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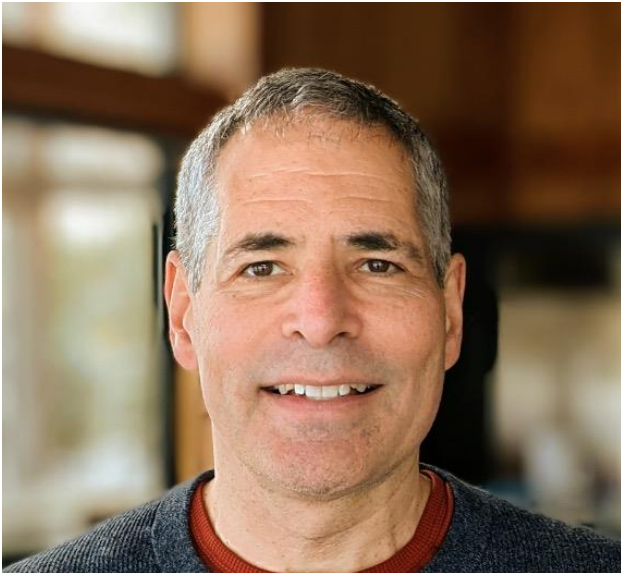
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Commercial/Faculty Disclosures

I have no financial disclosures



Goals

Acute and Chronic Diarrhea
Focus on essentials
New developments



Topics Covered

Definitions

Approach to acute diarrhea

- Differential diagnosis
- Diagnostic approach
 - When to watch
 - When to test
 - When to treat

Approach to chronic diarrhea

- Most common etiologies by age group
- Phenotypically: watery, inflammatory or fatty
- Diagnostic evaluation
 - Initial testing
 - Follow-up testing



Diarrhea: Definitions

Objective definition

- Excessive stool weight: $>200\text{gm/day}$

Subjective definition

- Excessive frequency of defecation (≥ 3 stools)
- Less-than-normal form and consistency

Acute diarrhea: < 4 weeks duration

Chronic diarrhea: > 4 weeks duration

Persistent diarrhea: 2-4 weeks duration



Normal Intestinal Physiology

10 L of fluid enters the jejunum daily

- 2 L: Food and drink
- 8L: Salivary, gastric, biliary, pancreatic, intestinal secretions

1L enters the colon

80-100 mL excreted daily



Abnormal Intestinal Physiology

Loosening of stools: 50-60mL increase daily fecal water

Diarrhea: 100mL (1-2%) increase in fecal water

Many disorders disrupt intestinal fluid and electrolyte absorption by at least this amount

- Frequent event
- Extensive differential diagnosis



Acute Diarrhea: Major Causes

Infectious: Most common

- Viral: Noroviruses , Rotavirus
- Bacterial: Food poisoning, C. difficile
- Parasitic/protozoal

Noninfectious

- Medications
- Consumption of poorly absorbed sugars (e.g. sorbitol)
- Enteral feeding
- Ischemic colitis
- Fecal impaction: “paradoxical diarrhea”



Diagnostic Evaluation

Majority of cases are mild and self-limited

90% of cases need no diagnostic evaluation

Treat symptomatically for several days

Likely etiologies:

- Viral (>75%)
 - Noroviruses (71%), Rotavirus
- Bacteria elaborating preformed toxin
 - *S. aureus*, *B. cereus*, *C. perfringens*

Stool culture positive: 1.5-5.6%



Stool Tests for Bacterial Pathogens

- Inflammatory Diarrhea:
 - Bloody/mucoid diarrhea
 - Dysentery: Bloody stools, fever, cramps, tenesmus
 - Stool culture positive up to 87%
- Severe Illness:
 - Volume depletion: eg orthostatic, scant or dark urine
 - Severe abdominal pain (also consider imaging)
 - Temperature $> 38.5^{\circ}\text{C}$ (101.3°F)
- History of inflammatory bowel disease
- Immunocompromised or elderly (≥ 70 yrs) with significant cardiovascular disease
- Pregnancy
- Public Health Concerns:
 - Food Handlers, healthcare and daycare workers



