Chapter 18
Chronic Diarrhea

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Case Study

A 58-year-old woman presents to clinic for the evaluation of a 4-month history of progressive diarrhea. She describes 6–8 watery bowel movements each day without abdominal pain. She notes urgency, occasional incontinence, and nocturnal stools at least twice weekly. She denies symptoms of hematochezia, melena, weight loss, or fever. She has not had any recent hospitalizations, medication changes, foreign travel, or exposure to antibiotics or sick contacts. Her past medical history is significant for Hashimoto's thyroiditis, depression, and osteoarthritis. She has had a cholecystectomy. Medications include levothyroxine, fluoxetine, and ibuprofen as needed. There is no family history of inflammatory bowel disease, celiac disease, or gastrointestinal neoplasia. She consumes one glass of wine daily. Review of systems is negative for ocular complaints, arthralgias, back pain, or skin rashes. A screening colonoscopy at age 50 was normal.

On examination, she is afebrile, with normal blood pressure and pulse and without orthostatic changes. Oral mucous membranes are moist, while a skin exam is negative for rashes or lesions. Her thyroid is normal size on palpation. Her cardiopulmonary exam is within normal limits, while examination of her abdomen reveals a scar, but is otherwise soft and non-tender. Rectal examination is notable for normal perineal sensation, resting tone, and squeeze tone, with no palpable masses or impacted stool. The remainder of the examination is normal.

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Laboratory studies reveal a normal complete blood count, thyroid-stimulating hormone, IgA tissue transglutaminase antibody, and C-reactive protein. Stool studies, including bacterial cultures and ova and parasite exam, are negative. Colonoscopy shows normal colonic mucosa, with random biopsies noting increased intraepithelial and lamina propria lymphocytes, with a thickened subepithelial collagen band.

Introduction

Diarrhea is common in clinical practice, and the ability to evaluate a patient who presents with diarrhea requires an understanding of the definition, pathophysiology, differential diagnoses, testing algorithms, and management strategies.

Diarrhea can be defined in various ways (see Table 18.1), but generally is considered to represent an increase in frequency and/or fluidity of stool. Since stool weight is proportionally related to fiber intake, stool weight in excess of 200 g daily should be used with caution as the sole defining criteria of "diarrhea." Chronic diarrhea has been defined as diarrhea lasting in excess of 4 weeks, whereas acute diarrhea typically lasts less than 2 weeks and is often self-limited.

Establishing the chronicity of diarrhea can help narrow the diagnostic considerations and facilitate testing strategies. Given the broad differential diagnosis that needs to be considered in a patient with chronic diarrhea (see Table 18.2), a thorough history is one of the most important parts of the diagnostic evaluation and allows the provider to approach the work-up in a stepwise, high-value, cost-conscious approach.

Epidemiology

The prevalence of chronic diarrhea is directly related to hygiene and sanitation practices and, therefore, varies widely throughout the world. The prevalence of chronic diarrhea in developed countries is 3–5 % but has been reported in up to 18 %

Table 18.1 Definitions of diarrhea

Stool frequency	>3 bowel movements daily
Stool weight	>200 g of stool daily
Stool form	Bristol stool type 6 (mushy) or 7 (watery)
Functional diarrhea	Loose (mushy) or watery stools without pain occurring in at least 75 % of stools[a]
Irritable bowel syndrome	Recurrent abdominal pain or discomfort at least 3 days/month associated with 2 or more of the following:[a] • Improvement with defecation • Onset associated with a change in stool frequency • Onset associated with a change in form (appearance) of stool

[a]Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Table 18.2 Differential diagnosis of chronic diarrhea

Category	Conditions[a]
Functional bowel disorders	Functional diarrhea
	Diarrhea-predominant IBS
	Mixed-type IBS
Medications	Antibiotics
	Metformin
	NSAIDs
	Proton pump inhibitors
	Colchicine
	Chemotherapeutic agents
	Others
Infection	Giardiasis
	Strongyloides
	Yersinia
	Mycobacteria
	Clostridium difficile
	Other parasites and bacteria
	Human immunodeficiency virus
Carbohydrate malabsorption	Lactose
	Fructose
	Sucrose
Other osmotic etiologies	Magnesium-containing antacids
	Sorbitol-containing elixirs
	Artificial sweeteners (xylitol, mannitol, others)
	Others (phosphates, sulfates)
	Iatrogenic (lactulose, polyethylene glycol)
Pancreatic insufficiency	Chronic pancreatitis
	Cystic fibrosis
Small bowel mucosal disorders	Celiac disease
	Collagenous sprue
	Tropical sprue
	Small intestinal bacterial overgrowth
	Autoimmune enteropathy
	Eosinophilic gastroenteritis
Inflammatory bowel disease	Ulcerative colitis
	Crohn's disease
	Microscopic colitis
Infiltrative disorders	Amyloid
	Whipple's disease
Bile salt abnormalities	Postcholecystectomy
	Terminal ileal resection
	Biliary obstruction

