Oral rehydration therapy: WHO at 40, ORT at 30

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ABSTRACT: Oral rehydration therapy may prove to be mankind's most significant therapeutic advance this century. Diarrheal disease remains the number one killer of children in the world and is a major cause of illness within Canada and other developed countries. Since its discovery 30 years ago, oral rehydration therapy, comprising glucose, salt and water, has been a simple and low cost treatment for people with life threatening diarrheal disease. Recent developments in solutions for oral rehydration therapy have led to the recognition that the existing World Health Organization glucose based oral replacement salt could be improved. In commercially available rehydration solutions, the sodium concentration has been lowered to reduce hypernatremia in noncholera induced diarrhea. Citrate has replaced bicarbonate as the base in oral replacement solutions to prolong shelf life. Organic substrates to replace glucose and enhance intestinal fluid and electrolyte absorption without osmotic penalty are being examined. However, their acceptance and proper utilization in developing countries remains to be determined. **Can J Gastroenterol 1989;3(1):7-14**

Key Words: *Absorption, Diarrhea, Glucose cotransport, Intestine, Oral rehydration salt, Oral rehydration therapy, Sodium, World Health Organization*

La thérapie de réhydratation par voie orale

RESUME: La réhydratation par voie orale pourrait bien s'avérer le progrès thérapeutique le plus significatif pour l'humanité. Dans le monde, les maladies accompagnées de diarrhées sont toujours la cause première de mortalité infantile et un facteur important d'affections au Canada et dans les autres pays développés. Depuis sa découverte il y a 30 ans de cela, la thérapie de réhydratation orale à base de glucose, de sel et d'eau, est demeurée un traitement simple et peu onéreux pour ceux dont la vie est menacée par les diarrhées graves. Des progrès récents dans le domaine des solutions destinées à ce mode de traitement ont permis de reconnaître que les sels de remplacement à base de glucose, administrés oralement, pouvaient être améliorés. Dans la composition des solutions disponibles sur le marché, la concentration de sodium a été diminuée pour réduire l'hypernatrémie propre aux diarrhées noncholériques provoquées. La durée de vie des produits a été prolongée grâce à l'utilisation du citrate plutôt que du bicarbonate. Sont présentement à l'étude les substrats organiques destinés à remplacer le glucose, à promouvoir les sécrétions intestinales et l'absorption des électrolytes sans encourir d'inconvénient osmotique. Leur adoption par les pays en voie de développement et leur utilisation correcte restent cependant à déterminer.

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Oral rehydration salts (ORS): The salt solution mixed for oral rehydration. When glucose is replaced by another substrate the resulting ORS is termed by the substrate name, ie, sucrose ORS, rice powder ORS.

Oral rehydration therapy (ORT): The administration of a physiologically appropriate fluid by mouth to prevent or correct dehydration that is a consequence of diarrhea.

THE CONSTITUTION OF THE WORLD Health Organization (WHO) was formally established at the first World Health Assembly which took place on June 24, 1948. It was held in the Palais des Nations which overlooks Lake Geneva. Over the past 40 years, WHO has stimulated enormous advancement in health care around the world. Progressing from a brilliant victory over smallpox, they are presently endeavouring to achieve health for all.

During the past decade, there has been increasing awareness among those involved in health care that diarrhea is one of the most destructive of global health problems. According to the best available estimates, diarrhea kills more individuals, mainly children, than any other disease or group of diseases. From one-third to one-half of all childhood deaths are due to diarrhea. If the complications of malabsorption and malnutrition are included in these estimates, then the toll is even greater.

Derived from well focused research efforts, the development of oral rehydra-

tion therapy (ORT) has provided a highly effective, low cost method of treating diarrhea. ORT ameliorates not only the immediate complictions of diarrhea related to dehydration but also the later, more devastating, chronic problems of poor nutrition and retarded growth. The use of ORT has returned us to an era when high technology health care is not necessarily required for treatment of a very common illness. This has greatly reduced the cost of health care in developing countries, which can ill afford to spend limited resources on the costly hospitals and clinics needed to provide intravenous fluids to large numbers of patients.

