Evaluation and Management of Diarrhea in the ED

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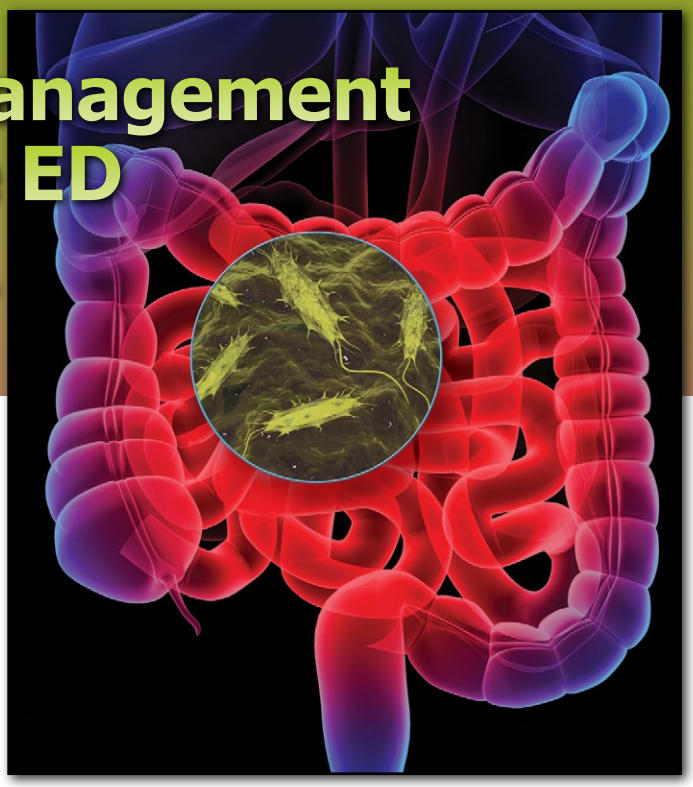

Diarrhea is a common symptom with a potentially serious etiology. Although most cases are self-resolving, a focused history may alert the emergency physician to risk factors that mandate further evaluation. Careful workup is warranted in patients who are elderly or immunocompromised, as well as in those who have traveled recently. Herein, the authors review current recommendations for diagnosis and treatment and provide guidance on which patients should be considered for hospital admission.

Diarrhea is estimated to account for 5% of ED visits, with a higher incidence in the fall and winter months.[1] This symptom poses a challenge to emergency physicians in light of its extensive differential diagnosis. Diarrheal illnesses span the gamut from mild, self-resolving conditions to potentially life-threatening pathology. The evaluation of diarrhea has changed in that the increasing frequency of world travel, an aging population, and the increasing numbers of patients with immunosuppression are all factors that must be considered. Although it is important to be aware of these considerations and the fact that they may represent a more serious etiology, most patients have self-limited disease that requires only supportive care. As EDs are facing increasing volumes and demands to efficiently and rapidly evaluate patients, it is important to be able to differentiate between potentially serious and self-limited illnesses in a timely manner. This article reviews current recommendations for the evaluation and management of diarrhea in the ED, with a focus on "red flags" that should alert emergency physicians to potential significant pathology.

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EPIDEMIOLOGY

Adult diarrhea occurs frequently in the United States, with an estimated incidence of 200 million to 300 million cases annually.[2] Diarrhea in the United States is more likely to be associated with morbidity than mortality; each year, approximately 900,000 patients require hospital admission.[2] Although diarrhea can present with simple abdominal discomfort and increased frequency of bowel movements, it can also lead to severe dehydration. Worldwide, there are more than 2.5 million deaths annually from diarrheal illness.[3] In the United States, diarrhea-related mortality most frequently occurs in the elderly. One study that reviewed national mortality data reported more than 28,000 deaths due to diarrhea over a 9-year period, with 51% of deaths occurring in persons older than 75 years.[4] Despite advances in rehydration, prevention, and treat-

ment, diarrhea remains the leading cause of childhood death worldwide (with the death of a child younger than 5 years occurring about every 10 seconds) and the second overall cause of mortality.[5]

PATHOLOGY

The pathophysiology of diarrheal illness can be categorized into four basic mechanisms: secretory, osmotic, motility, and inflammatory. On average, healthy intestines secrete more than 10 L of fluid (in the form of water and digestive enzymes) per day in addition to the fluid from oral ingestions.[6] The function of colonic epithelium is to reabsorb these fluids to prevent disequilibrium and dehydration. Changes in the colon's ability to handle this fluid burden can lead to increased frequency and decreased consistency of stools.

