CHAPTER 22
INFECTIONS OF
THE DIGESTIVE SYSTEM

WHY IS THIS IMPORTANT?

The digestive system is the second leading portal of entry into the body. As a health care professional you will see many patients with infections of the digestive system.

OVERVIEW
OVERVIEW

- The digestive system is a major portal of entry.
- Many pathogens enter the body when we ingest water and food.
- Defenses of the digestive system are very strong.
  - Keep many infections from ever happening.
- Digestive infections are a major cause of morbidity and mortality.
  - Cause the death of millions of children
    - Immune system is not mature.

BACKGROUND

- The mouth and large intestine are crowded with microorganisms.
  - Part of the normal oral flora
- Digestive diseases are usually associated with:
  - Crowding
  - Poor hygiene
  - Contaminated food or water

BACKGROUND

- Digestive infections in developed and undeveloped countries are associated with different pathogens.
- Developed countries:
  - Campylobacter
  - Salmonella
  - Shigella
- Undeveloped countries:
  - Vibrio cholerae
BACKGROUND

A variety of pathogens cause infections in the digestive system.
- Nosocomial infections are a serious problem in healthcare.
  - *Clostridium difficile* causes serious gastrointestinal infections.
- Opportunistic infections normally prevented by microbial flora are becoming more common.
  - They are associated with the overuse of antibiotics.
**BACKGROUND**

- Decreased saliva production can result in significant dental decay.
- Instead of being churned from the flora bacteria in the oral cavity, the pathogenic flora, enter the parotid, lymphatics, and from there the gastrointestinal tract.
- Antibiotics alter the normal flora of the colon by killing sensitive organisms; the normal flora can be replaced by more antibiotic-resistant bacteria.

**CLASSIFICATION OF INFECTION**

- Infections in the digestive system are classified in two groups:
  - Exogenous infections – pathogens that come into the body
  - Endogenous infections – organisms that are part of the normal microbial flora

**TYPES OF INFECTION**

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<td>Enterococcus faecalis</td>
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- Typhoid fever
- Septicemia
- Bacillary dysentery
- Cholera
- Typhoid fever
**TYPES OF INFECTION**

**EXOGENOUS INFECTIONS**
- Exogenous infections are brought in with contaminated food or water.
- *C. difficile* and other exogenous infections are frequently acquired in hospital environments.
- *Helicobacter pylori* spreads through oral-oral or fecal-oral contact.
- Exogenous infections can cause nausea and vomiting within 6 hours.

**ENDOGENOUS INFECTIONS**
- Endogenous infections are caused by organisms that are part of the normal flora.
  - *Streptococcus* and *Enterococcus* are examples.
- In the right circumstances they can cause:
  - Dental diseases.
  - Infections of the bowel, appendix, and liver.
  - Diverticular abscesses.
CLINICAL SYMPTOMS OF GASTROINTESTINAL INFECTIONS

- Most common symptoms are:
  - Fever
  - Vomiting
  - Abdominal pain
  - Diarrhea
- Symptoms vary with infection and with stages of infection.

The central feature in all cases is diarrhea.
- The nature of the diarrhea is used to classify gastrointestinal infections into three categories:
  - Watery diarrhea
  - Dysentery
  - Enteric fever

WATERY DIARRHEA

- Most common type of gastrointestinal infection.
  - Develops rapidly
  - Results in frequent voiding
  - May be accompanying vomiting, fever, and abdominal pain
  - Usually self-limiting
  - Caused by pathogenic mechanisms that attack the intestines
**WATERY DIARRHEA**

- Purest form is caused by enterotoxin-secreting bacteria.
  - *Vibrio cholerae*
  - Enterotoxigenic *Escherichia coli*
- Symptoms are usually acute but brief (last 1 to 3 days).
- Watery diarrhea caused by *V. cholerae* or *Giardia* can last for weeks and is very severe.

**DYSENTERY**

- Rapid onset with frequent evacuations
  - Smaller in volume than watery diarrhea
  - Contain blood and pus
  - Can be accompanied by cramps and abdominal pain
  - Little vomiting
- Caused by organisms that cause damage to the colonic mucosa
  - Either directly or production of toxins
- Not as much fluid loss as in watery diarrhea but lasts longer
  - Most cases resolve in 3 to 7 days.

**ENTERIC FEVER**

- Systemic infection focused in the gastrointestinal tract.
- Prominent features are fever and abdominal pain.
  - Take days to develop
  - Diarrhea is mild until late in the infection.
- Pathogenesis involves the penetration of enterocytes.
ENTERIC FEVER

Pathogens spread to biliary (bile) tract, liver, and organs of the reticuloendothelial system.
Most investigated form is typhoid fever.
Caused by *Salmonella enterica* serotype Typhi
Usually self-limiting
Can be serious and result in significant mortality.

TYPES OF INFECTION

There are five major types of gastrointestinal infection:
- Endemic
- Epidemic
- Traveler’s diarrhea
- Food poisoning
- Nosocomial infections

ENDEMIC GASTROINTESTINAL INFECTIONS

Defined as infections that occur sporadically
- Some are worldwide.
- Some are geographically restricted.
- There can be seasonal variation.
- They can be age-related.
**ENDEMIC GASTROINTESTINAL INFECTIONS**

- The major pathogens in developed countries are:
  - *Campylobacter*
  - *Salmonella*
  - *Shigella*
  - Infections are more commonly seen in children.
- Some organisms geographically restricted to warm climates:
  - *Vibrio cholerae*

**EPIDEMIC GASTROINTESTINAL INFECTIONS**

- Defined as infections involving regional, national, and international populations.
- Most common epidemic infections are:
  - Cholera
  - Typhoid fever
  - Shigellosis
- All are directly related to failures in public health.
  - Cholera and typhoid fever are associated with contamination of water.
  - Shigellosis is associated with wars, crowding, and poor sanitation.
  - *Shigella* infection is easily spread.

**EPIDEMIC GASTROINTESTINAL INFECTIONS**

- Most frequent epidemic infections in the US are:
  - *E. coli* O157:H7
  - Cryptosporidium
  - Giardia
**TRAVELER’S DIARRHEA**

- 20-50% of travelers to undeveloped countries will get diarrhea in the first week.
  - Usually brief and self-limiting
  - Can be serious
- Most studied cases are travelers from the US to Latin America.
  - 50% of cases are caused by enterotoxigenic strains of *E. coli*.
  - 10-20% are caused by *Shigella*.
  - The major source is ingestion of improperly cooked food.
    - Some toxigenic *E. coli* is found in salads and vegetables.

**FOOD POISONING**

- Usually connected to one meal
  - Single source of contamination
  - Typically involves multiple patients
- Almost always involves improper food handling
- Has increased with the popularity of fast food

**FOOD POISONING**

- Can result in two ways:
  - Infection – involves a pathogen directly
  - Intoxication – involves a toxin produced by a pathogen
- Incubation time and severity depend on:
  - Number of pathogens ingested – infections.
  - Amount of toxin ingested – intoxications.
- Incubation time is usually shorter in intoxications.
- Intoxication may involve organs outside the digestive tract.
  - Botulism affects the central nervous system.
**FOOD POISONING**

- Food poisoning is usually caused by:
  - Failing to cook food adequately.
  - Allowing undercooked food to sit.
    - Pathogens can enter, multiply, and produce toxins.
  - Improper storage is an additional factor.

