ORAL REHYDRATION AND FEEDING: STATE OF THE ART IN DIARRHEA MANAGEMENT

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INTRODUCTION

Until the early 1970s, the standard and recommended medical therapy for all patients with dehydration due to diarrhea included intravenous (IV) therapy to replace water and electrolyte losses, the restriction of oral intake ("bowel rest") for at least 24 hours, and the gradual reintroduction of foods, beginning with clear fluids.

During the last two decades, revolutionary discoveries have led specialists in the field of diarrheal diseases to recommend dramatic changes in the clinical management of acute diarrhea, both in health care facilities and community settings. Since 1970, it has been recognized that most episodes of diarrhea-associated dehydration can be prevented and treated by the oral administration of fluids that have an appropriate electrolyte composition. Case management guidelines provided by the World Health Organization (WHO) recommend that intravenous rehydration be reserved for children with "severe dehydration" (as defined by the presence of two or more specified signs and symptoms) and for patients who are unable to take oral fluids, (such as patients with paralytic ileus). Patients who are initially rehydrated intravenously should be changed to an oral solution as rapidly as possible, usually within six hours. Optimal and appropriate management of diarrhea also includes continued feeding of solid foods during the episode and supplementary feedings after symptoms resolve.

The advocates of this approach point to a number of advantages of oral rehydration and continued feeding over the traditional approach relying on IV rehydration and "resting the bowel":

-Fewer complications of therapy occur with oral rehydration than with IV lines.

-Oral rehydration is less physically and emotionally traumatic for young patients than IV therapy.

-Oral rehydration and feeding during diarrhea prevent some of the adverse nutritional consequences of diarrhea.

-Oral rehydration and feeding during diarrhea provide nutrients necessary to heal the gut.

-The skill and training needed to prepare the solution and administer ORT are less than the skill and training needed to properly insert and monitor an intravenous line.

-Oral rehydration is substantially less expensive than IV rehydration.

Despite extensive evidence regarding the efficacy of oral solutions in correcting diarrheal dehydration and in lowering dehydration-associated mortality, (Cash et al., 1970; Mahalanabis et al., 1973; Rahaman et al., 1979; Lasch et al., 1983; Parker et al., 1984), oral rehydration therapy and continued feeding are not universally implemented in health care settings. The World Health Organization's reviews of diarrheal disease control programs in developing countries indicate that physician resistance is a common and major obstacle to the adoption of oral rehydration and feeding by other health workers and by parents (WHO, 1985b; WHO, 1985c; WHO, 1986b; WHO, 1990). Despite the endorsement of oral rehydration by the Committee on Nutrition of the American Academy of Pediatrics (AAP, 1985), the most common hospital approach to managing diarrhea in the United States remains intravenous rehydration and delayed resumption of full feeding (Snyder, 1987). Some prominent pediatric textbooks refer to WHO's guidelines, but then recommend withholding oral intake in patients on IV therapy until the rate of stooling decreases (Robson, 1987).

A broad range of reasons have been suggested to explain the reluctance of physicians to adopt the new therapeutic approach to diarrhea management. Among the most common are:

-Perceptions that oral rehydration is a second line or "poor man's substitute" for IV therapy, and not as effective as the more expensive therapy in treating dehydration.

-Concerns about the safety of the electrolyte composition of solutions prepared from ORS packets[1], particularly when given to neonates and young infants.

-Fears that giving food and fluids orally will increase the volume or frequency of stools and give the impression that the diarrhea is getting worse.

-Beliefs that oral rehydration and feeding are inappropriate whenever vomiting is present.

-Reluctance to change or give up existing practices.

-Failure to recognize the cost and potential risks of IV therapy.

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[1]In this document, the term "ORS" solution (Oral rehydration salt solution) refers to a solution prepared from packets that have been manufactured according to the formula recommended by the WHO. The term "Oral rehydration therapy" (ORT) is used generically to refer to any fluid that is given by the oral route for the purpose of preventing or treating dehydration.

-Perceptions that oral rehydration and continued feeding are not technically sophisticated and therefore not as "modern" as intravenous therapy.

-Folk traditions as well as medical traditions that discourage feeding during diarrhea.

-Concerns that administering fluids orally requires more staff time than inserting and monitoring an intravenous line.

-Institutional characteristics and reimbursement policies that encourage the routine use of intravenous therapy.

This paper critically considers some of these concerns regarding current recommendations for diarrhea management. It begins with a description of the physiologic basis of oral rehydration. The following sections examine the available evidence concerning the advantages and disadvantages of using oral rehydration versus intravenous therapy for the treatment of diarrhea-induced dehydration. The final sections review the literature regarding the effects of continued feeding during diarrhea. The discussion focuses on the management of diarrhea in young children (under five years of age) in the health facility setting. The use of ORT in the home for the prevention of dehydration will not be addressed.

The Physiologic Basis of Oral Rehydration

The concept underlying oral rehydration is that fluids and electrolytes lost during diarrhea can be replaced by solutions that are administered by mouth and absorbed through the gut. Work done by Darrow in 1946 laid the foundation for developing this concept (Darrow, 1949). He determined that sodium chloride, potassium, and base are the essential electrolyte components needed for fluid replacement therapy.

ORT was initially developed for use in adults during cholera epidemics. Its scientific basis rests on the finding that sodium and certain food-derived molecules such as glucose are linked in their active transport across the mucous membrane of the small bowel. Thus the presence of glucose, galactose, neutral amino acids, some disaccharides, and some dipeptides stimulates and enhances the rate of sodium absorption by the small intestine. As water passively follows sodium molecules across the mucous membrane, the absorption of water from the small intestine is also increased in the process (Hirschhorn, 1982).

