Enteric Infections- Infectious Diarrhea

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Learning objectives

- Identify common causes of infectious diarrhea in adults in developed countries
- Describe patient history and clinical presentation distinguishing viral vs. bacterial causes
- Recognize warning signs for severe diarrheal disease
- Describe management approach and treatment

Overview — Global burden

- Infectious diarrhea: top 10 cause of death worldwide (Troeger et al., 2018)
- 1.7 billion cases annually
- Leading cause of death in children under 5 years (Liu et al., 2016)
- In adults in resource-rich settings: often “nuisance disease” with key clinical decision points

Definitions and duration

Diarrhea

- Passage of loose or watery stools
- ≥3 times in 24 hours
- Abnormal stool frequency or consistency

Duration Categories

- Acute: <14 days
- Persistent: 14-30 days
- Chronic: >30 days

Dysentery: diarrhea with visible blood, associated with fever and abdominal pain

These definitions are important clinically. Acute diarrhea typically has different etiologies and investigations than chronic diarrhea. Dysentery—bloody diarrhea—has a more restricted differential diagnosis and often indicates invasion of the colonic mucosa. Duration

Pathophysiology of diarrhea

Normal intestinal physiology

- GI tract absorbs 8-9 L fluid daily
- Net secretion only 100-200 mL/day
- Pathogen virulence factors disrupt this balance

Three mechanisms of pathogen damage

- Altered ion absorption/secretion
- Disruption of epithelial barrier
- Villus atrophy and enzyme deficiency

Understanding pathophysiology helps predict clinical presentation. Pathogens that cause secretory toxins lead to watery diarrhea because they increase intracellular cyclic nucleotides, driving electrolyte secretion. Pathogens that invade the mucosa cause inflammatory diarrhea

Small bowel vs. large bowel diarrhea

Small Bowel Pattern

- Large volume stools (>200 mL/stool)
- Watery consistency
- Cramping periumbilical pain - 4-8 stools daily

Associated Symptoms: Nausea/vomiting common, weight loss possible

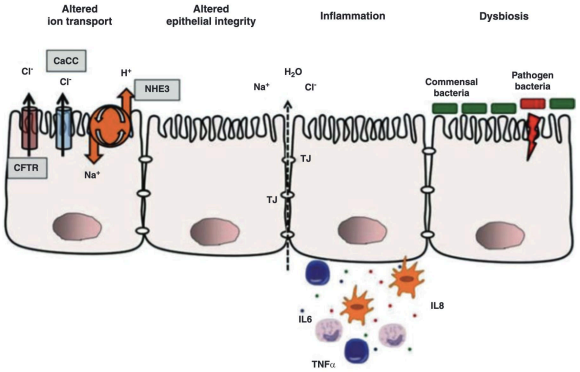
Large Bowel Pattern

- Small volume stools (<200 mL/stool)
- Frequent passage (>5-6/day)
- Painful tenesmus and urgency
- Bloody or mucoid stools

Associated Symptoms - Abdominal cramping/pain -sytemic symptoms less common

The pattern of diarrhea itself tells you about the location of infection and helps narrow the differential. Small bowel pathogens like norovirus or cholera produce large-volume watery stools because they affect water and electrolyte balance across a larger absorptive surface. Large

Overview of infectious etiologies



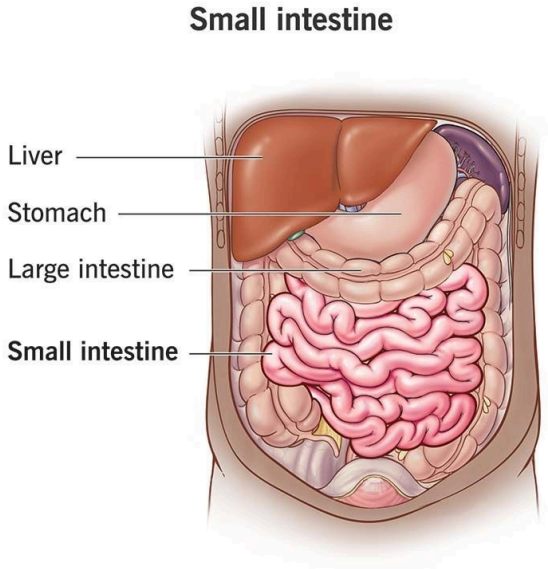
- **Most diarrhea is viral**: stool cultures positive only 1.5-5.6%
- **Viral**: norovirus (most common), rotavirus, adenoviruses 40/41, astrovirus
- **Bacterial**: Salmonella, Campylobacter, Shigella, ETEC, EHEC/STEC
- **Parasitic**: Cryptosporidium, Giardia, Cyclospora, Entamoeba

Most diarrhea is viral and self-limited. Stool cultures are positive in less than 6% of cases of acute diarrhea, which means routine culture for every patient with diarrhea is impractical. We should be selective about testing. The major bacterial pathogens vary by geography and risk factors. In developing countries, bacterial and parasitic pathogens are more common. In developed countries, we see more norovirus

Norovirus — “The winter vomiting virus”

Key Features

- Most common cause of acute gastroenteritis worldwide (Ahmed et al., 2014)
- Affects all ages, including highly immune populations
- Mean incubation: 24-48 hours - “Winter vomiting disease” (Northern hemisphere)



Norovirus is the leading cause of foodborne disease outbreaks in Eruope and the United States. It’s notable for its ability to cause outbreaks in closed environments—schools, cruise ships, hospitals. Unlike rotavirus, which is primarily a childhood pathogen, norovirus affects older adults and immunocompetent individuals equally. The seasonal pattern varies by geography; in temperate climates, it peaks in winter,but

Norovirus epidemiology & transmission

Viral Characteristics

- Non-enveloped RNA virus, Caliciviridae family - Multiple genotypes; no lasting immunity after infection (Patel et al., 2008)
- Extremely stable: resists alcohol, chlorine, temperatures to 60°C

Transmission Routes

- Primarily fecal-oral >aerosol transmission documented
- Fomite transmission (contaminated surfaces)- Can survive environmental conditions for weeks

Norovirus's resistance to environmental conditions and disinfectants makes outbreak control challenging. Standard hand sanitizers with alcohol are ineffective; handwashing with soap and water is required. The lack of long-lasting immunity means people can be reinfected

Norovirus clinical manifestations

Symptoms

- Acute onset vomiting (prominent feature)
- Watery non-bloody diarrhea (4-8 stools/24 hours)
- Fever in 50% of cases
- Malaise and headache

Clinical Course

Duration typically 48-72 hours

Complete resolution expected

Dehydration is main complication

Secondary bacterial infection rare

Diagnosis & Management: Clinical diagnosis in outbreak setting - EIA or PCR for confirmation (primarily epidemiologic)

Treatment: supportive care and oral rehydration solution

Norovirus typically causes a self-limited illness, and the focus of management is prevention of dehydration. Unlike bacterial gastroenteritis, antibiotic therapy is ineffective and unnecessary. The combination of vomiting and diarrhea can lead to rapid fluid losses, particularly in the