(continued)

Table 18.2 (continued)

Category	Conditions[a]
Protein-losing enteropathies	Menetrier's disease
	Lymphangiectasia (primary/secondary)
	Retroperitoneal fibrosis
	Lymphoma
Endocrine disorders	Hyperthyroidism
	Adrenal insufficiency
	Diabetes mellitus
Motility disorders	Scleroderma
	Paraneoplastic syndrome
	Idiopathic
Neuroendocrine tumors	Gastrinoma
	Carcinoid
	VIPoma
	Glucagonoma
	Thyroid medullary carcinoma (calcitonin)
Other	Short bowel syndrome
	Laxative abuse
	Radiation enteritis/colitis/proctitis
	Chronic mesenteric ischemia
	Graft-versus-host disease
	Idiopathic

IBS irritable bowel syndrome, *NSAIDs* nonsteroidal anti-inflammatory drugs, *VIP* vasoactive intestinal peptide

[a]Some conditions may belong in more than one category

of the population when "diarrhea" was more loosely defined. According to the World Health Organization, diarrhea affects 17 billion people annually and is the second leading cause of death worldwide in children less than 5 years of age. Within industrialized countries, chronic diarrhea is not associated with high mortality rates but is associated with decreased quality of life and significantly increased work and activity impairment compared to population norms. The economic impact of chronic diarrhea is difficult to measure; however, data from 1994 suggested that $350 million was lost annually due to time away from work. This amount is much greater today, especially if one adds the financial loss associated with diagnostic testing and management. The indication of "diarrhea" or "malabsorption" accounts for approximately 3 % of upper endoscopies, 7 % of colonoscopies, and 15 % of flexible sigmoidoscopies performed in the United States, not including those performed for a "change in bowel habits." In 2009, the symptom of diarrhea accounted for over four million outpatient visits in the United States, second only to abdominal pain as a gastrointestinal complaint, and was the leading gastrointestinal symptom used as a search term by Internet users.

Pathophysiology

Stool weight and fluidity are directly related to the amount of water in the stool. The underlying pathophysiology in chronic diarrhea is either due to an increase in intestinal secretion of water or a decrease in net absorption of water. The amount of intestinal fluid is also inversely proportional to intestinal transit time, so any alteration that decreases intestinal transit time will increase stool frequency and fluidity.

Diarrhea is commonly divided into osmotic and secretory types based upon the pathophysiology. Osmotic diarrhea results from either the ingestion of nonabsorbable, osmotically active substances or the lack of small bowel mucosal disaccharidases that aid in carbohydrate absorption. Since the small bowel works to maintain an iso-osmolar state (290 mOsm/kg), any osmotically active substance within the small bowel creates an efflux of water into the intestinal lumen resulting in diarrhea. Osmotic diarrhea improves with fasting or discontinuation of the offending agent. Secretory diarrhea can be caused from many things, but in the case of infectious etiologies with toxin production (a common phenomenon), stimulation of cAMP, cGMP, or calcium-mediated pathways results in a transition from net absorption to net secretion within the small bowel. This results in a large volume of liquid stool reaching the colon, overwhelming its absorptive capacity. In secretory diarrhea, stool volume tends to be high and is not affected by fasting.

Diarrhea can also be characterized on the basis of its underlying pathophysiology. Inflammatory causes of diarrhea typically cause either macroscopic or microscopic damage to the intestinal mucosa surface, decreasing the overall absorptive surface area of the bowel. Carbohydrate malabsorption causes an osmotically mediated diarrhea. Bacterial fermentation of undigested carbohydrates also causes an increase in intestinal gas production. Fat malabsorption can result from pancreatic lipase deficiency (e.g., chronic pancreatitis), inactivation of pancreatic enzymes as occurs with Zollinger–Ellison syndrome, small bowel mucosal diseases, or impairment in the enterohepatic circulation of bile (e.g., hepatic dysfunction, biliary obstruction, extensive terminal ileal resection or disease). With resection of <100 cm of terminal ileum, excess bile spills into the colon causing a secretory diarrhea, with subsequent liver upregulation of bile production to counteract intestinal loss and maintain an adequate bile salt pool. In contrast, as alluded to previously, with >100 cm of resected terminal ileum, the hepatic production of bile is inadequate to compensate for the degree of intestinal loss, resulting in bile salt deficiency and fat malabsorption from impaired micelle production, which is required for intestinal transport of long-chain triglycerides. Protein malabsorption rarely occurs in isolation, but can be seen with mucosal erosive diseases (e.g., inflammatory bowel disease [IBD], ischemia, graft-versus-host disease), nonerosive diseases with increased permeability (e.g., eosinophilic gastroenteritis, and celiac, Whipple's, and Menetrier's disease), or conditions with altered lymphatic drainage (e.g., right heart failure, constrictive pericarditis, lymphoma, retroperitoneal fibrosis, lymphangiectasia).

