Update on Diarrhea

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Practice Gaps

The mainstay of management of infectious diarrheal illness in children remains supportive care with oral or intravenous rehydration. In the postvaccine era, norovirus has supplanted rotavirus as the leading cause of gastroenteritis presenting to medical facilities in the United States.

Objectives After reading this article, the reader should be able to:

1. Recognize the common pathogens associated with infectious diarrhea and develop a management plan.
2. Identify the key differences between infectious and noninfectious causes of diarrhea.
3. Effectively treat a child with cow milk protein intolerance.
4. Recognize that antidiarrheal and antimotility agents are not indicated or recommended in the treatment of infectious diarrhea.
5. Understand the changing epidemiology of infectious diarrhea in the postvaccine era.

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INTRODUCTION

Diarrhea is a worldwide problem that is frequently encountered in the practice of pediatric medicine. According to the World Health Organization, diarrheal illness is the second leading cause of death in children younger than age 5 years, accounting for 760,000 deaths per year in this age group. (1)

The overwhelming majority of diarrheal illnesses are due to acute infectious diarrhea, commonly referred to as acute gastroenteritis (AGE). The degree of dehydration, assessed by both history and physical examination, is the most important indicator of disease severity. However, most children who have infectious diarrhea are not dehydrated and can be successfully treated at home with replacement of ongoing fluid losses using oral rehydration solution (ORS).

The routine use of antibiotics and antidiarrheal agents is not recommended for treatment of acute diarrhea and may cause harm. Restrictive diets are not necessary; the adverse effects on nutritional status during diarrheal illness can be

lessened or prevented by rapid reinstitution of a regular feeding regimen, which most often can include milk and milk products. (2)(3)

In this article, we provide an update on the diagnosis and clinical management of diarrheal illness for the general clinician.

DEFINITIONS

Stools that are more frequent or looser in consistency than an individual's regular stools are generally regarded as diarrhea. Stools may contain blood, mucus, fat, or undigested food particles. Parents frequently are anxious about differences in stool color, but only red (blood), black, tarry (melena, upper gastrointestinal bleeding), or white (acholic) stools are generally alarming.

Classifying diarrhea based on timing and content is clinically more useful. Categorization helps guide evaluation and management decisions. Four clinical classifications exist for diarrheal conditions:

- Acute watery diarrhea lasting several hours to days
- Acute bloody diarrhea or dysentery
- Prolonged diarrhea lasting 7 to 14 days and persistent diarrhea lasting 14 days or longer
- Diarrhea with severe malnutrition, which places the child at high risk for complications

Acute watery diarrhea is generally viral- or toxin-mediated. Replacement of ongoing fluid losses and reassurance usually are all that is required. Because the illness is typically self-limited, regardless of the etiologic microorganism, no specific testing is indicated.

Acute bloody diarrhea is an urgent issue that requires quick action. This is in contradistinction to blood in a non-diarrheal stool, which, in an otherwise well-appearing infant or child, is more likely to be associated with a less urgent problem such as a fissure, milk protein intolerance, or polyp. Blood in a diarrheal stool is a sign of infection, allergic reaction, or immune-mediated inflammation, as seen in inflammatory bowel disease. At a minimum, the presentation of acute bloody diarrhea necessitates collection of a stool sample for culture. This allows identification and proper management of potentially life-threatening illnesses such as hemolytic-uremic syndrome (HUS) caused by *Escherichia coli* O157:H7.