Norovirus in immunocompromised patients

Unique Clinical Course

- Chronic infection: shedding for months to years
- Viral evolution occurs during infection
- Severe, refractory symptoms possible
- May lead to malnutrition and functional decline

Treatment Challenges

- No specific antiviral therapy proven effective
- Supportive care remains cornerstone
- Probiotic therapy: insufficient evidence
- Management: supportive nutrition, hydration

Immunocompromised patients, particularly those with severe T-cell defects (advanced HIV, post-transplant), can develop chronic norovirus

Norovirus outbreak management

Prevention Measures

- Hand hygiene with soap and water (alcohol ineffective)
- Environmental cleaning with chlorine-based disinfectants (0.5-1% bleach)
- Surface decontamination: quaternary ammonium compounds
- Isolation precautions for symptomatic patients

Outbreak Control

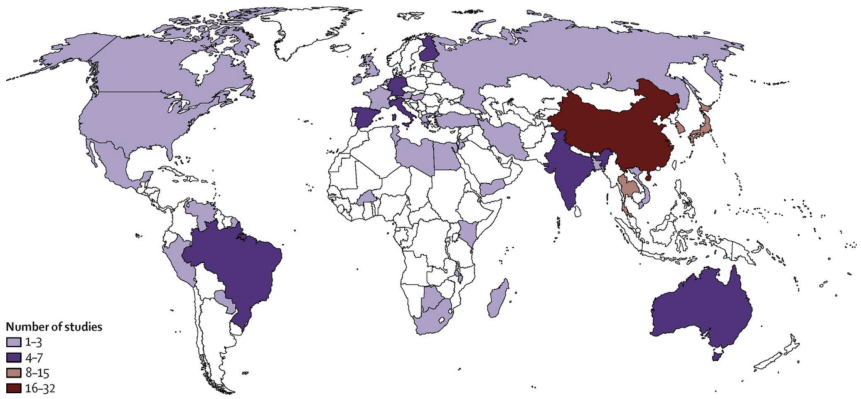
- Early detection and reporting to public health
- Exclusion of food handlers until 48 hours symptom-free
- Restriction of admitted patients in healthcare settings

Norovirus outbreak management requires understanding of the virus's stability and transmission. Simply using hand sanitizer won't prevent transmission—patients must wash with soap and water to mechanically remove virus. Environmental cleaning is critical; bleach solutions are

Rotavirus overview

Epidemiology

- Most common cause of severe diarrhea in children worldwide (Parashar et al., 2006) - >100 million cases annually
- Approximately 150,000 deaths in children <5 years (Tate et al., 2016)
- Peak incidence: 6-24 months age

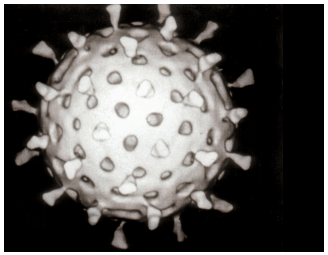


Clinical Course

- Duration 3-8 days , often more severe than norovirus
- Dehydration: primary complication

Before rotavirus vaccines, rotavirus was the leading cause of severe diarrhea in children globally. It caused significant morbidity and mortality, particularly in developing countries. The introduction of rotavirus vaccines (RotaTeq and Rotarix) has dramatically changed the

Rotavirus pathophysiology



Viral Characteristics

- 70 nm non-enveloped RNA virus (Reoviridae family)
- Segmented genome with multiple genes encoding virulence factors

Mechanisms of Diarrhea - Villus shortening and disruption - Brush-border enzyme deficiency (lactase, sucrase) - Calcium-dependent enterotoxin production (NSP4) - Impaired water and ion absorption

Rotavirus's pathophysiology is complex and explains some clinical features. The villus disruption impairs absorption and leads to nutritional losses. The enterotoxin activates fluid secretion, contributing to large stool volumes. The brush-border enzyme deficiency explains why secondary lactose intolerance is common—the damaged epithelium cannot produce lactase, so milk products worsen diarrhea temporarily.

Rotavirus vaccines

Available Vaccines

RotaTeq (Pentavalent) - Manufactured by Merck - 3-dose series - RV1, RV2, RV3, RV4, RV5

Rotarix (Monovalent) - Manufactured by GSK - 2-dose series - RV1 genotype coverage

Impact on Disease:

- Dramatic reduction in hospitalizations (>90%) (Ruiz-Palacios et al., 2006; Vesikari et al., 2006)
- $1.2 billion in healthcare cost savings in US per year
- Significant reduction in mortality globally in vaccinated populations

Both available vaccines are live attenuated oral vaccines given to infants. The vaccines are highly effective at preventing severe disease,

Rotavirus — Key clinical points

Typical presentation

- Watery, non-bloody diarrhea
- Vomiting less prominent than with norovirus
- Respiratory symptoms occasionally present (suggests dual viral infection)

Risk factors for severe disease

- Age <24 months
- Malnutrition
- Lack of prior exposure/vaccination
- Comorbid conditions

Epidemiology

- Common in daycare settings and seasonal: winter months and dry seasons in temperate climates

Other viral pathogens

Virus	Age Group	Key Features
Sapovirus	Children	Similar to norovirus; outbreaks
Astrovirus	Young children	Milder than rotavirus
Adenovirus 40/41	Infants/toddlers	Winter seasonality
Enteroviruses	Variable	Rash sometimes present
Coronaviruses (SARS-CoV-2)	All ages	Mild GI symptoms often with respiratory

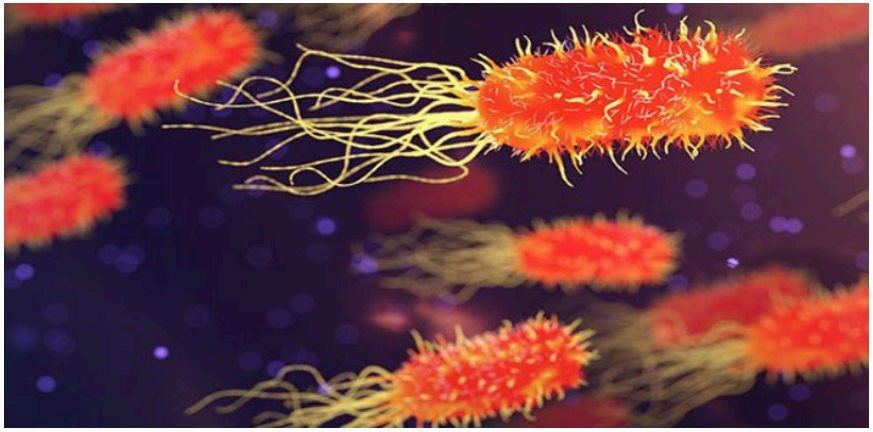
This table summarizes other viral pathogens that cause diarrhea. While less common than norovirus and rotavirus in most settings, these agents still cause significant disease. Sapovirus resembles norovirus clinically and epidemiologically. Astrovirus and Adenovirus 40/41 are primarily pediatric pathogens. Enteroviral infections may have systemic manifestations beyond GI symptoms. The COVID-19 pandemic has

Bacterial etiologies

Enterotoxigenic E. coli (ETEC) overview

Epidemiology & Pathogenesis

- Leading cause of acute diarrhea in developing countries (Qadri et al., 2005)
- Survives in water; transmitted via contaminated food/water
- Produces enterotoxins: heat-labile (LT) and heat-stable (ST) toxins



Clinical Presentation

- Watery diarrhea, often dehydrating
- Nausea common; vomiting less frequent
- Fever absent or mild
- Duration typically 3-5 days

Understanding the toxin-mediated mechanism explains the large-volume watery stools—these are secretory diarrhea similar to cholera.