The development of ORT had its origins in the 1958 Bangkok cholera epidemic. During this epidemic, Phillips (1), in his classic study, examined stool water from 25 patients with cholera. He found that the stool water was isotonic with plasma water but contained slightly higher concentrations of potassium and bicarbonate. With this finding and the realization that the intestinal enterocyte was not damaged by vibrio cholera, the concept of ORT was born. Prior to 1958 the 'intestinal overproduction' theory prevailed in explanations of diarrhea associated with cholera. Such eminent investigators as John Snow (2) believed that the cholera vibrio caused mucosal cells to slough off from their basement membrane, resulting in the outpouring of a transudate. Yet Cohnheim had analyzed the protein concentration of the cholera stool in 1902 and found it too low for a true transudate (2). This discrepancy remained unexplained until Goodpasture's definitive studies in 1923 showed that the sloughing of mucosa seen post mortem was due to post mortem autolysis (2). Despite this fact, textbooks prior to 1958 still supported a belief in mucosal sloughing and transudation.

In 1959, Dr Eugene Gangarosa from Walter Reid Army Hospital joined Dr Phillips and his team in Bangkok (1). He brought the newly developed Crosby capsule which he passed into the small bowel and, via a rectal tube, into the distal colon, thus obtaining specimens for histological analysis from patients with cholera. In no instance was there evidence of loss of mucosal integrity. In that same year, Dr Robert Gordon from the National Institute of Health joined Dr Phillip's team. He infused ^{131}I labelled polyvinylpyrrolidone intravenously and demonstrated that cholera patients had no greater ^{131}I activity per unit time in their stool than did patients without diarrhea. This confirmed once and for all that the diarrhea associated with cholera was not due to mucosal sloughing and denudation of intestinal villi (1).

With this information, Dr Phillips postulated that cholera induced diarrhea was a consequence of a greater than normal flow of protein-free plasma into the gut lumen, with an impaired transport from the lumen back into the intestine. Consequently, Ussing chamber studies were carried out during the 1960 Bangkok cholera epidemic. These demonstrated that the stools of cholera patients indeed contained an agent which inhibited the active transport of sodium.

Using this information, Dr Phillips and his colleagues, now at the San Larenzo Hospital in Manila, performed balance studies to ascertain what the precise effect of oral solutions would be in the treatment of cholera induced diarrhea. They demonstrated that sodium alone, as an isotonic electrolyte solution, was not absorbed well across the intestine. However, when glucose, at a concentration of 100 mM, was added to the oral isotonic electrolyte solution, sodium and chloride ions, along with water, were rapidly absorbed across the intestinal epithelium. This provided the first evidence suggesting that, "...by incorporation of glucose in an oral electrolyte solution one may be able to develop an oral treatment regimen which in the average case of cholera might completely eliminate the requirements for intravenous fluids" (1). Subsequently, enhancement of net sodium and water absorption was confirmed by Taylor and others (3) during intestinal glucose lavage in acute cholera patients. Hirschhorn et al (4) and Banwell et al (5) in follow-up studies, similarly described reduction in stool output in cholera during glucose and electrolyte lavage.

It was not until the studies of Schultz (6) emerged a decade later that the physiological basis of these findings could finally be interpreted. The effectiveness of ORT was shown to be based on the presence of sodium coupled glucose cotransport across the brush border of intestinal epithelium (6). Furthermore, this active carrier process remained intact during cholera stimulated intestinal