Stool Culture

Routine culture:

- Campylobacter, Salmonella, Shigella

Notify lab:

- E. Coli O157:H7, Yersinia, Aeromonas, Vibrio
- Bloody stools: STEC, amebiasis, shigella
 - Confirm lab checks Shiga toxin (Sensit: PCR >>EIA)
 - Lack of fecal leukocytes: Amebiasis

Single specimen: Bacteria shed continuously

Clostridium difficile toxin assay

- Antibiotic/Chemotherapy within preceding 2 weeks
- Hospital-acquired diarrhea

Stool cultures: Low yield if diarrhea develops after hospitalization > 72 hours.



Multipathogen/Multiplex Molecular Diagnostic Panels

- Up to 22 pathogens with fast turnaround (few hours) and more sensitive than stool culture: Bacterial, viral and parasitic;
- Replace stool culture in select cases
 - Very sick (bloody diarrhea/fever), immunocompromised, hospitalized
 - Epidemiological risk factors: Travel, high risk food or untreated water exposure
 - Caveat: Detect genetic material: Not necessarily viable organisms
- May detect more than one organism
- Positive test for bacteria: Send confirmatory culture.
 - Susceptibility testing
 - Public health reporting



Stool For Ova and Parasites

Cost-effective in high-risk groups

- Persistent diarrhea (>14 days)
- Community waterborne outbreak
- Exposure to untreated water (e.g. streams)
- Daycare center exposure
- Travel to Russia, Nepal
 - Giardia, Cryptosporidia
- MSM: Giardia, E.histolytica
- Advanced HIV: CD4<200cells/microL
 - Giardia, E.histolytica, Microsporidia

Intermittent shedding



- 3 specimens on consecutive days



Who needs Endoscopic Evaluation?

Bloody diarrhea

- IBD versus infectious diarrhea
- Suspected ischemic colitis

Pseudomembranous colitis

Immunocompromised or other high-risk patients: Look for CMV

Flexible sigmoidoscopy versus colonoscopy



Supportive Therapy

Rehydration: Glucose- Na^+ co transporter

- WHO oral rehydration solution (per liter of water)
 - 20gm glucose or 40gm sucrose, NaCl , NaHCO_3 , KCl
- Alternative rehydration solution (per liter of water)
 - 4 tablespoon sugar
 - $\frac{1}{2}$ teaspoon salt
 - $\frac{1}{2}$ teaspoon baking soda
- Rice-based oral rehydration solution (e.g. Cera-lyte)

Fluids for sweat replacement (e.g. Gatorade, Powerade, Propel)

- Not equivalent to ORS. Sufficient for mild cases
- Diluted fruit juice plus saltine crackers

Dietary modification

- Lactose free diet for several weeks
- Avoid food with high fat content
- Boiled starches or cereals with salt
- BRAT diet: Bananas, rice, apple sauce, toast



Supportive Therapy: Other Measures

Stop all sugar substitutes

Review medications

Assess for fecal impaction and treat

Adjust tube feeds: Dilute, decrease rate or add fiber



Antidiarrheal agents

Stools nonbloody and fever low-grade

Antimotility agents: Decrease peristalsis

- Loperamide (Imodium)
 - 4mg initially, then 2mg after each loose movement
 - Maximum: 16mg/day for 2 days
- Diphenoxylate atropine (Lomotil)
 - Central opiate and anti-cholinergic side-effects (atropine)
 - 1-2 tabs tid/qid

Other agents

- Pepto-Bismol: 2 tabs every 30 minutes (up to 8 doses/day)
 - Can also help vomiting
- Kaopectate: Improves stool consistency
- Racecadotril, aka acetorphan: Peripherally acting enkephalinase inhibitor; Reduces the secretion of water and electrolytes



