

# Gastrointestinal Infections

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# Introduction

- Acute gastrointestinal illnesses rank second only to acute upper respiratory illnesses as the most common diseases worldwide
- The incidence of diarrhea for all children under 5 years is estimated to be 2.9 episodes per child per year
- Younger children also have a higher risk of death from acute dehydrating diarrhea, and diarrheal disease

## Cont....

- **Gastroenteritis** is an illness characterized by diarrhea which may be accompanied by nausea, vomiting, fever, and abdominal pain.
- **Diarrhea** is usually defined as a decrease in consistency of bowel movements (i.e., unformed stool) and an increase of stools to  $\geq 3$  per day.
- For best diagnosis and management, it is important to distinguish *secretory diarrhea* that produces watery diarrhea from **inflammatory diarrhea**.
- *inflammatory diarrhea* caused by invasive pathogens, often presents as fever, tenesmus, or bloody stool.

## Watery vs. Inflammatory diarrhea

	Watery	Inflammatory
Percentage of patients	90	5–10
<b>Stools</b>		
Appearance	Watery	Bloody
Volume	Increased: ++/+++	Increased: +/++
Number per day	<10	>10
pH	5.0–7.5	6.0–7.5
Occult blood	Negative	Positive
Fecal PMN cells	Absent or few	Many

## Watery vs. Inflammatory.....

	Watery	Inflammatory
<b>Mechanisms</b>	Production of toxins	Mucosal invasion
<b>Complications</b>		
Dehydration	Could be severe	Mild
Others	Acidosis, shock, electrolyte imbalance	Tenesmus, rectal prolapse, seizures

Watery	Inflammatory
<b>Etiology</b> <i>Vibrio cholerae</i>	<i>Shigella</i>
Enterotoxigenic <i>Escherichia coli</i> (ETEC)	<i>Salmonella</i>
Enteropathogenic <i>E. coli</i> (EPEC)	<i>Campylobacter</i>
Rotaviruses	<i>Yersinia</i>
Noroviruses	Enterohemorrhagic <i>E. coli</i> (EHEC)
	Enteroinvasive <i>E. coli</i> (EIEC)
	Enteraggregative <i>E. coli</i> (EAEC)
	<i>Cytotoxigenic C. difficile</i>

# Bacillary Dysentery (Shigellosis)

- The shigellae are **gram-negative** bacilli belonging to the family Enterobacteriaceae.
- usually affects children **6 months to 10 yrs** of age.
- more common in **daycare centers** and in areas with **crowded** living conditions or poor sanitation
- transmitted through the **fecal–oral route**
- the bacteria multiply and spread within the submucosa of the small bowel

# Pathogenesis

- Infection with *Shigella* occurs after ingestion of as few as 10 to 100 organisms
- *Shigella* strains invade intestinal epithelial cells, with subsequent multiplication, inflammation, and destruction.
- This organism only rarely invades the bloodstream;
  - But, bacteremia may occur in malnourished children and in immunocompromised patient



# Clinical presentation and Diagnosis

- Early—high fever, watery diarrhea without blood
- Later— colitis develops with urgency, tenesmus, and dysentery, low-grade fever, vomiting
- Complication
  - proctitis (infant and young children)
  - intestinal obstruction
  - colonic perforation
  - bacteremia
  - metabolic disturbance
- Diagnosis
  - Stool examination (show leukocytosis, RBC)

# Treatment

- Infection with shigella is generally self-limited but **antibiotic** therapy is indicated to **shorten duration** of illness and to reduces the **risk of transmission**
- **First-line drug:** is ciprofloxacin
- **Children :** Ceftriaxone/Azithromycin
- **Duration of treatment:** five days

# Salmonellosis

- Salmonella enterica are **gram-negative** bacilli belonging to the family Enterobacteriaceae
- Nontyphoidal Salmonella (NTS) are important causes of food-borne infection.
- Risk factors for salmonellosis include
  - extremes of age
  - alteration of endogenous GI flora due to ab use
  - acid suppressive therapy
  - diabetes , malignancy, HIV
  - immune suppressive therapy

# Pathogenesis

- The inoculum necessary for clinical illness is estimated to be  **$10^6$  organisms**
- Once ingested and successfully beyond host defense mechanisms organisms can attach and invade the **distal ileum** and **proximal colon**.
- Gastroenteritis often is characterized by massive neutrophil infiltration followed by lymphocytes and macrophages

## Cont....

- Release of toxic substances by neutrophils may contribute to inflammation and result in:
  - tissue damage,
  - fluid secretion, or
  - leakage across the intestinal mucosa

# Clinical presentation

- Most patients experience symptoms within 48 hours of ingestion of contaminated food or water.
- Patients often complain of nausea and vomiting followed by abdominal cramps, headache, fever, and diarrhea
- bacteremia is the most common complication of gastroenteritis.
- High-risk patients include
  - Infants,
  - Elderly, and
  - Patients with immunosuppression