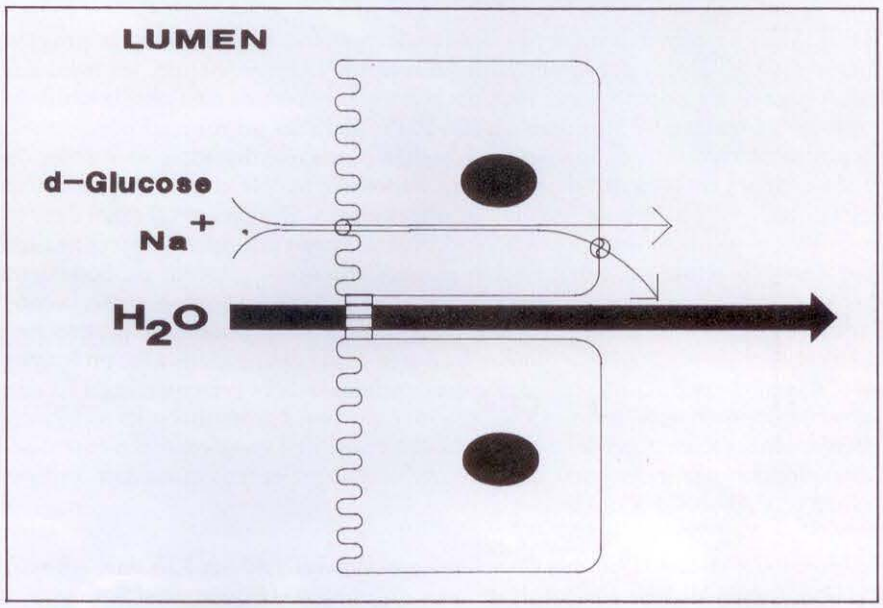

Figure 1) *Glucose stimulation of intestinal sodium and water absorption. The movements of sodium and that of the cotransported glucose across the brush border membrane of the enterocyte are coupled between sodium, D glucose and a carrier molecule in the membrane. Glucose stimulates sodium and, therefore, water absorption across the intact intestine. D hexoses, L amino acids and oligopeptides utilize similar sodium coupled transport processes*

transport. Figure 1 depicts the role of the sodium dependent glucose cotransporter in the physiological basis of ORT.

The first randomized trial using ORT was conducted by Nalin and colleagues (7) at the Pakistan-Seato Cholera Research Laboratory in Dacc, Pakistan. Twenty-nine patients with documented vibrio cholera were randomly assigned to either an oral solution containing glucose, sodium chloride, sodium bicarbonate and potassium chloride or to intravenous therapy. Patients receiving oral therapy for replacement to stool fluid and electrolyte losses required 80% less intravenous fluid than was required by control patients. ORT rapidly became the mainstay of maintenance therapy for cholera. Nevertheless, controversies over the ideal ORT continue to this day.

ORS SODIUM COMPOSITION

The WHO has adopted a formula for preparing a single oral rehydration salt (ORS) which may be used for treating diarrhea in all age groups regardless of etiology. A major concern in the initial trials with ORT was whether it would be possible to provide enough sodium to replace the high losses associated with cholera (8). Studies in Calcutta (9,10) and Bangladesh (11) reported success using solutions containing 90 to 120 mmol sodium/L. In mmol/L, the concentrations of the WHO ORS are: sodium 90; potassium 20; chlorine 80; bicarbonate 30; and glucose 111 (Table 1) (12).

TABLE 1
World Health Organization oral rehydration salt

Substance	Quantity
Sodium chloride	3.5 g/L
Sodium bicarbonate*	2.9 g/L
Potassium chloride	1.5 g/L
Glucose	20.0 g/L

* *May be replaced by 2.9 g sodium citrate*

A controversial issue has been whether or not a concentration of 90 mmol sodium/L is too high in an ORS used to treat noncholera induced diarrhea. Molla and co-workers (13) found stool sodium concentration and mean purging rate were significantly higher with vibrio cholera than with enterotoxigenic *Escherichia coli* or rotavirus induced diarrhea. Mean stool sodium concentrations averaged 88.9 mmol/L for cholera, 53.7 mmol/L for enterotoxigenic *E coli* and 37.2 mmol/L for rotavirus (13). Nevertheless, several trials have reported success in treating noncholera induced diarrhea with either high sodium (90 mmol/L) or low sodium (50 to 60 mmol/L) solutions. Santosham and colleagues (14) compared therapies of intravenous fluids, 50 mmol sodium/L ORS and 90 mmol sodium/L ORS, in 146 well nourished diarrhetic children from the United States and Panama. The regimens were equally effective and safe. No patient developed hypernatremia or hyponatremia during treatment.

