

# **The Management of Acute Diarrhea in Children: Oral Rehydration, Maintenance, and Nutritional Therapy**

U.S. Department of Health and Human Services Public Health Service Centers for Disease Control and Prevention (CDC) Atlanta, Georgia 30333

The MMWR series of publications is published by the Epidemiology Program Office, Centers for Disease Control and Prevention (CDC), Public Health Service, U.S. Department of Health and Human Services, Atlanta, Georgia 30333.

SUGGESTED CITATION Centers for Disease Control and Prevention. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. MMWR 1992;41(No. RR-16):(inclusive page numbers).

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The production of this report as an MMWR serial publication was coordinated in:

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Copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402-9325. Telephone: (202) 783-3238.

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Contents

PREFACE INTRODUCTION HISTORICAL BACKGROUND PHYSIOLOGIC AND CLINICAL BASIS FOR USING ORS

Initial ORS Composition Studies of ORS in the United States AVAILABILITY OF ORS IN THE UNITED STATES OTHER FORMS OF ORS

Home Use of Oral Rehydration and Maintenance Solutions LIMITATIONS AND ADVANTAGES OF ORT DIETARY THERAPY OF ACUTE DIARRHEA

Reduced Oral Intake Versus Continued Feeding Lactose Malabsorption Continuation of Regular Diet PHARMACOLOGIC THERAPY OF ACUTE DIARRHEA PRINCIPLES OF CASE MANAGEMENT

Clinical Assessment RECOMMENDATIONS FOR CASE MANAGEMENT

Patient Assessment Rehydration Therapy Based on Degree of Dehydration Replacement of Ongoing Fluid Losses Dietary Therapy Drug Therapy Vomiting Home Management of Acute Diarrhea and Instructions to

Parents CONCLUSION

References

Preface

Twenty-four years ago, oral rehydration therapy was first proven to be effective in the outpatient management of patients with severe dehydrating diarrhea caused by cholera. The development of this simple therapy for the treatment of diarrhea, one of the most common illnesses of humankind, was heralded as one of the great medical achievements of the 20th century. Oral therapy has now become the mainstay of the World Health Organization's efforts to decrease diarrhea morbidity and mortality, and Diarrheal Disease Control Programs have been established in more than 100 countries worldwide.

Although diarrhea kills about four million people in developing countries each year, it remains a problem in developed countries as well. In the United States, each child will have had 7-15

episodes of diarrhea by the age of 5 years, 9% of all hospitalizations of children less than 5 years old are associated with diarrhea, and 300-500 children die each year from this potentially preventable condition. This report on "The Management of Acute Diarrhea in Children" is CDC's first statement regarding the important use of oral therapy for rehydration and maintenance of children in the United States with dehydrating diarrhea, as well as for nutritional support. Because diarrhea is so common and can be severe, CDC believes the proper management of acute diarrhea in children by parents of small children and by physicians could markedly decrease national rates of hospitalization and death. Guidelines provided in this MMWR Recommendations and Reports concerning the proper management of childhood diarrhea have been compiled by CDC with the review of many experts in the field, including representatives of the American Academy of Pediatrics.

William L. Roper, M.D., M.P.H. Director Centers for Disease Control and Prevention

The Management of Acute Diarrhea in Children: Oral Rehydration, Maintenance, and Nutritional Therapy

### Summary

Worldwide, diarrhea remains one of the most common illnesses among children. In the United States, children less than 5 years of age experience greater than 20 million episodes of diarrhea each year, leading to several million doctor visits, 200,000 hospitalizations, and approximately 400 deaths. Much of this morbidity is due to the dehydration associated with acute watery diarrhea. Consequently, the proper management of children with acute diarrhea is important for all practitioners as well as for parents of small children.

The development of oral therapy for the rehydration and maintenance of children with dehydrating diarrhea has become the worldwide mainstay of national diarrheal control programs. More recently, proper nutrition for children with diarrhea is viewed as an important adjunct to therapy, whereas antibiotics and other drugs play only a limited role. Intravenous therapy remains essential for diarrheal episodes associated with severe dehydration. This document reviews the proper management of diarrhea among children. Particular attention is given to the use of oral therapy for rehydration and maintenance therapy for the dehydrated child and nutritional management. In the United States, the improved management of children with diarrhea could lead to a noticeable decrease in the number of children who are hospitalized or die as a result of diarrheal illness. This report contains recommendations prepared by the Centers for Disease Control and Prevention (CDC), with input from a panel of pediatric and diarrheal management experts, which are consistent with recommendations endorsed by the American Academy of Pediatrics.

## INTRODUCTION

In the United States, diarrhea remains one of the most common illnesses of children, and it is associated with 9% of all hospitalizations of children less than 5 years of age. Most hospitalizations and deaths due to diarrhea occur in the first year of life.

One hundred years ago, diarrheal diseases were among the principal causes of death of children in the United States, with seasonal epidemics occurring during summer. Today, this pattern of illness is replicated on a wider scale in many developing countries, where 1.5 billion episodes of diarrhea and 4 million associated deaths occur among children each year (1,1a). These statistics translate to an average of 3.3 episodes of diarrhea per year for a child less than 5 years of age and greater than 10,000 childhood deaths worldwide per day. The current epidemic of cholera in South and Central America serves as a conspicuous reminder of the morbidity and mortality associated with diarrheal diseases.