**NOSOCOMIAL GASTROINTESTINAL INFECTIONS**

- Acquired in a hospital and usually traced to:
  - Employees.
  - Contaminated food prepared outside the hospital.
- Two major pathogens responsible:
  - *E. coli*
  - *C. difficile*
- *C. difficile* accounts for 90% of infections.
  - Symptoms range from mild diarrhea to fulminant pseudomembranous colitis.
  - Colitis arises either during or after treatment with antibiotics.
TREATMENT & MANAGEMENT OPTIONS FOR GASTROINTESTINAL INFECTIONS

- Treatment involves supportive care with liquid replacement rest.
- Substantial liquid loss requires intravenous replacement.
- Infection with *E. coli* O157:H7 can result in renal failure.
  - Requires dialysis or transplant.

DENTAL AND PERIODONTAL INFECTIONS

- Mouth is the portal of entry for many pathogens.
- Many opportunistic pathogens reside in the mouth.
- Most commonly seen infections in the mouth are:
  - Dental caries.
  - Infections of the gum tissue.
- In both cases, the major source of infection is plaque.
  - Forms as a result of bacterial colonization on surface of teeth

FORMATION OF DENTAL PLAQUE

- Tooth surface is normally covered by pellicle.
- Bacteria adhere to the pellicle.
  - Facilitated by bacterial adhesion molecules
  - Initial adherent is usually *Streptococcus mutans*
FORMATION OF DENTAL PLAQUE

Adhered bacteria grow and are joined by additional organisms.

- Gram-positive cocci
- Gram-positive rods

After 2 to 4 days, new layers of organisms have joined.

- These are followed by Gram-negative motile anaerobes.
- There can be as many as 400 species in mature plaque.
FORMATION OF DENTAL PLAQUE

- Dental plaque is a biofilm.
  - Also a mediator for many types of interaction between organisms.
- Antiseptic substances can inhibit plaque formation and reduce plaque buildup.

DENTAL CARIES

- Caries are the single greatest cause of tooth loss.
- Several factors are involved in its development.
  - Tooth structure
  - Types of microflora
  - Types of substrate available
- Saliva normally protects against carries.
  - Contains lysozyme, IgA, and other antibacterial products

DENTAL CARIES

- Organisms that produce acid can cause dental caries.
  - *S. mutans* is the major cause.
  - Other organisms contribute.
- Carbohydrates easily enter the plaque and are readily metabolized.
  - Repeated snacking on sugar keeps acid level high.
  - This continues demineralization of the tooth.
GINGIVITIS & PERIODONTITIS

There are two forms of plaque-induced periodontal disease.

- Gingivitis
  - Inflammatory condition
  - Limited to the marginal surfaces of the gingival
  - Does not involve loss of bone
  - Can be corrected
  - Will continue as long as dental plaque remains

GINGIVITIS & PERIODONTITIS

- Periodontitis
  - Infection of the gingival
  - Results in loss of supportive bone and ligaments
  - Responsible for most tooth loss in adults

If plaque is removed and teeth kept plaque-free, gingivitis will completely resolve.

- When the supporting bone begins to be resorbed:
  - Condition escalates to periodontitis.
  - Bone is not replaced.
NECROTIZING PERIODONTAL DISEASE

- Previously referred to as Vincent’s disease or trench mouth.
- Spectrum of acute inflammatory diseases
  - Onset can be acute.
  - Associated with emotional stress and poor oral hygiene
  - Rapid ulceration of tissues
  - Pronounced bone loss

NECROTIZING PERIODONTAL DISEASE

- Bacteria invade the tissues
  - Very painful
  - Causes extremely bad breath
  - Requires systemic and topical administration of antibiotics

HAZARDS OF DENTAL PLAQUE

- Dental plaque is a serious hazard for:
  - Immunocompromised patients.
    - Can give rise to systemic infections
    - Frequent source of lethal infection in leukemia patients
  - Patients with heart valve malfunctions.
    - Can cause increased incidence of endocarditis
ENTEROBACTERIACEAE

- Many digestive infections caused by Enterobacteriaceae.
  - Diverse family of Gram-negative rod-shaped bacteria
  - Some are part of the indigenous microflora
  - Grow rapidly in aerobic and anaerobic conditions
  - Damage the human intestines only
  - Some are etiologic agents of diarrheal diseases
  - Spread to the blood can cause endotoxic shock

ENTEROBACTERIACEAE

- Enterobacteriaceae include some of the largest bacteria known and have a variety of morphologies.
- Some structures are antigenic.
  - Lipopolysaccharide in the outer membrane – O antigen
  - Surface polysaccharides may form a capsule – K antigen
  - Flagella proteins of motile strains – H antigens
ENTEROBACTERIACEAE

- Most colonize the lower gastrointestinal tract.
  - Many are components of the normal colonic flora.
  - *Shigella* and *Salmonella* are not part of the normal flora.
  - Strictly human pathogens

ENTEROBACTERIACEAE

- *Salmonella, Shigella, Yersinia, some E. coli*: produce disease in the gastrointestinal tract.
  - Some have invasive properties
  - Some produce virulence factors
    - Cytotoxins and enterotoxins
    - Correlate with the type of diarrhea

ENTEROBACTERIACEAE

- Enterotoxins usually cause watery diarrhea.
- Invasive and cytotoxic strains cause dysentery.
- Enterobacteria also produce a variety of virulence factors.
  - Some use a contact secretion system to get them into the cytoplasm of the host cell.
  - Genes for either are organized into pathogenicity islands.
    - On the chromosome or in a plasmid (or both)
**E. coli**

- Gram-negative rods.
- Can be distinguished by biochemical reactions they perform
- Over 150 different groups of *E. coli*
  - Classified according to O, K, and H antigens
- Many use fimbriae and pili to attach to host cells.
  - Also important virulence factors.

**E. coli**

- Enteric bacteria can produce different toxins.
  - Pore-forming toxin
  - Shiga toxin
  - Heat labile toxin
  - Heat stable toxin
  - All are produced by *E. coli.*

**E. coli:** Pore-forming toxin

- A form of hemolysin
- Inserts into the plasma membrane
  - Destroys the integrity of the cell
**E. coli:**

**Shiga toxin**

- Two-chain toxin
  - B chain attaches to host cells
  - A chain enzymatically modifies host ribosomal RNA
    - Blocks protein synthesis

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**E. coli:**

**Heat-labile toxin**

- Sensitive to heat
- Two chain toxin
  - B chain attaches to host cells
  - A chain disrupts host cell signaling
    - Results in accumulation of liquids in the lumen of intestine
    - This is the basis for diarrhea.

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**E. coli:**

**Heat-stable toxin**

- More resistant to heat than heat-labile toxin
- Small peptide
  - Binds directly to glycoprotein receptors
    - Results in the secretion of liquids and electrolytes into the lumen
CATEGORIES OF E. COLI

- E. coli can be divided into the following:
  - Enterotoxigenic E. coli (ETEC)
  - Enteropathogenic E. coli (EPEC)
  - Enteroinvasive E. coli (EIEC)
  - Enterohemorrhagic E. coli (EHEC)
  - Enteroaggretive E. coli (EAEC)
- Each type causes disease by a different mechanism.
- Diseases differ clinically and epidemiologically.