Similar results emerged from a study in India of 50 children with noncholera diarrhea treated with either high or low sodium solutions (15). In Costa Rica, 234 of 242 neonates, with a mean dehydration of 5.1% body weight, were successfully rehydrated with 90 mmol sodium/L ORS in an average time of 44 h. Hypernatremia, hyponatremia and acidosis present on admission were also corrected within several hours. Electrolyte abnormalities did not develop as a consequence of ORS therapy (16). Finally, Saberi and Assaee (17) have successfully rehydrated 27 20-month-old infants in Iran with either high or low sodium ORS without complications.

Certainly the high stool sodium loss associated with cholera demands an ORS with sodium concentration of 90 mmol/L. The treatment of enterotoxigenic *E coli* and rotavirus induced diarrheas with a low sodium ORS appears to be a theoretical consideration only. In control trials, the actual sodium concentration in ORS did not affect outcome. Nevertheless, commercially available oral replacement solutions marketed within North America do contain lower sodium concentrations (45 to 75 mmol/L).

ORS FREE WATER COMPOSITION

Techniques for replacing free water vary from study to study. One successful approach has been to use two parts ORS with one part free water in an attempt to avoid hypernatremia through providing the kidney with free water for homeostasis (12). Several studies have used this method during the rehydration phase with success (16,18-20).

Trials using ORS without free water during the initial rehydration phase have differed in their incidence of hypernatremia. While Santosham and co-workers (14) reported no hypernatremia in their group of well nourished, noncholera diarrhetic children over three months of age, Bhargava and colleagues (21) noted the onset of hypernatremia (serum sodium above 150 mmol/L) in 11 out of 22 infants under three months of age. Associated symptoms included periorbital edema, irritability and, in one case, a generalized convulsion. Reports from Jamaica (20) and Turkey (22) have noted asymptomatic, transient hypernatremia in several infants receiving a 90 mmol sodium/L ORS without free water. In contrast, none of 43 infants receiving either a 60 mmol sodium/L solution or intravenous therapy became hypernatremic (21).

Investigators have emphasized that, once the patient's volume status has been normalized (the rehydration phase of therapy), a modification in oral solutions is required for the maintenance phase of therapy (5,16). Initially, regardless of the serum sodium concentration, patients with volume depletion due to diarrhea have a total body deficit of sodium (23). Nalin and colleagues (20) found that net intestinal sodium absorption and correction of volume depletion during the first 24 h was significantly higher with a 90 mmol sodium/L ORS given via the 2:1 ORS to water method than with a single 60 mmol sodium/L solution. However, even proponents of a 90 mmol sodium/L ORS recommend increasing free water intake (or low solute fluids) to a 1:1 ORS to water ratio during the maintenance phase (following repletion of initial deficits) (12,24). For example, Sharifi and Ghavami (25) successfully treated 104 severely dehydrated infants with a two phase regimen, using an 80 mmol sodium/L solution for deficit therapy and a 40 mmol sodium/L solution for maintenance therapy.

What about the subset of patients who have high serum sodium concentrations on admission? Is the WHO's ORS safe in the treatment of hypernatremic diar-

rhea in parts of the world where rotavirus, rather than cholera, predominates? Pizarro and co-workers (24) specifically addressed these questions in a Costa Rican study of 61 well nourished, diarrhetic infants admitted with hypernatremia. In the rehydration phase, a 2:1 ORS to water regimen of the WHO's ORS successfully rehydrated all 61 patients. During maintenance therapy with a 9.5 mmol sodium/L milk formula, two infants required some intravenous fluids to keep up with ongoing losses. An 8% incidence of hypernatremia induced convulsions compared favourably, retrospectively, with the 14% rate encountered with intravenous rehydration. The mean rate of fall in serum sodium between admission and rehydration was 2.7 ± 1.0 mmol/L/h in patients with convulsions versus 1.6 ± 0.2 mmol/L/h in patients without convulsions, but the difference was not statistically significant.

