Oral Rehydration Therapy: An Annotated Bibliography

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An Annotated Bibliography

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INTRODUCTION

This collection of annotated abstracts on oral rehydration therapy (ORT) has been compiled to assist in understanding the large amount of information which has recently evolved concerning this method of treating diarrhea.

Diarrheal diseases are one of the major public health problems in the developing world, are a leading cause of death in small children and constitute an important contributing factor to malnutrition.

Acute diarrheal episodes, which are caused by a number of agents, are most often self-limited. Dehydration, the major cause of diarrheal disease morbidity and mortality, results from the loss of fluid and electrolytes in diarrheal stools.

The long-term reduction in incidence and severity of diarrhea will continue to depend on comprehensive programs to improve nutritional status, water supplies, personal hygiene and environmental sanitation. However, an immediate impact on mortality due to dehydration can be achieved by treatment based on early administration of oral glucose electrolyte solution. The cornerstone of this therapeutic plan is the use of an inexpensive, easily administered, and universally available oral rehydration solution.

The use of oral rehydration solutions to provide water and electrolytes for persons with diarrhea has long been advocated. Darrow (1949) and Harrison (1955) reported successful use of oral rehydration to provide maintenance fluid and electrolyte therapy in dehydrated children and infants. A salt and glucose oral rehydration solution was successfully used to treat persons with mild cholera in India in 1953.

In the late 1950s and early 1960s, studies demonstrated the glucose-enhanced uptake of sodium and water in the small intestine. In 1964, Phillips showed that persons with cholera could absorb oral glucose-electrolyte solutions, and in 1968 the first comprehensive metabolic balance studies were done, clearly demonstrating that oral infusions could maintain fluid and electrolyte balance in persons with cholera. Over the next decade a large number of hospital, treatment center, and field-based clinical trials, in all age groups, showed that oral rehydration solutions could be used to effectively treat mild and moderate dehydration resulting from both cholera and non-cholera diarrhea. These trials were carried out in many countries under widely varying conditions.

Severely dehydrated persons (10% or greater weight loss) may require initial intravenous (IV) rehydration, but the subsequent use of oral therapy to complete rehydration and to supply maintenance
fluids and electrolytes has led to an overall 80% reduction in the need for IV fluids. An implicit advantage is the virtual elimination of complications (e.g., septicemia) associated with IV therapy. Persons with severe, protracted vomiting, other medical complications, rarely-seen glucose (or sucrose) intolerance, and those whose oral intake cannot match losses also require IV therapy.

Most present oral rehydration programs use a single solution containing the WHC-recommended composition (ORS) to treat all age groups with all types of diarrhea. The electrolyte composition of the solution was initially developed to approximate the concentration of electrolyte losses in stools of persons with cholera. The concentration of glucose, the most expensive ingredient in the solution, represents the minimum amount needed to provide optimal sodium and water uptake.

There are obvious administrative and operational advantages to using a single oral solution, and the optimal concentration of each of the ingredients has been carefully determined. Sucrose, which in many countries is a less expensive and more easily obtained sugar than glucose, has proved a possible substitute for glucose. However, if sucrose is substituted, twice the amount of sucrose is needed (40 g vs 20 g) as in the glucose-electrolyte solution. The recommended sodium concentration (90 mEq/l) has been amply shown to be highly effective and safe for deficit replacement and maintenance needs of individuals with either cholera or non-cholera diarrhea; additional water need during maintenance of small infants is easily met by providing breastmilk, diluted cows' milk or plain water.

A large number of hospital and treatment center trials have demonstrated that oral rehydration therapy (ORT) reduces the clinical severity and mortality caused by diarrhea. The early reports from field studies are similarly encouraging. These studies have convincingly shown that dependence on expensive IV therapy to treat dehydration can be greatly diminished. When combined with educational efforts stressing the need to continue feeding (especially breastfeeding in infants) during and after diarrheal episodes, ORT is expected to have a favorable impact on malnutrition by reducing the severity and duration of dehydration and acidosis associated with diarrhea and by improving appetite and food intake. However, because of the complex interactions of social, economic, health, and environmental factors related to malnutrition, this impact has been difficult to quantify.

A key to implementing country oral rehydration programs is devising distribution and administrative systems which incorporate the customs, beliefs, practices and facilities of the target populations. Prepackaged preparations of ORS distributed through rural treatment centers and primary health care workers have proved effective, but as knowledge and acceptance of oral rehydration grows, home-prepared solutions using locally available household sugar and salt may become
practical and inexpensive. However, much more information concerning the efficacy of home preparation is required before the home-based mode can be recommended.

National efforts to implement oral rehydration therapy must be part of the general program for delivery of all basic health services. Use of oral rehydration therapy in the treatment of diarrhea in infants and children acts as a highly effective entry point for appropriate health education measures, particularly promotion of breastfeeding, appropriate dietary practices including weaning foods and personal hygiene. The practice of oral rehydration therapy should be implemented through the primary health care approach by integrating it into other primary health care activities, such as immunizations, family planning, nutrition and maternal and child health.

On the following pages, annotated abstracts of oral rehydration articles are arranged under 5 categories: history, clinical trials, composition, impact, and implementation. If information in an article pertains to more than one category, the abstract appears in the section corresponding to the major thrust of the article, while the citation is cross-listed in each other appropriate category. Abstracts appear in approximately chronological order.

WHO-Recommended Formulation of ORS:

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<table>
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I. HISTORY

These annotated abstracts trace the physiologic and clinical rationale behind the development of oral rehydration solutions.

Oral solutions containing glucose (historically first used for its nutritional value) and electrolytes have been used successfully in treating dehydrated persons for over 30 years. A physiologic basis for such treatment has been established in the past 2 1/2 decades by studies which showed that coupled transport of glucose and sodium in the small intestine results in accelerated transport of electrolytes and water. Clinical trials were subsequently performed to determine whether persons with cholera could absorb oral glucose-electrolyte solutions and, if so, whether maintenance fluid and electrolyte requirements could be met.


Detailed metabolic balance studies were performed on 7 hospitalized infants with moderate to severe diarrhea. The results showed that an oral solution containing Na⁺, Cl⁻, K⁺, HCO₃⁻, and glucose could be tolerated and that the solution could aid replacement of body water and electrolyte losses without prolonged parenteral therapy. After one day of intravenous therapy, most of the children received their fluid and electrolyte requirements orally.

These findings provided early evidence for the efficacy of oral rehydration therapy.


The efficacy of an oral solution to treat cholera patients was evaluated while controlling vomiting with an antiemetic agent.

During 2 epidemics of cholera in Calcutta in 1952 and 1953, 59 and 127 persons, respectively, were treated with 14 mg tablets of promethazine and 8-chlorotheophylline to control vomiting. A solution of Na⁺(114 mEq/l), K⁺(28 mEq/l), and glucose (137 mmol/l) was administered by mouth to 33 of these persons with mild cholera and by mouth and rectum to 153 with moderate to severe disease. All 186 treated persons recovered without sequelae.
This historic report demonstrated the potential usefulness of non-parenteral glucose-electrolyte solutions for the treatment of cholera.


This early physiologic study demonstrated that a relatively small number of cells in a rat small intestine preparation were involved in glucose translocation from the lumen and that the remaining cells were impermeable to glucose translocation. From this evidence, it was possible to postulate the existence of specific receptor sites for glucose uptake.


A general review of the etiology, physiology, clinical and laboratory assessment and therapy of pediatric diarrheal disease was presented. Intravenous rehydration was identified as the initial therapy of choice for dehydrated children. However, administration of oral electrolyte-carbohydrate solutions was recommended as a suitable method for supplying maintenance water, electrolyte, and carbohydrate requirements. The oral solution used contained 50 mEq/l of Na⁺ and Cl⁻ and 20 mEq/l of K⁺, in addition to citrate, phosphate and glucose or maltose.

After 6 years of experience at Baltimore City Hospital the investigators reported most patients were kept in water and electrolyte balance and that there was no evidence of exacerbated or prolonged diarrhea using oral solutions for maintenance hydration.


Unwittingly high sodium concentrations in oral formulas given at home for the early treatment of mild to moderate diarrheal disease may contribute to an increased incidence of hypernatremia.

Thirty-two children with gastroenteritis (consecutive admissions at 2 urban American hospitals) were studied. Careful feeding histories were obtained. Where possible, samples of pre-admission oral feedings where tested for solute concentration, as were samples of water from particular homes. Solutions made by using heaping measures of a commonly used commercial oral electrolyte solution were analyzed for solute concentrations.
Seventeen of the thirty-two cases had confirmed hypernatremia (sodium greater than 150 mEq/l) on admission, and four of those died. Three others had neurologic sequelae at discharge. There were no deaths or neurologic sequelae in the non-hypernatremic patients. The major difference in the hypernatremic group was the high solute load in their predishission feedings. Reasons for the high solute loads included errors in formula preparation and high concentrations of sodium in the water used for mixing.

This study was one of the first to point out the pitfalls inherent in home preparation of oral rehydration fluid for children, especially when measurement of all constituents is performed in the home.


The dependence of active absorption of sugars (glucose, galactose, and fructose) on cation concentrations bathing the intestine was clearly shown in these classic studies performed on isolated surviving guinea pig intestine. Both sodium and potassium ions were shown to be required for the process of active transport of glucose. This was one of the first studies to demonstrate the physiologic link between glucose and sodium transport in the small intestine.


The study discussed hypernatremic dehydration, defined as fluid losses amounting to 10-15% of body weight associated with an elevated serum sodium concentration. Predisposing factors were described including prematurity, decreased free water intake, increased solute-free evaporative water loss, increased stool loss of free water, increased solute load to a sick infant, salt poisoning, and diabetes insipidus (both central and nephrogenic). Associated clinical findings were also described and a treatment rationale was outlined, including mention that oral therapy with "glucose-water and electrolytes" can be given within 12-24 hours of admission to the hospital or earlier.


To determine the interrelationships of cellular metabolism, transport of NaCl and water and the effects of glucose and metabolic poisons on ion transport, in vitro studies were carried out on rat ileum preparations.
Net water transport was shown to be dependent on the rate of net sodium transport. In the presence of glucose increased Na⁺ and Cl⁻ uptake was seen. The presence of metabolic poisons inhibited Na⁺ and Cl⁻ uptake.

The data presented indicated that water transport is a passive process and is dependent on Na⁺ and Cl⁻ transport. Na⁺ and Cl⁻ influx was shown to be significantly affected by the presence of glucose. The active-transport nature of ion uptake was demonstrated by inhibition of ion influx with metabolic poisons.

This study helped to establish the biophysical rationale for the use of glucose-electrolyte solutions to provide effective oral rehydration.


This paper traced the development of programs for treating cholera which were based on studies of the mechanism of production and electrolyte composition of diarrheal stools. To determine if oral rehydration could be used to treat persons with cholera, oral solutions of varying compositions were administered to hospitalized Filipino patients and to healthy volunteers.

Electrolyte solutions were shown to replace water, K⁺, and some of the HCO₃⁻ losses in cholera. Addition of glucose to an isotonic electrolyte solution allowed the uptake of sodium and chloride which were not otherwise absorbed.

The physiologic evidence for the coupling of sodium and glucose transport in the small intestine provided the rationale for this successful demonstration that an oral glucose-electrolyte solution could be used to treat the fluid and electrolyte losses of cholera.


This symposium report detailed the biophysical evidence supporting the hypothesis of coupled glucose and sodium transport in the small intestine. Transport appears to be related to the energy-dependent translocation of Na⁺ at the cellular level.


To show the relationship of diarrhea and the active transport of sodium, quantitative and qualitative stool, serum, and urine studies
were performed on 12 hospitalized Filipino adults with onset of cholera within 24 hours of admission. Initial intravenous hydration corrected acid-base and fluid deficits.

During study periods, one of 3 oral solutions containing 10 mmol/l KCl, 45 mmol/l NaHCO₃, and either 0, 100 or 185 mmol/l NaCl were administered, and uptake of electrolytes was measured.

Absorption of H₂O, K⁺, and HCO₃⁻ was demonstrated but NaCl was not absorbed during acute, severe cholera. However, net absorption of all ions was seen during convalescence.

These results demonstrated that sodium is not absorbed from the gut in the absence of glucose in patients with severe, acute cholera regardless of whether a hypotonic, isotonic, or hypertonic sodium solution is used.


Glucose-, galactose-, and fructose-electrolyte solutions were infused into 8 hospitalized adults with cholera, and the effect on net stool output was evaluated. Each of the persons studied had culture-proven V. cholera, (El Tor-Inaba), infections, were admitted in shock, had high stool purging rates, and received initial intravenous correction of fluid and electrolyte deficits. Warmed electrolyte solutions (mEq/l: Na⁺-133, K⁺-6.1, Cl⁻92, HCO₃⁻-48) with varying amounts of glucose, galactose, or fructose were infused. IV hydration was continued in order to supply maintenance fluid and electrolytes. Intake, output, stool composition, and serum chemistries were serially monitored. Controls consisted of 25 people treated for cholera from 3 previous epidemics who had received IV therapy along with some water and small snacks taken by mouth.

The net stool output decreased when glucose was added to the perfusion solution and increased when glucose was removed. Galactose was as effective as glucose in reducing net stool output but fructose had no effect on stool rate. Stool electrolyte concentrations during perfusion were similar to that of the perfusing solution, indicating that no one component of the solution was selectively absorbed.

Decreases in the net stool rate and net stool losses of Na⁺, K⁺, Cl⁻, and HCO₃⁻ were observed during the infusion studies. These results suggested that oral glucose-electrolyte solutions could be of value in reducing the intravenous fluid requirement for cholera.

Twenty-nine Bangladeshi adults hospitalized with bacteriologically confirmed V. cholerae infections were studied. Each was initially treated intravenously until hypotension was corrected. Ten controls continued to receive only IV hydration, while ten received intragastric perfusion of a glucose-electrolyte solution, and nine drank the rehydration solution. The latter two groups also received IV hydration whenever necessary to maintain plasma specific gravity of less than 1.030. The IV solution contained sodium chloride (5 g/l), sodium bicarbonate (4 g/l), and potassium chloride (1g/l). The intragastric solution contained sodium chloride (4.22 g/l), sodium bicarbonate (4 g/l), potassium chloride (0.5 g/l), and glucose (20 g/l). The oral solution was the same as the intragastric except for the substitution of potassium citrate (9.25 mEq/l) for potassium chloride to improve the taste. The intragastric solution was infused at a rate of 750 cc per hour for those patients weighing more than 25 kg and at 500 cc per hour for those weighing less.

Patients receiving intragastric perfusion required 78.8% less IV fluid than controls, while those patients drinking rehydration fluid required 81% less IV fluid than controls (these percentages include the initial IV rehydration which all patients received). A net positive gut fluid balance was achieved in less than eight hours in 80% of patients receiving intragastric or oral fluids. Serum electrolytes were normal throughout the study in all patients. No increased stool output was noted in either intragastric or orally treated patients vis-à-vis controls.

The study demonstrated that an oral rehydration solution can provide maintenance fluid and electrolytes to cholera patients and that, in the authors' opinions, mild cases of cholera (those presenting without shock) may be treated solely with an oral solution.


The authors wished to determine whether sodium participates in carrier-facilitated entry of glucose into intestinal cells or whether intracellular sodium produces the energy required for the "uphill" transport of sugars.

Twenty-four "healthy young people" were studied on 53 occasions. Their small bowels were infused with one of two groups of solutions: one group containing various concentrations of glucose (1.0, 1.7, 3.4, 6.0, 11.1, 20.0, 27.8 mmol/l) and 140 mEq/l of sodium and the second
group containing glucose (same concentrations as above) and mannitol as an osmotic replacement for sodium. One infusion followed the other in each subject. Serum and intraluminal concentrations of sodium and glucose were determined, as were intraluminal concentrations of a non-absorbable polyethylene glycol (PEG) marker.

Serum glucose did not change appreciably in any of the studies in which it was measured. When sodium was infused, intraluminal sodium concentration was always 140 mEq/l. During sodium infusions, intraluminal PEG concentration always increased, indicating net absorption of water, (although this effect diminished in distal portions of the bowel). Dilution of PEG occurred when sodium-free solutions were infused.

Significant (p less than 0.01) inhibition of uphill glucose absorption (i.e., when infusate glucose concentration was less than serum) occurred when sodium was replaced by mannitol or tris-HCl. "Downhill" glucose absorption was not impaired. Hypotonic infusions (without sodium, containing less mannitol) did not enhance glucose transport and may have inhibited it (PEG concentrations increased, indicating water absorption).

After typical meals, intraluminal glucose concentrations were all greater than 6.0 mmol/l, a level at which downhill absorption occurs and sodium is not necessary. The amount of sodium required for optimal absorption of glucose was inversely related to intraluminal glucose concentration.


To determine whether glucose-enhanced sodium and water absorption occurs in the small bowel of persons with cholera, 9 adult males hospitalized with severe V. cholera, (El tor, Ogawa) infections were studied. Two oral solutions were used; solution 1 contained (in mEq/l): Na⁺- 118, K⁺-8.5, Cl⁻-86.5, HCO₃⁻-40, and glucose 40 mmol/l; and solution 2 contained (in mEq/l): Na⁺-110, K⁺-90, Cl⁻-79, HCO₃⁻-40 and glucose 160 mmol/l. All patients initially received 12 hours of IV therapy followed by 12 hours of intragastric infusion of one of the 2 solutions. This was followed by an additional 12 hours of IV therapy. Intake, output, specific gravities, and serum electrolytes were monitored.

Net stool losses of water and electrolytes were less during the intragastric infusions. Significantly greater volumes of the 40 mmol/l glucose solution (No. 1) were required to improve net water balance vis-à-vis the 160 mmol/l glucose solution (No. 2). Stool volumes were significantly greater in the patients receiving solution No. 1 than in those receiving solution No. 2. One patient in each
group received supplemental IV fluid during intragastric infusion because of elevated plasma specific gravities; one of these patients had significant vomiting.

Absorption of water and electrolytes was documented in both study groups and water, electrolyte, and acid-base balances were maintained in patients with severe cholera.

The 160 mmol/l glucose solution was better absorbed as evidenced by smaller stool output and reduced fluid requirement in patients receiving solution No. 2.

