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## DIARRHEA

## Diner's Diarrhea . . . . . Level I

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CHANGES IN THIS EDITION

## CASEBOOK

*Patient Presentation*

- New patient (25-year-old woman) with different history of present illness, past medical history, social history, medication list, allergies, and physical examination and laboratory findings.

## INSTRUCTOR'S GUIDE

*Problem Identification*

- The patient has a history of migraine headaches and irritable bowel syndrome (IBS) (but not hypertension or dyslipidemia as in the previous case).
- Possible drug-related causes of diarrhea include over-the-counter (OTC) psyllium, St. John's wort, and valproic acid.
- Consideration should be given to the patient's IBS as a contributing cause of diarrhea.
- Acid suppression therapy, if taken chronically, could be a predisposing factor for infectious diarrhea development.
- New information provided on whether stool cultures should be obtained in patients with similar situations.

*Therapeutic Alternatives*

- Additional information provided on the BRAT diet and probiotics.
- Adsorbents are not routinely used to treat nonspecific diarrhea due to questionable effectiveness.
- Azithromycin added as another antibiotic option for infectious causes of diarrhea.

*Optimal Plan*

- Revised based on the medications this patient was taking prior to the diarrheal episode.

*Patient Education*

- Information on polycarbophil removed since it is no longer recommended.

*Follow-Up Questions*

- Added questions about management of contraception post-therapy, changes in therapy for migraine headache prophylaxis, management of IBS, and the possible link between bacterial gastroenteritis and IBS.

*References*

- Updated with nine new references added.

## CASE SUMMARY

A 1-day history of nausea, vomiting, diarrhea, and mild fever causes a 25-year-old woman to seek treatment at an outpatient clinic. Her medications include valproic acid for migraine headache prophylaxis, omeprazole for GERD, triphasic oral contraceptives for birth control, St John's wort for depression, psyllium for irritable bowel disease, and Prilosec OTC (omeprazole) and Maalox Plus, which she took for acute nausea. Physical exam findings indicate the presence of dehydration, and the patient is admitted for treatment overnight and discharged the next day. The case requires students to ask questions to obtain the additional information needed for a complete patient assessment. Treatment modalities should be directed toward replacement of fluid and electrolyte losses, discontinuation of any offending drugs, and provision of symptomatic relief with antidiarrheal compounds.

## QUESTIONS

## Problem Identification

## 1.a. Create a list of the patient's drug therapy problems.

- Diarrhea, requiring fluids and possibly other symptomatic treatment
- Nausea, cramping, vomiting, and fever, possibly requiring symptomatic treatment
- Orthostasis and moderate to severe dehydration (secondary to diarrhea, vomiting, and fever), requiring fluid replacement
- History of migraine headaches
- History of IBS

## 1.b. What signs and symptoms indicate the presence or severity of the diarrhea?

- Four to six liquid stools since yesterday<sup>1,2</sup>
- Cramping with bowel movements
- Dry mucous membranes
- Drop in blood pressure (BP) (35 mm Hg systolic, 22 mm Hg diastolic) and increased pulse on standing (orthostatic changes); weakness and dizziness on standing
- Temperature of 38°C (100.4°F)
- Decreased urination, amber-colored urine, and high urine specific gravity indicating intravascular volume depletion
- Symptom duration of about 24–48 hours

## 1.c. What questions should you ask the patient or members of the medical team to obtain the additional information needed for a complete assessment of this patient?

*Note to instructors:* The questions that follow also have the answers provided. After you discuss the reason for asking each question with the students, provide them with the response given by the patient or members of the medical team.