In a subsequent study, Pizarro et al (19) slowed the rate of rehydration by 50%, in an attempt to decrease the incidence of seizures among 35 infants with hypernatremia and diarrhea. In addition, 11 of the 35 infants received the WHO's ORS without free water, instead of the standard 2:1 ORS to water regimen. There were no convulsions in either group. The authors suggested that, in addition to rapidly falling sodium, precipitous changes in other electrolytes and in pH were important factors involved in the development of convulsions during rehydration.

Pizarro and colleagues (24) also reported success using a 2:1 ORS to water concentration of the WHO's ORS in treating patients with hyponatremia and diarrhea. At the end of the study they withheld free water from the treatment regimen of eight infants with particularly severe hyponatremia; the net sodium gain and the rate of change in serum sodium concentration was greater than in the group receiving the 2:1 ORS to water therapy. These authors suggested that giving ORS without additional water may be the optimal regimen for treating hyponatremic diarrhea.

In general, the amount of free water replacement remains a confusing and complex issue. Since the majority of severely volume depleted patients have a total body sodium deficit, a 2:1 ORS to water is appropriate during the rehydration stage to be followed by a 1:1 ORS to water concentration of the ORS during the maintenance phase.

ORS POTASSIUM COMPOSITION

Several studies have suggested that the WHO's ORS potassium concentration may be too low. Molla and co-workers (13) found that potassium levels of fecal effluent in diarrhea induced by cholera, enterotoxigenic *E coli* or rotavirus, averaged 31, 38 and 37 mmol/L, respectively. These values are all higher than the 20 mmol of potassium/L found in the WHO's ORS. In a study by Nalin et al (20), an ORS containing 35 mmol of potassium/L was found to be significantly better in correcting potassium deficits than the standard WHO ORS.

Despite these findings, the 20 mmol/L potassium concentration in the WHO ORS and the commercially available ORS have repleted and maintained adequate potassium concentrations.

ORS BASE COMPOSITION

In addition to the concerns about sodium and potassium content in ORS, recent research has focused on the appropriate base for an ORS. Since bicarbonate forms insoluble lumps in humid climates, citrate (2.9 g/L) has replaced bicarbonate during the past year and now extends the shelf life of the ORS packet. Animal experiments have shown that citrate is actively absorbed by rabbit ileum via a ouabain sensitive chloride independent mechanism. It also stimulates the absorption of sodium and chlorine via a chloride dependent mechanism (26). Clinical studies have suggested that sodium citrate can be satisfactorily substituted for sodium bicarbonate (27).

Indeed, an ORS from effervescent tablets containing a sodium citrate base has proven as effective as the standard WHO's ORS packets in the management of enterotoxigenic *E coli* diarrhea in both adults and children (28). These effervescent tablets present a convenient and compact alternative to packets of ORS ingredients and may become a 'travelling companion' for visitors to developing countries.

TABLE 2
Substrates for oral rehydration solutions

Carbohydrates
Glucose
Sucrose
Glucose polymers (maltodextrins)
Amino acids
Alanine
Glycine
Dipeptides
Glycyl glycine
Rice
Cereals
Maize
Wheat
Lentil

ORS ORGANIC SUBSTRATE COMPOSITION

Glucose is the original organic substrate and is still the standard being universally used in ORS packets. Recently, other organic substrates for ORS have been investigated (Table 2). Field (29) pointed to the likely importance of polymers of glucose and amino acids in optimal transport of sodium and water from the gut lumen into the blood stream. Using a children's rhyme by Maurice Sendak to make his point: "Sipping once, sipping twice, sipping chicken soup with rice," he noted that biophysical considerations and transport studies had indicated a significant advantage in using larger cotransporting substrates to maximize the absorption of salt and water during diarrhea.