Secretory Diarrhea

Secretory diarrhea is caused by an increased flow of ions, fluid, and digestive enzymes into the intestinal lumen, overwhelming the colon's ability to handle reabsorption. This form is most commonly seen in acute bacterial infections, where a bacterial enzyme targets intracellular messengers (cAMP, gAMP, Ca^{2+}, and NO) to cause an increase in transmembrane fluid shifts into the intestinal lumen. Infections with agents such as *Vibrio cholerae* and *Escherichia coli* (notably the strains capable of producing the heat-stable enterotoxin) work via this mechanism. The cholera and cholera-like toxins activate intracellular cAMP or gAMP to cause massive volumes of water secretion to a level that far exceeds the colon's reabsorption capability. Clinically, this leads to acute, severe dehydration from intestinal water loss.[6,7] Secretion can reach levels of 1 L per hour in adults.[7] In "true" secretory diarrhea, there will be a large volume of fluid loss, regardless of oral intake, and neither blood nor white blood cells will be present in the patient's stool.[7] Of note, it is worthwhile to remember that not all cases of secretory diarrhea are due to infections. Secretory diarrhea may also be due to hormonal disequilibrium. Examples of hormonal causes include gastrinomas, pancreatic cholera/VIPomas (vasoactive intestinal polypeptide tumors), and carcinoid syndrome.[8] Although these conditions may not be formally diagnosed in the ED, they are important to consider in the differential diagnosis for chronic diarrhea.

Osmotic Diarrhea

Osmotic diarrhea can result from infection or inflammation that causes damage to intestinal epithelial cells, preventing functional reabsorption of fluid contents. However, more commonly, this mechanism may be seen following enteric ingestion of contents that cannot be absorbed by epithelium, producing an osmotic gradient that pulls water from intracellular compartments into the intestinal lumen. This ultimately leads to an increased fluid burden in the colon that cannot be successfully reabsorbed and is consequently propelled through the bowels. In brief, ingestion of substances such as sorbitol (as found in sugar-free foods) or lactose (in those with lactase deficiency) can trigger this mechanism of diarrheal illness.[7] Medications such as laxatives, lactulose, or magnesium-containing antacids may also create diarrheal symptoms, as they increase osmotic burdens within the intestinal lumen. Thus, it is important to inquire about a patient's eating habits as well as his or her medication regimens.

Motility-Related Diarrhea

Irregularity in intestinal motility and peristalsis is the third major cause of diarrhea. Any state that increases the rate of transport through the intestines decreases the amount of time available to reabsorb fluid. The jejunum is capable of absorbing about 75% of the water content it is exposed to, while the colon can normally reabsorb the remainder, so that only a minimal amount is lost in feces. However, when the rate of transport exceeds the rate of reabsorption, the result is a stool with higher fluid load and decreased consistency of bowel movements.[8] Causes include thyrotoxicosis, diabetic autonomic neuropathy, anxiety states, opiate withdrawal, and medications that increase intestinal peristalsis.[7] This can also occur postoperatively in patients who have undergone gastrectomy, vagotomy, pyloroplasty, or antrectomy.[8] Irritable bowel syndrome (IBS) is one of the most common causes of functional bowel dysmotility and accounts for 25% of visits to gastroenterologists.[7] This category also includes overflow diarrhea, in which a distal constipation prevents fur-

ther motility. This leads to loose stools being propelled around the stagnant region and presenting as diarrhea.[9]

Inflammatory Diarrhea

Inflammation of the bowel epithelium can cause alterations in a patient's bowel regimen. This class of diarrheal illnesses is also referred to as exudative diarrhea. It may be caused by damage to the intestinal villi, such as from enteroinvasive infections, or from autoimmune destruction, such as that which occurs in inflammatory bowel diseases; with either etiology, compromise of the epithelium's barrier function allows protein and blood to leak into the intestinal lumen.[8] Some microbacterial pathogens cause bloody diarrhea, or dysentery, by damaging the intestinal cells and allowing direct invasion.[10] This is the mechanism by which *Clostridium difficile* toxin causes diarrhea. When the epithelium is damaged, the tissue is unable to function appropriately, preventing absorption of water through ion channels. Again, the epithelial damage may result in bloody or mucus-laden bowel movements.

FAST TRACK

Symptoms occurring less than 6 hours since oral intake suggest exposure to a preformed toxin, such as Staphylococcus aureus *or* Bacillus cereus *in food products.*

An understanding of these mechanisms is crucial for emergency physicians to rapidly create a differential diagnosis and differentiate between benign and malignant causes for their patients' presenting complaints.

