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Evaluating the Patient With Diarrhea: A Case-Based Approach

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Abstract

The evaluation of the patient with diarrhea can be complex and the treatment challenging. In this article, the definition of diarrhea and the pathophysiologic mechanisms that lead to diarrhea are reviewed. A simplified 5-step approach to the patient with diarrhea is provided and applied in a case-oriented manner applicable to everyday clinical practice. On completion of this article, you should be able to (1) define diarrhea, (2) outline various pathophysiologic mechanisms of diarrhea, and (3) describe a simplified 5-step approach to facilitate the evaluation of diarrhea.

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Diarrhea can be defined by increased stool frequency, liquidity, or volume. Health care professionals typically think of diarrhea as an increase in stool frequency[1]; however, for most individuals, the essential characteristic of diarrhea is the passage of loose stools.[2] Diarrhea is objectively defined as passing a stool weight or volume greater than 200 g or 200 mL per 24 hours.[3] Diarrhea is common, with most episodes being short-lived. However, in the course of a year, approximately 5% of the US population experiences chronic diarrhea as defined by liquid stools lasting longer than 4 weeks.[4] Therefore, diarrhea is a major cause of morbidity. It is important to recognize that diarrhea is a symptom or sign, not a disease, and can be caused by numerous conditions. Given the multitude of possible causes, the evaluation and treatment of the patient with diarrhea can be challenging. An understanding of the basic mechanisms of diarrhea can help facilitate diagnosis and management.

PATHOPHYSIOLOGY

The fundamental process causing all diarrheal diseases is incomplete absorption of water from intestinal luminal contents. Water itself is not actively transported across the intestinal mucosa but moves across secondary to osmotic forces generated by the transport of solutes, such as electrolytes and nutrients. Normally, absorption and secretion take place simultaneously, but absorption is quantitatively

greater. Either a decrease in absorption or an increase in secretion leads to additional water within the lumen and diarrhea. Excess stool water then causes decreased stool consistency.

Thus, diarrhea is a condition of altered intestinal water and electrolyte transport. The pathophysiologic mechanisms of diarrhea include osmotic, secretory, inflammatory, and altered motility. Osmotic diarrhea involves an unabsorbed substance that draws water from the plasma into the intestinal lumen along osmotic gradients. Secretory diarrhea results from disordered electrolyte transport and, despite the term, is more commonly caused by decreased absorption rather than net secretion. Inflammatory diseases cause diarrhea with exudative, secretory, or osmotic components. Altered motility of the intestine or colon may alter fluid absorption by increasing or decreasing the exposure of luminal content to intestinal absorptive surface. However, from a pathophysiologic perspective, no single cause of diarrhea is truly unifactorial.

A SIMPLIFIED 5-STEP APPROACH

The initial approach to the patient with diarrhea is to obtain a detailed history and perform a physical examination. An understanding of the epidemiological settings in which diarrhea occurs (eg, community acquired, hospital acquired, or travel related) will also help direct diagnosis and treatment. Often, after history and physical examination, the cause of diarrhea is not obvious. In this situation, a simple 5-step evaluation (Table 1) can facilitate the workup of the patient with diarrhea.

Does the Patient Really Have Diarrhea? Beware of Fecal Incontinence and Impaction

The first step in the clinical appraisal of the patient with diarrhea is to identify what the patient means by *diarrhea*. Fecal incontinence is often reported as diarrhea because of embarrassment associated with this condition rather than because the patient has any real difficulty distinguishing diarrhea from incontinence.[5] This possibility should be addressed by direct questioning and assessment of anal squeeze on digital examination. Incontinence is defined as the involuntary release of rectal contents. Continence requires intact anorectal structure and neuromuscular function. Although many incontinent patients have loose stools, their predominant problem is anal sphincter dysfunction and not dysregulated intestinal fluid or electrolyte absorption. If fecal incontinence is frequent, especially if it occurs in the absence of rectal urgency or loose stools, the patient should be evaluated for incontinence and not diarrhea.