In the United States, despite the many improvements in water treatment, sanitation, education, and medical care, diarrhea remains one of the most common pediatric illnesses. Each year, children less than 5 years of age experience 20-35 million episodes of diarrhea, which result in 2-3.5 million doctor visits, greater than 200,000 hospitalizations, and 325-425 deaths (2-5). Approximately 65% of the hospitalizations and 85% of the diarrheal deaths occur in the first year of life.

During the past two decades, research has provided important new insights about the etiologic characteristics of acute diarrhea. In the early 1970s, an infectious agent could be identified in 15%- 20% of episodes of diarrhea. Today, when extensive diagnostic techniques are used, a causative agent is found in 60%-80% of cases. Many infectious agents of diarrhea are common in North America (Table 1). Rotavirus is the most common cause of acute diarrhea among children, accounting for one-fourth of all cases (6), but many other viruses can cause childhood diarrhea as well, including Norwalk-like viruses, enteric adenoviruses, astroviruses, and caliciviruses. Important bacterial pathogens include Salmonella, Shigella, Yersinia, Campylobacter, and certain strains of Escherichia coli. Common parasitic causes of diarrhea include Giardia, Cryptosporidium, and Entamoeba histolytica. Despite the wide range of organisms associated with gastrointestinal infections, the mainstay of the treatment of a person with acute watery diarrhea is appropriate fluid and electrolyte therapy and nutritional management, as outlined below.

This report summarizes the historical and physiologic principles behind the development of oral therapy for rehydration and maintenance, discusses recent advances in the field, addresses frequently asked questions concerning the use of oral therapy, and provides recommendations for clinical assessment and case management, including appropriate dietary therapy. This document addresses the treatment of acute diarrhea rather than persistent diarrhea lasting 2 weeks or longer and is aimed primarily at watery diarrhea rather than bloody diarrhea (dysentery). Oral rehydration therapy (ORT) encompasses two phases of treatment: a) the rehydration phase, in which water and electrolytes are given as oral rehydration solution (ORS) to replace existing losses, and b) the maintenance phase, which includes both replacement of ongoing fluid and electrolyte losses and adequate dietary intake (7). It is important to emphasize that although ORT implies rehydration alone, in view of present advances, knowledge, and practice, our definition has been broadened to include maintenance fluid therapy and nutrition.

## HISTORICAL BACKGROUND

Early attempts at treating patients with dehydrating diarrhea were first published in the 1830s during epidemics of *Vibrio cholerae* infections (8,9). These initial reports recorded the physiologic disturbances associated with diarrhea. Further, the reports described the rationale for intravenous (IV) therapy as an attempt "first to restore the blood to its natural specific gravity; second to restore its deficient saline matters" (10). The first use of IV saline therapy by Latta (11) had only limited success because of the selection of moribund patients, inadequate maintenance therapy, and complications, including chills and sepsis, resulting from inadequate knowledge concerning sterilization techniques.

The use of IV fluids did not become widespread until 100 years later. In the 1930s, important landmarks included the development of Hartman's solution. In the 1940s, the first oral rehydration solutions were developed by Harrison in Baltimore, Maryland, and Darrow in New Haven, Connecticut (12). This demonstration by Harrison and Darrow proved the importance of replacing potassium in the solution. Accurate chemical analysis of diarrheal stools eventually permitted the formulation of physiologically appropriate replacement solutions (13). By the 1950s, cholera was successfully treated with IV fluids (14). In the early 1960s, research teams in both Dhaka, Bangladesh, and Calcutta, India, further refined effective IV solutions for cholera patients (15).

Studies documenting the effectiveness of IV rehydration fluids among economically disadvantaged populations provided an impetus to develop less expensive, but equally effective, oral solutions. These solutions are less invasive and reduce the need for hospital admissions. Harrison's solution contained (in mmol/L): sodium, 62; potassium, 20; chloride, 52; lactate, 30; and glucose, 183 (3.3%). A commercial preparation (Lytren, Mead Johnson) was soon available in the United States, but its use in the 1950s coincided with an increased incidence of hypernatremia (16). Several factors contributed to this problem, including a) the product's high carbohydrate concentration (8%), which causes osmotic diarrhea; b) dispensing the product in a powdered form with instructions to mix with an appropriate volume of water; c) incorrect mixing, resulting in a hypertonic solution; and d) certain dietary practices (e.g., ingestion of boiled skim milk), resulting in ingestion of milk with a high solute load. Because of this experience, U.S. physicians are often reluctant to use ORS, despite many worldwide scientific studies demonstrating the physiologic basis, safety, and efficacy of oral rehydration and maintenance therapy.

## PHYSIOLOGIC AND CLINICAL BASIS FOR USING ORS

### Initial ORS Composition

ORS can be used to treat diarrhea regardless of the patient's age, causative pathogen, or initial sodium values. Many physicians continue to prescribe a variety of "clear liquids" to treat patients with diarrhea instead of an appropriately composed ORS.

In the 1950s and 1960s, researchers delineated in various animal tissue models and later in human tissue and in vivo systems the molecular process of cotransport. During this process, the

absorption of one sodium ion was linked with that of one glucose molecule at the intestinal brush border (17-19). It was later demonstrated that other organic molecules, such as amino acids, dipeptides, and tripeptides, contributed to this cotransport phenomenon (20) and that this process remained intact during acute diarrhea (21). Phillips initially demonstrated that adding glucose to saline solutions during cholera induced net absorption of sodium and water in patients who did not absorb intestinal salt solutions in the absence of glucose. Phillips also demonstrated effective intestinal absorption of potassium and bicarbonate in cholera patients (13).