A number of key studies conducted in the 1960s showed that the intestinal co-transport of glucose (and the other compounds listed above) and sodium remains relatively unaffected in secretory diarrheas such as cholera. This was followed by the clinical demonstration that orally administered solutions containing glucose can sufficiently enhance the absorption of salt and water during cholera diarrhea so that substantial ongoing fluid and electrolyte losses can be replaced by this mechanism (Phillips, 1964; Hirschhorn et al., 1968; Pierce et al., 1968a, 1968b). This approach has been successful in treating dehydrated patients of all ages (Pizarro et al., 1983a; Abdalla et al., 1984), and in diarrheas caused by a range of infectious agents in addition to V. cholerae (Sack et al., 1978; Taylor et al., 1980; McLean et al., 1981; Santosham et al., 1982). When WHO established its Control of Diarrhoeal Diseases (CDD) program in 1978, case management (defined as oral rehydration and continued feeding for the majority of cases) was the cornerstone of that program. Since then, policies on appropriate case management have been adopted by over 100 national CDD programs.

To standardize therapy, facilitate distribution, and simplify instructions on preparation and use, WHO has recommended that a single universal formula be used for the manufacture of oral rehydration salt (ORS) packets. For patients who require IV therapy initially (patients in shock or with severe dehydration), this single ORS formulation is recommended for use as soon as the patient's condition has stabilized.

The standard ORS formula recommended by WHO is given below:

Ingredients (grams/l)	Resulting electrolytes (mMol/l)
sodium chloride 3.5	sodium 90
potassium chloride 1.5	potassium 20
trisodium citrate 2.9	chloride 80
(or sodium bicarbonate 2.5)	citrate (or bicarbonate) 10 (30)
glucose 20 (or sucrose 40)	glucose (or sucrose) 111

A base is included in the formula to correct acidosis. Although either can be used (Hoffman, 1985; Salazar-Lindo, 1986), trisodium citrate is preferred to sodium bicarbonate because of its longer shelf life. Potassium chloride is added to correct the hypokalemia that typically results from excessive diarrheal losses.

Despite variations in stool electrolyte losses in diarrheas of different etiologies (Molla et al., 1981; Mahalanabis et al., 1974), diarrheal dehydration is usually isotonic. Physiologically, the optimal solution for rapid rehydration should be isotonic or hypotonic to plasma (300 mosmoles/l or

less) to minimize osmotic water shifts into the intestinal lumen. The sodium concentration should approximate that of plasma to sufficiently replace deficits and ongoing losses. With the addition of glucose (to stimulate sodium absorption) and other electrolytes, it is necessary to use a lower sodium concentration than the plasma level in order to maintain isotonicity of the solution. Balancing these considerations, the 90 mMol/l sodium concentration in the standard ORS has been found to be the optimal amount in an oral rehydration fluid. More sodium might risk dangerous salt overload or osmotic diarrhea. Rehydration can be achieved with a lower sodium concentration, but would require the administration of larger volumes of fluid, the excretion of a large amount of dilute urine, and would probably occur more slowly. Chloride should be replaced at the same concentration as sodium since sodium and chloride losses and absorption are closely linked. The recommended ratio of glucose to sodium concentration is 1 to 1 for maximal glucose ennancement of sodium absorption (WHO, personal communication).

The Efficacy of Oral Rehydration Salt Solution (ORS) in Treating Dehydration

Various criteria can be used as indicators of efficacy in treating dehydration. This section will focus on the ability of ORS solution and IV therapy to replace fluid and electrolyte losses, as indicated by resolution of symptoms of dehydration and normalization of laboratory values.

A number of randomized controlled trials, conducted in both developed and developing countries, have compared clinical and physiologic aspects of different rehydration regimens (Table 1). Only randomized studies that compared ORS with intravenous administration of fluids during the rehydration phase of therapy were included. These studies varied in the composition of the ORS and IV rehydration solutions used (particularly in relation to sodium content), in the rehydration and feeding regimens adopted, and in the types of patients, severity of dehydration, and etiology of diarrhea studied. Most did not provide detailed data on the type and amount of foods or fluids given in addition to the rehydration fluids.

In four of the nine studies reviewed, the ORS failure rate was either zero or less than one percent[2]. In eight of the nine studies, the failure rate was less than ten percent. As expected, ORS failure rates are higher in cases of severe

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[2]ORS failure rate is defined as the percentage of patients who could not be successfully rehydrated and maintained orally and who therefore required intravenous therapy.

dehydration, especially those caused by infection with V. cholera (Mahalanabis et al., 1974). In one very small study conducted in the United States, the slightly higher failure rate (13%) due to persistent vomiting may have been caused by concomitant urinary tract infection in two patients (Listernick, 1986).

Data on the relative speed with which ORS or IV therapy corrects metabolic abnormalities and dehydration are limited. Many of the studies cited in Table 1 did not specifically comment on these parameters. The four studies that examined the speed of correction of acidosis (Vesikari et al., 1987; Tamer et al., 1985; Listernick et al., 1986; Brown et al., 1988) suggest that ORS is at least as efficient as IV therapy in correcting acidosis. In one of the studies (Tamer et al., 1985), correction occurred more rapidly in patients undergoing oral rehydration with ORS than in the group receiving IV therapy.

In a number of studies, laboratory parameters indicative of rehydration status (such as hematocrit, BUN, and plasma protein) normalized faster in the IV groups. However, the rate of improvement in signs of dehydration was similar in the ORS and the IV groups, suggesting that the more rapid correction of electrolyte abnormalities achieved with IV therapy is not clinically important.