HISTORY AND PHYSICAL EXAMINATION

Diarrhea is a difficult entity to assess and treat in the ED. One of the emergency physician's initial challenges is lack of uniform definition. The classic definition for diarrhea is "greater than three loose stools or bowel movements over a 24-hour period."[3] Another technical definition for diarrhea is "stool weight > 200 grams/day."[11] In addition, the patient's interpretation must be understood by the ED team. Patients may present with any increase in bowel frequency or decrease in solidification of stools. It is important to have patients describe their normal bowel regimen in order to ascertain how their current presentation differs. Additionally, duration of symptoms (acute vs chronic) and the characteristics of the stools themselves (watery, mucus-laden, bloody, fatty) should be documented.[2] Acute diarrhea is defined as lasting less than 14 days; subacute diarrhea, 2 to 3 weeks; and chronic, more than 4 weeks.[11-13] Symptoms occurring less than 6 hours since oral intake suggest exposure to a preformed toxin, such as *Staphylococcus aureus* or *Bacillus cereus* in food products.[11] In patients with chronic diarrhea, it is also important to determine what, if anything, affects symptoms. For example, if the patient reports that the symptoms stop during periods of fasting, this would suggest an osmotic rather than secretory etiology, as symptoms persist throughout in the latter. The patient's current medication list should also be reviewed to assess for drugs that could cause diarrhea. Examples include broad-spectrum antibiotics, promotility agents, antiarrhythmics, antineoplastic agents, antacids (especially those containing magnesium and phosphate compounds), and antihypertensive agents.[12,14] The history should also focus on recent travel, recent antibiotic use, ill contacts (especially in nursing home patients), water source, oral intake (recent meals, tolerance), sexual practice, and exposure to pets (particularly turtles, amphibians, small lizards, and snakes).[11,15]

Many patients presenting to the ED have an acute diarrheal illness. However, patients may come in seeking aid for symptoms that have persisted beyond the 2 weeks associated with acute illness. In these patients, it is important to consider the etiologies of chronic diarrheal illness. Table 1 lists causes of acute versus chronic diarrheal illness.[8,9,11,13] The etiology in chronic diarrhea tends to lean away from infectious causes (unless there is an underlying immunodeficiency) and instead toward underlying medical conditions.[13] For example, potential etiologies may include malignancy, inflammatory bowel disorders, malabsorption (celiac disease), functional bowel disorders (IBS), endocrine disorders (thyroid disease, parathyroid disease, and diabetic autonomic neuropathy), factitious diarrhea, or medication side effects.[13]

Table 1. Etiologies of Diarrheal Illness

	Acute	Chronic
Secretory	Infectious causes: viral, bacterial (*Vibrio cholerae*), parasitic	Tumors: VIPomas, carcinoid syndrome, gastrinomas
Osmotic	Unabsorbed substrates (sorbitol, lactose), poor fat absorption, laxatives	Celiac disease, postsurgical changes (short gut syndrome), pancreatic insufficiency
Dysmotility	Thyrotoxicosis, anxiety, medications, opiate withdrawal	Functional causes: IBS, hyperthyroidism, autonomic neuropathy, surgical changes (eg, gastrectomy, vagotomy)
Inflammatory	Infectious, mesenteric ischemia	Inflammatory bowel diseases, bowel malignancies

VIPoma = vasoactive intestinal polypeptide tumor; IBS = irritable bowel syndrome.
Information extracted from Sabol and Friedenberg[8]; Akhtar[9]; Helton and Rolston[11]; Thomas et al.[13]

The physical exam should focus first on signs of dehydration, as the most common cause of morbidity and mortality from diarrhea is severe dehydration.[5] This can be quickly assessed by evaluating the patient's vital signs (hypotension, tachycardia, tachypnea), mucous membranes, mental status, eyes (for sunken orbits), and skin (for increased turgor).[11] A rectal exam should be performed to assess for blood or mucus in the stools and for evidence of hard stool in the vault (to suggest loose stool circumventing it to cause diarrhea).[9]

Although most diarrheal illness in the United States tends to have a self-limited and benign course, the potential for a more serious pathology must be recognized. Review of the current literature reveals several signs and symptoms that may serve as "red flags" upon a patient's presentation to the ED (Table 2).[9,11,16,17] Some of the most important ones include fever, worsening symptoms after 48 hours, and bloody stools.[11] There are also several patient populations with higher risk for severe illness with increased morbidity and mortality.

RED FLAGS AND HIGH-RISK POPULATIONS

When evaluating a patient, it is always important to consider his or her risk factors for potential complications. Some of the most common risk factors seen today include older age, immunosuppression (from HIV infection, solid organ transplantation, chronic steroid use), exposures to food sources, and recent travel.