Devising ORS solutions with minimal osmotic loads and maximal nutritional values is a major focus of current research. Simply raising the glucose concentration, in an attempt to increase sodium and chloride absorption (through the sodium dependent glucose cotransporter), is ineffective because of the increased osmotic penalty. Therefore, one approach has been to enhance sodium and water absorption by exploiting glucose independent transport. Recent studies in animals and humans have shown that water soluble organic molecules, such as amino acids, dipeptides and tripeptides, also enhance the absorption of sodium and water in the small intestine (6). As the sodium coupled carrier for these solutes is not competitive with the sodium dependent glu-

cose cotransporter, additional fluids and electrolytes can be absorbed.

Clinical trials in developing countries, one utilizing adults (30) and one utilizing children (31), demonstrated that, when glycine was added to a glucose-ORS, both the duration of diarrhea and the stool output were considerably reduced, in comparison with the use of an ORS without glycine. In contrast, Santosham and co-workers (32) evaluated the safety and efficacy of a glycine-ORS, comparing it to a standard glucose-ORS without glycine, in a randomized double blind trial of infants from the United States who were being treated (either as inpatients or outpatients) for acute gastroenteritis. The glycine-ORS and the glucose-ORS were identical in all respects, except for an addition of 111 mmol/L glycine and a subsequently higher osmolatity, 389 mOsm/L (glycine) compared to 278 mOsm/L (glucose). Among the 66 inpatients, stool volume and duration of illness were similar. However, 13% of the infants receiving glycine-ORS developed hypernatremia compared to none of those receiving the glucose-ORS. Among the 77 outpatients there were no differences in stool volume, duration of illness or serum sodium concentrations between those receiving the glycine-ORS and those receiving the glucose-ORS (32).

A further reason for examining the role of glucose in ORS is its limited availability and high cost in many developing countries, where the incidence of diarrhea is high. Consequently, the use of alternative carrier substances, such as sucrose, has been explored (33-36). Rice powder is an alternative currently attracting interest because, in many countries, rice is cheaper than glucose or sucrose, it is available in virtually every home and it is readily accepted as a traditional food. This is a promising strategy as rice is a polymer which hides its eventual osmotic load from the intestine until its subunits have been liberated by digestion. Exerting minimal osmotic force as an intact substrate, the polymer travels down the intestine as a molecular Trojan horse, slowly hydrolyzing into glucose, glycine and lysine, and thus avoiding osmotic diarrhea. A rice-ORS has been found effective in treating dehydration due to diarrhea caused by vibrio cholera and *E coli* in adults and children (37).

In separate studies Patra and co-workers (38) and Mohan and co-workers (39) replaced the 20 g/L glucose found in a glucose-ORS with 50 and 30 g/L rice powder, respectively. The electrolyte composition of both solutions was otherwise identical. In these studies the two rehydrating solutions proved comparable to the WHO's ORS in correcting and maintaining hydration status and serum electrolyte values. Mean rehydration time, stool output, stool frequency, ORS intake, weight gain and urine output were similar in both groups. Rice powder-ORS thus appears to be a satisfactory alternative to the WHO's glucose-ORS.

Furthermore, basic salt ingredients may be stored as premeasured packages and reconstituted with rice powder water, thereby prolonging shelf life. Unlike the WHO's glucose-ORS, boiling is necessary for the reconstitution of a rice powder-ORS, thus minimizing the risk of initial bacterial contamination of an ORS prepared with well water (40). In comparison with that of the WHO's glucose-ORS, however, rice powder-ORS preparation is fairly cumbersome and time consuming.

