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Oral Rehydration Therapy: An Annotated Bibliography

Second edition

A project of the WHO/PAHO Program for the Control of Diarrheal Diseases

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PREFACE

Each year an estimated five million of the world's children die of diarrheal dehydration. Worldwide, it may be the leading cause of infant mortality.

In many countries diarrheal diseases account for twenty-five percent or more of pediatric hospital admissions. Treating these hospitalized cases with costly intravenous therapy and the requisite medical supervision places a heavy burden on already scant health resources. And yet we know those fortunate enough to receive such treatment are only a fraction of those in need.

Surveys in various parts of the world indicate that children below the age of five commonly experience as many as ten episodes of diarrhea annually. The deleterious nutritional consequences of these repeated infections have been well described.

Fortunately, recent developments in gastrointestinal physiology, and enteric diseases in general, have led to the refinement of an appropriate technology innovation of tremendous significance: oral rehydration therapy (ORT).

The key finding was that glucose, in the correct concentration, dramatically enhances the absorption of water and sodium in the small intestine. Moreover, this active transport mechanism remains largely intact despite the presence of diarrhea. The problem of rehydration and maintenance of fluid and electrolyte balance during acute diarrhea is thus immensely simplified; patients need only drink ORT solution in volumes approximately equal to their stool losses.

Data from many sources indicate mortality from diarrheal dehydration can be virtually eliminated once the routine use of ORT is established. More importantly, ORT is so safe and effective it can be given in the home by nearly anyone with minimal training.

The task of disseminating ORT comprises a key strategy of the WHO Program for the Control of Diarrheal Diseases (CDD). Begun in 1978, this high priority program forms an essential element of primary health care. Taking a comprehensive approach, the program seeks not only to promote ORT but also to reduce the incidence and severity of diarrheal diseases through improved child care practices (including the promotion of breastfeeding and proper weaning), the use of safe water and adequate sanitary facilities, and the early detection and control of epidemics through improved epidemiological surveillance. To implement these strategies, new approaches to training, communications, information dissemination as well as program delivery and evaluation are essential, particularly in light of the Organization's goal of achieving "health for all by the year 2000."

With a view toward making the information as widely available as possible, the major published literature on ORT has been collected and abstracted in this annotated bibliography. Both continuing demand for information on ORT and rapid technical advances as ORT programs are implemented worldwide have led us to publish this updated second edition.

Dr. Carlyle Guerra de Macedo
Director

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

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WHO-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. More recently, investigators have focused on the feasibility of substituting other carbohydrates for glucose or sucrose, and of using a more stable base, citrate, in place of bicarbonate.

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. While numerous recent studies have shown that such "simple salt/sugar (SSS)" solutions are efficacious, they have also determined that correct home measurement and administration of SSS solutions depend on careful calibration of local measures, repeated face-to-face instruction and some form of supervision on the village level.

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.

First-edition abstracts, numbered 1–133, were drawn from the published literature up to and including early 1980. Most of the 144 second-edition abstracts, numbered 134–277, were published between early 1980 and the end of 1982. A few pre-1980 articles, which for various reasons were not abstracted in the first edition, also appear in the newer material.

WHO-Recommended Formulation of ORS:

Ingredients	*gram/liter of water*
Sodium chloride	3.5
Sodium bicarbonate	2.5
Potassium chloride	1.5
Glucose	20.0

Composition	*mmol/liter of water*
Sodium	90
Potassium	20
Chloride	80
Bicarbonate	30
Glucose	111

Chapter 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.

1. Darrow, D. C., et al., Disturbances of water and electrolytes in infantile diarrhea, *Pediatrics* 3:129-156, 1949.

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^+, HCO_3^-, 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.

2. Chatterjee, H. N., Control of vomiting in cholera and oral replacement fluid, *Lancet* 2:1063, 1953.

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 promethozine 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.

3. Fisher, R. B., Glucose movements across the wall of the rat small intestine, *J Physiol* 119:210-223, 1953.

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.

4. Harrison, H. E., The treatment of diarrhea in infancy, *Ped Clinics N Am* 1:335-348, 1954.

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.

5. Colle, E., et al., Hypertonic dehydration (hypernatremia): the role of feedings high in solutes, *Pediatrics* 22:5–12, 1958.

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 sequellae in the non-hypernatremic patients. The major difference in the hypernatremic group was the high solute load in their preadmission 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.

6. Riklis, E., et al., Effects of cations on sugar absorption by isolated surviving guinea pig intestine, *Can J Biochem Physiol* 36:347–362, 1958.

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.

7. Harrison, H. E., et al., Hypernatremic dehydration, *Ped Clin N Am* 6:193–199, 1959.

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.

8. Curran, P. F., Sodium, chloride, and water transport by rat ileum in vitro, *J Gen Physiol* 43:1137–1148, 1960.

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 depen-

dent 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.

9. Phillips, R. A., Water and electrolyte losses in cholera, *Fed Proc* 23:705-712, 1964.

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 HCO_3^- 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.

10. Crane, R. K., Na^+-dependent transport in the intestine and other animal tissues, *Fed Proc* 24:1000-1008, 1965.

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.

11. Phillips, R. A., et al., Water and electrolyte absorption by the intestine in cholera, *Cholera Res Symp* 299-311, Honolulu, 1965.

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 defecits.

During study periods, one of 3 oral solutions containing 10 mmol/l KCl, 45 mmol/l $NaHCO_3$, and either 0, 100 or 185 mmol/l NaCl were administered, and uptake of electrolytes was measured.

Absorption of H_2O, K^+, and HCO_3^- 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.