TABLE 1. Simplified 5-Step Approach to Diarrhea

1. Does the patient really have diarrhea? Beware of fecal incontinence and impaction.
2. Rule out medications as a cause of diarrhea (drug-induced diarrhea).
3. Distinguish acute from chronic diarrhea.
4. Categorize the diarrhea as inflammatory, fatty, or watery.
5. Consider factitious diarrhea.

Another condition that is often misinterpreted as diarrhea is fecal impaction. Patients with chronic constipation may develop fecal impaction from the inability to expel a large fecal mass through the anus. Rectal distention causes relaxation of the internal anal sphincter, and there is induction of secretions proximal to the obstructing stool. An overflow diarrhea results from liquid stool passing around the impaction and may be reported as diarrhea. A careful rectal examination will allow identification and treatment of this condition.[6]

Rule Out Medications as a Cause of Diarrhea (Drug-Induced Diarrhea)

The second simple step is to consider medications as a potential cause of the diarrhea. Medications serve an important role in maintaining health and well-being. However, many medications are associated with adverse effects, particularly diarrhea. Drug-induced diarrhea is common because nearly all medications may cause diarrhea.[7] The key to diagnosing drug-induced diarrhea is to establish the temporal relationship between starting use of the drug and onset of diarrhea. The medications that most frequently cause diarrhea include antacids and nutritional supplements that contain magnesium, antibiotics, proton pump inhibitors, selective serotonin reuptake inhibitors, and nonsteroidal anti-inflammatory drugs.

The pathophysiology of drug-induced diarrhea is complex and varied. Drugs can cause diarrhea by several different mechanisms.[8] Specific mechanisms of drug-induced diarrhea may include activation of specific receptors and transporters, alteration in colonic bacterial flora, changes in mesenteric blood flow, provocation of intestinal inflammation, and apoptotic enteropathy.[9,10] Caffeine is an agent that may cause increased intestinal fluid secretion by elevating intracellular cyclic adenosine monophosphate levels.[11] Antibiotics alter colonic bacterial flora that may then decrease colonic bacterial fermentation of malabsorbed carbohydrates or lead to *Clostridium difficile* infection. Mesenteric vasoconstricting agents may decrease mesenteric blood flow

and cause malabsorption. Nonsteroidal anti-inflammatory drugs or mycophenolate mofetil are agents that may incite intestinal inflammation, causing diarrhea. Lastly, diarrhea is common immediately after chemotherapy because these agents may cause intestinal or colonic crypt damage, thus impairing water absorption[12] and resulting in an apoptotic enterocolopathy.

To identify drug-induced diarrhea, it is imperative that the physician take a complete medication history and inquire about over-the-counter medications and supplements (eg, vitamin C and magnesium). Treatment involves withdrawal of the offending drug.

Distinguish Acute From Chronic Diarrhea

If a drug-induced cause of diarrhea seems unlikely, then the third step that can help direct evaluation is the duration of the diarrhea. The duration of diarrhea may be an important clue to the cause. Diarrhea is acute if it lasts fewer than 2 weeks and chronic if it lasts more than 4 weeks. The approach to acute diarrhea is straightforward because it is most commonly caused by infection and is self-limited. Often, no evaluation or treatment is required. However, stool testing and other studies are often indicated in the presence of certain clinical or epidemiological features, including age older than 65 years, immune compromise, volume depletion, hematochezia or blood-tinged stool, fever, severe abdominal pain, recent antibiotic use, known or suspected inflammatory bowel disease, community infectious disease outbreaks, and employment as a food handler. In contrast to acute diarrhea, chronic diarrhea typically warrants a diagnostic evaluation, is less likely to resolve on its own, and presents a broad differential diagnosis.