Studies in Dhaka and Calcutta confirmed that the addition of glucose to sodium-containing solutions resulted in net movement of salt and water from the intestinal lumen to the bloodstream of patients with severe cholera (22-25). These studies established that the use of a glucose-electrolyte solution provided safe, effective, and practical maintenance therapy for severely dehydrated patients who typically required IV rehydration to correct shock. The solution was tested for both rehydration and maintenance therapy among patients with severe and moderate dehydration (26) and was found effective and safe when appropriately used. Providing additional drinking water at the bedside of rehydrated patients allowed for excretion of any excess salt intake. More importantly, oral therapy -- first introduced at Dhaka -- allowed fluid losses to be replaced in a timely manner and on a volume-for-volume basis with rehydration solution (21,24,25). Since the purging rate of patients declines with time (especially for cholera, when an appropriate antibiotic is administered concurrently), this therapeutic method proved essential for safe and effective practical oral therapy that included maintenance of electrolyte and water balance without causing either excessive or inadequate replacement of water or salts.

These methods were later further adapted and developed into simple guidelines suitable for use in less severely ill patients with cholera, for the treatment of persons with noncholera diarrheas (21), and for the instruction of nurses, paramedicals, and parents. Field testing of these solutions was performed initially in rural Bangladesh (26,27), and then in India during an epidemic of cholera affecting war refugees (28).

Concern was eventually raised whether a solution designed for the treatment of severe, secretory diarrhea such as cholera would be appropriate for the management of a less severe gastrointestinal tract infection (29). Indeed, stool losses of water and electrolytes are more pronounced in cholera than in noncholera diarrhea (30). Early compositions of ORS, based on data from studies of patients with cholera, contained 100-120 mmol/L of sodium.

In 1975, the World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) agreed to promote a single solution (WHO-ORS) containing (in mmol/L): sodium, 90; potassium, 20; chloride, 80; base, 30; and glucose, 111 (2%). This solution, representing a compromise between stool sodium losses in cholera compared with noncholera diarrhea, was selected because of the realization that promotion of a single solution among populations with all levels of education in different countries would be simpler and more practical than multiple solutions of different compositions. Indeed, clinical studies soon indicated that ORS was as effective in treating diarrhea caused by enterotoxigenic *E. coli* as when used to treat cholera (21).

In the late 1970s, other concerns about ORS surfaced when rotavirus was identified as an important cause of diarrhea. Since rotavirus causes a diffuse enteropathy that is sometimes associated with glucose malabsorption, the appropriateness of ORS was questioned. However, studies demonstrated the efficacy of ORS for the treatment of children with rotavirus diarrhea as well (30-32).

The acceptance and use of ORS for treating diarrhea regardless of patient age, etiologic agent of diarrhea, and initial serum sodium value (21,33,34) have been important to the development of WHO Global Diarrheal Diseases Control Programs. As a result of these successful ORT programs, diarrhea case-fatality rates have declined dramatically (35). Despite these results, many clinicians in industrialized countries have been reluctant to use ORS. This reluctance has persisted, although multiple clinical trials have documented the safety and efficacy of this therapy in developing countries. This resistance has been partially ascribed to the unsubstantiated concern that WHO-ORS may induce hypernatremia. Many physicians continue to recommend a variety of "clear liquids" to treat patients with diarrhea, instead of an appropriately composed ORS (36). These "clear fluids" can cause osmotic diarrhea and electrolyte imbalance, and they often contain inadequate sodium bicarbonate and excess sugar for appropriate replacement of stool losses (Table 2).

#### Studies of ORS in the United States

Studies of U.S. children have confirmed the usefulness of ORS as well. For example, a randomized, controlled clinical trial of well-nourished Panamanian and U.S. children hospitalized with acute diarrhea demonstrated no differences in stool output or duration of diarrhea among three groups who received WHO-ORS, standard IV therapy, or ORS with a reduced sodium content (50 mmol/L). All patients with hypernatremia or hyponatremia had safe resolution of these electrolyte imbalances with ORS alone (37).

In another study, four different oral solutions with sodium concentrations ranging from 30 to 90 mmol/L were administered to children with less than 5% dehydration (38). Ninety-eight percent (137/140) of these children were successfully treated as outpatients, and no differences in duration of diarrhea or amount of fluid ingested were found among the children. In another study, ORT for infantile diarrhea proved to be as successful as IV fluid therapy in a U.S. hospital emergency room (39). Other investigators have confirmed the safety and efficacy of ORS for infants hospitalized in the United States (40) and for the outpatient management of children with mild diarrhea.

A key factor in the excellent therapeutic and safety record of ORT has been the development of simple rules that can be successfully taught by hospital and community clinic medical staff. These simple rules effectively teach the proper procedure for mixing and administering the solution, when to change to other dietary fluids and foods, and how to avoid therapeutic starvation. Several approaches are effective, but all of them include communicating to the parent or guardian simple guidelines enabling him or her to mix the solution appropriately. These guidelines also permit the amount of oral solution administered to be related to the condition of the child and the frequency of stools. Additionally, all rules encourage the parent or guardian to begin appropriate dietary liquids and foods early in the maintenance phase.