ETEC Toxins and mechanisms

Heat-Labile Toxin (LT)

- Similar to cholera toxin
- Activates adenylate cyclase
- Increases cAMP
- Stimulates secretion

Heat-Stable Toxin (ST)

- Smaller molecular weight
- Activates guanylate cyclase
- Increases cGMP
- More tissue-specific

Result: Increased intestinal cyclic nucleotides → electrolyte and water secretion → watery diarrhea

The toxin-mediated secretory mechanism explains the clinical and pathophysiologic features of ETEC infection. Both toxins work through G-protein coupled signaling but use different second messengers. The LT toxin's similarity to cholera toxin means the diarrhea can be severe and dehydrating. **Importantly, the epithelial barrier remains intact in toxin-mediated disease—there's no blood in stool and no**

Other Pathogenic *E. coli* Strains

EPEC (Enteropathogenic E. coli)

- Primarily affects children <6 months
- Contains Eae gene encoding adhesin
- Causes attaching and effacing lesions - **Non-bloody watery diarrhea**

EIEC (Enteroinvasive E. coli)

- Invasive mechanism similar to *Shigella*
- **Bloody diarrhea with systemic symptom**s - Fever and abdominal pain common

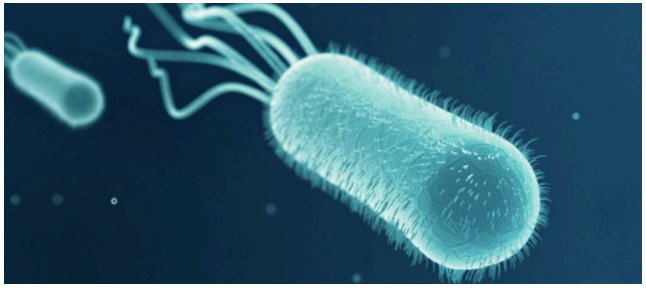
EAEC (Enteroaggregative E. coli)

- Biofilm formation on epithelium- causes persistent or chronic **non-bloody** diarrhea (>14 days)
- Often associated with travel to developing countries

EHEC/STEC overview

Clinical Significance

- Shiga toxin-producing E. coli (STEC) strains
- *E. coli* O157:H7 most common in North America (Karch et al., 2005)
- Multiple non-motile serotypes cause disease
- Shiga toxin causes microangiopathic hemolytic damage (Tarr et al., 2005)



STEC infections are notably important because of the potential for life-threatening complications, particularly **hemolytic uremic syndrome**. While the initial presentation is typically bloody diarrhea, the systemic complications distinguish this from other bacterial diarrheal pathogens. The Shiga toxins (Stx1 and Stx2) are AB toxins that inhibit protein synthesis in endothelial cells, leading to thrombotic

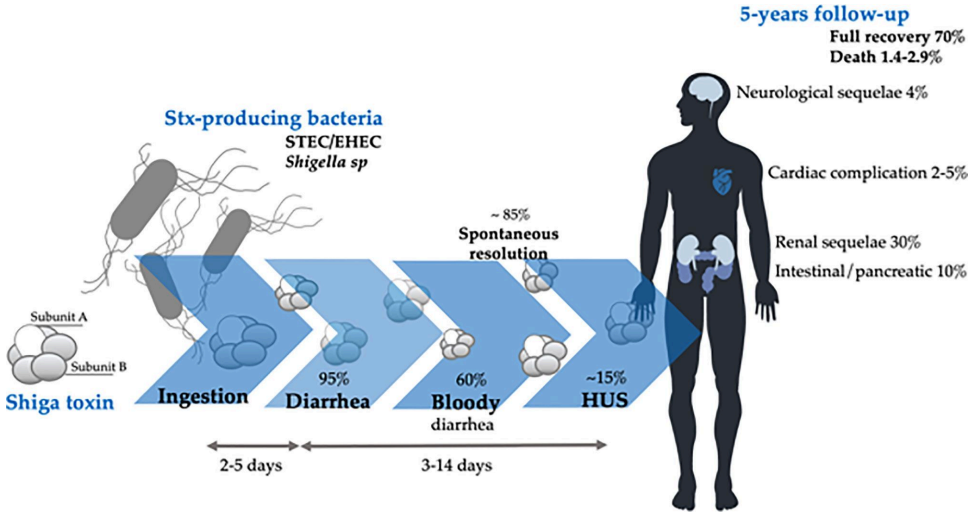
Hemolytic Uremic Syndrome (HUS)

STEC-Associated HUS

- Occurs in approximately 5-15% of STEC infections
- Often follows 3-5 days of hemorrhagic diarrhea
- Triad**:** microangiopathic hemolytic anemia (schistocytes on blood smear), thrombocytopenia, acute kidney injury

Prognosis and Sequelae

- 5-year outcomes: ~70% complete recovery Mortality: 1.4-2.9%
- Chronic sequelae: renal dysfunction (8-50%), neurological (5-25%), cardiac (5%)



The pathophysiology involves Shiga toxin-mediated endothelial injury, leading to platelet activation, fibrin deposition, and mechanical hemolysis (schistocytes on blood smear). Children under 5 have

HUS management

Critical Principle: Avoid Antibiotics !!!