- Could a parasitic infection be responsible for this patient's diarrhea?
  - ✓ This is a possibility. A stool specimen was obtained on admission for culture and examination for ova, parasites, and white blood cells/red blood cells. Eosinophilia may result from parasitic infections but is absent in this case.
- What else has the patient eaten over the past 48 hours? Has anyone who has dined with her during this time also complained of the same symptoms? This will help you to determine

whether bacteria from contaminated food (e.g., *Escherichia coli*, *Staphylococcus*, *Salmonella*, *Shigella*, *Vibrio*) could be responsible for the diarrhea. If others who ate the same food have similar diarrhea symptoms, then bacterial infection becomes a more likely cause. *Staphylococcus aureus* and *Bacillus cereus* are the primary bacteria that cause food-borne illness within 7 hours of ingestion due to preformed enterotoxins in the food. *B. cereus* can also cause a longer-incubation food-borne illness due to in vivo enterotoxin production.<sup>1</sup>

- ✓ She had granola and yogurt for breakfast and a chicken pesto and avocado sandwich for lunch the day her symptoms began. Her boyfriend ate Miso soup and beef teriyaki for dinner while she had sushi (containing some raw seafood), and he has felt fine.
- Has she complained of similar diarrhea episodes in the past? This would allow you to determine whether the diarrhea is acute or chronic in nature.
  - ✓ She last experienced a diarrhea episode with a flare-up of her IBS 1 month ago. This was followed by periodic episodes of constipation, which she often has with her IBS.
- How frequent is the vomiting? The nausea and vomiting help support an infectious cause (e.g., viral or bacterial) and could result in a greater risk of fluid depletion and electrolyte abnormalities.
  - ✓ She vomited at least four to five times yesterday but only once today (earlier in the morning).
- How often has she been using the Prilosec OTC? Frequent use or high doses of the Prilosec OTC could result in diarrhea.
  - ✓ The patient was already taking omeprazole 20–40 mg daily for gastroesophageal reflux disease and with the two extra OTC omeprazole doses taken 1 day prior to admission, her total dose that day was 60 mg. Prilosec OTC is a proton pump inhibitor that inhibits gastric acid secretion. Although adverse effects are uncommon, diarrhea can occur in some patients. However, since the patient was already taking omeprazole without apparent problems and due to the other symptoms present (nausea, vomiting, fever), the two additional doses from Prilosec OTC are not a likely cause of this patient's diarrhea.
- Is she taking any other OTC medication or herbal products? It is possible that a patient could be taking another OTC medication (e.g., a different antacid) or a natural product that might cause diarrhea?
  - ✓ She is taking a multivitamin.
  - ✓ She is taking Metamucil.
  - ✓ She is taking St. John's wort.
  - ✓ St. John's wort is a dietary supplement used for a variety of purposes, including depression, anxiety, and insomnia. There are reports of mild GI disturbances with the product, including nausea and diarrhea. In general, side effects from St. John's wort are uncommon.<sup>3</sup> The patient's dosing regimen is consistent with established recommendations, namely 900–1,800 mg per day. Although the abrupt onset of the patient's symptoms 24 hours ago (with fever) rules against St. John's wort as the cause, it is always important to consider the use of dietary supplements or herbal products when evaluating a patient's drug therapy. Various herbal remedies, such as *Ginkgo biloba*, feverfew, ginseng, and pau d'arco, have also been implicated in causing GI distress including diarrhea.
- Does she have a history of lactose intolerance? Since she did not remember taking any milk or other dairy-related foods at

the restaurant, it is unlikely that lactose intolerance could cause diarrhea and cramps in this patient. Additionally, the other symptoms (e.g., vomiting, fever) are not consistent with lactose intolerance.

✓ She has no history of lactose intolerance.

- Has she traveled recently outside the United States? Traveler's diarrhea is usually caused by bacteria and might require anti-bacterial therapy. Although it occurs most commonly during the 2–3 weeks of travel, it can occur at any time while traveling even after returning home.<sup>4,5</sup>
  - ✓ Her only travel has been to Key West, Florida, 1 month ago on vacation. Florida is not a destination associated with traveler's diarrhea. High-risk destinations include Africa (excluding South Africa), South and Central America, most of the Middle East, Oceania, and southern Asia.<sup>5</sup>
- Has she taken ciprofloxacin since her last UTI?
  - ✓ No, that was the last time she had taken any antibiotic.