Empiric Antibiotic Therapy

Severely ill immunocompetent individuals

- Fever, bloody diarrhea
- Exception!: STEC (shiga toxin-producing E. Coli)
- Dehydration
- >8 stools/day or symptoms for > 1 week

Immunocompromised patients

- AIDS, malignancy, transplant recipients

Drugs of choice

- Quinolone: Ciprofloxacin, levofloxacin (3-5 days)
- Azithromycin (3 days)
 - Suspect fluoroquinolone resistance (eg. travel to Southeast Asia)
 - Campylobacter infection
- Vancomycin: C. difficile suspected



Probiotics: Mixed Results

Prevention of travelers diarrhea

- Supportive studies/meta-analysis
- Lactobacillus GG and acidophilus
- Saccharomyces boulardii: N. Africa, Turkey

Infectious diarrhea

- Mixed data: Lactobacillus species
- Reduce duration of diarrhea: about 24 hours
- 10 billion CFU within first 48 hours

Antibiotic associated diarrhea: Need more studies



Acute Diarrhea

Select Infectious Causes



Campylobacter jejuni

A leading cause of bacterial diarrhea: 4-11%

Source - Contaminated poultry: 50-70%

Relapsing course: 15-20%

Drugs of choice:

- Fluoroquinolones
- Azithromycin
- Rising rates of resistance
 - Check sensitivities



Campylobacter: Complications

Reactive arthritis/Reiter's Syndrome: 1%

- 1-2 weeks after diarrhea onset
- Self-limited: several months

Guillain-Barré Syndrome

- Responsible for 25% cases
- Symptoms within 3 months of diarrhea onset
- May be Culture negative but serology positive

Antibiotics do not prevent these complications



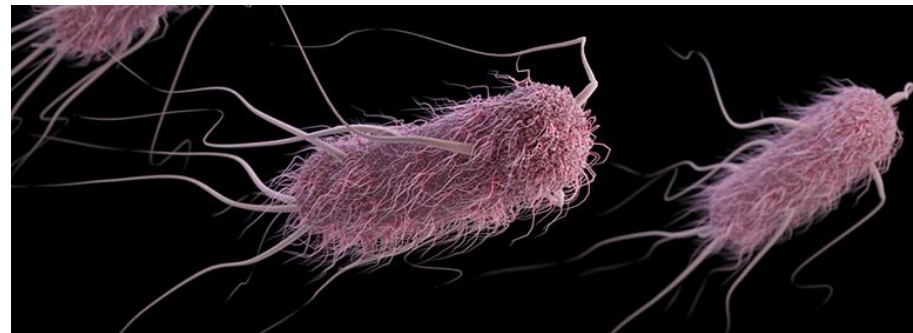
STEC (Shiga toxin-producing E. coli).

Most prevalent in U.S.: E. coli 0157: H7

- Undercooked meat ingestion
- Predisposing factors: Age < 10 or > 50
- Watery diarrhea → bloody diarrhea
- Often afebrile

May elaborate 2 proteins:

- Shiga toxin = verotoxine
- Intimin= Adhesine protein



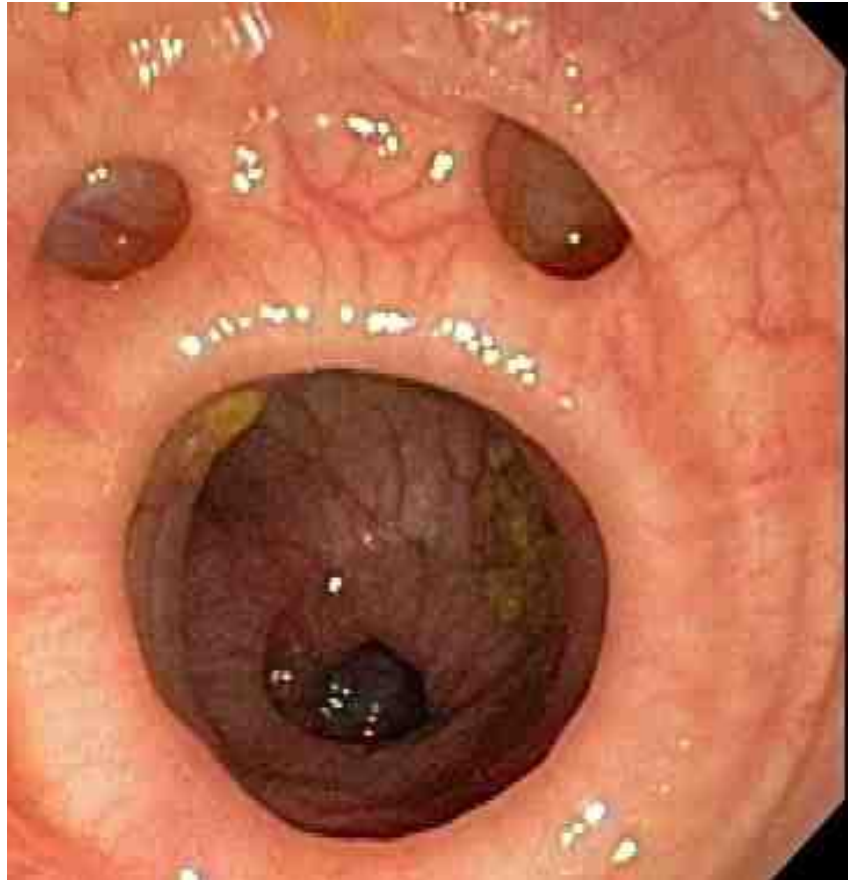
STEC Infections: Complications

STEC with both proteins

- Potentially lethal
- Increase risk of Hemolytic-uremic Syndrome (HUS)
 - Acute renal failure
 - Microangiopathic hemolytic anemia
 - Thrombocytopenia
- Selective culture required: Multiplex much faster
- Many labs: Test for shiga toxin: PCR more sensitive than EIA
- **Avoid Antibiotics:**
 - Increased production of shiga toxin
 - Increased risk of HUS
 - Especially fluoroquinolones, β -lactams, TMP-SMX, and metronidazole should be avoided
 - Fosfomycin and Azithromycin appear to be safer



Chronic Diarrhea: A Systematic Approach



Chronic Diarrhea in Resource-abundant Settings

Afflicts 6-7% of adults in the US

90% have a noninfectious etiology

Myriad of disorders

Order of prevalence varies

- Age of the patient
- Practice setting

Optimum evaluation strategy

- Not established
- Expert opinion
 - JAMA review: March 2026
 - AGA (American Gastroenterological Association) Guidelines 2019
 - UpToDate 2026