ENTEROTOXIGENIC E. COLI

- Disease is caused by a toxin.
- The most frequent cause of traveler’s diarrhea.
- Produces diarrhea in infants
  - Leading cause of morbidity and mortality in first two years in developing countries
ENTEROTOXIGENIC *E. COLI*

- Transmission is by consumption of contaminated food or water.
  - Contaminated by actively infected individuals or by carriers
  - Uncooked foods are the greatest risk.
  - Person-to-person transmission is very rare.

ENTEROTOXIGENIC *E. COLI*: Pathogenesis

- Organisms adhere to the cells of the small and large intestine.
- Diarrhea is caused by heat-labile or heat-stable toxin.
  - Toxin causes water and electrolytes to flow into the intestine.
- Genes for the toxins are on plasmids.
  - Can be readily moved from organism to organism
  - No invasion of the host cells, no damage to cells, and no inflammatory response

ENTEROPATHOGENIC *E. COLI*

- First seen in hospital outbreaks of diarrhea in the 1950s.
- Essentially disappeared in developed countries
  - Account for 20% of diarrhea seen in bottle-fed infants in developing countries
  - Transmission is by the fecal-oral route.
  - Infants are the reservoir.
ENTEROPATHOGENIC E. COLI: Pathogenesis

- Organisms attach to cells in the intestine.
  - Use fimbriae to form colonies on surface of cells
  - Causes effacement of the microvilli
- Secretion system delivers at least five different proteins into host cell cytoplasm.
  - Inhibit cell signaling
  - Cause modifications of cytoskeletal proteins
  - Cause of the diarrhea not understood
  - May involve the changes to the microvilli

ENTEROHEMORRHALGIC E. COLI

- So called because they produce the Shiga toxin which causes:
  - Capillary thrombosis.
  - Blood in stool.
- Transmission is via consuming infected animal products.
  - Person-to-person transmission can occur.
  - Infection is more common in developed industrialized countries.

ENTEROHEMORRHALGIC E. COLI

- *E. coli* O157:H7 is a well known enterohemorrhagic *E. coli*.
  - Causes bloody diarrhea
  - Associated with ground meat and unpasteurized juices
ENTEROHEMORRHAGIC E. COLI: Pathogenesis

- Two factors make human infection likely:
  - Very low ID₅₀.
  - Common reservoir – cattle.
- Changes in the food processing industry that provide “fresher” meat have caused outbreaks.
  - Worst outbreaks seen in countries with the most modern food processing.
- Fruits and vegetables can also be contaminated.

ENTEROHEMORRHAGIC E. COLI: Pathogenesis

- Distinguishing clinical factors are:
  - Production of Shiga toxin.
  - Effacement of intestinal microvilli.
  - Attack the colon by adhering through attachment proteins
    - Use the secretion infection system to deliver proteins into target cells
    - These proteins alter cytoskeletal components.

ENTEROHEMORRHAGIC E. COLI: Pathogenesis

- Attachment and effacement cause diarrhea
- Shiga toxin causes capillary thrombosis and inflammation of the colonic mucosa.
  - Leads to hemorrhagic colitis
- Shiga toxin can circulate in the blood and bind to renal tissue causing.
  - Glomerular swelling
  - Deposition of fibrin platelets in blood vessels
TREATMENT OF ALL FIVE FORMS OF E. COLI

- Most E. coli diarrhea is mild and treatment is not required.
- If diarrhea is severe, liquid replacement is required.
- Enterohemorrhagic infections may require heroic measures such as dialysis.
- Treatment with antibiotics can reduce the duration of illness.
  - Trimethoprim/sulfamethoxazole or quinolones are effective.
- Antibiotics have no effect if hemorrhagic colitis has occurred.

SHIGELLA

- Shigella species are closely related to E. coli but:
  - Cannot ferment lactose.
  - Lack flagella.
  - Cannot be identified by H antigens.

SHIGELLA

- Four species can invade and multiply inside a wide variety of cells.
  - S. dysenteriae
  - S. flexneri
  - S. boydii
  - S. sonnei
- All species produce Shiga toxin.
  - S. dysenteriae produces most.
**SHIGELLA**

- *Shigella* species cause dysentery.
  - Spread from person to person in unsanitary conditions
- Strictly human pathogen
- Shigellosis is one of the most common causes of diarrhea worldwide.
  - More than 600,000 deaths each year
  - *S. dysenteriae* causes the most severe form of infection - bacillary dysentery.

**SHIGELLA**

- Transmission can occur by:
  - Fecal-oral route.
  - Person-to-person transmission.
  - Consumption of contaminated food or water.
- ID₅₀ is fewer than 200 organisms.
  - It is easily transmissible.
  - 40% of patients get infection from family member.
- Direct connection between *Shigella* infections and community sanitary practices

**SHIGELLOSIS: Pathogenesis**

- *Shigella* is acid-resistant.
  - Survives passage through the stomach
- Invade the cells of the colonic mucosa
  - Intense acute inflammatory response
  - Causes mucosal ulcerations and abscess formation
**SHIGELLOSIS:**
Pathogenesis

- *Shigella* is nonmotile.
  - Creates an actin tail and uses it as a means of transport
  - *Shigella* moves to the membrane of the host cell.
  - Some push into the adjacent cell.
  - Causes the formation of a fingerlike projection into the next cell
  - This pinches off, forming a vacuole.
  - *Shigella* lyases the vacuole membranes.
  - Pathogen is released into the cytoplasm.
  - The process starts again.

- Cell-to-cell extensions cause localized ulcers in the mucosa, particularly in colon.
  - Adds a hemorrhagic component to the infection
  - Allows *Shigella* to enter the lamina propria
  - Causes the intense inflammatory response
  - Diarrhea stools are small.
    - Contain white blood cells, red blood cells, and bacteria
**SHIGELLOSIS: Pathogenesis**

- Shiga toxin contributes to the overall severity of the illness causing:
  - Inflammatory colitis.
  - Bloody diarrhea.
- Inflammatory colitis presents as dysentery with cramps and bloody mucoid discharges.
  - Initial indications are fever, malaise, and anorexia.
  - Dysentery follows later.

**TREATMENT OF SHIGELLOSIS**

- Majority of shigellosis spontaneously resolve in 2 to 5 days.
  - Mortality can be as high as 20%.
- Antibiotics are effective at shortening the period of illness.
  - Trimethoprim and sulfamethoxazole are the drugs of choice.
- Standard sanitation disposal and water chlorination are important in prevention.

**SALMONELLA**

- All types of *Salmonella* are now classified as one species, enteric.
- *Salmonella enterica* is divided into serotypes based on its antigens.
  - O antigens identify the serogroup.
  - K and H antigens are used for further subdivision.
- Can also distinguish *Salmonella* by host range
  - Some are strictly adapted to humans.
**SALMONELLA**

- *Salmonella* possess multiple pili.
  - Bind to mannose receptors on eukaryotic cells
  - Most *Salmonella* are very motile.