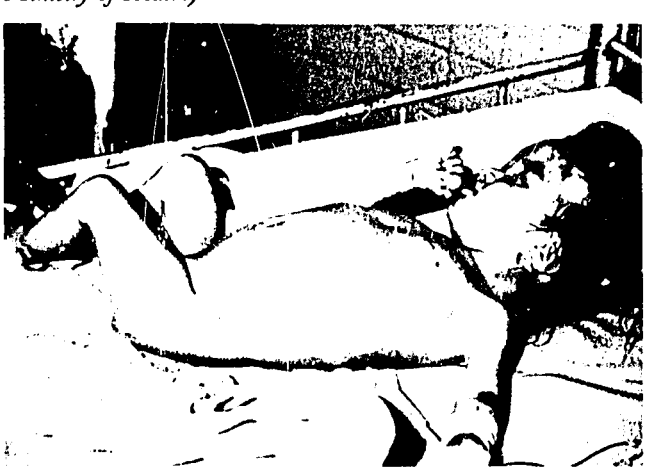
12. Hirschhorn, N., Decrease in net stool output in cholera during intestinal perfusion with glucose containing solutions, *N Engl J Med*, 279:176-180, 1968.

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 defecits. Warmed electrolyte solutions (mEq/l: Na^+-133, K^+-6.1, Cl^-92, HCO_3^--48) with varying amounts of glucose, galactose, or fructose were infused. IV hydration was continued in order to supply maintenance

Until the advent of ORT, costly, hospital-based intravenous therapy was the treatment of choice for diarrheal dehydration. (Photo: WHO)

Malnutrition and diarrhea are intimately related. (Photo: Ecuador Ministry of Health)

In many countries acute diarrhea is still the leading cause of pediatric hospital admissions. (Photo: Ecuador Ministry of Health)



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 HCO_3^- 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.

13. Nalin, D. R., et al., Oral maintenance therapy for cholera in adults, *Lancet* 2:370-2, 1968.

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 (1 g/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.

14. Olsen, W. A., et al., The role of sodium in intestinal glucose absorption in man, *J Clin Inv* 47:1133-1142, 1968.

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.

15. Pierce, N. F., et al., Oral replacement of water and electrolyte losses in cholera, *Ind J Med Res* 57:848-855, 1968.

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, HCO_3^--40, and glucose 40 mmol/l; and solution 2 contained (in mEq/l): Na^+-110, K^+-90, Cl^--79, HCO_3^--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.

16. Pierce, N. F., et al., Effect of intragastric glucose-electrolyte infusion upon water and electrolyte balance in Asiatic cholera, *Gastroent* 55:333-343, 1968.

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 HCO_3^- 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 chemis-

tries 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.

17. Turnberg, L. A., et al., Mechanism of bicarbonate absorption and its relationship to sodium transport in the human jejunum, *J Clin Invest* 49:548–556, 1970.

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.

Second Edition Abstracts

134. Nalin, D. R., et al., Oral therapy for cholera, In Barua and Burrows (eds) *Textbook of Cholera*. 1st Edition, Chapter 13, pp. 253–261, Philadelphia, Saunders, 1974.

The authors reviewed the major clinical and field studies that led to the development of oral rehydration therapy (ORT). They described how the elegant mechanisms by which the gut absorbs water and electrolytes in the presence of glucose were not clearly elucidated until the late 1960's although various investigators had observed the apparent feasibility of ORT a century ago. The successful use of a specific glucose-electrolyte solution in a clinical setting was first reported by Chatterjee et al, in 1953. By 1968, Nalin et al, had shown ORT provided a useful adjunct to IV therapy in that, after initial IV treatment, it successfully maintained hydration even in severe cholera cases. These findings were soon confirmed in large-scale field trials. In 1970 Cash et al, showed ORT was effective in severe cholera without initial IV rehydration. Others soon showed this was true even for small children.

Considering public health aspects and noting that ORS ingredients are inexpensive and widely available and that ORT can reduce IV fluid use by 80% or more, the authors recommended that cholera vaccination programs in

endemic areas be replaced with treatment programs based on ORT.

Finberg, L., et al., The role of oral electrolyte-glucose solutions in hydration for children—international and domestic aspects, *J Pediatr* 96(1):51-54, 1980.

Anonymous, Oral rehydration therapy (ORT) for childhood diarrhoea. *Population Reports, Series L, No. 2, (75 pages), Nov-Dec 1980*, (available in several languages from the Population Information Program, the Johns Hopkins University, Hampton House, 624 N. Broadway, Baltimore, Md. 21205, USA).

Parker, R. L., Oral fluid therapy in diarrhea and dehydration: Current concepts and practical considerations, (*Unpublished Document available from*: Dept. of International Health, Johns Hopkins Univ. School of Hygiene and Pub Health, Baltimore, Maryland, USA), July 1980.

Levine, M. M., Oral therapy for diarrhoea: past, present and future (editorial), *J Trop Med Hyg*, 84:185-187, 1981.

Chapter II. CLINICAL TRIALS

With the encouraging results of the initial physiologic and clinical studies, investigators 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.

Chatteree, H. N., 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).

Phillips, R. A., Water and electrolyte losses in cholera, *Fed Proc* 23:705-712, 1964 (see No. 9).

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

Hirschhorn, N., Decrease in net stool output in cholera during intestinal perfusion with glucose containing solutions, *N Engl J Med* 279:176-181, 1968 (see No. 12).

Nalin, D. R., et al., Oral maintenance therapy for cholera in adults, *Lancet* 2:370-372, 1968 (see No. 13).

Olsen, W. A., et al., The role of sodium in intestinal glucose absorption in man, *J Clin Invest* 47:1133-1142, 1968 (see No. 14).

Pierce, N. F., et al., Oral maintenance of water-electrolyte and acid-base balance in cholera: a preliminary report, *Ind J Med Res* 6:640-645, 1968 (see No. 15).

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

Nalin, D. R., et al., Reduction of maintenance intravenous fluid needs in cholera by means of an oral therapeutic solution, *J Pakistan Med Assoc* 19:373-379, 1969 (see No. 69).

18. Pierce, N. F., et al., Replacement of water and electrolyte losses in cholera by an oral glucose-electrolyte solution, *Ann Int Med* 70:1173-81, 1969.