Geriatric Population

Elderly patients typically present later in the course of their illness. They often have increased comorbidities and decreased physiologic reserve. As mentioned earlier, about half of diarrhea-related deaths in the United States occur in the elderly.[4] Besides having more physiologic risk factors, elderly patients residing in nursing homes are at risk for diarrhea from infectious etiologies. Close boarding conditions and exposures to antibiotics increase the incidence of *C difficile* infection. Chronic medical comorbidities and polypharmacy also do much to obscure the underlying etiology of an elderly patient's diarrhea. The differential diagnosis, therefore, should include vascular causes (mesenteric ischemia), medication side effects (antacids, laxatives, cholinergics), endocrine disorders (thyroid disease), and dietary causes (hyperosmolar feeds, high sorbitol or lactose content in food) among the numerous possibilities.[12] Diarrhea can have serious sequelae in this population, eg, in bedridden patients, the formation of pressure ulcers secondary to skin breakdown from frequent watery stools. Despite the extensive possibilities and range of severity of illness, there are several signs and symptoms that should alert an emergency physician to a more serious underlying condition: severe dehydration, bloody diarrhea, fever exceeding 101.3°F, evidence of systemic illness, abdominal pain, and (if the patient resides in a nursing home) reports of the same signs and symptoms in other nursing home resi-

Table 2. Red Flags Suggesting Dangerous Pathology

History and Physical Exam Findings

- Fever >101.3°F (38.5°C)
- Severe abdominal pain, especially in patients age >50 years
- Recent hospitalization
- Residency in a nursing home
- Recent antibiotic use
- Dysentery (blood and mucus in stool)
- ≥ 6 stools in 24-h period
- Symptoms that worsen after 48 h
- Evidence of severe dehydration (lightheadedness, excessive thirst, decreased urine output)

High-Risk Populations

- Older patients (≥70 years)
- Immunocompromised patients
- Foreign travelers

Information extracted from Akhtar[9]; Helton and Rolston[11]; Ball[16]; Thom and Forrest.[17]

dents,[9,11] The presence of these features should trigger a more extensive workup upon presentation to the ED, as discussed under "ED Workup."

Immunocompromised Patients

With the rapidly increasing prevalence of immunosuppression, opportunistic infections must be included in the differential diagnosis for diarrhea. When a patient with AIDS and low CD4 counts (especially <50/μL) presents with diarrhea, infections such as cryptosporidiosis, cytomegalovirus (CMV), *Mycobacterium avium* complex (MAC), and microsporidiosis must be considered.[18] Among these, CMV is the most common cause of opportunistic infection, causing symptoms that affect the entire gastrointestinal system.[6] Moreover, if a patient presents with additional complaints of lethargy and spiking fevers, disseminated MAC should be strongly considered.[16] HIV infection itself, as well as treatment with protease inhibitors as part of HAART, can cause diarrhea.[17] Patients immunosuppressed for other reasons, such as the treatment of chronic inflammation, cancer, and solid organ transplants, are at risk for the same infectious etiologies as HIV/AIDS patients. In cancer patients, the possibility of diarrhea caused by chemotherapy and radiation should be kept in the differential diagnosis. Of note, CMV is the most common cause of diarrheal illness in solid-organ transplant patients; however, the incidence of reactivation of this virus has been greatly reduced with the use of valganciclovir prophylaxis.[17] According to the National Cancer Institute, 50% to 80% of patients receiving chemotherapy experience moderate to severe episodes of diarrhea.[19] Additionally, certain surgical interventions, such as a Whipple procedure or Roux-en-Y, may lead to the development of bacterial overgrowth or a short gut syndrome, which in turn can lead to diarrhea from decreased intestinal absorption.[20] Patients receiving anti–tumor necrosis factor α therapy have been found to be at increased risk for infections with *Salmonella* and *Listeria* species.[17] However, it is important to keep the differential diagnosis broad because immunosuppressed patients remain at risk for the same infectious and noninfectious etiologies as immunocompetent patients (eg, dysmotility, dietary, medication side effects)[21]; rather than focus solely on opportunistic infectious causes, it is best to keep them in mind in the global evaluation of patients in this population.