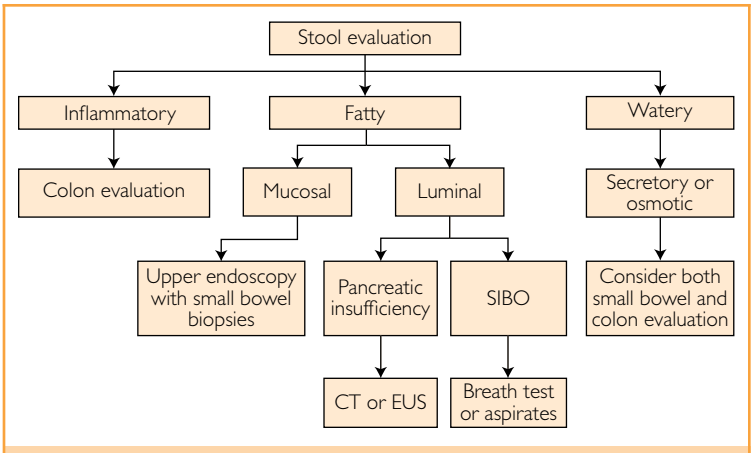

FIGURE. Categorization of diarrhea. CT = computed tomography; EUS = endoscopic ultrasonography; SIBO = small intestinal bacterial overgrowth.

Categorize the Diarrhea as Inflammatory, Fatty, or Watery

If the patient has chronic diarrhea, then the fourth step is to categorize the diarrhea into inflammatory, fatty, or watery type on the basis of presentation and simple stool tests (Figure). Grouping patients with chronic diarrhea into one of these categories is most easily accomplished noninvasively at the front end of the evaluation by stool testing, a strategic initial step that will narrow the differential diagnosis and rationally direct the investigation.

Inflammatory diarrhea is characterized by frequent, small-volume, bloody stools and may be accompanied by tenesmus, fever, or severe abdominal pain. Inflammatory diarrhea is suspected with the demonstration of leukocytes or leukocyte proteins (eg, calprotectin or lactoferrin) on stool examination. Other laboratory studies that may indicate an inflammatory diarrhea include elevated C-reactive protein level or sedimentation rate and low serum albumin level. Inflammatory diarrhea fundamentally indicates disrupted and inflamed mucosa, such as that caused by idiopathic inflammatory bowel disease (Crohn disease or ulcerative colitis), ischemic colitis, and infectious processes, such as *C difficile*, cytomegalovirus, tuberculosis, or *Entamoeba histolytica*. Radiation colitis and neoplasia are uncommon causes of inflammatory diarrhea. When history or stool analysis suggests chronic inflammatory diarrhea, flexible sigmoidoscopy or colonoscopy should be the initial study to look for structural changes.

Fatty stools are suggested by a history of weight loss, greasy or bulky stools that are difficult to flush, and oil in the toilet bowl that requires a brush to remove.[13] A common misconception is that floating stools are indicative of steatorrhea. Floating stools indicate gas production by colonic bacteria, not steatorrhea.[14] The basic mechanisms of chronic fatty diarrhea are malabsorption and maldigestion. Fat malabsorption results from inadequate mucosal transport, and fat maldigestion results from defective hydrolysis of triglycerides. Malabsorption is caused by mucosal diseases, most commonly celiac disease, whereas the maldigestion results from pancreatic exocrine insufficiency (eg, chronic pancreatitis) or inadequate duodenal bile acid concentration (eg, small intestinal bacterial overgrowth [SIBO] or cirrhosis). A simple test to screen for excess fecal fat is a Sudan stain, which will detect most cases of clinically significant steatorrhea. However, the criterion standard for steatorrhea is a quantitative measurement on a timed stool collection while patients consume a 100-g fat diet, and steatorrhea is defined as more than 7 g of fat per 24 hours. When fatty diarrhea is identified, the initial goal is to distinguish malabsorption from maldigestion. The evaluation