Despite the ability to characterize diarrhea based on pathophysiology, this characterization is rarely pure, and many conditions will often have more than one mechanism involved in causing diarrhea.

Diagnosis and Evaluation

The diagnostic approach to the patient with chronic diarrhea (see Fig. 18.1) begins with a detailed clinical history, noting the timing and features at onset, and the relationship to other events (e.g., surgery, new medications, self-limited illness, ingestion of specific foods). The frequency and pattern (e.g., postprandial, nocturnal) of bowel movements should be obtained. Details on stool characteristics should be reviewed including the presence of blood, which may indicate an infectious or inflammatory condition, or an oily appearance, which may be evidence of fat malabsorption. Small, low-volume frequent stools may imply a distal colonic or rectal disorder, while large-volume watery stools imply a small bowel disorder. Patients should be asked about the presence of fecal incontinence, although it should be noted that not all patients with fecal incontinence have a primary diarrheal condition, as spinal cord injuries and anal sphincter defects may also cause incontinence. The presence of associated gastrointestinal and systemic symptoms should be noted. The patient's past medical history should be reviewed for evidence of autoimmune diseases (e.g., celiac disease, thyroid dysfunction, diabetes mellitus, adrenal insufficiency, microscopic colitis), immunosuppression (e.g., human immunodeficiency virus, chemotherapy, medication-induced), abdominopelvic radiation (e.g., colorectal,

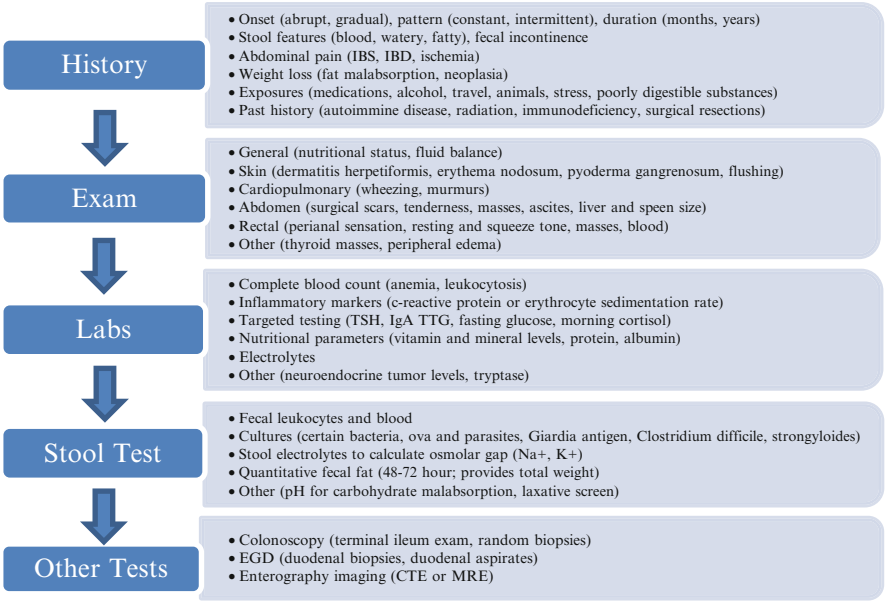

Fig. 18.1 Algorithmic approach in the evaluation of the patient with chronic diarrhea. Adapted from Schiller LR. Chronic diarrhea. Gastroenterology. 2004;127:287–93. *IBS* irritable bowel syndrome, *IBD* inflammatory bowel disease, *TSH* thyroid-stimulating hormone, *TTG* tissue transglutaminase, *Na+* sodium, *K+* potassium, *CTE* computed tomography enterography, *MRE* magnetic resonance enterography