MAJOR CAUSES IN DEVELOPED COUNTRIES

Irritable bowel syndrome (IBS-D) or functional diarrhea

Inflammatory bowel disease

- Ulcerative colitis, Crohn's disease
- Microscopic colitis

Malabsorption syndromes

- Lactose intolerance, Celiac disease, SIBO, Pancreatic insufficiency

Medications

Chronic infections

- Immunocompromised
- Bacterial, parasitic

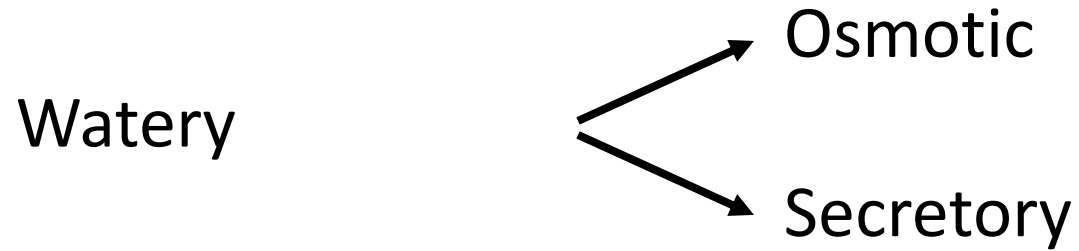


How the Differential Diagnosis of Chronic Diarrhea Changes with Age

- Young adults: 18-44 years old
 - Functional disorders (IBS-D, Postinfectious IBS-D, Functional diarrhea), carbohydrate malabsorption, celiac disease, and early-onset IBD (Crohns/UC) predominate. Colorectal neoplasia uncommon but look for red flags
- Middle Age: 45-64 years old
 - Functional disorders, Medication-induced diarrhea and microscopic colitis become increasingly common; colorectal neoplasia should be considered and ruled-out.
- Older Adults: $\geq$ 65 years old
 - Polypharmacy, fecal incontinence/overflow (18%), SIBO, exocrine pancreatic insufficiency, microscopic colitis, recurrent *C. difficile*, and colorectal cancer assume greater importance.



Categorization of Chronic Diarrhea



Inflammatory

Fatty

Several mechanisms may coexist



Osmotic Diarrhea

Hallmarks

- Diarrhea stops with fasting
- Generally not nocturnal
- Large osmotic gap: $> 125 \text{ mOsm/kg}$

Mechanism

- Ingestion of osmotically active solutes
- Retention of water in intestinal lumen
- Electrolyte absorption (Na^+ , K^+) is normal
- Large osmotic gap between expected (290mOsm) and calculated

Stool osmotic gap = $290 - 2([\text{Na}^+] + [\text{K}^+])$

Logistical hurdles: Reserve for diagnostically challenging cases



Osmotic or Malabsorptive Diarrhea

Exogenous Causes:

- Antacids: Mg^+
- Laxatives:
 - Polyethylene glycol (PEG)
 - Poorly absorbed anion (PO_4^{-3} , SO_4^{-2} , citrate)
- Sugar substitutes: Sugar-free candy/gum or medication elixirs:
 - Sorbitol, mannitol, Splenda, lactulose
- Nonabsorbable fats: Olestra

Endogenous Causes:

- Congenital: Disaccharide deficiencies: Lactose intolerance
- Acquired
 - Post-enteritis: Lactose intolerance
 - Pancreatic insufficiency
 - Celiac disease
 - Olmesartan (ARB): Collagenous sprue and collagenous colitis



Secretory Diarrhea

Hallmarks

- Persists with fasting
- Nocturnal diarrhea
- Large volume ($> 1\text{L}$)
- Small stool osmolar gap $< 50 \text{ mOsm/kg}$



Secretory Diarrhea

Exogenous:

- Stimulant laxatives: Bisacodyl, senna
- Prostaglandins, theophylline, colchicine
- Dietary secretagogues: Ethanol, caffeine, colas

Endogenous:

- Bile acid malabsorption:
 - Crohn's ileitis, SB resection, bacterial overgrowth, cholecystectomy
- Hormone-producing tumors: Carcinoid, gastrinoma, Glucagonoma, VIPoma
- Systemic mastocytosis



Bile Acid Diarrhea (BAD)

IBS-D: up to 50% with bile acid malabsorption

Post cholecystectomy: 5-12%; Often improves over weeks to months

Bile acids: Stimulate colonic motility and secretion

Treatment: Bile acid sequestrants

- Colestipol (tablet): 1 gm twice daily
- Cholestyramine (powder): 4 gms daily
- Colesevelam/Welchol (tablet): 1.875gm twice daily
 - Average delay in transit time of 4 hours c/w placebo

Potential side effects: Bloating, flatulence, abdominal discomfort and constipation

- Need to be separated from other medication by > 2 hours.



