

# Oral Rehydration Therapy and Dietary Therapy for Acute Childhood Diarrhea

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During the past 15 years, oral rehydration therapy has been extensively and increasingly used in developing countries for the treatment of dehydration in acute infantile diarrhea.<sup>1</sup> It has been shown that mortality from this disease, which is the leading cause of infant deaths in developing countries, can be reduced dramatically by using oral rehydration therapy.<sup>1,2</sup> Despite this experience, many physicians from developed countries, such as the United States, have been reluctant to adopt oral rehydration therapy for the treatment of acute diarrhea in infants. In this discussion we will review the accumulated data from different countries supporting the safety and efficacy of using this form of therapy with particular emphasis on studies conducted in the United States. In addition, the role of feeding during an acute episode of diarrhea will be discussed.

## ORAL GLUCOSE ELECTROLYTE SOLUTIONS

### Background

Different oral solutions have been used by mankind throughout history for the treatment of diarrhea. The first sophisticated oral rehydration solution (ORS) was introduced by Harrison in Baltimore and Darrow at Yale University at approximately the same time in the middle 1940s.<sup>3</sup> The solution used by Harrison contained (in mmol/L): sodium 62, potassium 20, chloride 52, lactate 30, and glucose 183 (3.3%). This composition was developed on a theoretical basis to approximate electrolyte deficits from losses in the stools, and the glucose

was added for its protein-sparing property. This solution was successfully used by Harrison to prevent dehydration in outpatients with diarrhea. A commercial product (Lytren, Mead Johnson Company) was produced, based on this information, which was dispensed in powder form. When reconstituted with the appropriate volume of water, it contained 50 mmol/L of sodium and 8% carbohydrates. This solution was extensively used in different parts of the United States during the 1950s.

Simultaneous to the widespread use of Lytren, hypernatremia (which resulted in some deaths) was being reported in increasing numbers in different parts of the country.<sup>4</sup> One or more of the following factors may have contributed to the increased incidence of hypernatremia: (1) a high carbohydrate content in the ORS which aggravated the diarrhea due to the osmotic load; (2) because of poor training and instructions, many mothers incorrectly mixed ORS resulting in very high concentrations of sodium; and, (3) the common practice of giving fluids such as boiled skim milk, which contained a high solute load to infants with diarrhea, increased the diarrhea due to the osmotic load in the gut. As a result of these unfortunate events, ORS was no longer used by pediatricians as the standard form of therapy for the treatment of dehydration secondary to diarrhea. Instead, ORS containing less sodium (25 to 30 mmol/L) and 5% to 8% carbohydrates was used for maintenance therapy in outpatients without signs of dehydration and in hospitalized patients for maintenance therapy after initial rehydration therapy with intravenous fluids.

In the 1960s, careful physiologic studies demonstrated the coupled absorption of sodium and glucose in the small intestine.<sup>5</sup> The studies showed that optimal absorption of sodium and water occurred when the ORS contained 110 to 140 mmol/L (2% to 2.5%) glucose. It was later shown that the absorption of glucose

### EDUCATIONAL OBJECTIVE

18. Appropriate knowledge of the controversies regarding oral nutritional management of acute diarrhea (Recent Advances, 86/87).

in the small intestine and its cotransport with sodium remained intact during acute diarrhea.<sup>1</sup>

Based on these physiologic studies, a glucose-electrolyte solution was developed which contained sodium, potassium, chloride, bicarbonate, and glucose. The initial solutions contained 100 to 120 mmol/L of sodium. Later, the sodium content of the solution was reduced to 90 mmol/L (Table 1). The latter product was initially tested and shown to be safe and efficacious in treating, first, adults and, then, infants with cholera. Subsequently, in developing countries, it was also shown to be effective and safe in treating dehydration secondary to noncholera diarrheas including rotavirus diarrhea in adults and children of all ages, including newborns. Based on these studies, the World Health Organization recommended the use of this solution (WHO-ORS) for the treatment of diarrhea in children and adults of all ages regardless of the etiology of diarrhea.

In the United States, however, ORS was not used because of the fear of hypernatremia and the relatively small amount of data available on the use of the WHO-ORS in developed countries. Therefore, we conducted studies in hospitalized and ambulatory children in the United States to evaluate the safety and efficacy of ORS of different sodium concentrations in treating diarrhea.<sup>6,7</sup>

In the first study, conducted in the United States and Panama,<sup>6</sup> we com-

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**TABLE 1.** Oral Rehydration Solution Recommended by the World Health Organization\*

Component	mmol/L
Sodium	90
Potassium	20
Chloride	80
Citrate†	30
Glucose	111

\* Solution is made by adding the following to 1 L of water: sodium chloride, 3.5 g; trisodium citrate dihydrate, 2.9 g; potassium chloride, 1.5 g; and glucose, 20 g.