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focuses on looking for a structural problem involving the small intestine or pancreas. Endoscopy with small bowel biopsies allows evaluation of the small intestinal mucosa for celiac disease. Small bowel aspiration can be performed to look for SIBO, which causes steatorrhea by deconjugation of bile acids with resultant low duodenal bile acid concentrations. In addition, hydrogen breath tests may be used to diagnose SIBO. The diagnosis of SIBO requires consideration of a predisposing factor, such as intestinal stasis, achlorhydria, pancreatic insufficiency, or immune deficiency. If small bowel disease is excluded, computed tomography or endoscopic ultrasonography may be useful to identify morphological changes of chronic pancreatitis. If no intestinal abnormalities are found and there is no evidence of chronic pancreatitis, abnormal pancreatic exocrine function should be considered. An empiric trial of pancreatic enzyme supplementation may be used to assess for the presence of pancreatic exocrine insufficiency. If such a trial is conducted, high doses of enzymes should be prescribed, and some objective measurement, such as fecal fat excretion or weight gain, should be monitored to assess response.[10]

Watery diarrhea can be further classified as osmotic or secretory in origin. Osmotic diarrhea is due to the ingestion of poorly absorbed ions or sugars. Secretory diarrhea is due to disruption of epithelial electrolyte transport. Two ways to distinguish an osmotic from a secretory process is by response to fasting and calculating the fecal osmotic gap. An essential characteristic of osmotic diarrhea is that stool volume decreases with fasting, whereas secretory diarrhea typically continues unabated with fasting. Another way to clinically differentiate osmotic diarrhea from secretory diarrhea is by calculating the fecal osmotic gap. The fecal osmotic gap is calculated by adding the stool sodium and potassium concentration, multiplying by 2, and subtracting this amount from 290 mmol/L. Measured stool osmolality should not be used because it largely reflects bacterial metabolism in vitro, not intraluminal osmolality. A fecal osmotic gap greater than 50 mmol/L suggests an osmotic cause for diarrhea, whereas a gap less than 50 mmol/L supports a secretory origin.

If a diagnosis of osmotic diarrhea is made, the differential diagnosis is limited and the evaluation is relatively straightforward. Osmotic diarrhea is usually due to ingestion of poorly absorbed cations (eg, magnesium) or anions (eg, phosphate, or sulfate), which are often contained in laxatives and antacids, or to carbohydrate malabsorption from ingestion of poorly absorbed sugars or sugar alcohols (eg, sorbitol or xylitol). Lactose intolerance is by far the most common type of carbohydrate malabsorption, with prevalence rates up to 100% in Africa, Asia, and Latin America.[15] Measuring a stool pH can help distinguish between osmotic diarrhea due to poorly absorbed ions and that due to poorly absorbed sugars.[16,17]

Carbohydrate malabsorption will result in a stool pH less than 6 because as carbohydrates reach the colon they are fermented by bacteria, releasing short-chain fatty acids and making the stool water acidic.[15,16] Numerous disease processes can produce secretory diarrhea; the major causes are listed in Table 2. The basic pathophysiologic mechanism involves either net secretion of ions (chloride or bicarbonate) or inhibition of net sodium absorption.[18] The most common cause of secretory diarrhea is infectious[18]; however, infection is an uncommon cause of chronic secretory diarrhea. Therefore, noninfectious causes of secretory diarrhea should be sought. Of the many causes of secretory diarrhea, peptide-secreting endocrine tumors (eg, carcinoid or gastrinoma) deserve mention. Endocrine neoplasms are a rare cause of chronic diarrhea and account for less than 1% of patients who present with chronic diarrhea.[6] Therefore, the pretest probability of detecting a peptide-secreting tumor in an individual with chronic diarrhea is low, and there is a high probability of false-positive screening test results.[19] Hence, testing for peptide-secreting tumors should only be pursued if there is more direct evidence of one of these conditions. For example, an enlarged nodular liver, skin flushing, and wheezing would support small intestinal carcinoid metastatic to liver. Because diarrhea associated with endocrine neoplasms can cause significant morbidity and mortality, it is important for physicians to recognize the diarrheal syndromes associated with endocrine neoplasms (Table 3). Once the type of diarrhea is categorized and the differential diagnosis minimized, directed testing can usually lead to a diagnosis.