Travelers

One of the largest populations to present with diarrheal illnesses is those who have recently traveled abroad. It is estimated that each year, approximately 34 million persons from industrialized countries travel to locales such as Africa, Latin America, the Caribbean, and Southeast Asia, where there is a high prevalence of diarrhea.[10] Between 20% and 50% experience "traveler's diarrhea," with many having to shorten their vacation or limit business travel activities and 20% becoming confined to bed due to illness.[22] Symptoms generally begin within 1 week of arrival/exposure and resolve within 3 to 5 days of onset.[10] Patients may complain of loose stools, abdominal pain or cramps, nausea, vomiting, fever, and tenesmus. Traveler's diarrhea is usually caused by the consumption of contaminated food and water. These commonly include undercooked seafood,

unclean tap water, and raw fruits and vegetables.[23] Epidemiologic studies have demonstrated that certain populations are at higher risk for infections: the very young, those with blood type O, and patients taking proton pump inhibitors.[10] Stool studies have shown that 60% to 85% of cases are caused by bacterial infections, particularly *E coli* strains, including those that produce enterotoxins (heat-labile and heat-stable variants).[10,22,23] The remaining causes include parasitic and viral infections, most notably noroviruses, rotaviruses, and enteric adenoviruses.[10,23] Treatment is aimed primarily at reducing symptoms and facilitating rapid return to functionality. However, there is also concern that some causes of traveler's diarrhea may lead to long-term sequelae, such as Reiter syndrome (associated with *Campylobacter jejuni* and *Yersinia* species infections), Guillain-Barré syndrome (*C jejuni*), hemolytic uremic syndrome (*Shigella* and enterohemorrhagic *E coli* infections), and postinfectious IBS.[3,22,23] Although these complications are infrequent, they serve as further justification for empiric treatment of traveler's diarrhea. Most cases of traveler's diarrhea do not require hospital admission and should resolve with the therapy described under "Treatment."

THE ED WORKUP

With so many potential causes for diarrheal illnesses, it is crucial to tailor the workup to be cost-effective and focused on potential underlying etiologies. As suggested above, it is critical to obtain a thorough history to ascertain any specific risk factors for more deleterious causes. Reviewing the patient's medical history, current signs and symptoms, and physical exam findings (with attention to fevers and evidence of dehydration/shock) will help alert the physician to any etiologies that may be associated with high morbidity or mortality. This method should help distinguish ED patients who may be safely discharged home from those who need more extensive inpatient workup. Stool samples can be sent for evaluation for fecal leukocytes, cultures, ova and parasites, and *C difficile* toxins. However, due to their cost and turnaround time, these studies are not always practical for ED use.

Traditionally, it has been taught that evaluation of stool for fecal leukocytes is one method of differentiating secretory from inflammatory/infectious diarrhea.[24] However, this test has poor sensitivity and cannot discern definite etiologies. A meta-analysis of multiple studies evaluating the sensitivity and specificity of fecal screening tests in the workup of inflammatory diarrhea has found that stool leukocyte testing does not consistently diagnose invasive diarrhea or predict response to antimicrobial therapy.[25] A positive result may simply prompt further culture and sensitivity testing. From a cost-efficacy standpoint, stool cultures yield an identified organism in 1.5% to 5.6% of samples, at a cost of $950 to $1,200 per positive study.[11] Therefore, "routinely" testing stool samples offers little benefit. If a particular bacterial organism is suspected based upon the patient's risk-factor profile, stool culture and sensitivities may be ordered. The laboratory should be advised to test for the organism in question, since standard stool culture and sensitivity evaluates only for *Campylobacter*, *Salmonella*, and *Shigella* species. *Vibrio*, *E coli* O157:H7, and *Yersinia* require special growth media.[8,11]

Stool samples should be sent expeditiously for *C difficile* toxin detection, given the high incidence of *C difficile* diarrhea. Ideally, cytotoxicity testing should be used, but unfortunately, these studies have a turnaround time of 1 to 2 days. However, immunoassay testing for the *C difficile* toxins is completed in a shorter time frame.[26] Enzyme immunoassay has an estimated sensitivity of 63% to 99% and a specificity of 93% to 100%, with results typically available within 2 to 6 hours.[27] With newer tests, sensitivity is reported at 85% to 95%.[27] Ultimately, several sets of stool samples should be sent for the *C difficile* toxin assay to increase sensitivity and specificity.[14] In the interim, empiric antibiotic therapy with oral metronidazole or vancomycin should be started if there is sufficient suspicion of *C difficile*.[9] Patients with a history of recent hospitalization or recent antibiotic use and those who reside in a nursing home are at the greatest risk. Infections with *C difficile* can range from asymptomatic carriage to life-threatening colitis, toxic megacolon, or abdominal compartment syndrome.[26]