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 ad-

mission to the cessation of diarrhea) was greater, but not significantly so, in the orogastric group. Although stool output during orogastric replacement was 21% greater then 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 intragrastric solution could be administered orally and that its efficacy should be evaluated in children and persons with non-cholera diarrhea as well.

19. Nalin, D. R., et al., Oral therapy for cholera, (letter) *Ann Intern Med* 72:288-289, 1970.

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 hyponatremic. 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.

20. Pierce, N. F., et al., Oral electrolytes in cholera, (letter) *Ann Intern Med* 72:959, 1970.

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.

21. Pierce, N. F., et al., Oral replacement of water and electrolyte losses in cholera, *Ind J Med Res* 57:848-855, 1969 (see No. 15).

An oral rehydration solution (containing in mEq/l: Na^+-100, K^+-10, Cl-70, HCO_3^- 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 maintain 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.

22. Bart, K. J., Pediatric cholera, pathophysiology and treatment, *Pak Pediatr J* 1:45-53, 1970.

This review article on treatment of pediatric cholera briefly discussed the *V. cholera* 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, HCO_3^- 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.

23. Cash, R. A., et al., A clinical trial of oral therapy in a rural cholera-treatment center, *Am J Trop Med Hyg* 19:653-656, 1970.

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, HCO_3^- 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. cholera* 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, R. A., et al., Rapid correction of acidosis and dehydration of cholera with oral electrolyte and glucose solution, *Lancet* 2:549-550, 1970 (see No. 70).

24. Mahalanabis, D., et al., Water and electrolyte losses due to cholera in infants and small children: A recovery balance study, *Pediatrics* 45:374-385, 1970.

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 in-

travenously 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 CO_2 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.

25. Nalin, D. R., et al., Oral or nasogastric therapy for cholera, *WHO Public Health Paper No. 40*, Chapter 11, pp. 73-76, 1970.

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, $NaHCO_3$-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, D. R., et al., Oral (or nasogastric) maintenance therapy for cholera patients in all age-groups, *Bull WHO* 43:361-363, 1970 (see No. 46).

Nalin, D. R., Oral or nasogastric maintenance therapy for diarrhea of unknown aetiology resembling cholera, *Trans Roy Soc Trop Med Hyg* 64:769-771, 1970 (see No. 47).

26. Sack, R. B., et al., The use of oral replacement solutions in the treatment of cholera and other severe diarrhoeal disorders, *Bull WHO* 43:351-360, 1970.

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, HCO_3^--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 vomit-

ing 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.

27. Nalin, D. R., Oral or nasogastric maintenance therapy in pediatric cholera patients, *Trop Ped* 78:355-358, 1971.

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, HCO_3^--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.

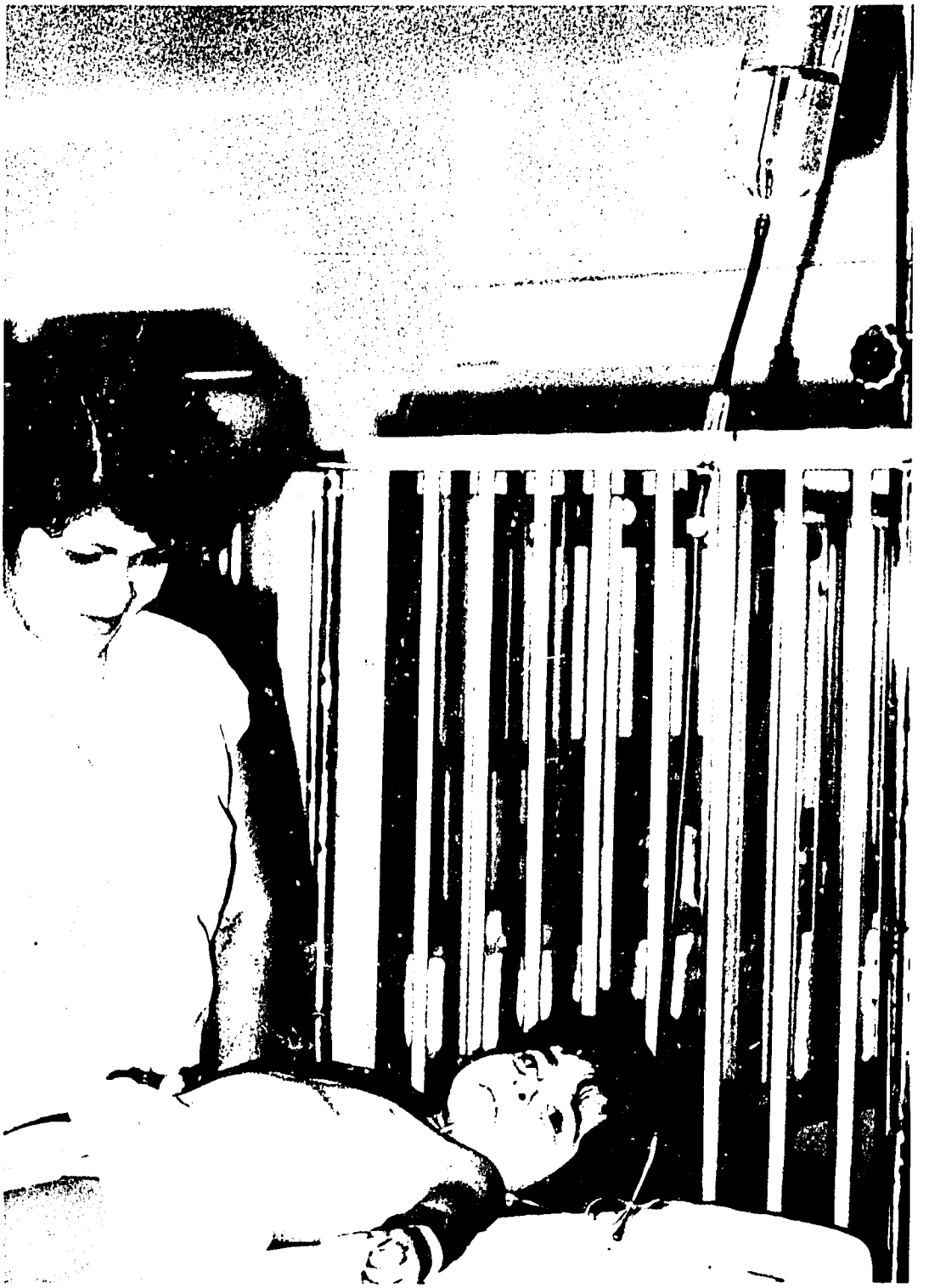
28. Hirschhorn, N., et al., Oral fluid therapy of Apache children with acute infectious diarrhea, *Lancet* 2:15-18, 1972.