Overall the studies of Table 1 indicate that in a small proportion of all cases of diarrhea (estimated at less than one percent), IV therapy will be required at some time during treatment. Among patients presenting to ambulatory facilities, approximately five percent will require in-hospital IV therapy.

The Safety of the Current Formulation of ORS

Some physicians voice concern that the 90 mMol/l sodium concentration in the WHO formula is too high and potentially dangerous for neonates whose immature kidneys may not be able to excrete excess sodium. The issue has been of particular concern in developed countries where the most prevalent diarrhea in young children is due to rotavirus for which stool sodium concentrations average less than 40 mMol/l (Aballi, 1975; Finberg, 1984; Bart and Finberg, 1976). This has led some pediatricians to be reluctant to use ORS solution in neonates, and others to suggest that there be two solutions: one with a sodium concentration in the range of 75-90 mMol/l for treating dehydration in children; and one with a lower sodium concentration (40-60 mMol/l) for treating dehydration in neonates and for maintenance therapy in older children (Finberg, 1984; AAP, 1985).

A few studies have reported some transient hypernatremia during rehydration with ORS, but this has been for the most part asymptomatic. One study reported symptomatic hypernatremia in infants under three months of age, but the ORS was given in large volumes and through a nasogastric tube (Bhargava et al., 1984). Other studies have shown that there is no reason to advocate a solution with a sodium concentration less than that in the WHO formula. Hypernatremia rarely occurs during rehydration with the WHO formula, if given according to established guidelines (Merson, 1985). During the rehydration period, usually lasting four to six hours, ORS may be safely given without other fluids to children over six months of age. The continuation of breast-milk (which is low in sodium) during the rehydration phase will avoid the risk of hypernatremia in children less than six months of age (Datta et al., 1984). Non-breastfed infants less than six months of age should be offered additional fluids that are low in sodium (such as plain water) during rehydration. For all children, additional fluids and food should be given along with ORS during the maintenance phase (Pizarro, 1980).

One of the chief reasons the risk of hypernatremia is of concern to pediatricians is that it may cause convulsions. However, a review of the complications of rehydration therapy indicates that the incidence of convulsions associated with rehydration therapy has been at least as great with IV therapy as with the use of ORS (Table 3). In fact, there is some evidence that ORS can be better than IV therapy for the treatment of hypernatremic dehydration. One study (Pizarro et al., 1983b), carried out in well-nourished, bottle-fed infants in Costa Rica showed that when ORS (with some plain water) was used to rehydrate infants with hypernatremic dehydration, the incidence of convulsions was eight percent compared to a rate of 14% in comparable children receiving IV therapy.

These considerations lead to the conclusion that the concerns about ORS-related hypernatremia leading to convulsions are unfounded. WHO's recommendations regarding the administration of supplemental water or breastmilk along with ORS avoid the confusion and potentially dangerous errors that might occur if two different formulations (one with a higher sodium concentration for maximally effective rehydration, the other at a lower concentration for maintenance) were made available. In fact, when used properly, ORS is less likely to result in hypernatremia than IV therapy, and has been demonstrated to be more effective in actually treating hypernatremic diarrheal dehydration than intravenous fluids.

The Nutritional Effects of Oral versus Intravenous Rehydration

In developing countries where many children suffer from some degree of malnutrition, diarrhea is both an important nutritional disorder as well as a fluid and electrolyte problem (Rohde and Northrup, 1986). Failure to gain weight or actual weight loss over the course of a diarrheal episode is also observed in children from developed countries (Vesikari et al, 1987). Thus when comparing the advantages and disadvantages of IV versus oral rehydration, it is important to consider whether either affects the intake or absorption of nutrients during or following the acute diarrheal episode.

There are a limited number of studies that address the nutritional effects of the method of rehydration separately from the effects of feeding. In a well designed study reported from Finland, 37 children hospitalized for acute diarrhea and dehydration were randomly assigned to receive oral rehydration or intravenous rehydration with nothing by mouth for 12 hours (Vesikari et al., 1987). The reintroduction of normal feedings was successful in 17 out of 22 orally rehydrated children after 12 hours, but was successful in only six of 15 children receiving intravenous therapy. This difference was statistically significant. Furthermore, the orally rehydrated children showed a 2.9% weight gain by the time of discharge whereas the intravenously treated children did not gain weight by the time of discharge. The authors concluded that the oral fluid administration had stimulated the recovery of appetite and normal feeding behaviors.

A community-based study in the Philippines (International Study Group, 1977) gave identical dietary messages to mothers bringing their children to clinics in two communities. The importance of continued feeding and giving fluids was stressed in both areas. ORS was provided in one of the study areas. Children between one and five years of age in the ORS group had a greater average weight gain during episodes of diarrhea and over a seven-month period compared to the group that did not receive ORS. There was no significant difference between groups in children under one year of age. Because the intervention was given to non-dehydrated or mildly dehydrated children in a community setting, the effect of IV rehydration was not evaluated.

Another community-based study was reported from The Gambia (Rowland and Cole, 1980). However, in this study, no dietary or feeding instructions were given to either the experimental or the control subjects. Families in the experimental group were visited by a field worker every day and a glucose-electrolyte mixture was given to mothers of children with diarrhea. The earlier introduction of ORS was associated with a greater mean

weight gain during a three-month study period compared to the control group receiving ORS later in the course of illness, although the difference was not statistically significant. The fact that families in the control group were not visited at home raises the alternative explanation that any observed differences may be due to the effect of daily monitoring.

The mechanism by which ORT increases dietary intake and weight gain cannot be determined from these studies. The results are nevertheless reassuring and suggest that the administration of ORS during diarrhea may have positive nutritional consequences.