The laboratory tests commonly ordered in the ED are rarely helpful in the evaluation and management of diarrhea. Outside of stool studies, there are some blood

studies that may also be used for evaluation and management of patients with diarrhea. If hyperthyroidism is suspected (diaphoresis, tachycardia, elevated temperature), obtaining levels of thyroid-stimulating hormone and T_3/T_4 can aid in the diagnosis. A complete blood count (CBC) would act as a nonspecific screening tool for infection, which would be reflected by an elevation in the patient's white blood cell count. However, infection should be inferred from the patient's history and physical exam findings rather than from this lab value. A CBC would be useful, however, to determine the red blood cell and platelet counts when there is concern for inflammatory etiologies with potential for anemia and thrombocytopenia, such as in hemolytic uremic syndrome or inflammatory bowel disease.[8,9,11,12] A basic metabolic panel (BMP) can provide the examiner with information regarding a patient's hydration status (blood urea nitrogen, creatinine levels); however, such information can also be determined from the physical exam. The BMP can provide an estimate of acid-base and electrolyte shifts seen in diarrheal states.[11] Liver function tests are beneficial when the patient has abdominal pain or signs of acute hepatitis, pancreatitis, or gallbladder disease. Serum lactate levels should be ordered if there is concern for mesenteric ischemia or severe dehydration/septic shock. Blood cultures should be obtained only if there is suspicion for systemic involvement of an infectious etiology.[8,12]

FAST TRACK

Liver function tests are beneficial when the patient has abdominal pain or signs of acute hepatitis, pancreatitis, or gallbladder disease.

The use of imaging studies should be reserved for specific concerns. An abdominal radiograph may be obtained in the evaluation of patients with abdominal pain and distention. However, this would be helpful only in cases where there is concern for perforation (to visualize free air in the abdomen), obstruction (dilation proximal to a lead point for rotation), or colonic distention (as in toxic megacolon).[5,11] CT, however, has limited utility in the further workup of potential infectious/inflammatory etiologies and has lower levels of sensitivity and specificity.[28] Conversely, it can reveal other serious conditions which create diarrheal symptoms, such as pneumointestinalis, obstruction, or mesenteric ischemia.[29] CT can also demonstrate underlying tumors that may be causing a chronic diarrheal illness. Again, these studies should be reserved for individual cases with a particular finding that warrants investigation. They should not be used indiscriminately for all cases of diarrheal illness, as they are expensive and time-consuming, involve radiation exposure, and may ultimately not be necessary.

TREATMENT

As with the treatment of any ED patient, it is important to start with the basics. Patients who present with severe dehydration require fluid resuscitation. Moreover, patients with grave systemic illness and sepsis require aggressive early goal-directed therapy. However, in the more common and less acute presentations, it is important to decide how to best manage symptoms in order to sustain healthy hydration and return the patient to baseline functionality.

One of the paramount goals of treatment is rehydration. This therapy has contributed the most to reducing mortality worldwide from secretory diarrhea, such as that seen in *V cholerae* infections.[5,7,30] In patients with severe dehydration (as identified by vital signs and exam), resuscitation with isotonic IV fluids should be initiated. Once a patient is able to tolerate oral hydration, has improving vital signs, and does not appear toxic, the transition should be made from IV to oral fluids. If the patient is to be discharged to home, aggressive fluid hydration should be continued to keep up with stool losses while symptoms resolve. The World Health Organization (WHO) recommends use of a hypotonic solution rich in glucose with a sodium concentration of 75 mmol/L.[3] These solutions are designed to promote intestinal reabsorption of water and sodium through glucose uptake among enterocytes.[5,10] Treatment is not limited to specific solutions but may also incorporate soups, fruit juices, or foods with high carbohydrate compositions (eg, crackers, bread).[5] There is also on-

going research to investigate the use of starch-based solutions, with early studies suggesting these solutions provide better oral rehydration compared to the glucose-based solutions recommended by WHO.[5] "Sports drinks" are *not* considered appropriate in this patient population.[31] As soon as patients are able to tolerate oral intake, their diet should be advanced as tolerated to return to normal enteric functioning.[10,31,32] The traditionally recommended "BRAT diet" is now considered restrictive, and diet should be "as tolerated," using foods from the patient's normal routine.[31] Although it was once believed that high stool output "washes out" lactase enzymes in the intestines, even milk products may be ingested, unless there is already an underlying lactase deficiency due to mild to moderate diarrhea.[33] Infants who are breastfeeding should continue to do so to maintain hydration.[32]