**SALMONELLA**

*Salmonella* infections are divided into five groups:
- Gastroenteritis
- Bacteremia
- Enteric fever
- Chronic infections
- Typhoid fever
**SALMONELLA: Bacteremia**

- Bacteremia is an acute form of gastroenteritis.
  - Approximately 70% of AIDS patients are affected.
  - Can lead to septic shock and death
  - Pathogens can spread to the meninges, bones, or sites of malignancy.

**SALMONELLA: Enteric Fever**

- Enteric fever is a multiorgan *Salmonella* infection
  - Sustained bacteremia.
  - Profound infection of organs.
    - Particularly the lymph nodes, liver, and spleen
  - First symptoms are fever and headache.
    - Fever increases over 72 hours.
      - Can last for weeks if untreated
    - Some patients have constipation, others have diarrhea.

**SALMONELLA: Chronic Infection**

- Chronic infection is very serious if bacteria enter the blood.
- Continuous release of endotoxin can cause:
  - Myocarditis.
  - Encephalopathy.
  - Intravascular coagulation.
  - Infection of distal sites.
    - Biliary tract continues to harbor organisms and cause reinfection.
**SALMONELLA GASTROENTERITIS**

- Occurs both in the stomach (gastro) and intestines (entero).
- Disease of industrialized societies.
  - Results from improper food handling
- Transmission is from animal or human reservoirs to humans.
- ID$_{50}$ is higher than that seen with *Shigella*.
  - Less infectious problem
  - 1,000 or more organisms required for infection.

**SALMONELLA GASTROENTERITIS**

- *Salmonella* is the leading cause of food-borne gastrointestinal infections.
  - Poultry and infected eggs are most often the cause.
  - Poor food handling and preparation are also implicated.
  - Can also be transmitted by exotic pets

**SALMONELLA GASTROENTERITIS**

- 40,000-50,000 cases are reported each year in the US.
  - This may be only 1-4% of the total cases.
  - Nearly 30% of cases are in nursing homes, hospitals, and mental health facilities.
  - 5% of patients recovering will shed the organism in their feces for up to 20 weeks.
  - Chronic carriers are an important reservoir.
**SALMONELLA GASTROENTERITIS:**
**Pathogenesis**

- Ingested *S. enterica* pass through the stomach.
  - Swim through the intestinal mucous layer
  - Reach enterocytes and M cells
  - Use pili to adhere to M cells
  - Cause the surface of M cells to ruffle

**SALMONELLA GASTROENTERITIS:**
**Pathogenesis**

- Ruffles on M cells are specialized sites.
  - Rearrangement of the filamentous actin occurs here.
  - Rearrangement is stimulated by 12 or more proteins.
    - Coded for by genes located on pathogenicity islands
  - Ruffled surface engulfs bacteria.
    - Forms an endocytic vacuole
    - Transcytoses to the basolateral surface
**SALMONELLA GASTROENTERITIS:**

- Bacteria enter the lamina propria.
  - Initiate powerful inflammatory response
- *Salmonella* can withstand the phagocytic response.
  - Induce apoptosis of the host phagocytic cell
- Transcytosis and the inflammatory response cause the onset of diarrhea.

**TYPHOID FEVER**

- Caused by *Salmonella enterica* serotype Typhi.
- Strictly human disease
  - Chronic carriers are the primary reservoir.
    - Some carry disease for years.
    - Bacteria become sequestered in the gall bladder.
- Bacteria are transmitted to water after sewage contamination.
  - Passed from human to human by the fecal-oral route.
- ID$_{50}$ can become lower if the organism is encapsulated.
- Causes significant morbidity and mortality in Latin America and India
**TYPHOID FEVER:**

**Pathogenesis**

- Lack of animal model makes it difficult to study.
- *S. enterica* serotype *Typhi* can survive for long periods inside viable host macrophages.
  - Inhibits the release of oxidative poisons used by macrophages
  - Allows it to multiply and infect new macrophages
  - Bacteria eventually spill into the lymphatic circulation.
  - Migrates to lymph nodes, spleen, liver, and bone marrow.

- Systemic infection is exacerbated by release of lipopolysaccharide endotoxin.
  - Causes a fever to increase and persist
  - Bacteria can spread to the urinary system and other organs.
    - Bowel becomes reinfected.
    - Entire cycle takes only two weeks
  - Most important complication is hemorrhaging causing perforation of the wall of the colon or ileum.
    - Peyer’s patches become necrotic.

**SALMONELLA INFECTIONS:**

**General Treatment**

- Primary therapy is replacement of fluid and electrolytes.
  - Control of nausea and vomiting is also used.
- Antibiotics are not appropriate.
  - Increase the duration and frequency of the carrier state
  - Can be used prophylactically to prevent disease spreading
- A vaccine has been available for many years.
- Essential to provide clean water and treat those carrying the disease.
VIBRIO

- Gram-negative, non spore-forming, and rod-shaped
- Commonly found in salt water
- Have a unique morphology
  - Form S shapes and half spirals
- Highly motile by means of a single polar flagella

VIBRIO

- Can grow either aerobically or anaerobically
- Cell structure similar to that of Gram-negative bacteria
- Low tolerance for acidic conditions
  - Grow well in mildly alkaline environments
- *Vibrio cholerae* produces a toxin.
  - Causes a devastating intestinal infection
- There have been eight cholera pandemics lasting 5-25 years.
**V. CHOLERAE: Pathogenesis**

- Spread primarily by contaminated water and poor sanitation.
- Short incubation of 2 days
  - Rapid epidemic cycle
- Bacteria possess long filamentous pili.
  - Form bundles on the bacterial surface
  - Used for colonization
- Colonizes the entire intestinal tract
  - Jejunum to the colon

**V. CHOLERAE: Pathogenesis**

- Liquid loss is the major clinical problem and depends on:
  - Bacterial growth.
  - Toxin production.
  - Host liquid secretion and absorption.
- Loss of liquids and electrolytes can amount to multiple liters a day.
  - Greatest in the small intestine
  - Results in dehydration, hypokalemia, and metabolic acidosis

**V. CHOLERAE: Pathogenesis**

- *Vibrio cholerae* does not invade or damage enterocytes.
  - Uses its toxin plus a variety of virulence factors to cause disease.
- Virulence factors are part of a controlled, coordinated system involving environmental sensors.
  - All coded for by genes located on pathogenicity islands.
**V. CHOLERAE: Pathogenesis**

- Cholera has a rapid onset characterized by:
  - Abdominal fullness.
  - Discomfort.
  - Rushes of peristalsis.
  - Loose stools.

- Stools quickly become watery, voluminous, and almost odorless.
  - Can progress to rice stool containing mucus
  - No fever
  - No blood in stool

**TREATMENT OF CHOLERA**

- Outcome depends on balancing liquid and electrolyte loss.
  - Liquid replacement is all that is required except in the most severe cases.
  - Tetracycline shortens duration of diarrhea and magnitude of liquid loss.
**CAMPYLOBACTER ENTERITIS**

- Caused by *Campylobacter jejuni*
- Not recognized as a human pathogen until 1973
  - Now one of the most common causes of diarrhea
  - Leading cause of gastrointestinal infection in developed countries
  - More than 2 million cases in US each year
- ID₅₀ of only a few hundred

**CAMPYLOBACTER ENTERITIS**

- Primary reservoir is animals.
- Transmitted to humans by:
  - Ingestion of contaminated food.
  - Direct contact with pets that harbor the organism.
- Most common source is undercooked poultry.
- Can also be contaminated water and unpasteurized milk
- *Campylobacter* commonly found as part of the gastrointestinal and genitourinary tract flora of animals.
- Domestic pets may have a significant role in transmission to humans.