Inflammatory Diarrhea

Hallmarks

- Mucoid, bloody stool
- Tenesmus, abdominal pain, fever: Dysentery
- FOBT positive
- Can be nocturnal
- Fecal leukocytes:
 - Low sensitivity (70%) /specificity (50%)

Elevated Fecal calprotectin (or Fecal lactoferrin: less sensitive)

- Zn/Ca binding protein
- Derived from neutrophils and monocytes
- Levels increased in intestinal inflammation
- Distinguish inflammatory from noninflammatory causes of chronic diarrhea



Inflammatory Diarrhea

IBD: Crohn's, ulcerative colitis

Chronic infections

- C. difficile
- Invasive bacteria: eg. TB, yersinia
- Invasive parasites: eg. ameba, strongyloides

Radiation or chemo-induced mucositis

Colonic ischemia



Fatty Diarrhea

Oil droplets in stool, floating stool

Diagnosis

- Positive Sudan III stain: Qualitative
- 72 hour stool collection
 - Abnormal: > 7gm fat/day
 - Rarely done (limited reproducibility)
- Stool acid steatocrit
 - Acidify stool
 - Separate fecal homogenate into lipid, water, solid phases; Measure lipid
 - Good correlation with quantitative fecal fat



Fatty Diarrhea: Causes

Maldigestion and/or Malabsorption
Pancreatic insufficiency

Inadequate luminal bile acids
Crohn's disease
Short bowel syndrome
SIBO



History

Stool characteristics: Watery, bloody, fatty/oily

Epidemiological factors: Travel, sick contacts

Aggravating/mitigating factors: Diet, stress

Presence or absence:

- Fecal incontinence, abdominal pain, weight loss

Past history:

- Diabetes, Hyperthyroidism, surgery, XRT, CAD

Medication history

Sexual history: Risk factors for HIV

Family history: IBD, neoplasm, celiac disease

Markers of eating disorder, malingering



PHYSICAL EXAM

Extent of fluid and nutritional depletion

Skin rashes or flushing

Mouth ulcers

Thyroid masses or exophthalmos

Arthritis

Hepatomegaly or abdominal masses

Anorectal exam: sphincter tone, perianal fistula/abscess

Scars (suggesting prior abdominal surgery)



Initial Laboratory Testing

AGA (American Gastroenterological Association) Initial Evaluation:

- Fecal calprotectin (or lactoferrin): Screen for IBD
- TTG IgA and total IgA level: Celiac disease
- Stool: Giardia
- Future: Testing for bile acid diarrhea (BAD)
 - SeHCAT (75Selenium-Homocholic Acid Taurine Test) measures retention of a radiolabeled synthetic bile acid 7 days after oral ingestion.
 - Inverse relationship between 7-day retention and response to bile acid sequestrants
 - 80% of patients with <10% retention respond to treatment, compared with 70% at <15% retention. Not available in US.
 - Fasting serum C4 level (serum 7 α -hydroxy-4-cholesten-3-one): marker of bile acid synthesis by the liver
 - Elevated in bile acid diarrhea
 - Limited availability and lack of regulatory approval
- Empiric therapy with bile acid binders is used instead in clinical practice.



Additional Laboratory Testing: Other Guidelines

Also include

- CBC with differential
- Electrolyte panel
- Thyroid function tests

Strongly consider

- Iron studies, vitamin B12



Initial Stool Testing

- Elisa for Giardia Ag
- Fecal calprotectin or lactoferrin
- C. Difficile toxin: Antibiotic or chemotherapy history



Endoscopic Evaluation

Colonoscopy: Required for evaluation of many patients

- Rather than flexible sigmoidoscopy
- Age appropriate: ≥ 45 yo
- Any age: Alarm features
 - Patients with iron deficiency anemia
 - Rectal bleeding
 - Unexplained weight loss
 - Nocturnal diarrhea or change in bowel habits
 - Patients with suspected Crohn's disease
- Biopsy normal-appearing mucosa
 - Collagenous/lymphocytic colitis
 - 10% right-sided only