#### 1.d. Could any of this patient's problems have been caused by her prescription drug therapy?

- *Valproic acid* can also cause GI symptoms including nausea, vomiting, and diarrhea. Because this patient's GI symptoms were of acute onset and she had been taking the valproic acid for 6 years for migraine prophylaxis, valproic acid-induced diarrhea is an unlikely cause of her current complaints. Diarrhea can also be a sign of hepatotoxicity, but there is no objective evidence of valproic acid-induced liver disease. Selected liver function tests were normal.
- *Triphasil*, a triphasic oral contraceptive, is associated with nausea and less commonly diarrhea. Because the patient had been on the drug for 3 years (without adverse effects), it is an unlikely cause of her acute-onset GI symptoms.
- *Ciprofloxacin* can cause diarrhea or colitis even after therapy has been stopped. However, it has been 6 months since the drug was taken. The patient does not have a history of recent use of ciprofloxacin or other antibiotics that might cause these problems.

#### 1.e. What are other possible causes of this patient's diarrhea?

- *Infections (bacterial or viral)*. This is a likely possibility although a specific causative agent is usually not able to be identified. Because of this, stool cultures are not routinely recommended unless the following are present: severe diarrhea (passage of six or more unformed stools per day), diarrhea persisting for longer than a week, fever, dysentery, and illness that appears to represent an outbreak.<sup>1</sup> Bacteria and viruses are common causes of watery, noninflammatory diarrhea, and noncholeraic vibrios are often associated with diarrhea occurring after eating contaminated seafood or shellfish.<sup>1</sup> Bacterial, toxin-induced food poisoning can occur within the time frame experienced by this patient. Regardless of whether the etiology is bacterial or viral, the diarrhea is usually self-limited (generally resolves within 48–72 hours) and does not generally require diagnostic testing.<sup>1,2</sup>

## Desired Outcome

### 2. What are the goals of therapy for this patient?

- Rehydrate the patient.
- Prevent further excessive water and electrolyte losses and acid-base disturbances.
- Provide symptomatic relief to reduce fluid loss and increase patient comfort.
- Manage any underlying causes of the diarrhea.

- Provide better control of the IBS on a long-term basis (a secondary goal).

## Therapeutic Alternatives

### 3.a. What nonpharmacologic therapies should be considered for this patient?

- Dietary management (refer to the treatment section of the textbook chapter on nausea and vomiting for more detailed information):
  - ✓ Although stopping solid foods for 24 hours or eating a digestible, low-residue diet for 24 hours such as the BRAT diet (bananas, rice, applesauce, toast) has been traditionally recommended for adults, there is disagreement about the role of restrictive diets with diarrhea, and there are no well-controlled trials that show these diets facilitate recovery.<sup>1,6</sup> It is best to avoid heavy, fatty, spicy, or stimulant-containing foods or beverages such as caffeine-containing drinks during this time. It can also be helpful to avoid lactose-containing foods during the acute episode. This should be followed by resumption of the patient's normal diet as tolerated and desired.<sup>6</sup>
  - ✓ Rehydration and maintenance of water and electrolytes. Use of IV fluids with electrolytes (e.g., normal saline with KCl) if the patient is dehydrated and in the hospital, or oral rehydration solutions for outpatients. In general, oral rehydration should be used whenever possible. This is critical if the frequency and severity of the diarrhea increase. It is important that fluid intake be maintained during acute diarrheal episodes.<sup>1,2,5</sup>
- Management of any underlying causes.