**CAMPYLOBACTER ENTERITIS: Pathogenesis**

- Oral ingestion is followed by colonization of the intestinal mucosa.
  - Bacteria adhere to and enter cells in endocytic vacuoles.
  - Move in association with microtubule structures
  - Produce lethal distending cytotoxin
    - Arrests cell division
    - Cytoplasm continues to increase.
    - Leads to diarrhea
**CAMPYLOBACTER ENTERITIS: Pathogenesis**

- Illness begins about seven days after ingestion.
  - Includes fever and lower abdominal pain
  - May be severe enough to mimic appendicitis
  - Within hours there are dysenteric stools containing blood, mucus, and pus.
- Association between *C. jejuni* and Guillain-Barré syndrome
  - An acute demyelinating disease
  - Up to 40% of patients with it also have evidence of infection with *Campylobacter*.

**CAMPYLOBACTER ENTERITIS: Treatment**

- Infection is self-limiting.
  - Signs and symptoms last for only 3 to 5 days.
  - Up to 2 weeks in severe cases
- Fewer than 50% of patients benefit from antibiotic treatment.
  - Erythromycin is the treatment of choice for severe infections.

**HELICOBACTER PYLORI**

- Similar to *Campylobacter* in morphology and growth characteristics
  - Slender
  - Microaerophilic
  - Gram-negative curved rod
  - Polar flagella
Lipopolysaccharides in the outer layer may be more toxic than those in other Gram-negative pathogens.

- A unique feature is the production of a urease.
  - Generates ammonia
  - Allows it to survive in very acidic environments
- Produces a circulating protein – vacuolating cytotoxin
  - Causes apoptosis in eukaryotic cells

Infected cells have large vacuoles throughout their cytoplasm.

- H. pylori cells possess a contact injection system.
  - Introduces proteins that disrupt proteins in the infected cell.
- Virulence factors are coded for by genes located on pathogenicity islands.
**HELICOBACTER PYLORI**

- *Helicobacter pylori* infection causes ulcers.
- Found in 30-50% of all adults in developed countries
  - Practically 100% of adults in developing countries
- Mode of transmission is not known.
  - Presumed to be person-to-person by the fecal-oral route

**HELICOBACTER PYLORI**

- Colonization increases with patient’s age and persists for decades.
- Most common cause of:
  - Gastritis.
  - Gastric ulcers.
  - Duodenal ulcers.
- Predisposing factor for gastric adenocarcinoma
**H. PYLORI GASTRITIS:**

**Pathogenesis**

- Uses multiple mechanisms to adhere to the gastric mucosa and survive the acidic environment
- Highly motile and swims to less acidic areas
  - In less acidic areas, it adheres using surface proteins.

---

**H. PYLORI GASTRITIS:**

**Pathogenesis**

- Colonization is usually accompanied by cellular infiltration.
  - Part of the inflammatory response
- Inflammatory response can be extensive.
  - Causes the formation of microabscesses
  - Contributes to the ulceration
- Virulence factors enhance cellular erosion.

---

**H. PYLORI GASTRITIS:**

**Pathogenesis**

- Primary infection shows no symptoms or some nausea and mild upper abdominal pain.
  - Usually lasts two weeks
- Gastritis or peptic ulcer disease can develop years later.
  - Nausea, anorexia, vomiting, and pain
  - Many patients asymptomatic even up to perforation of the tissue
  - Perforation leads to extensive internal bleeding.
**H. PYLORI GASTRITIS:**

**Treatment**

- Sensitive to a wide variety of antimicrobial agents
  - Bismuth salts (Pepto-Bismol) is one of the best.
- Treatment with bismuth salts and a combination of tetracycline plus clarithromycin cures 95% of cases.

---

**VIRAL INFECTIONS OF THE DIGESTIVE SYSTEM**

- Digestive system is an important portal of entry for viruses.
- For some it is only an entry point
  - Disease occurs somewhere else.
- Most common sign of viral infection is diarrhea.
  - Rapid onset – within hours
  - Lasts for less than three weeks
  - Abundant excretion of virions in the stool
    - $10^8$ per gram of stool

---

**VIRAL INFECTIONS OF THE DIGESTIVE SYSTEM**

- Specific criteria must be met to implicate viruses in digestive infections.
  - Virus must be detected in ill patients..
  - Viral shedding must correlate with onset of symptoms.
  - Must be a significant antibody response
  - Disease must be reproduced.
    - Experimental inoculation of nonimmune humans or animals
    - Difficult requirement to satisfy as many viruses cannot be grown in culture
  - Other causes of the signs and symptoms must be excluded.
VIRAL INFECTIONS OF THE DIGESTIVE SYSTEM

Several groups of viruses cause gastrointestinal infections:
- Rotavirus
- Calicivirus
- Astrovirus
- Some serotypes of adenovirus
- Enterovirus

VIRAL INFECTIONS OF THE DIGESTIVE SYSTEM

Infections all have similar characteristics
- Brief incubation periods
- Fecal-oral routes of transmission
- Vomiting that either precedes or accompanies diarrhea

<table>
<thead>
<tr>
<th>Surface Antigens</th>
<th>Envelope</th>
<th>Capsid</th>
<th>Stool</th>
<th>Normal Intestinal Mucosa</th>
<th>Other Mucous Membranes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenesis</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
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</tr>
</tbody>
</table>

VIRAL INFECTIONS OF THE DIGESTIVE SYSTEM

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Laboratory Findings</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Note: (c) Microbiology: A Clinical Approach © Garland Science
**ROTA VIRUS**

- Rotaviruses belong to the family *reoviridae*.
  - Non-enveloped
  - Spherical
  - Double-stranded RNA
  - Have a double-capsid structure
    - Outer capsid is attached to the inner by spoke-like structures.

- Not discovered until 1973
  - Now found around the world
  - Believed to account for 40 - 60% of cases of acute gastroenteritis
  - Can undergo genetic re-assortment
    - Difficult to deal with immunologically

- Outbreaks of rotavirus infections common in infants and children under 2.
  - Adults are usually only minimally affected.
  - Can affect the elderly or institutionalized
  - Usually causes little or no clinical illness
**ROTA VIRUS**

- Rotavirus infections kill more than 1 million infants worldwide each year.
  - In the US there are fewer than 100 deaths each year.
  - Infection is still a major cause of hospitalization early in life.

**ROTA VIRUS INFECTION: Pathogenesis**

- Localizes primarily in the duodenum and proximal jejunum
  - Blunts the microvilli of epithelial cells
  - Causes infiltration of mononuclear and polymorphonuclear leukocytes
    - Decreased absorptive surface on the microvilli
    - Decreased enzymatic function
  - End result is malabsorption and defective handling of fats and carbohydrates.
  - Gastric colonic mucosa is not affected.

- Normal histology and function takes 8 weeks to restore.
- Incubation is between 1 and 3 days.
  - Begins with the abrupt onset of vomiting
  - Within hours there are frequent copious watery brown stools
    - Often low-grade fever as well
    - Vomiting and diarrhea last for several days.
  - Major complication of these effects is dehydration.