† Previously, bicarbonate was used instead of citrate.

pared the clinical outcome in three groups of well-nourished infants younger than 2 years of age who were hospitalized for dehydration secondary to acute diarrhea. One group (group A) received the WHO-ORS that contained 90 mmol/L of sodium; the other group received an ORS that was similar in composition but contained only 50 mmol/L of sodium (group B); the third group (group C) received the standard intravenous therapy. Patients in group A and group B were given intravenous therapy on hospital admission if they were assessed to have severe dehydration. There were 146 children studied: 50, 48, and 48 in groups A, B, and C, respectively. Of the 98 patients in the two ORS groups, 97 (99%) successfully completed therapy according to protocol. One patient in group A whose stool output was 11 mL/kg/h required unscheduled intravenous therapy. Eighty-one (82%) of the patients in the two ORS groups who presented with vomiting were successfully hydrated with ORS alone. In addition, six patients (three in group A and three in group B) who presented with hypernatremia (serum sodium >150 mmol/L) and two patients with hyponatremia (one group A and one group B) were successfully hydrated with ORS alone, and their serum sodium levels returned to normal within eight to 24 hours (Figure). There were no differences in stool output or duration of diarrhea among the three groups. Two patients in group A who were given excessive amounts of ORS had periorbital

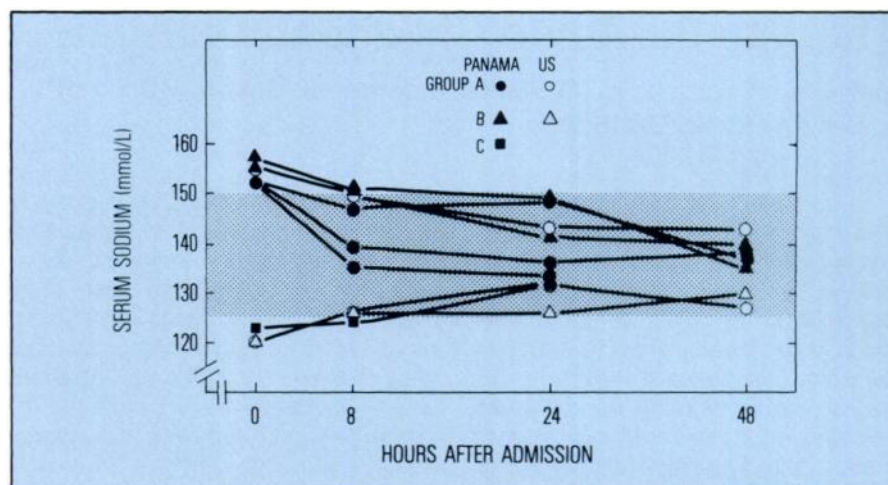


Figure. Serum sodium concentrations during therapy in patients who had abnormal values on hospital admission, plotted according to treatment group. Each symbol denotes one patient. Groups A and B received oral fluid containing sodium 90 mmol/L and 50 mmol/L, respectively; group C received primarily intravenous fluids. Only one patient in oral therapy groups (group B, United States [US, hyponatremia]) received initial intravenous therapy. Shaded area represents expanded normal range that is considered clinically safe. Reprinted with permission of The New England Journal of Medicine 1982;306:1072.

edema, which resolved spontaneously after ORS was discontinued.

In the second study,<sup>7</sup> we compared the use of four different ORSs (sodium concentrations ranging from 30 to 90 mmol/L) in treating outpatients with acute diarrhea but with less than 5% dehydration (Table 2). In three of the solutions, either citrate or phosphate or a combination of the two was used as base instead of bicarbonate. Of the 140 patients, 137 (98%) were successfully hydrated as outpatients. The duration of diarrhea and amount of fluid intake were similar in all groups. The mean serum bicarbonate values at resolution of illness were also similar in all groups. Two patients were hospitalized due to persistent vomiting, and one patient was hospitalized because of an inability to drink fluids due to severe monilial lesions of the buccal mucous membrane. This patient was hospitalized and rehydrated successfully with the ORS administered by nasogastric gavage.