## AVAILABILITY OF ORS IN THE UNITED STATES

ORS can be distributed premixed with water or as dry ingredients in packets. Packets are more common in developing countries, where low cost, long shelf life, and ease of transport make them particularly suitable. The disadvantage of packets is the potential for mixing with inappropriate volumes of water, resulting in ORS that is either too diluted or too concentrated. When caretakers are asked to mix ORS from packets at home, detailed written and oral instructions should be given (41). With premixed solutions, the concentration can be ensured, but cost can limit access (42).

Recently, the bicarbonate component of the WHO-ORS has been replaced with the bicarbonate precursor, citrate, because it has a longer shelf life. Citrate-containing solutions are as efficacious as those containing bicarbonate (43), and both components aid in the intestinal absorption of sodium and water (44).

In the United States, several different formulations of premixed ORS are available commercially (Table 3). In the past 5 years, U.S. manufacturers of ORS have altered their formulations to contain lower, more appropriate concentrations of carbohydrate. The sodium concentrations of the fluids have also increased compared with previously available ORS.

The American Academy of Pediatrics (AAP) (45) recommends that oral solutions used for rehydration should contain 75-90 mEq/L of sodium. However, AAP recommends use of fluids containing 40-60 mEq/L of sodium for the prevention of dehydration or maintenance of hydration status (45). These lower sodium solutions more closely approximate the stool-sodium losses encountered in patients with viral diarrhea, which occurs commonly in the United States. Thus, there is a wide range of sodium content in commercially available products.

When fluids with greater than 60 mEq/L of sodium are used for maintenance, other low-sodium fluids, such as breast milk, diluted or undiluted infant formula, or water, need to be administered as well to prevent sodium overload.

The most widely used solutions in the United States, Pedialyte and Ricelyte, contain 45 and 50 mEq/L of sodium, respectively. These fluids are intended for maintenance of hydration and prevention of dehydration in clinical practice. Ricelyte has been used successfully for rehydration and maintenance therapy in one study; however, the effectiveness of Pedialyte for rehydration has not been studied. Although solutions with higher sodium concentrations (75-90 mEq/L) are preferable, Pedialyte, Ricelyte, and other similar low-sodium solutions can be used for rehydration when the alternative is physiologically inappropriate liquids or IV fluids. When the rate of purging is very high (e.g., greater than 10 ML/kg/hour), solutions with 75-90 mEq/L are recommended for rehydration.

## OTHER FORMS OF ORS

Glucose-based ORS does not reduce the duration of illness or the volume of stool output. Early feeding, however, can reduce the severity, duration, and nutritional consequences of diarrhea.

A perceived weakness of the glucose-based ORS is its inability to reduce the duration of illness or volume of stool output. Caretakers and practitioners frequently resort to multiple, costly, and often ill-advised therapies to reduce diarrhea. In the past decade, several attempts have been made to improve the standard WHO-ORS by adding other substrates or by replacing glucose with other ingredients. It is anticipated that such formulations will cause an improved clinical response. Many different substrates have been evaluated: sucrose (46-48), glycine (49-51), alanine (52), and, more recently, glutamine (53). Initial studies using glycine-based ORS found the formula superior to glucose-based ORS in efficiency of absorption and in reducing both stool volume and duration of diarrhea. This finding was replicated chiefly for diarrhea associated with cholera. However, in one study (50), the use of a glycine-based ORS predisposed patients to the development of hyponatremia.

With the use of glucose or amino acid substrates for sodium cotransport, there is a limit to the concentration of substrate that can be added. When the concentration of substrate in the solution is too high, then osmolar forces carry water into the gut lumen and exacerbate diarrhea. In contrast, cereal-based ORS contains large polymers that may not create an excessive osmotic load (54-58). Rice-based ORS, for instance, contains cooked rice powder instead of the glucose found in the WHO and other commercially available solutions. Complex carbohydrate molecules are slowly digested by intestinal enzymes and then absorbed as glucose; larger proteins in the cereals are digested and absorbed as smaller peptides and amino acids.

Ricelyte, a commercial preparation containing 30 g/L of rice-syrup solids, differs from a cereal-based solution in that the preparation contains only small glucose polymers derived from rice. In one study, the use of this solution, which differs from rice-based ORS in that it lacks whole rice, reduced stool output during the first 6 hours of therapy when compared with a standard, glucose-based solution (59). No differences in the duration of diarrhea or in total stool output were found, although stool output after 48 hours was not reported. Therefore, it is difficult to draw firm conclusions about the relative efficacy of Ricelyte in comparison with glucose-based ORS.

One advantage of cereal-based ORS, at least in developing countries, is that these solutions can be easily prepared in the home. However, the solutions require time and effort to prepare, and they can become contaminated if left unrefrigerated. Standardization of cereal-based solutions may prove difficult; in India, for example, several food-based solutions made by mothers revealed a wide range of sodium content and generally inadequate amounts of cereal base and glucose (60).

Clinical trials in developing countries have reported that cereal-based ORS reduces stool output and duration of diarrhea (54-58). Critical analysis of these studies, however, reveals that the quantity and quality of the maintenance diet often were not standardized, measured, or described adequately. Therefore, the possibility exists that variations in diet accounted for the differences in results. As discussed below, the practice of early feeding reduces the severity, duration, and nutritional consequences of diarrhea (61-63). In Egypt and Pakistan, large-scale, ongoing studies comparing cereal-based ORS with glucose-based ORS -- in which all case-patients receive standardized, early feedings -- will address the issue of the comparative efficacies of these two types of solutions.