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/l: Na^+-90, K^+-20, Cl^--65, HCO_3^--45, and glucose) and received either cow's milk or one of 2 hypotonic (Na^+-19 mmol/l) 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.



Careful balance studies led to the formulation of WHO-recommended ORS.
(Photo: D. Pizarro, Costa Rica)

Hirschhorn, N., et al., Ad libitum oral glucose-electrolyte therapy or acute diarrhea in Apache children, *J Pediatr* 83:562-571, 1973 (see No. 50).

29. Ludan, A. C., The efficacy of oral electrolyte fluid in the therapy of diarrhea, *J Philip Med Ass* 49:243-252, 1973.

Intravenous (IV) and oral rehydration therapies were compared for fluid balances in Filipino children hospitalized with acute gastroenteritis. Initial hydration defecits 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/l; 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.

Mahalanabis, D., et al., Oral fluid therapy of cholera among Bangladesh refugees, *Johns Hopkins Med J* 132:197-205, 1973 (see No.71).

30. Mazumdar, H., et al., Oral rehydration in gastroenteritis in children, *Indian Pediatrics* 10:315-322, 1973.

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.

31. Mahalanabis, D., et al., Use of an oral glucose-electrolyte solution in the treatment of paediatric cholera—a controlled study, *J Trop Pediatr Environ Hlth* 20:82-87, 1974.

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. cholera* 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.

32. De, S., et al., Oral fluid therapy for cholera and non-choleraic diarrhoeas in children, *J Comm Dis* 7:124-128, 1975.

To assess the efficacy of oral rehydration treatment of pediatric diarrhea caused by *V. cholera* and non-*V. cholera* 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 $NaHCO_3$, 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, M. R., 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).

33. De, S., Oral glucose-electrolyte solution in the treatment of cholera and other diarrhoeas, *J Ind Med A* 65:230-232, 1975.

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, Ca^{++} 4, Cl^- 62, SO_4^{--}, PO_4^{--}, HCO_3^- 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; 16 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. cholera* in 29 specimens and no pathogens in 89.

Oral rehydration proved to be an inexpen-

Increased dietary intake during and immediately after diarrheal episodes is an important adjunct to ORT. (Photo: M. McQuestion, PAHO/WHO)

sive, effective, and easily administered mode of therapy, especially for mild and moderate dehydration.

34. Editorial, Oral glucose-electrolyte therapy for acute diarrhea, *Lancet* 1:79-80, 1975.

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

Nalin, D. R., Sucrose in oral therapy for cholera and related diarrhoeas, *Lancet* 1:1400-1402, 1975 (see No. 53).

Naik, N. V., et al., Oral rehydration in acute gastro-enteritis in young children, *Ind Pediatr* 13:127-133, 1976 (see No. 56).

Rahilly, P. M., 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).

Bollag, U., Cup-and-spoon rehydration of children with acute diarrhea, *J Trop Ped Env Child Hlth* 23:268-270, 1977 (see No. 101).

Chatterjee, A., et al., Evaluation of a sucrose/electrolyte solution for oral rehydration in acute infantile diarrhoea, *Lancet* 1:1333-1335, 1977 (see No. 58).

Gracey, M., et al., ROSE system for treatment of cholera dehydration (letter), *Br Med J* 1:839-840, 1977 (see No. 104).

International Study Group, A positive effect on the nutrition of Philippine children of an oral glucose-electrolyte solution given at home for the treatment of diarrhoea, Report of a field trial by an international study group, *Bull WHO* 55:87-94, 1977 (see No. 75).

35. Lishnevsky, M. S., et al., Oral rehydration treatment benefits Lao children with diarrhoea, *WHO Chron* 31:421-22, 1977.

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 diarrhea." 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.

Palmer, D. L., et al., Comparison of sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrhea, *N Engl J Med* 297:1107-1110, 1977 (see No. 59).

Sandle, G. I., et al., Oral therapy in cholera (letter), *N Engl J Med* 298:797-798, 1978 (see No. 61).

36. **Pierce, N. F.**, et al., Oral fluid—a simple weapon against dehydration in diarrhoea, *WHO Chron* 31:87-93, 1977.

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 substained 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.

37. **Barzgar, M. A.**, et al., Evaluation of the effectivness of oral rehydration in gastro-enteritis in children under 3 years of age, West Azerbaijan, Iran, 1977, presented to the Regional Scientific Meeting on the Epidemiology of Enteric Infections of the International Epidemiological Association (Alexandria, May 27-31, 1978), *WHO Document:Ent Inf WP No. 18.*

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.

Chatterjee, A., et al., Oral rehydration in infantile diarrhoea, Controlled trial of a low sodium glucose electrolyte solution, *Arch Dis Child* 53:284-289, 1978 (see No. 62).

Fortin, J., et al., Dehydration scoring system for infants, *J Trop Pediatr Env Child Hlth* 24:110-114, 1978 (see No. 113).

Moenginah, P. A., et al., Sucrose electrolyte solution for oral rehydration in diarrhea, *J Trop Ped Env Child Hlth* 24:127-129, 1978 (see No. 63).

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

Sack, D. A., et al., Oral hydration in rotavirus diarrhoea: A double-blind comparison of sucrose with glucose electrolyte solution, *Lancet* 2:280-283, 1978 (see No. 65).

