Diarrhea and Hypovolemia in Older Individuals

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ABSTRACT

PURPOSE: To review the risks associated with diarrhea and hypovolemia in the older US population, and discuss how and why to administer oral rehydration therapy (ORT) for this group.

EPIDEMIOLOGY: Older patients are involved in 26% of hospitalizations for diarrhea in the United States and 51% to 85% of diarrheal deaths.

REVIEW SUMMARY: Certain risk factors for diarrhea are more common in older than in younger adults, including institutional exposure to infectious agents, diminished host defenses, and increased use of antimicrobials and other diarrhea-inducing medications. Compared with their younger counterparts, older adults are less likely to be able to compensate for hypovolemia from diarrhea, placing them at a greater risk of cardiovascular, cerebral, and renal complications. ORT usually can be initiated by patients themselves without waiting for a diagnostic evaluation. With the exception of *Clostridium difficile* infection, antibiotics are of marginal value in treating diarrheas and pose a risk of exacerbating postantibiotic diarrhea. Early feeding with complex carbohydrates (eg, banana, rice, or cereal) is indicated. Antimotility drugs are contraindicated for diarrhea because of the presence of invasive organisms, but preparations containing bismuth subsalicylate often are helpful in stopping diarrhea.

TYPE OF AVAILABLE EVIDENCE: Prospective cohort studies, systematic reviews, and meta-analyses.

GRADE OF AVAILABLE EVIDENCE: Good.

CONCLUSION: ORT is a simple, inexpensive, science-based treatment for volume depletion resulting from diarrhea. It is likely to be as effective in older adults as in young children, and it is as applicable in the United States—given the need to contain healthcare costs—as in developing countries that often lack basic facilities for intravenous therapy.

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Diarrheal diseases are the cause of a great deal of disability and death among older individuals. Awareness of their importance has increased as their hemodynamic consequences have become better understood. Atherosclerosis and poor vascular responsiveness, which occur with aging, place older patients at higher risk for complications from volume depletion resulting from diarrhea. This article focuses on the timely use of oral rehydration therapy (ORT), a simple and low-cost therapy that should be initiated as soon as possible in anyone experiencing diarrhea, but which is of special importance to older adults as they are at increased risk for vascular events resulting from reduced perfusion of vital organs. In-depth discussion of the potential causes of diarrhea in older adults is beyond the scope of this article (Table 1).[1-3]

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Conflict of Interest: Dr Greenough reports that he is a consultant for, holds stocks in, and receives royalties from Cera Products Inc.

Off-Label Product Discussion: The author of this article does not discuss off-label/unapproved uses of drugs or products.

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Epidemiology, Etiology, and Natural History

Important risk factors for diarrhea shared by the very young and very old include diminishing hygiene (eg, incontinence and inability to bathe), institutional exposure to resistant bacteria and viruses, contact with other children or grandchildren who carry viruses such as rotavirus or the noroviruses, diminished host defenses, and increased use of laxatives and antimicrobials, a particular hazard in acute hospitalizations and long-term care. Nonmicrobial causes of diarrhea include[1,2]:

- Laxatives
- Chemotherapies for cancer
- Cardiovascular drugs (antiarrhythmics, antihypertensives, diuretics, cholesterol-lowering agents)
- Central nervous system drugs (antiparkinsonism drugs, antianxiety drugs, lithium)
- Gastrointestinal drugs (antiulcer drugs, cathartics, lactulose, bile salts)
- Nonsteroidal anti-inflammatory drugs
- Methylxanthines
- Colchicine
- Certain foods (heavily spiced dishes, sorbitol-containing dietetic food, candy, or gum)

Of the microbial causes, *Clostridium difficile, Escherichia coli* O157:H7, and *Salmonella* are the most common bacterial infections seen in older patients who reside in long-term care facilities.[3] *C difficile* infection is especially noteworthy because it typically follows courses of antibiotics. Because of insensitive diagnostic methods, *C difficile* infection is an underestimated cause of morbidity and mortality in older people.[4,5] Salmonella causes most deaths attributed to outbreaks of diarrhea that occur in nursing homes.[3]