Upper Endoscopy

- Useful to rule-out sprue or Whipple's



Difficult to Diagnose Cases

- Common problems overlooked
 - Lactose intolerance
 - Fecal incontinence
 - Review medications again
- Stool culture: Aeromonas and pleisiomonas
- O&P: Cryptosporidium, Cyclospora, E. Histolytica, Microsporidia if immunocompromised
 - 3 samples
- Breath test for small intestinal bacterial overgrowth (SIBO)
- Calculate the osmotic gap



Difficult Cases: Osmotic

Laxative screen

- Inadvertent or surreptitious laxative use
 - Melanosis coli
- Anthraquinones (eg. Senna, cascara, aloe), bisacodyl and phenolphthalein (eg. ExLax) in urine
- magnesium and phosphate in stool.

Stool pH < 5.3

- Carbohydrate malabsorption (e.g. lactulose, sorbitol)



Difficult Cases: Secretory

24 hour urine collection: 5-HIAA (carcinoid)

Plasma peptides: Neoplasms and systemic mastocytosis

- VIP, gastrin, glucagon (NETs), calcitonin (thyroid), tryptase

Imaging:

Dotatate PET scan: Good for NETs

VIPomas, gastrinomas, glucagonomas are typically located in the pancreas or duodenum

Carcinoid tumors: Most often small intestine but can occur throughout the GI tract, including the appendix and rectum.

Endoscopic Ultrasound: Particularly sensitive for small pancreatic NETs



Difficult Cases: Inflammatory and Fatty

Fecal fat assessment

- Stool sudan stain

Suspect pancreatic insufficiency

- Pancreatic imaging: Chronic pancreatitis
 - MRI/MRCP
- Stool: Fecal elastase (<100 µg/g of stool)
 - Reliable only in moderate to severe insufficiency
- Urine collection: Pancreolauryl test
- Trial of pancreatic enzymes

MR or CT enterography, intestinal ultrasound (spec. for T.I.)

- Rule-out IBD

Small bowel biopsies for sprue, Whipple's

Breath test for SIBO

- Trial of antibiotics



SYMPTOMATIC THERAPY

- **Supportive therapy:** ≥ 8 cups noncaffeinated fluids daily, limit caffeine: ≤ 3 cups/day, avoid alcohol and carbonated beverages
- **First-line pharmacotherapy:**
 - loperamide, diphenoxylate atropine for stool consistency
 - Anticholinergics for cramping: Dicyclomine (Bentyl), hyoscyamine
 - Ondansetron (Zofran) for urgency/loose stools: Emerging evidence of benefit
- **Targeted therapy:** After a specific etiology is identified
 - Bile acid sequestrants for BAD
 - Budesonide for microscopic colitis
 - Gluten-free diet for celiac disease
 - Pancreatic enzyme replacement for EPI (exocrine pancreatic insufficiency)
 - Antibiotic for SIBO
- **Octreotide:** Disabling diarrhea



Summary and MOC Reflections: Acute Diarrhea

- Infections: Most common cause of acute diarrhea
 - Viral more common than bacterial etiology
 - 90% self-limited, require no further evaluation
- Further evaluation with stool studies:
 - Bloody/Inflammatory diarrhea**
 - Multiplex diagnostic panel: Supplanting stool culture
 - Sick (blood/fever), immunocompromised, hospitalized, outbreak detection
 - Higher sensitivity, faster turnaround, and broader pathogen detection.
 - Standard culture: outpatients, antimicrobial susceptibility testing is needed, public health reporting, outbreak tracking
 - Antibiotic exposure, hospitalized → C. Diff. Toxin
- Empiric Antibiotics: Severely ill, immunocompromised
 - Quinolone
 - Azithromycin: Fever, bloody stool, suspected quinolone resistance
 - Vancomycin: C. difficile suspected
- Avoid antibiotics: E. coli 0157:H7