cervical, or prostate cancer), and psychiatric conditions. Medications should be scrutinized, paying attention to timing of medication initiation, antibiotic use, and over-the-counter products (e.g., magnesium-containing antacids, herbal products containing laxatives, nonsteroidal anti-inflammatory drugs [NSAIDs]). The patient's surgical history should be reviewed for prior intestinal resections (including bowel segment and length removed), creation of blind loops of bowel (a risk factor for SIBO (small intestinal bacterial overgrowth)), and pancreaticobiliary surgeries. A family history of gastrointestinal and other relevant disorders should be obtained. Social history should focus on excessive alcohol consumption (pancreatic insufficiency), infectious exposures (e.g., daycare setting, animals, water sources), travel history, sexual preference, and dietary behavior patterns (e.g., excessive caffeine intake or gum chewing, ingestion of sugar-free foods or sugar substitutes). Review of systems should include asking about fever, which may indicate an inflammatory or infectious condition; weight loss; extraintestinal manifestations of IBD (e.g., pyoderma gangrenosum, erythema nodosum, ankylosing spondylitis, sacroiliitis, uveitis, or episcleritis); and celiac disease (e.g., dermatitis herpetiformis, infertility, premature metabolic bone disease, iron deficiency anemia).

The examination of a patient with chronic diarrhea is useful in assessing the nutritional status of the patient (e.g., muscle wasting, low body mass index) and evaluating for evidence of dehydration (e.g., orthostasis, dry mucous membranes, skin tenting). Occasionally, clues to a specific diagnosis can be found on examination of the skin. On abdominal examination, tenderness, fullness, and hepatomegaly should be noted as these may be signs of neoplasia, Crohn's disease, a neuroendocrine tumor, amyloid, or other infiltrative disorders. Perianal examination is important to assess for intact sensation and tone, presence of fissures or fistulae, and to rule out mass lesions or stool impaction.

The diagnostic evaluation of a patient with chronic diarrhea needs to be tailored based on the historical details obtained and the conditions that are most likely (see Table 18.3). Irritable bowel syndrome (IBS) is the most common cause of chronic diarrhea in Western societies. The diagnosis of IBS can be made in patients with abdominal pain and altered bowel movements in the absence of alarm features with little exclusionary testing (see Fig. 18.2). Given that the prevalence of celiac disease is 0.41–1.0 % and many of these patients fulfill the Rome criteria for IBS, many experts suggest that all patients with diarrhea-predominant IBS (or those with a mixed bowel pattern) be serologically tested for celiac disease, although prospective studies to validate this practice have not been performed. Similarly, some patients with microscopic colitis fulfill the Rome criteria, a fact that must be considered in patients who do not respond to antidiarrheal therapy, and in those with more recent onset of diarrhea, especially in older patients.

Laboratory testing for patients with chronic diarrhea needs to be logical and individually tailored and may include one or more of the following: complete blood count (to assess for anemia or leukocytosis), serum electrolytes (to evaluate for metabolic acidosis, hypokalemia, hyponatremia), IgA tissue transglutaminase antibody (to screen for celiac disease), C-reactive protein, endocrine testing (e.g., sensitive thyroid-stimulating hormone, fasting glucose, morning cortisol), serum protein

Table 18.3 Diagnostic testing in chronic diarrhea

Categories	Associated conditions	Diagnostic tests
Functional	Irritable bowel syndrome (diarrhea, mixed) Functional diarrhea	Clinical diagnoses; consider excluding celiac disease (see below)
Osmotic	Carbohydrate malabsorption Sugar alcohol consumption Magnesium-containing products	Breath testing (lactose, fructose, sucrose); stool pH <6 Avoidance trial after careful history (sugar-free substances, elixirs) Avoidance of offending medication; stool magnesium (factitious)
Secretory	Infections Bile-acid induced diarrhea Neuroendocrine tumors Motility disorders	Stool cultures (including parasites); often negative Trial of cholestyramine Gastrin, VIP, calcitonin, urine 5-HIAA Transit tests; fasting glucose (diabetes); anti-scl70 (scleroderma)
Inflammatory	Inflammatory bowel disease • Ulcerative colitis • Crohn's disease • Microscopic colitis Chronic mesenteric ischemia Infection	Combination of clinical, endoscopic, histologic, and radiographic • Colonoscopy (biopsies) • Colonoscopy (biopsies) and enterography imaging (CTE or MRE) • Flexible sigmoidoscopy or colonoscopy (biopsies) Mesenteric ultrasound; CTA; MRA; angiography Stool cultures
Malabsorptive	Fat malabsorption • Pancreatic insufficiency • Celiac disease • Small intestinal bacterial overgrowth Carbohydrate malabsorption Protein malabsorption	Quantitative fecal fat (48–72 h) • Imaging (CT, EUS); pancreas function tests; empiric enzymes • Celiac serology (TTG) and duodenal biopsies • Small bowel aspirates; hydrogen breath test; empiric antibiotics Breath testing (lactose, fructose, sucrose); stool pH <6 Alpha-1 antitrypsin stool clearance

