Chapter 23: Diarrhea

INTRODUCTION

- *Diarrhea* is an increased frequency and decreased consistency of fecal discharge as compared with an individual's normal bowel pattern. Diarrhea can be thought of as both a symptom and a sign of a systemic disease.
- Acute diarrhea is commonly defined as shorter than 14 days' duration, persistent diarrhea as longer than 14 days' duration, and chronic diarrhea as longer than 30 days' duration. Most cases of acute diarrhea are caused by infections with viruses, bacteria, or protozoa, and are generally self-limited.

PATHOPHYSIOLOGY

- Although viruses are more commonly associated with acute gastroenteritis, bacteria are responsible for more cases of acute diarrhea. Common causative bacterial organisms include *Shigella*, *Salmonella*, *Campylobacter*, *Staphylococcus*, and *Escherichia coli*. Acute viral infections are attributed mostly to the Norwalk and rotavirus groups.
- Diarrhea is an imbalance in absorption and secretion of water and electrolytes. It may be associated with a specific disease of the gastrointestinal (GI) tract or with a disease outside the GI tract.
- Four general pathophysiologic mechanisms disrupt water and electrolyte balance, leading to diarrhea: (1) a change in active ion transport by either decreased sodium absorption or increased chloride secretion, (2) a change in intestinal motility, (3) an increase in luminal osmolarity, and (4) an increase in tissue hydrostatic pressure. These mechanisms have been related to four broad clinical diarrheal groups: secretory, osmotic, exudative, and altered intestinal transit.
- Secretory diarrhea occurs when a stimulating substance (eg, vasoactive intestinal peptide [VIP] from a pancreatic tumor, unabsorbed dietary fat in steatorrhea, laxatives, hormones [such as secretion], bacterial toxins, and excessive bile salts) increases secretion or decreases absorption of large amounts of water and electrolytes.
- Inflammatory diseases of the GI tract can cause exudative diarrhea by discharge of mucus, proteins, or blood into the gut. With altered intestinal transit, intestinal motility is altered by reduced contact time in the small intestine, premature emptying of the colon, or bacterial overgrowth.

CLINICAL PRESENTATION

- Acute diarrhea is usually self-limiting and subsides within 72 hours of onset, whereas chronic diarrhea involves frequent attacks over extended time periods. However, infants, young children, the elderly, and debilitated persons are at risk for morbid and mortal events in prolonged or voluminous diarrhea.
- Signs and symptoms include:
    - ✔ Abrupt onset of nausea, vomiting, abdominal pain, headache, fever, chills, and malaise
    - ✔ Bowel movements are frequent and never bloody, and diarrhea lasts 12–60 hours
    - ✔ Intermittent periumbilical or lower right quadrant pain with cramps and audible bowel sounds is characteristic of small intestinal disease
    - ✔ When pain is present in large intestinal diarrhea, it is a gripping, aching sensation with tenesmus (straining, ineffective, and painful

stooling)

✔ In chronic diarrhea, a history of previous bouts, weight loss, anorexia, and chronic weakness are important findings

- Physical examination typically demonstrates hyperperistalsis with borborygmi and generalized or local tenderness.
- Laboratory tests:

  ✔ Stool analysis studies include examination for microorganisms, blood, mucus, fat, osmolality, pH, electrolyte and mineral concentration, and cultures

  ✔ Stool test kits are useful for detecting GI viruses, particularly rotavirus

  ✔ Antibody serologic testing shows rising titers over a 3- to 6-day period, but this test is not practical and is nonspecific

  ✔ Occasionally, total daily stool volume is also determined

  ✔ Direct endoscopic visualization and biopsy of the colon may be undertaken to assess for the presence of conditions such as colitis or cance

- Radiographic studies are helpful in neoplastic and inflammatory conditions.
- Many agents, including antibiotics and other drugs, cause diarrhea (**Table 23-1**). Laxative abuse for weight loss may also result in diarrhea.