Most diarrheal deaths in the United States involve individuals older than 55 years of age, rather than young children. In a study conducted between 1979 and 1987 by the (then called) Centers for Disease Control (CDC), diarrhea was listed on the death certificates of 35 274 people. In 28 538 of those deaths, diarrhea was listed as the immediate cause of death (55%) or as an underlying cause (45%). Altogether, 78% of the 28 538 diarrheal deaths occurred among individuals 55 years of age and older, and 51% occurred among those older than age 74.[6] In a later study, individuals 80 years of age or older accounted for 85% of 514 diarrheal deaths, and the case-fatality ratio increased exponentially with advancing age (Figure 1).[7] Of 87 181 hospitalizations for which gastroenteritis was one of the top 3 discharge diagnoses, adults 60 years of age or older accounted for 26%, nearly equal the percentage of children aged 0 to 4 years who were hospitalized (25%).[7]

Good epidemiologic studies that clearly demonstrate a relationship between an episode of diarrhea-induced hypovolemia and a subsequent myocardial infarction, stroke, or worsening renal failure are lacking. However, anecdotal evidence points to the likelihood of such a relationship.[8] In 1970 there was an outbreak of *Salmonella* enteritis at a nursing home in Baltimore. During a 10-day period, 104 of 145 patients (72%) became ill, and 25 (24%) of those affected patients died. Patients sustained volume depletion with inadequate replacement and generally succumbed a week later from the secondary effects of cardiovascular, cerebral, or renal damage. Autopsy data in one of the cases confirmed a vascular mechanism of death.

Table 1. Causes of Diarrhea in Older Adult Patients*

Noninfectious Causes

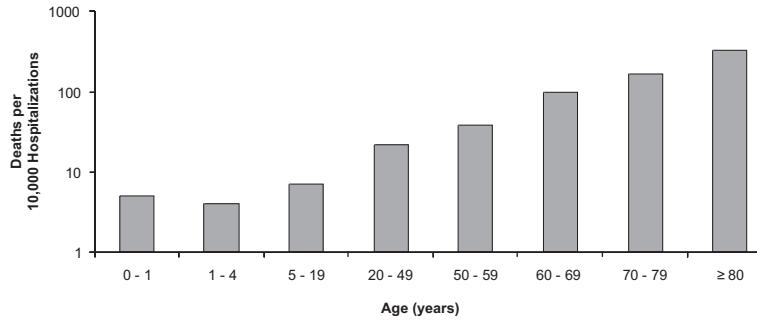
- Drugs and food (see text)
- Neoplasia (obstructive lesions, secretory adenomas, hormone-secreting tumors)
- Gastrointestinal disease (obstructive lesions, dysmotility with constipation and impaction, inflammatory bowel disease, malabsorption, mesenteric atherosclerosis and ischemia, portal hypertension)
- Systemic illness (diabetes mellitus, thyrotoxicosis, uremia)

Infectious Causes

- Bacteria (*Campylobacter* sp, *Clostridium difficile*,† *Clostridium perfringens*,† *Escherichia coli*,† *Salmonella* sp,† *Staphylococcus* sp, *Shigella* sp, *Vibrio cholerae*, *Vibrio* sp)
- Viruses (astrovirus,† calicivirus,† Norwalk-like virus,† rotavirus†)
- Parasites (*Cryptosporidium*, *Cyclospora*, *Entamoeba histolytica*, *Giardia*)

*Adapted with permission from Bennett RG, Greenough WB III.[8]
†Reported as the cause of at least 1 outbreak of diarrhea in a nursing home.

Figure 1. Deaths Increase With Age: Case Fatality Ratio for Gastroenteritis*



*Reprinted with permission from Gangarosa RE, Glass RI, Lew JF, Boring JR.[7]

Older individuals are more vulnerable to volume-depleting events as a result of diminished circulatory reserve, partial atherosclerotic occlusion of arteries to vital organs, lowered thirst drive, less effective homeostasis or "homeostenosis," or geater use of diuretics, antihypertensive drugs, and low-salt diets.

In many older patients, comorbidities also exacerbate the compensatory response to hypovolemia. For example, dementia can impair the perception of thirst and the ability to obtain fluids, and physical disability from arthritis, stroke, or neurologic disease can impede a person's ability to obtain or to swallow adequate amounts of fluids. Medications such as diuretics and agents to lower blood pressure can aggravate volume loss and limit the normal response to hypovolemia that maintains perfusion of vital organs.

PATHOPHYSIOLOGY

The digestive system typically processes 8 L to 12 L of fluid per day, not counting food or drink. Salivary, gastric, pancreatic, and biliary secretions help with digestion, and most of this fluid is absorbed in the small intestine. Anything that interferes with absorption or enhances secretion can overwhelm absorption capacity, resulting in diarrhea. Diarrhea causes loss of solutes and water from the body. Repair of these losses is the first priority in all patients with diarrhea.