- Antibiotic use associated with 25% increase in HUS risk
- Proposed mechanism: bacterial lysis releases Shiga toxin
- Even fluoroquinolones and azithromycin increase risk
- Avoid antimotility agents

HUS Management

Renal replacement therapy: essential in ~50% of cases

Blood product support: transfusions for anemia, platelets carefully

Plasma exchange: controversial but may help neurologic complications

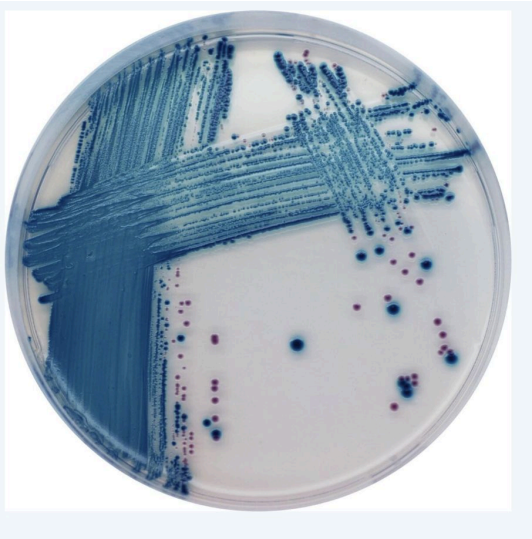
ICU-level supportive care often required

The association between antibiotics and HUS progression is one of the most clinically important “don’ts” in infectious diseases. Multiple studies have demonstrated this increased risk. The mechanism likely involves stimulating toxin release during bacterial lysis. This creates a

EHEC Detection Methods

Diagnostic Approaches

- Sorbitol MacConkey agar: STEC O157:H7 appears non-sorbitol fermenting (colorless)
- Chromogenic agar: substrate produces color with specific enzymes
- EIA for Shiga toxins: rapid detection from stool
- PCR for Stx genes: confirmatory molecular testing

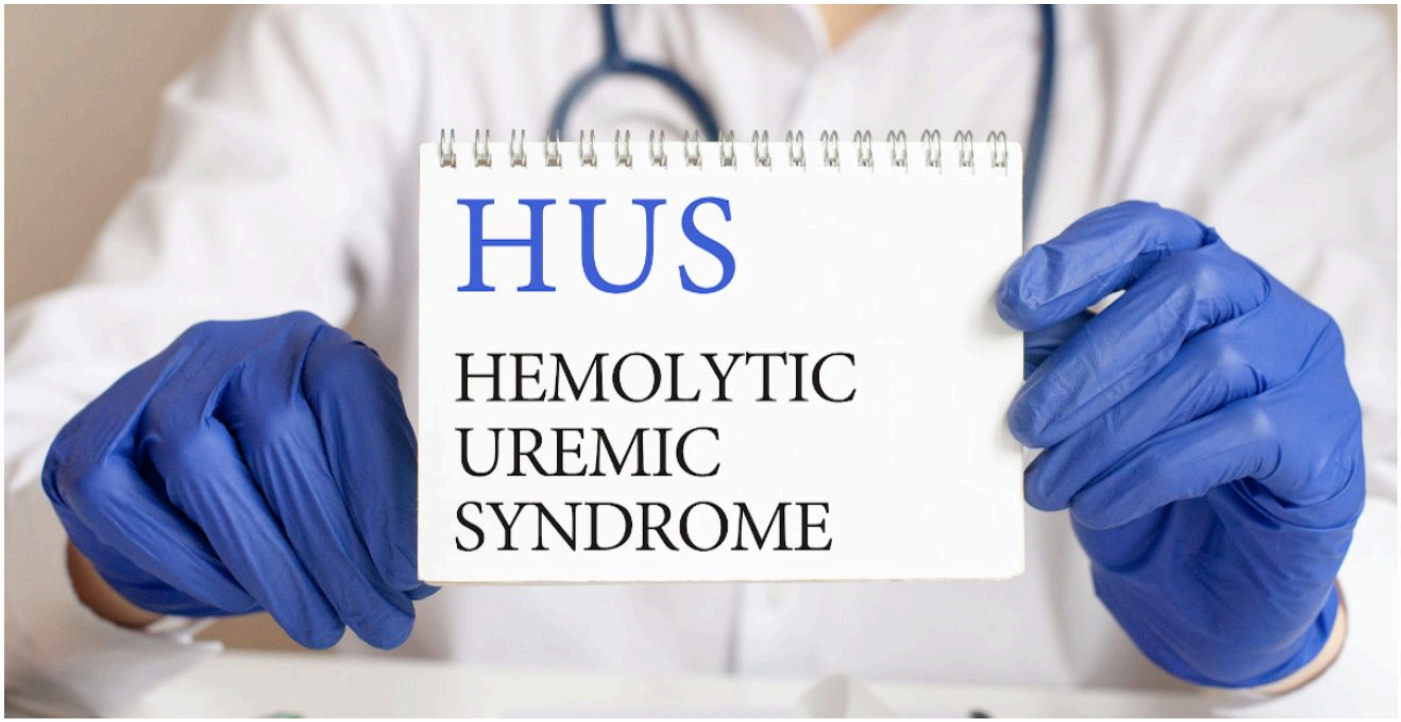


Chromogenic agar: STEC strains grow as mauve colonies, while other bacteria grow as blue, colorless, or are inhibited

Routine culture on standard media will miss many STEC strains. Sorbitol MacConkey agar is the classic selective medium for O157:H7 detection; the characteristic non-sorbitol fermentation creates a visible phenotype. Chromogenic agar media have improved sensitivity and specificity. Direct toxin detection by EIA is rapid and available at many centers. PCR-based testing for Stx genes is increasingly standard and

EHEC Outbreaks — Germany 2011

HUS in Italy?



Italy sees most HUS cases for decades

By Joe Whitworth on March 1, 2023

Italy has reported the highest annual total of Hemolytic Uremic Syndrome (HUS) cases since records began.

From January to December 2022, 91 cases were recorded. This is the most observed in a single year since the start of surveillance in 1988. HUS is a severe

Campylobacter infections

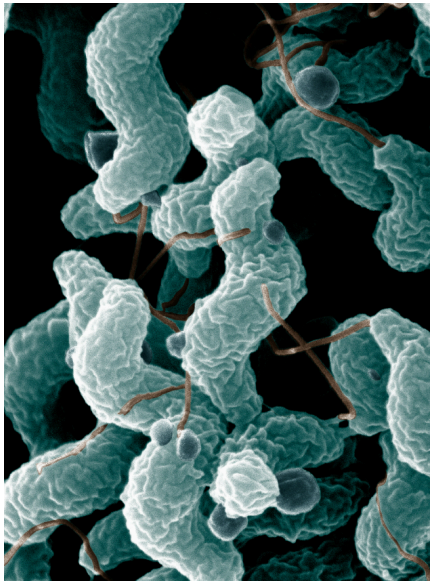
Campylobacter overview

Epidemiology - Most common bacterial cause of gastroenteritis globally (Kaakoush et al., 2015)

- Primarily *Campylobacter jejuni* (90% of infections) - Also: *C. coli*, *C. lari*, and other species

Characteristics

- Gram-negative, microaerophilic curved rod
- Minimal growth on routine culture media
- Fastidious organism; requires special handling



Campylobacter is arguably the leading bacterial cause of diarrhea in developed countries, though because it's less reported than Salmonella and Shigella, its true burden is underappreciated. It's fastidious and easily missed on routine stool culture, requiring selective media and microaerophilic conditions. The curved morphology is characteristic but requires careful observation on microscopy or culture.