38. Seriki, O., Management of moderately severe dehydration by continuous intra-gastric infusion of electrolyte solution, *Trop Doc* 8: 134-136, 1978.

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.

39. Thomas, K., et al., Oral rehydration therapy in childhood diarrhea, a comparative study, *Indian Ped* 15:791-796, 1978.

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.

Hutchins, P., et al., Comparison of oral sucrose and glucose electrolyte solutions in the out-patient management of acute gastroenteritis in infancy, *J Hyg (Camb)* 82:15-19, 1979 (see No. 66).

40. Nalin, D. R., et al., Oral rehydration and maintenance of children with rotavirus and bacterial diarrhoeas, *Bull WHO* 57:453-459, 1979.

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.

41. Nalin, D. R., et al., The problem of emesis during oral glucose-electrolyte therapy given from the onset of severe cholera *Trans Roy Soc Trop Med Hyg* 73:10-14, 1979.

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 10^5 to 10^6 *Vibrio cholera* organisms. The incubation period was 37 ± 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.

Rahaman, N. M., et al., Diarrheal mortality in two Bangladeshi villages with and without community-based oral rehydration therapy, *Lancet* 2:809-812, 1979 (see No. 78).

42. Fazil, et al., Treatment of children with diarrhea with UNICEF's oral rehydration salts in rural areas by midwives, *Unpublished Document.*

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.

Hirschhorn, N., The treatment of acute diarrhea in children: a historical and physiological perspective, *Am J Clin Nutr* 33:637-663, 1980. (see No. 133).

International Study Group, Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea (Part 1): Stud-

ies in two ambulatory care clinics *J Trop Ped* 27(2):62-67, 1981, (see No. 79).

International Study Group, Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea (Part 2): Studies in seven rural villages *J Trop Ped* 27(3):136-139, 1981, (see No. 80).

43. Nalin, D. R., 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; evalution 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 antiemetic agents as adjuncts to diarrhea therapy.

Nalin, D. R., et al., Comparison of low and high sodium and potassium content in oral rehydration solutions *J. Pediatr* 97(5):848-853, 1980, (see No. 67).

44. Pizarro, D., Oral rehydration of neonates with dehydrating diarrheas, *Lancet* 12:1209-1210, 1979.

Observing that ORT has been found highly effective in all but very young children with dehydrating diarrhea, the authors performed an uncontrolled clinical trial to examine its efficacy in neonates.

Forty Costa Rican children (mean age 20.3 days, range 7 to 30 days) with uncomplicated, acute diarrhea and mean dehydration equivalent to 6.7% of body weight were selected for study. The patients were similar with respect to duration (mean 2.6 days) and intensity of diarrhea (mean 7.3 stools/previous 24 hours) and vomiting (58%) prior to admission. Serum electrolyte determinations were made for 22 patients at admission, after initial rehydration and 24 hours after ORT was begun.

The WHO-recommended ORS composition—with slightly more potassium added—was used. After practical training, mothers gave their children 2 parts ORT solution followed by one part free water until initial rehydration was achieved. Once rehydrated, breastmilk or half-strength formula was reinstituted, patients were sent home where ORT was continued and mothers were asked to return for follow-up the next day.

Oral rehydration was successful in 39 of the 40 neonates. Nasogastric tubes were used in three patients while one patient required intravenous fluids due to excessive vomiting. Oral maintenance in the home was successful in 34 of 40 neonates. Five children who were brought back dehydrated were again successfully orally rehydrated within 6-10 hours. Mean rehydration time was 8.2 $\pm$ 0.8 hours (range 2-25 h). Forty-five percent were initially rehydated in less than 6 hours, 90% in less than 15 hours.

Seven of eight patients with hypernatremia upon admission (serum Na^+ over 150 mmol/l) were normonatremic after initial rehydration. One had borderline high plasma sodium. There was no hyponatremia. Normal K^+ concentrations were restored in two hyperkalaemic patients after 24 hours of therapy. Two hypokalaemic neonates became normal with additional oral K^+. There were no deaths.

The authors concluded ORT is as effective in neonates as in older patients.

(See also abstracts No. 141, 155).

45. Taylor, P. R., et al., Oral rehydration therapy for treatment of rotavirus diarrhea in a rural treatment center in Bangladesh *Arch Dis Child* 55(5):376-379, 1980.

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.

Second Edition Abstracts

Once clinical and early field studies had shown the feasibility of substituting ORT for intravenous therapy, many workers did so. Other investigators turned to more specific issues that had to be addressed before ORT could be fully "routinized" in the clinical setting. Some of these issues included the use of ORT in neonates, optimal refeeding schedules, disaccharidase deficiency, the use of antibiotics and the merits of adding flavoring to ORS.

Nalin, D. R., et al., Oral therapy for cholera. In: Barua and Burrows (eds.), *Textbook of Cholera*. 1st Edition, Chapter 13, pp. 253-261, Philadelphia, Saunders, 1974.

135. Taindel, C., et al., Metoda simpla si eficienta de reechilibrare hidroelectrolitica orala a copiilor cu infectii digestive acute. (A simple, efficient method for restoring water-electrolyte balance orally in children with acute enteric infections), *Rev Pediatr Obstet Ginecol (Pediatr)* 26(1):71-78, 1977, (Article in Bulgarian).

The authors reported the results of a sequential, uncontrolled ORT trial in Bucharest, Rumania.

During 1975-1976, 2,000 patients with acute diarrhea of various etiologies presented to a Bucharest hospital. One thousand six-hundred twelve of these patients (81%) were successfully treated with the WHO-recommended oral rehydration solution. Three hundred eighty-eight patients (19%) were severely dehydrated and, of these, 230 (60%) needed initial IV therapy. Forty percent of the severely dehydrated patients, however, were successfully treated with ORT alone. Of the 230 patients needing initial IV therapy, adequate hydration was later successfully maintained in 146 (40%) with ORT alone. Only 4% of the 2,000 patients required continuous IV therapy.