Diarrhea that persists longer than 14 days may be infectious, may represent the unmasking of a chronic illness, or may be a complication of AGE. *Giardia* and *Cryptosporidium* species are the most common enteric protozoan infections that cause persistent diarrhea. *Clostridium difficile* infection should also be considered when diarrhea is persistent. Chronic illnesses that may present as acute and persistent diarrhea include celiac disease and inflammatory bowel disease. Diarrhea-predominant irritable bowel syndrome can present as a complication of postinfectious diarrhea in adults. The equivalent illness in children may be chronic nonspecific diarrhea (CNSD). In children, another cause of postinfectious persistent diarrhea is villous atrophy related to mucosal injury by an infectious agent or an allergen. Historically, this illness was associated with enteropathogenic *E coli* infection. Villous atrophy appears to have decreased in frequency with the disappearance of this infection in many developed countries and with the use of age-appropriate regular diets either during the acute or prolonged phase of illness. Reinstitution of feeding is believed to aid in mucosal healing and recovery of the absorptive potential of the intestine. (4)

Diarrhea in the setting of severe malnutrition, especially vitamin A deficiency and zinc deficiency, is deserving of its own category due to the increased risk of severe complications and even death. This scenario is rarely encountered in developed nations, but it remains a problem in many parts of the world. Global health efforts to reduce this category of diarrheal illness have the potential to drastically decrease mortality and morbidity in children worldwide.

ETIOLOGY OF DIARRHEAL ILLNESS

Although most diarrheal illness is due to viral, bacterial, or parasitic infections, the noninfectious causes of childhood diarrhea are important for clinicians to consider and differentiate from infectious causes. (5) Of particular importance are the noninfectious causes in the very young infant (<30 days of age) or where diarrhea is prolonged or persistent.

VIRAL GASTROENTERITIS

The most common viral pathogens encountered in the United States are norovirus and rotavirus. Viral infections typically cause low-grade fevers and watery nonbloody diarrhea.

Norovirus

Recent publications indicate that norovirus has overtaken rotavirus as the leading cause of medical visits related to viral gastroenteritis in the United States, with an estimated 1 million health care visits annually. (6) Norovirus is the leading cause of foodborne disease outbreaks and is frequently implicated in traveler's diarrhea. Typically, infections with norovirus result in a less severe gastroenteritis than infections with rotavirus and are characterized by

frequent vomiting. Due to antigenic diversity, norovirus infection does not lead to lasting host immunity in subsequent seasons when another variant emerges.

Rotavirus

Rotavirus is a key pathogen in global childhood morbidity and mortality related to diarrheal illness. The burden of disease is especially high in developing countries, where poor sanitation and close living quarters contribute to the spread of this highly infectious disease. Very few infectious virions are required to cause disease in a susceptible host. Before widespread vaccination in the United States beginning in 2006, nearly every child was infected with rotavirus by age 5 years. (7) Rotavirus infections tend to cluster in the winter months in temperate climates, while more tropical climates have less specific seasonality. Infections with rotavirus generally are more severe and protracted than infections that have other causes, leading to more severe dehydration. Rotavirus was the cause of 20% to 50% of severe AGE cases in young children worldwide. In areas where vaccine implementation has been successful, rotavirus-related hospitalizations and death have declined dramatically. This success is somewhat less pronounced in developing countries. (8)

BACTERIAL GASTROENTERITIS

Although less common than viral causes, bacterial infections are an important cause of acute diarrheal disease in children. Certain clinical findings, including high temperature (>40°C [104°F]), bloody stools, severe abdominal pain, and central nervous system involvement, suggest a bacterial pathogen; vomiting and respiratory symptoms are more consistent with viral causes. (2)

Salmonella Species

Salmonella species are commonly implicated in bacterial gastroenteritis worldwide. Children infected with nontyphoidal *Salmonella* species typically have a mild, self-limited gastroenteritis characterized by watery, bloody, or nonbloody diarrhea; vomiting; and fever. Extraintestinal complications are common in children younger than age 3 months, including bacteremia, meningitis, and osteomyelitis. Diagnosis is confirmed on stool culture. Treatment with antibiotics is reserved for special populations, including those at high risk of disseminated disease (age younger than 3 months, immunocompromised patients, and those with sickle cell disease) and those with suspected or proven sepsis or who appear toxic. Recommended treatment regimens are based on local resistance patterns, culture susceptibility data, patient age, and risk of extraintestinal complications. Antimicrobials with activity against *Salmonella* species include ampicillin/amoxicillin, trimethoprim-sulfamethoxazole, tetracyclines, third-generation cephalosporins, macrolides, and fluoroquinolones. The optimal duration of treatment for *Salmonella* gastroenteritis has not been defined, but expert opinions call for a 5- to 7-day course.