Based on these data, we offer the following conclusions about the use of oral rehydration therapy in the United States: (1) ORS containing 50 or 90 mmol/L of sodium are equally safe and efficacious in treating hospitalized infants with diarrhea. (2) ORS containing 30, 50, or 90 mmol/L of sodium are equally efficacious in

treating ambulatory patients with mild diarrhea.

In the past 2 years, studies have been conducted in other centers in the United States<sup>8,9</sup> that confirm the safety and efficacy of ORS for the treatment of dehydration secondary to diarrhea in infants.

### Recommendations

Based on our experience, we recommend the following schedule of treatment for patients with acute diarrhea in the United States: (1) Assess the patient for degree of dehydration as shown in Table 3. (2) Patients who are mildly or moderately dehydrated should be given 60 and 80 mL/kg, respectively, of ORS during a four-hour period. If the patient is severely dehydrated, give intravenous therapy (Ringer's lactate or similar solution) at the rate of 40 mL/kg/h until pulse and blood pressure and state of consciousness return to normal levels. Reassess patient for degree of dehydration and proceed as in mild to moderate dehydration. (3) Maintenance phase (after first four hours): Give a lactose-free formula at the rate of 150 mL/kg/24 hours. (4) Replacement of ongoing stool losses: Ongoing stool losses should be replaced with ORS on a 1:1 basis. (5) Monitoring: Intake and output should be



**TABLE 2.** Four Oral Rehydration Solutions Used in Outpatient Study

Component of Solution	Solution			
	A	B	C	D
Sodium (mmol/L)	90	50	30	30
Potassium (mmol/L)	20	20	20	20
Magnesium (mmol/L)	0	4	4	4
Calcium (mmol/L)	0	4	4	4
Chloride (mmol/L)	80	50	30	30
Citrate (mmol/L)	0	23	23	28
Bicarbonate (mmol/L)	30	0	0	0
Phosphate (mmol/L)	0	5	5	0
Glucose (g/L)	20	20	20	50
Calories (per L)	80	80	80	200
Osmolality (mosm/kg)	333	251	211	388

measured every four hours. Patients should be reexamined at least every eight hours for signs of dehydration.

The following points are helpful in the practical management of patients receiving oral rehydration therapy. (1) If patients present with vomiting, ORS should be given in small volumes (5 to 10 mL) every five minutes. The volume given can be gradually increased until the patient can drink ad libitum. More than 90% of infants will tolerate ORS if it is given gradually. Nasogastric gavage can also be used to deliver ORS slowly to patients with vomiting; intravenous fluid is rarely required. (2) Nasogastric tubes can also be used for delivering ORS to patients who are unable to drink due to ulcers in their buccal mucous membranes. (3) ORS containing 50 to 90 mmol/L of sodium should be used alone only during the rehydration phase. After this period, a source of free water should be given. This can be done by resuming feeding (such as a lactose-free formula, breast-feeding, etc) or providing free water in addition to ORS. (4) Patients whose stool output exceeds 10 mL/kg/h will often require intravenous fluids.

Patients with less than mild dehydration who are treated as outpatients can be given 75 mL/kg/24 hours of an ORS containing 50 or 90 mmol/L of sodium. The ORS should be alternated with fluids such as a lactose-free formula or other fluids that do not have a high carbohydrate content and have a low sodium content. We do not recommend ORS containing 30 mmol/L of sodium for

treatment of diarrhea because this sodium concentration would not be adequate to treat moderate to severe diarrhea.

The compositions of the different ORS formulations that are available in the United States are shown in Table 4.

Recently, some investigators have attempted to improve the WHO-ORS by adding substrates such as glycine or rice powder to the WHO-ORS.<sup>10</sup> Preliminary studies in developing countries suggest that both glycine-based ORS and rice powder-based ORS reduce stool output and duration of diarrhea by 30% to 50% compared to the WHO-ORS. We were not able to show the same effect when we used a glycine-based ORS in US children.<sup>11</sup>

## DIETARY THERAPY

### Background Considerations

The scientific literature on the oral nutritional management of children with acute diarrhea is not as richly developed as the respective information on fluid and electrolyte therapy. Therefore, it is not surprising that the optimal approach to dietary management remains controversial. The reasons for this controversy have been reviewed in detail previously.<sup>12</sup>

When the ingestion and/or absorption of nutrients are insufficient to satisfy maintenance nutrient requirements, tissue nutrient stores are catabolized to meet those needs, and secondary growth-faltering occurs. Moreover, intestinal mucosal renewal