Stool electrolyte determinations in 40 randomly selected cases showed the WHO-recommended ORS corrected both sodium and potassium levels within 72 hours.

The authors showed in this relatively early trial that ORT is safe and effective for treating the majority of patients presenting to hospital with diarrheal dehydration.

136. Sunoto, et al., Treatment of acute infantile gastroenteritis, *Paediatr Indones* 17: 351-360, 1977.

Noting that many Indonesian physicians routinely employ antibiotics in the treatment of acute diarrhea, the authors performed a con-

trolled clinical trial evaluating their efficacy as an adjunct to oral rehydration therapy.

One hundred children under the age of two years, admitted to a Jakarta hospital over a five-month period with mild to moderate diarrheal dehydration, were randomly divided into 2 groups. For each, clinical histories were elicited, nutritional and clinical status assessed and stool samples bacteriologically examined. All patients were also screened for sugar intolerance. The first group of 42 children was treated with the WHO-recommended glucose-electrolyte solution while the second group of 58 children was given the same oral solution plus antibiotics (tetracycline, chloramphenicol or ampicillin).

Age, sex, nutritional status and duration of diarrhea were comparable between the two groups. Initial degree of dehydration and prevalence of concomitant infections, however, appeared to be more serious in Group II. No significant differences were observed in the rate of rehydration, weight gain or "acceptability" of ORT. Bacteriological isolates (*Salmonella* and/or *Shigella*) were found in 13% of the cases; resistance was shown in 3/5 and 4/8 isolates in Group I and II, respectively.

The authors concluded there was no differences in either clinical or microbiological outcome between the groups.

This study indicates that the routine use of antibiotics is not beneficial in the treatment of acute diarrhea.

137. Shyamsunder, P., Oral hydration therapy in the management of cholera and other diarrhoeal diseases, *Antiseptic (India)* 74(10):633-638, 1977.

This relatively early report on the use of ORT in a Hyderabad, India hospital outlined the manifold advantages of oral vs. parenteral rehydration. The report was based on the findings of 401 patients admitted to hospital during March, 1977 with acute diarrheal diseases. Virtually all had received ORT.

After presenting the physiologic rationale for ORT, the author described the composition of ORS, its preparation, use and obvious operational advantages. Five locally available ORS formulations were compared, leading the author to recommend "Orosol" packets, (WHO-recommended composition), although purely on a cost basis. The author calculated ORT was only 1/15th as expensive as traditional IV therapy and that total savings for the 401 cases reached US$1,600.

Although clinical results were not given, the author stated ORT can replace up to 80% of all fluid requirements and that its many advantages over IV therapy make its use highly desirable.

138. Carraza, F. R., et al., Ensaio clinico comparativo sobre aceitacao de duas solucoes hidratantes orais em criancas com diarréia aguda (Comparative clinical trial of the acceptability of two oral rehydration solutions in children with acute diarrhea), *Folha Med (Brazil)* 77(5):611-614, 1978 (Article in Portuguese).

To determine the effects of adding flavoring to glucose-electrolyte solutions, the authors performed a double-blind trial among 39 children presenting with diarrheal dehydration to a Sao Paulo hospital.

Only mildly to moderately dehydrated children were studied. Ages ranged from one month to 9 years (mean 8 months). Twenty (51%) children judged moderately dehydrated were initially given IV therapy, then switched to ORT. In double-blind fashion, patients were assigned to one of 3 ORT groups: Group A (10 children) received only a cherry-flavored ORT solution; Group B (9) was given only an unflavored solution and Group C (20) was alternatively offered both solutions.

Although composition was not described, both solutions were isotonic and contained glucose and electrolytes. In all 3 groups, patients were offered the solutions *ad libitum* at fifteen-minute intervals. Acceptance was considered "good" if the recommended amounts were ingested and if fluid losses did not exceed intake over a three-hour period; acceptance was judged "regular" if fluid intake was not sufficient unless observers actively intervened; refusal to drink the solution in three successive

fifteen-minute intervals or presence of vomiting in two successive intervals indicated "bad" acceptance. Group C children who rejected both solutions were offered a third, 3% glucose solution and its acceptance was rated.

The groups were similar with respect to sex and nutritional status; however, Group C patients appeared to be older and more likely to have required initial IV therapy (levels of significance not given). Twenty-one (54%) children were either mildly or moderately malnourished.

Acceptance appeared best in Group B (unflavored); of 9 subjects, acceptance was judged "good" in 7 and "regular" or "bad" in 2. Over the first 3 hours, Group B subjects ingested a mean of 12 ± 4.5 ml/kg/hr each of the unflavored fluid.

In Group A, 7 of 10 subjects rejected the solution ("bad"); the mean age of the remaining 3, in whom acceptance began as "good" but deteriorated over time, was less than 3 months. Mean fluid intake over the 3 hours was 9 ± 6.5 ml/kg/hr in Group A.

Among the 20 Group C subjects, overall acceptance of the unflavored solution was judged "good" in 14 compared to only 4 for the flavored solution. Eleven subjects rejected the flavored solution, compared to only 4 for the unflavored; median age of the latter 4, who rejected both solutions, was over 5 years.

The authors concluded unflavored ORT solution was significantly more acceptable than flavored, that acceptance of both solutions decreased over time and that older children are more likely to refuse the flavored solution.

Although the design of this study was interesting, these findings cannot be easily generalized due to methodological problems (composition of the ORT solution, initial IV fluid volumes and other treatment details were not given). They do, however, agree with the general observation that adding flavoring does not improve and may decrease acceptability of ORT solutions.

By some little-understood mechanism, thirst appears to naturally regulate ORT fluid intake. Many observers have noted that, once rehydrated, children will refuse the unflavored solution. Masking this natural mechanism by adding flavoring could lead to overconsumption (often indicated by transient periorbital edema).