Shigella Species

Shigella species are the most common cause of bloody diarrhea in children. Only 10 to 100 organisms are required for person-to-person transmission via the fecal-oral route. Children infected with *Shigella* species generally present with fever, malaise, watery diarrhea, tenesmus, and crampy abdominal pain. Blood and mucus are typically present in the stools by the second day of illness. Routine stool culture can differentiate this organism from other invasive pathogens. The infection usually is self-limited, resolving in 48 to 72 hours after symptom onset. Treatment with antibiotics is reserved for those who are severely ill or hospitalized. Antimicrobial resistance to first-line agents is common in *Shigella* infections. Accordingly, antimicrobial selection should be guided by local resistance patterns and culture susceptibility data. Strains susceptible to ampicillin or trimethoprim-sulfamethoxazole can be treated for 5 days. Infection control measures, including strict handwashing, should be implemented in outbreaks at schools and child care facilities, where infections may spread quickly. The high temperature often seen at the onset of illness has been associated with febrile seizures.

Campylobacter jejuni

Bacterial gastroenteritis caused by *Campylobacter jejuni* is common worldwide. In developed countries, infection follows a bimodal pattern, with peaks in children younger than age 2 years and again in young adults. The illness can range in severity from mild diarrhea to frank dysentery. Fever, malaise, nausea, and abdominal pain are common. Stool culture is the gold standard for diagnosis. Most children recover in 1 week without specific antimicrobial treatment. Treatment is reserved for severe disease and for outbreaks in child care settings. The primary benefit of treatment is the reduction of fecal shedding from 2 weeks to 48 hours. The recommended treatment regimen is a 5-day course of erythromycin.

DIARRHEAGENIC *ESCHERICHIA COLI*

Escherichia coli are both part of the normal human large intestinal microbiota and important pathogens associated

with diarrheal illnesses worldwide. Diarrheagenic strains of *E coli* have virulence factors that produce distinct clinical presentations. Of particular clinical importance is *E coli* O157:H7 infection, which presents with bloody diarrhea and can lead to HUS in up to 20% of affected individuals. (9) Experts recommend that children infected with *E coli* O157:H7 or other shiga-like toxin producing *E coli*, be hospitalized for volume expansion with intravenous (IV) fluids. By hospitalizing such children for careful monitoring, clinicians can judiciously hydrate patients, avoid unintentional harm resulting from antibiotic or antimotility medication, and minimize secondary spread. Patients with confirmed *E coli* O157:H7 are highly infectious, and infection control is more easily achieved in the hospital. IV volume expansion with fluids appears to protect the kidneys. Careful monitoring of urine output is critical to avoid fluid overload in patients at risk for HUS. The goal of volume expansion is to avoid the anuric phase of HUS because this portends a worse prognosis. Most experts agree not to treat children with *E coli* O157:H7 with antimicrobials due to concern that this increases the risk of developing HUS.

Clostridium difficile

Clostridium difficile is an increasingly prevalent cause of diarrhea in both hospitalized and nonhospitalized children. Historically, *C difficile* infection was believed to affect only high-risk populations following exposure to antibiotics. Community-acquired *C difficile* infection rates have increased over the past decade, now accounting for about 25% of all *C difficile* infections. Although exposure to antibiotics remains a risk factor, it is no longer considered requisite in the pathogenesis of *C difficile* infection. (10) In addition, although *C difficile* diarrhea in children was classically described as bloody, it may be nonbloody.