According to a 1978 editorial in *Lancet*, "The discovery that sodium transport and glucose transport are coupled in the small intestine, so that glucose accelerates absorption of solute and water, was potentially the most important medical advance this century."[9] This finding was the basis for the development of ORT. It is now known that in addition to sugars, some amino acids and some peptides also are absorbed across the intestinal brush border membrane by separate carrier molecules that couple their movements to that of Na+ (Figure 2). Salt is absorbed along with these carrier substances and water follows, because transport from the intestinal epithelial cell to the lateral intercellular space creates both an osmotic and electrochemical gradient that draws water and solutes from the intestinal lumen to the circulation.[9]

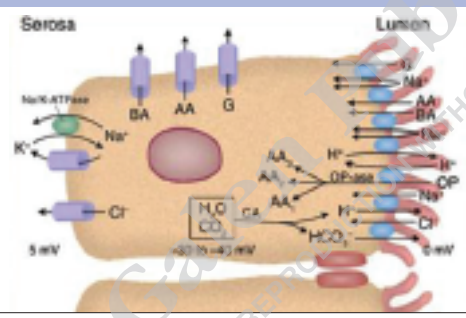
In general, secretion in the small intestine arises from crypts, and absorption takes place at the villus tips. Cyclic adenosine monophosphate (cAMP) or guanosine monophosphate (cGMP) and agents that increase their intracellular concentration stimulate active Cl secretion and inhibit active NaCl absorption ("active" here signifies transport against an electrochemical gradient). Regulation of absorption and secretion in the intestine is accomplished by hormones, neurotransmitters, paracrine agents, and substances released by inflammatory cells.[10]

A high osmotic load also causes diarrhea. If a large amount of osmotically active nonabsorbed solute is ingested, or if the individual has an absorptive defect, osmotic force pulls water and solutes into the intestinal lumen.[10] Osmotic diarrhea often is associated with ingestion of sorbitol in dietetic foods, lactulose and magnesium sulfate in laxatives, and magnesium in antacids and bowel purgatives.[2] Another major mechanism of diarrhea is excess secretion, which can be stimulated by bacterial enterotoxins, hormones generated by endocrine neoplasms, or inflammatory mediators.[10] Diarrhea is, in fact, a defense mechanism. The gut flushes noxious materials out from the top down; crypt cells secrete fluid, and villus tip cells fail to absorb it. The fluid flows from the duodenum and jejunum, overwhelming the absorptive capacity of the ileum and colon and resulting in watery diarrhea. Inflammation that compromises the intestinal epithelium's barrier function, as well as increases or decreases in gut motility, also can influence fluid loss.[10]

EVALUATION

It is not necessary to know the cause of the diarrhea in order to start effective replacement of volume losses. As long as the patient is conscious and can swallow, self-

Figure 2. Ileal Absorptive Cell*



Multiple brush border transporters couple ion influxes (Na+ and, in one instance, H+) to organic solute influxes or exchange one ion for another. Basolateral-membrane carriers facilitate diffusion of organic solutes and are not coupled to ion movements. Na/K-ATPase in the basolateral membrane uses energy from ATP hydrolysis to drive Na+ extrusion and K+ uptake (3:2 stoichiometry), both moving against their electrochemical gradients. K+ and Cl-channels in the basolateral membrane open in response to cell swelling and elevations of intracellular Ca2+. Some of the cellular H+ and HCO_3—extruded in exchange for Na+ and Cl—is provided through the action of carbonic anhydrase (CA). Additional HCO_3- may enter the cell through the basolateral membrane NHE1 or the Na(HCO_3)3 cotransporter (not shown). The cell electric potential is 30 to 40 mV negative relative to the lumen, providing an electric, as well as a chemical, driving force for Na+ entry via Na-organic solute cotransport.

G = glucose or galactose; AA = amino acid (there are actually several amino acid carriers); BA = bile acid anion; OP = oligopeptide; OPase = oligopeptidase (almost all oligopeptides entering the cell intact are quickly hydrolyzed).

*Reprinted with permission from Field M.[10]

treatment with ORT should begin before dehydration ensues. A good output of pale-colored urine every 2 to 4 hours indicates an adequate replacement of fluid relative to stool output. Diagnostic evaluation is desirable, but not necessary, for initiating treatment for fluid losses.