Campylobacter transmission

Campylobacter clinical features

Incubation Period

- Mean: 3 days (range 1-7 days) - Longer than many bacterial pathogens

Typical presentation

- Affects both small and large bowel → mixed diarrhea pattern
- Watery AND bloody diarrhea common
- Febrile prodrome in ~1/3 of cases (fever, malaise, myalgias)
- Abdominal pain often prominent and severe

Systemic complications

- Bacteremia in 0.1-1% (higher in immunocompromised)
- Septic arthritis, osteomyelitis, meningitis (rare)
- Post-infectious syndromes (see next slide)

Campylobacter's clinical presentation is diverse. The fever and severe abdominal pain can sometimes lead to concern for appendicitis or other surgical abdomen; one must maintain a high index of suspicion and send stool cultures in appropriate patients. The combination of watery and bloody stool reflects both secretory toxin production and mucosal invasion. The relatively long incubation

Campylobacter complications

Post-infectious complications

Guillain-Barré Syndrome (GBS)

- Estimated 3-40% of GBS cases linked to prior Campylobacter (Nachamkin et al., 1998)
- Mechanism: molecular mimicry
- Antibodies cross-react with GM1 ganglioside
- Ascending paralysis 1-3 weeks after diarrhea

Reactive Arthritis

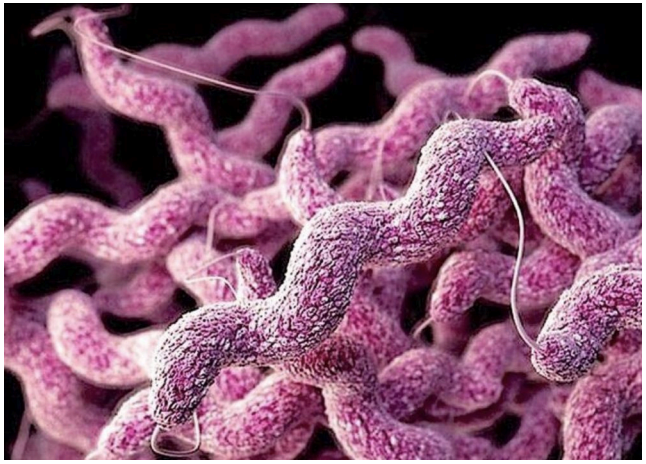
- Occurs in 2.6% of infections
- HLA-B27 association
- Arthralgia/arthritis weeks after diarrhea
- Can be prolonged and disabling

GBS is a post-infectious autoimmune complication that develops after the acute diarrhea has resolved, typically 1-3 weeks later. The molecular mimicry mechanism reflects LPS epitopes on certain *Campylobacter* strains that resemble human nerve tissue. This complication emphasizes that some patients with Campylobacter infection experience significant morbidity beyond the acute gastroenteritis. Reactive

Campylobacter diagnosis

Laboratory Detection

- Stool culture on selective media (Campy agar, CCDA agar) -
- Requires microaerophilic conditions
- Gram-negative, S-shaped or curved rods on microscopy
- Culture takes 48-72 hours minimum



Molecular Methods

- PCR increasingly available at reference labs
- Rapid diagnosis possible
- Higher sensitivity than culture

Salmonella infections

Salmonella overview

Epidemiology

- Motile gram-negative Enterobacterales
- Non-typhoidal: common cause of gastroenteritis (Majowicz et al., 2010)
- Typhoidal (*S. typhi, S. paratyphi*): invasive systemic illness (Crump and Mintz, 2010)

Diversity

- >1,400 serotypes identified
- Two major clinical syndromes: gastroenteritis vs. enteric fever
- Highest incidence globally: South Asia

Salmonella is diverse in both its serotypes and clinical presentations. Understanding whether you're dealing with non-typhoidal gastroenteritis or enteric fever (typhoid) is crucial for prognosis and treatment. Non-typhoidal Salmonella causes self-limited gastroenteritis in most immunocompetent hosts. Typhoidal Salmonella causes invasive systemic infection with distinctive clinical features. The

Non-typhoidal *Salmonella* epidemiology

Serotype distribution - *S. enteritidis*: most common globally

- *S. typhimurium*: second most common
- Both associated with poultry and poultry products
- Transovarial transmission in hens explains egg contamination

Geographic & seasonal patterns

- Incidence highest in South and Southeast Asia
- Seasonal peaks: summer and autumn in temperate climates
- Year-round in tropical regions

The predominance of *S. enteritidis* and *S. typhimurium* reflects the importance of poultry in global food supply. The discovery of transovarial transmission (passage of bacteria through the ovaries to contaminate eggs) was important **because it explained why even properly handled eggs could transmit disease.** The seasonal pattern in temperate climates likely relates to food handling practices and

Non-typhoidal *Salmonella* transmission

Reptile-associated Salmonella is an underappreciated source in developed countries, particularly among children who have pet turtles or iguanas. Public health campaigns have promoted awareness, but reptile ownership continues to result in Salmonella infections. Understanding transmission routes helps guide prevention counseling with patients. The ability to transmit via fomites means that

Non-typhoidal Salmonella clinical features

Incubation Period : 8-72 hours (typically 12-36 hours)

Typical Presentation :

- Diarrhea with abdominal pain and cramping
- Fever in ~50% (often high—>39°C)
- Nausea and vomiting common
- Systemic symptoms: malaise, headache

Risk Factors for Severe Disease

- Extremes of age (<5 or >65 years)
- Achlorhydria or antacid use, Inflammatory bowel disease
- Sickle cell disease, immunosuppression

Prognosis

- Self-limited in immunocompetent hosts, bacteremia in <5% (higher with underlying conditions)
- Duration typically 4-7 days

Most non-typhoidal Salmonella gastroenteritis is indistinguishable from other bacterial causes of diarrhea. The fever, abdominal pain, and watery diarrhea constitute a typical presentation. Risk factors for invasive disease and bacteremia guide clinical decision-making about antimicrobial therapy. Achlorhydria increases risk because stomach acid normally kills some bacteria; patients on acid

Non-typhoidal Salmonella — Asymptomatic Carriage

Chronic Carriers

- Shedding bacteria >1 year after infection
- Prevalence: 0.6-2% of infected individuals
- More common with *S. enteritidis* than other serotypes
- Risk factors: female sex, older age, biliary disease

Clinical Implications

- Potential source for transmission to others - Important for food handlers and healthcare workers
- Prolonged antibiotics (e.g., fluoroquinolone) may clear carriage
- Cholecystectomy eradicates infection in some biliary carriers

Asymptomatic carriage represents an important public health consideration. While most infected people shed for days to weeks, a small proportion become chronic carriers. For food handlers, carriage poses ongoing transmission risk. The association with biliary disease

Enteric/typhoid Fever

Epidemiology : Caused by *Salmonella typhi* (endemic in South Asia, Africa)

- Also *S. paratyphi* (Asia-Pacific region)
- Humans are the only reservoir - ~21 million cases and 200,000 deaths annually globally
- Mortality 1-4% with treatment; 20-30% without

Risk Factors for Acquisition - Travel to endemic areas (South Asia especially)