TABLE 2. Major Causes of Secretory Diarrhea

Infection
Bile acid malabsorption
Nonosmotic laxatives
Inflammatory bowel disease (microscopic colitis, Crohn disease, ulcerative colitis)
Disordered regulation (eg, post vagatomy, diabetic neuropathy)
Peptide-secreting endocrine tumors
Neoplasia (colon carcinoma, lymphoma, villous adenoma)
Idiopathic or epidemic secretory diarrhea

TABLE 3. Endocrine Neoplasms Associated With Diarrhea

Tumor	Associated findings
Gastrinoma	Abdominal pain, erosive esophagitis, enlarged gastric folds, duodenal ulcers
Carcinoid	Flushing, enlarged nodular liver from metastases
VIPoma	Hypokalemia, achlorhydria
Somatostatinoma	Diabetes mellitus, cholelithiasis, hypochlorhydria
Glucagonoma	Diabetes mellitus, deep vein thrombosis, depression, necrolytic migratory erythema

Consider Factitious Diarrhea

Factitious diarrhea is an intentionally self-inflicted disorder. The most frequent cause of factitious diarrhea is surreptitious laxative ingestion. Physicians usually assume that patients are being truthful, but up to 15% of patients who undergo an evaluation for chronic diarrhea may be surreptitiously ingesting laxatives.[20] The key to diagnosing factitious diarrhea is suspecting it. A factitious origin should be considered for persons in whom diarrhea remains undiagnosed after thorough evaluation.

Individuals with factitious diarrhea are most commonly women of higher socioeconomic status and often employed in the medical field. There is frequently a history of multiple medical consultations or hospitalizations in an effort to establish the cause of diarrhea. Evaluation of the patient with suspected factitious diarrhea consists of measuring stool osmolality, performing endoscopy, and analyzing stool water or urine for laxatives.

Measurement of stool osmolality can be useful in detecting factitious diarrhea caused by the addition of water or dilute urine to the stool.[21-23] Because stool osmolality can never be less than that of plasma, a low osmolality (<290 mOsm/kg) can only result by adding a hypotonic solution, such as water or urine, to stool. In addition, a very high stool osmolality (>600 mOsm/kg) may be a clue to stool diluted with hypertonic solutions, such as tomato juice or blood.[24] A stool osmolality of less than 600 mOsm/kg often indicates prolonged storage and carbohydrate fermentation. Therefore, a measured stool osmolality of less than 290 mOsm/kg or greater than 600 mOsm/kg is a potential clue to factitious diarrhea.

Colonoscopy may be helpful in evaluating factitious diarrhea. Pseudo–melanosis coli may be a potential clue found on colonoscopy. Pseudo–melanosis coli is a brownish discoloration of the colonic mucosa caused by the accumulation of lipofuscin pigment in macrophages of the lamina propria.[25] It occurs with the use of anthraquinone laxatives, such as senna, cascara, and rhubarb, and takes on average 9 months to develop. It is benign and reversible, disappearing within 1 year of discontinuing use of anthraquinone laxatives.[26] Before confronting the patient with this finding, it is important to realize that pseudo–melanosis coli is not pathognomonic for anthraquinone laxative use and may be seen in other conditions that cause chronic colonic inflammation. In addition, patients may be unaware that they are ingesting anthraquinone like laxatives because they may be "natural" ingredients in herbal teas and other health supplements. Finally, if measurement of stool osmolality and colonoscopy do not provide potential clues to factitious diarrhea, then stool, urine, and serum can be tested for laxatives.

The following 3 cases illustrate the application of the simplified 5-step approach to the patient with diarrhea.