Rotavirus infections kill more than 1 million infants worldwide each year. In the US there are fewer than 100 deaths each year. Infection is still a major cause of hospitalization early in life.

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TREATMENT OF ROTAVIRUS INFECTION

- No specific treatment
  - Severe cases require vigorous fluid replacement.
- Rotavirus is highly infectious.
  - Can spread rapidly in institutional settings
- Requires strict control of hygienic practices

ENTEROVIRUS

- Enteroviruses are members of the *picornaviridae*.
- Very resistant to acidic environments
  - Can survive in the stomach
- Also resistant to common disinfectants and various detergents
- Humans are the natural hosts.
  - Asymptomatic infection is common.
  - Whether infection is symptomatic or not depends on the species of enterovirus.

ENTEROVIRUS

- All enterovirus infections:
  - Show a seasonal infection pattern.
  - Are predisposed to temperate climates.
  - Transmission is by direct or indirect fecal-oral route.
    - Person-to-person is most common.
  - Virus will normally spend 1 to 4 weeks in the oropharynx.
    - Can be shed for 18 weeks in the feces
ENTEROVIRUS INFECTION: Pathogenesis

- 60% of infections occur in children of 9 and younger.
- Incubation time is 2 to 10 days.
- Virus is brought into the host cell by envelopment in the host membrane.
  - Viral RNA is released into the cytoplasm.
  - Binds directly to cellular ribosomes
  - Begins synthesis of viral proteins

- Enteroviruses are lytic.
  - End result is destruction of host cell
  - Primary infection in the digestive system
    - Spreads to other sites

TREATMENT OF ENTEROVIRUS INFECTION

- None of the currently available antiviral agents is effective.
HEPATITIS VIRUSES

- Hepatitis describes any disease that affects the hepatocytes of the liver.
- Diseases can be caused by a variety of agents:
  - Bacteria
  - Protozoans
  - Viruses
  - Toxins
  - Drugs
- At least 6 different viruses cause hepatitis
  - They are distinctly different from one another.

HEPATITIS A

- Classified as a member of the genus \textit{hepatovirus}, family \textit{picornaviridae}
  - Non-enveloped, single-stranded RNA virus with cubic symmetry
  - Resists inactivation
  - Stable at -20°C and low pH
- Only one serotype

HEPATITIS A

- Humans are the most common natural host.
- Transmission is usually via the fecal-oral route.
  - Infections are common where there is crowding and poor hygiene.
  - Rates of infection are higher in lower socioeconomic groups.
  - Up to 90% of the population of developing nations show evidence of previous infection.
HEPATITIS A INFECTION:
Pathogenesis

- Infection often results from poor personal hygiene in food handlers.
  - Patients are contagious 1 to 2 weeks before the onset of clinical symptoms.
  - Virus is believed to replicate initially in intestinal mucosa.
  - Seen in feces 10-14 days before onset of symptom.
  - When symptoms begin, virus is no longer being shed.

- Multiplication in the intestines is followed by spread to liver
  - Causes lymphoid infiltration into the liver
    - Necrosis of the parenchymal cells
    - Proliferation of Kupffer cells
  - Extent of necrosis correlates to the severity of infection.

- Immune response is protective.
  - Patients with antibodies cannot be reinfected.
  - Incubation times vary from 10 to 50 days, followed by:
    - Fever
    - Anorexia
    - Nausea
    - Pain in the abdomen
    - Jaundice
**HEPATITIS A INFECTION: Pathogenesis**

- In infected patients with jaundice:
  - Urine becomes dark.
  - Stool can become clay-colored 1 to 5 days before onset of jaundice.

**HEPATITIS A INFECTION: Pathogenesis**

- Many of those infected will be asymptomatic or mildly affected.
  - Do not develop jaundice
  - Referred to as anicteric hepatitis A infection
  - Function of the patient’s age
    - Seen more in children, less in adults

**HEPATITIS A INFECTION: Treatment**

- No drugs are effective – supportive measures are recommended.
- There is an active immunization protocol for those who are repeatedly exposed to hepatitis A virus.
HEPATITIS B

- Classified as a member of the family *hepadnaviridae*
  - Unrelated to any other human virus
  - DNA virus
  - Spherical shape with a surrounding envelope

HEPATITIS B

- Viral genome is unique.
  - Only partly double-stranded
  - Contains short stretch that is single-stranded
  - Carries with it viral DNA polymerase
- Envelope contains viral surface antigens HBsAg.
  - Aggregates of these often found in abundance during the infection.

HEPATITIS B

- Replication cycle is unique because of its genome.
  - Full-length positive viral RNA transcripts are inserted into the virus core.
  - Used as a template for reverse transcription
  - Negative DNA strand is made
  - Positive DNA strand is begun but never finished.
HEPATITIS B

- Hepatitis B is found worldwide.
  - Prevalence varies between countries.
- Chronic carriers are the main reservoir.
- An estimated 1.5 million people in the US are infected with hepatitis B yearly.
  - 300,000 new cases each year

- 5-10% of those infected become chronic carriers.
  - 0.1% will die of acute viral infection.
- Up to 4,000 of the 300,000 new cases in the US develop hepatitis B cirrhosis.
  - 1,000 will get hepatocarcinoma.
- 50% of infections are sexually transmitted.
- Screening of blood donors has markedly reduced the incidence of transfusion transmission.

HEPATITIS B INFECTION: Pathogenesis

- Major modes of transmission are:
  - Close contact with body liquids from infected individuals
  - Inadequately sterilized hypodermic needles or instruments.
    - Tattooing or piercing can easily transmit this viral infection.

- 300,000 new cases each year
- 5-10% of those infected become chronic carriers.
  - 0.1% will die of acute viral infection.
- 1,000 will get hepatocarcinoma.
- 50% of infections are sexually transmitted.
- Screening of blood donors has markedly reduced the incidence of transfusion transmission.
HEPATITIS B INFECTION:
Pathogenesis

- Mechanisms involved in the appearance of clinical symptoms are not yet understood.
  - Seem to involve the immune response
- Lesions in acute hepatitis B infections resemble those seen with other hepatitis viruses.
  - Chronic active infection causes a continued inflammation resulting in necrosis of hepatocytes.
    - Collapse of the reticular framework of the liver
    - Progressive fibrosis

HEPATITIS B INFECTION:
Pathogenesis

- Clinical symptoms are variable.
  - Incubation time is 7-160 days.
- Acute infection shows as a gradual onset of symptoms.
  - Onset of fatigue
  - Loss of appetite
  - Nausea
  - Pain the upper right abdominal quadrant

HEPATITIS B INFECTION:
Pathogenesis

- Early in the infection there may be:
  - Painful swollen joints and arthritis.
  - A rash.
  - Jaundice.
- Symptoms can last for months.
HEPATITIS B INFECTION:  
Pathogenesis

- Fulminant hepatitis is seen in less than 1% of infections.
- Approximately 10% of infected individuals will develop chronic hepatitis.
  - Risk is higher in children and the immunocompromised.
- Chronic hepatitis B can lead to:
  - Cirrhosis.
  - Liver failure.
  - Hepatocellular carcinoma.