One of the most common debates in medicine concerns the use of antibiotics and antidiarrheal medications. It is not infrequently taught that patients with diarrheal illness should not receive these agents, as it places them at risk for prolonged illness, carrier state, and possible systemic illness from bacterial toxins.[34,35] One example of the rationale behind this medical misconception is seen in a 1969 article studying the duration of *Salmonella* infection in patients treated with antibiotics compared with those who were not.[35] The reluctance to use antimotility agents arose from studies in the 1960s and 1970s evaluating the use of opiates or diphenoxylate-atropine in diarrheal states.[34,36,37] However, given the lack of human subjects in one study[34] and the insufficient power and design to prove statistical significance in another,[36] adverse outcomes from use of these agents were not clearly established. Subsequent studies have failed to demonstrate true harm from the use of antibiotic agents and antimotility agents, particularly in the absence of fever exceeding 101.3°F or dysentery.[11,23,37] Conversely, the evidence suggesting a clear benefit is limited as well.[5] Antimotility agents in combination with antibiotics have been used safely in patients with dysentery with limited evidence for worsening morbidity or mortality.[5] Formal CDC guidelines nevertheless recommend against using antimotility agents in patients with fever or bloody stools.[31] If there is suspicion for *C difficile* infection, antimotility agents should also be avoided to prevent complications from continued intracolonic toxin accumulation.[26] This can lead to life-threatening abdominal distention with subsequent abdominal compartment syndrome and toxic megacolon. In terms of antimotility agents, loperamide and diphenoxylate-atropine are two of the most commonly used agents.[5] They function to increase transit time through the intestines, with the goal of promoting fluid reabsorption and decreasing fluid losses. They may be prescribed for use as needed throughout the course of the diarrheal illness. Another option is the use of bismuth subsalicylate. This agent has demonstrated anti-inflammatory, antisecretory, and even minimal antibiotic properties.[10,23] Additionally, it is widely available and generally well tolerated, with limited side effects—most commonly tinnitus from the salicylates and (guaiac-negative) darkened stools from the bismuth. However, dark (guaiac-positive) stools may also indicate gastrointestinal bleeding related to the salicylates. It has been advocated for prophylactic use to prevent contamination with potential pathogens for travelers abroad.[23]

For patients who likely have traveler's diarrhea, treatment consists of empiric antibiotic therapy aimed at likely causative pathogens. However, prior to treatment, it is important to consider the risk of side effects and concerns about antibiotic resistance, as well as the fact that traveler's diarrhea is associated with limited morbidity and very rare mortality. As above, the choice to treat should be made with the objective of timely relief of symptoms or for concerns of potential sequelae. Numerous studies have evaluated the utility of several classes of antibacterial agents, including fluoroquinolones, trimethoprim/sulfamethoxazole (TMP/SMZ), azithromycin, and newer agents such as rifaximin.[23] Rifaximin is a synthetic antimicrobial that is not absorbed by the intestines, leading to higher enteral concentrations. Research has shown substantial benefit from rifaximin in the treatment of traveler's diarrhea without evidence of systemic infection, again due to very limited intestinal absorption.[22] There is also evidence for rifaximin's potential in the treatment of HIV/AIDS patients with acute diarrheal illnesses. In addition to its broad coverage for common enteric

pathogens, emerging evidence suggests rifaximin may be used to treat *Cryptosporidium parvum* infections, which previously have only been treated through immune reconstitution.[38] Other agents currently being investigated include newer fluoroquinolones such as prulifloxacin, which has been shown to have an appropriate spectrum of coverage and greater potency than ciprofloxacin.[39] This agent is currently in phase 3 clinical studies but has been approved for use in Europe and Japan.

The following recommendations have emerged for the treatment of traveler's diarrhea: (1) for noninvasive moderate to severe traveler's diarrhea, a single oral dose of a fluoroquinolone (ciprofloxacin 500 mg or levofloxacin 500 mg) is the treatment of choice; (2) a 3-day course of a fluoroquinolone is recommended for cases with evidence of invasive diarrhea (ie, with dysentery); (3) TMP/SMZ is no longer recommended, due to significant widespread bacterial resistance; (4) single-dose azithromycin (1,000 mg) has equal efficacy to that of fluoroquinolones and is particularly effective in cases of fluoroquinolone resistance seen in resistant *Campylobacter* infections in Mexico or in children (in whom quinolones are contraindicated); and (5) rifaximin has demonstrated slightly better tolerability, a lesser side-effect profile, and better ability to reduce duration of illness compared to TMP/SMZ and ciprofloxacin.[22,23]

Patients who are confirmed to have *C difficile* infectious diarrhea should be treated with oral metronidazole (500 mg tid) or oral vancomycin (125 mg/qid) for 10 to 14 days; there is no statistical difference in outcome between either medication, but oral vancomycin is much more expensive.[14] Fidaxomicin is a macrolide that recently received FDA approval for the treatment of *C difficile* diarrhea.[40] If there is suspicion that the *C difficile* diarrhea is antibiotic induced, the antibiotic should be discontinued.[14,26] If the patient lives in a nursing home, it is important to report the findings to staff at that facility to initiate source control and prevent spread among other residents.[9]