## Home Use of Oral Rehydration and Maintenance Solutions

Management of acute diarrhea should begin at home. Families with infants and small children should be encouraged to keep a supply of ORS at home at all times and use the solution when diarrhea first occurs in the child.

Ideally, management of acute diarrhea should begin at home, since effective early interventions can reduce complications, such as dehydration and poor nutrition. Thus, early home management will result in fewer office or emergency room visits, hospitalizations, and deaths. This type of management is best realized through support and education of mothers by health-care personnel at centers that use oral therapy. All families, particularly those in rural areas or poor urban neighborhoods where access to health care may be delayed, should be encouraged to have a supply of ORS in the home at all times, much in the same way that acetaminophen and syrup of ipecac are viewed as staples of the medicine chest.

A recent conference on the household management of acute diarrhea (64) outlined several important points concerning the choice of an appropriate rehydration or maintenance fluid for home use. When diarrhea begins, a commercially available product can be administered at home. Alternatively, food-based fluids (e.g., cereals or gruels) or other plain fluids can be used to prevent dehydration. Regardless of the type of fluid used, an appropriate diet should be administered as well.

The most crucial aspect underlying home management of diarrhea is the need to administer increased volumes of appropriate fluids as well as to maintain adequate caloric intake. Medications, other treatments, or inappropriate home remedies should be avoided. Infants should be offered more frequent feedings at the breast or bottle, and children should also be given more fluids. Further research is needed to identify cultural, dietary, and educational factors that affect the home management of the child with diarrhea (65).

### LIMITATIONS AND ADVANTAGES OF ORT

Although ORT is recommended for all age groups and for acute diarrhea caused by any etiologic agent, several limitations to its use exist.

#### Bloody diarrhea

ORT is not sufficient therapy for some cases of bloody diarrhea (dysentery) since patients with bloody diarrhea may have a bacterial or parasitic infection requiring treatment with an antimicrobial agent. These patients need to seek medical care immediately.

#### Severe dehydration

Patients in shock or near shock should be treated initially with IV solutions. Also, patients with intestinal ileus should not be given oral fluids until bowel sounds are audible.

#### Intractable vomiting

Many patients with clinically significant acute diarrhea have concomitant vomiting. Nevertheless, greater than 90% can be successfully rehydrated or maintained with oral fluids when small volumes of ORS (5-10 mL) are administered every 1-2 minutes, with a gradual increase in the amount consumed. A frequent mistake is to allow a thirsty child to drink large volumes of ORS fluids (ad libitum) from a cup or a bottle; the caretaker should be instructed to administer ORS in small amounts via a spoon, syringe, cup, or feeding bottle. Continuous, slow nasogastric infusion of ORS via a feeding tube can be helpful for the child who is vomiting.

### High stool output

Stool output greater than 10 mL/kg/hour is associated with a lower rate of success of oral rehydration (48), although these data are derived from a study performed among patients who had cholera. In general, no patient should be denied ORT simply because of a high purging rate, since most patients will respond well when administered adequate replacement fluid. In severely purging patients, subtle differences in substrate and electrolyte composition of oral solutions play a critical role in the success of therapy.

### Monosaccharide malabsorption

The presence of glucose or reducing substances in the stools, accompanied by a dramatic increase in stool output with the administration of ORS, is an indication of glucose malabsorption. The presence of stool-reducing substances alone is not sufficient to make the diagnosis, since this is a common finding among patients with diarrhea and does not indicate failure of oral therapy. Patients with true glucose malabsorption will show an immediate reduction in stool output when IV therapy is begun instead of oral therapy. The incidence of clinically evident glucose malabsorption during acute diarrhea is approximately 1%, although rates as high as 8% have been reported among selected populations (43). Malabsorption of lactose, maltose, and sucrose can also occur because of deficiencies of their respective enzymes or starvation associated with the lack of enzyme induction.

Nonetheless, ORT is often the optimal method for the treatment of acute diarrhea. Its ability to be administered at home promotes earlier treatment and prevention of dehydration, as well as active involvement of parents in the medical care of their children. Oral fluid administration is safer and more physiologic than IV fluids, and the risks of phlebitis and IV infiltrates are avoided. Finally, the use of ORS with early feeding (discussed below) is not only safer, but more efficacious than IV therapy for the treatment of acute diarrhea.

## DIETARY THERAPY OF ACUTE DIARRHEA

Although dehydration is the most serious direct effect of diarrhea, adverse nutritional consequences also can occur when nutritional management is not appropriate.

Acute diarrhea can endanger the nutritional status of affected children for the following reasons: a) anorexia and food withdrawal interfere with adequate intake; b) carbohydrates, fats, proteins, and micronutrients are often malabsorbed; c) excess urinary and stool nitrogen losses are likely, even with subclinical infections; and d) metabolic demands are generally higher with fever and

systemic illness (66). The long-term effects of repeated gastrointestinal tract infections include growth failure and malnutrition (67-69) and possibly impaired cognitive development (70). The nutritional consequences of diarrheal illnesses among well-nourished children or adults in developed countries are less dramatic but have not been extensively investigated.