APPLYING THE 5-STEP APPROACH

Case 1

A 50-year-old man with type 2 diabetes mellitus presents with a 6-month history of diarrhea. He has up to 10 explosive watery stools a day with occasional fecal incontinence. There is no associated bleeding or pain. He has not lost weight. Complete blood cell count and chemistry analysis results are unremarkable for contributing conditions. Prior testing shows multiple negative stool study results for white blood cells, occult blood, and pathogens. He had a normal flexible sigmoidoscopy with biopsy result. A serologic test result for celiac disease with tissue transglutaminase antibodies was negative.

This patient with diabetes mellitus appears to have chronic diarrhea with fecal incontinence as a complication and not primary contributor to symptoms. When applying the simple 5-step approach to diarrhea further, the next step is to consider a drug-induced cause. Further history in this case revealed that the patient was prescribed metformin 2 weeks before the onset of symptoms. By far the most common cause of diarrhea in those with type 2 diabetes is therapy with metformin.[27] This case illustrates the importance of taking a detailed medication history in the patient with chronic diarrhea. A medication history is particularly salient in the diabetic patient because medications such as metformin and acarbose commonly cause diarrhea. Features of metformin-induced diarrhea include watery stools that are often explosive and associated with fecal incon-

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tinence. The resolution of diarrhea after cessation of metformin therapy is indicative of this diagnosis. Other causes of chronic diarrhea to consider in diabetic patients include celiac disease, microscopic colitis, exocrine pancreatic insufficiency, "sugar-free" foods that may contain poorly absorbable sugar alcohols, and bile acid malabsorption.

Case 2

A 25-year-old Asian woman presents with intermittent diarrhea, abdominal bloating, and excess flatus for the past 5 years. Several times per week she experiences mild cramping abdominal pain that is followed by explosive watery bowel movements with a large amount of flatus. She denies blood in stool, fever, weight loss, anorexia, or fecal incontinence. She has not traveled internationally or taken any antibiotics. She takes no medications and has not been able to associate her symptoms with dietary triggers. Physical examination reveals normal thyroid, no hepatomegaly, and no rashes. Laboratory studies reveal a normal complete blood cell count. Stool studies performed during an episode of diarrhea show a sodium level of 80 mmol/L, a potassium level of 30 mmol/L, and stool pH of 5.

This individual has intermittent diarrhea without fecal incontinence. She takes no medications, making a drug-induced cause unlikely. Symptoms have persisted for more than 4 weeks, making this chronic diarrhea and unlikely to be infectious in origin. The next step in the simplified 5-step approach would be to categorize the diarrhea as inflammatory, fatty, or watery. An inflammatory cause is unlikely given the absence of fever, severe abdominal pain, or blood in stool. She has lost no weight and has no descriptors, such as oil droplets in toilet water or difficult to flush stools, which would raise suspicion for fatty stools. Correct categorization of the stools in this case would be watery diarrhea. The next step when confronted with a chronic, watery diarrhea is to determine whether it is an osmotic or secretory process by calculating the stool osmotic gap. In this case, the patient had a stool osmotic gap ($290 - 2[80+30]$) of greater than 50 mmol/L, suggesting an osmotic cause of diarrhea. The evaluation of osmotic diarrhea is relatively straightforward because there are only a few causes. The 2 major causes of osmotic diarrhea are ingestion of poorly absorbed ions, such as magnesium, or ingestion of poorly absorbed sugars. Assessing the pH of stool water helps to distinguish these 2 conditions. Carbohydrate malabsorption will result in a stool pH less than 6 because as carbohydrates reach the colon they are fermented by bacteria, releasing short-chain fatty acids and making the stool water acidic.[15,16] Stool analysis in this case revealed a stool pH of 5, which is indicative of colonic fermentation of malabsorbed carbohydrates. Initially, the patient did not associate any of her symptoms with dietary triggers; however, on further questioning there was some correlation of symptoms with ingestion of milk products. Subsequently, her symptoms improved on a lactose-free diet. Intolerance to lactose-containing foods (primarily dairy products) is common, with a particularly high prevalence in Asians. Ingestion of the disaccharide lactose requires digestion by the disaccharidase lactase to its constituent components of glucose and galactose to permit absorption because monosaccharides are the only sugars absorbed across the small intestinal epithelium. Absence of disaccharidases as in lactase deficiency results in an osmotic diarrhea, abdominal pain, and excess flatulence.