Probiotics have been advocated for the treatment of diarrheal illness since the early 1980s.[5] This therapy is targeted at the disturbance in colonic microbiologic balances. Multiple studies have investigated the utility of providing particular species of benign bacteria to repopulate the flora of a host's gastrointestinal tract. Species that have received the most study include *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces* for the treatment of acute infectious diarrhea.[41] To date, studies have demonstrated limited benefit, particularly for mild, self-resolving causes of diarrhea.[41,42] However, some evidence supports the use of *Lactobacillus* GC in addition to traditional therapy for antibiotic-associated *C difficile* diarrhea.[41] Ultimately, the medical literature shows only weak evidence for using probiotics as sole prevention or treatment of acute diarrhea, but it suggests probiotics may have some benefit as an adjunct to other treatment modalities.[42] This would limit use of these therapies in emergency medicine.

For patients with suspected etiologies other than an infectious etiology, the goal of therapy should be to target the underlying cause in combination with symptomatic relief. For example, if the diagnosis of thyroid disease is suspected, thyrotoxicosis should be evaluated and treated emergently. Once immediately life-threatening etiologies have been ruled out, the patient should be treated for symptomatic relief either until symptoms resolve or until outpatient follow-up with a primary care physician and/or gastroenterologist.

DISPOSITION

In most cases, discharge to home is appropriate. Criteria for hospitalization include evidence of systemic illness, hemodynamic instability, evidence of sepsis, or unexplained findings. Treatment should be started early in the ED as clinically warranted (fluid resuscitation, antibiotics), as should any testing deemed worthwhile (blood/stool cultures). For transplant patients, the transplant coordinator should be contacted for further direction in care. Patients with HIV/AIDS who present with chronic diarrhea may also require inpatient workup, as the estimated 10-month mortality rate is 72% in this group.[13] Those with sepsis, severe dehydration, and hemodynamic instability should be admitted to the ICU. If mesenteric ischemia is suspected, prompt consultation with a general or vascular surgeon is required. Other patients may be admitted to a general medical or gastroenterology service as

appropriate.

Patients deemed stable enough for discharge should receive written instructions indicating signs and symptoms that warrant immediate return to the ED. They may also be treated symptomatically as described. If an infectious etiology is suspected, the decision to use antibiotics is made by the treating physician, based on the patient's risk factors. It may be beneficial to order laboratory studies in the ED for use by the patient's primary physician during follow-up: thyroid cascades, stool cultures, or stool samples for ova and parasites, if they are expected to be of high yield. Patients who are discharged to home should have primary care follow-up established, at a minimum. Patients with chronic diarrhea may be referred to a gastroenterologist for continued evaluation.

CONCLUSION

Diarrheal illness is a common presentation in the ED, with most cases having a benign, self-limited course that does not require extensive workup (Table 3).[2,5,9] However, patient groups such as the elderly, recent travelers, and those who are immunocompromised are at risk for more serious etiologies or prognoses that mandate further evaluation. Antimotility agents may be used in most patients for symptomatic relief and return to functionality. Antibiotics may be prescribed at the physician's discretion for suspected traveler's diarrhea. Patients in the groups mentioned above or those with concerning signs and symptoms should be considered for admission for comprehensive workup and treatment. In the absence of risk factors and "red flags," patients who are hemodynamically stable may be discharged to home with continued outpatient follow-up. EM

Table 3. Summary of Recommendations for Emergency Physicians

- Obtain focused history, perform physical examination
  - Determine acuity of disease (acute, subchronic, chronic)
  - Identify risk factors/red flags
- Assess hydration status, determine need for oral vs IV hydration
- Perform targeted workup, based on identified risk factors
  - *Clostridium difficile* toxin assay
  - Stool cultures (only high-risk populations)
  - Ova and parasites (as directed by patient's risk factors)
  - CBC, BMP, LFTs, lactate, thyroid cascade (should not be ordered indiscriminately)
- Treat for symptomatic relief
  - Consider empiric antibiotics for traveler's diarrhea (based on region of travel) vs symptomatic support
  - Avoid antimotility agents if there is concern for *C difficile*
  - Start early therapy if there is high suspicion for *C difficile*

IV = intravenous; CBC = complete blood count; BMP = basic metabolic panel; LFT = liver function test.

Information extracted from Baldi et al[2]; Casburn-Jones and Farthing[5]; and Akhtar.[9]

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