This early study demonstrated the potential usefulness of orally administered glucose-electrolyte solutions in the clinical management of cholera.


Intragastric infusion of a glucose-electrolyte solution was used to determine whether glucose absorption occurs in cholera patients and whether administration of such a solution would alter cholera stool production or composition. The effect of the solution on water, electrolyte, and acid-base balance in cholera patients with severe diarrhea was also studied.

Fourteen hospitalized adults with severe dehydration, high stooling rates, and culture-proven V. cholerae infection were administered intravenous hydration to correct deficits and then received one of 3 oral rehydration solutions pumped intragastrically. None of the patients had received antibiotics. The solutions varied in glucose concentration from 40 to 220 mmol/l, Na+ from 118 to 101, K+ from 8.5 to 9.0, Cl− from 86.5 to 74.5, and HCO3− from 40 to 35 mmol/l. IV hydration was used during control periods when oral fluid was not administered or when oral fluid infusion could not maintain water balance. Intake, output, fluid and electrolyte balances, plasma chemistries and specific gravities were monitored. Admission data were not significantly different in the 3 treatment groups nor were there significant differences after the initial IV hydration.

Positive water balance and decreased net electrolyte loss during ORS infusion were demonstrated. Although actual stool output increased on intragastric infusion, the net balance of water and electrolytes improved. Stool composition studies showed glucose present in stools of only 2 patients while sodium and chloride concentrations decreased and bicarbonate increased as intragastric treatment progressed. Vomiting was seen in only 3 persons.
A 160 mmol/l glucose-electrolyte solution required one-half the infusion rate to balance stool losses as compared to a 40 mmol/l solution. No advantage was seen with a 220 mmol/l solution. In most of the patients, water, electrolyte, and acid-base balances were maintained during 12 hour periods of intragastric ORS infusion.

The complete absorption of glucose in all but 2 persons and the improvement of water and electrolyte balances were consistent with the postulated enhancement of water and NaCl absorption by active transport and by glucose. Moreover, this enhanced absorption gave no evidence of altering the mechanism by which cholera stools are formed. Of the three solutions used, the 160 mmol/l glucose-electrolyte solution demonstrated the highest ratio of water and electrolyte absorption to concentration of glucose.


Using a constant perfusion technique, factors affecting sodium and bicarbonate absorption from the gut were described. An unspecific number of normal persons as well as 11 persons with pernicious anemia underwent infusion and gut content sampling studies in which various electrolyte solutions were used.

Sodium absorption was markedly influenced by bulk water flow, being zero when flow was zero, and sodium was absorbed against an electrochemical gradient in the presence of bicarbonate. Bicarbonate transport was shown to occur against a steep electrochemical gradient and was inhibited by acetazolamide.

These results indicated that a mechanism for active transport of sodium exists and that it may be linked to absorption of bicarbonate.
II. CLINICAL TRIALS

With the encouraging results of the initial physiologic and clinical studies, investigations next sought to describe etiological and host factors affecting the efficacy of ORT with a view towards formulating specific treatment regimens. A succession of trials yielded information on methods of administration, reduction of IV requirements and the limitations of ORT. More recent studies have tested the feasibility of delivering ORT in differing cultural and non-clinical, field settings.

Chatterjee HN, Control of vomiting in cholera and oral replacement fluid, Lancet 2:1063, 1953 (see No. 2).

Colle E et al, Hypertonic dehydration (hypernatremia): the role of feedings high in solutes, Pediatrics 22:5-12, 1958 (see No. 5).


Pierce NF et al, Effect of intragastric glucose-electrolyte infusion upon water and electrolyte balance in Asiatic cholera, Gastroenterology 55:333-343, 1968 (see No. 16).


This study examined the efficacy of an oral rehydration solution in providing maintenance therapy in males over the age of twenty with bacteriologically proven ("clinically severe") cholera.

All patients were initially treated with IV fluids for six hours. They were then randomized to either a control group, which continued to receive IV therapy, or a treatment group, which was given an intragastric oral fluid infusion to match output plus 100 cc per hour, with IV therapy added as necessary to maintain a plasma specific gravity of less than 1.030. The orogastric solution contained sodium (100 mEq/l), potassium (10 mEq/l), chloride (70 mEq/l), bicarbonate (40 mEq/l) and glucose (120 mmol/l) with an osmolality of 327 mOsm/l.

Controls did not differ demographically, clinically, or biochemically from the orogastric study patients at admission or at the conclusion of the study. Total fluid administered (from admission to the cessation of diarrhea) was greater, but not significantly so, in the orogastric group. Although stool output during orogastric replacement was 21% greater than expected, measurements indicated that study patients retained a mean of 87% of the orogastric solution. Net electrolyte balances deviated less from zero in study patients than in controls, although some study patients had negative balances of individual electrolytes. Study patients did not differ from controls in total stool volume, duration of diarrhea, or duration of vibrio excretion.

The authors maintained that their intragastric solution could be administered orally and that its efficacy should be evaluated in children and persons with non-cholera diarrhea as well.


This letter was in response to an article by Pierce, et al (see preceding abstract, "Replacement of water and electrolyte losses in
cholera by an oral glucose-electrolyte solution," Ann Intern Med 70:1173-81, 1969). The authors felt the solution used by Pierce and Sack was low in sodium (100 mEq/l) as compared to the concentration of sodium (120 mEq/l) found optimal in their studies. In the absence of glycine, which along with glucose enhances sodium absorption, patients treated with the solution containing 100 mEq/l sodium might become dangerously hypotonic. They presented the same argument for potassium (advocating 15 mEq/l, compared to the 10 mEq/l recommended by Pierce, Sack, et al).

The authors also stated that recording intake and output measurements every 4 hours provides sufficient data and is less time consuming and less misleading than the "cumbersome" hourly intake and output monitoring of Pierce, Sack, et al.


In this response to a critical letter by Nalin and Cash (see preceding abstract) the authors noted that the designation of an "optimal" composition for oral rehydration solutions must await controlled studies comparing various solutions in children and adults with both cholera and acute non-cholera diarrhea. The results of their studies and the studies of Nalin and Cash indicated that both solutions were equally effective in cholera therapy, they felt, and probably no single ideal oral replacement solution would be found.


An oral rehydration solution (containing in mEq/l: Na⁺-100, K⁺-10, CI⁻-70, HCO₃⁻ 40, and glucose 120 mmol/l) was compared to intravenous therapy in a controlled treatment trial of hospitalized cholera patients in order to evaluate the effectiveness of oral solution in maintaining water, electrolyte, and acid-base balance.

Twenty adult males with bacteriologically confirmed severe (hypotension) cholera were treated for 6 hours with intravenous therapy to correct their dehydration and metabolic acidosis. Each patient received tetracycline therapy. At the end of 6 hours of therapy the patients were randomly assigned to either a control group (continued IV therapy plus up to 500cc of water orally per 12 hours) or to an orogastric group in which calculated volumes of the oral solution were administered by a nasogastric tube. In addition to bacterial cultures, serial stool compositions and plasma chemistries and pH measurements were assessed in each patient.

The two groups were similar with respect to history, physical examination, and laboratory findings except that mean plasma
bicarbonate was significantly lower in the control group. Only 1 of the 10 orogastrically-treated patients required additional IV fluid, and he had the most severe diarrhea of those studied—greater than one liter/hr. Significantly less IV fluid was required by the orogastric group. The total stool output, duration of diarrhea, and duration of detectable vibrio excretion were similar in the 2 groups.

Plasma studies showed that fluid, electrolyte, and acid-base balance were maintained by oral fluid therapy. Except for one orogastric patient who received the largest volumes of OG fluid, significant vomiting was not seen. No mortality nor "unusual" morbidity was noted.

In demonstrating that oral fluid can maintan satisfactory water, electrolyte, and acid base-balance while reducing the requirement for IV fluids, oral rehydration therapy proved to be a successful, easily administered, and inexpensive adjunct to IV therapy.


This review article on treatment of pediatric cholera briefly discussed the V. cholerae organism, cholera infection, and detailed primarily intravenous and antibiotic methods of treatment. An oral therapy solution no longer recommended (in mEq/l: Na+120, K+25, HCO3- 48, Cl- 97, in a 2% glucose solution) was described. The main advantage of oral therapy noted by the author was that it could reduce the need for over 75% of the intravenous maintenance requirements.


The use of oral rehydration therapy (ORT) to treat cholera patients was assessed in a large-scale clinical trial at a rural treatment center in Bangladesh. Persons over 15 years of age with severe dehydration and no underlying disease were included in the study. Clinical assessment, weights, fluid balance measurements, and bacterial cultures were obtained on each of 135 patients.

The oral solution was composed of (in mEq/l): Na+120, K+15, Cl-72, HCO3- 48, and glucose 110 mmol/l. Patients were initially rehydrated with IV therapy and were given ORT as soon as they were alert. The oral solution was administered both oro- and naso-gastrically. When oral intake exceeded the volume of stool and vomitus output, IV hydration was stopped. Each patient was treated with tetracycline.
ORT successfully maintained positive fluid and electrolyte balance in 133 of 135 patients with culture-proven V. cholerae infection. The 2 treatment failures occurred in 1 person who died (the death was not felt to be directly attributable to cholera or to therapy) and in 1 person with persistent vomiting. Oral rehydration was the sole therapy in 12 moderately dehydrated patients who were successfully rehydrated.

Comparing this treatment group to a group of 135 persons treated with IV therapy during a previous epidemic, the investigators found a 70% reduction in use of IV fluids. Oral therapy was shown to be an effective method for supplying maintenance fluids in conjunction with IV hydration of severely dehydrated patients and was the successful sole therapy for 12 moderately dehydrated persons.

Cash RA et al, Rapid correction of acidosis and dehydration of cholera with oral electrolyte and glucose solution, Lancet 2:549-550, 1970 (see No. 70).


Cholera stool electrolyte compositions were determined in children in the following age groups: less than 2 years, less than 5 years, and 5-10 years, and the results compared to electrolyte concentrations in stools of adults with cholera. Ileal fluid compositions in 4 children 4-6 years of age with cholera, were also compared to those found in adults with cholera. Complete recovery fluid and electrolyte balance studies were done in 6 children less than 2 years of age with cholera. Stool compositions of group of healthy children were also measured.

In severely dehydrated cases, one of two approximately isotonic solutions were given intravenously during the first hours of treatment. A second solution was given over the succeeding 7 hours to complete rehydration, and a third IV solution was used for maintenance. Oral tetracycline was given and water and reconstituted powdered milk feedings were begun 24 to 48 hours after admission. Intake and output volumes along with stool and urine compositions were carefully monitored. Fluid balance studies continued 5 to 8 days—at least 2 days after IV fluids were stopped, stools were formed, and milk feedings were tolerated.

The electrolyte composition of the stools of children in the 3 age groups were not significantly different, but the sodium and CO₂ content were significantly lower and the potassium content significantly higher than in stools of adults with cholera. As the
rate of stool loss in children declined, sodium loss decreased while potassium loss increased.

This study showed that the stool composition in children with cholera differs from that of adults. The authors presented a biochemical basis for rational guidelines to fluid and electrolyte replacement in pediatric cholera. Replacement therapy should be similar to that used in infant diarrhea with isotonic dehydration, emphasizing rapid restoration of effective plasma volume.


This chapter described the rationale and mechanics of operating a treatment center-based oral maintenance therapy program for cholera patients. A fluid composed of (in mmol/l): glucose-110, NaCl-72, NaHCO3-48, and KCl-25 was administered both orally and nasogastrically to children and adults. Patients were given nothing by mouth except the oral solution and tetracycline. Intravenous fluids were used if diarrhea volume significantly exceeded oral intake. Although vomiting was frequently encountered in cholera patients, most could tolerate oral solution.

The oral maintenance solution was effective in maintaining positive water and electrolyte balance and greatly reduced the need for use of IV fluids.

Nalin DR et al., Oral or nasogastric maintenance therapy for cholera patients in all age-groups, Bull WHO 43:361-363, 1970 (see No. 46).


This controlled study examined the efficacy of an oral rehydration solution in providing maintenance fluids and electrolytes to hospitalized persons with cholera and severe non-cholera diarrhea. The effect of adding charcoal to the solution was also evaluated.

Fifty-one males (above the age of 15 years) with watery diarrhea of less than 24 hours duration, no antibacterial medication prior to hospitalization, and with hypotension on admission were included in
the study. Serial intake, output, fluid and electrolyte balances, plasma chemistries and specific gravities, and vibrio excretion rates were followed. After 3 hours of initial intravenous (IV) rehydration, the patients were randomly assigned to one of 3 groups. A control group received IV replacement therapy along with small amounts of oral water ad libitum. Calculated volumes of oral fluid (in mEq/l: Na⁺-90, Cl⁻-56, HCO₃⁻-30, and glucose 115 mmol/l) or oral fluid plus charcoal (in mEq/l: Na⁺-89, K⁺-10, Cl⁻57.5, and glucose -97 mmol/l) were administered to the other 2 groups.

Fluid and electrolyte balances for both cholera and non-cholera patients were maintained equally well in the three treatment groups. No treatment failures using oral fluid occurred in the non-cholera group; of the 3 failures in the cholera treatment group, one temporarily refused to take ORS and 2 had excessive vomiting of the ORS-charcoal solution. There were no significant increases in the duration of diarrhea, duration of vibrio excretion, or in volume of stool produced in those treated with ORS. The addition of charcoal to oral fluid was associated with a significant increase in the volume of diarrheal stools and in prolongation of vibrio excretion.

Oral rehydration was shown to be an inexpensive and effective method for providing maintenance fluids to persons with severe cholera and non-cholera diarrhea. The addition of charcoal proved to be of no benefit.


Fluid and electrolyte balance studies were performed on 12 Bangladeshi children, aged 2 to 9 years, hospitalized with severe cholera in order to determine whether a glucose-electrolyte solution given orally or by nasogastric tube could maintain positive water and electrolyte balance in patients in the pediatric age group.

Intravenous fluids were used to rehydrate the severely dehydrated children on admission. Fluid intake and output, serial weights, and plasma chemistries were carefully evaluated. After initial rehydration, oral rehydration solution (in mEq/l: Na⁺-120, K⁺-25, HCO₃⁻48, Cl⁻-97, and glucose-110 mmol/l) was administered either orally or by nasogastric tube and the IV rate was slowed. NG tubes were of special benefit in those children who did not drink enough voluntarily to match stool volumes. Nothing was given by mouth except ORS and tetracycline.

Eight of the 12 children required no IV therapy for maintenance fluids and the other 4 required small amounts of IV fluid only during the first 8 hours of treatment with oral fluid. No electrolyte abnormalities were observed and positive water and electrolyte
balances were demonstrated. No glucose was found in the stools, indicating complete absorption.

Pediatric cholera patients were shown to absorb oral fluid in sufficient quantity to maintain positive fluid and electrolyte balance. A decreased requirement for IV fluid was demonstrated.


This study assessed the use of oral rehydration therapy combined with early and uncomplicated feeding of 68 Apache children (median age 13 months) admitted to hospital with diarrhea. The children, 25% of whom had signs of undernutrition, were evaluated clinically, with serial weights, plasma and stool chemistries, careful fluid balance studies, and stool cultures for bacterial pathogens.

Children who were conscious and had bowel sounds were rehydrated with calculated volumes of oral fluid (in mmol/1: Na+ -90, K+ -20, Cl- -65, HCO3- -45, and glucose) and received either cow's milk or one of 2 hypotonic (Na+ -19 mmol/1) commercial formulas containing casein hydrolysates, medium-chain triglycerides, electrolytes, and glucose. Fluid was administered by professional and non-professional personnel.

About 40% of the children showed signs of dehydration, and 5 were in shock on admission. Admission electrolyte abnormalities, including hyponatremia and acidosis, were corrected during therapy. When compared to Apache children hospitalized the previous summer, there was no evidence that institution of early feeding predisposed to relapse of diarrhea.

ORS was shown to be easily administered by professional and non-professional personnel with a minimum of training. Severely dehydrated children required only partial rehydration with intravenous fluids before oral therapy was begun. Although a matched control group was not used, the study indicated that initiation of early and uncomplicated feeding during a diarrheal episode may not predispose to relapse of diarrhea. The effect of such early feedings on the duration of a diarrheal episode could not be assessed.


Intravenous (IV) and oral rehydration therapies were compared for fluid balances in Filipino children hospitalized with acute
gastroenteritis. Initial hydration deficiencies had been corrected by 8 hours of IV fluids. Thirty children aged 2 months to 6 years with mild to moderately severe dehydration but without clinical evidence of malnutrition or concomitant serious illness were randomly assigned to one of two groups. The control group received IV therapy, and the study group received a commercial rehydration fluid (in mEq/1; Na\(^+\)-30, K\(^+\)-20, Ca\(^{++}\)-4, Mg\(^{++}\)-4, Cl\(^-\)-30, lactate-8, citrate-10, HCO\(_3\)-10, glucose-not given).

Both groups of children increased their admission weight on therapy and showed no statistical difference in urine, stool, and vomitus output nor in Na\(^+\), K\(^+\), or HCO\(_3\) levels after 24 hours of treatment. All 13 children treated with IV therapy and 15 of 17 receiving oral fluid had completely recovered by 24 hours. The 2 children who had received oral fluid and had minimal dehydration at 24 hours had vomited their initial feedings.

A low-sodium oral solution was shown to provide adequate maintenance therapy in most children whose fluid deficits were initially corrected by IV hydration. Since oral fluid was also easier and less expensive to administer, it was recommended for use as the maintenance fluid for children with acute diarrhea.


To assess the effectiveness of using oral rehydration solutions to treat children with dehydration from acute gastroenteritis, 30 hospitalized Indian children, aged 17 days to 5 years, were orally rehydrated. Intravenous (IV) fluids were used only for the treatment of shock and for persistent vomiting.

On admission 12 children had severe dehydration, 9 moderate, and 9 mild. Eight children received initial IV therapy - three for shock and 5 for persistent vomiting. Of the 22 children who received initial oral therapy (composition closely approximating the WHO-recommended solution), 2 subsequently required IV fluids. Both oral and nasogastric administration were used. No stool pathogens were found on stool culture.