Summary and MOC Reflections: Chronic Diarrhea

- Broad differential diagnosis: Categorize the diarrhea
 - Differential by age group
 - Phenotype: Watery, Inflammatory or Fatty
- Initial testing:
 - Fecal calprotectin: Screen for IBD, other inflammatory diarrhea
 - Stool: Giardia
 - TTG IgA and total IgA level: celiac disease
 - Future: Testing for bile acid diarrhea; Current: empiric trial bile acid-binding med.
- Keep in mind possibility of fecal incontinence
- Many patients with chronic diarrhea require endoscopic evaluation with colonoscopy and endoscopy
- Acute and chronic diarrhea:
 - Supportive measures: Rehydration, antidiarrheal agents
 - Targeted therapies



Question 1

Which is a hallmark of watery secretory diarrhea?

- A) Diarrhea improves with fasting
- B) Stool osmotic gap >125 mOsm/kg
- C) Nocturnal diarrhea
- D) Steatorrhea
- E) Symptoms triggered by lactose-containing foods



Question 1: Answer C

The correct answer is **Nocturnal diarrhea**.

Secretory diarrhea: Large volume, watery stools that persist during fasting and often occur at night. Bile acid diarrhea is an example.

Osmotic diarrhea typically abates with fasting and is associated with a high stool osmotic gap ($>125\text{mosm/kg}$). Lactose intolerance falls into this category.

Steatorrhea/fatty diarrhea, is distinguished from watery diarrhea. Presence of excess fat in the stool, typically due to malabsorption or maldigestion of lipids, as seen in conditions such as exocrine pancreatic insufficiency or celiac disease.



Question 2:

In patients with acute diarrhea, empiric antibiotic therapy should be avoided in one of the following contexts:

- a. Fever and bloody diarrhea
- b. Moderate to severe travelers diarrhea
- c. Known or suspected *E. coli* 0157: H7
- d. Elderly and immunocompromised
- e. Hospitalization under consideration



Question 2: Answer C

Known or suspected E. coli 0157: H7

Most common STEC infection

- Avoid antibiotics:
 - Increases production of shiga toxin
 - Increases risk of Hemolytic-uremic Syndrome (HUS)
 - Acute renal failure
 - Microangiopathic hemolytic anemia
 - Thrombocytopenia



Commercial/Faculty Disclosures

None



References

1. LaRoque R, Harris JB , Approach to the adult with acute diarrhea in resource-rich settings In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA (accessed on June 26, 2026).
2. Singh P, MBBS; Lee A, MD, MS; Sheth N, MD; Chey WD, MD. Chronic, Noninfectious Diarrhea: A Review JAMA, March 2026; 335(14): 1250-1262. doi:10.1001/JAMA.2026.0872
3. Smalley W, Falck-Ytter C, Carrasco-Labra A, et al. AGA Clinical Practice Guidelines on the Laboratory Evaluation of Functional Diarrhea and Diarrhea-Predominant Irritable Bowel Syndrome in Adults (IBS-D). Gastroenterology. 2019;157(3):851-854.
4. Bonis PA, LaMont JT, Approach to the patient with chronic diarrhea in resource rich settings In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA (accessed on June 26, 2026).
5. Schiller, LR, Pardi, DS, Sellin, JH, Chronic Diarrhea, Diagnosis and Management, Clinical Gastroenterology and Hepatology; February 2017; Vol 15, Issue 2, 182-193.
6. Gunn D, Topan R, Barnard L, et al. Randomised, placebo-controlled trial and meta-analysis show benefit of ondansetron for irritable bowel syndrome with diarrhoea: The TRITON trial. Alimentary Pharmacology and Therapeutics. June 2023, Volume57, Issue11, 1258-1271; <https://doi.org/10.1111/apt.17426>Digital Object Identifier (DOI)