VIP vasoactive intestinal peptide, *5-HIAA* 5-hydroxyindolacetic acid, *CTE* computed tomography enterography, *MRE* magnetic resonance enterography, *CTA* computed tomography angiography, *MRA* magnetic resonance angiography, *CT* computed tomography, *EUS* endoscopic ultrasound, *TTG* tissue transglutaminase

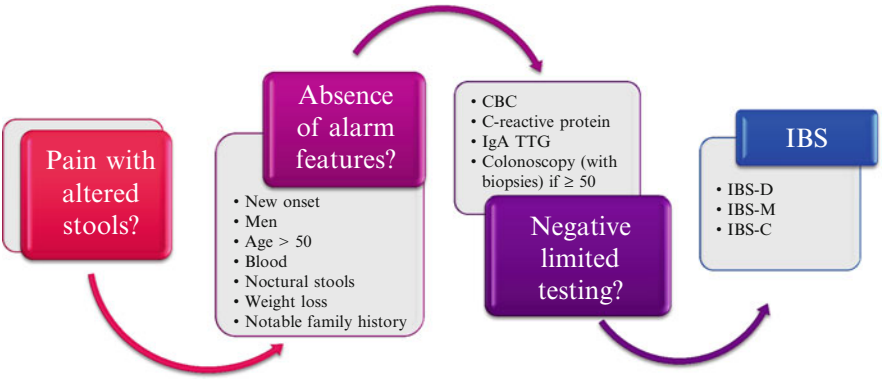

Fig. 18.2 Algorithmic approach in the diagnosis of irritable bowel syndrome. Adapted from: Spiller RC, Thompson WG. Bowel disorders. Am J Gastroenterol. 2010;105:775–85. *CBC* complete blood count, *TTG* tissue transglutaminase, *IBS* irritable bowel syndrome, *IBS-D* diarrhea-predominant, *IBS-M* mixed type, *IBS-C* constipation-predominant

electrophoresis, and, occasionally, an assessment of micronutrients (e.g., vitamin B12, vitamin D, iron, folate). The pattern of low vitamin B12 and elevated serum folate may be seen in SIBO. While a number of other laboratory studies can be considered, they should only be performed when the clinical suspicion of the associated disease states is high—such as serum tryptase (mastocytosis), gastrin (gastrinoma), vasoactive intestinal peptide (VIPoma), calcitonin (medullary carcinoma of the thyroid), urinary 5-hydroxyindolacetic acid (carcinoid), and plasma and urinary metanephrines (pheochromocytoma). It is important to recognize that because these conditions are rare, if these tests are performed indiscriminately, a positive test is more likely to be false positive than true positive.

During the evaluation for chronic diarrhea, a number of stool tests can be considered. Stool tests for inflammation including fecal leukocytes, calprotectin, or lactoferrin are easily performed. Stool cultures are usually sent to check for general enteric pathogens; however, atypical organisms including *Yersinia*, *Aeromonas*, *Plesiomonas*, and mycobacteria should be considered as well in the appropriate setting. Testing for *Clostridium difficile*, ideally with polymerase chain reaction, should be performed. Testing the stool for parasites such as *Giardia* and *Strongyloides* should be considered; in immunocompromised patients, additional parasitic studies should include those for cryptosporidia, *Cyclospora*, microspora, and *Cystoisospora*. Although uncommonly performed, a stool pH < 6 suggests carbohydrate malabsorption. Stool sodium and potassium may be useful to calculate the stool osmotic gap with the calculation as follows: 290 − 2[stool sodium + stool potassium]. A stool osmotic gap of ≥100 indicates an osmotic cause of diarrhea, whereas a gap ≤50 suggests a secretory cause of diarrhea. The gold standard test to document fat malabsorption is a quantitative fecal fat, often collected over 48–72 h while consuming a standardized high fat diet (e.g., 100 g daily) both before and during the collection. Fecal fat is considered normal if <7 g/daily, indeterminate if 7–14 g/daily, and abnormal if >14 g/daily.

An esophagogastroduodenoscopy (EGD) with small bowel biopsies should be considered in all patients with positive celiac serologies (see Fig. 18.3). Small bowel biopsies can also be used to diagnose Whipple's disease (positive periodic acid Schiff stain, negative acid fast stain, and positive polymerase chain reaction), amyloid (positive Congo red stain), autoimmune enteropathy (a celiac disease mimic), infectious conditions (*Giardia*, cryptosporidia), and other infiltrative processes. An EGD should, therefore, be considered in any patient with diarrhea and clinical or laboratory features of malabsorption. A colonoscopy with terminal ileal examination and random colonic biopsies should also be considered in all patients with chronic unexplained diarrhea, particularly where there is concern of IBD. Random colonic biopsies are essential in the diagnosis of microscopic colitis, which includes both lymphocytic and collagenous colitis types (see Fig. 18.4).