- Poor sanitation exposure
- Close contact with chronic carriers

Typhoid fever is an invasive systemic infection distinct from non-typhoidal gastroenteritis. It's primarily a disease of developing countries with inadequate sanitation. For travelers to endemic areas, typhoid represents a significant health risk. The clinical syndrome develops

Typhoid fever — Clinical progression

Week 1: Septicemia Phase

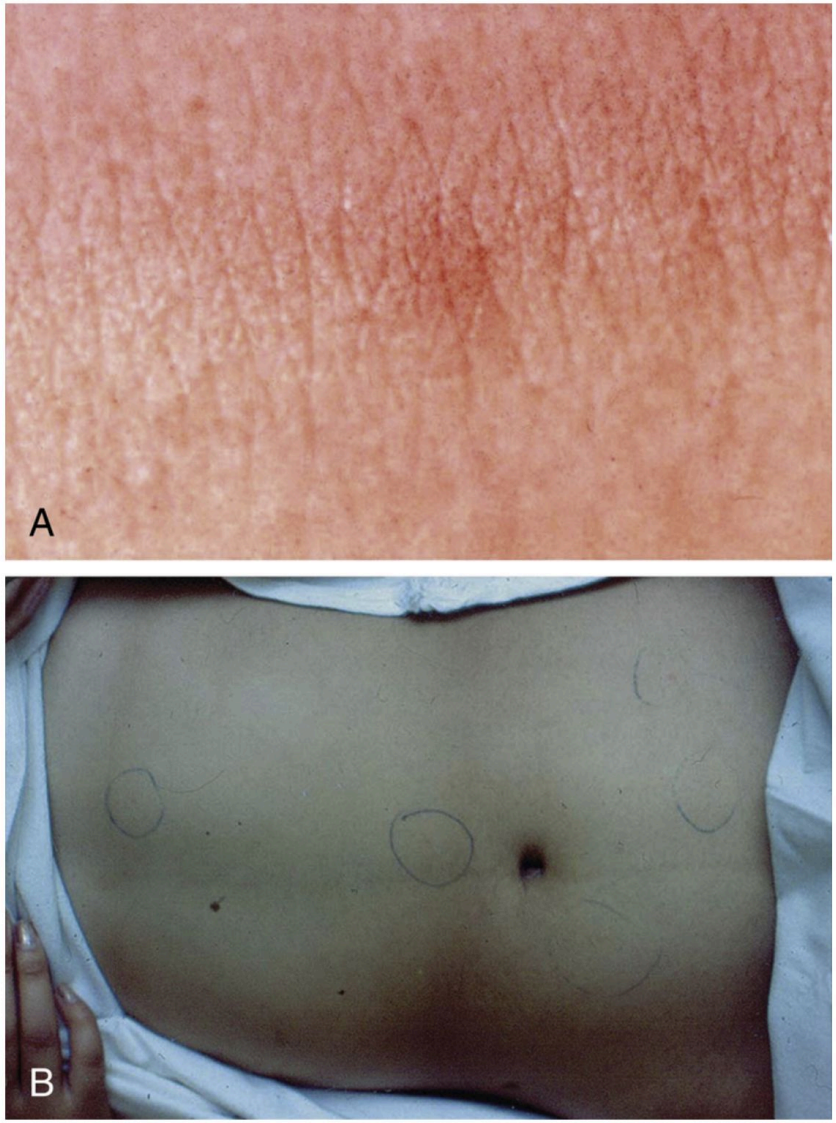
- Gradual fever onset (prodrome over days)
- High fever develops, continuing to rise
- Bacteremia present
- Relative bradycardia (unusual for degree of fever)
- Malaise, headache, myalgias

Week 2-3: Systemic Phase

- Sustained high fever (often continuous pattern—“staircase fever”)
- Rose spots rash (evanescent, 2-3mm rose-colored papules on trunk)
- Hepatosplenomegaly with abdominal pain and distension, diarrhea or constipation

Week 3-4: Crisis Phase

- Risk of intestinal perforation (Peyer’s patches ulcerate)
- Septic shock possible
- Delirium and altered mental status (“typhoid state”)
- Myocarditis, pneumonia



Typhoid fever — Treatment

- **Antimicrobial challenges**
  - Fluoroquinolone resistance increasing in South Asia
  - Multidrug-resistant strains (TMP/SMX, chloramphenicol, ampicillin) common
  - Extensively drug-resistant (XDR) strains emerging
- **Treatment options** - **First-line (susceptible)**: Fluoroquinolone (ciprofloxacin)
  - **Alternatives**: Third-generation cephalosporins (ceftriaxone, cefixime)
  - **Resistant strains**: Azithromycin (5-day course) for nalidixic acid-resistant strains
  - **Duration**: 7-14 days depending on severity and response
- **Prognosis with treatment** - Defervescence typically 4-6 days after starting therapy
  - Relapse possible 1-2 weeks after apparent cure - Follow-up cultures recommended to document clearance

The emergence of XDR typhoid in Pakistan in recent years is concerning and may require cephalosporins as first-line. The delayed response to therapy (4-6 days for fever to resolve) requires clinical judgment about treatment failure versus expected slow response. Relapse in 5-10%

Shigella overview

Microbiology

- Non-motile gram-negative Enterobacterales
- Four serogroups: dysenteriae, flexneri, boydii, sonnei (Kotloff et al., 2018)
- Humans are the only reservoir (crucial difference from Salmonella)

Clinical Significance

- Third most common bacterial cause of diarrhea (after Salmonella and Campylobacter)
- Associated with severe dysentery and complications
- Rapid person-to-person spread in closed environments

Unlike Salmonella with its animal reservoir or Campylobacter with widespread animal colonization, Shigella is person-to-person spread. This makes it particularly problematic in crowded conditions, daycare, and institutions. The serogroups vary geographically; *S. flexneri* and *S.*

Shigella pathophysiology and complications

Shigella diagnosis and treatment

Laboratory Diagnosis

- Stool culture on selective media (HE agar, XLD agar)
- Preferred: culture from mucoid/blood-stained stool
- Non-motile gram-negative colonies - PCR for Stx gene (*S. dysenteriae*)

Resistance Patterns

- Asia/Africa: 20-30% resistance to third-generation cephalosporins
- TMP/SMX resistance: 65-85% in some regions
- Fluoroquinolone resistance increasing (esp. *S. sonnei* in Asia)

Treatment

- First-line: Fluoroquinolone or ceftriaxone (when fluoroquinolone susceptibility uncertain)
- Alternative: Azithromycin
- Duration: 5-7 days

Shigella's high rates of antimicrobial resistance necessitate knowledge of local epidemiology. In developed countries, fluoroquinolones remain effective, but in many developing countries, resistance is common. Third-generation cephalosporins maintain good coverage for most strains. Macrolides are useful alternatives. Most shigellosis is self-limited without therapy, but treatment is recommended

Shigella — When to treat

Standard Recommendation

- Most infections resolve without antibiotics
- Treatment doesn’t significantly alter outcomes in mild-moderate disease