Two children died; a 3-month-old who received oral and IV fluids before developing paralytic ileus and a 5-month-old who initially did well on oral fluid but then became severely dehydrated and developed paralytic ileus. The remaining 28 children (8 on IV's and 20 on oral fluid) were adequately rehydrated and discharged.
This non-controlled study showed that oral therapy could be used successfully to treat dehydrated children, even some with severe dehydration. However, the deaths of 2 infants demonstrated the need for intravenous fluids and careful fluid and electrolyte monitoring in complicated patients.

A controlled trial comparing intravenous hydration with intravenous plus oral therapy was carried out in 32 children under 6 years of age hospitalized in Calcutta for watery diarrhea due primarily to V. cholerae infection. The children, who had received no previous antibiotic therapy and were approximately 10% dehydrated on admission, were randomly assigned to 3 groups. A control group of 15 children received IV therapy and 5% oral glucose ad libitum. The study group of 17 children was divided into 2 treatment sections, A and B. Children in Group A received IV therapy for 3 hours, after which the remainder of their deficits, maintenance fluid needs and replacement of ongoing losses was supplied by oral or nasogastric administration of an oral rehydration solution (containing 80 mEq/l Na+ and 15 mEq/l K+). The 9 children in Group B received 8 hours of IV therapy to replace their fluid and electrolyte deficits before beginning oral rehydration. Rehydration was monitored by use of serial clinical assessments, hematocrits, electrolytes, and plasma specific gravities. Each of the 32 children received tetracycline and 4 mEq/kg of oral potassium hydrogen citrate per 24 hours.

One child in Group A died, presumably due to aspiration of vomitus, and persistent vomiting caused 3 of the remaining 7 children in the group to required additional IV therapy after initiation of oral therapy. The mean hemodynamic measures of the survivors of the control and both treatment groups were within normal limits at the end of therapy.

Under these conditions, initial IV rehydration of severe dehydration was needed to correct fluid and electrolyte deficits. Use of nasogastric administration of oral fluid may have improved results, especially in the children with vomiting. Requirements for intravenous fluid volume needed to treat pediatric cholera were reduced by use of oral rehydration.

To assess the efficacy of oral rehydration treatment of pediatric diarrhea caused by V. cholerae and non-V. cholerae pathogens, 80 hospitalized, dehydrated Indian children less than 5 years of age were
treated with either oral therapy or intravenous fluid. Each child weighed less than 15 kg and was 8 to 10% dehydrated. The children were alternately assigned to either the oral or intravenous therapy group (except the final 8 children who were given oral therapy), and all received tetracycline. The oral solution contained 3.5 g NaCl, 2.5 g NaHCO₃, 1.5 g KCl, and 20.5 g glucose dissolved in 1 liter of water.

Recovery was successful in 40 of the 44 children receiving oral therapy and in all 36 who received IV's. Because of vomiting, refusal to drink, and/or severe diarrhea, 4 children who were started on oral therapy were subsequently treated intravenously.

In a majority of cases small children with significant dehydration managed under close supervision were shown to be effectively rehydrated by means of oral therapy. Reduced cost and ease in preparing and administering oral therapy as compared to intravenous therapy were emphasized.

Baral MR, Experience with 100 diarrhoea cases treated at Narayani Zonal Hospital Rehydration Therapy Centre, Birgunj, J Nep Med Assoc 13:77-87, 1975 (see No. 92).


This study assessed the use of oral rehydration in 118 males, aged 6 to 70 years, hospitalized with mild to severe diarrhea and dehydration. The oral solution consisted of (in mEq/l): Na⁺115, K⁺25, Ca²⁺-4, Cl⁻-62, SO₄-4, PO₄-5, HCO₃⁻48, lactate-4, citrate-25.

The patients were divided into three groups: 60 with severe dehydration marked by blood pressures less than 80 mm Hg; 15 with moderately severe dehydration and blood pressures between 80 and 90 mm Hg; and 42 with mild dehydration and blood pressures greater than 90 mm Hg. All were initially treated with oral fluid; intravenous (IV) hydration was used only if stool and vomitus output exceeded oral intake. Tetracycline was given to all patients.

None of the patients died, and 84 required no IV therapy (53 of 58 in the mild and moderately severe groups). All patients had vomiting but in only a few was vomiting persistent enough to require IV therapy. Stool culture results identified V. cholerae in 29 specimens and no pathogens in 89.

Oral rehydration proved to be an inexpensive, effective, and easily administered mode of therapy, especially for mild and moderate dehydration.

This review outlined the development of oral therapy as a practical and efficient method of treating diarrheal dehydration. To meet the realities of supply and preparation in underdeveloped areas, use of a single fluid having a WHO-recommended composition to treat persons of all age groups was supported. A combination of biophysical, medical and managerial technology will be needed the article stated, to ensure that the optimal oral solution will be available and effectively used at the home and village level.

Moenginah PA et al, Oral sucrose therapy for diarrhoea (letter), Lancet 2:323, 1975 (see No. 52).

Nalin DR, Sucrose in oral therapy for cholera and related Diarrhoes, Lancet 1:1400-1402, 1975 (see No. 53).


Rahilly PM et al, Clinical comparison between glucose and sucrose additions to a basic electrolyte mixture in the outpatient management of acute gastroenteritis in children, Arch Dis Child 51:152-154, 1976 (see No. 57).


In this study village health workers demonstrated the efficacy of oral rehydration therapy in Lao children with diarrhea.

A test area (3 villages with 373 households, 1884 inhabitants, 356 children aged 0-4) and control area (3 villages, 322 households, 2,223 inhabitants, 406 children aged 0-4) with comparable demographic and socioeconomic characteristics and with equal access to the same district health center were chosen. The study period was six weeks, during which children with diarrhea in the test area were treated with oral fluid (WHO-recommended ORALYTE) prepared by health workers and administered by them and by mothers. Children in the control area were treated with traditional methods and breast feeding.

Ninety children in both areas had attacks of gastroenteritis over the 6-week period (9 children had two attacks for a total of 99 attacks). Sixty-two percent of the cases were in children less than 2 years of age. Twenty-two had clinical dehydration (only 5 were severe). Mean duration of illness was 2-4 days (range 1-10 days). There were no deaths. Thirty-six children had enteropathogenic E. coli, seven had shigella species and 56 had "acute undifferentiated diarrhoea." Oral rehydration was well accepted by mothers and children in the test area. The mean duration of diarrhea was not significantly different in the 2 groups of children. Test area children gained an average of 187 grams during their illness, while control children lost 170 grams (significance not noted).

Oral rehydration was found to be acceptable and at least as efficacious as traditional therapy in this setting.


The problem of acute diarrhea and the physiological basis of oral therapy and its limitations were discussed in a concise and thorough manner. The effect of repeated diarrheal episodes on nutrition, growth, and development was also described.
The two major objectives of treatment, the authors stated, are the very early replacement of water and electrolyte losses to prevent or correct dehydration and the maintenance of adequate food intake to prevent malnutrition. Early treatment, the authors felt, can be accomplished by means of oral therapy solutions distributed at neighborhood or rural primary health centers and can be administered by instructed family members. Family members could potentially learn to institute treatment at home as soon as diarrhea starts.

The WHO-recommended packet was described, and sucrose-electrolyte solutions were noted to be almost as effective as glucose-electrolyte solutions. To provide extra water requirements when the stool sodium concentration is lower than that in the oral solution, continued intake of water and oral feedings were encouraged. Normal renal function is essential to managing salt and fluid balances.

Intravenous fluid therapy was recommended for persons with severe dehydration; those unable to drink because of fatigue, stupor, or coma; those with prolonged oliguria or anuria; those with severe and sustained vomiting; the approximately 3% of persons with acute diarrhea who have serious glucose malabsorption; and those unable to orally replace their ongoing losses. Oral therapy has not been evaluated in premature infants or in babies less than 1 month old, (see abstract No. 44).

Oral therapy has been shown to be a safe, effective method of treating mild and moderate acute diarrhea in children and adults. The mortality due to dehydration as well as the need for intravenous fluids have been greatly reduced.


Two geographically and socioeconomically similar communities in northwestern Iran, both served by trained local family health workers, were chosen for study. All children aged 3 to 36 months who developed diarrhea between May 10, 1977, and September 29, 1977, were included in the study. Each child was examined and weighed daily during illness and weighed six months after illness. The children in the study community were given WHO-recommended oral rehydration salt solution (ORS or "Oralyte") and other fluids (breast milk, rice water, water, diluted cow's milk, and tea) during their diarrheal illnesses, while those in the other (control) community were given the same fluids except for ORS (Oralyte).

Of two hundred thirty children with diarrhea in the study community, each consumed a mean of 2.73 liters of oral rehydration
fluid during their illnesses. They were clinically comparable to the 3300 ill children in the control community. Mean six-month weight gain were greater (p less than 0.01) in the study community for each age group studied. There was one fatality in the study community while seven children in the control village died. Oral rehydration was well accepted in the community where it was used.

Despite some methodological defects (e.g., the etiologies of illnesses in the two villages were not determined, limiting the comparability of the two groups of children), there is reasonable evidence presented in this study that the use of oral rehydration during childhood diarrhea may have a positive effect on diarrheal morbidity and mortality and may improve nutrition and post-episodal weight gain.


Nalin Dr et al, Comparison of sucrose and glucose in oral therapy of infant diarrhoea, Lancet 2:277-279, 1978 (see No. 64).


The effectiveness of nasogastric administration of an oral rehydration solution was tested in 15 dehydrated, hospitalized children greater than 6 months of age in Ibadan, Nigeria. Children with diarrhea of less than 3 days duration with approximately 7% dehydration were included in the study. The admission weights, clinical appearances, blood smears, hematocrits, stool cultures, serum ureas and electrolytes were evaluated but not the stool volumes, plasma specific gravities or osmolarities. Two oral solutions were
used: normal saline + 1/6 M lactate (Na*, approximately 158 mEq/l) to correct initial deficits and 0.45% normal saline in a 2.7% glucose solution for fluid maintenance.

In 11 of the 15 children, clinical improvement and subsequent hospital discharge resulted. Because of either vomiting or profuse stooling, 3 children had to be switched to IV therapy. One child died 12 hours after admission, an 8 kg 2-year-old with marked hyponatremia and hypokalemia on admission.

Nigerian children with moderate dehydration were treated with a hypertonic oral rehydration solution, most without difficulty. The death of the one child with electrolyte imbalance was probably not directly related to the oral therapy but serves as a reminder of the importance of electrolyte considerations when treating small children.


A comparison was made of intravenous (IV) and oral rehydration therapy to treat children hospitalized with dehydration from acute gastroenteritis in Kottayam, India. From 1970 to 1972, 1800 consecutively-admitted children with diarrhea and dehydration were treated with conventional therapy, including IV fluids whenever necessary, and received no oral therapy. Beginning in 1972, the next 1200 consecutively-admitted children with diarrhea and dehydration received oral therapy (closely approximating the WHO-recommended formula) unless dehydration was severe enough to require IV's. Most children in both groups presented with moderate to severe diarrhea. Fewer children in the orally-treated group, including those with severe diarrhea, required IV fluids. Those who received oral fluid required lower volumes and shorter durations of IV therapy than did those in the IV-only group. The mortality rate was significantly less for the orally-treated group compared to the IV group, but infectious agents, concomitant illnesses, and causes of death were not listed.

In the conventional therapy group, 38 of 454 children receiving IV fluids developed phlebitis and 8 children developed septicemia. Only one case of phlebitis and one case of septicemia were seen in the 48 children receiving IV therapy in the orally-treated group.

Despite the inherent risks of comparing results in non-matched patients, oral rehydration was shown to be an effective method of treating diarrheal dehydration, and use of oral therapy decreased the amount and duration of IV therapy needed with subsequent reduction of complications associated with IV use.

To determine the usefulness of oral fluid in treating hospitalized, dehydrated infants with bacterial and viral diarrhea, oral therapy was administered in a setting where intravenous fluid had previously been used to treat such patients. Since animal studies had shown that rotavirus causes a defect in glucose-coupled sodium absorption, the author elected to compare the efficacy of oral therapy in treating bacterial vis-à-vis rotaviral diarrhea.

The study included 62 Costa Rican children hospitalized for diarrhea and 5 to 10% dehydration. Their nutritional levels were comparable to that of the general population. The WHO-recommended oral solution was used. Fluid was administered by nurses and auxiliaries and given by sips with no more than 100 cc permitted in any 20 minute period.

Skin turgor was monitored to assess rehydration, and when normal, the child was switched to half-strength milk formula. Free water was encouraged. Serial weights and serum protein and electrolyte determinations were obtained and oral intake and stool, urine and vomitus outputs were closely monitored. Stools were cultured for bacteria and assayed (ELISA technique) for rotavirus.

Using improvement in clinical and laboratory measures of dehydration as criteria, 94% of the infants were successfully treated. Although vomiting was common, the emesis volumes were small, infrequent, and had little effect on the results. No electrolyte abnormalities were seen.

Four children required IV therapy: 2 who refused oral therapy, one who was hypotensive and had a complicating pneumonia on admission, and one child who showed clinical evidence of glucose malabsorption.

This study showed oral therapy to be effective in treating almost all children with 5 to 10% dehydration caused by either bacterial pathogens or rotavirus. No electrolyte abnormalities were found at the end of therapy in either treatment group. Administering plain water may have helped children to tolerate intake of a sodium concentration higher in the oral solution than that excreted in their stools. By reducing the need for intravenous fluids, oral therapy was shown to be both cost-beneficial and less traumatic to patients.

One assumption underlying the concept of home-based oral rehydration is that oral therapy given early would eliminate the need
for IV therapy. This assumption was tested in 57 U.S. adult volunteers who had experimentally-induced cholera as part of a vaccine study.

Clinical cholera developed in 57 unvaccinated or ineffectively vaccinated volunteers after the ingestion of $10^9$ to $10^8$ Vibrio cholerae organisms. The incubation period was $37 \pm 2$ hours (range 11-63 hours). Cholera was defined by the production of at least three culture-positive liquid to watery stools within 24 hours. Twenty-six individuals received oral therapy with the Dacca formula (20 grams/l glucose, 4.2 grams/l sodium chloride, 4.0 grams/l sodium bicarbonate, 1.8 grams/l potassium chloride) in amounts equal to the volume of stool lost. Thirty-one patients received the WHO-recommended oral therapy formula (20 grams/l glucose, 3.5 grams/l sodium chloride, 2.5 grams/l sodium bicarbonate, 1.5 grams/l potassium chloride) at 1.5 times stool volume. All volunteers were allowed food and other beverages ad libitum. Serum electrolytes, plasma specific gravities, hematocrits, and intake and output were serially monitored. Intravenous therapy was initiated whenever water or electrolyte balance could not be satisfactorily maintained.

Seventy-seven percent of the volunteers were maintained satisfactorily by oral therapy alone, and this proportion was independent of the formula of rehydration fluid used. In the successfully treated oral group, biochemical values were normal from onset to convalescence. The remaining 23% required intravenous therapy. Need for IV therapy was significantly related to total stool volume greater than 8 litres (p less than 0.003) and to emesis (p less than 0.001). Eighty-five percent of patients receiving IV fluids had diarrhea of greater than 50 hours duration. Use of nasogastric tubes did not curtail emesis.

These data are relevant to field conditions because the fluid losses of the patients requiring IV therapy were similar to those in patients presenting in shock at the cholera treatment center in Dacca. The Dacca patients also typically give a history of vomiting, the authors pointed out, and "like the severely ill volunteers, would not be saved by oral therapy alone." The implication is that cholera mortality occurs in the severest cases and that the mortality in these cases would not be significantly reduced by encouraging home oral rehydration therapy. Severely ill patients will require judicious initial IV therapy at regional treatment centers to be followed by oral therapy. Since only 5% of all cholera cases become severely dehydrated, a widely available home-based rehydration program would expend a large amount of resources to reach only a few people. The authors felt that use of existing rural treatment centers to provide oral maintenance therapy for severe diarrhea and initial IV therapy to severely dehydrated persons would constitute a more effective use of resources. If practical and effective emesis control were to become available, it might be possible to treat even severe cases with oral therapy alone.


This study assessed the impact of oral rehydration therapy in rural Turkey.

During the period July-August 1977, the authors investigated 169 cases of diarrhea in children less than six years of age. Cases diagnosed as salmonellosis or shigellosis were excluded from the study. Midwives administered oral fluids to 124 of the children while 45 were used as a control group. All children were seen by the midwife and the physician. Patients showing deterioration were hospitalized. Seven children in the control group and no children in the oral rehydration group required intravenous fluids.

In addition, 23 of 50 pediatric outpatients were treated with oral fluids while 27 served as controls. Two of the controls required intravenous therapy and two died. No patients in the oral therapy group required hospitalization or intravenous therapy.

In both the outpatient and the community study, weight gains after treatment were greater in the oral therapy group than in the control group.


43. Nalin DR et al, Research on oral rehydration therapy for diarrhoeal dehydration, unpublished manuscript.
This paper presented a review of oral rehydration studies including discussions of composition, use in infantile diarrhea, nutritional benefit, and methods of delivery. Priority areas for future research were listed: investigation of the accuracy of salt and sugar solutions made at home and their impact on diarrheal disease morbidity and mortality; determination of the most suitable methods of administering the WHO-recommended solution to infants; evaluation of an oral solution containing a higher potassium concentration; determination of the efficacy of adding other nutritional agents to ORS; assessment of the nutritional benefits of ORS; evaluation of antisecretory and anti-emetic agents as adjuncts to diarrhea therapy.

Nalin DR et al, Comparison of low and high sodium and potassium content in oral rehydration solutions (in preparation), (see No. 67).

44. Pizarro D et al, Rehidratación por la vía oral en niños menores de un mes de edad, unpublished manuscript.

This paper examined the efficacy of oral rehydration therapy in infants less than one month of age.

Forty children of both sexes, less than one month of age, with 1-14% clinical dehydration secondary to acute diarrhea who presented to the emergency room of the National Children's Hospital, in San Jose, Costa Rica, were studied. After a brief examination and weighing, children were begun on oral rehydration solution (containing in g/l: sodium chloride 3.5, sodium bicarbonate 2.5, potassium chloride 2.25, and glucose 20). Oral fluid was given 50 or 100 cc at a time with two parts solution followed by one part water. Mothers were taught to administer oral fluid and to recognize signs of dehydration. When these signs had disappeared, one-half strength formula or breast milk was begun. As feedings were tolerated and stooling had improved, the infants were sent home. Mothers were instructed to return if signs of dehydration reappeared. Stool cultures were obtained, and serum electrolytes were measured before and after initial rehydration was completed. Rotavirus and E. coli were the most common pathogens found in the stools.