The Effect of ORS on Stool Volume, Stool Frequency and Duration of Diarrhea

The effect of ORS on stool volume and stool frequency is difficult to assess because there are a number of confounding factors, including the types and varying administration of additional fluids and food. Five of the randomized controlled studies in Table 1 examined stool volume (Santosham et al., 1982 in both Panama and the USA; Brown et al., 1988; Sack et al., 1978; Vesikari et al., 1987). Of these studies, two reported similar stool volumes initially (ranging from the first eight to 24 hours) in children treated with ORS solution and children treated with IV therapy. In both of these, the total stool volume over the duration of the episode was greatest in the IV-treated group. In the third study, total stool output was significantly less in the IV group. The fourth study reported a lower purging rate in the ORS group, but the difference was not statistically significant. The fifth study noted higher initial stool volumes in patients treated with ORS solution, but there was a "compensatory" increase in stool volume in the IV group after the first two days.

Two studies examined stool frequency (Tamer et al., 1985; Singh, 1982). One of the studies reported that stools were more frequent in the ORS group during the first day of treatment, and one found that the reduction in stool frequency was similar in both groups.

Seven of the nine studies listed in Table 1 reported the duration of the diarrhea episode. In five of the studies, the duration was the same with oral rehydration as with intravenous rehydration. Two studies reported a shorter duration in the ORS treated groups. A number of studies suggest that treatment with ORS is often associated with reduced mean duration of hospital stay (Vesikari et al., 1987; McLean et al., 1981; Listernick et al., 1985).

Although the studies reviewed report inconsistent findings, it is helpful to note that the weight of the evidence does not justify concerns that ORS substantially increases stool output, frequency or duration. The results of a few studies indicated an increase in stool output with use of ORS, but none reported an increase in stool frequency or diarrhea duration with ORS. Most concluded that ORS is superior or equal to IV rehydration in terms of these three parameters.

It is important to note that the nine studies referenced above compared glucose- or sucrose-based ORS with intravenous fluids. It has more recently been shown that the administration of ORS prepared from certain cereal starches or proteins (instead of simple sugars) causes a decrease in total stool output and duration of the diarrhea when compared with glucose based ORS (Molla et al., 1989; Greenough, 1987; Mehta and Subramaniam, 1986; Molla et al., 1985; Mahalanabis and Patra, 1983; Patra et al., 1982). The reduction in stool output is greatest (as much as 50%) in cases associated with severe purging due to cholera. Therefore, it can be extrapolated that food-based ORS is far superior to IV therapy in terms of reducing stool output and duration. Its potential use in health facilities strengthens the argument against the routine use of intravenous therapy in all cases of diarrhea-associated dehydration.[3]

The Use of Oral Rehydration During Vomiting

Vomiting and high purging rates in the face of insufficient intake account for many of the ORS failures, but these must be seen in light of the overall failure rates. The failure rate due to vomiting is very low despite the fact that the majority of patients who present with diarrheal dehydration have a history of vomiting (Table 2). In the one IV-ORS comparison study that reported the frequency of vomiting during the different treatment regimens, the frequency was similar in the ORS group to that in the IV group (Sack et al., 1978).

Thus vomiting is not a reason to withhold therapy with ORS and rarely prevents successful oral rehydration. As more ORS is given and dehydration improves, vomiting will decrease (Pizarro, 1980). Also, most patients who vomit put out much less than the amount administered, resulting in a net gain of fluid.

It should be recognized, however, that vomiting is very disconcerting and discouraging for the mother, as well as the

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[3]The topic of food-based ORT is reviewed in another PRITECH manuscript entitled "Food-Based ORT: Is it the magic solution for diarrhea?"

physician or health worker. Special education is essential to convince those involved in the rehydration process that the patient is being rehydrated despite the losses due to vomiting. It is often helpful to tell the mother to wait ten minutes before resuming rehydration, and then to give ORS more slowly. In a small proportion of cases, the severity of vomiting may necessitate the use of an IV until the dehydration and acidosis are sufficiently corrected and the vomiting lessens.

The Complications and Risks Associated with Oral Rehydration Therapy and Intravenous Rehydration Therapy

Hypernatremia was discussed as a potential complication of rehydration therapy in a preceding section. However, other risks are associated with IV rehydration as well as with oral rehydration.

The complications of peripheral infusion therapy have been well described in developed countries (Maki, 1976; Maki, 1986; Hamory, 1987), and include local infection, sepsis, phlebitis, fluid overload resulting in pulmonary edema, severe electrolyte and metabolic imbalances, emboli, and infective endocarditis. These complications are generally more common with the use of catheters over prolonged periods of time. As such they do not reflect the level of risk associated with IV rehydration therapy, which theoretically should be completed in 4-6 hours.

Potential complications of IV use in the setting of rehydration therapy in children include fluid overload and pulmonary edema from over-aggressive treatment or poor supervision, convulsions from IV fluids with inappropriate compositions, skin necrosis at the site of the needle or catheter, local infection, and emotional trauma. In addition to problems relating to the IV line per se, there is the potential problem of contamination of IV fluids, either at the time of original constitution or as a result of subsequent manipulation (Lapage, Johnson, Holmes, 1973; Stjernstrom, Gunnarsson, Wikner, 1978). Finally, the expense of IV hydration and difficulties in placing and maintaining IV lines in developing countries may result in a delay of treatment and worsening of hydration status, or failure to receive treatment at all if the patient's family cannot afford to buy the IV fluid and IV set.