Treat When

- Immunocompromised patients (including HIV)
- Severe diarrhea or dysentery
- Bacteremia or extraintestinal infection
- High risk for transmission (food handlers, daycare workers)

Benefit of Treatment

- Decreases symptom duration by ~2 days
- Reduces fecal shedding (may reduce transmission)
- Prevents complications in vulnerable populations

Yersinia

Species of clinical importance:

- *Yersinia enterocolitica - Yersinia pseudotuberculosis*

Key characteristics - Zoonotic infections: wild and domestic animals

- Transmission: undercooked pork, contaminated water
- Can survive refrigeration (cold enrichment aids culture)

Clinical features : Watery diarrhea or dysentery

- **Distinctive: pharyngitis in ~20% (pharyngitis-gastroenteritis pattern)**
- **Acute mesenteric lymphadenitis: can mimic appendicitis**
- Fever and abdominal pain prominent
- Can cause arthralgia (particularly HLA-B27 associated)

Lab diagnosis - Culture on selective media (CIN agar)

- Overgrowth by normal flora; requires selective medium or cold enrichment

The combination of pharyngitis with gastroenteritis is unusual and should raise suspicion for Yersinia. The risk of acute mesenteric lymphadenitis misdiagnosed as appendicitis is clinically important.

John Snow- Birth of medical epidemiology

Vibrio cholerae

Epidemiology

- Endemic in South Asia (particularly Bangladesh, India) (Sack et al., 2004)
- Seventh pandemic ongoing since 1961
- Transmitted via contaminated water in areas with poor sanitation
- Epidemic potential high; 3-5 million cases, 100,000-300,000 deaths annually (Ali et al., 2015)

Clinical Presentation

- Acute watery non-bloody diarrhea
- Characteristic “rice-water stools” (clear, watery, with flecks)
- Severe dehydration and shock possible
- Vomiting common
- Can be fulminant with progression to hypovolemic shock

Cholera is primarily a disease encountered in endemic areas or during humanitarian crises with disrupted water systems. In developed countries, it is usually associated with travel to endemic regions or consumption of raw seafood from contaminated waters. The toxin-mediated secretory diarrhea can be massive—patients may produce 10-20 liters of stool daily. The fulminant nature of severe cholera

Cholera management

Traveler’s Diarrhea

Traveler’s diarrhea — Overview

Epidemiology

- Affects 300-500 million travelers annually
- Attack rate varies by destination: 5-50% depending on region (Steffen et al., 2015)
- Onset typically 5-15 days after arrival in endemic region
- Duration usually 1-5 days (self-limiting in 90%)

Clinical Presentation

- Watery diarrhea most common (80%)
- Some bloody stools possible (10-20%)
- Fever in 20-30%
- Cramping abdominal pain
- Systemic symptoms mild

Definition

- ≥3 unformed stools in 24 hours plus 1+ GI symptom
- Occurring in someone traveling to area of higher risk

The pathogenesis is multifactorial: combination of unfamiliar microbiota, altered diet, dehydration, and exposure to enteropathogens. The risk varies dramatically by destination; highest risk areas

Traveler’s diarrhea — Etiology by region

Pathogen	Frequency	Geographic Notes
ETEC	40-50%	Most common worldwide
Campylobacter jejuni	5-30%	Higher in Asia
Salmonella spp.	5-20%	Variable by region
Shigella spp.	5-15%	Higher in developing regions
Enteroinvasive E. coli	5-10%	Variable
Protozoa (Giardia, Crypto)	2-5%	More in rural areas
Viral	5-10%	Norovirus, Rotavirus, Adenovirus
Noninfectious	10-20%	Dietary changes, altitude

Traveler’s diarrhea — Prevention

Food and water precautions

- Drink bottled or boiled water
- Avoid ice, raw vegetables, raw/undercooked meat
- Peel own fruits
- Avoid street food and unpasteurized dairy

Antimicrobial prophylaxis

- Not routinely recommended (resistance, adverse effects)
- Consider for high-risk patients (immunocompromised, severe underlying disease)
- Bismuth subsalicylate: effective prophylaxis (2 tablets QID)
- Duration: maximum 3 weeks

Food and water safety counseling is the most important prevention strategy. Travelers should be cautious about water quality even in urban areas; boiling, bottled water, or water purification tablets provide protection. The decision to use antimicrobial prophylaxis should be individualized. For most healthy travelers, the small risk of side effects outweighs benefits. Bismuth subsalicylate is effective

Traveler's Diarrhea — Self-treatment

Treatment Options

Preferred Approach

- Azithromycin 500 mg once daily, 3 days (Riddle et al., 2016)
- Covers ETEC, *Campylobacter, Shigella*
- Lower resistance rates than fluoroquinolones

Alternative Approaches

- Fluoroquinolone (levofloxacin, ciprofloxacin) if available
- Rifaximin 200 mg TID, 3 days (non-absorbed, minimal resistance)
- Symptomatic Therapy - Loperamide (Imodium): effective for cramping
  - Combine with antibiotic for faster resolution - Bismuth subsalicylate: both treatment and symptomatic relief

Self-treatment of traveler's diarrhea with antibiotics can dramatically reduce duration and severity. The combination of a motility agent and antibiotic provides both symptomatic relief and pathogen eradication. Counseling patients about when to self-treat versus seek care is

Diarrhea in HIV/AIDS

Epidemiology

- Affects 30-60% of patients with AIDS (CD4 <200) (Sanchez et al., 2005)
- Incidence decreased markedly with antiretroviral therapy
- ART with immune reconstitution reduces diarrheal disease

Infectious Etiologies in AIDS

- Cryptosporidium parvum: most common parasitic cause
- Cytomegalovirus: causes ulcerative colitis pattern
- Microsporidium: can cause chronic diarrhea
- Mycobacterium avium complex: systemic infection
- Conventional pathogens remain common (*Salmonella, Campylobacter*)

Management - Start/optimize antiretroviral therapy (most important) - Ganciclovir for CMV colitis - Multipathogen testing recommended - Empiric therapy based on CD4 count and epidemiology

Diarrhea in transplant recipients

Diarrhea in immunocompromised patients — General approach

- **Key Diagnostic Principles**
  - Identify etiologic agent whenever possible (broad differential)
  - Multipathogen testing: stool culture, parasitic studies, molecular panel
  - Lower threshold for colonoscopy and biopsy
  - Consider unusual pathogens based on immune defect
- **Treatment Considerations**
  - Pathogen-specific therapy when identified
  - Avoid empiric broad-spectrum antibiotics when possible
  - Address underlying immune defect (ART, immunosuppression optimization)
  - Monitor for immune recovery inflammation (MAC disease, IRIS)