Case 3

An 80-year-old woman with hypertension presents with a 3-year history of nonbloody diarrhea. She reports 3 to 6 moderate-sized bowel movements per day without a nocturnal component. Her appetite is intact, and she has had no fever, weight loss, or blood in the stool. She has occasional fecal incontinence, but these episodes are less common now because she does not eat out and stays home to be close to the bathroom. She has tried eliminating milk products, gluten, and caffeine from her diet without improvement. Physical examination revealed a woman physically younger than her stated age, and rectal examination revealed adequate resting and squeeze anal sphincter tone without stool in the rectum. Laboratory studies revealed a normal complete blood cell count. Colonoscopy revealed pseudo–melanosis coli.

The simple 5-step approach to diarrhea should be applied to this 80-year-old woman: (1) determine whether the patient really has diarrhea; (2) rule out medications as a cause of diarrhea; (3) distinguish acute from chronic diarrhea; (4) categorize the diarrhea as inflammatory, fatty, or watery; and (5) consider factitious diarrhea.

The patient appears to have diarrhea that is complicated by mild fecal incontinence. A drug-induced cause is unlikely based on review of medications. The duration of the diarrhea is greater than 4 weeks, indicating it is chronic. The diarrhea is watery because there are no symptoms or signs of inflammatory diarrhea, and the absence of weight loss makes fatty diarrhea unlikely. Stool electrolytes reveal no fecal osmotic gap, indicating a secretory origin. On the basis of the differential diagnosis of secretory diarrhea and considering the patient's demographic features, a colonoscopy was performed to evaluate for microscopic colitis. The colonoscopy revealed pseudo–melanosis coli, suggestive of anthraquinone laxative use; how-

ever, she denied laxative ingestion. On further questioning, the patient admitted to drinking herbal tea on a daily basis. The tea contained sennosides, which are hydroxyanthracene glycosides derived from senna leaves. Her diarrhea resolved when she stopped drinking the herbal tea. This case illustrates 2 important points. First, a complete dietary history is crucial when evaluating the patient with chronic diarrhea. Second, when confronted with chronic, secretory diarrhea, it is helpful to review its differential diagnosis and pursue testing based on clinical suspicion.

CONCLUSION

Evaluation of the patient with diarrhea can often be complex and time-consuming. Hence, a methodical approach to the patient with diarrhea can facilitate diagnosis and management. One such simplified method is the 5-step approach as outlined and applied in the clinical cases described in this report. This approach helps to limit the differential diagnosis and direct testing. It is meant as a guide for the physician and is not a substitute for a thorough history. With this approach, a large percentage of patients with diarrhea can be evaluated and treated by a primary care physician. More complex scenarios should be referred to a gastroenterologist.