Fluid overload is a potential complication of oral rehydration therapy as well. However, the decrease in thirst that occurs when the patient has been adequately rehydrated may guard against excessive ingestion. There has been an ongoing concern that the use of flavoring in ORS might lead children to

overdrink, thus bypassing this protective advantage. However, evidence that this is a problem is limited to a single report (Nayyar, Ramzan, Khan, 1987). Recent studies done in Egypt show no increased risk of fluid overload with flavored ORS (WHO, personal communication).

Based on the reported complications in the randomized controlled trials comparing IV therapy with ORS during the rehydration or maintenance phase of therapy, it appears that ORS is safer than IV therapy (Table 3). Although most patients in both groups experienced no complications, the more serious complications (electrolyte imbalances, convulsions, phlebitis, sepsis, paralytic ileus, and hydrothorax) occurred in the IV treated groups. Less serious complications (peri-orbital edema and abdominal distension) tended to occur in groups receiving oral therapy.

The Psychological and Social Benefits of Oral and Intravenous Rehydration

There is no direct information about the psychological stress of rehydration in young children. However, diarrheal diseases commonly occur in the age group (six months to four years) identified as being most vulnerable to the stress of the hospital environment (Thompson 1985).

There are several theoretical advantages of oral rehydration over IV rehydration in reducing stress in the hospital setting:

1- A number of studies have documented that rehydration with ORS is associated with reduced hospital stays (Vesikari, 1987; McLean et al., 1981; Listernick et al., 1985). If reducing the amount of time in the hospital reduces stress, rehydration with ORS may be advantageous.

2- Unlike intravenous therapy, administration of ORS requires the presence and active participation of a caretaker, usually the mother or other family member. This may be comforting and reassuring to the child.

3- Rehydration with ORS solution is a non-invasive and painless treatment that does not require needles or other equipment unfamiliar to a child. The only exceptions to this are the few cases in which a naso-gastric tube is used to administer ORS. In contrast, children receiving IV therapy are often restrained.

An additional advantage of oral rehydration in the health facility is that it teaches, models and reinforces behavior that can continue at home and that can be used to prevent dehydration during future diarrheal episodes.

The Relative Costs of Oral and Intravenous Rehydration Therapies

Oral rehydration salts are composed of inexpensive raw materials. The cost of producing a packet of ORS is estimated at less than 10 U.S. cents. If the cost of materials and supplies is the only consideration, ORS packets will consistently prove to be cheaper than the materials and supplies needed for IV rehydration.

The few studies that compare the total cost per patient of IV rehydration with oral rehydration show that considerable savings can be realized with ORS in developing countries (Phillips et al., 1989; Samadi et al., 1983; Srivastava et al., 1985; WHO, 1984). The difference in cost is especially large, even in developed countries, if patients treated with intravenous fluids are routinely admitted to the hospital, whereas patients treated with ORS solution can be treated in an outpatient or "holding" area. In the United States, Listernick et al. (1986) did cost calculations as part of a randomized controlled trial comparing intravenous and oral rehydration. They found that the mean costs of outpatient therapy with ORS (US$ 272.78) was significantly less than the mean cost of IV therapy, either given in the outpatient area (US$ 379.20) or in the hospital (US$ 2,299.50). The study did not report the costs of inpatient hydration with ORS solution, nor did it take into account the different amount of staff time required to administer each of the treatments.

The Effect of Feeding on Stool Volume, Stool Frequency and Duration of Diarrhea

Appropriate diarrhea management includes not only the replacement of water and electrolytes, but also continued feeding during and extra feeding after an acute episode. Continued feeding not only protects against the adverse nutritional consequences of diarrhea, but may also decrease total stool output and shorten the duration of the episode. The following sections explore the scientific background and clinical evidence behind these feeding recommendations.

Studies that evaluate the effect of feeding on stool volume and frequency must be reviewed cautiously because there are many factors (in addition to whether the child is fed or starved) that influence these indicators. The total osmolality of oral

rehydration solutions, foods, and other liquids administered is an important factor in determining stool output. High concentrations of glucose contained in sugared tea, soft drinks, and certain commercial fruit juices are incompletely absorbed in more severe cases of diarrhea, and can cause net water loss from osmotic diarrhea.

The first study that measured the effect of feeding during diarrhea was done by Chung in 1948. The study evaluated male infants between 12 days and three months of age presenting with acute diarrhea, dehydration and acidosis. All were rehydrated orally while intake and outputs were measured in a metabolic unit. The effects of giving a formula consisting of evaporated milk, corn syrup and water were evaluated. Chung reported increased stooling with early feeding of this formula. However, he argued against the practice of "therapeutic starvation" because he found that, despite the increased stooling, the absorption of nutrients continued, and the greater the intake, the greater the absorption.

Later studies suggested that the continuation of breast-feeding does not increase stool output and may have a beneficial effect on stool frequency and consistency. In Egypt, Kassem et al. (1983) divided infants presenting with diarrhea into two groups. One group received nothing by mouth except for ORS until rehydration was complete; the other group received ORS and breast-milk from the start of therapy. Twenty-four hours after admission, both groups showed a similar drop in the frequency of stools, and the breast-fed group showed a statistically significant improvement in stool consistency. Results of another study in Burma indicate that a regimen consisting of breast-milk plus standard ORS is superior to ORS alone: stool frequency and volume were less, while clinical recovery was more rapid in the group receiving breast milk (Khin-Maung et al., 1985).

In a recent study conducted in Peru, Brown et al. (1988) studied the effects of feeding a formula diet of different dilutions to infants with diarrhea, compared with giving ORS alone and with giving IV fluids alone during the initial two days of therapy. Stool output was lower initially in infants receiving IV therapy and delayed feeding. This effect, however, lasted only for the period of fasting (two days). There was no difference in stool output between the groups receiving full strength and dilute formula.