# Treatment

- Salmonella gastroenteritis is usually self-limited,
  - fluid and electrolyte replacement is the primary mode of treatment
  - most patients respond well to ORT
- Antibiotic therapy
  - used in high-risk patients
    - neonates or infants
    - persons older than age 50 years
    - immunodeficiency
  - Ciprofloxacin for 5–7 days is recommended.
  - Alternatives: azithromycin, Cotrimoxazole

# Campylobacteriosis

- *Campylobacter jejuni* is the most commonly identified cause of bacterial diarrhea worldwide.
- is primarily a pediatric disease
- Risk factors
  - contaminated foods of animal origin
  - unpasteurized milk
  - contaminated water
  - contact with farm animals and pets
  - use of antimicrobial therapy
  - foreign travel
  - poor sanitation



# Pathophysiology

- *Campylobacter spp.* are *gram-negative bacilli*
- are sensitive to **stomach acidity**; as a result, diseases or medications that buffer gastric acidity may increase the risk of infection
- after an incubation period, infection is established in the jejunum, ileum, colon, and rectum

# Clinical presentation

- Incubation period of 1 to 7 days.
- fever, headache, and myalgias is followed by crampy abdominal pain, and several bowel movements
- **Abdominal pain** is more prevalent in Campylobacter infection than shigella/salmonella
- Tenesmus occurs in approximately 25% of patients.
- Diagnosis of Campylobacter is established by stool culture.

# Treatment

- Fluid replacement is the cornerstone of therapy
- Antibiotic therapy should be considered in patients with
  - high fevers, bloody stools, symptoms lasting longer than 1 week, pregnancy,
  - Immunocompromising conditions
- First line: Macrolides
- Alternative: fluoroquinolone
- N:B antimotility agents should be avoided
  - Prolong the duration of symptoms and associated with worse outcomes

# Escherichia Coli

- Diarrheagenic E. coli is differentiated into several distinct categories based on pathogenic features of diarrheal disease:
  - Enterotoxigenic E. coli (**ETEC**)
  - Enteropathogenic E. coli (**EPEC**)
  - Enteroinvasive E. coli (**EIEC**)
  - Enteroaggregative E. coli (**EAEC**)
  - Enterohemorrhagic E. coli (**EHEC**)

## Cont....

- The most common diarrheagenic *E. coli* infection is caused by **ETEC** manifested by **watery** (enterotoxigenic) diarrhea.
- **Dysentery** is caused by **EHEC**.
- Infections with **EIEC** and **EPEC** are primarily a disease of **children** in developing countries.
- **EAEC** strains are implicated in persistent diarrhea ( $\geq 14$  days) in HIV-infected patients.

# Pathogenesis

- **Enterotoxigenic *E. coli*** are capable of producing enterotoxins
- luminal accumulation of electrolytes that draws water into the intestine, and production of a cholera-like secretory diarrhea
- **EHEC** is able to produce shiga-like toxins
- the cytotoxic effect of shiga-like toxins disrupts the mucosal integrity of the large intestine, causing diarrhea

# Clinical presentation

- **ETEC:**
  - watery stools, nausea and abdominal cramp
  - abrupt in onset and resolves within 24 to 48 hours without complication
- **EHEC:**
  - as many as 12 bloody stools per day
  - cramping abdominal pain, abdominal distension
  - nausea occurs in about two-thirds of patients, and vomiting occurs in less than half.
  - the white blood cell count is elevated and accompanied by a left shift

## Cont....

- **EPEC**
  - Acute onset of profuse watery diarrhea, vomiting, and low-grade fever.
- **EAEC**
  - Persistent, watery, mucoid, secretory diarrhea with low-grade fever
- **EIEC**
  - Presents most commonly as watery diarrhea



# Treatment

- Prevent dehydration by correcting fluid and electrolyte imbalances.
- **ETEC:** antibiotics are rarely needed except in severe cases. Recommended antibiotics include TMP-SMX and quinolones
- **EHEC:** the only recommended treatment is supportive, including fluid and electrolyte replacement
  - antibiotics are CI because they can induce the expression and release of toxin.
  - antimotility agents should be avoided because they delay clearance of the pathogen and toxin,

# Cholera (*Vibrio Cholerae*)

- is caused by the bacterium *vibrio cholerae* that leads to a massive loss of fluid loss
  - results in life-threatening dehydration
- cholera can be transmitted by contaminated water or food
- A relatively large inoculum of  $10^3$  to  $10^6$  organisms is required for infection if water is the vehicle, and  $10^2$  to  $10^4$  if the vehicle is food.

# Pathophysiology

- vibrios cholerae is a **gram-negative** bacillus
- pathology of cholera results from an **enterotoxin (cholera toxin)** produced by the bacteria
- vibrios pass through the stomach to colonize the upper small intestine.
  - They possess filamentous protein extensions that attach to receptors on the intestinal mucosa, and
  - their motility assists with penetration of the mucus layer

## Cont....

- The enterotoxin causes an increase in cyclic adenosine monophosphate (cAMP), and results in inhibition of sodium and chloride absorption by microvilli
- The net effect of the cholera toxin is isotonic fluid secretion by SI that exceeds the absorptive capacity of duodenum
- This results in the production of watery diarrhea with electrolyte concentrations similar to that of plasma.

