febrile dysentery, which may be exacerbated or prolonged by them. Bismuth subsalicylate may reduce symptoms of vomiting and diarrhea but should not be used to treat immunocompromised patients or those with renal impairment because of the risk of bismuth encephalopathy.

Judicious use of antibiotics is appropriate in selected instances of acute diarrhea and may reduce its severity and duration (Fig. 55-2). Many physicians treat moderately to severely ill patients with febrile dysentery empirically without diagnostic evaluation using a quinolone, such as ciprofloxacin (500 mg bid for 3–5 d). Empirical treatment can also be considered for suspected giardiasis with metronidazole (250 mg qid for 7 d). Selection of antibiotics and dosage regimens are otherwise dictated by specific pathogens, geographic patterns of resistance, and conditions found **(Chaps. 160, 186, and 190–196)**. Antibiotic coverage is indicated, whether or not a causative organism is discovered, in patients who are immunocompromised, have mechanical heart valves or recent vascular grafts, or are elderly. Bismuth subsalicylate may reduce the frequency of traveler's diarrhea. Antibiotic prophylaxis is only indicated for certain patients traveling to high-risk countries in whom the likelihood or seriousness of acquired diarrhea would be especially high, including those with immunocompromise, IBD, hemochromatosis, or gastric achlorhydria. Use of ciprofloxacin, azithromycin, or rifaximin may reduce bacterial diarrhea in such travelers by 90%, though rifaximin is not suitable for invasive disease, but rather as treatment for uncomplicated traveler's diarrhea. Finally, physicians should be vigilant to identify if an outbreak of diarrheal illness is occurring and to alert the public health authorities promptly. This may reduce the ultimate size of the affected population.

## CHRONIC DIARRHEA

Diarrhea lasting >4 weeks warrants evaluation to exclude serious underlying pathology. In contrast to acute diarrhea, most of the causes of chronic diarrhea are noninfectious. The classification of chronic diarrhea by pathophysiologic mechanism facilitates a rational approach to management, although many diseases cause diarrhea by more than one mechanism **(Table 55-3)**.

**Secretory Causes** Secretory diarrheas are due to derangements in fluid and electrolyte transport across the enterocolonic mucosa. They are characterized clinically by watery, large-volume fecal outputs that are typically painless and persist with fasting. Because there is no malabsorbed solute, stool osmolality is accounted for by normal endogenous electrolytes with no fecal osmotic gap.

***MEDICATIONS*** Side effects from regular ingestion of drugs and toxins are the most common secretory causes of chronic diarrhea. Hundreds of prescription and over-the-counter medications (see earlier section, "Acute Diarrhea, Other Causes") may produce diarrhea. Surreptitious or habitual use of stimulant laxatives (e.g., senna, cascara, bisacodyl, ricinoleic acid [castor oil]) must also be considered. Chronic ethanol consumption may cause a secretory-type diarrhea due to enterocyte injury with impaired sodium and water absorption as well as rapid transit and other alterations. Inadvertent ingestion of certain environmental toxins (e.g., arsenic) may lead to chronic rather than acute forms of diarrhea. Certain bacterial infections may occasionally persist and be associated with a secretory-type diarrhea.

***BOWEL RESECTION, MUCOSAL DISEASE, OR ENTEROCOLIC FISTULA*** These conditions may result in a secretory-type diarrhea because of inadequate surface for reabsorption of secreted fluids and electrolytes. Unlike other secretory diarrheas, this subset of conditions tends to worsen with eating. With disease (e.g., Crohn's ileitis) or resection of <100 cm of terminal ileum, dihydroxy bile acids may escape absorption and stimulate colonic secretion (cholerheic diarrhea). This mechanism may contribute to so-called *idiopathic secretory diarrhea or bile acid diarrhea (BAD)*, in which bile acids are functionally malabsorbed from a normal-appearing terminal ileum. This *idiopathic bile acid malabsorption (BAM)* may account for an average of 40% of unexplained chronic diarrhea. Reduced negative feedback regulation of bile acid synthesis in hepatocytes by fibroblast growth factor 19 (FGF-19) produced by ileal enterocytes results in a degree of bile-acid synthesis that exceeds the normal capacity for ileal reabsorption, producing BAD. An alternative cause of BAD is a genetic variation in the receptor proteins (β-klotho and fibroblast growth factor 4) on the hepatocyte that normally mediate the effect of FGF-19. Dysfunction of these proteins prevents FGF-19 inhibition of hepatocyte bile acid synthesis.

Partial bowel obstruction, ostomy stricture, or fecal impaction may paradoxically lead to increased fecal output due to fluid hypersecretion.

***HORMONES*** Although uncommon, the classic examples of secretory diarrhea are those mediated by hormones. *Metastatic gastrointestinal*

**TABLE 55-3 MAJOR CAUSES OF CHRONIC DIARRHEA ACCORDING TO PREDOMINANT PATHOPHYSIOLOGIC MECHANISM**

| |
|---|
| **Secretory Causes** |
| Exogenous stimulant laxatives |
| Chronic ethanol ingestion |
| Other drugs and toxins |
| Endogenous laxatives (dihydroxy bile acids) |
| Idiopathic secretory diarrhea or bile acid diarrhea |
| Certain bacterial infections |
| Bowel resection, disease, or fistula (↓ absorption) |
| Partial bowel obstruction or fecal impaction |
| Hormone-producing tumors (carcinoid, VIPoma, medullary cancer of thyroid, mastocytosis, gastrinoma, colorectal villous adenoma) |
| Addison's disease |
| Congenital electrolyte absorption defects |
| **Osmotic Causes** |
| Osmotic laxatives ($Mg^{2+}$, $PO_4^{-3}$, $SO_4^{-2}$) |
| Lactase and other disaccharide deficiencies |
| Nonabsorbable carbohydrates (sorbitol, lactulose, polyethylene glycol) |
| Gluten and FODMAP intolerance |
| **Steatorrheal Causes** |
| Intraluminal maldigestion (pancreatic exocrine insufficiency, bacterial overgrowth, bariatric surgery, liver disease) |
| Mucosal malabsorption (celiac sprue, Whipple's disease, infections, abetalipoproteinemia, ischemia, drug-induced enteropathy) |
| Postmucosal obstruction (1° or 2° lymphatic obstruction) |
| **Inflammatory Causes** |
| Idiopathic inflammatory bowel disease (Crohn's, chronic ulcerative colitis) |
| Lymphocytic and collagenous colitis |
| Immune-related mucosal disease (1° or 2° immunodeficiencies, food allergy, eosinophilic gastroenteritis, graft-versus-host disease) |
| Infections (invasive bacteria, viruses, and parasites, Brainerd diarrhea) |
| Radiation injury |
| Gastrointestinal malignancies |
| **Dysmotile Causes** |
| Irritable bowel syndrome (including postinfectious IBS) |
| Visceral neuromyopathies |
| Hyperthyroidism |
| Drugs (prokinetic agents) |
| Postvagotomy |
| **Factitial Causes** |
| Munchausen |
| Eating disorders |
| **Iatrogenic Causes** |
| Cholecystectomy |
| Ileal resection |
| Bariatric surgery |
| Vagotomy, fundoplication |

***Abbreviation:*** FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.