HEPATITIS B INFECTION:  
Treatment

- No effective treatment for acute hepatitis B infection, but can be prevented by:
  - Using safe sex practices.
  - Avoiding needle sticks.
- Hepatitis B serum globulin can reduce development of disease.
- A vaccine made in yeast provides excellent protection.
  - Health care workers required to receive it.

HEPATITIS C

- Classified as a member of the *flaviviridae* family
  - RNA virus
  - Very simple genome consisting of only eight genes
- Six major genotypes and multiple subtypes
  - Geographic distribution and severity of disease is related to the genotype.
HEPATITIS C

- Major transmission mechanisms are:
  - Blood transfusions
  - Sexual transmission
  - Needle sharing accounts for 40% of infections.
  - Hemodialysis patients are also at risk.
- More than 3.5 million in the US are infected with hepatitis C.

HEPATITIS C INFECTION: Pathogenesis

- Incubation time is 6-12 weeks.
- Infection is usually mild or asymptomatic.
- 85% of those infected will become carriers of the infection.
  - Progress to chronic hepatitis
  - Can take 10-18 years
- Late consequences of chronic hepatitis C infection are:
  - Cirrhosis,
  - Hepatocellular carcinoma.
- Hepatitis C is the leading cause of liver transplants.

HEPATITIS C INFECTION: Pathogenesis

**Image of a liver with cirrhosis.**
HEPATITIS C INFECTION: Treatment

- Combination therapy with interferon-α and ribavirin is the treatment of choice.

HEPATITIS D

- Small, single-stranded RNA virus.
- Referred to as a satellite virus
  - Requires the presence of hepatitis B
- Seen only in people infected with hepatitis B
  - Seen most often in intravenous drug abusers

HEPATITIS D INFECTION: Pathogenesis

- Two types of infection:
  - Co-infection with hepatitis B
  - Superinfection of people already infected with hepatitis B
- Superinfection with hepatitis D infection can cause a relapse.
  - Recurrence of jaundice
  - Increased risk of cirrhosis
  - Rapid progression of liver disease
  - Death in 20% of these cases
HEPATITIS D INFECTION: Treatment

- Interferon-α is given to doubly infected patients.
  - Only about 15 - 25% of patients improve.
- Preventative methods include safe sex and no sharing of needles.

HEPATITIS E

- Classified in the family caliciviridae
- Different family to hepatitis A virus, but similar structure
  - Non-enveloped RNA virus
  - Pronounced spikes on the capsid
- Causes a form of hepatitis that is transmitted by the fecal-oral route.

- Infection is frequently subclinical.
  - Causes acute disease only in pregnant women
- Highest attack rates in young adults.
- Infection is associated with contaminated drinking water.
  - Does not seem to be transmitted person-to-person
- Incubation time is about 40 days.
- No treatment
HEPATITIS G

- Classified in the family flaviviridae
  - Same family as and similar to hepatitis C
  - RNA virus
  - Discovered in 1995
  - 2% of blood donors are positive for hepatitis G RNA.
  - Pathogenesis and disease process not yet understood.
  - No Treatment

PARASITIC INFECTIONS OF THE DIGESTIVE SYSTEM

- Several protozoan and helminthic infections of the human digestive system
- Common parasitic diseases are caused by:
  - Giardia
  - Cryptosporidium
  - Whipworms
  - Hookworms

GIARDIASIS (GIARDIA DUODENALIS)

- Giardiasis is caused by the flagellate protozoan parasite Giardia duodenalis.
  - Found throughout world
  - Large in size
  - Exists in both a trophozoite form and cyst form
    - Trophozoite has four pairs of flagella.
GIARDIASIS (GIARDIA DUODENALIS)

- Reside in the duodenum and jejunum
  - Absorb nutrients from the host digestive tract.
- Move about and through mucous layer in two ways:
  - Using a tumbling motion
  - Through a large ventral sucker that attaches to the epithelium

GIARDIASIS (GIARDIA DUODENALIS)

- Unattached Giardia is carried in the fecal stream to large intestine.
- While in the descending colon a cyst is formed.
  - Flagella are retracted.
  - Clear cyst wall is secreted.
    - Encloses the organism

GIARDIASIS (GIARDIA DUODENALIS)
### GIARDIASIS
**(GIARDIA DUODENALIS)**

- In the cyst, *Giardia* divides to produce
  - A quadri-nucleate organism with two sucking disks.
- Mature cyst is the infectious form.
  - Can survive in cold water for months
  - Resistant to chlorine
  - Transmission is by the fecal-oral route.

---

| **GIARDIASIS**
<table>
<thead>
<tr>
<th><strong>(GIARDIA DUODENALIS)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inside a host, the cyst divides into two trophozoites.</strong></td>
</tr>
<tr>
<td><em>Giardia</em> is one of the most widely distributed intestinal protozoans and is found in:</td>
</tr>
<tr>
<td>- Fish.</td>
</tr>
<tr>
<td>- Amphibians.</td>
</tr>
<tr>
<td>- Reptiles.</td>
</tr>
<tr>
<td>- Birds.</td>
</tr>
<tr>
<td>- Mammals.</td>
</tr>
</tbody>
</table>

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<table>
<thead>
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<th><strong>(GIARDIA DUODENALIS)</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Three morphologically distinct groups.</strong></td>
</tr>
<tr>
<td><strong>Infection can be through contaminated water or food.</strong></td>
</tr>
<tr>
<td>- In children and young adults is highest in areas of poor hygiene and sanitation.</td>
</tr>
<tr>
<td>- With endemic infections, more than 60% can be asymptomatic.</td>
</tr>
<tr>
<td>- In acute outbreaks most patients show symptoms.</td>
</tr>
</tbody>
</table>
GIARDIASIS:  
Pathogenesis

- Disease is associated with malabsorption by the intestinal tract.
  - Particularly of fats and carbohydrates
- Pathogenic mechanisms are unknown but could involve:
  - Blockage of the intestine by large numbers of parasite
  - Destruction of microvilli
  - Damage to bile-production pathways
  - Altered intestinal motility
  - Accelerated turnover of the mucosal epithelium
  - Invasion of the mucosal tissue

When symptoms occur they begin 1-3 weeks after exposure.
- Sudden onset and explosive diarrhea
- Stool is foul-smelling and greasy
  - No blood or mucus
- Abdominal cramping
- Large amounts of gas
  - Abdominal distension
  - Abundant flatulence
- Nausea and low-grade fever are also possible.

Acute illness usually resolves itself in 1-4 weeks.
- May persist in children causing significant weight loss and malnutrition.
- In adults, acute phase may give way to sub-acute or chronic stage.
  - Lasts for weeks to months
  - Causes heartburn, weight loss, and flatulence

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GIARDIASIS:
Treatment

- Four drugs are currently available:
  - Quinacrine hydrochloride
  - Metronidazole
  - Furazolidone
  - Paromomycin
- All require five to seven days of therapy.
- None should be used during pregnancy.