There are several studies that suggest that early feeding does not prolong the duration of the diarrhea, and may shorten it. In Indonesia, Soeprapto et al. (1979) compared early reintroduction of foods, proceeding to a normal diet on the fourth day, with a regimen of slower reintroduction over nine to

11 days. The duration of diarrhea was not affected by the feeding schedule.

In Finland, Isolauri et al. (1985) randomized patients to various treatment groups. Regardless of the type of oral fluid or the presence or absence of cholestyramine in the treatment regimen, rapid feeding (full feeding at 24 hours) was associated with a statistically significant decrease in diarrhea duration.

In a recent outpatient study conducted in the U.S.A., infants were randomly assigned to receive either a treatment diet (24 hours of electrolyte solution then dilute soy formula, dilute cow's milk formula, or undiluted soy formula) or their usual formula. Patients on an unrestricted diet averaged fewer days of diarrhea, fewer total stools, and less weight loss than those receiving a treatment diet, although the differences were not statistically significant (Margolis et al., 1990).

Concerns about diarrhea-induced lactase deficiency and the osmotic effect of undigested lactose has sometimes led to recommendations to eliminate, delay, or dilute milk during diarrhea. However, the data indicate that breast-milk is universally well tolerated during diarrhea (Khin-Maung et al., 1985; Kassem et al., 1983) and that clinically significant lactose intolerance with feeding non-human milks occurs in only a small proportion of cases (Haffejee, 1990). Simple alteration of feeding practices such as mixing milk with cereals, will obviate the complications of non-human milk feeding. This approach is preferable to recommending discontinuation of non-human milk as it avoids the danger of mothers misunderstanding instructions and withholding milk following resolution of the diarrhea. A few experts recommend that infants who are exclusively fed with non-human milk should either be given diluted milk or be managed in a hospital under clinical supervision due to the potential for life-threatening complications of severe lactose intolerance (Brown, 1989). Although this recommendation is controversial, it is generally advised that these infants be closely monitored for worsening of their diarrhea.

In summary, there is no support for the practice of "resting the bowel" during diarrhea. Continued feeding reduces the duration of the diarrhea and improves the consistency of the stools, and most studies conclude that continued feeding does <u>not</u> increase stool output or frequency.

The Anatomical and Physiological Effects on the Gut of Feeding versus Starvation During Diarrhea

At least part of the rationale behind the practice of "therapeutic starvation" is the belief that the bowel is injured during diarrhea and requires a period of "rest" in order to promote healing. Animal and human studies related to this issue focus either on the small bowel mucosal damage and repair during diarrhea, or on the effect of diarrhea on intestinal enzyme production.

Acute diarrhea has been shown to be associated with mucosal cell damage, both structural and functional. Recovery of normal structure and function depends on healing or replacement of the damaged cells or cell components. Although there is no existing evidence that early feeding speeds cell regeneration, animal studies have shown that the process of cell renewal and bowel healing are adversely affected by protein deprivation and starvation (Brown et al., 1963; Deo and Ramalingaswami, 1965; Hopper et al., 1968).

Studies in humans have shown the sensitivity of the intestine to decreased food intake. One early response is a decrease in enzyme activity. Adibi and Allen (1970) found reduced absorption rates of essential amino acids following starvation or protein deprivation in human subjects. In another study, Rosensweig and Herman (1970) showed that the level of disaccharidase activity depends on the amount and type of carbohydrates ingested. Knudsen et al. (1968) reported that healthy humans show a prompt decrease in disaccharidase activity early in fasting (at three days), followed by a slower but progressive decrease as fasting continues. In their study, refeeding for ten days after 14 days of fasting did not bring enzyme levels back to normal. Unfortunately, the researchers did not examine the effects of refeeding after a shorter duration of fasting (which may more closely approximate common practices during diarrhea episodes). In developing countries in which children may have multiple episodes of diarrhea each year, frequent and prolonged food withholding in response to diarrhea may be particularly detrimental to intestinal enzyme activity and nutrient absorption.

Therefore, there is no evidence that "resting the bowel" or withholding food during diarrhea is beneficial in terms of speeding the healing process. Quite the contrary, there is good evidence that withholding necessary nutrients delays healing and may cause further decreases in mucosal function.

The Effects of Continued Feeding on the Adverse Nutritional Consequences of Diarrhea

It has been estimated that a child with diarrhea may lose up to two percent of his body weight per diarrhea-day, especially if the child is fasting (Rohde and Northrup, 1986). For many children, particularly the already malnourished, this amount of weight loss may take place many days each year. It is important, therefore, to determine whether feeding during diarrhea can prevent or decrease the adverse nutritional consequences of the disease.

The most comprehensive study on dietary aspects of diarrhea management has been done in Peru by Brown et al. (1988). Children were randomized into four groups. Groups I to III were rehydrated with ORS (WHO formula) and group IV received intravenous therapy. After two to four hours, maintenance diets were started. Maintenance diets consisted of a formula of casein, sucrose, dextrimaltose, and vegetable oil (CSO) provided at 110 kcal/kg body weight/day (group I) or provided at CSO 55 kcal/kg/day for two days, then increased to 110 kcal/kg/day (group II). Group III received only ORS for the first two days, then gradually increasing amounts of CSO. Group IV received nothing by mouth for the first 48 hours of therapy and then CSO was begun slowly.

The groups that showed the greatest nutritional gains were those started early on the formula diet (groups I and II). Absorption of macronutrients and retention of nitrogen were directly related to the amount of food consumed, with groups I and II showing the best results in the first few days of therapy. Group I was the only group to consistently gain weight. Following an initial weight gain related to fluid therapy, the other groups lost weight and only began to gain weight after receiving CSO at 110 kcal/kg/day. Groups I and II showed significantly greater weight gains at weeks one and two than the other two groups. Similarly, increments in arm circumferences and skinfold thicknesses were greater in groups I and II than in the other two groups.