### Reduced Oral Intake Versus Continued Feeding

Two opposing approaches to the nutritional management of acute diarrhea have been recommended (71). One approach favors reducing oral intake during illness to avoid diarrhea that occurs because of intestinal malabsorption, while the other approach favors continued feeding to avoid the nutritional consequences of fasting. The first approach, the tradition of "gut rest," still in wide practice, probably evolved from the observation that stool output was reduced in patients who fasted. However, fasting can reduce enterocyte renewal (72). Enteral nutrition stimulates intestinal cell renewal in several ways. In the short bowel syndrome, for example, villous hypertrophy and increased absorptive capability are stimulated by the direct effects of nutrients on the mucosa and by the nutrient-induced secretion of trophic hormones in the gastrointestinal tract (73). Further, intestinal permeability is increased in fasting (as opposed to fed) children with acute diarrhea (74). Thus, there are several theoretical reasons to avoid fasting.

Until recently, few controlled clinical trials had evaluated the dietary management of acute diarrhea. In one study in Arizona (61), well-nourished Apache infants were administered either a full-strength, lactose-free, soy-based formula immediately upon rehydration, or the infants were first fed ORS for 48 hours, then half-strength, lactose-free, soy-based formula for 24 hours, and finally administered a full-strength formula. Both the stool output and the duration of diarrhea were reduced by approximately 50% for infants who were administered full-strength, lactose-free, soy-based formula immediately after rehydration compared with the stool output and duration of illness for infants whose formula was gradually reintroduced. Similarly, in Peru (62), four different feeding regimens were compared in a group of 128 children ages 3-36 months with acute diarrhea. Two groups were administered a formula containing casein, sucrose, corn-syrup solids, and vegetable oil, either full- or half-strength; two other groups were administered either glucose-based ORS or IV fluids and then advanced to formula feeding. Stool output in the last two groups was noticeably lower than in the other groups for the first 48 hours. However, this difference disappeared when these groups were given food. Moreover, the duration of diarrhea and failure rates among all four groups were similar. More importantly, nitrogen balance, energy absorption, weight gain, and change in arm circumference and skinfold thickness were positively related to the level of dietary energy intake. These studies provide strong evidence for the recommendation that full-strength, lactose-free formulas can be safely introduced immediately after rehydration therapy and that such therapy can improve nutritional outcome as well as reduce stool output.

### Lactose Malabsorption

Although recent data support the introduction of a full diet soon after rehydration, the content of this diet, especially for infants receiving most of their calories from milk-based formulas, is controversial. Acquired lactase deficiency, which is a reduction in the intestinal brush border enzyme responsible for lactose digestion, is frequently associated with diarrhea (75). One study

reported that 88% of patients hospitalized with rotavirus diarrhea had evidence of lactose malabsorption (76). However, lactase deficiency must be distinguished from lactose malabsorption (a clinical diagnosis based on signs and symptoms of carbohydrate malabsorption), since many infants with lactase deficiency will not have clinical malabsorption.

Despite concerns about lactose malabsorption in breast-fed and bottle-fed children with diarrhea, continued breast-feeding or bottle-feeding during illness is clinically well tolerated and advantageous. A study of breast-fed children selected at random to receive either ORS or ORS-plus, who continued breast-feeding during the first 24 hours of hospital treatment, found that the breast-fed group had reduced stool output (63). The AAP recommends the gradual reintroduction of milk-based formulas in the management of acute diarrhea, beginning with diluted mixtures (45). This recommendation, however, is being reevaluated. Breast-feeding should continue immediately after rehydration.

### Continuation of Regular Diet

Older children accustomed to eating a variety of table foods should continue receiving a regular diet; cereal-milk and cereal-legume diets have been used successfully for the dietary management of these children (77-79). Other recommended foods include starches (e.g., rice, potatoes, noodles, crackers, and bananas), cereals (e.g., rice, wheat, and oat cereals), soup, yogurt, vegetables, and fresh fruits. Foods to be avoided are those that are high in simple sugars, which can exacerbate diarrhea by osmotic effects. These foods include soft drinks, undiluted apple juice, Jell-O, and presweetened cereals. In addition, foods high in fat may not be tolerated because of their tendency to delay gastric emptying.

Although there have been no controlled trials concerning its efficacy, the "BRAT" diet (bananas, rice, applesauce, and toast) has long been used as a dietary-management tool among pediatric practices in the United States. To the extent that it includes starches and fruits, it is a reasonable dietary recommendation. However, prolonged use of the BRAT diet, or a protracted course of diluted formulas, can result in inadequate energy and protein content in the recovering child's diet.

### PHARMACOLOGIC THERAPY OF ACUTE DIARRHEA

Antimicrobial agents and other drugs have limited usefulness in the management of acute diarrhea. Antimicrobial therapy of acute diarrhea varies depending on the etiologic agent. Since viral agents are the predominant cause of acute diarrhea, antimicrobial agents play only a limited role in case management. Certain diarrheal diseases, however, require appropriate drugs in addition to fluid and nutritional therapy. Identification of patients requiring antimicrobial therapy relies on clinical, epidemiologic, and laboratory evidence. For instance, bloody diarrhea or the presence of white blood cells on methylene blue stain of the stool specimen suggests a bacterial agent causing invasive mucosal damage and indicates that stool cultures should be performed to identify the organism. Other clinical clues suggesting a cause of infectious diarrhea amenable to antimicrobial therapy include a history of recent antibiotic use (in which case *Clostridium difficile* should be suspected), exposure to children in day care centers where *Giardia* or *Shigella* is prevalent, recent foreign travel, and immunodeficiency, in which infectious causes of diarrhea

should be diligently evaluated. Conversely, watery diarrhea and vomiting in a child less than 2 years of age most likely represent viral gastroenteritis and therefore do not require antimicrobial therapy. A full discussion of antimicrobial therapy for gastrointestinal tract infections is found in other published reports (80-82).