139. Levine, M. M., et al., Acute diarrheal infections in infants, I. Epidemiology, treatment and prospects for immunoprophylaxis, *Hosp Pract*, December, pp. 89–100, 1979.

Writing to U.S. clinicians, the authors reviewed various epidemiological data on diarrheal diseases worldwide, described its main risk factors, outlined therapeutic approaches to dehydration and reviewed the prospects for developing vaccines against major enteric pathogens.

The authors compared diarrheal disease prevalence in most of the developing world today to that of New York City, circa 1900. The data show that diarrheal diseases present a significant health problem until massive infrastructural and socioeconomic improvements can take place. Today, the relative prevalence of bacterial diarrheas in the developing world, compared to the primarily viral diarrheas in industrialized countries, points up the continuing environmental disparities.

The authors presented a lucid explanation of the mechanisms of dehydration and, referring to data from India, Guatemala and Africa, described the nutritional consequences of recurrent diarrhea in already marginally nourished children. The advantages of ORT were discussed and the importance of involving the mother in the actual treatment was stressed.

The use of antibiotics and drugs in treating simple diarrhea was discouraged. Kaolin-pectin preparations, they stated, "make useful placebos" but do not diminish stool electrolyte and water losses. Antibiotics are only indicated in suspected bacillary dysentery or in suspected cases of glucose malabsorption (less than one percent of cases) where heavy bacterial colonization of the upper bowel may be a risk.

The authors felt prospects for vaccines against rotavirus and enterotoxigenic *E. coli*

(ETEC), the two leading diarrhea pathogens, are mixed. The difficulty of culturing rotavirus and lack of cross-antigenicity between types 1 and 2 make vaccine development problematic. Immunoprophylaxis in ETEC, however, may be feasible as work on adhesion pili progresses.

The authors concluded by stressing the importance of nature's own way of conferring diarrheal immunity: breastfeeding.

Sack, D. A., et al., Sucrose or glucose: which sugar to use in oral rehydration solution? A summary of four clinical trials, In: Takeya, K. and Zinnaka, Y., (eds.), *Symposium on Cholera*, Karatsu (Japan) 1978. (*Proceedings of 14th Joint Conference, U.S.-Japan Cooperative Medical Science Program, Cholera Panel*, Tokyo, Japanese Cholera Panel), pp. 154-164, 1979, (Also reported in: *Lancet* 2, 280, 1978).

Djoeanda, P., et al., Oral rehydration of infants and children in the Dr. Hasan Sadikin General Hospital, Bandung, *Paed Indones* 19:72-78, 1979.

140. Greenough, W. B., III, Principles and prospects in the treatment of cholera and related dehydrating diarrheas, In: *Cholera and Related Diarrheas*, 43rd Nobel Sypm, Stockholm, pp 211-218, Karger Press, Basel, 1980.

Pertinent biological and operational issues concerning ORT and other aspects of treating diarrheal diseases were discussed in this thoughtful article. Among biological issues which the author felt required further research were the role of carrier molecules other than glucose in ORS (which enhance transluminal sodium absorption), and the effectiveness of ORT in diarrheas due to invasive organisms. Operational issues for further study included the development of effective alternate oral solutions to meet differing geocultural and economic situations; the development of a cheap, foolproof method for mothers to measure and mix an oral solution in the home; and the testing of various approaches to introducing ORT into the community.

The discovery of new antisecretory agents which would reduce fluid losses to the point where intravenous treatment would be unnecessary would constitute a real breakthrough, felt the author. Another important area for research is the possibility of developing blocking agents for toxin receptor sites in the gut epithelium. (Such receptors are known to exist for cholera toxin and may exist for others as well.) Alternately, there may be a way either to interrupt the biochemical pathway by which adenylate cyclase is produced by the receptor or to suppress the enzyme itself.

A great deal more biological and sociological research is needed into all aspects of diarrhoeal diseases, concluded the author, if improvements in their treatment and prevention are to continue.

Sack, D. A., et al., Oral therapy in children with cholera: A comparison of sucrose and glucose electrolyte solutions, *J Pediatr*, 96(1):20-25, 1980.

Greenough, W. B., III, Oral replacement therapy in diarrhea: consensus and controversy, In: Field, M., et al., (eds.), *Secretory Diarrhea*, Bethesda, MD, American Physiological Society, 1980.

141. Pizarro, D., et al., Rehidratación por via oral y su mantenimiento en pacientes de 0 a 3 meses de edad deshidratados por diarrea (Oral rehydration and its maintenance in patients 0 to 3 months old with diarrheal dehydration), *Bol Méd Hosp Infantil Mex* 37(5):879-891, 1980, (Article in Spanish).

As a follow-up to an earlier study, the authors performed this uncontrolled, sequential trial to assess the clinical efficacy of ORT in very young children.

Between March 1978 and May 1979, 106 patients ranging in age from 7 days to 3 months (mean 44.7 days) and weighing 1,900 to 6,080 grams, were treated at a Costa Rican hospital for diarrheal dehydration. The degree of dehydration was determined by comparing weight upon admission with weight on discharge.

Thirty-eight percent of patients were less than 5% dehydrated, 44% were moderately dehydrated (5-10% loss of body weight) and 18% were severely dehydrated (greater than 10% loss of body weight).

The composition of the ORT solution used was (in g/l): NaCl 3.5, KCl 2.25, $NaHCO_3$ 2.5 and dextrose 20; (in mmol/l): Na^+ 90, Cl^- 90, K^+ 30, HCO_3^- 30, and dextrose 111. The solution, which had slightly more potassium than the WHO-recommended formula (30 vs. 20 mEq/l), was mixed in 50, 100 and 200 ml. bottles and fed to the babies by their mothers. One part free water was administered for every two parts ORT solution until normal hydration was achieved. The total quantity of ORT solution administered was at least twice the clinically estimated losses, depending on the degree of initial dehydration. Mothers were encouraged to continue breastfeeding their babies while non-breastfed patients received diluted milk formula once initial rehydration had been achieved. After initial rehydration, mothers were instructed to continue ORT at home and to return for follow-up the next day.