A stool culture is appropriate in the setting of an epidemic outbreak and for patients with new-onset bloody diarrhea, recurrent bouts of diarrhea, or severe symptoms such as fever, leukocytosis, and lethargy. Stool cultures have a very low yield among patients with diarrhea who have been hospitalized for 3 days or more,[2] but a *C difficile* toxin assay or antigen test should be ordered for patients who have recently been treated with antibiotics—especially in the case of institutionalized patients.[11] For immunocompromised patients such as frail, older adults or HIV-positive patients, investigations should include cryptosporidia, microsporidia, cytomegalovirus, *Mycobacterium avium* complex, and a search for parasites.[2]

Consultation with a gastroenterologist is appropriate for individuals with recurrent diarrhea that does not appear to be infectious, at which time patients should be evaluated for possible inflammatory bowel diseases, ischemia, or malignancies.

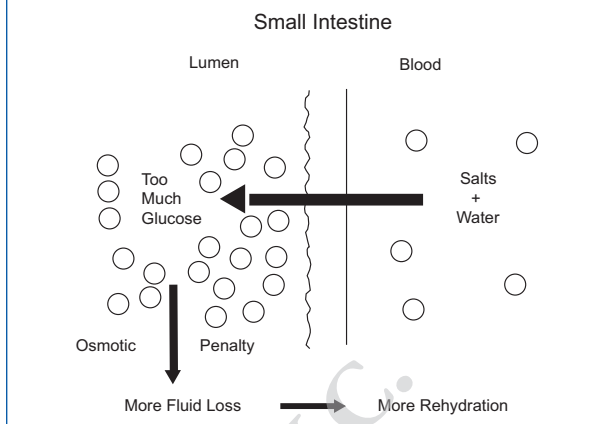
Rationale for Oral Rehydration Therapy

A general principle of medicine that seems simple and intuitive is that, when a patient is losing a vital body fluid, it should be replaced with a fluid similar in amount and composition. Historically, early efforts to replace fluids lost in diarrhea employed only salt and water by mouth, but those methods simply increased diarrheal volume[11] because, in diarrhea, the normal mechanism of salt absorption is blocked by the mechanisms that govern secretion and absorption in the gut. Observations in rabbit intestinal loops showed that if glucose were added to a properly constituted saline solution, absorption was increased.[11,12] This was an early demonstration of the glucose-sodium cotransport mechanism of the intestinal tract.

Later studies of patients with cholera[13,14] showed that properly constituted glucose solutions with appropriate electrolytes corrected dehydration in heavily purging individuals, but did not reduce the diarrhea itself. In these studies, the solution was given by intestinal tube. However, subsequent research in Bangladesh and India demonstrated that an oral glucose solution could maintain normal hydration after intravenous (IV) replacement had rehydrated collapsed cholera patients.[15] Shortly thereafter, it was shown that most patients with cholera could be rehydrated using ORT alone.[16]

In 1992, 25 years after the discovery of ORT, the CDC made a public statement about its value in the United States.[11] However, to this day ORT is not used nearly as often as it might be. Several recent publica-

Figure 3. The Addition of Small Substrate Molecules to Oral Rehydration Therapy Creates an "Osmotic Penalty"



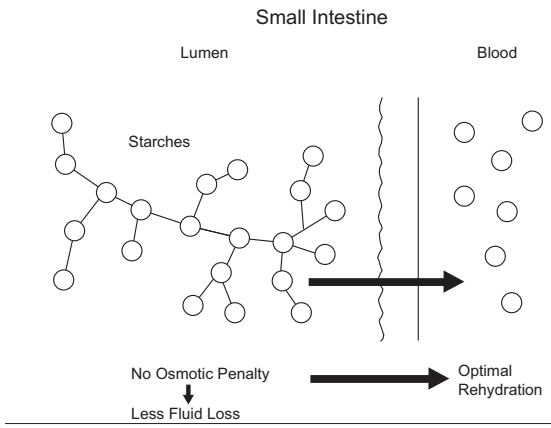
When small osmotically active molecules (in this case glucose) are presented to the small intestine, there is a rapid equilibration with the extracellular fluids and blood circulation. There is a rapid net flow of solutes and water from the portal circulation into the gut lumen, which in extreme cases can cause a "dumping syndrome" and syncope due to decrease in circulating volume and cardiac output.