Discontinuation of antimicrobial agents is often the first step in treating *C difficile* infection and may suffice when appropriate. For patients not receiving concurrent antimicrobial agents and for those with moderate or severe disease, proper empiric antibiotic treatment should be started as soon as the diagnosis is suspected. The initial treatment recommendation is a course of oral metronidazole for 10 to 14 days. Recurrent *C difficile* infection in children is increasing and often presents a treatment challenge. A repeated course of oral metronidazole is recommended for primary relapse; a course of oral vancomycin is recommended for subsequent relapse. Prolonged therapy and pulse therapy have also been used to treat recurrent disease. The use of fecal microbiota transplant (FMT) in treatment of refractory *C difficile* infection in children and adults is gaining widespread acceptance, although its long-term safety is uncertain. The US Food and Drug Administration (FDA) recently approved FMT as a treatment for recurrent *C difficile* infection. Additional evidence suggests that probiotics and prebiotics can decrease the severity and duration of *C difficile* infection. (11)

SPECIAL POPULATIONS

Children who are immunodeficient, malnourished, or have an underlying chronic medical condition are at higher risk for a more severe and prolonged disease course with common diarrheal pathogens. Opportunistic microorganisms such as *Cytomegalovirus* species can also cause persistent and severe diarrhea in these populations.

NONINFECTIOUS DIARRHEA

Noninfectious causes of diarrhea represent a broad range of disease states (**Table 1**). A few general principles are helpful in differentiating the relatively uncommon noninfectious causes of diarrheal diseases from infectious causes. Onset of diarrhea at birth or in children younger than age 30 days is concerning for a congenital diarrheal disorder and warrants prompt evaluation by a subspecialist.

Food protein–induced proctocolitis ("cow milk protein intolerance"), a nonimmunoglobulin E-mediated process, usually presents in the first postnatal month in otherwise healthy infants who have blood-streaked stools. Diarrhea is notably absent in this condition. Up to 60% of cases occur in exclusively breastfed infants. Cow milk protein

TABLE 1. **Noninfectious Causes of Diarrhea in Children**

• Carbohydrate malabsorption, congenital or acquired
• Functional diarrhea, eg, diarrhea-predominant irritable bowel syndrome, "chronic nonspecific diarrhea"
• Inflammatory bowel disease
• Pancreatic insufficiency
• Immunodeficiency syndromes
• Motility disorders
• Neuroendocrine tumors
• Hyperthyroidism
• Congenital diarrhea
• Drug-related

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intolerance is primarily a clinical diagnosis. A complete blood cell count can be useful because most infants have normal-to-borderline low hemoglobin values. Additional laboratory testing, including assessing peripheral eosinophilia and the presence of fecal leukocytes, is limited by poor specificity. Symptoms typically resolve within 1 to 3 weeks after the elimination of milk- and soy-containing products in the maternal diet in breastfed infants or transition to a partially hydrolyzed formula. A trial of soy-based formula can be attempted, but up to 40% of infants react to both cow milk and soy proteins. Reintroduction of milk- and soy-containing products may be attempted as early as age 6 months, and most individuals achieve clinical tolerance by age 1 year. (12) The long-term prognosis is excellent, with no increased incidence of (immunoglobin) IgE-mediated allergies to milk or soy proteins.

PERSISTENT DIARRHEA

Most acute diarrheal episodes resolve in less than 1 week; prolonged diarrhea that lasts for 7 to 14 days is a risk factor for development of persistent diarrhea. Persistent diarrhea in children has an age-related spectrum of disease. In infants and young children, the typical causes include persistent intestinal infections, intractable diarrhea of infancy (postinfectious diarrhea), intolerance to specific nutrients such as cow milk protein (allergic colitis) or dietary carbohydrates (sucrose and lactose), pancreatic insufficiency, and chronic nonspecific diarrhea (CNSD or toddler's diarrhea).