Small intestinal bacterial overgrowth can be diagnosed by quantitative culture of small bowel aspirates obtained during EGD ($>10^5$ colony-forming units/mL), by hydrogen breath tests (glucose or lactulose) or by evaluating response to an empiric antibiotic trial. Specific hydrogen breath tests (lactose, fructose, sucrose) can be performed to assess for specific carbohydrate malabsorption; a positive test is suggested by a rise usually greater than 10–20 parts per million in breath hydrogen due to colonic bacterial fermentation of the malabsorbed substance. Many factors can cause both false-positive and false-negative breath test results, however (see Chap. 11).

Abdominal imaging is typically reserved for patients where there is strong concern over a small bowel process (e.g., Crohn's disease, radiation enteritis) or complications thereof and also enables the assessment of altered small bowel fold patterns (seen in celiac disease) and other anatomic abnormalities (such as small bowel diverticula, which is a risk factor for SIBO). Additionally, cross-sectional abdominal imaging allows the pancreas to be viewed and assessed for pancreatic atrophy or calcifications (chronic pancreatitis) and tumors (neuroendocrine tumors). Small bowel barium radiography has largely been replaced by enterography imaging, either with computed tomography or magnetic resonance.

Treatment

The management of chronic diarrhea is directed at the underlying diagnosis uncovered during the course of the evaluation (see Table 18.4). For patients with functional diarrhea or IBS, reassurance should be provided, invasive or excessive testing should be avoided, and symptomatic treatment recommended. In cases where there is an exposure causing the diarrhea (e.g., lactose, medications), avoidance of the offending agent is recommended. Other patients will require disease-directed therapy (e.g., amyloid, IBD, celiac disease), while some may require surgery (neoplasia).

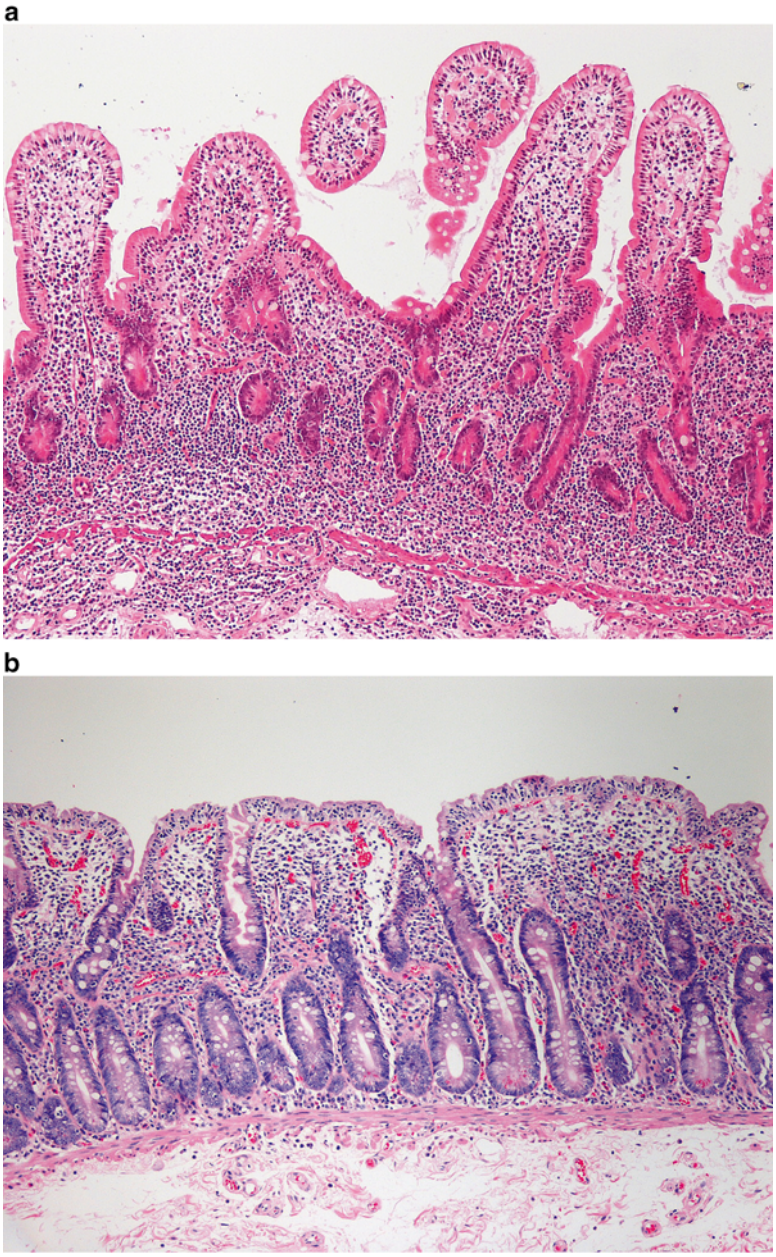

Fig. 18.3 Small bowel histology in celiac disease. Duodenal biopsy specimens showing: (**a**) partial villous atrophy, with a villous/crypt ratio of 1:1 and increased intraepithelial lymphocytes (40/100 surface epithelial cells); (**b**) total villous atrophy with markedly increased intraepithelial lymphocytes (>100/100 surface epithelial cells) (hematoxylin and eosin staining: original magnification ×100)