A number of other studies have documented that weight gain may be augmented during diarrheal episodes with the early administration of breast-milk (Kassem et al., 1983), milk-based formula (Chung, 1948), and a variety of other diets (Soeprapto et al., 1979; Isolauri et al., 1985).

The studies referenced above clearly demonstrate the nutritional benefits of feeding during diarrhea. They confirm that there is a net absorption of nutrients presented to the

intestine even in the face of continuing stool losses and transient increases in stool volume.

CONCLUSIONS

For many physicians, the term "gastroenteritis" immediately triggers the response "clear fluids", "NPO", or "intravenous" (Goldbloom, 1984). The situation is slowly changing, and it is the developing rather than the developed world that is leading the way. Physicians in developed countries may feel that ORS and continued feeding are not important in the context of high living standards and the generally good nutritional status of children. This situation has had unfortunate repercussions in parts of the developing world where pediatricians, often drawing on Western education and medical texts, frequently impede acceptance of oral rehydration therapy and continued feeding.

Is there any basis for reservations about the use of ORS and continued feeding during diarrhea? To answer this question, it is important to realize that the patient's clinical hydration status is the best indicator of the success of any given therapy. The patient's stools or laboratory tests may contribute useful information but should not be relied upon exclusively as an indicator of success. The studies cited indicate that patients given oral fluids and food during diarrhea do better, as determined by weight gain and return of appetite, than patients treated with intravenous fluids and withholding of food. The slight increase in initial stool output seen in some patients treated orally (although not in many) should not distract the clinician from noting the more effective recovery of the patients treated in this fashion.

There is clearly a role for both ORS and IV therapy in the management of acute diarrhea. This review of a number of issues makes it clear, however, that in those patients who can take ORS (more than 90% of all patients presenting with diarrheal dehydration), oral rehydration therapy is as good as or <u>better</u> than IV therapy -- physiologically, nutritionally, and psychologically. IV therapy should be reserved for those few patients who are in shock, who have paralytic ileus, or in whom purging rates are so high or vomiting so great that the oral intake cannot keep up with the stool losses. Patients initially begun on IV therapy should rapidly be switched over to ORS solution once they are able to drink.

Feeding is a further critical element in the management of the child with diarrhea. Its early implementation will help to avoid the serious nutritional consequences of diarrhea, and may

shorten the duration of the episode. Any increase in stool output due to early feeding will be of limited duration and should not discourage the adoption of this very important practice.

Many topics related to the management of acute diarrhea are currently under investigation -- the identification of the best foods for use during and after diarrhea, the use of non-human milk in non-breast-fed children with diarrhea, and the use of cereal-based ORS. These unanswered questions do not alter the conclusion that rehydration with ORS solution and continued feeding are the optimal management strategies for the vast majority of children with diarrhea, including those with diarrhea-induced dehydration.

TABLE 1

Randomized Controlled Trials Comparing IV and ORS Therapy: Summary of Results

Country	Comparison Groups	Additional Feeding or Oral Fluids	Stool Volume or Frequency	Duration of Diarrhea	Speed of Correction of Metabolic Abnormalities	Speed of Rehydration	Length of Hospital Stay	ORS Failure Rate	Comments	Reference
Afghanistan n=100	ORS_{90}[1] IV	?	Similar reduction in frequency in both groups	Similar in both groups	N G[2]	Dehydration corrected within 24 hours in both groups	N.G.	0	*Chloramphenicol was given to all. *Patients with shock, acidosis, abdominal distension, persistent vomiting were excluded, representing 20% of admissions. *One death - complication of therapy in IV group.	Singi et al, 1982
Bangladesh n=101	ORS_{90} glucose ORS_{90} sucrose IV	Yes (ORS groups) ? IV group	Purging (ml/kg) lower in ORS glucose group but differences not statistically significant	Similar in all groups	N G	*IV group had lower serum specific gravity at 4 hrs and 24 hrs *Time to first urination similar in all groups	N G.	0	*Patients all had rotavirus diarrhea *Randomization was only between sucrose glucose groups	Sack et al, 1978
Finland n=37	ORS_{60} IV	Yes, from 12 hours onward.	Stool volume similar in first 24 hours, greater in IV group in second 24 hours	Shorter in ORS group	Rate of correction of acidosis similar in both groups during the first 12 hours	Similar in both groups. hematocrit, plasma protein, weight gain	Shorter in ORS group	9% (insufficient intake (1), & continuous vomiting (1))	*ORS group showed significantly better weight gain at time of discharge.	Vesikari, Isolauri, Baer, 1987
Iran n=470	ORS_{80} ORS_{40} IV	Yes, within 24 hours in ORS group. Oral feedings were begun in IV group when diarrhea lessened.	N.G.	Shorter in ORS group	N G	N G	N G	<1% (signs of dehydration increased)	*Patients all had severe or moderately severe dehydration *Rehydration with ORS_{80} was done by nasogastric tube. *Maintenance ORS had 40 mMol/l of sodium.	Shanfi et al, 1985
Panama n=94	ORS_{90} ORS_{50} IV	Yes, from 8 hours onward.	Stool output similar in first 8 hours. Total output significantly greater in IV group	Similar in all groups	N G	N G.	N G	0	*Severely dehydrated patients were partially rehydrated with IV therapy	Santosham et al, 1982
U.S.A. n=52	ORS_{90} ORS_{50} IV	Yes, after the diarrhea stopped In IV group pedialyte given for 8 hrs before formula	Total stool output significantly greater in ORS groups	Similar in all groups	N G	N G.	N G	3%	*Severely dehydrated patients were partially rehydrated with IV therapy	Santosham et al, 1982