The use of nonspecific antidiarrheal agents such as adsorbents (e.g., kaolin-pectin), antimotility agents (e.g., loperamide), antisecretory drugs, or toxin binders (e.g., cholestyramine) is a common practice in many developed and developing countries (1). Despite the theoretical benefits from their use, available data do not demonstrate their effectiveness in reducing diarrhea volume or duration (80). For example, although stool consistency can be improved by binding agents, stool water losses are unchanged and electrolyte losses may increase (83,84). Indeed, side effects of these drugs are well known, including opiate-induced ileus, drowsiness and nausea due to atropine effects, and binding of nutrients and other drugs. One report from Pakistan detailed 18 cases of severe abdominal distention in association with use of loperamide, including at least six deaths (85). Another study reported that even in a controlled clinical setting, six of 28 patients administered loperamide experienced side effects (i.e., ileus, drowsiness) requiring discontinuation of therapy (86). In addition, reliance on antidiarrheal agents shifts the therapeutic focus away from appropriate fluid, electrolyte, and nutritional therapy; can interfere with oral therapy; and can unnecessarily add to the economic cost of the illness. Little evidence exists to support the use of nonspecific drug therapy in children, and much information exists to the contrary.

## PRINCIPLES OF CASE MANAGEMENT

### Clinical Assessment

Fever, vomiting, and loose stools are the common symptoms of acute gastroenteritis. Among infants and children, however, these can be the symptoms of many nongastrointestinal illnesses as well, including meningitis, bacterial sepsis, pneumonia, otitis media, and urinary tract infection. Vomiting alone can be the first symptom of metabolic disorders, congestive heart failure, toxic ingestions, or trauma. As such, a detailed history and physical examination are important in identifying acute gastroenteritis as a likely diagnosis when symptoms and signs are nonspecific and for ruling out other serious illnesses.

Besides a complete physical examination, an accurate body weight must be obtained. Auscultation for adequate bowel sounds is important before oral therapy is initiated. Visual examination of the stool can confirm abnormal consistency and determine the presence of blood or mucus.

Signs and symptoms of dehydration are crucial in guiding therapy. Infants with acute diarrhea are more apt to dehydrate than are older children because they have a higher body surface-to-weight ratio (i.e., somewhat high insensible loss/kg of body weight), have a higher metabolic rate, and are dependent on others for fluid (87). Although the most accurate assessment of fluid status is acute weight change, the patient's premorbid weight often is not known. The clinical signs and symptoms of mild dehydration (3%-5% fluid deficit) include increased thirst and slightly dry mucous membranes, whereas moderate dehydration (6%-9% fluid deficit) is

associated with loss of skin turgor, tenting of skin when pinched, and dry mucous membranes (88) (Table 4). Signs and symptoms of severe dehydration (greater than or equal to 10% fluid deficit) are severe lethargy or altered state of consciousness, prolonged skin tenting and skin retraction time (greater than 2 seconds), cool and poorly perfused extremities, and decreased capillary refill. Rapid, deep breathing (a sign of acidosis), prolonged skin retraction time, and decreased perfusion are more reliably predictive of dehydration than sunken fontanelle or absence of tears (89). A good correlation has been reported between time of capillary refill and fluid deficit (90). However, fever, ambient temperature, and age can affect capillary refill time as well (91).

Supplementary laboratory studies in the assessment of the patient with acute diarrhea are rarely needed. However, serum electrolytes can be measured when the physician recognizes clinical signs or symptoms suggesting abnormal sodium or potassium concentrations. Stool cultures are indicated for dysentery (bloody diarrhea) but are not needed to initiate treatment in the usual case of acute watery diarrhea in the immunocompetent patient.

## RECOMMENDATIONS FOR CASE MANAGEMENT

Successful case management of children with diarrhea depends on the principles of appropriate fluid, electrolyte, and nutritional therapy (Table 4) (92). Treatment of symptomatic and dehydrated children who seek medical evaluation should include two phases: rehydration and maintenance. In the rehydration phase, the fluid deficit should be replaced and clinical hydration attained. In the maintenance phase, adequate dietary and fluid intake should be maintained. In both phases, excess fluid losses must be replaced continuously.

### Patient Assessment

The patient should be clinically evaluated to assess the degree of dehydration (Table 4), as well as to rule out other medical conditions, and the patient's body weight should be measured.

### Rehydration Therapy Based on Degree of Dehydration

For the mildly dehydrated patient (3%-5% fluid deficit), oral rehydration should commence with a fluid containing 50-90 mEq/L of sodium. The amount of fluid administered should be 50 mL/kg over a period of 2-4 hours. Using a teaspoon, syringe, or medicine dropper, the caregiver should initially provide small volumes of fluid (e.g., one teaspoon) and then gradually increase the amount, as tolerated. After 2-4 hours, hydration status should be reassessed. If the patient is rehydrated, treatment should progress to the maintenance phase of therapy (see below). If the patient is still dehydrated, the fluid deficit should be reestimated and rehydration therapy should begin again.

For the moderately dehydrated patient (6%-9% fluid deficit), ORS should be administered by the same procedures as used for the mildly dehydrated patient. The initial amount of fluid administered for rehydration should be increased to 100 mL/kg, administered over 2-4 hours.