TABLE 23-1

Drugs Causing Diarrhea

Laxatives
Antacids containing magnesium
Antineoplastics
Auranofin (gold salt)
Antibiotics
- Clindamycin
- Tetracyclines
- Sulfonamides
- Any broad-spectrum antibiotic

Antihypertensives
- Reserpine
- Guanethidine
- Methyldopa
- Guanabenz
- Guanadrel
- Angiotensin-converting enzyme inhibitors

Cholinergics
- Bethanechol
- Neostigmine

Cardiac agents
- Quinidine
- Digitalis
- Digoxin

Nonsteroidal anti-inflammatory drugs
Misoprostol
Colchicine
Proton pump inhibitors
H_2-receptor blockers

TREATMENT

- Goals of Treatment: To manage the diet, prevent excessive water, electrolyte, and acid–base disturbances; provide symptomatic relief; treat curable causes of diarrhea; and manage secondary disorders causing diarrhea. Diarrhea, like a cough, may be a body defense mechanism for ridding itself of harmful substances or pathogens. The correct therapeutic response is not necessarily to stop diarrhea at all costs. If diarrhea is secondary to another illness, controlling the primary condition is necessary.

General Approach to Treatment

- Management of the diet is a first priority for treatment of diarrhea (**Figs. 23-1** and **23-2**). Most clinicians recommend stopping solid foods for 24 hours and avoiding dairy products.

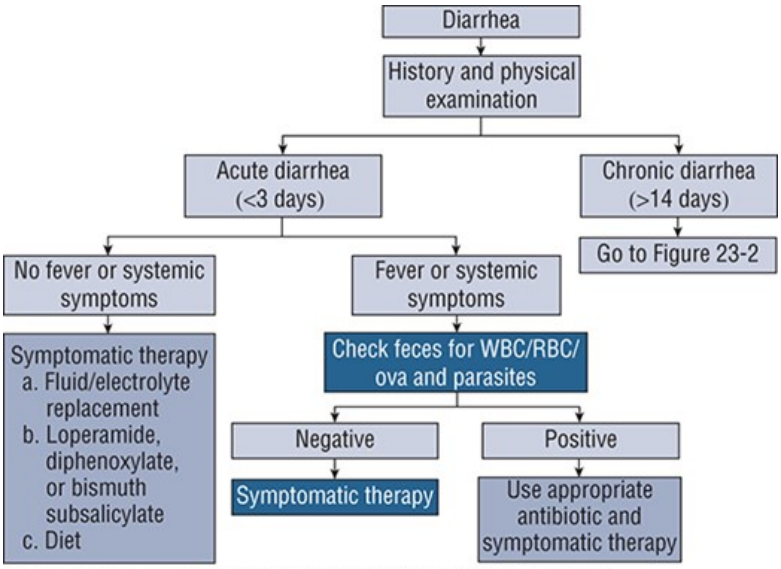
- Dietary management is a first priority in the treatment of diarrhea. Feeding should continue in children with acute bacterial diarrhea.

- If vomiting is present and is uncontrollable with antiemetics, nothing is taken by mouth. As bowel movements decrease, a bland diet is begun.
- Rehydration and maintenance of water and electrolytes are the primary treatment measures until the diarrheal episode ends. If vomiting and dehydration are not severe, enteral feeding is the less costly and preferred method. In the United States, many commercial oral rehydration preparations are available (**Table 23-2**). The WHO now recommends an oral rehydration solution (ORS) with a lower osmolarity, sodium content, and glucose load (see **Table 23-2**).
- Oral supplementation of zinc 20 mg daily for 10 days in addition to ORS significantly reduces the severity and duration of acute diarrhea in developing countries.

FIGURE 23-1

Recommendations for treating acute diarrhea. Follow these steps: (1) Perform a complete history and physical examination. (2) Is the diarrhea acute or chronic? If chronic diarrhea, go to Figure 23-2. (3) If acute diarrhea, check for fever and/or systemic signs and symptoms (ie, toxic patient). If systemic illness (fever, anorexia, or volume depletion), check for an infectious source. If positive for infectious diarrhea, use the appropriate antibiotic/anthelmintic drug and symptomatic therapy. If negative for infectious cause, use only symptomatic treatment. (4) If no systemic findings, use symptomatic therapy based on severity of volume depletion, oral or parenteral fluid/electrolytes, antidiarrheal agents (see Table 23-3), and diet.

(RBC, red blood cells; WBC, white blood cells.)