CRYPTOSPORIDIOSIS
(CRYPTOSPORIDIUM)

- Cryptosporidiosis is caused by the protozoan parasite Cryptosporidium.
  - Infects the intestinal tract of humans and other animals
  - Obligate intracellular parasite
  - Alternates between sexual and asexual reproduction
    - Both in the gastrointestinal tract
  - Small and spherical
  - Arranges itself in rows along the microvilli of the intestinal tract
CRYPTOSPORIDIOSIS (CRYPTOSPORIDIUM)

- Parasites remain external to the cell cytoplasm.
  - Eventually become covered over by the membrane
    - Referred to as intracellular
- Oocysts are excreted in the stool of infected persons.
  - Fully mature and infectious

- On ingestion, sporozoites are released from the oocyte.
  - Attach to the microvilli of the epithelial cells of small intestine
  - Transform into trophozoites
  - Divide by schizogony to form schizonts containing eight daughter cells
  - Each daughter cell attaches to another epithelial cell.
  - Schizogony cycle is repeated.

- After several rounds of schizogony:
  - Trophozoites develop into male and female forms.
  - Sexual reproductive cycle takes place.
  - Resulting zygote develops into an oocyte
  - Shed into the lumen of the small intestine.
### CRYPTOSPORIDIOSIS (CRYPTOSPORIDIUM)

- Zygote develops a thick protective wall.
  - Ensures safe passage in the fecal stream and externally.
- 20% of zygotes will not develop walls.
  - Oocytes rupture
  - Sporozoites are released back into the lumen

### CRYPTOSPORIDIOSIS (CRYPTOSPORIDIUM)

- Various species of *Cryptosporidium* can infect most vertebrates.
  - Domestic animals are the reservoir.
- Most human infections result from person-to-person transmission.
  - Principal route is fecal-oral.
  - Contaminated food and water can also transmit.

### CRYPTOSPORIDIOSIS (CRYPTOSPORIDIUM)

- In developed countries:
  - 1 - 4 % of children harbor oocytes.
- In undeveloped countries:
  - 4 - 8 % of children are infected.
- Highest rate of infection is seen in:
  - Children
  - Families of infected children
  - Medical workers
  - Travelers
CRYPTOSPORIDIOSIS: Pathogenesis

- Jejunum most heavily involved area.
  - Some severe cases can involve the entire digestive system.
- Bowel changes are minimal.
  - Mild to moderate destruction of microvilli
  - Some mononuclear cell infiltration
- Pathology of the resulting diarrhea is not understood.

CRYPTOSPORIDIOSIS: Pathogenesis

- CD4 T cells and interferon have a role in clearance of parasites.
- Immunocompetent patients have an onset of profuse, explosive watery diarrhea.
  - Appears 1-2 weeks after exposure to the parasite
  - Lasts for about 5 days then rapidly clears

CRYPTOSPORIDIOSIS: Pathogenesis

- Diarrhea can be more severe in immunodeficient patients.
  - Liquid loss can be 25 liters per day.
  - Disease can last for life.
  - Half of the cryptosporidiosis patients with AIDS die within 6 months.
CRYPTOSPORIDIOSIS: Treatment

- In immunocompetent patients:
  - Disease is self-limiting and no treatment is required.
  - May be necessary to rehydrate small children.
- In immunocompromised patients:
  - Diarrhea is so pronounced rehydration is essential.
  - No uniformly effective therapy.

WHIPWORM (TRICHURIS TRICHIURA)

- Adult whipworm is 30-50mm in length.
  - First two-thirds are thin.
  - Last third is bulbous.
WHIPWORM (TRICHURIS TRICHIURA)

- Female worm can produce 3000-10,000 eggs per day.
- Infects about 1 billion people worldwide and is most common in:
  - Areas where indiscriminate defecation occurs.
  - Warm and humid environments.
    - Infection rate in tropical environments is up to 80%.
    - Affects people in rural areas of southeastern US.
- Adult worm can live for eight years.

WHIPWORM INFECTION:
Pathogenesis

- Adult worms live with anterior end attached to the host colonic mucosa.
  - While attached female releases eggs.
  - Eggs are passed out of the body, with feces, and deposited in soil.
  - In this stage, eggs are immature not infective.
    - They must incubate in the soil for 10 days to become infectious.

- Infectious eggs are picked up on hands.
  - Passed into the mouth and swallowed
  - Move into the duodenum
  - Larvae mature for about one month.
  - Migrate to the cecum
WHIPWORM INFECTION: Pathogenesis

- Attachment of adult worms produces hemorrhaging and localized ulcerations.
  - Lesions can be used as portals of entry for bacterial infections.
  - Concomitant bacteremias can often be seen.
- Light infections are usually asymptomatic.
- Moderate worm loads damage the intestinal mucosa.
  - Accompanied by nausea, diarrhea, and abdominal pain
- Some children have worm loads as high as 800.
  - Significant mucosal damage, blood loss, and anemia
  - Strain to defecate can cause prolapse of the colonic or rectal mucosa.

WHIPWORM INFECTION: Treatment

- No need for treatment of asymptomatic infections.
- Mebendazole is the treatment of choice for more severe disease.
  - Cure rate is 60-70% with 90% of the worms being expelled.
  - Even though the patient becomes asymptomatic worms may still be present.
- Prevention involves good sanitation.
HOOKWORMS

- Two species of hookworm infect humans:
  - *Necator americanus*
  - *Ancylostoma duodenale*

- Adult worms are:
  - About 10 mm long.
  - Pinkish in color.
  - Hook-like in appearance.
  - Found worldwide.

- Transmission is through deposition of eggs into shady, well-drained soil.
- Infection can be significant in densely populated communities.
- *Necator americanus* is found in:
  - Southern Asia, Africa, and the Americas.
- *Ancylostoma duodenale* is found in:
  - Mediterranean, Middle East, northern India, China, and Japan.

HOOKWORM INFECTION: Pathogenesis

- *Ancylostoma duodenale* uses four sharp tooth-like structures.
HOOKWORM INFECTION: Pathogenesis

- *Necator americanus* uses dorsal and ventral cutting plates for attachment.
- Fertilized females release 10,000-20,000 eggs per day.
  - Passed in feces
- Eggs are passed in a four-cell or eight-cell stage.
  - On reaching soil, they hatch within 48 hours.
  - Larvae feed on soil bacteria.
  - Double in size and molt
  - Become infectious
- Infectious larvae can survive for 4-6 weeks in soil.

- On contact with human skin:
  - Larvae penetrate the epidermis and move into the blood and lymph.
  - Move to the heart and eventually the lungs.
  - Rupture in the alveolar spaces and are coughed up and swallowed.
  - Move into the small intestine and mature into adult worms.

- As worms migrate in the intestine, they leave behind bleeding points.
  - Worms can live up to 14 years.
  - Blood loss can be enormous.
  - Vast majority of patients have a small worm load and are asymptomatic.
  - Symptomatic cases can have:
    - Rash and swelling for several days where worm enters.
    - Pulmonary problems – infrequent and less severe.
    - Abdominal pain and abnormal peristalsis.
HOOKWORM INFECTION:
Pathogenesis

- Major clinical manifestation is blood loss and concomitant anemia.
  - Depends on worm load and patient’s dietary iron intake
  - Development of severe anemia can take months or even years.
- Other problems can develop earlier in children.
  - Heart failure
  - Retardation of mental and physical development

HOOKWORM INFECTION:
Treatment

- Anemia is the primary consideration and must be corrected.
- The three most widely used anti-helminthic drugs are:
  - Pyrantel pamoate
  - Mebendazole
  - Albendazole
- All are highly effective.
- Prevention is tied to proper sanitation.