**TABLE 3.** Clinical Assessment of Degree of Dehydration

<b>MILD (5%–6%)</b>
Watery diarrhea
Increased thirst
Slightly dry mucous membranes
<b>MODERATE (7%–9%)</b>
Loss of skin turgor
Sunken eyes
Very dry mucous membranes
Depressed anterior fontanel
<b>SEVERE (&gt;9%)</b>
Signs of moderate dehydration plus one or more of the following:
Rapid weak pulse
Cold extremities
Coma

and brush border enzyme production can be impaired by fasting. Thus, food withholding may actually contribute to prolonged malabsorption and secondary diarrhea. Recognizing the important negative impact of enteric infections on children's nutritional status,<sup>13</sup> pediatricians and public health specialists are reevaluating whether the common clinical practice of food withdrawal during diarrhea is appropriate. Attempts to prevent the nutritional deficits that unavoidably accompany the interruption of feeding, however, must be balanced against the possibility that continued feeding may increase diarrheal severity because of enhanced intestinal secretion in response to enteral feedings and/or infection-induced malabsorption of the ingested foods.

Specific recommendations for the dietary management of children with diarrhea must consider the age of the patient, the preillness feeding patterns, and possibly the type of infection. Age is an important factor because selected digestive pathways are not fully developed at birth. Pancreatic amylase, for example, is not secreted in adequate levels until an infant is approximately 6 months of age. Thus, some limitation in starch absorption might be anticipated, especially if colonic absorption of the starch metabolites that are produced by intracolonic bacteria is reduced because of the limited "contact time" permitted by frequent bowel evacuations. Likewise, the bile acid pool size

**TABLE 4.** Oral Rehydration Solutions Available in the United States\*

Component of Solution	Solution (Manufacturer)						
	WHO	Resol† (Wyeth)	Pedialyte (Ross)	Pedialyte RS (Ross)	Lytren (Mead Johnson)	Infalyte (Pennwalt)	Hydralyte (Jayco)
Sodium (mEq/L)	90	50	45	75	50	50	84
Potassium (mEq/L)	20	20	20	20	25	20	10
Chloride (mEq/L)	80	50	35	65	45	40	59
Bicarbonate (mEq/L)						30	15
Citrate (mEq/L)	30	34‡	30	30	30		
Glucose (g/L)	20	20	25	25	20	20	12
Sucrose (g/L)							12.6

\* WHO, Infalyte, and Hydralyte are dispensed in packets; Resol, Pedialyte, Pedialyte RS, and Lytren are dispensed in 240-mL (8-oz) bottles. Composition of solutions taken from package inserts.

† Also contains magnesium 4 mmol/L, calcium 4 mmol/L, and phosphate 5 mmol/L.

‡ 11 mmol/L added as citric acid.

of young infants may be especially reduced during diarrhea because of their relatively limited ability to increase the rate of bile synthesis. This reduced pool size can result in an intraluminal concentration of bile salts that is insufficient to achieve solubilization of long-chain dietary fatty acids.

Preillness feeding patterns are important, because it is unlikely that a young patient will change markedly from customary patterns of intake in the event of an acute illness. Thus, infants who have been receiving an exclusively liquid diet will require a liquid diet during therapy. Because milk is the usual dietary source for these infants, special considerations might be necessary for their management, as will be discussed.

The infectious agents are important when planning dietary therapy because individual microbial agents produce specific pathophysiologic changes in intestinal function. Viral agents, which may cause substantial patchy inflammation and disruption of mucosal structure and function, have been associated with greater malabsorption of carbohydrates.<sup>14</sup> However, because microbiologic diagnoses are often not available until relatively late in the course of therapy (and in many cases may not be available at all), the practical importance of this knowledge is limited.

### General Recommendations

Alternative approaches to nutritional therapy include either continued feeding during acute illness or

reduced or interrupted feeding during the acute stage and a compensatory increase in feeding during convalescence. Often a combination of these two approaches is required. In both cases, the patient's nutritional status should be the guide to indicate when nutritional recovery is complete. In simplest terms, this means that patients should be followed at least until their preillness body weight is achieved. In more severe or complicated illnesses, it might be advisable to monitor additional anthropometric and biochemical indicators of nutritional status.

When appetite is not impaired and it can be assured that the diet is being reasonably well absorbed, there is no advantage to interrupted feeding during diarrhea. On the other hand, when anorexia is a prominent feature of the illness or when the diet is being malabsorbed to such an extent that clinical complications occur, some reduction in dietary intake or change in dietary sources may be unavoidable.