Celiac disease is an important cause of persistent diarrhea throughout childhood, and inflammatory bowel disease is a consideration, especially when there is bloody diarrhea, poor growth, or other extraintestinal manifestations. (4) Food allergy is often suggested as a cause for persistent diarrhea. When food allergy is the cause, diarrhea occurs most commonly in immediate relationship to the ingested food in question, and there are other manifestations of allergy, including hives or wheezing. Eosinophilic gastroenteritis may be a cause of diarrheal disease and requires endoscopy and biopsy for diagnosis.

According to the Rome III criteria, CNSD is defined as toddler's diarrhea in children younger than age 4 years and as irritable bowel syndrome in children ages 5 to 18 years. (13) Children with CNSD do not have evidence of weight loss or blood in the stool, and they maintain a normal appetite and activity level. The diarrhea in CNSD only occurs during the waking hours. Typically, affected children have a large formed or semiformed stool upon awakening and have frequent smaller, watery stools as the day progresses.

DIAGNOSTIC CONSIDERATIONS

A stepwise approach to the evaluation and treatment of children with persistent diarrhea is necessary. History and the child's age are among the most important guides.

In a child who is not gaining weight, evaluation for persistent infections, celiac disease, intractable diarrhea of infancy, pancreatic insufficiency, and inflammatory bowel disease is indicated. For example, preliminary evaluation might include bacterial stool culture, testing for *C difficile*, evaluation for parasites with direct fluorescent antigen, inflammatory markers (complete blood cell count, erythrocyte sedimentation rate, fecal calprotectin), specific serologic tests for celiac disease (tissue transglutaminase-IgA or antiendomysial antibodies-IgA), or fecal elastase.

Diarrhea in a child who is otherwise well and gaining weight is more likely to be due to functional causes or dietary intolerance. Most adults and many older children and adolescents develop relative lactase deficiency, also known as primary lactase deficiency, due to age-related declines in the intestinal enzyme lactase. The rate of primary lactase deficiency is higher in patients of Asian (80% to 100%) or African (70% to 95%) descent than those from Europe (15% to 70%). (14) Transient lactase deficiency following AGE is common in infants. Persistent lactase deficiency is exceedingly rare in infants and is overdiagnosed. Sucrase (sucrose-isomaltase) deficiency is less common following AGE but is a rare cause of persistent diarrhea in children. The diagnosis of dietary carbohydrate intolerance can be established with a trial of avoidance (eg, lactose-free diet) or treatment (eg, lactase-treated milk, hydrogen breath testing, or intestinal biopsy).

EVALUATION OF ACUTE DIARRHEA

Infectious diarrheal illness is typically a mild, self-limiting disease process that can be successfully treated at home. Uncomplicated cases of AGE can be managed via telephone consultation, with a focus on obtaining sufficient information to evaluate the child's clinical condition and risk for dehydration. (2)

Infants and toddlers should be referred for medical evaluation if any of the following is present:

- Moderate-to-severe illness in a child younger than 3 months (eg, fever, irritability, or abdominal distention)
- Severe underlying disease such as diabetes or renal failure, which increases the risk for complications
- Persistent vomiting

- High-output diarrhea with large stool volumes (>8 episodes per day) or reported signs of severe dehydration

ASSESSMENT OF DEHYDRATION

Accurate assessment of the degree of dehydration in children with AGE serves as a basis for management decisions. Dehydration in AGE occurs due to the increased loss of water and electrolytes (principally sodium, chloride, potassium, and bicarbonate) in the diarrheal stool with inadequate replacement. The ideal method of assessing fluid losses is to compare the pre-illness bodyweight to the current weight to calculate the percentage of weight loss. Real-world application of this method is limited, and clinicians typically rely on a global assessment: e.g., skin turgor, sunken eyes, general appearance, capillary refill time and mucous membranes, or a validated scoring tool to assist them in the assessment of dehydration in children. The Clinical Dehydration Scale is an easy-to-use and well-validated tool in the assessment of dehydration (**Table 2**). There are 3 generally accepted categories of dehydration severity: 1) no or minimal dehydration, 2) mild-to-moderate dehydration, and 3) severe dehydration.