Thirty-nine children were successfully rehydrated orally and 34 were successfully maintained orally. Five patients required readmission and all were successfully rehydrated again with oral therapy. Mean rehydration time was 8.23 hours, and mean time in the emergency room was 13.39 hours. Forty-five percent of patients stayed less than six hours and 90% stayed less than 15 hours. Bicarbonate level, pH, and osmolality were all significantly improved after oral therapy. Five of 8 patients with hyponatremia on admission were maintained with oral therapy alone and sodium values were normal for all but one at follow-up. No neurologic complications were
encountered. Potassium values after oral fluid administration were all within normal limits. There were no deaths.

This study demonstrated that very young infants can be rehydrated and maintained successfully with oral therapy.

45. Taylor PR et al, Oral rehydration therapy for treatment of rotavirus diarrhea in a rural treatment center in Bangladesh (accepted for publication, Arch Dis Child).

Over a 5-week period at a rural Bangladesh treatment center, the WHO-recommended oral rehydration solution was used to treat hospitalized children less than 5 years of age presenting with diarrhea associated with ELISA-proven rotavirus infection. Brief histories and pretreatment weights were obtained and stool volumes recorded.

Oral fluid was given ad libitum to 207 rotavirus-infected children with 5% or less dehydration and continued breastfeeding was encouraged. In 19 children with greater than 5% dehydration IV hydration was used to replace initial deficits while oral therapy was used for maintenance requirements. Children who could not ingest enough oral solution to keep up with stool and vomitus losses were considered treatment failures.

The failure rate was 5%. Vomiting was statistically more frequent in the failures (82%) than in the successes (32%).

The WHO-recommended oral rehydration solution was shown to be effective in treating mildly or non-dehydrated children with rotavirus infection in rural Bangladesh. Although stool sodium losses are generally much smaller in rotavirus diarrhea than in cholera, the 90 mEq/l of sodium in the solution caused no clinically evident problems.
III. COMPOSITION

The studies abstracted in this section deal with the development and evaluation of a single oral rehydration solution for use in all ages with all types of diarrhea.

To arrive at the WHO-recommended formula investigators have addressed several important points, among which are: the use of a single sodium concentration for all diarrheal cases, regardless of age or etiology; the feasibility of substituting sucrose or other sugars for glucose; the effects of adjuvants such as glycine and antisecretory agents; determination of the optimal potassium concentration.

Chatterjee HN, Control of vomiting in cholera and oral replacement fluid, Lancet 2:1063, 1953 (see No. 2).


Phillips RA et al, Water and electrolyte absorption by the intestine in cholera, Cholera Res Symp, Honolulu, pp. 299-311, 1965 (see No. 11).


Because of the greater potassium losses in stools of children with cholera, an oral rehydration solution was developed for children containing more potassium (25 mEq/l) than previous solutions. This solution was shown in this study to be effective in maintaining fluid and electrolyte balance in 56 children (age range not given) and 50 adults treated at a field hospital with severe, uncomplicated, culture-proven cholera.

Initial intravenous therapy was administered until signs of hypotension and dehydration disappeared. Calculated amounts of oral or nasogastric fluids (in mEq/l: Na⁺-120, K⁺-25, HCO₃⁻-48, Cl⁻-97, and glucose 110 mmol/l) were then given. Careful fluid balance measurements were kept, and serial plasma potassium determinations were performed on the 50 adults.
Following correction of severe dehydration by intravenous therapy, all patients were maintained in positive fluid balance with oral fluids alone. Of the children studied, 80% were in positive fluid balance within 6 hours of instituting oral therapy. Vomiting was commonly seen but not in volumes sufficient to affect oral fluid administration. Plasma potassium levels monitored in the adults were normal.

This study demonstrated the ability of adult and pediatric cholera patients to absorb oral fluid and of adults to be successfully treated with a solution containing 25 mEq/l K+. Oral fluid therapy effectively met maintenance fluid and electrolyte needs of cholera patients and reduced the need for IV fluids.


Two trials were carried out in this study. The first evaluated the effectiveness of an oral rehydration solution consisting of (in mEq/l): Na⁺-120, K⁺-25, HCO₃⁻-48, Cl⁻-97, and glucose-110 mmol/l, in treating persons hospitalized with diarrheal dehydration, and the second compared treatment with the above solution with and without glycine (110 mmol/l).

The number, age distribution, and degrees of dehydration of persons studied were not included although adults and children were differentiated. Initial intravenous therapy was given to correct shock, and calculated amounts of oral fluids (given by mouth or nasogastric tube) were then used to meet maintenance fluid and electrolyte requirements. Mildly dehydrated cases were treated with oral therapy alone. Careful intake and output measurements were made. Tetracycline was given to each patient. Bacterial culturing of stools was not mentioned.

Fluid balances were adequately maintained by oral therapy in all cases after initial IV correction of shock. Persons receiving the glycine solution had much lower stool volumes and diarrhea of shorter duration than those receiving only oral fluid, indicating that glycine may enhance the absorption of oral fluid. Use of oral therapy reduced the amount of IV fluid required for management of dehydration.

Although the addition of glycine to oral fluid was shown to reduce the volume and duration of stool output in this study, incorporation of glycine into oral solutions may be limited by cost and availability factors.
To determine whether glycine can promote net sodium and water absorption in cholera patients and increase the absorptive effect of glucose, 2 clinical trials were carried out in Bangladesh.

In the first trial, 48 hospitalized patients 12 years of age or older with hypovolemia and laboratory confirmed cholera were initially treated with IV therapy until their plasma specific gravities were less than 1.030. The patients were then treated with one of four oral solutions, (the basis on which persons were assigned to treatment groups was not specified). Nine patients received only electrolytes (in mEq/l: Na⁺-120, K⁺-15, HCO₃⁻-48, Cl⁻-72, citrate-15); 12 were given electrolytes and 110 mmol/l of glycine; 17 received electrolytes (including K⁺-6 or 9 mEq/l, plus 110 mmol/l of glucose, and 10 patients received electrolytes (including Na⁺-100 mEq/l, Cl⁻-52 mEq/l) and both glucose and glycine. Net gut balance was calculated and serum, stool, and urine electrolytes, urea, and creatine were determined, all every four hours.

In the second study, 136 persons were admitted to a field hospital with severe cholera. Sixty-eight patients were treated, after initial IV rehydration, with electrolytes plus either 110 mmol/l or 220 mmol/l of glucose (shown by the authors to be equivalent in effect), and sixty-eight were treated with electrolytes plus 110 mmol/l each of glucose and glycine. Intake and output were calculated every six hours. Laboratory determinations were not performed.

Clinical and laboratory measures of severity at admission were similar for all four groups in the first study. Patients in that study given electrolytes alone had a greater volume of diarrhea and prolonged (20 hours) negative water and sodium balance compared to the other three groups. Patients given glycine experienced a sharp rise in serum urea nitrogen, demonstrating glycine absorption. Serum electrolytes were generally stable and within normal limits in all groups. Mean duration of diarrhea was 49 hours in the plain electrolyte group, 46 hours in the glucose group, 31 hours in the glycine group, and 27 hours in the glucose plus glycine group. The differences between the plain electrolyte group and each of the other groups were all significant. Differences between the glucose, glycine, and glucose-glycine groups were not discussed. All oral solutions containing glucose or glycine were absorbed well enough to supply maintenance fluid and electrolyte requirements (positive balance was usually achieved in 8-12 hours). Net absorption was highest in the glucose plus glycine group.

The field hospital study results were similar. The patients in each group had similar severity of disease on admission, but the
glucose plus glycine group had diarrhea of significantly less volume and shorter duration than the glucose group.

The authors felt that any sugar or amino acid which normally enhances sodium absorption will do so in cholera patients. An additive effect of glucose and glycine was demonstrated in that those patients treated with both agents had the shortest duration of diarrhea and the greatest net water and sodium absorption. This additive property was valuable in the field situation because it shortened the duration of illness and hospitalization.

Nalin DR et al, Oral or nasogastric therapy for cholera, WHO Public Health Paper No. 40, Chapter 11, pp. 73-76, 1970 (see No. 25).


The authors outlined their rationale for advocating the use of an oral rehydration solution consisting of, (in mEq/l): Na⁺-120, K⁺-25, Cl⁻-97, base (a sum of bicarbonate plus citrate or acetate)-48, and glucose 110 mmol/l, to treat diarrheal dehydration.

Clinical studies comparing the efficacy of various concentrations of glucose and electrolytes were analyzed to obtain an optimal concentration of ingredients for a proposed oral rehydration solution. A 2% glucose solution (110 mmol/l) was found to provide the maximum induced sodium and water absorption and an acceptable osmotic load, while minimizing the most costly ingredient of the solution. The electrolyte concentrations were selected by use of electrolyte balance studies, and on the basis of these studies no magnesium or calcium was added to the solution. Glycine was not included as an ingredient because of cost and availability considerations.

The authors felt that the proposed solution would be beneficial for treating persons of all ages with cholera-like diarrhea and that any excess sodium load could be handled by the kidneys. However, the
The authors noted, with the 48 mEq of \( \text{HCO}_3^- \) used, alkalosis leading to tetany could result in persons with low serum calcium and magnesium concentrations.

The authors described the ease of preparing and administering oral therapy and emphasized that management of cholera epidemics should rely on effective treatment utilizing oral therapy, and not on ineffective vaccination programs. Promotional efforts to demonstrate the ease of mixing and administering oral fluid should be directed to local public health officials and paramedical personnel.


A hypotonic oral rehydration solution was used to treat 47 Apache children hospitalized with diarrhea. Only 2 of the children were older than 2 years and none were currently breastfeeding. The extent of dehydration on admission ranged from inapparent to severe with shock.

Determinations included careful fluid balance measurements, serum chemistries, and bacterial stool cultures. Hypotonic oral fluid, consisting of (in mmol/l): \( \text{Na}^+ - 81 \), \( \text{K}^+ - 18 \), \( \text{Cl}^- - 17 \), \( \text{HCO}_3^- - 18 \), and glucose-139, was administered to children strong enough to drink and having bowel sounds, using thirst as the regulator of volume intake.

Clinically apparent fluid volume depletion, moderate hypo- and hypernatremia, and acidosis were readily corrected. Vomiting, when present, did not impede oral fluid administration. Children in shock could drink oral fluid after rapid intravenous volume replacement.

Untoward effects were seen in 3 children who drank excessive amounts of fluid and developed mild periorbital edema which resolved after formula feedings began. Two other children demonstrated reversible glucose malabsorption.

Use of a hypotonic oral fluid (the \( \text{Na}^+ \) concentration of 81 mmol lies midway between the 101 mmol in pediatric cholera stools and the 56 mmol in noncholera stools), was shown to be effective in treating inapparent to moderate dehydration and in correcting moderate hypo- and hypernatremia and acidosis using thirst as the volume intake regulator. The study demonstrated the ease and economy with which an oral rehydration program can be administered.


The editors emphasized the danger of administering homemade oral rehydration solutions too high in sodium and other solutes during diarrheal episodes, especially to infants with physiologic renal immaturity. The risk is largely due to erroneous or poorly understood instructions given to the mother. The editors stated that "...in the absence of a convenient and safe electrolyte mixture it is safer to give water without added salt--but not for longer than 24 hours.... There is no advantage in offering a child fluids with glucose alone added."

The editorial recommended the removal of solid food and cow's milk from the diet of children under one year of age during the first 24 hours of diarrhea. Persistence or recurrence of diarrhea in spite of food and milk withdrawal would warrant hospital referral.


The author hypothesized that sucrose may be preferable to glucose as the carbohydrate constituent of oral rehydration solutions because of its lower cost and wider distribution.
Thirty-three children (whose ages were not stated) with mild to moderate dehydration secondary to diarrhea were randomly divided in a double-blind fashion into four treatment groups. Groups I and II were given (by unstated means) a solution containing sodium chloride (2.0 g/l), sodium bicarbonate (2.0 g/l), potassium chloride (1.0 g/l), and either glucose (30 g/l — Group I, 10 patients) or sucrose (30 g/l — Group II, 8 patients). Groups III and IV were given a solution containing sodium chloride (3.5 g/l), sodium bicarbonate (2.5 g/l), potassium chloride (1.5 g/l), and either glucose (20 g/l — Group III, 7 patients) or sucrose (20 g/l — Group IV, 8 patients). Demographic, nutritional, and biochemical characteristics of patients prior to admission were not described. When 50% of patients in Groups I and II were found to have reducing substances in their stools, the study was "switched" to Groups III and IV.

Mean patient body weight, mean stool output, and mean net fluid balance were similar for all four groups, as was the percentage of patients "failing" oral treatment and requiring IV's. One Group-III and five Group-IV patients had reducing substances in their stools. No data on serum electrolytes, volume of solution required, or duration of symptoms were given.

Since information on the comparability of the treatment groups was not presented, it is difficult to draw conclusions concerning the comparative efficacy of the glucose and sucrose solutions. However, the similar clinical outcomes of the treatment groups indicated that the sucrose solution may be effective in orally rehydrating children with diarrhea.


The proven efficacy of a glucose-containing oral rehydration fluid suggested that sucrose, which is hydrolyzed to glucose and fructose in the small bowel and is cheaper and more widely available than glucose, ought to be examined as a possible replacement for glucose in oral rehydration solutions.

Eighteen adult patients with severe dehydration secondary to diarrhea (13 with proven cholera, one with a non-01 Vibrio, and four without recognized pathogens) were studied. Mean age was thirty-two (range 11-65). All patients were initially rehydrated with IV fluids and then begun on oral or nasogastric maintenance. The oral solution contained either 48 grams/l (5 patients) or 38 grams/l (13 patients) of sucrose as well as sodium chloride (4.2 grams/l), sodium bicarbonate (2.0 grams/l), and potassium citrate (2.7 grams/l). Patients were permitted measured quantities of water and milk orally ad libitum. Stool reducing substances, plasma specific gravities, and serum electrolytes were monitored.
Two cholera patients and one non-cholera patient developed negative water and electrolyte balances and needed re-institution of IV therapy. All other patients were adequately maintained on oral therapy, but diarrhea rates increased substantially (two- to four-fold) in three. All 12 patients whose stools were tested had reducing substances present in their stools, both before and after hydrolysis.

The author concluded that sucrose is potentially useful but less effective than glucose and should be reserved for situations where glucose is unavailable.


The author questioned the effectiveness of the "recommended" oral rehydration solution (containing 90 mmol/l of sodium) for children less than two years of age in developed countries. Since children under two have relatively large insensible losses and relatively low renal concentrating capacity (700-1000 mOsm/l) even under normal circumstances, they are at higher risk of developing hypernatremia if given oral fluids with a high sodium concentration and high solute load.

Studies of the efficacy of the WHO "recommended" solution had been carried out in developing nations in children over two years of age, some of whom were chronically malnourished and have hypotonic body fluids. Studies in Apache Indian children under two were carried out with success, but these children may be "closer to a developing-world population than the rest of the U.S. infant population." The authors felt that developing world and Apache Indian infants may be more tolerant of higher oral sodium concentrations because they are more likely to be poorly nourished and have hypotonic body fluids than are children in developed countries.

As the authors suggested, studies are needed to assess the efficacy of oral rehydration solutions in treating children in developed countries.


Responding to the letter of Bart and Finbey (see abstract, Bart KJ, et al: "Single solution for oral therapy of diarrhoea." (letter) Lancet: 2:633-634, 1976.), these investigators pointed out that the quantity of oral fluid received (and therefore the total sodium load) will be commensurate with losses of stool and vomitus. Those with minimal losses will receive minimal therapy (and sodium) and vice-versa. The authors provided evidence that, as the diarrhea rate increases so does stool sodium concentration, implying that those with profuse diarrhea will require more sodium to maintain net balance.
Further, due to the equilibration of plasma and luminal sodium concentration, a hypotonic sodium oral solution may increase diarrheal sodium loss. The authors recommended a rehydration solution containing 120 mmol/l of sodium.

The heart of Bart and Finbey's concern—that data obtained from children in developing countries may not apply to children from developed countries—was not directly addressed here. The authors did, however, reaffirm the appropriateness of their solution for the population where it will be most required and beneficial—the children of the developing nations.


The authors sought to study the efficacy of oral rehydration in treating non-specific acute gastroenteritis in children and to compare results using two different oral solutions.

Fifty hospitalized Indian children less than 5 years of age were studied, all of whom were admitted with either no dehydration (5), mild dehydration (27), or moderate dehydration (18), based on established clinical criteria. The children were given one of two oral solutions (C-concentrated or D-dilute) in a double-blind fashion. Solution C contained sodium (115 mEq/l), bicarbonate (48 mEq/l), chloride (62 mEq/l), potassium (25 mEq/l), calcium (4 mEq/l), magnesium (4 mEq/l), sulfate (4 mEq/l), phosphate (4 mEq/l), lactate (4 mEq/l), and dextrose (3.68%). Solution D was the same with the exception of sodium (60 mEq/l), chloride (35 mEq/l), bicarbonate (80 mEq/l), and dextrose 4.035%). Children who could not be successfully rehydrated orally were removed from the study and treated with IV fluid. Neither criteria for exclusion nor the number of cases excluded from each treatment group were stated. Serum sodium, chloride, and potassium were determined at admission and after 24 and 48 hours of therapy.

Thirty-seven of forty-five dehydrated children were successfully treated; 19 given C and 18 given D. Twenty-five of 27 mildly dehydrated and 12 of 18 moderately dehydrated children were treated successfully. Of the eight treatment failures, three had clinical acidosis, three had persistent vomiting, and two were not described. One child with acidosis died. Two-thirds of all children were rehydrated with 24 hours and 89% within 36 hours. Results were similar for both solutions used. Mean serum sodium levels at admission were not stated by treatment group; although higher at 24 and 48 hours in patients given solution C, statistical significance was not demonstrated. The mean serum sodium level was in the hypernatremic range (150 mEq/l) after 48 hours of treatment in those children with absent or mild dehydration who were treated with the concentrated solution. Results for chloride were similar for both
groups, and mean potassium levels appeared to be comparable for both
groups throughout the study.