The following 2 cases demonstrate the difference between rehydration via IV vs ORT:

A 72-year-old woman with pneumonia who had been in an acute-care hospital for 3 days had a systolic blood pressure (BP) of about 95 (her normal BP was 120). When seen by the attending physician, house staff, and students on morning rounds the patient reported having had watery diarrhea the previous evening. She was not passing urine. It was recognized that she needed prompt volume replacement, but she did not have an IV in place at that time. During the next 30 minutes 3 nurses, 2 physicians, the medical students, and the attending physician worked on placing the IV line and struggled with the IV pump, which kept alarming because it balked at providing more than 800 mL/hr. The patient became anxious and upset by all the noise and people surrounding her. However, she responded well, her vital signs returning to normal over the course of the next hour.

The following morning, an 81-year-old man with pneumonia and severe psoriatic arthritis was found to have a systolic BP of 98 and reported watery diarrhea during the night. The attending physician had a packet of standard WHO glucose oral replacement solution, which was mixed in a liter of water. The physician spent the next 30 minutes conversing with the patient while offering him frequent sips of 50 to 100 mL every 2 to 4 minutes. Within 30 minutes, the patient had consumed 800 mL of the solution, his BP was back up to 120, and he felt much better and began to pass urine. In the meantime, the clinician had been able to learn a lot about the patient's life and illness, spending a very pleasant half hour with no IV team, no noise or running around, no machines or needles, and no pain or anxiety.

Figure 4. Digestible Food Polymers (Starches and Proteins) Provide More Cotransporting Substrates With Little Increase in Osmoles



By employing covalently linked digestible polymers (starches and proteins), cotransporting substrates can be presented to the intestinal epithelium with little "osmotic penalty" (eg, increase in luminal osmolarity).

tions from pediatric centers in the United States have confirmed that ORT is as effective and applicable in the United States as it is in resource-poor countries.[17-19] A recent review from the Mayo Clinic also has commented on its applicability in the United States.[20]

Oral Rehydration Therapy Solutions

Because a glucose-based electrolyte mixture works well it was originally thought that the solution could be improved by adding more sugar (ie, more cotransporting substrate). This was not so, however, because of the "osmotic penalty" (Figure 3). If too many glucose molecules enter the lumen of the gut, osmotic forces increase a net flow of fluid from the bloodstream into the gut lumen, the exact opposite of the desired result.[21] This is why, for instance, hyperosmotic drinks such as colas and fruit juices can aggravate diarrhea losses.

Patients can be instructed to make a homemade solution, stirring 1 handful of sugar and 1 "3-finger pinch" of salt into 1 pint of water. Unfortunately, many people think that if a little bit is good, more is better, and when too much sugar and salt are used there is a danger of a hyperosmolar solution with the risk of increased diarrhea and hypernatremia. A safer method is to prepare an instant rice cereal (eg, precooked rice cereal for babies) so that it is thick but drinkable, and add 1 pint of water and 1 3-finger pinch of salt, or use cooked cereals in place of precooked varieties. Potassium may be replaced by eating fruits or unsweetened fruit juices.

Research on ORT over the last 25 to 30 years has shown that cotransporting substrates can be provided at a low osmotic cost to improve the performance of ORT solutions. This has been accomplished by adding starches and proteins, which are digestible polymers made up of covalently linked glucose or amino acid molecules. Mammals are designed to digest starches and proteins by cleaving them into smaller chains that are then further processed to individual glucose or amino acid molecules at the intestinal brush border membrane.[9,22] Hence, more glucose or amino acids can be presented to the cotransporting system of the intestinal epithelium without generating excessive luminal osmoles, thus rapidly moving more salt and water into the bloodstream (Figure 4).

A meta-analysis conducted by the World Health Organization (WHO) evaluated 24-hour stool output with glucose ORT solutions compared with rice-based solutions. In almost all instances, the rice-based solutions were associated with a lower volume of stool output and shorter duration of diarrhea.[14] Therefore, the WHO now recommends feeding patients a carbohydrate (eg, banana, rice, or cereal) along with the standard glucose-based ORT solution. Another option is to use CeraLyte®, a rice-based oral hydration solution of an electrolyte composition appropriate to correct losses from diarrhea.[23]

Administering Oral Rehydration Therapy

If the patient is aspirating or having trouble swallowing, the rehydration solution should be administered through an enteral feeding tube. Otherwise, anyone can administer ORT. There is no specific dose; the goal is to simply replace the volume of fluid that has been lost in order to avoid intravascular volume depletion. ORT should be started with the first watery stool, even if the patient also has been vomiting. The patient should take small sips of 2 to 4 ounces every 2 to 4 minutes. Intensity of thirst is ordinarily a good guide for monitoring repletion, but the thirst drive is diminished in many older adults, and cognitive impairment may further limit the usefulness of this symptom. In this case, rehydration is considered adequate when the patient begins to urinate a reasonable volume (more than 200 cc) every 2 to 4 hours. If there is concern about urinary retention in debilitated patients, it may be necessary to check for urinary retention via ultrasound or to temporarily insert a urinary catheter.