Laboratory tests are not recommended in the routine assessment of dehydration. The results of testing in the setting of mild-to-moderate dehydration may distract the clinician from signs and symptoms that have proven diagnostic utility. Recent evidence suggests that urinary indices, including specific gravity and the presence of ketones, are not useful in the assessment of dehydration. However, electrolytes should be measured in all hospitalized patients who have severe dehydration and in children requiring IV rehydration therapy to assess hyper- or hyponatremia. It is important to remember that the early stages of dehydration are asymptomatic, and early initiation of fluid replacement is critical in the prevention of worsening dehydration.

DIAGNOSTIC EVALUATION

Episodes of AGE in children do not generally require a specific diagnostic evaluation. Microbiologic investigation is not indicated in most cases of AGE because most pathogens do not require treatment with a specific antimicrobial agent. Investigation is warranted for outbreaks in child care, school, or hospital settings; children who have bloody diarrhea (dysentery); or for patients who have underlying chronic illness or immunodeficiency.

Routine microscopic stool examination for polymorphonuclear cells is of limited clinical utility because a large number of children with gastroenteritis have a negative test result (<5 polymorphonuclear cells per high-powered field).

PREVENTION AND TREATMENT

Vaccinations

There are currently 2 licensed rotavirus vaccines in the United States, Rotarix® (GSK, Middlesex, United Kingdom) and RotaTeq® (Merck Sharp & Dohme Corp, Kenilworth, NJ). Since the introduction of rotavirus vaccine in the United States in 2006, diarrhea-associated health care use and medical expenditures have declined substantially. (7) From 2007 to 2009, there was an estimated reduction of 64,855 hospitalizations related to diarrheal illness associated with an approximately $278 million decrease in treatment costs. More recent studies have found even greater reductions, which have been attributed to herd immunity.

Rehydration

Oral and Enteral Rehydration. Oral rehydration and replacement of ongoing fluid losses with reduced-osmolarity (50-60 mmol/L sodium) ORS has replaced isotonic ORS as the first-line treatment for children with AGE. Recent studies

TABLE 2. **Clinical Dehydration Scale (CDS) for Children**

CHARACTERISTICS	0	1	2
General appearance	Normal	Thirsty, restless, or lethargic but irritable when touched	Drowsy, limp, cold, or sweaty ± comatose
Eyes (periorbital skin turgor)	Normal	Slightly sunken	Extremely sunken
Mucous membranes (tongue)	Moist	Sticky	Dry
Tears	Tears	Decreased tears	Absent tears

A score of 0 represents no dehydration, a score of 1 to 4 represents some dehydration, and a score of 5 to 8 represents moderate/severe dehydration.

have shown that reduced-osmolarity ORS is more effective than full-strength ORS, resulting in reduced stool output, reduced vomiting, and reduced need for supplemental IV therapy. The oral route is preferred, but when this is not feasible, enteral instillation via nasogastric (NG) tube is a secondary option. The use of oral and/or enteral rehydration is safer, reduces hospital stay, and is equally successful compared to IV rehydration in most children. (2)

The worldwide reduction of morbidity and mortality associated with AGE following the introduction of ORS is one of the true success stories of the past 50 years. ORS has become the cornerstone of therapy in the management of acute diarrheal illnesses worldwide.

Parenteral Rehydration. The use of IV rehydration should be limited to select circumstances, including:

- Shock
- Dehydration with altered level of consciousness or severe acidosis
- Worsening of dehydration or lack of improvement despite oral or enteral rehydration therapy
- Persistent vomiting that compromises oral or NG tube hydration
- Severe abdominal distention and ileus

Children presenting with shock due to AGE need rapid IV infusion of crystalloid solution as a 20-mL/kg bolus, followed by repeated boluses as needed, based on clinical response. Glucose-containing replacement fluids should be initiated in the maintenance phase of IV rehydration. Once the clinical condition permits, a switch to oral hydration is appropriate.