When mucosal digestive and transport mechanisms are impaired by enteric infections, simple dietary manipulations are advisable to take optimal advantage of the remaining intestinal capacity. Absorptive efficiency depends on the relationship between the amount of nutrients presented to the available intestinal transport pathways per unit time. Because we do not have the therapeutic ability to correct impaired transport, restriction of the amount of nutrients presented to the gut at any given moment is the only therapeutic option when absorp-

tive efficiency is diminished. This can be accomplished either by reducing the total dietary intake or, preferably, by increasing the feeding frequency. By increasing the frequency of feedings, while holding the total dietary intake constant, the amount of nutrients entering the intestine following each meal can be reduced. The nutritional advantage of the latter approach is suggested by metabolic balance studies which have demonstrated more complete nutrient absorption by infants with chronic diarrhea when they received continuous rather than bolus feedings.<sup>15</sup>

Another general recommendation is to avoid hyperosmotic foods or liquids, such as heavily sweetened juices and soft drinks. When absorption is incomplete, these solutions will draw more fluid into the intestinal lumen than hypo- or isoosmotic diets. Thus, the common practice of treating children with diarrhea with soft drinks should be discouraged.

Studies by Torres-Pinedo et al<sup>16</sup> demonstrated elegantly that some children with acute diarrhea will not absorb lactose completely, and the unabsorbed carbohydrate can contribute to the severity of diarrhea and metabolic acidosis. Malabsorption of other carbohydrates is less common, but when malabsorption of other disaccharides or monosaccharides occurs, similar clinical complications can ensue.

Although questions are often raised about the potentially negative effects of other specific food components, such as fats and dietary fiber,



during the course of diarrhea, there is little scientific evidence on which to base these concerns. Because most dietary triglycerides contain long-chain fatty acids that are not soluble in water, they do not contribute to the intraintestinal osmolality. Thus, when they are incompletely absorbed during diarrhea, they will not affect the severity of diarrhea by osmotic mechanisms. By contributing to the energy density of the diet, fats may facilitate adequate energy intake when appetite is impaired, and, by delaying gastric emptying time, dietary fats would tend to lower the amount of nutrients presented to the gut per unit time, a potential advantage as discussed before. On the other hand, unabsorbed fatty acids can be metabolized by colonic bacteria to hydroxylated fatty acids, which are able to stimulate some increase in colonic secretion. The practical importance of these observations for the dietary management of acute diarrhea in otherwise healthy children remains unknown.

### Specific Dietary Recommendations

**Breast-Fed Infants.** Despite the concern about malabsorption of lactose in human milk by infants with diarrhea, continued breast-feeding during illness has been promoted for several reasons. Stimulation of the mechanoreceptors of the nipple is necessary to maintain milk production. Thus, continued suckling has been advocated because the maintenance of lactation is deemed a higher therapeutic priority than protection from the potential complications of hypothetical lactose malabsorption. Furthermore, the antiinfective properties of breast milk might actually shorten the duration of symptomatic illness. Recently completed studies of infants randomized to either continued or interrupted breast-feeding in addition to glucose-electrolyte solution during the first 24 hours of inpatient therapy for diarrhea indicated that continued breast-feeding produced a reduction in the severity of diarrhea.<sup>17</sup> Although additional studies would be of interest, these results support the recommen-

dation that breast-feeding should be continued throughout illness.

**Milk- or Formula-Fed Infants.** Young infants who receive the majority of their nutrient intake from cow milk or milk-derived infant formulas and who are not yet consuming solid or semisolid complementary foods require special consideration during therapy. Because these products contain lactose and lactose is the food component most commonly malabsorbed during enteric infections, a change or reduction of the diet may be necessary. Although some researchers report no increase in the rate of complications when milk is continued ad libitum during the early stage of illness, others have noted explosive diarrhea and evidence of carbohydrate malabsorption in a subgroup of their patients. Whereas some clinicians suggest that milk feedings can be continued during the early stages of treatment, others recommend partial dilution or elimination of lactose-containing milks. If milk is continued, it is prudent to monitor for evidence of malabsorption, such as an abrupt increase in fecal excretion with the introduction of milk and the presence of fecal reducing substances or acidic pH. Our own practice is to replace milk with a lactose-free diet or to dilute milk by one half during the first 24 hours of therapy and then introduce milk while the patient remains under observation.