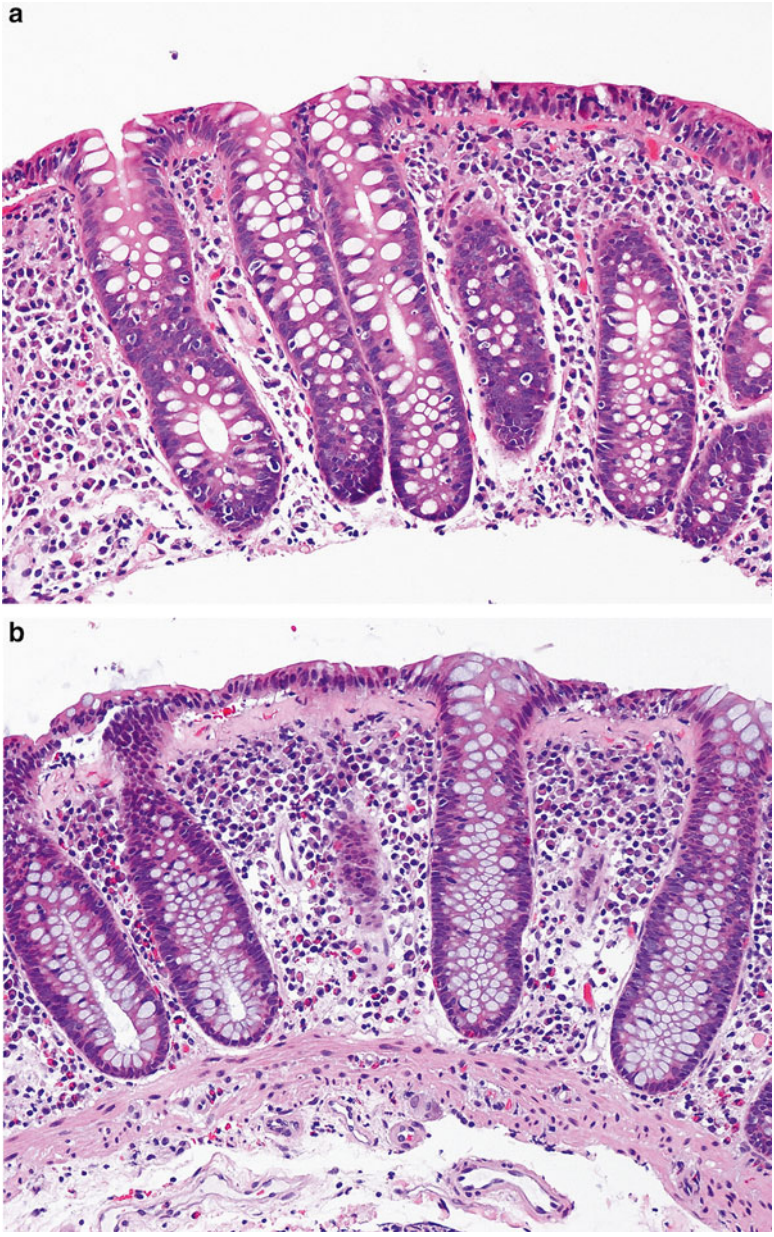

Fig. 18.4 Colonic histology in microscopic colitis. Colonic biopsy specimens showing: (**a**) lymphocytic colitis, with an inflamed lamina propria and increased intraepithelial lymphocytes within the surface and crypt epithelium; (**b**) collagenous colitis, with the surface epithelium containing increased intraepithelial lymphocytes and a thickened subepithelial collagen band measuring 40–50 μm (normal is 5 μm) (hematoxylin and eosin staining: original magnification ×200)