The authors concluded that oral rehydration is an effective tool
in the treatment of childhood gastroenteritis, that their dilute
formula (D) was better suited to these children because it did not
produce hypernatremia, and that constituents of oral rehydration fluid
other than sodium, potassium, bicarbonate, chloride, and glucose are
unnecessary and expensive. The data supported the first two
conclusions but did not prove them (no control group of non-orally
treated children was used to compare outcomes and serum electrolytes
were not statistically different). The final claim regarding added
constituents was unsupported by the study.

Moran M, Oral rehydration therapy in home and hospital, experience

57. Rahilly PM et al, Clinical comparison between glucose and sucrose
additions to a basic electrolyte mixture in the outpatient management

This study compared the clinical efficacy of a sucrose- and
sucrose-electrolyte solution in outpatient oral rehydration at a
London hospital.

One­hundred-twenty children treated on an outpatient basis for
mild gastroenteritis were consecutively studied. A basic electrolyte
solution (in mEq/l: potassium-28, sodium-26, hydrogen-4, chloride-24,
phosphate-9, and citrate-3) was provided and on a randomized,
double-blind basis, mothers were given sucrose or glucose to add to
the electrolytes. The osmolality of the 5% glucose solution was 216
mOsm/l and that of the 5% sucrose solution was 351 mOsm/l.

Children were given 150-170 ml/kg/day of either of the two
solutions and milk of increasing strength was added to their diets as
they recovered. Patients were monitored continuously and if the child
failed to recover, he was admitted to the hospital and considered a
clinical failure.

Ninety-four children met the criteria and could be studied - 50 in
the sucrose group and 44 in the glucose group. The number of clinical
failures in the glucose group (12) was significantly greater (p less
than 0.05) than in the sucrose group (5). Serum electrolytes and
stool output were not assessed nor were the clinical, biochemical, or
demographic characteristics of the treatment groups.

The authors concluded that glucose held "no practical advantage"
over sucrose, but critical evaluation was limited by their failure to
more rigorously assess both groups.

Realizing that sucrose could be of great practical importance in oral rehydration the authors sought a more complete understanding of the physiology of sucrose absorption in infants with acute diarrhea.

Twenty consecutively hospitalized Indian children with acute diarrhea and clinically moderate to severe dehydration were studied. Nineteen were less than two years old. Two were hypotensive on admission and were treated with IV fluids for one hour and then begun on intragastric rehydration, which the others started at admission. The rehydration solution consisted of sodium (50 mmol/l), potassium (15 mmol/l), chloride (30 mmol/l), bicarbonate (15 mmol/l), and sucrose (130 mmol/l), had an osmolality of 260 mOsm/l, and was infused at a mean rate of 15 ml/kg/hour. Infants were allowed to drink dilute milk after initial hydration. Stools were cultured and volume, pH, and reducing substances were monitored. The clinical hydration state and serum sodium, potassium, and bicarbonate were followed. Seventeen children had sucrose tolerance tests done on the second day of admission and sixteen had glucose tolerance tests done on day 3. Sixteen children had upper jejunal biopsies done to assay for sucrase, maltase, and lactase. There were no control patients.

All but one child were treated successfully by oral means alone. The one failure had sucrose intolerance as indicated by the tolerance test. All other patients had satisfactory clinical and biochemical responses even though 13 of 19 had reducing substances present in their stools. Excluding the patient who failed oral therapy, all others had normal and statistically similar oral sucrose and glucose tolerance test response curves. Low levels of sucrase, lactase, and maltase were seen in 3, 12, and 2 of the children, respectively. One of these children had cholera, and the others had non-cholera disease.

This study demonstrated that most infants and children with diarrhea have the ability to hydrolyze sucrose and absorb its component monosaccharides. Nineteen of these twenty children were treated successfully, but the lack of appropriate controls limits the conclusions that can be drawn regarding the relative efficacy of this therapy versus glucose oral rehydration or no oral rehydration at all.


Assuming the clinical acceptability of glucose-electrolyte solutions for oral rehydration therapy, these investigators described the relative efficacy of a sucrose-electrolyte solution in a controlled clinical trial.

One hundred twenty-two hospitalized Bangladeshi patients, aged 6-80, with clinical cholera and severe dehydration (estimated at greater than eight percent) were included in the study if they had a stool volume greater than 10 cc/kg/hour during initial IV rehydration. IV fluids were stopped and the patients were randomly assigned in a double-blind fashion to receive one of two oral fluids. Each solution contained sodium (96 mEq/l), potassium (25 mEq/l), chloride (72 mEq/l), bicarbonate (24 mEq/l), citrate (25 mEq/l) and either glucose (20 grams/l) or sucrose (40 grams/l). Solutions were prepared by the nursing staff which mixed the contents of pre-weighed, coded packets with tap or well water. Stools were cultured and monitored for reducing substances before and after acid hydrolysis. Intake, output and plasma specific gravities were followed, but serum electrolytes were not monitored. Oral therapy was considered to have failed if an IV was necessary. IV therapy was instituted if plasma specific gravity was greater than 1.030.

Both treatment groups were statistically similar with respect to demographic, nutritional, etiological, clinical and biochemical characteristics at admission and thereafter except that there were proportionately more males in the sucrose group. Eighty-six percent of those treated with sucrose and 87% of those given glucose were successfully treated orally. Of the patients with confirmed cholera, the success rates were 68% with sucrose and 78% with glucose—significantly different. Significantly more failures occurred in those patients with higher purging rates (oral treatment failed in 13/17 patients with stool rates greater than 20 cc/kg/hour during the first 24 hours). Volumes of oral fluid required were similar for both groups overall as were purging rates. Less than 1% of the glucose administered was recovered in the stools. Those given sucrose failed to hydrolyze about 5% of the sugar and failed to absorb 5% of the monosaccharides generated by hydrolysis; no significance was noted between this and the glucose group. Nutritional status was not statistically related to failure of oral hydration.
This study demonstrated that, in patients over five years of age with clinically severe diarrhea and dehydration caused by cholera and non-cholera agents, sucrose and glucose appear to be equally effective carbohydrate substrates in oral rehydration solutions. Failure of oral rehydration is most directly related to failure to keep up with the volume needs generated by high diarrhea rates. The clinic staff had no difficulties preparing the solution from pre-mixed packets and administering it under standard rural hospital conditions, a point of great practical importance.


This is a companion editorial to the paper by Palmer (see preceding abstract, "Comparison of sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrheas"), in which the pathophysiology of cholera and the intestinal transport mechanisms which provide the rationale for use of oral therapy are clearly described.

The demonstrated efficacy of the sucrose-electrolyte solution supports the use of this widely available sugar in home-based oral rehydration programs. In addition, the results of Palmer's study suggested that other substances requiring hydrolysis, such as starches, might be equally or more effective in aiding salt and water uptake. Since neutral amino acids such as glycine share the same sodium-coupled absorption mechanism as glucose, postulated the author, polypeptides added to oral rehydration solutions might offer the additional theroretical advantage of treating malnutrition simultaneously with diarrhea.

Finally, although effective, currently available oral therapy only fosters absorption of the fluid administered and does not reverse the secretory diarrhea caused by cholera and other agents. Studies to discover rehydration fluid constituents which would foster such a reversal are still needed.


In light of certain findings by Palmer, et al, (see abstract No. 59, "Comparison of sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrheas") this study augmented findings regarding disaccharide absorption and net intestinal water flux in normal volunteers.

Seven normal volunteers had jejunal segments infused with one of 2 solutions: 1) 55.5 mmol (1%) glucose with 122 mmol sodium or 2) 28 mmol (1%) maltose with 122 mmol sodium. Five other normal volunteers had infusions of either 111 mmol glucose, 21 mmol sodium, and 146 mmol mannitol or 111 mmol maltose, 21 mmol sodium, and 146 mmol mannitol.
In the first study, glucose absorption was significantly greater with the maltose infusion, but water absorption was significantly greater with the glucose infusion. Sodium absorption was also greater with the glucose infusion, but not significantly so. Both infusions in the second study produced net water and sodium secretion despite glucose absorption. Secretion was significantly greater with the maltose solution.

In persons with diarrhea, glucose has therapeutic advantages over glucose-containing disaccharides, especially in persons with high stooling rates. When oral rehydration is used, glucose solutions should be used whenever practicable.

Pierce NF et al, Oral fluid - a simple weapon against dehydration in diarrhoea. WHO Chron 31:87-93, 1977 (see No. 26).


Considering that the average fecal sodium concentration in infantile diarrhea is 56 mmol/l, the authors compared an oral rehydration solution with 50 mmol/l sodium to the WHO-recommended solution (90 mmol/l) for treatment of children with non-cholera diarrhea.

Thirty-nine hospitalized children with clinically moderate to severe dehydration were randomized (not blindly) into two treatment groups. Group A (19 patients) was given a solution containing sodium (90 mEq/l), potassium (15 mEq/l), chloride (75 mEq/l), bicarbonate (30 mEq/l), and glucose (90 mmol/l) by intragastric drip at 10 cc/kg/hr. Group B (20 patients) was given a solution containing sodium (50 mEq/l), potassium (15 mEq/l), chloride (50 mEq/l), bicarbonate (15 mEq/l), and glucose 170 mmol/l at 12.5 cc/kg/hr. Both solutions had 300 mOsm/l, and were given until complete hydration was achieved. Children with continuing diarrhea were given the same solution orally to replace stool losses and Group-A children were actively encouraged to drink additional water after four hours of hydration "for ethical reasons." Clinical features, hematocrit, and serum electrolytes and specific gravities were followed. Stools were cultured for bacterial pathogens and examined for reducing substances.

The demographic, clinical, biochemical, and nutritional characteristics of both groups were comparable at admission and biochemical values remained comparable throughout the study. The percentage and type of bacterial pathogens isolated were also similar in both groups. All children were adequately rehydrated orally, although two Group B infants with underlying illnesses died. One of two Group-A patients and one Group-B patient with hypernatremia on
admission still had hypernatremia at the end of oral treatment. Two other Group-A patients became hypernatremic during rehydration. None of these patients had neurological manifestations. Seven Group-A and 3 Group-B patients had periorbital edema.

Difficulties in interpreting the results of this study arise from the non-blind assignment of children to treatment groups and from the presence of a number of uncontrolled variables including varying glucose concentrations, differing infusion rates, and the active encouragement of free water intake in Group A only. The incidence of hypernatremia was not significantly greater in A than in B and the significance of the reported periorbital edema is unclear. Both solutions were equally effective clinically, but the results do not adequately support the authors' hypothesis that a 50 mEq/l Na+ solution would be superior.


After the distribution of glucose-electrolyte packets for oral rehydration in rural health centers in an Indonesian province, the percentage of pediatric hospital admissions attributed to diarrheal disease dropped from 32% (1972) to 22%. Because sucrose is only 20% as costly as glucose in Indonesia, a comparative study of sucrose-versus glucose-electrolyte solutions was conducted.

Sixty-seven children between 2 and 28 months with mild to moderate dehydration secondary to non-cholera diarrhea were studied in a double-blind fashion. Eighteen children were given solution I and 49 solution II. Solution I consisted of (in g/l): sodium chloride, 2.0; sodium bicarbonate, 2.0; potassium chloride, 1.0; and either glucose, 30, or sucrose, 20. Of the 18 persons given solution I, 10 received the glucose version and 8 that containing sucrose. Solution II consisted of (g/l): sodium chloride, 3.5, sodium bicarbonate, 2.5; potassium chloride, 1.5; and either glucose, 20, or sucrose, 20. Of the 49 given solution II, 23 received the glucose and 26 the sucrose versions. Oral solutions were given ad libitum. Clinical condition, body weight, stool output, net fluid balance, emesis, stool for reducing substances, and total consumption of rehydration fluid were monitored. Serum and stool electrolytes were not evaluated.

There were no significant differences for all the above characteristics among patients receiving solutions I and II with either glucose or sucrose. Those given sucrose solutions did have greater (not significantly) mean stool volume than those given glucose solutions in both treatment groups. Three patients given glucose solutions and four patients given sucrose solutions failed to respond to oral therapy.
Comparable clinical results were obtained from each treatment group. When glucose is unavailable, the authors concluded sucrose may be an adequate (and less expensive) carbohydrate constituent of oral rehydration solutions.


The comparative clinical efficacy of oral rehydration solutions containing sucrose and glucose was assessed in this study.

Fifty-one hospitalized Costa Rican infants, aged 3 to 12 months, with clinical signs of greater than five percent dehydration were included in the study. There was no mention of their nutritional status. After admission, they were randomly assigned in a double-blind fashion into one of two groups: The first received a glucose-containing oral solution (20 grams/l) and the second received a sucrose solution (40 grams/l, yielding 2% glucose). The remaining constituents were the same for both solutions (in grams/l: sodium chloride, 3.5, sodium bicarbonate, 2.5, and potassium chloride, 1.5). The possible influence of intraluminal fructose was ignored. Children were fed rehydration solution and water in a 2:1 ratio by trained staff. Serial serum, urine, and stool samples were collected for electrolyte, osmolality, sucrose, and glucose determinations. Stools were cultured for bacterial pathogens and examined for rotavirus by the ELISA technique.

The two groups were similar demographically and clinically at admission and were found to have diarrhea of similar etiologies. Oral rehydration was successful clinically and biochemically in 100% of the glucose group and 92% of the sucrose group. Stool biochemistries were similar except for mean osmolality, which was significantly greater between 6 and 24 hours in the sucrose group. Presence of sugar in stools was significantly related only to the presence of rotaviral infection and not to other etiologic agents or to the type of sugar in the solution consumed. The glucose solution corrected serum electrolyte abnormalities significantly more rapidly than did the sucrose solution, and significantly fewer glucose-group patients required more than 24 hours of therapy. Other differences between the groups (including urine output in males, diarrhea rate, initial weight gain, IV fluid needs, and net absorption) were all suggestive of greater efficacy for glucose but were not statistically significant.

The authors stated that, in the face of the small failure rate demonstrated, sucrose can be used in oral rehydration solutions in areas where it is available and glucose is not. Because the evidence presented indicated that sucrose is less efficient than glucose, use of glucose was recommended whenever possible.
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The authors stated that, in the face of the small failure rate demonstrated, sucrose can be used in oral rehydration solutions in areas where it is available and glucose is not. Because the evidence presented indicated that sucrose is less efficient than glucose, use of glucose was recommended whenever possible.


A sucrose-electrolyte solution was compared to a glucose-electrolyte solution in the outpatient management of acute gastroenteritis in infants. Seventy-eight children less than 18 months of age presenting consecutively to 2 London hospital outpatient facilities with acute gastroenteritis were studied.

All patients were treated at home with 150 ml/kg/day of oral carbohydrate electrolyte solution (composition not given) for 24 hours and then advanced in quarter strength measurements daily to full strength milk. Children were clinically assessed daily. Those requiring hospital admission were classified as clinical failures. Mothers were provided with a concentrated out-patient electrolyte mixture to be diluted one part to five parts of boiled water and, in a randomized, double-blind fashion, were given packets of either sucrose or glucose. Mothers were instructed to add one flat teaspoonful (5 ml) of sugar to each 120 ml of diluted electrolyte solution prepared at home. At the first return visit, a sample of the solution prepared by the mother was obtained for osmolality testing. No laboratory determinations were performed on the infants.

Seventy-three children (57 under one year of age) completed the study—39 received sucrose and 34 glucose. Approximately half of the mothers in each group submitted samples for analysis. There was no significant difference for mean osmolality between the solutions of the treatment failures and successes in either group. Variances in the osmolality of the solutions of the failures and successes were not significant in the sucrose group, but the failures in the glucose group had received fluids with significantly greater variance in osmolality than did the successes. Recovery times (both mean and range) was similar for both groups. Seven of 39 given sucrose and 11 of 34 given glucose were admitted to hospital, but most admissions were often unrelated to treatment failure (e.g., social reasons, intercurrent infections, etc.) so that this difference, although statistically significant, may not be of practical importance.

This study indicated that sucrose-containing solutions are at least as effective as glucose-containing solutions in the outpatient management of infant diarrhea. If a solution is prepared incorrectly, sucrose may be less liable to produce hyperosmolar feeds. Finally, sucrose is cheaper and more widely available than glucose.

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A problem with this study was that the clinical and laboratory indicators of diarrheal severity were not measured and compared for the study groups. If diarrhea in the sucrose group had been significantly less severe, the equivalent clinical outcomes noted above may not be meaningful. In addition, the authors did not describe the underlying nutritional condition of the infants studied.


The composition of coconut water was analyzed to assess its potential use as an oral rehydration fluid. The fluid of 51 coconuts taken from 5 coconut palm trees (2 varieties) was examined.

The mean sodium concentration was 2.9 mmol/l; potassium was 9.9 mmol/l; and glucose 114 mmol/l. Composition varied with the age of the coconut (10-month-old coconuts had 1/3 the glucose and slightly more sodium and potassium than 5-month-old coconuts) and with location (coconuts closer to the ocean had proportionately more potassium than did those taken from inland areas).

The extremely low sodium and sometimes dangerously high potassium concentrations make coconut water a less than ideal oral therapy solution.


The authors compared clinical results in Jamaican children hospitalized with diarrhea who were given oral solutions containing low and high concentrations of sodium and potassium. The authors felt this comparison was warranted because children with cholera have lower stool sodium losses and higher stool potassium losses than adults with cholera, for whom the WHO oral rehydration solution (90 mEq/l sodium, 20 mEq/l potassium) was initially formulated. Use of the WHO-recommended solution the authors hypothesized, may place small children at risk of hypernatremia and hypokalemia, respectively.

Seventy-three infants (age range not given) were studied for 24 hours. All had watery diarrhea of undetermined etiology and at least one had clinical signs of dehydration. All received 240 ml/hour of oral fluid therapy until signs of dehydration disappeared, at which point one-quarter strength milk formula was given. In the first part of the study fifty-eight of the infants were randomly given either a low sodium (60 mEq/l) or high sodium (90 mEq/l) solution. These infants received no additional plain water during rehydration. In a second study, 25 infants were randomly given low potassium (20 mEq/l) or high potassium (35 mEq/l) solutions and extra water (two parts oral solution followed by 1 part water) until normally hydrated. Intake and output volumes were recorded. Serum and stool electrolytes were analyzed at six and 24 hours.