Randomized studies have also been carried out comparing hydrolyzed wheat-ORS and lentil-ORS with the WHO's glucose-ORS in the treatment of non-cholera diarrhea in children. The basis for the use of these solutes is similar, with enhanced sodium and water absorption, without an osmotic penalty, through delivery down the intestine of a complex molecule which hydrolyzes into smaller molecules which stimulate optimum absorption of sodium. In these studies, the alternate solutions worked equally as well as, or slightly better than, the standard WHO glucose-ORS or a rice-ORS solution in reducing stool output and stimulating rehydration (41-43).

Although the concept of using local cereals and carbohydrates in mixing an ORS is attractive physiologically, economically and culturally, it is necessary that natural foods chosen for use in rehydration solutions be hydrolyzed within the gastrointestinal lumen at standard rates. This allows optimal solute concentrations without excess osmotic load. Significant differences in the composition of these natural foods will be important considerations in ensuring adequate rehydration without complications. Although a cereal based ORS may be superior to a glucose-ORS, most cereal-ORS preparations tested so far need boiling before they are suitable for use in an ORS (41). This precludes their use in a premixed packet form and reduces their convenience. In addition, once they are mixed, cereal based ORS turn sour and undrinkable within 6 to 8 h.

ORS NUTRITIONAL VALUES

The nutritional impact of diarrhea is a result of reduced consumption, withholding of food and impaired absorption of nutrients (44-46). Studies have indicated that a reduction in food intake of approximately 30% occurs in acute cases of diarrhea (47,48). ORT is thought to improve nutritional status by correcting dehydration, by normalizing metabolic derangements and possibly by restoring appetite through a recovery from diarrhea (49).

However, Molla and associates (47) studied food consumption and absorption of nutrients in children with cholera. They compared 22 children treated with intravenous solutions with 25 others given ORT, along with intravenous supplementation as necessary. Intake of fats and proteins but not carbohydrates was lower in the ORT treated group during the acute state of diarrhea. Differences in the consumption and absorption of nutrients between the two groups were transient and returned to equal levels within two weeks after recovery. Although ORT intervention alone may not alter malnutrition during diarrhea, Santosham and colleagues (50,51) have presented compelling evidence to show that early feeding of lactose-free soy based formula, along with ORT, reduces duration of diarrhea and stool output as well as allowing better weight gain and nutritional status.

In the North American adult population, a short period of malnutrition and weight loss during an acute diarrheal illness is not likely to be harmful and for some, may even be desirable. Nevertheless, in the pediatric population similar

malnutrition can have severe consequences. The old adage of withholding food during acute diarrheal illness appears to be falling by the wayside as early feeding of lactose-free formulae during acute diarrhea maintain a better nutritional status.

ORS — IS THERE A CHOICE?

Results of an Australian study emphasized the importance of giving standardized oral replacement solutions rather than commercially available products not designed for this purpose. Dibley and co-workers (49) found wide nutrient and electrolyte variations among 91 commercial clear fluids, including fruit juices, cordials, carbonated beverages, powdered drinks, syrups, soups and jellies. The range was between 0 to 175 mmol/L for sodium, 0 to 52 mmol/L for potassium, 0 to 839 mmol/L for solutes and 50 to 914 mmol/kg water for osmolality (Table 3). Snyder (52), in his review of departments of pediatrics at medical schools in the United States and Canada, found many to be using these common household fluids for oral rehydration during acute diarrhea. In general, these common household beverages do not provide adequate sodium and/or glucose to 'drive' intestinal water and electrolyte absorption via the sodium coupled glucose cotransporter. In addition, their high glucose concentration may actually worsen symptoms by inducing an osmotic diarrhea.

During the last several years, commercial sugar-salt solutions have become available which more closely approach a solution based on physiological principles and studies (Table 4). The lower sodium concentration of commercially available solutions reduces the risk of hypernatremia in noncholera induced diarrhea.