An obvious alternative to the dilution of lactose-containing milks or formulas would be a temporary change to a low-lactose or lactose-free product. A recent study has shown that patients who received (in addition to glucose-electrolyte solution) a formula composed of soy protein isolate and sucrose/corn syrup solids had less severe diarrhea than a control group randomized to treatment with glucose-electrolyte solution alone.<sup>18</sup> These studies and other unpublished observations with a casein-sucrose formula indicate that it is safe and nutritionally advantageous to introduce nonlactose-containing formulas immediately following rapid oral rehydration. The only disadvantages of a change in formula are the problems of introducing a new food (and a new taste) to infants who are acutely ill

and the questions of increased cost and availability that may be of particular concern in some populations.

**Weanlings.** Infants and young children who are receiving a mixed diet with or without human or other milks are less problematic to manage. Because these patients can often meet their nutrient requirements from non-milk foods, the concerns related to malabsorption of lactose are not relevant. Moreover, results of several studies indicate that the reduced amounts of lactose present in milk-containing mixed diets are generally well tolerated even by known lactose malabsorbers and by patients with acute diarrhea.<sup>19,20</sup>

Information on the digestibility of common foods during the early stages of acute diarrhea is extremely limited. Some evidence is available that wheat noodles, rice, and potatoes are well tolerated, but additional quantitative, controlled studies are needed. In the meantime, there is no compelling reason to discontinue feeding children with their usual diets during illness, with the exceptions noted. To the contrary, evidence is mounting that continued feeding during diarrhea is the correct approach to therapy, not only to reduce the adverse nutritional consequences of diarrhea but also to reduce its clinical severity.

### SUMMARY

1. Oral rehydration therapy can be used to treat acute diarrhea of all ages, regardless of etiology and initial serum sodium value.

2. Vomiting is not a contraindication for oral rehydration therapy.

3. Intravenous fluids must be used in the initial management of children with severe dehydration.

4. Enteral feeding should be continued during diarrhea. If anorexia or malabsorption prevents sufficient intake during illness, compensatory nutritional therapy must be provided during convalescence to assure complete nutritional recovery.

5. Breast-fed infants should continue nursing during illness.

6. Infants who usually receive only cow milk or lactose-containing milk-derived formula should be monitored for lactose malabsorption during diar-

rhea. Reduction in milk intake or a temporary change to a lactose-limited formula may be necessary in some cases.

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## Point—Counterpoint

### Oral Rehydration Therapy

The Committee on Nutrition of the American Academy of Pediatrics strongly supports the concept of the use of the oral route for rehydration and maintenance hydration of infants with enteritis as reviewed in this issue by Santosham et al. We place emphasis more forcefully on distinguishing the different stages of physiologic disturbance in such infants which, therefore, slightly changes our emphasis in the recommendations for therapy.

Even for mild dehydration, three stages are recognized: a state of clinical dehydration requiring *rehydration*, a *maintenance fluid* stage after hydration is achieved, and an *early refeeding* stage in which nutrition is restored. These stages may merge into one another quickly, and in some patients the rehydration period may not ever present.

The *rehydration* stage for the seriously ill infant is customarily subdivided into an emergency phase and

a repletion phase. The emergency phase (less than one hour) is for the restoration of plasma volume in the moderately or severely dehydrated infant with a capillary filling (turgor) time of greater than 2 seconds. For mild illness, no emergency phase exists. However, for any rehydration stage to exist, there must be a deficit, which may be estimated from clinical history and findings. The recommended therapeutic volume for the oral rehydration stage is the estimated deficit; the time is two to six hours. The oral fluid should contain, optimally, 60 to 90 mEq/L of sodium and 100 to 120 mmol/L (2%) of glucose. Lower concentrations of sodium in the oral solution will suffice in mild illness as pointed out by Santosham et al.

The *maintenance* stage (also a preventive stage, prior to dehydration) should contain less sodium (eg, 40 to

50 mEq/L) because of the high insensible water losses in infancy. This can be accomplished by either alternating the rehydrating fluid (Na = 60 to 90 mEq/L) with breast-feeding or water or by using a maintenance solution designed for the purpose with, for example, 50 mEq/L of sodium. If such a solution has been used in the rehydration stage, it should *not* be alternated with water, an interpretation possible from the review article.

Finally, we concur that *early refeeding* is desirable, tempered by common sense when, as occasionally happens with a small infant, the stool-purging rate remarkably accelerates. Even then, neither repeated nor prolonged starvation should be permitted. When necessary, both fluid and nutrients can be administered parenterally.

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