Each study group had similar characteristics on admission, and clinical and laboratory indicators of rehydration were also similar after six hours. The groups given high sodium and high potassium solutions had significantly (p less than 0.02) higher mean sodium and potassium absorption, respectively, during the first six hours and at 24 hours. Transient asymptomatic hypernatremia was seen in five infants given the high sodium solution but disappeared after they were switched to a dilute milk formula. A significantly (p less than 0.025) greater number of infants given the low potassium solution were hypokalemic at the end of treatment compared to those given high potassium solution. Twenty-eight percent of infants given low sodium solution had hyponatremia at a one-week follow-up (nineteen percent were hyponatremic at the close of the study). In the potassium study, where both solutions had a "high" sodium concentration (90 mEq/l) and extra water was consumed, sodium absorption levels were between those seen with the high and low sodium concentration solutions with which no extra water was given. There was no hypernatremia in the patients given solutions with extra water.

These results showed that a solution containing 90 mEq/l of sodium is safe and effective and may produce no hypernatremia if extra water is allowed. A solution containing 90 mEq/l of sodium could be used in infants and adults with either cholera or non-cholera diarrhea. The
WHO-recommended formula may result in hypokalemia in infants with diarrhea and may play a role in producing total body potassium depletion in infants with repeated diarrheal attacks. If a single formula is to be used, tests to determine the efficacy and safety of solutions containing 35 mEq/l of potassium given to adults with cholera are indicated.

Pizarro D et al, Rehidratación por la vía oral en niños menores de un mes de edad, (Unpublished manuscript) (see No. 44).

Taylor PR et al, Oral rehydration therapy for treatment or rotavirus diarrhea in a rural treatment center in Bangladesh (accepted for publication, Arch Dis Child), (see No. 45).
IV. IMPACT

The abstracts in this section are of studies which attempted to measure the effect of oral rehydration therapy on diarrheal disease morbidity and mortality and on the nutritional status of the persons treated.

In these studies both methodological limitations and intervening sociocultural factors often confounded impact measurement. Among the former were poorly chosen or nonexistent comparison groups, variable levels of training and expertise on the part of those administering oral rehydration interventions and often unreliable disease and nutrition surveillance data. Intervening factors included widely varying environmental, cultural and socioeconomic characteristics.


Pierce NF et al, Effect of intragastric glucose-electrolyte infusion upon water and electrolyte balance in Asiatic cholera, Gastroenterology 55:333-343, 1968 (see No. 16).

To determine whether oral therapy could provide a safe and effective means of supplying maintenance fluids, hospitalized persons with uncomplicated cholera were treated with either standard intravenous therapy or with intravenous therapy followed by an oral rehydration solution (composition, in mmol/l: Na+120, K+15, HCO3-48, Cl-72, citrate-15 and glucose-110). Careful input-output balance studies were performed, and IV and oral needs were recalculated every four hours. The volume of oral fluid administered equaled the volume of stool and vomiting output.

29 persons received initial IV hydration, and 19 were then begun on oral therapy as soon as they were alert enough to drink. Both oral and oro- or nasogastric tube administration were used. Tetracycline was given to each patient.

"About one patient in 10" required continued IV therapy after oral hydration was begun. Vomiting occurred with equal frequency in both treatment groups and "ceased as dehydration and acidosis were corrected." Both groups had a similar decrease in the rate of stooling.

Oral therapy was shown to reduce the amount of IV fluids needed by 80%. As an adjunct to cholera therapy a major advantage of oral fluid is that the ingredients are inexpensive, widely available, and do not require sterile conditions for mixing.


To see if oral therapy alone could correct initial acidosis and dehydration caused by diarrhea, 5 persons with severe acidosis and moderate dehydration admitted to a rural treatment center were administered an oral rehydration solution closely resembling the WHO-recommended formula. All 4 controls, who had similarly severe diarrhea but who received only occasional water and no intravenous
therapy in the 6 hours of study, as well as 4 of the 5 persons receiving oral therapy had *V. cholerae* recovered from their stools.

Rapid correction of pH, specific gravity, and hematocrit had occurred by 6 hours in the oral treatment group, but there was no change in controls. The results indicated that oral fluid, even when given after marked acidosis and moderate dehydration have occurred, can obviate the need for intravenous therapy.

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An outbreak of cholera among war refugees from East Pakistan (now Bangladesh) necessitated the use of an oral rehydration solution to treat dehydration in a situation marked by a shortage of intravenous supplies, inadequate treatment facilities, and few trained personnel. Prior to intervention the diarrhea case fatality rate for these refugee camps had been estimated at 30%.

An oral rehydration solution (composition, in mEq/l: Na⁺-90, Cl⁻-60, HCO₃⁻-30, and glucose-121 mmol/l) was packaged in Calcutta for use in the camps at a cost of (U.S.) 1 1/2 cents per liter. Sufficient quantities of potassium were not available for inclusion in the solution. Intravenous therapy was begun only in the severe cases, and oral therapy was given for further correction of deficits as well as for maintenance and replacement of continuing losses. Antibiotics were given when available; normal diet was resumed as soon as possible.

3703 persons were treated during the 8 weeks of the outbreak with an overall diarrhea case fatality rate of 3.6%. The case fatality rate was only 1% in a facility manned entirely by trained personnel. Treatment failures were usually related to inadequate fluid volume
intake in patients supervised only by untrained attendants. Although vomiting was common, most persons retained enough oral fluid to sustain hydration.

These results, obtained under most difficult circumstances, demonstrated the simplicity and effectiveness of an oral rehydration program and the dramatic effect such a program can have on case fatality rates caused by cholera.


To determine whether negative nitrogen balance or insufficient oral intake was responsible for atrophy and hypoplasia of the small intestine in fasted rats, one study group of rats was given intravenous alimentation while a second group of rats was given the same solution orally. After one week the intravenously-fed rats showed decreases in gut weight (22%), mucosal weight (28%), mucosal protein (35%), DNA (25%), and mucosal height as compared to the orally-fed rats. Lower total intestinal maltase (62%), sucrase (62%), and lactase (64%) contents were noted and the specific activities of maltase and sucrase but not lactase were also decreased. The proximal-distal gradients of mass, protein, and DNA were reduced in the intravenously-fed rats.

Caution must always be used in applying results of animal experiments to humans. However, data in this study indicated that the physiologic responses related to food ingestion are important in maintaining small intestinal mass, disaccharidase activity, and the proximal-distal gradient. Withholding of food during diarrheal episodes, this study implied, is likely to depress these physiologic functions which would in turn impede food digestion and absorption during recovery.

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The article reviewed the epidemiology of acute diarrheal diseases in the developing world. The clinical effectiveness and cost-effectiveness of oral glucose-electrolyte therapy in the treatment of diarrheal diseases were described.


The relationship between repeated bouts of diarrhea and the development of malnutrition was explored. The rapid restoration of body fluids, especially by use of oral rehydration solution, and early feeding could help alleviate one of the principal causes of malnutrition.

Field trials using oral therapy to treat acute diarrhea in children were encouraged in order to study the potential effects of this therapy on nutrition and mortality.

To implement a successful oral rehydration program one should consider cultural attitudes regarding diarrheal disease and its treatment, the packaging and stability of the salts, the distribution of packets, and the cost.


To assess the effect of a home-administered oral therapy program on weight change during diarrheal episodes, children less than 5 years of age with diarrhea in one rural Philippine village received the WHO-recommended oral solution while children similarly ill in a comparable neighboring city received no oral therapy. Nutritional information, including the need to continue feedings during diarrheal episodes, was given to families in both villages. Ill children in both villages were initially examined by the medical staff, were given non-specific antidiarrheal and antibiotic medications according to local medical practices, and throughout illness were examined at home daily while the nutritional education program was continued. No routine stool culturing was done. Serial weights were obtained during illness and weight surveys of nearly all community children were done before and after the 7-month study.

Children given oral therapy gained nearly twice as much weight during an attack of diarrhea than did controls. The fluid was tolerated well in children with mild or moderate diarrhea with the exception of one child who may have had glucose intolerance. Hospitalization was not significantly reduced in the orally-treated group. Analysis of weight gain over the period of the study indicated an increase in the orally-treated group, but this was not consistent throughout the study (see later abstract).

Since both communities received nutritional and feeding instructions, the increased weight gain per episode noted in the orally-treated group was likely to be related to taking the fluid. The fact that no impact was made on hospitalization rates may be attributable to the study design which was based on answers to nutritional questions and not on the initiation of early treatment of diarrhea.


Lishnevsky MS et al, Oral rehydration treatment benefits Lao children with diarrhea, WHO Chron 31:421-422, 1977 (see No. 35).

Oral therapy for cholera patients has saved over $50,000 in parenteral fluid costs annually at the Infection Diseases Hospital in Calcutta, India. Oral therapy was instituted as a result of a study in which 92% of moderately to severely dehydrated patients were successfully maintained with frequent, small amounts of oral rehydration fluid (thus avoiding emesis problems). Oral therapy was publicized via mass media and lectures and seminars for health professionals, and the distribution of prepackaged glucose-electrolyte powder for oral rehydration was vastly increased, (600,000 packets requested in India in 1975). Training programs were planned for doctors and paramedics and studies were proposed to evaluate the feasibility of delivering oral rehydration at the village level.

Pierce NF et al, Oral fluid — a simple weapon against dehydration in diarrhoea. WHO Chron 31:87-93, 1977 (see No. 36).


Thomas K et al, Oral rehydration therapy in childhood diarrhea, a comparative study, Indian Pediatr 15:791-796, 1978 (see No. 39).


Based on an extensive and thoughtful review of the world's literature on oral rehydration, the author concluded that effective, readily available, safe, and inexpensive oral rehydration solution can decrease the morbidity, mortality, and associated malnutrition of diarrheal diseases. Specifically, oral fluids can be used as the sole treatment for mild to moderately dehydrated patients and can greatly reduce the volume of IV fluids used to treat severely dehydrated patients.

For easy distribution and to reduce the chance of errors in concentration, one prepackaged solution for use in all ages was recommended. Continued feeding during episodes of diarrhea was encouraged, especially in breast-fed infants. In cases of diarrhea in which stool electrolyte concentrations are lower than the oral fluid electrolyte concentrations, additional water intake may be required.
Oral therapy is effective in all but a small percentage of persons with dehydration. The major limitation is in the initial treatment of persons with severe dehydration or shock, altered state of consciousness, prolonged oliguria, severe vomiting, and severe stool losses.


The authors designed and carried out a community-based oral rehydration program administered without medically trained personnel in 2 socioeconomically and geographically comparable villages in rural Bangladesh.

In the study village, 18 local residents were selected for training in basic nutritional concepts and in the preparation and administration of the WHO-recommended ORS packet and were provided ORS packets for distribution in time of illness. A thorough community oral rehydration education program was also carried out. The second (control) village was informed that oral therapy was available in the nearby first village, but no education program or local distribution network were established. Neither village had qualified practitioners or easy access to a treatment center.

Diarrheal disease surveillance and mortality assessment were done by trained field workers who visited each household on a regular schedule. Families of persons whose deaths were attributed to diarrheal disease were interviewed by a physician, and a final review of the mortality assessment was made by an independent group of physicians.

During the study period, no evidence of diarrheal disease epidemics was seen, and both villages had comparable attack rates of diarrheal diseases. Oral therapy was given to 80% of the study village cases identified and to 30% in the control village. Only 3% of those with diarrhea in the study village took more than 2 packets of ORS per episode and only 2% of those in the control village took more than one packet. The case fatality rate for diarrheal diseases was significantly higher in the control village (2.4%) vis-a-vis the study village (0.5%) with the maximum difference in rates seen in infants.
This study indicated that an oral rehydration program which includes vigorous educative efforts and fosters a spirit of active community involvement can have a significant impact on diarrheal disease mortality.

Fazil et al, Treatment of children with diarrhea with UNICEF's oral rehydration salts in rural areas by midwives. (Unpublished document), (see No. 42).


In a continuation of a previous study of the effect of oral therapy on the nutrition of Filipino children, a treatment center in one rural village was provided the WHO-recommended glucose oral solution while a treatment center in a second, similar village dispensed an identical solution except that sucrose was substituted for glucose. The solutions contained equal weights of glucose and sucrose yielding glucose concentrations of 111 mmol/l and 56 mmol/l, respectively.

The investigators followed the methodology of the previous study which included medical staff evaluation of all ill children reporting to the treatment clinics and daily home visits during illness by the staff in order to continue education and encourage maintenance of a regular diet. Weights were monitored during illness and community-wide weight surveys were made four times annually with results compared to Philippine median standards.

Data from the current and previous studies showed no overall decrease in hospitalization or mortality with the oral therapy program. However, decreased rates of hospitalization and mortality from dehydration due to insufficient fluid intake were demonstrated. As found in the previous study, there were weight gains across individual episodes of diarrhea, even prolonged ones. Although the earlier report indicated greater weight gain over a period of months in children receiving oral therapy, no long-term effects on weight gain were shown at the conclusion of the second study. Use of non-specific anti-diarrheal agents were of no benefit and although the overall outcome was comparable, treatment with the sucrose solution did result in a 25% greater duration of diarrhea.

In treating over 1600 episodes of diarrhea of unspecified etiology, the study showed that oral therapy administered under close
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In treating over 1600 episodes of diarrhea of unspecified etiology, the study showed that oral therapy administered under close
Nalin DR et al, Comparison of low and high sodium and potassium content in oral rehydration solutions (in preparation) (see No. 68).

Pizarro D et al, Rehidratación por la vía oral en niños menores de un mes de edad. (Unpublished manuscript) (see No. 44).

Taylor PR et al, Oral rehydration therapy for treatment of rotavirus diarrhea in a rural treatment center in Bangladesh (Accepted for publication, Arch Dis Child) (see No. 45).
V. IMPLEMENTATION

Issues concerning implementation of oral rehydration programs are considered in this section. These include: the quality and type of training needed for those administering the program; location of administration facilities (e.g., rural treatment centers vs. homes); the method of distribution (e.g., packet vs. use of local sugar and salt); mode of preparation (e.g., packet vs. "scoop-and-pinch"); the assessment of fluid requirements and the provision of IV fluids to persons who cannot take initial oral rehydration treatment. There remains a need to develop oral rehydration programs incorporating the local cultural customs, beliefs, and practices.

Chatterjee HN, Control of vomiting in cholera and oral replacement fluid, Lancet 2:1063, 1953 (see No. 2).

Colle E et al, Hypertonic dehydration (hypernatremia): the role of feedings high in solutes. Pediatrics 22:5-12, 1958 (see No. 5).


This article included a general review of diarrheal disease in childhood including discussions of etiology and management. Some of the therapeutic techniques that were advocated by the author are now outmoded, but oral therapy was described as an effective means of rehydrating mildly dehydrated children. The solution recommended contained 2 grams each of sodium chloride and potassium chloride per liter of water. A home-prepared fluid containing 1 teaspoon of salt and 8 teaspoons of sugar per liter of water was also described. Either fluid is to be administered by cup and spoon. There was no discussion of the choice of composition of either formula.


The author outlined a plan for establishing rehydration centers in developing countries to deliver care for children with dehydration secondary to diarrhea. The author discussed the proposed administration of oral rehydration solutions by mothers under supervision. The possibility of then supplying mothers with a "saline mixture" for home maintenance was considered. The use of oral rehydration early in illness, proposed the author, could lead to reduced hospital admissions and reduced mortality secondary to diarrheal disease in children.


To try to find a method simpler than intravenous therapy to supply maintenance fluids to small children, intraperitoneal fluid administration was assessed in 8 adults and 26 children (aged 6 years or less). Children with significant dehydration, manifested by decreased blood pressure, were first rehydrated by intravenous therapy before maintenance intraperitoneal fluids were begun.

Intraperitoneal fluids were shown to be absorbed too slowly to be used for maintenance therapy in adults. In children, partial initial rehydration and maintenance (including replacement of on-going losses) therapy were successful in 16 of 19 patients. One of the failures had signs of peritonitis.

The limitations of intraperitoneal fluid hydration include the need for close supervision and sterile conditions. The 16% failure rate for treating children with mild to moderate dehydration was higher than the failure rate for treating such children with oral rehydration, which does not entail comparable risks of peritonitis and sepsis.

Nalin DR et al, Oral (or nasogastric) maintenance therapy for cholera patients in all age-groups, Bull WHO 43:361-363, 1970 (see No. 46).

The use of Kaolin, frequently recommended for the treatment of cholera prior to the introduction of fluid and electrolyte replacement therapy, had never been formally studied.

Cholera was experimentally induced in four adult dogs with surgically prepared jejunal loops, and the effects of Kaolin introduced into the prepared loops were studied. In human adults with cholera, a controlled trial of 300 cc. of Kaolin suspension instilled intragastrically was also conducted.

In the dog studies, Kaolin prevented diarrhea if it was mixed with cholera toxin before the latter was instilled into the prepared loops. Partial inhibition of diarrhea was produced if Kaolin was placed in the loop before toxin. Diarrhea volume did not differ from untreated controls if Kaolin was administered after toxin. Kaolin administration did not alter the diarrhea volume in humans, independent of treatment with tetracycline.

Kaolin was found to be an ineffective form of oral cholera therapy. The data suggested that agents which modify the intestinal response to cholera toxin may be more effective in reducing stool volume than agents which may neutralize the toxin.


Based on previous experience with 300 dehydrated young children during a gastroenteritis epidemic in Papua, New Guinea, a standardized approach to the management of diarrhoea was developed. From this experience, a decision was made to treat all dehydrated cases intravenously with standardized amounts of 2.5% Dextrose in half strength Darrow's solution followed by administration of oral therapy. Antibiotics were not routinely used. The mortality rate from diarrhoea during this epidemic was below 1%.
The standardized treatment regimen adopted was based on the five points: 1) dehydration, 2) diagnosis, 3) drugs, 4) diet, and 5) disaccharidase deficiency. Rehydration was accomplished intravenously (immediately following clinical detection of dehydration), through continued breast feeding, and by the use of oral fluid with electrolytes (either a sugar-salt solution with potassium and magnesium added or a sweetened condensed milk solution diluted with water 1:8). Starvation therapy for diarrhea was felt to be inappropriate for young children in developing countries since it can exacerbate malnutrition. Disaccharidase deficiency was a problem found in 25% of the malnourished children but in only 2% of those who were adequately nourished.