# Clinical presentation




- **Diarrhea:**
  - patients may lose up to **1 L** of isotonic fluid every hour
  - the onset of diarrhea is abrupt
  - is followed rapidly or sometimes preceded by **vomiting**
- **Fever:** < 5% of patients
- Abdominal distension and ileus
- Laboratory abnormalities: increased RBC volume and total protein, magnesium, and calcium levels

# Complication

- Hypoglycemia
- Seizures
- Fever
- Mental alterations
- Metabolic acidosis
- Prerenal azotemia
- Aspiration pneumonia

# Treatment

- **Goals of therapy**

-  rapid restoration of fluid losses,
-  correction of metabolic acidosis, and
-  replacement of potassium deficiency

- **Rehydration**

 Mild cases:

- ORS; for children: < 2yrs: 50 – 100ml; 2-10yrs: 100 – 200ml after each loose stool.

 For severe cases: **Ringer lactate/NS** 50-100ml/min until shock is reversed;

## Cont....

- Antibiotics are not necessary in most cholera cases
- However, in **severe cases**, antibiotics shorten the duration of diarrhea, decrease fluid loss, and shorten the duration of the carrier state.
- A single dose of
  - **Doxycycline**
  - **Ciprofloxacin**
  - Erythromycin/azithromycin
  - Cotrimoxazole



# Prevention

- ensuring a safe water supply
- safe food preparation,
- improving sanitation, and
- patient education
- Vaccination
  - In high-risk groups, such as children and patients infected with HIV, in countries where the disease is endemic.

# Clostridium difficile infection

- C. difficile is the primary cause of hospital-acquired infectious diarrhea in hospitalized patients, including children
- Common risk factors include
  - increasing age, severe underlying illness, ICU admission, gastric acid suppression, exposure to broad spectrum antimicrobials
  - Clindamycin, cephalosporins, quinolones and penicillins are the antibiotics most commonly associated with Clostridium difficile-associated diarrhea (CDAD)

# Pathophysiology

- C. difficile, a **gram-positive**, spore-forming anaerobe, is spread by the fecal–oral route,
- the organism is ingested either as the vegetative form or spores, which can survive for long periods
- once the GI tract is colonized with spores, disruption of the gut flora, which occurs with antibiotic therapy, allows C. difficile to proliferate.
- toxin production is responsible for the inflammation, fluid and mucus secretion and mucosal damage

# Clinical presentation

- Symptoms can start as first day of antibiotic therapy or several weeks after antibiotic therapy is completed
- **Colitis**
  - profuse, watery diarrhea, abdominal pain, abdominal distention, nausea, and anorexia
  - left or right lower quadrant abdominal pain
- **toxic megacolon:** suggested by acute dilation of the colon to a diameter greater than 6 cm
- **fulminant colitis:** Acute abdomen and systemic symptoms such as fever, tachycardia, dehydration, and hypotension

# Treatment

- Patients who develop CDI while receiving an antibiotic should have the antibiotic discontinued, if possible or switch to an agent with a lower risk of CDI.
- **First line: mild- moderate disease**
- Metronidazole (500 mg orally TID 7–14 days; or, 30 mg/kg/day divided q 6 hr for children)
- **Severe disease** (WBC greater than 15,000 cells/mm<sup>3</sup>)
- oral vancomycin (125 mg qid for 7-14 days or, 40-50 mg/kg/day divided q 6hr for children)
- use of antimotility agents should be avoided since they may precipitate toxic megacolon.

# Viral gastroenteritis

- Viruses are the most common cause of diarrheal illness in the world
- Many viruses may cause gastroenteritis, including rotaviruses, noroviruses, astroviruses, enteric adenoviruses, and coronaviruses

## Agents Responsible for Acute Viral Gastroenteritis and Diarrhea

Virus	Peak age	Transmission	Symptoms
Rotavirus	6month -2 years	Fecal–oral, water, food	Diarrhea, vomiting, fever, abdominal pain
Adenovirus	<2 years	Fecal–oral	Diarrhea, respiratory symptoms, vomiting, fever
Astrovirus	< 7 years	Fecal–oral, water	Vomiting, diarrhea, fever, abdominal pain
Noroviruses	> 5 years	Fecal–oral, food	Nausea, vomiting, diarrhea, abdominal cramps, headache, fever, chills, myalgia

# Cont...

- **Rotavirus**
- is a double-stranded, RNA virus accounts for the most common cause of infectious diarrhea in children
- The cornerstone of rotavirus treatment is supportive care and rehydration with ORT or IV fluids.
  - IV hydration in case of shock, severe emesis, and high stool output ( $>10$  mL/kg/hr).
- antimotility agents should be avoided
- zinc supplementation: shorten the duration and frequency of diarrhea
  - Dose:  $\leq 6$  month 10mg/d for 10 days  
 $> 6$  month 20mg/d for 10 days



# Prevention

- Promotion of exclusive breast-feeding (prevent through promotion of passive immunity)
- Improved complementary feeding practices
  - malnutrition is an independent risk for the frequency and severity of diarrheal illness
- Improved water and sanitary facilities
- Promotion of personal and domestic hygiene
- Rotavirus immunization

THANK YOU