### 3.b. What feasible pharmacotherapeutic alternatives are available for treatment of diarrhea in this patient?

- *Antimotility agents* (e.g., *opioids* and *opioid derivatives* including *loperamide* and *diphenoxylate/atropine*) are the most commonly used drugs to reduce stool frequency and cramping and are easy to administer. However, if used alone without an antibacterial agent, they may worsen an invasive bacterial infection of the colon and should be avoided in patients with frank bloody diarrhea and high fever.<sup>1,7</sup> They may cause drowsiness and constipation. In the absence of an invasive bacterial infection, loperamide is often considered the drug of choice. It does not require a prescription and avoids the habit-forming or abuse potential of opioids.<sup>7</sup>
- *Adsorbents* (*attapulgit*, *kaolin*, *pectin*, *polycarbophil*) are not currently used to treat nonspecific diarrhea. Data regarding their effectiveness and safety for this condition either are lacking or have been removed from the market/reformulated.
- *Bismuth subsalicylate* (an antisecretory agent) is indicated for the management of acute diarrhea, including traveler's diarrhea. It is less convenient to administer because of the need for frequent dosing. The salicylate content is a concern in children, and it is not generally recommended for persons younger than 12 years of age or for patients who are already receiving large dosages of salicylates, patients with aspirin sensitivity, and patients who are taking other medications that interact with aspirin (e.g., anticoagulants). Bismuth may cause dark-colored stools (which could be confused with melena).
- *Antibiotics* (e.g., *trimethoprim-sulfamethoxazole*, *fluoroquinolones*, *azithromycin*, *rifaximin*) act by treating the infection if bacteria are responsible for diarrhea. Conversely, they are ineffective if bacteria are not responsible for the diarrhea. Recommendations for therapy are dependent on the organism

responsible and patient age (e.g., child or adult).<sup>1</sup> Side effects vary depending on the antibiotic used and generally occur more frequently than with the other antidiarrheal agents listed.

- *Probiotics* (e.g., *Lactobacillus GG*, *Saccharomyces*) improve microbial balance in the intestine and exert an antimicrobial effect by competing with pathogens for nutrients and for adherence to intestinal mucosa, along with other favorable local actions. In addition, they may modulate the immune response by promoting production of peptides that exert an antimicrobial action or promoting antibody responses against specific pathogens, along with other postulated effects.<sup>8</sup> They have been studied to prevent or treat antibiotic-associated diarrhea and mild to moderate infectious diarrhea. However, study findings have generally been inconsistent. The role of probiotics in preventing and treating infectious diarrhea has not been established, with the possible exception of the use of *Lactobacillus GG* and *Saccharomyces boulardii* for adjuvant therapy of acute diarrhea in children.<sup>8</sup> The inconsistent formulation of probiotic products combined with their lack of FDA regulation underscores the need for further controlled studies of these agents before their use can be routinely recommended.

## Optimal Plan

### 4. What nonpharmacologic interventions and specific pharmacotherapeutic regimens would you recommend for treating this patient's diarrhea?

Refer to the textbook chapter for more detailed information on treatment recommendations for acute diarrhea.

- *Eliminate contributory factors.* The contribution of drugs to the diarrhea should be considered. The use of "as-needed" Prilosec OTC should be discouraged, but her usual daily omeprazole dose should continue since historically it was not associated with any GI adverse effects. The patient may continue taking the St. John's wort since there is little likelihood that it contributed to her diarrhea although its benefit for this patient should be documented.
- *Change diet temporarily.* Avoid heavy, fatty, spicy, and caffeine/lactose-containing foods or beverages until the diarrhea resolves. Easily digested foods or a BRAT diet may be tried. Resume normal diet as desired and tolerated.
- *Replace fluids.* This patient was admitted for observation and therapy because of the moderate to severe dehydration that was evident. Replace fluid/electrolyte losses with IV fluid administration (approximately 2.0–2.5 L of normal saline containing KCl 20–30 mEq/L adjusted depending on serum potassium concentration). This volume should be increased if vomiting continues or increases. Prior to discharge, fluid and electrolyte intake can be maintained with IV fluids until diarrhea stops. An oral rehydration solution could be used in this patient if diarrhea is still occurring after the IV fluids are stopped; however, noncarbonated drinks containing glucose and electrolytes could also be used in otherwise normal adults.
- *Provide symptomatic relief.* If symptomatic control of the diarrhea is desired (to reduce the discomfort and inconvenience), loperamide should be recommended. This drug has been shown to be effective in shortening symptom duration and the number of unformed stools.
  - ✓ *Loperamide* (e.g., Imodium AD caplets or generic versions) 4 mg initially followed by 2 mg after each unformed stool, not to exceed 16 mg per day (8 mg per day when self-medicating) for up to 48 hours.