Hospital-acquired diarrhea

- **Epidemiology**: Occurs in 10-15% of hospitalized patients
  - Clostridioides difficile: most common infectious cause (Lessa et al., 2015)
  - Associated with increased morbidity, mortality, and healthcare costs
- **Risk factors:** Recent or current antimicrobial therapy (strongest risk factor)
  - Advanced age
  - Severity of underlying illness
  - Prolonged hospitalization
  - Immunosuppression
- **Clinical features** : Occurs after ≥3 days hospitalization
  - Watery diarrhea most common
  - Fever, leukocytosis, abdominal pain -
  - Can progress to toxic megacolon or perforation
- **C. difficile-associated disease**
  - Toxin-mediated disease (toxin A, toxin B) -Antimicrobial exposure disrupts normal flora
  - Transmission via spores: contact precautions required (hand sanitizer not sufficient)
  - Increasing incidence of severe, recurrent disease

Diarrhea in institutional settings

- **Long-Term Care Facilities**
  - One-third of residents experience diarrhea annually
  - C. difficile most common
  - Rotavirus, G. lamblia seasonal outbreaks
  - Norovirus rapid spread in winter
  - **Nutritional impact: worsens outcomes in elderly**
- **Daycare and School Settings**
  - Rotavirus common in young children (prior to universal vaccination)
  - G. lamblia outbreaks in daycare
  - Shigella spread via fecal-oral route
  - ETEC in contaminated water/food
  - Exclusion policies important for control
- **Neonatal diarrhea**
  - Often caused by EPEC serotypes
  - Risk of severe dehydration in newborns
  - Historical mortality 24-50%; now <5% with rehydration therapy
  - Insidious onset; requires high clinical suspicion - May present with failure to thrive

Principles of treatment — Rehydration

- **Oral Rehydration Solution (ORS)**
  - First-line for mild-moderate dehydration
  - WHO-recommended formulation: sodium 75 mmol/L, glucose 75 mmol/L, chloride 65 mmol/L, potassium 20 mmol/L
  - Effective for >90% of acute diarrhea cases
- **Rehydration Approach**
  - Replace ongoing losses (10 mL/kg per stool)
  - Add maintenance fluids
  - Early rehydration prevents severe dehydration
  - Resume age-appropriate diet early
- **IV Rehydration** - Reserved for severe dehydration, vomiting, shock
  - Normal saline or Ringer's lactate preferred
  - Careful electrolyte monitoring - Transition to oral when feasible

Rehydration is the cornerstone of diarrheal disease treatment, and the introduction of ORS has been transformative in reducing mortality from diarrhea globally. The electrolyte composition of ORS is based on the sodium-glucose cotransport mechanism in the small intestine, which remains intact even in diarrheal disease. Most cases of acute diarrhea, even with significant initial dehydration, can

Symptomatic treatment

- **Bismuth Subsalicylate**
  - Reduces diarrheal volume by 30-50%
  - Antimicrobial properties against several pathogens
  - Useful for both prophylaxis and treatment
  - Avoid in salicylate allergy; concern for drug interactions - Useful in traveler's diarrhea management
- **Antimotility Agents: Use with Caution** - Loperamide (Imodium): effective for cramping
  - Risk: can precipitate toxic megacolon **(contraindicated in bloody diarrhea, fever, severe disease**)
  - Never use with suspected EHEC
  - Combined with antibiotics: effective for traveler's diarrhea
  - Generally safe in mild, watery, non-inflammatory diarrhea
- **Probiotics**
  - Insufficient evidence for general recommendation
  - May be role in specific contexts (antibiotic-associated diarrhea)
  - Not harmful but not proven beneficial in most diarrhea

Bismuth subsalicylate has both antimicrobial and symptomatic benefits, making it useful in traveler's diarrhea. Antimotility agents require clinical judgment; they're safe in uncomplicated watery diarrhea but contraindicated when there's concern for invasive infection, fever, or bloody stools because they increase risk of complications like toxic megacolon. The combined use of antimotility

When to use antibiotics

- **Empiric Antibiotics Recommended For:**
  - Severe diarrhea (bloody, fever, >8 stools/day)
  - Diarrhea in immunocompromised patients
  - Traveler's diarrhea (if symptomatic treatment not effective)
  - Suspected invasive pathogen (Salmonella bacteremia, Shigella in systemically ill)
  - Institutional outbreaks (control transmission)
- **Avoid Antibiotics:** Suspected or confirmed EHEC/STEC (increases HUS risk)
  - Viral diarrhea - Mild, watery, non-bloody diarrhea in immunocompetent hosts
  - Non-typhoidal Salmonella gastroenteritis in most patients

First-Line Empiric Choices

- Azithromycin 500 mg daily × 3 days (preferred for traveler's diarrhea)
- Fluoroquinolone (ciprofloxacin 500 mg BID × 3 days) where resistance is low
- Adjust based on local resistance patterns

Micronutrient supplementation

- **Zinc Supplementation**
  - Particularly in children <5 years in developing countries (Lazzerini and Wanzira, 2016)
  - Reduces duration and severity of diarrhea
  - Decreases risk of subsequent infections for 2-3 months
  - Dose: 10-20 mg elemental zinc daily for 10-14 days
  - Strong evidence supports benefit, especially in malnourished children
- **Other Micronutrients**
  - Vitamin A: benefit in deficient populations
  - Iron: avoid during acute infection (may worsen)
  - Folate, B vitamins: supportive during recovery

Role in Developed Countries - Less emphasis (better nutritional status baseline) - Consider in malnourished or vulnerable populations - Not harmful if administered

Zinc supplementation during diarrheal illness has strong evidence for benefit, particularly in developing countries where zinc deficiency is common. The mechanism involves improved intestinal barrier function and immune response. Even in developed countries, zinc supplementation during severe or prolonged diarrhea may be beneficial, though the evidence is less robust. The evidence for other

Key Take-Home Messages

1. **Most diarrhea is viral and self-limited —** reserve specific testing and antibiotics for cases suggesting bacterial infection
2. **Rehydration is the cornerstone of treatment —** ORS is highly effective and first-line for most cases (Munos et al., 2010)
3. **Identify patients needing hospitalization or antibiotics —** use clinical features, history, and exam to guide severity assessment and testing
4. **EHEC/STEC demands special attention —** antibiotics are contraindicated and increase HUS risk
5. **Geographic and risk-factor epidemiology matters —** tailor diagnostic approach and empiric therapy based on exposure history and patient factors

Clinical decision Framework

① Assess Severity

Dehydration • Vital signs • Systemic symptoms

⚠ Red flags: bloody stools | fever >39°C | altered mental status | shock

↓

② Targeted History

Travel • Food/water exposure • Sick contacts • Immunocompromise • Recent antibiotics • Medications

↓

③ Decide on Testing

✓ Send Testing

- Bloody diarrhea
- Fever >38.5°C
- Systemic illness
- Immunocompromised
- Duration >7 days

✗ No Testing Needed

- Mild watery diarrhea <7 days
- No red flags
- Immunocompetent host

↓

④ Treatment

Rehydration — first-line for all **Antibiotics** — only if bacterial criteria met; avoid for EHEC **Symptomatics** — if no contraindications

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