FEEDING

The two pillars of management in AGE are immediate attempts at oral rehydration and rapid reintroduction of regular feeding following initial fluid rehydration (generally within 4-6 hours). There is no difference in episodes of vomiting, diarrhea, or need for unscheduled IV fluids in patients with early versus late refeeding in the setting of AGE.

Breastfeeding should not be interrupted during episodes of AGE. Active breastfeeding may be associated with a reduced incidence of AGE. Most formula-fed infants can also resume a lactose-based diet once dehydration has been treated. Exceptions to this are infants who have severe diarrhea or diarrhea requiring hospitalization. In addition, if the infant is very young (<3 months old) or follow-up evaluation cannot be assured, a temporary switch to a non-lactose formula is appropriate.

MANAGEMENT OF HOSPITALIZED PATIENTS WITH AGE

No standardized admission criteria exist for children with AGE. Based on consensus guidelines, indications for hospitalization include the following:

- Shock
- Severe dehydration (>9% of body weight)
- Neurologic abnormalities (eg, lethargy, seizures)
- Intractable or bilious vomiting
- Failure of oral rehydration
- Concern for a surgical abdomen
- Inability to ensure that the caregivers or conditions at home will provide adequate monitoring, follow-up evaluation, or return to the hospital if needed

Contact precautions are indicated in addition to standard precautions in hospitalized children with AGE. Efforts to decrease the hospital length of stay in children with AGE are aimed at reducing the duration of symptoms and completing the transition to oral replacement of ongoing diarrheal losses.

Antiemetic Medication

The routine use of antiemetics in the treatment of AGE in children is controversial. Such use is not indicated for children younger than age 3 years. However, ondansetron therapy has been shown to decrease the risk for persistent vomiting, the need for IV fluids, and the risk of immediate hospital admission in children with vomiting related to AGE. (2) Prescribers should be aware that increased diarrhea frequency is one of the most common adverse effects of ondansetron. Safety considerations must also be taken into account, considering the FDA's "black box" alert recommending electrocardiographic monitoring in patients with electrolyte abnormalities who are receiving ondansetron because they may be at risk for developing prolongation of the QT interval that can lead to an abnormal and potentially fatal ventricular tachydysrhythmia. (2)

ANTIMOTILITY AGENTS

Antimotility agents, such as loperamide, are usually contraindicated in the treatment of childhood AGE. Although the risk for harm is based on only a few reports of toxic megacolon or ileus, there is minimal evidence of benefit in children. There is a much stronger case for potential harm with other opioids, especially those that cross the blood-brain barrier, including "third spacing of fluids in the intestine," and minimal benefit. Therefore, most guidelines state that antimotility agents are not indicated in

children with AGE, especially those younger than age 3 years.

PROBIOTICS AND PREBIOTICS

Probiotics are live microorganisms that are believed to work by stimulating the host immune system and competing for binding sites on intestinal epithelial cells. The use of probiotics in children with acute and persistent diarrhea is associated with reduced severity and duration of illness. (15)(16) The effect is modest, with an average decrease of 1 day of diarrheal illness. Controversy surrounds the routine use of probiotics in acute diarrheal illness, but they seem to be most effective when started early in the disease course in otherwise healthy individuals with viral gastroenteritis.

Prebiotics are oligosaccharides that stimulate the growth of commensal intestinal flora. Trials of these agents have failed to show a significant decrease in diarrheal severity or length of illness in children and, therefore, they are not routinely recommended.

ZINC SUPPLEMENTATION

The role of zinc supplementation in children with AGE is well established for developing countries where malnutrition is a significant risk factor.