TABLE 3
Composition of some common household beverages

Beverage	Glucose (mmol/L)	Sodium (mmol/L)	Potassium (mmol/L)	Osmolality (mOsm/L)
Jello water (one-half strength)	444	10.0	0.1	600
Apple juice	666	2.5	35.0	690
Grape juice	866	2.5	35.0	1180
Ginger ale	333	3.0	3.0	540
Pepsi Cola	589	1.3	0.1	591
Coca Cola	597	1.7	0.1	601
'Mother's' chicken broth	0	250.0	8.0	450
Tea	0	0.0	0.0	5

TABLE 4
Commercially available oral replacement solutions

Solution	Glucose (mmol/L)	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Base (mmol/L)	Osmolality (mOsm/L)
WHO Glucose-ORS	111	90	20	80	30 (bicarbonate)	331
Pedialyte RS	139	75	20	65	30 (citrate)	329
Pedialyte	139	45	20	35	30 (citrate)	269
Gastrolyte	100	50	20	52	18 (bicarbonate)	240
Lytren	100	50	25	45	30 (citrate)	250
Gatorade	277	22	3	27		330

ORT — IS IT WORKING?

Despite the above concerns, epidemiologic reports continue to support use of the WHO's oral replacement therapy. In the Gaza Strip, 35 health centres, serving approximately 60,000 children, began an ORT programme in 1979. Compared with statistics from 1977, hospital admissions for diarrheal illnesses dropped by 35% in 1980 and 42% in 1981; diarrheal mortality decreased 36% in 1980 and 53% in 1981 (53).

A study from Bangladesh retrospectively examined the effect of changing from intravenous therapy accompanied by ORT to ORT alone in the treatment of patients with moderate and severe diarrheal dehydration (54). In 1980, 93% of 10,379 patients received intravenous fluids compared with only 39% of patients in 1981 (54). There was no significant difference in mortality or complication rates. Use of ORT alone was, however, associated with a 33% reduction in health care cost (54). In New Guinea, the institution of an ORT programme in the treatment of children under five years of age was accompanied by a fall in diarrheal mortality from 3.3/1000 annually to 1.3/1000 annually (55).

Poor patient education continues to be an obstacle preventing the truly effective use of outpatient ORT (56,57). In the underdeveloped areas traditional remedies for diarrhea are often intended to dry the stool. Thus, a woman from New Guinea stated, "I took my child to the aid post for the first two days but the fluid [ORS] made the diarrhea worse and we decided to hold a prayer meeting instead" (55).

Another problem involves the correct mixing and usage of powdered ORS. In Cairo, the WHO's glucose-ORS costs about $0.40 Canadian per litre of reconstituted solution. Yet Cleary and colleagues (58) reported that only eight out of 100 children admitted with diarrhea dehydration had been given the solution prior to arrival at the hospital. In addition, despite instructions written in Arabic on each packet, none of the eight children received the ORS in an appropriate fashion. Mothers consistently mixed the packets with insufficient water and thus four of the eight children were hypernatremic on admission. In one case, the powdered ORS had been sprinkled over cereal!

A further study from Cairo found that differences in the capacity of home containers used in which to mix the powdered ORS contributed to its underdilution (59). Twenty-six mothers, using containers of varying sizes usually found in the home, mixed ORS solutions with a mean sodium concentration of 123 mmol/L. In contrast, 25 mothers given special standardized containers mixed solutions with a mean sodium concentration of 98 mmol/L. These findings are similar to those of studies done in India where ORS reconstitution and rehydrating instructions are misinterpreted 40%

of the time despite careful instructions to the mothers (60).

The health education program regarding oral rehydration therapy continues. If the grounds for oral rehydration are explained within the framework of the local culture's view of physiology, the program will likely be more successful. Otherwise, the use of ORT is likely to decline as more mothers become disillusioned when avoidable complications arise following incorrect use of an ORS.

Within the developed world, ORT continues to be the basis for pediatric treatment of diarrhea. In the adult population, commercially available ORT and the applied physiological concepts can play a major role in maintaining adequate hydration during acute and chronic diarrhea, acute volume depletion associated with exertion and short bowel states.

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