Severe dehydration (greater than or equal to 10% fluid deficit, shock or near shock) constitutes a medical emergency. IV rehydration should begin immediately. Boluses (20 mL/kg) of Ringer's lactate solution, normal saline, or a similar solution should be administered until pulse, perfusion, and mental status return to normal. This treatment may require two IV lines or even alternate access sites (e.g., venous cutdown, femoral vein, intraosseous infusion). When the patient's level of consciousness returns to normal, he or she can take the remaining estimated deficit by mouth. As with less severely ill patients, hydration status should be assessed frequently to monitor the adequacy of replacement therapy.

For patients with acute diarrhea, but without signs of dehydration, the rehydration phase of therapy should be omitted and maintenance therapy started immediately.

### Replacement of Ongoing Fluid Losses

During both rehydration and maintenance therapy, ongoing stool and vomit fluid losses must be replaced. If the patient is at a facility where such losses can be measured accurately, 1 mL of ORS should be administered for each gram of diarrheal stool. Alternatively, stool losses can be approximated by administering 10 mL/kg for each watery or loose stool passed, and 2 mL/kg of fluid should be administered for each episode of emesis. Excess fluid losses during maintenance therapy can be replaced with either low-sodium ORS (containing 40-60 mEq/L of sodium) or with ORS containing 75-90 mEq/L of sodium. When the latter type of fluid is used, an additional source of low-sodium fluid is recommended (e.g., breast milk, formula, or water).

### Dietary Therapy

Recommendations for maintenance of dietary therapy depend on the age and dietary history of the patient.

Breast-fed infants should continue nursing on demand. For bottle-fed infants, full-strength, lactose-free, or lactose-reduced formulas should be administered immediately upon rehydration in amounts sufficient to satisfy energy and nutrient requirements. When such formulas are unavailable, full-strength, lactose-containing formulas should be used under supervision to assure that carbohydrate malabsorption does not complicate the clinical course. Alternatively, diluted, lactose-containing formulas can be used for the initial infant feedings; however, the concentration of formula should be increased rapidly. Patients with true lactose intolerance will have exacerbation of diarrhea when a lactose-containing formula is introduced. The presence of low pH (less than 6.0) or reducing substances (greater than 0.5%) in the stool in the absence of clinical symptoms is not diagnostic of lactose intolerance; this diagnosis is indicated by more severe diarrhea upon introduction of lactose-containing foods. If lactose intolerance occurs, appropriate therapy includes temporary reduction or removal of lactose from the diet.

Older children receiving semisolid or solid foods should continue to receive their usual diet during diarrhea. Recommended foods include starches, cereals, yogurt, fruits, and vegetables. Foods high in simple sugars and fats should be avoided.

Despite the type of dietary regimen chosen, excess fluid losses via vomiting or diarrhea must be replaced with ORS as outlined above.

### Drug Therapy

Neither antibiotics nor nonspecific antidiarrheal agents are usually indicated for acute diarrhea. Antibiotics should be considered when dysentery or a high fever is present, when watery diarrhea lasts for greater than 5 days, or when stool cultures, microscopy, or epidemic setting indicate an agent for which specific treatment is required.

### Vomiting

In the child with vomiting, oral rehydration should proceed with small, frequent volumes at first (e.g., 5 mL every minute). Administration via a spoon or syringe -- with close supervision -- helps guarantee a gradual progression in the amount taken. Often, simultaneous correction of dehydration lessens the frequency of vomiting.

### Home Management of Acute Diarrhea and Instructions to Parents

Early administration of ORS at home should proceed as described above, with stool and vomit fluid losses replaced with appropriate volumes of ORS and adequate dietary therapy administered.

Education of parents and other caretakers should include the fluid and dietary principles noted above. Since morbidity and mortality from diarrhea in the United States usually occur in the first year of life, parents should be taught how to manage diarrhea and dehydration at the first newborn clinic visit or early during the first year of the child's life. Subsequent well-baby examinations should provide an opportunity to emphasize appropriate therapy as part of routine anticipatory guidance and nutritional counseling. During an acute illness, parents should be instructed to telephone or return to the clinic if the patient becomes irritable or lethargic, has decreased urine output, develops intractable vomiting, or has persistent diarrhea.

The management of diarrhea at home can be encouraged by physicians who care for children by supporting efforts to reduce the price and increase the insurance coverage of commercially available ORS. ORS should be available in every household, and a 24-hour supply of ORS should be provided to the parents of children with diarrhea upon clinic visits. Additional efforts regarding proper handwashing techniques, diaper changing practices, and hygiene can help prevent the spread of disease.

### CONCLUSION

For many years, the treatment of acute diarrhea has proven that oral therapy, with a fluid-electrolyte solution for rehydration and maintenance, is simple and effective. More recently, the important coprinciple in case management of early refeeding of children immediately upon

rehydration has also gained wider acceptance. The combination of oral rehydration and early nutritional support guides a patient through an episode of diarrhea safely and effectively. When the principles of therapy that are outlined are accepted by all levels of the U.S. medical community, and when education of parents includes instructions about how to begin ORT at home, then unnecessary hospitalizations and deaths can be prevented. Meanwhile, improvements in rehydration and maintenance solutions, vaccines, diapering practices, and food safety are anticipated that may help combat one of the most common public health problems of children.

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