[1] Subscripts following ORS indicate the sodium concentration

[2] N G. = Not given

TABLE 1 (Cont'd)

Randomized Controlled Trials Comparing IV and ORS Therapy: Summary of Results

Country	Comparison Groups	Additional Feeding or Oral Fluids	Stool Volume or Frequency	Duration of Diarrhea	Speed of Correction of Metabolic Abnormalities	Speed of Rehydration	Length of Hospital Stay	ORS Failure Rate	Comments	Reference
Peru n=128	ORS_{90} + 3 feeding regimens; IV + delayed feeding	Yes, after first 2 4 hours in 2 of the ORS groups, after 48 hours in 1 ORS group and the IV group.	Fecal output greater in ORS groups in first 2 days, then equal after 3 days.	Similar in all groups	Similar in all groups	*Clinical recovery from dehydration similar in all groups *More rapid decrease in hematocrit and total serum protein in IV group (all groups similar by 12 hours)	N G.	8.5%		Brown et al., 1988
USA n=100	ORS_{75} IV	Yes, in ORS groups, usually begun in first day IV group fasted for 18 24 hours	More frequent in ORS group in first day.	N G.	More rapid correction of acidosis in ORS group	More rapid decrease in hematocrit in ORS groups	same	6% (seizures (1), vomiting (1), unable to feed (1))	*ORS_{50} given for maintenance	Tamer et al., 1985
USA n=29	ORS_{60} IV	Yes, after about 30-36 hours	N G.	N G.	Similar at the end of 24 hours	N G	Mean hospital time less in ORS group	13%	*The 2 failures with ORS had urinary tract infections complicating their course. *Exclusions: serum sodium > 160mEq1L., need for intensive care.	Listernik et al., 1986

TABLE 2
Rates of Vomiting on Presentation and of ORS Failure Due to Vomiting

Country	No of Patients Receiving ORS	No (%) With Vomiting on Presentation	No (%) of Patients Who Could Not be Rehydrated with ORS Due to Vomiting	Total No (%) of ORS Failures	Reference
Bangladesh	57	56(98)	0	0	Sack et al, 1978
Brazil	29[1]	11(37)	1(3)	1(3)	Mclean et al, 1981
Costa Rica	100	N G.	2(2)	8(8)	Pizarro et al, 1979
India	8[1]	4(50)	3(37)	4(50)	Mahalanabis et al, 1974
India	9[2]	N.G	0	0	Mahalanabis et al, 1974
India	20	N G.	0	1(5)	Chatterjee et al, 1977
Iran	236	212(90)[3]	0	1(<1)	Sharifi et al, 1985
Panama	63	55(87)	0	0	Santosham et al., 1982
U.S A	35	26(74)	0	1(3)	Santosham et al, 1982
Peru	97	91(94)	4(4)[4]	15(15)	Salazar Lindo et al, 1986
U.S A.	47	42(84)	1(2)	3(6)	Tamer et al, 1985
U.S A.	15	15(100)	2(13)	2(13)	Listernick et al, 1986
U S A	57	42(74)	N G.	2(4)	Listernick, Zieserl, Davis, 1985
U S A	47	23(49)	0	2(4)	Hirshhorn et al, 1973
U.S A	140	55(39)	0[5]	0	Santosham et al, 1985

[1] ORS used for maintenance after 3 hrs of IV rehydration

[2] ORS used for maintenance after 8 hrs of IV rehydration

[3] 118(50) with history of severe vomiting on presentation

[4] Vomiting was a contributing factor

[5] 2 patients were hospitalized with vomiting but were not ORS failures by protocol criteria

TABLE 3

Complication Rates Reported in Studies Comparing
ORS and IV Therapy for Diarrheal Dehydration in Children

				No (%) of patients with listed complications								
Country	Comparison Groups	Overall Complication Rate (%)	Number of Deaths Due to Complications	Electrolyte Abnormalities[1]	Convulsions	Phlebitis	Sepsis	Peri orbital Edema	Paralytic Ileus	Abdominal Distension	Hydrothorax	Reference
Afganistan	ORS (n=50) IV (n=50)	0 20	0 1	N D.* N D.	0 1(2)	0 0	0 9(18)[2]	0 0	0 0	0 0	0 0	Singh et al., 1982
Brazil	ORS (n=29) IV (n=24)	0 0	0	0	0	0	0	0	0	0	0	McLean et al., 1981
Iran	ORS (n=236) IV (n=234)	10 22	0 0	14(6) 29(12)	2(1) 6(3)	0 5(2)	0 0	4(2) 4(2)	0 8(3)	4(2) 0	0 0	Sharifi et al., 1985
U.S.A.	ORS (n=15) IV (n=14)	7 0	0 0	0 0	0 0	0 0	0 0	1(7) 0	0 0	0 0	0 0	Listernick et al., 1986
U.S.A.	ORS (n=50) IV (n=50)	2 0	0 0	0 0	1(2) 0	0 0	0 0	0 0	0 0	0 0	0 0	Tamer et al., 1985
Panama	ORS (n=63) IV (n=31)	0 13	0 0	0 2(6)	0	0 1(3)	0	0	0	0	0 1(3)	Santosham et al., 1982
U.S.A.	ORS (n=35) IV (n=17)	6 6	0 0	0 0	0 1(6)	0 0	0 0	2(6) 0	0 0	0 0	0 0	Santosham et al., 1982

1 normal becoming abnormal
2 fever and rigors, presumed sepsis
* N.D. = no data presented

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