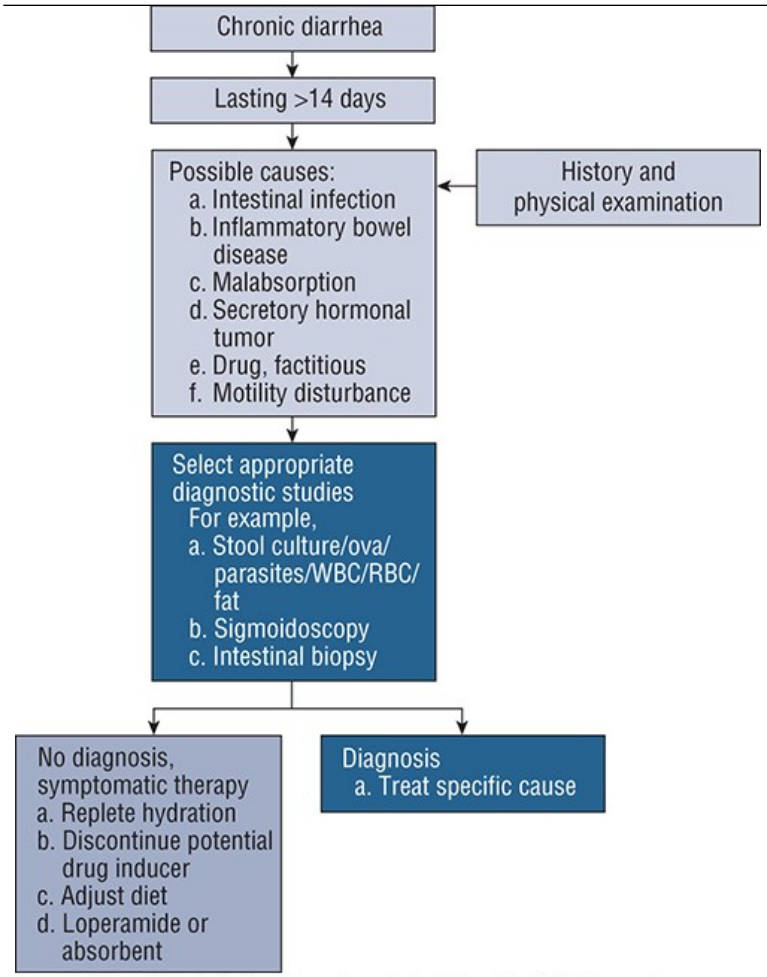


Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

FIGURE 23-2

Recommendations for treating chronic diarrhea. Follow these steps: (1) Perform a careful history and physical examination. (2) The possible causes of chronic diarrhea are many. These can be classified into intestinal infections (bacterial or protozoal), inflammatory disease (Crohn disease or ulcerative colitis), malabsorption (lactose intolerance), secretory hormonal tumor (intestinal carcinoid tumor or vasoactive intestinal peptide [VIP]–secreting tumors), drug (antacid), factitious (laxative abuse), or motility disturbance (diabetes mellitus, irritable bowel syndrome, or hyperthyroidism). (3) If the diagnosis is uncertain, appropriate diagnostic studies should be ordered. (4) Once diagnosed, treatment is planned for the underlying cause with symptomatic antidiarrheal therapy. (5) If no specific cause can be identified, symptomatic therapy is prescribed.

(RBC, red blood cells; WBC, white blood cells.)



Source: Terry L. Schwinghammer, Joseph T. DiPiro, Vicki L. Ellingrod, Cecily V. DiPiro: *Pharmacotherapy Handbook, 11e*

TABLE 23-2

Oral Rehydration Solutions

	WHO-ORSYT[a]	Pedialyte[b] (Ross)	CeraLyte (Cera Products)	Enfalyte (Mead Johnson)
Osmolality (mOsm/kg or mmol/kg)	245	250	220	167
Carbohydrates[b] (g/L)	13.5	25	40[c]	30[c]
Calories (cal/L [J/L])	65 (272)	100 (418)	160 (670)	126 (527)
Electrolytes (mEq/L; mmol/L)				
Sodium	75	45	50–90	50
Potassium	20	20	20	25
Chloride	65	35	40–80	45
Citrate	—	30	30	34
Bicarbonate	30	—	—	—
Calcium	—	—	—	—
Magnesium	—	—	—	—
Sulfate	—	—	—	—
Phosphate	—	—	—	—

[a]World Health Organization reduced osmolarity oral rehydration solution.

[b]Carbohydrate is glucose.

[c]Rice syrup solids are carbohydrate source.