Nalin DR, Oral or nasogastric maintenance therapy in pediatric cholera patients, Trop Pediatr 78:355-358, 1971 (see No. 27).


Ugandan mothers were taught a simple, replicable method for mixing oral rehydration fluid.

The mothers were taught to add two pinches of salt (using the thumb and two fingers) and a four-finger scoop of sugar to a mug (pint) of water. Juice from one orange was added as available. Training was performed by an experienced mother under the observation of a clinic medical staff.

When a series of thirty pinches of table salt (10 each by three participants) and thirty pinches of sea salt (same method) were weighed, the mean weights were found to be in the range of 0.41 to 0.61 grams, plus or minus 15-35%. The weight of sugar was not similarly tested, but was felt to be approximately 30 grams.

Salt concentration is a crucial aspect of oral rehydration fluid, and the method described provided a simple means of obtaining a roughly appropriate concentration under supervision. Field trials to assess accuracy of measurement and efficacy of solution administration under village conditions are needed.


The author described a glucose-electrolyte solution (GE-SOL) which could be prepared using reagent-grade chemicals and measuring spoons in the following manner: sodium chloride - 1/2 teaspoon, sodium bicarbonate - 1/2 teaspoon, potassium chloride - 1/4 teaspoon, glucose - 2 tablespoons. These powders could be combined in a plastic container ready for dissolving in one liter of warm water.

Ten containers were prepared in this fashion, resulting in the following mean millimole/l concentration (+ 5%): sodium-81, potassium-18, chloride-71, bicarbonate-28, glucose-139. One person could prepare 100 such containers in an hour.

The use of spoons for measuring volumes of solutes for oral rehydration fluids was shown to be quick and reliable in this hospital-based study.


The author compared the sodium content of milk prepared from powder by English mothers to the content in milk prepared in hospital milk kitchens or in a laboratory. The urine osmolarity and creatinine of breast-fed and cow's milk-fed infants presenting for their first well-baby visit (6-10 weeks of age) were also compared.

The mean sodium content (32.7 mEq/l, range 22-66) of milk prepared by mothers was significantly greater (p less than 0.01) than that of milk prepared by the hospital staff (mean 26 mEq/l, range 25-26.8). Urine osmolality and urine creatinine were significantly higher in infants fed cow's milk than in breast-fed infants.

Three cases of hypernatremic dehydration were described, all in infants fed powdered milk formula. The hypernatremia was attributed to mothers using heaping measures of the powder in preparation rather than level measures as directed.

The findings in this study supported the concern that complications such as hypernatremia may develop if electrolyte powders are measured by volume in the field rather than prepared and packaged centrally.


Universal treatment of dehydration due to diarrhea by use of oral therapy was encouraged in this general review article which recounted the successes of oral rehydration programs in India, Bangladesh, and Indonesia. Educational and promotional programs to make oral therapy available to all sectors of society were encouraged.


Using clinical examples for demonstration, a method for training medical personnel in the recognition, prevention, and treatment of dehydration was detailed, including instruction on the preparation and administration of oral rehydration solution. Diagnostic considerations, possible additional therapeutic interventions, and nutritional guidelines were discussed.


The writer expressed concern that stool sodium and potassium losses in children with diarrhea may vary in different populations due to underlying states of nutrition, climatic conditions, and the variable nature of locally common enteric pathogens. The writer felt the use of a single oral rehydration solution, although a practical idea, may not be ideal for use in all infants under all conditions. Studies in many different populations of children are needed to assess the efficacy of oral rehydration, the author concluded.

The impact of the first hospital-based oral rehydration program in Nepal was described. One hundred children, 2 days to 14 years of age, were treated with a locally-produced oral solution (closely approximating the WHO-recommended composition) for mild to moderate dehydration or with intravenous (IV) therapy for severe dehydration. The etiologies of the diarrhea were not reported; all children received antibiotic therapy. Systemic infections were noted in 6 children, and 11 were judged clinically to be malnourished.

Twenty-one children died, 17 within the first 24 hours of admission. Difficulties in initiating IV therapy in some severely dehydrated cases were noted and might have partially accounted for 18 of the 21 deaths occurring in the less than 1 age group. The comparatively lower fatality rate using oral therapy was felt to be an early indication favoring the use of oral rehydration in hospitals.

In addition to providing oral rehydration therapy, facilities for administering parenteral fluids to severely dehydrated and otherwise complicated patients should be included in any oral rehydration program.


The successful use of oral rehydration solutions in clinical and field trials to treat all types of diarrhea in all age groups was documented. To overcome major problems in delivery, measurement techniques involving use of a syringe barrel or a plastic spoon were
described. If prepackaged solutions are to be used, the authors recommended a "kangaroo packet" in which salts are separately packed from glucose to provide longer shelf life. Detailed information was provided on use of these techniques.


Simple guidelines for treatment and prevention of diarrhoeal dehydration were presented in order to aid the training of primary health workers to prepare their own guidelines adapted to local needs and resources.

The dangers, treatment, and prevention of diarrhea were discussed along with information on the preparation and administration of oral rehydration solutions. Methods for evaluating nutritional status and for implementing educational programs were also included.


This preliminary evaluation of the Indonesian oral rehydration program included a description of the country's environmental conditions and the nature of its diarrheal disease problem. A diarrheal disease control program has been developed with the long-term goal of reducing the incidence of diarrhea by providing a safe water supply, good latrines, improved health education, and a comprehensive nutritional program.

To accomplish the short-term goal of preventing or reducing deaths due to diarrhea, a program has been established which encourages early administration of oral therapy to all persons with diarrhea, use of oral therapy to treat mild to moderate cases of dehydration, and use of initial intravenous followed by oral therapy for treating severe dehydration.

In implementing the program, oral rehydration salts packets will be provided to public health nurses, field workers, social workers, and village volunteers as well as to hospitals and treatment centers. Mothers will be educated in the efficacy, preparation, and administration of oral solution. A marketing study will be carried out.
The preliminary results revealed that the case-fatality rate in severely dehydrated cases admitted to hospitals and health centers has been reduced from 10-30% to 0.5% after initiating the dehydration treatment program.


This is a brief but helpful review of the pathophysiology, differential diagnosis, and management of childhood diarrheal disease. Home management and preparation of an oral rehydration solution containing 5% glucose were discussed. Salt was excluded from this homemade solution because it is "potentially more dangerous than useful unless it is accurately measured." Strong recommendations against the use of Kaolin, opiates, codeine, lomotil and other medications directed at suppression of symptoms were presented.

Salt is no more likely to be inaccurately measured than sugar, and a hyperosmotic glucose solution can produce the same problems as a hypertonic salt solution, despite the opinion expressed in this article. Both should be included in home prepared oral rehydration fluid as long as the parents can be properly trained in the preparation. Barring that, oral rehydration should take place under closer supervision by health-care personnel.


A missionary nurse working in a rural Nigeria hospital found that oral rehydration solutions prepared from powdered electrolytes and glucose were practical and effective in treating diarrheal rehydration in children.

Two solutions were used. Initially, oral solutions were made using Morley's formula of a three-finger pinch of salt and a three-finger scoop of sugar dissolved in a pint of water with the addition of the juice from one orange, if available. However, when several unexplained sudden deaths occurred which were presumed to be due to hypokalemic cardiac anhythmias, the investigators utilized a second formula-Hirschhorn's GE-SOL. GE-SOL consists of 2 tablespoons of glucose, one-half teaspoon of sodium chloride, one-half teaspoon of sodium bicarbonate, and one-quarter teaspoon of potassium chloride dissolved in one liter of water. Infants were either fed this solution by cup and spoon or had it infused, alternating with expressed breast milk, via nasogastric tube.

The number of infants treated in this manner was not stated nor was the clinical success rate, but the implication was that the method was highly satisfactory, both to the mother and the health care workers.
This general review article traced the effect of laboratory cholera research studies on the advances in clinical treatment capabilities. The advent of oral rehydration therapy has greatly simplified treatment of dehydration. Experience from ORT trials has shown that most persons can be rehydrated and maintained using oral rather than intravenous fluids if oral rehydration is started early enough; that clinical rather than laboratory criteria can be effective in assessing fluid needs; and that thirst can serve as the main criterion for administering fluids. A recommended electrolyte composition of the fluid was not discussed, but studies reporting that sucrose can be effectively substituted for glucose were cited.

Considerations in implementing an oral rehydration program were discussed using the experience in Indonesia as an example. Oral rehydration salts packets have been distributed to 2000 rural health centers, but it was estimated that only a small percentage of diarrheal cases were using the treatment centers. Involving village leaders in providing initial therapy was one strategy the author recommended to obtain wider coverage. Another method identified was promoting the local production of oral rehydration salts packets and the utilization of existing local distribution networks for marketing the packets. The widespread acceptance of oral therapy depends on the development of effective education programs individualized to the beliefs, practices and traditions of the society involved.

This letter described a program to evaluate the feasibility of training poorly-educated Southern Indian mothers to prepare the WHO-recommended oral rehydration solution in their own homes. Mothers who had brought children with diarrhea and some degree of dehydration...
to a hospital outpatient clinic were taught by a native nurse to boil water, mix in the contents of the packet, let the mixture cool, and administer it to the child. Obtaining correct volume measurements was a major problem as several local cooking utensils and glasses of various sizes were used.

After instruction, the mothers prepared the solutions in their own homes while a control group of mothers who received the same instructions prepared oral solutions under supervision.

Sodium concentration, measured in 66 samples produced without supervision, had a mean of 120 mmol/l (versus the 90 mmol/l expected from the packet) and a range of 39 to 510 mmol/l. A mean of 105 mmol/l and a range of 61 to 163 mmol/l was found in the 12 samples produced under supervision.

To reduce the chance for producing hypertonic solutions, the authors suggested designing packets based on the volume of the smallest size of local container. Also, by using smaller volume preparation, the authors theorized, contamination of the solution would be less likely.

The importance of establishing a uniform volume measure vessel for oral solution preparation and the need to provide a thorough training program were clearly demonstrated by these results.


Hypernatremic dehydration resulted when the parents of a seventeen-month-old child with diarrhea were instructed to give him only "glucose water." In the absence of clearer instructions, a hyperosmolar 15-20% glucose solution was prepared and fed. This apparently caused osmotic diarrhea leading to hypernatremic dehydration.

This report served as a warning that without proper training, persons preparing oral rehydration solutions at home may cause rather than alleviate problems.


The results of a program introducing a cup and spoon rehydration method in a Jamaican child care center were described.

Sixteen children (age range: 6 months to 5 years) with "sporadic, unspecified" diarrhea were treated with an oral rehydration solution (prepared using one "3 finger pinch" of salt and sodium bicarbonate
and 2 teaspoons of "Mist. potassium chloride" dissolved in 100 cc. of water). None of these children had to be hospitalized.

The author supported the early administration of oral therapy for diarrheal illness and early resumption of feeding if tolerated by the child. Use of a cup and spoon to provide small amounts of fluid at frequent intervals was recommended. For community-based programs, the fluid must be simple to prepare from easily available ingredients.


The author outlined an essentially clinical approach to the diagnosis, continuing assessment, and management of childhood diarrheal disease. Oral therapy with the WHO packet (ORALYTE or ORS) was recommended where excessive vomiting does not preclude its use. According to the author, oral rehydration should only be used when initial rehydration has been completed via 24-36 hours of intravenous infusion. No reference was made to the use of oral rehydration fluid for rehydration therapy.


The reliability of the pinch technique for salt measurement was tested using 4 groups of people.

In India, 127 persons measured crude salt and 78 persons measured refined salt 10 times each using the pinch technique. Refined salt was measured by 51 people in Trinidad (5 determinations each) and by 2 English people (10 determinations each).

An "unacceptably wide variability" in measured weights was found. Finger size was not correlated with pinch weight.

It was speculated that variability in weights may be related to intercultural differences in the use of hands in cooking and eating. The study demonstrated that before techniques like the pinch method are employed in making oral rehydration fluid in any locale, they must be carefully tested under the conditions found there.
This letter reported the success of a simultaneously-administered IV and oral rehydration program in severely dehydrated, hospitalized Indonesian children (ROSE: Rehydration, Oral, Simultaneous IV, and Education of mothers about diarrhea and dehydration).

In February and May 1976, 2 groups of children with dehydration and shock secondary to severe diarrhea were rehydrated by simultaneous administration of IV Ringer's lactate and an oral solution given ad libitum (in mmol/l: Na⁺-85, Cl⁻-70, HCO₃⁻-30, K⁺-15, and glucose 120). Breastfed children continued breastfeeding during treatment. A total of 165 children were treated in the 2 studies (95 in February and 70 in May) with 15 less than 12 months of age, 73 aged 1-6 years, and 77 aged 6-13 years.

V. cholerae was found in 48 of 63 stool cultures performed. Most children were discharged following 8 hours of therapy and on follow-up at 3 days, no deaths or significant clinical complications were noted.

The authors supported their conclusion that a simultaneously administered IV and oral rehydration program is efficacious by noting that the mortality from childhood cholera in Indonesia had fallen from 46% in 1963 to 10% in 1973 (when NaHCO₃ was added to IV fluids), to 3.5% in 1974 (when therapy of IV Ringer's followed by oral rehydration was instituted) to zero in the present study.
experts advised by nutritionists, are often based on a different set of concepts than those held by villagers. Feeding a child who is suffering from diarrhea is a basic and correct health lesson, but the idea may be abhorrent to mothers because they believe it could increase the amount of diarrhea. The need to design health education programs based on local customs and beliefs was clearly stated.

Lishnevsky MS et al, Oral rehydration treatment benefits Lao children with diarrhoea, WHO Chron 31:421-422, 1977 (see No. 35).


Although effective oral rehydration treatment programs have been frequently carried out in institutional settings, the authors noted that relatively few reports of successful management have come from community-based programs. A discussion of the problems in instituting a village-based oral rehydration program to treat childhood diarrhea cases in 13 rural Indian villages was presented. Most children were treated with a solution made in the home from local sugar, salt, and water.

An intensive training program was required to change the existing village practices of treating diarrheal disease and restricting food and milk intake during illness. Mortality from diarrheal disease decreased after initiating this training program which had placed primary responsibility for treating all but the most severe cases in the hands of auxiliaries and mothers.

The authors noted that the cost of using prepackaged solutions to treat all cases of diarrhea (most of which are mild and self-limited) could be prohibitive in areas with limited monetary resources.


Diarrheal diseases are a major cause of death in children less than five years of age, and virtually all these deaths occur in the developing countries. A simple and easily administered therapeutic approach such as oral rehydration is essential to reduce diarrheal mortality rates.
Information regarding the design and composition of oral rehydration solutions was presented and the problems of trying to treat all varieties of fluid and electrolyte loss with one solution were discussed. Since treatment of acute diarrhea is concerned with 3 objectives (treatment of shock, replacement of losses, and provision of maintenance needs), one oral solution may not be appropriate in all treatment situations. To illustrate, the authors pointed out that high solute rehydration solutions may have a lower safety margin (more likely to produce hypernatremia) in persons with increased insensible water losses and decreased renal concentrating ability.

In designing ORT programs, the authors felt, knowledge of local beliefs, customs, and practices is essential and the use of locally available fluids, such as soft drink, soups, and teas should be investigated as to their potential efficacy. The continuation of breastfeeding and early initiation of regular food intake during diarrheal episodes was encouraged.


This letter commented on practical, conceptual, physiological, and historical "fallacies" in the review article by Nichols and Soriano (see preceding abstract, "A critique of oral therapy of dehydration due to diarrheal syndromes," Am. J. Clin. Nutr. 30:1457-1472, 1977). Hirschhorn contended that lower sodium concentrations in oral rehydration solutions could result in hyponatremia and that treatment of seriously dehydrated children requires a high sodium concentration which can, at any rate, be tolerated by children less seriously ill.


In responding to Dr. Hirschhorn's critique of his article, Dr. Nichols continued the debate concerning the optimal composition for oral rehydration solutions.

Balance studies done during oral rehydration of children in developing countries support Hirschhorn's recommendation of the use of a 90/mEq/l sodium solution. Whether such a solution would be efficacious in treating children in developed countries has not been determined.


Pierce NF et al, Oral fluid—a simple weapon against dehydration in diarrhoea, WHO Chron 31:87-93, 1977 (see No. 36).


The efficacy of oral rehydration in the treatment of acute diarrheal disease in children was clearly stated, as was the opinion that this technology must be removed from the "official" health-care establishment and placed in the hands of "the people themselves" at the village level. The mothers of the developing world must be given adequate training so that they can accept the responsibility for administering oral rehydration therapy. To achieve this methods of health care delivery the hard-sell techniques of private industry must be copied with doctors taking the lead in the campaign.


Diarrhea is a major public health problem, causing an estimated 5 to 18 million child deaths in 1976. In addition, diarrheal disease can play a significant role in the development of malnutrition.

Despite diverse etiologies, diarrhea treatment is uniform, consisting of replacement of salt and water losses. The administration
administration of oral rehydration solutions is a simple technique and can be carried out by the families of ill persons. Loss of water and electrolytes should be considered as fluid-electrolyte malnutrition (FEM); thirst is an early symptom and is naturally countered by drinking.

Salt, sugar and water are natural dietary ingredients and should be regulated as foods, not medicines. Glucose-electrolyte packets should be in every home and commercial firms could be encouraged to manufacture and distribute rehydration drinks. Since over half the price of a liter packet (US 12 cents) is for packaging, provision of bulk supplies distributed through village outlets could reduce the price. Home rehydration with sucrose electrolyte solutions is also feasible.

Government officials, physicians, and mothers must be persuaded that deaths from diarrhea need not occur. This education must be done in the context of local beliefs, customs and practices.

Recent Philippine studies indicate that oral rehydration may have a positive effect on malnutrition. When combined with early refeeding oral rehydration could potentially have an even greater effect on malnutrition. Maternal participation is indispensible to the success of the strategies outlined above.