Table 18.4 Management options for chronic diarrhea

Diagnosis	Management
Irritable bowel syndrome	Fiber
	Loperamide
	Tricyclic antidepressants (low-dose)
	Rifaximin (non-FDA approved for IBS)
	Alosetron
Celiac disease	Gluten-free diet
	Vitamin and mineral replacement
	Assessment of bone mineral density
Small intestinal bacterial overgrowth	Rotating antibiotics
	Manage secondary lactose malabsorption
Microscopic colitis	Discontinue offending medications
	Loperamide
	Bismuth subsalicylate
	Budesonide
Ulcerative colitis	Mesalamine
	Immunomodulators (AZA, 6-MP)
	Biologic agents
Crohn's disease	Immunomodulators (AZA, 6-MP, MTX)
	Biologic agent
Pancreatic insufficiency	Modified fat diet
	Pancreatic enzyme replacement
Infectious	Antimicrobial therapy as indicated
	Manage postinfectious lactose malabsorption
	Manage postinfectious IBS
Medication-induced diarrhea	Discontinue or use lowest effective dose
	Loperamide as needed
Carbohydrate malabsorption	Reduce ingestion of offending agent
Bile salt-induced diarrhea	Cholestyramine
Bile salt deficiency	Medium-chain triglyceride-based diet
Others	Target treatment toward specific condition

IBS irritable bowel syndrome, *AZA* azathioprine, *6-MP* 6-mercaptopurine, *MTX* methotrexate

Case Resolution

The clinical presentation and diagnostic evaluation demonstrate typical features of collagenous colitis, a form of microscopic colitis. While the patient's age and underlying autoimmune thyroid disease are clues to the diagnosis, this condition is also associated with certain medication use. In this case, fluoxetine and nonsteroidal anti-inflammatory drug use has previously been implicated. Assessing the temporal association and the underlying necessity of each would be important. She was treated with a 2-month course of bismuth subsalicylate (three tablets three times daily) with a rapid return of her normal bowel pattern.

Key Clinical Teaching Points

- A careful clinical history is essential in the evaluation of the patient with chronic diarrhea in order to categorize features and approach the testing in an organized, cost-effective approach.
- Irritable bowel syndrome is the most common cause of chronic diarrhea and is a clinical diagnosis; minimal testing is required in the absence of alarm features.
- The evaluation of a patient with chronic diarrhea is individualized and stepwise and may include blood and stool testing, upper and lower endoscopy with histologic assessment, and radiographic imaging. Additional testing is reserved for those with negative first-line testing and targeted toward clinical features.

Teaching Questions

1. A 28-year-old woman presents to the clinic for an evaluation of diarrhea that has been present for more than 2 years. She reports 4–5 bowel movements daily without blood. She describes cramping abdominal pain that is relieved after a bowel movement. She complains of mild bloating but no nausea or vomiting. Her weight has been stable and she denies nocturnal diarrhea. Past medical history is notable for depression and chronic headaches. She has been on sertraline for 5 years and takes acetaminophen as needed. There is no family history of gastrointestinal diseases or neoplasia. She has not responded to simple dietary interventions such as excluding caffeine, lactose, fructose, or extra fiber from her diet. Her examination is normal.

   Which one of the following is the next best step in management of this patient?

   (A) Reassurance
   (B) IgA tissue transglutaminase antibody
   (C) Colonoscopy
   (D) Stool bacterial cultures
   (E) Trial of nortriptyline

2. A 52-year-old woman presents to the clinic for an evaluation of diarrhea that has been present for the past 3 months. She reports a history of travel to Mexico immediately prior to symptom onset. During her vacation, she had several days of diarrhea that was self-limited in nature. Symptoms recurred shortly after her return home. She reports 3–5 bowel movements daily associated with increased bloating and flatus. She denies fever, hematochezia, weight loss, or nocturnal stools. Her past medical history is significant for hypothyroidism and a cholecystectomy 3 years ago. Her only medication is levothyroxine. Examination is normal. Stool for bacteria (including *Clostridium difficile*) and ova and parasites is negative. Stool sodium is 40 mmol/L and stool potassium is 20 mmol/L.

Which one of the following is the most likely diagnosis?

(A) Postinfectious irritable bowel syndrome
(B) Microscopic colitis
(C) *Vibrio cholera* infection
(D) Lactose malabsorption
(E) Bile salt-induced diarrhea

3. A 72-year-old man presents to the clinic for evaluation of diarrhea that has been present for 6 months. He describes 6–8 stools daily that are small in volume and associated with blood and mucous. He also describes bothersome tenesmus. He denies abdominal pain, fever, or weight loss. Past medical history is significant for hypertension, hyperlipidemia, and prostate cancer, for which he underwent prostatectomy and external beam radiation 4 years ago. Medications include hydrochlorothiazide, olmesartan, and atorvastatin. His last colonoscopy was at age 70.

Which one of the following is the most likely diagnosis?

(A) Colorectal cancer
(B) Ischemic colitis
(C) Radiation proctitis
(D) Ulcerative proctitis
(E) Medication-induced colitis

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