All commercial oral rehydration solutions contain potassium (Table 2). If the patient is in renal failure, an ORT solution without potassium can be made by mixing a liter of tap water with a 1-L bottle of intravenous 5% dextrose and saline.

The principal risk of ORT in older patients is that, for patients with impaired cardiac function, overhydra-

tion can result in congestive heart failure. Therefore, it is important to watch for signs of heart failure, including rales at the lung bases, jugular vein distension, and sacral or peripheral edema. However, it is far less likely that overhydration will occur when using ORT as compared with IV routes, because the taste of the solution is such that overdosing rarely has been seen. With escalating hospital costs, inexpensive and more effective measures are needed to approach common causes of diarrhea in the elderly, such as *C difficile*.[24]

Other Treatment Measures

Feeding should be encouraged if there are no contraindications with foods containing proteins and complex carbohydrates. Foods with sugars and high osmolarity should be avoided. Unless there is clearly infection with an invasive organism, such as *C difficile*, antibiotics are contraindicated for older patients with acute watery diarrhea. Any benefits from antibiotic use are far outweighed by the risk of postantibiotic diarrhea, which may be more serious.

Bismuth subsalicylate (eg, Pepto-Bismol) is a rational therapy for any diarrhea because it is antisecretory and has some microbicidal activity. The recommended dosage is 30 mL every 30 minutes for up to 8 doses or until diarrhea stops, followed by a maintenance dosage of 60 mL 4 times a day for 5 days or until the diarrhea has stopped, if it stops in fewer than 5 days. The risk of toxicity is minimal, and there is a possibility of increasing patient comfort and shortening illness duration. Recently, Kaopectate has added bismuth subsalicylate to its formulation. The kaolin increases stool bulk and makes it less watery but neither approach influences fluid loss.

When an older individual presents for the first time with diarrhea of unknown cause, it is important to inquire about medications and over-the-counter agents that could be responsible for diarrhea or might aggravate volume depletion.

Conclusion

ORT is a simple, inexpensive treatment for volume depletion resulting from diarrhea. It is likely to be as effective in older adults as in young children, and it is as applicable in the United States, as it is in developing countries that often lack basic facilities for IV therapy. As yet, there are no randomized prospective studies to prove this assertion, but the data from ORT use in children is persuasive. In virtually all cases of acute watery diarrhea, ORT should be started as soon as pos-

Table 2. Analysis of 7 Commercially Available Oral Rehydration Solutions and a Homemade Rice-Based Solution*

ORT Solution	Na (Mmol/Liter)	K (Mmol/Liter)	Osmolality (Mmol/Liter)	Base† (Mmol/Liter)	Carbohydrate‡ (g/Liter)	Calories (Kcal/Liter)
CeraLyte (Cera Products)	50	20	220	30	40	165
Infalyte (Mead Johnson)	50	25	200	50	13	50
Kao Lectrolyte (Pharmacia & Upjohn)	50	20	232	30	20	80
ORS§ (Jianas Bros)	90	20	310	30	20	80
Pedialyte (Ross)	45	20	250	30	25	100
Pediatric Electrolyte (NutraMax Products)	45	20	250	30	25	100
Rehydralyte (Ross)	75	20	310	30	25	100
Rice-based (homemade)	90	20	—	30	80	320

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†Bicarbonate or citrate.
‡The commercial ORT solutions except CeraLyte contain glucose. CeraLyte contains a complex mixture of rice carbohydrates and proteins. The homemade rice-based ORT can be made from precooked instant rice cereal (eg, Gerber's Rice Cereal for Baby).
§This is the WHO/UNICEF-sanctioned formula.

sible. In view of the well-established record of ORT for reducing morbidity and mortality as well as the costs of hospitalization for children, careful studies in older adults are overdue. Other treatment measures should include early feeding with complex carbohydrates and proteins (eg, banana, rice, cereal, or meat broths), prescription of bismuth subsalicylate, avoidance of other antidiarrheal drugs, and cancellation or modification of potential diarrhea-causing drugs or diets.

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