- ✓ *Bismuth subsalicylate* (e.g., Pepto-Bismol 262-mg tablets, two chewable tablets [524 mg] every 30–60 minutes as needed; maximum 8 doses per day) could also be used.
- ✓ *Antibiotics* would only be indicated if a bacterial cause is identified, bloody diarrhea develops, or symptoms are severe or persistent.

## Outcome Evaluation

### 5. What clinical and laboratory parameters are necessary to evaluate the diarrhea therapy for achievement of the desired outcome and to detect or prevent adverse effects?

- Diarrhea is usually a self-limiting symptom of an underlying cause. If Prilosec OTC or valproic acid were contributing factors, discontinuation of the drugs should help relieve the diarrhea. Acute diarrhea should generally resolve within 48–72 hours; thus, the problem should lessen noticeably within the next 24 hours in this patient. Because a fever was initially present, an infectious cause should be considered. Other specific monitoring parameters include:
  - ✓ Bowel movement frequency and character (e.g., liquid, semiformal) with each bowel movement.
  - ✓ BP and pulse rate (to assess fluid status) during each hospital shift.
  - ✓ Intake and output daily to assess fluid status.
  - ✓ Body weight daily (for weight loss and to assess fluid status).
  - ✓ Serum electrolytes daily while diarrhea persists.
  - ✓ Other signs of dehydration daily (e.g., dry mucous membranes, skin turgor, weakness or dizziness on arising).
  - ✓ Body temperature during each hospital shift until afebrile.

## Patient Education

### 6. What information should be provided to this patient to enhance adherence, ensure successful therapy, and minimize adverse effects?

#### General information:

- If anorexia, nausea, vomiting, or diarrhea persists or recurs after returning home, consult your physician immediately.

#### Loperamide:

- The drug may cause you to become sleepy. Determine how much this affects you before driving or performing other tasks that require you to be fully alert.
- Do not exceed the recommended maximum dosage of 8 mg per day (for self-management without a physician's approval) or use for more than 2 days.
- Do not use this medication if you develop a high fever or if blood appears in the stool.

## ■ FOLLOW-UP QUESTIONS

### 1. How should this patient's contraception be managed after she is rehydrated and returns home?

- Diarrhea may adversely affect the absorption of oral contraceptives rendering them less effective. It was learned that she took the oral contraceptive the evening that she became ill. Whether its absorption was affected given her vomiting and diarrhea is unknown. The patient should be advised to take her regularly

scheduled tablet the evening following her hospital discharge and then one daily at bedtime as before. No additional backup contraceptive method would be required.

### 2. Does the patient need any changes in her prophylactic migraine headache therapy?

- The patient's GI symptoms were of acute onset, and she had been taking the valproic acid for 6 years for migraine prophylaxis with apparent benefit. Therefore, valproic acid–induced diarrhea is an unlikely cause of her current complaints. If the patient or provider wanted to change therapy, beta-blockers, calcium channel blockers, the antiepileptic agents gabapentin and topiramate, and several antidepressants might be appropriate alternative options. Nondrug choices include cognitive behavioral therapy, acupuncture, and surgery.

### 3. How should her IBS be managed?

- The patient is receiving a bulk-forming agent (psyllium) for her IBS. These products are often used to treat IBS. Other types of therapy include modifying the diet to exclude foods known to trigger symptoms in a specific patient, laxatives (particularly osmotic laxatives) on occasion to treat constipation, alosetron (severe IBS when other therapies have failed), and antidepressants.<sup>9</sup> Due to the varying efficacy of many of these agents and the potential role of psychological treatments for IBS, it is important that this patient be under the routine care of her primary care physician.

### 4. Is there a relationship between the development of IBS and bacterial gastroenteritis?

- There has been an association between the occurrence of bacterial gastroenteritis and the subsequent development of IBS, with postgastroenteritis IBS or risk estimates ranging up to 12–32%. In one study in which known postgastroenteritis IBS patients were followed, approximately half had resolution of the IBS within 5 years.<sup>10</sup> Whether there was any apparent link between this patient's IBS and a previous episode of bacterial gastroenteritis has not been documented.

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