,

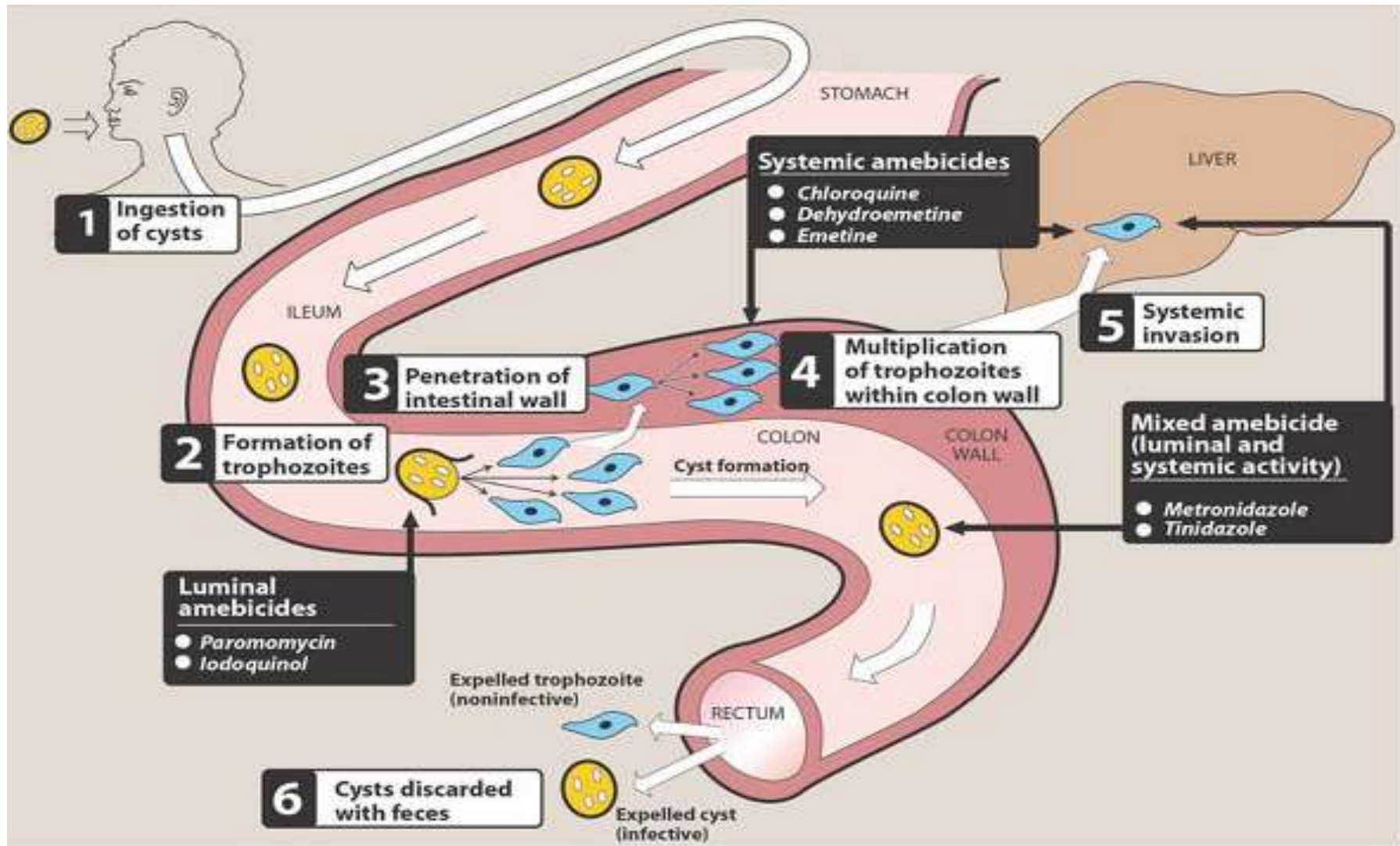
Protozoan Gastrointestinal Diseases

Disease	Pathogen	Comments
Protozoan Diseases of the Digestive System		
Giardiasis	<i>Giardia lamblia</i>	Protozoan adheres to intestinal wall, may inhibit nutritional absorption. Causes diarrhea.
Cryptosporidiosis	<i>Cryptosporidium parvum</i>	Shed in animal feces, protozoan enters water supply; causes self-limiting diarrhea but may be life-threatening if immuno-suppressed.
<i>Cyclospora</i> diarrheal infection	<i>Cyclospora cayetanensis</i>	Usually ingested with fruits and vegetables; causes watery diarrhea.
Amoebic dysentery (amoebiasis)	<i>Entamoeba histolytica</i>	Amoeba lyses epithelial cells of intestine, causes abscesses; significant mortality rate.

Protozoan Gastrointestinal Diseases

- **Amoebic dysentery & chronic amebiasis**
- Caused by *Entamoeba histolytica*, a pathogenic amoeba
- Transmission: fecally contaminated water or food
- Amebiasis can be severe acute disease called amoebic dysentery or chronic amebiasis (invade intestinal mucosa & live indefinitely) which can suddenly revert to acute stage
- The parasites may invade liver and lung tissue, & cause abscesses
- symptoms: severe diarrhea contain mucus & blood, causes dehydration from excessive fluid loss.
- Treatment: metronidazole

Life cycle of *Entameba histolytica* and the sites of action of amebicidal drugs



Helminth Gastrointestinal Diseases

- A wide variety of helminths can parasitize the human intestinal tract, and some also invade other tissues.
- Most are prevalent only in tropical regions.
- Tapeworms
- Hydatid Disease
- Nematodes(Pinworms, Hookworms, Ascariasis,)