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REFERENCES

1. Talley NJ, Zinsmeister AR, Van Dyke C, Melton LJ III. Epidemiology of colonic symptoms and irritable bowel syndrome. *Gastroenterology*. 1991;101(4):927-934.
2. Talley NJ, Weaver AF, Zinsmeister AR, Melton LJ III. Self-reported diarrhea: what does it mean? *Am J Gastroenterol*. 1994;89(8):1160-1164.
3. Davies GJ, Crowder M, Reid B, Dickerson JW. Bowel function measurements of individuals with different eating patterns. *Gut*. 1986;27(2):164-169.
4. Schiller LR. Diarrhea. *Med Clin North Am*. 2000;84(5):1259-1274.
5. Leigh RJ, Turnberg LA. Faecal incontinence: the unvoiced symptom. *Lancet*. 1982;1(8285):1349-1351.
6. Schiller LR. Diarrhea and malabsorption in the elderly. *Gastroenterol Clin N Am*. 2009;38(3):481-502.
7. Chassany O, Michaux A, Bergmann JF. Drug-induced diarrhoea. *Drug Saf*. 2000;22(1):53-72.
8. Abraham B, Sellin JH. Drug-induced diarrhea. *Curr Gastroenterol Rep*. 2007;9(5):365-372.
9. Ratnaike RN, Jones TE. Mechanisms of drug-induced diarrhoea in the elderly. *Drugs Aging*. 1998;13(3):245-253.
10. Schiller LR, Sellin JH. Diarrhea. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management*. 9th ed. Philadelphia, PA: Saunders; 2010:211-231.
11. Wald A, Back C, Bayless TM. Effect of caffeine on the human small intestine. *Gastroenterology*. 1976;71(5):738-742.
12. Gibson RJ, Stringer AM. Chemotherapy-induced diarrhoea. *Curr Opin Support Palliat Care*. 2009;3(1):31-35.
13. Donowitz M, Kokke FT, Saidi R. Evaluation of patients with chronic diarrhea. *N Engl J Med*. 1995;332(11):725-729.
14. Levitt MD, Duane WC. Floating stools—flatus versus fat. *N Engl J Med*. 1972;286(18):973-975.
15. Scrimshaw NS, Murray EB. The acceptability of milk and milk products in populations with a high prevalence of lactose intolerance. *Am J Clin Nutr*. 1988;48(4, suppl):1079-1159.
16. Eherer AJ, Fordtran JS. Fecal osmotic gap and pH in experimental diarrhea of various causes. *Gastroenterology*. 1992;103(2):545-551.
17. Hammer HF, Fine KD, Santa Ana CA, et al. Carbohydrate malabsorption: its measurement and its contribution to diarrhea. *J Clin Invest*. 1990;86(6):1936-1944.
18. Schiller LR. Secretory diarrhea. *Curr Gastroenterol Rep*. 1999;1(5):389-397.
19. Schiller LR, Rivera LM, Santangelo WC, et al. Diagnostic value of fasting plasma peptide concentrations in patients with chronic diarrhea. *Dig Dis Sci*. 1994;39(10):2216-2222.
20. Bytzer P, Stokholm M, Andersen I, et al. Prevalence of surreptitious laxative abuse in patients with diarrhoea of uncertain origin: a cost benefit analysis of a screening procedure. *Gut*. 1989;30(10):1379-1384.
21. Thomas PD, Forbes A, Green J, et al. Guidelines for the investigation of chronic diarrhea, 2nd edition. *Gut*. 2003;52(suppl 5):1-15.
22. Topazian M, Binder HJ. Brief report: factitious diarrhea detected by measurement of stool osmolality. *N Engl J Med*. 1994;330(20):1418-1419.
23. Pollock RC, Banks MR, Fairclough PD, Farthing MJ. Dilutional diarrhea: underdiagnosed and over-investigated. *Eur J Gastroenterol Hepatol*. 2000;12(6):609-611.
24. Zimmer KP, Marquardt T, Schmitt GM. More on factitious diarrhea. *J Pediatr Gastroenterol Nutr*. 2002;35(4):584-585.
25. Ewe K, Karbach U. Factitious diarrhoea. *Clin Gastroenterol*. 1986;15:723-740.
26. Speare GS. Melanosis coli: experimental observations of its production and elimination in twenty-three cases. *Am J Surg*. 1951;82(5):631-647.
27. Lysy J, Israeli E, Goldin E. The prevalence of chronic diarrhea among diabetic patients. *Am J Gastroenterol*. 1999;94(8):2165-2170.