Pharmacologic Therapy

- Drugs used to treat diarrhea (**Table 23-3**) are grouped into several categories: antimotility, adsorbents, antisecretory compounds, antibiotics, enzymes, and intestinal microflora. Usually, these drugs are not curative but palliative.
- Opiates and opioid derivatives delay the transit of intraluminal content or increase gut capacity, prolonging contact and absorption. The limitations of the opiates are addiction potential (a real concern with long-term use) and worsening of diarrhea in selected infectious diarrheas.
- **Loperamide** is often recommended for managing acute (including traveler's diarrhea) and chronic diarrhea. Diarrhea lasting 48 hours beyond initiating loperamide warrants medical attention.
- **Diphenoxylate and difenoxin (a diphenoxylate derivative)** are combined with **atropine** and have the same uses, precautions, and side effects.

- **Bismuth subsalicylate** is often used for treatment or prevention of diarrhea (traveler's diarrhea) and has antisecretory, anti-inflammatory, and antibacterial effects. Bismuth subsalicylate contains multiple components that might be toxic if given in excess to prevent or treat diarrhea.

- **Probiotics**, including microorganisms such as *Saccharomyces boulardii*, *Lactobacillus* GG, and *Lactobacillus acidophilus* decrease the duration of infectious and antibiotic-induced diarrhea in adults and children. The dosage of probiotic preparations varies depending on the brand used. Intestinal flatus is the primary patient complaint experienced with this modality.

- **Octreotide**, a synthetic octapeptide analogue of endogenous somatostatin, is prescribed for the symptomatic treatment of carcinoid tumors and other peptide secreting tumors, dumping syndrome, and chemotherapy-induced diarrhea. The dosage range for managing diarrhea associated with carcinoid tumors is 100–600 mcg daily in two to four divided doses, subcutaneously, for 2 weeks. Octreotide is associated with adverse effects such as cholelithiasis, nausea, diarrhea, and abdominal pain.

- Vaccines. An oral vaccine for cholera (Vaxchora®) is licensed and available in the United States. The Advisory Committee for Immunization Practices (ACIP) recommends the vaccine for adults aged 18–64 years old who are traveling to an endemic area. Two orally administered rotavirus vaccines (RotaTeq and Rotarix) prevent gastroenteritis due to rotavirus infection in infants and children.

TABLE 23-3

Selected Antidiarrheal Preparations

	Dose Form	Adult Dose
Antimotility		
Diphenoxylate	2.5 mg/tablet 2.5 mg/5 mL	5 mg four times daily; do not exceed 20 mg/day
Loperamide	2 mg/capsule	Initially 4 mg, and then 2 mg after each loose stool; do not exceed 16 mg/day
Paregoric	2 mg/5 mL (morphine)	5–10 mL one to four times daily
Opium tincture	10 mg/mL (morphine)	0.6 mL four times daily
Difenoxin	1 mg/tablet	Two tablets, and then one tablet after each loose stool; up to eight tablets per day
Antisecretory		
Bismuth subsalicylate	1050 mg/30 mL 262 mg/15 mL 524 mg/15 mL 262 mg/tablet	Two tablets or 30 mL every 30 minutes to 1 hour as needed up to eight doses per day
Enzymes (lactase)		
	1250 neutral lactase units/4 drops	Three to four drops taken with milk or dairy product
	3300 FCC lactase units per tablet	
Bacterial replacement (*Lactobacillus acidophilus*, *Lactobacillus bulgaricus*)		Two tablets or one granule packet three to four times daily; give with milk, juice, or water
Octreotide	0.05 mg/mL 0.1 mg/mL 0.5 mg/mL	Initial: 50 mcg subcutaneously One to two times per day and titrate dose based on indication up to 600 mcg/day in two to four divided doses

EVALUATION OF THERAPEUTIC OUTCOMES

- Therapeutic outcomes are directed to key symptoms, signs, and laboratory studies. The constitutional symptoms usually improve within 24–72 hours. Monitoring for changes in the frequency and character of bowel movements on a daily basis in conjunction with vital signs and improvement in appetite are of utmost importance.

- Monitor body weight, serum osmolality, serum electrolytes, complete blood cell count, urinalysis, and cultures (if appropriate). With an urgent or emergency situation, any change in the volume status of the patient is the most important outcome.
- In the urgent/emergent situation, restoration of the patient's volume status is the most important outcome. Toxic patients (fever dehydration, hematochezia, or hypotension) require hospitalization, IV fluids and electrolyte administration, and empiric antibiotic therapy while awaiting culture and sensitivity results. With timely management, these patients usually recover within a few days.

See Chapter 53, Diarrhea, Constipation, and Irritable Bowel Syndrome, authored by Patricia H. Fabel and Kayce M. Shealy, for a more detailed discussion of this topic.