This report included a brief review of the epidemiology and public health importance of diarrheal diseases in children and described the WHO program for controlling these diseases.

Oral rehydration therapy has made possible an immediate program of mortality reduction. Feasibility and acceptability studies of oral therapy have been undertaken in Costa Rica, Egypt, El Salvador, Guatemala, India, Iran, The Lao People's Democratic Republic, Liberia, Nigeria, the Philippines, and Turkey in order to determine whether oral rehydration can be effectively administered through existing health services in countries with different cultures and health care methods. WHO-supported studies in the Philippines and Turkey have shown that oral rehydration may improve weight gain during diarrheal episodes and thus may have an ameliorative effect on malnutrition.

The proposed mechanism for the WHO program is to promote a partnership arrangement between WHO and national health authorities. The national programs should operate through existing primary health care infrastructures as much as possible.
The authors described a scoring system for grading severity of dehydration in Tunisian infants which permitted nursing staff to classify a patient as mildly, moderately, or severely dehydrated in under one minute. The system was based on observation of seven physical signs, using descriptive terms chosen by the nursing staff. Low-scoring infants were put on oral therapy; moderate-scoring infants were put on oral therapy if they accepted it without vomiting; high-scoring infants were treated intravenously, with scoring repeated every three hours. In each case, antibiotics were given only in the presence of specific indications. After a month of use, close agreement was achieved among the medical and nursing staff who scored the patients.

Eight hundred forty-one children aged one to 24 months were scored for dehydration during one summer. Gomez scores were presented. Seventy percent of admissions for diarrhea and rehydration were of undernourished children. Outpatients seen at the hospital often showed dehydration; those seen at the MCH center rarely did. Many children with low dehydration scores were admitted to hospitals because of malnutrition as evidenced by skin-fold.

Of all patients, 75 were admitted to the hospital and 44 treated intravenously. Thirty-one patients were treated intravenously in the MCH centers. Thirty patients died, including 27 who were undernourished. The authors felt that use of the clinical scoring system was preferable to attempting to ascertain exact loss of weight. Moreover, the resoring at three-hour intervals required nursing staff to observe the patient more thoroughly. Fatalities in the pediatrics department dropped from 26.1% to 13% after the introduction of the scoring system.

The advantages of this system included standardization of management norms for non-medical staff and reduction of physician workload. Undernourished children are a high-risk group among the dehydrated; the scoring system distinguished between malnutrition and dehydration. While the scoring system under discussion was used for summer diarrhea, the criteria chosen are independent of etiology and can be used in other circumstances in which dehydration might result, such as diabetes, hyperpyrexia, and "salt-losing" syndromes.

The author described the development of a simple plastic spoon with two deep cylindrical wells for measuring sugar and salt,
respectively, for preparing oral rehydration fluids in Indonesian homes. Cost of the spoon was 0.5 cents, U.S..

The spoon measured 4 grams of granulated sugar and 0.9 grams of table salt to be added to 200 cc of water (chosen because of the ubiquity of drinking glasses with 185-220cc capacity in Indonesia). In the study, mothers generally mixed "safe" concentrations of sodium chloride.

This letter described in general terms the reliability of a fluid preparation method in which measuring and mixing are done by the provider. Studies to determine the accuracy of solution preparation in the home remain to be done.

This study utilized a more "culturally available" volume for dilution than the liter. Such cultural differences in volume determinations may make worldwide standardization of oral rehydration fluid volumes difficult.


This was a review of the available alternatives for composition, production, distribution, preparation, and use of oral rehydration solutions. Although some questions remain unanswered in all of these categories, the author felt we should "get on" with utilizing oral rehydration therapy.


This book offered a comprehensive, well written and concise chapter on diarrhea, including associated complications and appropriate treatments. Diarrhea was clearly defined and a discussion of its various etiologies (cholera, giardiasis, dysentery, etc.) and specific clinical assessment was included. Breastfeeding throughout the diarrheal episode was strongly encouraged. The authors urged that giving food throughout the diarrheal episode is important because the child has a better chance of maintaining his nutritional state. Clinical signs of dehydration and methods of determining use of oral versus intravenous rehydration were reviewed. The section on rehydration covered intravenous and intraperitoneal rehydration and use of two kinds of oral rehydration.

Mothers should be taught to mix the oral fluids in a clinic setting before using it at home. Clinical examples can be helpful in showing the relationship between dehydration and diarrhea. Drugs are not necessary for most children with diarrhea unless a
causative agent is found. Some drugs may cause diarrhea and can harm the normal gut flora. The entire chapter (and book) was illustrated with helpful diagrams and charts about measuring, mixing and giving oral, intravenous, or intraperitoneal fluids.

The efficacy of oral rehydration in treating diarrheal dehydration was stressed along with the need to provide an educational program to supply information on diarrheal diseases, nutrition, and personal and food hygiene.


While evaluating childhood mortality data in 13 rural Indian villages the authors found oral rehydration therapy was not well accepted by mothers and was considered inferior by the village medical auxiliaries. A training program for the health workers was instituted, resulting in greater utilization of oral rehydration and a statistically significant decrease in the diarrheal disease mortality rate despite an increase in incidence of diarrheal disease over the same period of time (January 1971 to May 1973).

To provide a successful oral rehydration program, a continuous analysis of effectiveness of the program and in-service training based on the analysis is essential.


The reliability of using measuring spoons to determine the amount of sugar and salt needed to prepare oral rehydration solutions may be significantly compromised by the grade of solute available.

Using the spoons described by Morley and King (see abstract No. 120, "Spoons for making glucose-salt solution," (letter) Lancet 1:53, 1978), five grades of sodium chloride (reagent grade to coarse) as well as glucose and brown sugar were measured and then weighed at least five times each under the following four conditions - damp (normal climate circumstances) and leveled; damp, packed, and leveled; dried and leveled; and dried, packed, and leveled.

Coarse salt in the normal damp state, leveled but unpacked, had a mean weight of 1.8 to 2.4 grams, depending on the grade, instead of the expected 3.5 grams. Reagent-grade dried, packed and leveled sodium chloride had a mean weight of 3.5 grams. Glucose measured with the described spoon weighed less than expected unless it was dried, packed, and leveled (mean weight 19.3 grams; expected - 20 grams), whereas brown sugar had a mean weight of 19.6 grams damp and leveled.
and 23.4 grams damp, packed, and leveled. When a "pinch-and-scoop" method was used, two three-finger pinches of coarse salt delivered a mean of 4.4 grams, and a four-finger scoop of sugar delivered a mean of 18.3 grams.

Certainly the quality of local salt and sugar supplied and the contribution of absorbed or adsorbed water to their volume and weight must be considered when use of measuring spoons is advocated. Local variability of environment and supplies must be taken into account when standardized approaches are advocated.


The authors described a set of individually labeled measuring spoons with cylindrical wells to be used by junior health workers, not mothers, to measure the 20 grams of glucose, 3.5 grams of sodium chloride, 2.5 grams of sodium bicarbonate, and 1.5 grams of potassium chloride needed to produce 1 liter of oral rehydration solution. The spoons could be used at health posts to provide an easy and accurate method of preparing oral rehydration solution. Although the potassium spoon is red and the others blue, the potential of using the wrong spoon to measure an ingredient must be explored.

Nalin DR et al, Comparison of sucrose with glucose in oral therapy of infant diarrhea, Lancet 2:277-279, 1978 (see No. 64).


The author described the vagaries of home preparation of oral rehydration fluid, especially the variabilities in the quality and measurement of constituent (including the volume of dilution). A plastic bag containing pre-measured ingredients with instructions to fill it with water to a marked volume level was proposed. Such a bag could be locally manufactured and, according to the author, ought not to add substantially to the cost of packaging.

The problems of local availability of the high grade reagents needed and the technology for calibrating the volume of the plastic bag were not addressed.

The authors stated that immediate institution of maternal home oral therapy using a sugar-salt solution could decrease gastroenteritis mortality in preschoolers in the developing world.

The idea of oral rehydration has spread rapidly in Lago, Nigeria, based on a survey of new mothers, but less than 1/2 of the women aware of the treatment knew the correct proportions of the ingredients. Use of too much salt was a common error.

The authors felt that a simple measuring spoon giving the actual quantities of ingredients would improve the accuracy of mixing.


Rohde believes that the application of our present knowledge in public health and preventive medicine is more important than continued research. "Knowledge is not enough, and the quest for more often hinders the field application of what we already know."

Not usually considered in the realm of preventive medicine, Rohde feels effective home-based convalescent care is the first important step in preventing future illness in children. Rather than as a passive recipient of health services, the mother should be supported as the basic health worker providing primary care for her child. Greater attention must be paid to "mothering"—the poorly defined but crucial interaction between mother and child.

Not all illnesses have the same nutritional impact. Respiratory illnesses do not have the same effect as diarrheal diseases. More frequent diarrheal illnesses result in more severe weight deficits.

Rohde reported on a successful program in Java where mothers gather once a month to weigh their own children and record their weights. A remarkable finding was the large number of well-nourished, healthy children in poor communities. The mothers of these children are the real experts and they are encouraged in the monthly gatherings to share their experiences and child-rearing practices with their neighbors. The mothers become responsible for the program, view it with pride and concern; this, Rohde feels, accounts for much of its success. With UNICEF and World Bank assistance, Indonesia is trying to expand this approach to many of its 65,000 villages.


An evaluation of the efficacy of oral rehydration therapy to treat diarrheal dehydration was presented. Hospital, clinical, and home-based trials were cited and nutritional impact was discussed.

The controversy over the optimal composition for oral solutions was detailed as were alternative methods of delivery. The effect of oral rehydration on nutrition and its efficacy in very young infants, wrote the author, are areas requiring further studies.


This was a review, in news report style, of the importance of childhood diarrhea as a cause of morbidity and mortality in the developing world and of the efficacy of oral rehydration therapy in treating diarrhea. The WHO/UNICEF approach of distributing packaged glucose-electrolyte powder for dilution in a liter of water was described and compared to home preparation of oral rehydration fluid. Conflicting viewpoints on the composition, preparation, and delivery of the fluid were presented.


Encouraging oral rehydration therapy as a means of reducing acute diarrheal disease mortality is an immediate WHO objective. Use of a single, prepackaged mixture of sodium chloride, sodium bicarbonate, potassium chloride, and glucose was recommended. Such a mixture was shown to be acceptable to mothers of children with diarrhea in a study done in Turkey. UNICEF will assist in establishing local production and distribution of the prepackaged mixture and will cooperate with WHO in assessing the efficacy of various production and delivery strategies as well as their impact on diarrheal mortality.

The use of oral rehydration therapy to meet the varying needs of local programs was discussed as a major strategy in the Global WHO Diarrheal Disease Control Program. In addition to providing oral solution, facilities for parenteral fluid administration would be required for treating severely dehydrated patients, oral fluid treatment failures, and patients with complications.

The importance of using a single formulation (of the WHO-recommended composition) was stressed because of the administrative and logistical advantages. However, the need for providing additional water, especially to infants with non-cholera diarrhea or with only maintenance fluid and electrolyte requirements, was emphasized.

Prepackaged ingredients to be mixed with a volume corresponding to a readily available local vessel were recommended. A smaller-sized packet for a proportionately smaller volume of fluid may be more useful in infants. Further field evaluation must be done to determine the efficacy of the pinch-and-scoop or spoon methods of measurement.

In discussing research priorities, the authors identified a critical need for field studies to evaluate the accuracy, concentration, safety, and efficacy of oral solutions made from local ingredients in the home.


Diarrhea accounts for at least 25% and perhaps as much as 50% of all deaths among Egyptian children less than five years old. Approximately 75% of these deaths occur in the summer months. Breast milk and other foods are often withheld from children during bouts of diarrhea.

This paper described a project to distribute Oralyte to households in the Menoufia governorate of Egypt. The project represents the largest, most intensive effort to date to make oral rehydration salts and treatment information available for home use. The goal of the project is to reach the entire population of Menoufia governorate (population 1.7 million) by the end of 3 years.

Despite the rarity of liter-size containers in Egyptian households, Oralyte packets containing rehydration salts for mixture in one liter of water will be used in the project with instructions to mix one teaspoon per 200 cc glass. "Rehydran", an Egyptian-made packet, contains only 1/5 the salts of Oralyte and would be preferable to Oralyte but production cannot match the needs of this project. In a field test of mixing instructions given by community canvassers to village women, 75% of the women produced acceptable solutions but 25% prepared solutions with hazardous sodium concentrations.

This article examined the hypothesis that children with acute gastroenteritis will do well if full-strength milk feedings are continued throughout their illness.

Forty-six children between the ages of 6 weeks and 4 years who had diarrhea with no other underlying illness and who were less than 5% dehydrated clinically were randomly divided in a non-blind fashion into three study groups. Group I received full-strength milk feedings, and Group II received clear fluids (30 mEq/l sodium chloride and 220 mmol/l dextrose in water) until diarrhea "settled" and then full-strength milk. Group III received clear fluids until diarrhea "settled" followed by concentrations of milk increased by a quarter-strength every eight hours. Patients were discharged when full-strength milk could be tolerated without diarrhea. Stools were
examined for bacterial and viral pathogens. Number of stools and number of episodes of vomiting were noted but no determination of serum electrolytes, stool volume or duration of diarrhea were included.

Mean length of hospital stay was not significantly different for any group; median length of stay was not given. No effort was made to assess the comparability of the three groups in terms of demographic factors, clinical severity, prior nutritional status, nature of pathogens isolated, or duration or volume of diarrhea. Patients in Groups I and II did vomit significantly more frequently, but this was dismissed as being "not of sufficient severity to warrant a change in regimen." The authors concluded that children with acute gastroenteritis can tolerate full-strength milk. However, because the comparability of the three groups was not clearly described the data presented did not fully support this conclusion.


The report of a WHO Expert Scientific Working Group meeting reviewed the "state-of-the-art" regarding the interrelationship of childhood diarrheal disease and what has come to be termed "maternal technology." This includes child feeding practices, personal hygiene and food handling, and the provision of overall child care. The effects of maternal health on that of the child were also explored and a brief discussion of the use of oral rehydration solutions in the treatment of acute diarrheal disease was presented. The Group also formulated exhaustive recommendations for child care practices and for prospective research activities.


This was a useful review of studies that established the theoretical and practical bases for the current WHO-recommended oral rehydration solution composition and implementation scheme. Other aspects of the medical management of childhood diarrhea were discussed, including the importance of continued feedings and the use of intravenous therapy and drugs. The paper also contained recommendations for further research on the composition, effectiveness, production and delivery of oral rehydration fluid.


After reviewing the rationale for oral rehydration, this paper identified potential problems of implementation: shelf life of oral...
rehydration salts, delivery systems, maternal diagnosis of dehydration, mixing inaccuracies, and the need for nutrition and health education. A proposed operational study, adapted for ongoing revisions, would prepare for the integration of an oral rehydration program into the general health system.

Several service areas totaling 50,000 population would be included in the study, and a National Project Team would see the project through from inception to nationwide implementation. One group would produce and distribute oral rehydration powder and another would organize delivery of services. The functions of each group were described in detail; field operations were also outlined.

Evaluation is based on field data gathered through a simple recording system. Procedures were outlined to permit ongoing correction of operational defects through analysis of monitoring data.


The author presented an extensive and thoughtful analysis of the historical, physiologic, clinical, and epidemiologic evidence to support a treatment plan of rapid restoration of extracellular fluid, electrolytes, and bases for persons with diarrheal dehydration. This treatment plan has its basis in the use of a single oral rehydration solution for all ages. The sodium concentration of this fluid must be high enough to replace deficits on a volume-for-volume basis and, with the use of increased water and low solute fluid, be able to provide maintenance requirements without the use of adjunct therapy. In addition to oral fluid intake, early initiation of tolerated foods during a diarrheal episode was encouraged.

In a critical review of pertinent literature, the author disputed practices encouraging slow repletion of fluid losses, supplying lower sodium loads, (especially to infants), tailoring fluid therapy to each individual, and resting the bowel before beginning feeding.

The successful impact of oral rehydration on diarrheal disease morbidity and mortality was documented and the potential effect on malnutrition discussed.

Delivery of oral therapy was identified as the major target for future research efforts. For effective implementation of oral rehydration programs, the production, distribution, and administration of oral rehydration salts must be tailored to locally available supplies, containers and customs.


Nalin DR et al, Comparison of low and high sodium and potassium content in oral rehydration solutions (In preparation), (see No. 68).

Pizarro D et al, Rehidratación por la vía oral en niños menores de un mes de edad, (Unpublished manuscript), (See No.44).


In the emergency room of the National Children's Hospital, San Jose, Costa Rica, where 90% of infants with diarrheal dehydration had previously been treated with intravenous fluids, the authors examined the efficacy of oral rehydration treatment.

One hundred infants aged 18 days to 20 months with varying degrees of dehydration due to diarrhea were studied. They were examined and weighed on presentation and treatment with an oral rehydration solution was instituted (in g/l: glucose-20, sodium chloride-3.5, sodium bicarbonate-2.5, and potassium chloride-2.0). Mothers were taught to administer oral rehydration therapy and, as soon as clinical dehydration had disappeared, the infants were sent home to continue on oral fluid and/or milk. Normal feedings were instituted when stools became pasty or semi-formed. Mothers were to return with the child if illness worsened at home. In an effort to mimic field conditions, no laboratory determinations were performed. Antibiotics were given only for complicating infections or clinical evidence of shigellosis.

Ninety-two patients were successfully rehydrated without major complications using oral fluid alone. Mean rehydration time was 6.4 hours, and mean emergency room stay was 15.6 hours. Seventy-four percent stayed less than 24 hours. Thirteen infants returned after discharge, all because of inadequate instructions given to the mothers concerning oral fluid administration. Seven of these children required intravenous therapy. Discharged infants were not followed-up.
This study showed the feasibility of rapid rehydration by means of oral therapy and demonstrated that hospital stay and expense were dramatically reduced. Because patients were not followed up at home, the effectiveness of the program in teaching mothers the techniques of home oral rehydration was difficult to assess.
ORAL REHYDRATION THERAPY SEQUENTIAL BIBLIOGRAPHY

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II. CLINICAL

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III. COMPOSITION

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IV. IMPACT

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V. IMPLEMENTATION

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