Summary

- On the basis of recent epidemiologic evidence, norovirus has supplanted rotavirus as the most common cause of infectious diarrhea in the postvaccine era in the United States.
- On the basis of some research evidence as well as consensus, infants with milk protein-induced proctocolitis ("cow milk protein intolerance") may attempt reintroduction of milk- and soy protein-containing products as early as age 6 months.
- On the basis of strong evidence, using a validated tool to assess and classify the severity of dehydration in children with acute diarrheal illness is recommended to guide management decisions.
- On the basis of strong evidence, rapid initiation of oral rehydration with oral rehydration solution is the preferred method for replacing fluid and electrolyte losses in the setting of acute gastroenteritis.
- On the basis of strong evidence, reintroduction of regular age-appropriate feedings, including milk, after initial fluid resuscitation is the standard of care for acute diarrheal illnesses.
- On the basis of some research evidence as well as consensus, ondansetron therapy in select patients with vomiting related to acute gastroenteritis may be effective, but safety in children remains to be established.

CME Quiz and References for this article are at http://pedsinreview.aappublications.org/content/37/8/313.

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1. A 6-month-old infant presents with a 2-day history of 6 to 8 loose stools per day. In the past, she typically had 1 to 2 formed stools per day. The stools are nonbloody yet contain some undigested food particles. She has been irritable these past 2 days, but there is no change in her appetite; she is eating and drinking. Review of her growth chart reveals she is at the 50th percentile for height and weight. She is afebrile, has tears, and has moist mucous membranes. The rest of her physical examination findings are unremarkable. Which of the following is the best description of the patient's presenting condition?
    A. Acute watery diarrhea.
    B. *Shigella* diarrhea.
    C. Prolonged diarrhea.
    D. Diarrhea with severe malnutrition.
    E. Normal stool pattern.
2. A 3-year-old boy presents with a 2-day history of high temperature, malaise, and frequent watery diarrhea. He periodically complains of acute, sharp abdominal pain. There is no vomiting. On physical examination, he has a temperature of 40°C (104°F) and dry mucous membranes. Findings on the remainder of his physical examination are unremarkable. Suddenly he complains of abdominal pain, which is followed by defecation of a watery, bloody, slimy stool. Which of the following is the most likely cause of this patient's diarrhea?
    A. Rotavirus infection.
    B. Norovirus infection.
    C. *Salmonella* infection.
    D. *Shigella* infection.
    E. Food protein-induced proctocolitis.
3. A 1-year-old girl presents with a 3-month history of daily frequent loose, watery stools. She had a bout of acute viral gastroenteritis with mild fever, vomiting, and diarrhea that resolved approximately 3.5 months ago. She continues to grow and gain weight. Vital signs are normal for age. Her physical examination yields unremarkable findings. Which of the following is the most likely reason for her loose, watery stools?
    A. Dietary intolerance.
    B. Inflammatory bowel disease.
    C. *Salmonella* infection.
    D. Pancreatic insufficiency.
    E. Diarrheagenic *Escherichia coli* infection.
4. A 6-month-old boy presents with a 2-day history of mild fever, vomiting, and diarrhea. Vital signs include a temperature of 38°C (100.4°F), pulse of 120 beats per minute, and respiratory rate of 40 breaths per minute. He is lethargic but arousable and has slightly decreased periorbital skin turgor, "sticky" mucous membranes, and decreased tears. Which of the following is the infant's Clinical Dehydration Score?
    A. 0.
    B. 3.
    C. 4.
    D. 5.
    E. 8.

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5. For the 6-month-old boy described in the previous question, which is the most appropriate next step in management?

   A. Observation.
   B. Prescribe ondansetron therapy.
   C. Begin intravenous fluid bolus and ongoing fluid loss replacement.
   D. Begin oral rehydration and ongoing fluid loss replacement.
   E. Prescribe loperamide.

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