The results showed that 97% of the patients were successfully rehydrated with ORT alone (4 patients by nasogastric route). The only complication was one case of moderate transient edema. Three patients needed IV therapy because of persistent vomiting and 10 patients were admitted to hospital due to profuse, frequent stools. The mean time to reach initial rehydration was 7 hours; 55% were rehydrated in 6 hours or less. The average treatment time in the clinic was 12 hours (range 2.5-26 hours).

Of eleven cases presenting with hypernatremia (i.e., serum Na^+ greater than or equal to 150 mmol/l), ten were corrected within 24 hours using the above regimen alone. The only case not to respond had not received either free water or milk feedings over the initial 18 hours of home treatment.

The authors concluded that ORT using the the WHO-recommended formula, is efficacious in neonates as well as infants.

(See also abstracts No. 44, 155.)

142. Rahaman, M. M., et al., Evaluation of oral rehydration as the only therapeutic measure in acute diarrhoea: a treatment centre experience with home follow-up, ICDDR, Bangladesh, (Presented at: *VI Asian Pacific Congress of Gastroenterology*, Auckland, 10-14 February, 1980).

The authors described an uncontrolled clinical trial in which patients with moderate to severe dehydration, (as defined by serum refractive index of 1.029 or greater), without shock, were managed exclusively by ORT (UNICEF supplied, WHO-recommended ORS packets), first at the ICDDR,B Treatment Center in Dacca, Bangladesh and then at home during follow-up.

Of 451 patients (all ages) initially screened, 277 (61%) whose serum refractive indices exceeded 1.029 were selected for study. Of these, 257 (93%) were successfully rehydrated in the clinic with ORT alone. Twenty (7%) were judged treatment failures and were given intravenous rehydration while another 21 patients developed fever above 39°C or signs of dysentery and were therefore excluded from the study.

Following successful rehydration, 215 patients were sent home with instructions to continue ORT. Patients were visited daily by health workers over a five-day period. Eighteen (8%) were lost to follow-up. Six (3%) of the 201 remaining cases required subsequent IV therapy and were thus judged treatment failures.

The high ORT success rates observed in mildly as well as moderately to severely dehydrated patients, the authors concluded, suggest ORT is a very useful method for both home and clinical management of dehydration.

143. Bai, K. I., et al., A study of oral rehydration therapy in childhood diarrhea, *Indian J Pediat* 47:279-282, 1980.

The author reported the results of a large, uncontrolled, sequential clinical trial of ORT in Tirupati, Andhra Pradesh, India.

A total of 877 children (72% below 5 years of age) presenting to hospital with diarrhea and vomiting, were studied. Five hundred-ten children (58%) who presented with mild dehydration were treated with ORT using WHO-recommended ORS alone on an outpatient basis, while 367 (42%) with either moderate (320) or severe (47) dehydration were first admitted to hospital where most were initially rehydrated with IV therapy, then switched to ORT.

Of the 510 mildly dehydrated cases, 84.1% were successfully treated with ORT alone. Of the 320 moderately dehydrated cases admitted to hospital, 64 (17%) were treated only with ORT. Three common complications of IV therapy—abdominal distension, venesection and thrombophlebitis—were observed in 54 (91%) seriously dehydrated, 90 (27%) moderately and in no mildly dehydrated cases.

The authors concluded ORT was highly effective, even in the presence of vomiting. ORT is inexpensive, non-invasive, easily administered and does not require constant monitoring by skilled personnel, they found. They added that ORT can also be used in other disorders such as encephalitis, meningitis and pyrexia of unknown origin, which require prolonged rehydration therapy.

144. Ghisolfi, J., et al., Traitement par voie orale par une solution hydroélectrolytique sucrée des diarrhées aiguës de l'infantile (Oral treatment of acute infantile diarrhoea with sucrose-electrolyte solution), *Arch Fr Pediatr* 37:93-98, 1980, (Article in French).

Despite the fact that oral fluids for treating diarrheal dehydration had gained wide acceptance in many countries, little is known about ORT in France, observed the authors. They therefore carried out a one-year, uncontrolled, sequential clinical trial to evaluate ORT among children presenting with uncomplicated acute diarrhea to a French treatment centre.

One hundred sixty-one well-nourished children, ages 1-26 months (mean 6.8 months), were selected for study. After initial physical examination, stool and serum specimens were collected and the degree of dehydration assessed. Over the first 24 hours all solid foods and milk were withheld and the children were given ORT *ad libitum*.

The authors used an isotonic oral solution which contained both glucose and sucrose (composition: Na^+ 50 mEq/l; K^+ 30 mEq/l; HCO_3^- 24 mmol/l; glucose 111 mmol/l; sucrose 55 mmol/l).

Over the first 6 hours the children were given volumes equal to two-thirds of their estimated fluid losses. By 24 hours, they had been offered volumes equivalent to at least twice their initial losses. Milk and other foods were gradually reintroduced the second and third days.

One hundred-twenty (74.5%) of the children did not show overt signs of dehydration at admission; 19 (11.8%) were judged moderately and 22 (3.7%) severely dehydrated. Acidosis was found in 69 (46%) cases, other electrolyte imbalances in only 18 (11.2%). Stooling rates averaged 6 stools/24 hours, but in 38 (23.6%), the rates exceeded 10 stools/24 hrs.

Volume of ORT solution ingested was significantly related to initial degree of dehydration (p less than 0.01) and, over the first 24 hours, exceeded initial fluid losses in all cases. Fluid intake over the second 24 hours, however, varied only with age (p less than 0.01) and not with degree of initial dehydration. Although vomiting was observed in 88 (54.6%) children it was not an obstacle to treatment and in all cases dehydration disappeared within three days.

Over 5 days of treatment, significantly dehydrated children gained weight while those not presenting with overt signs of dehydration lost weight. Of 5 children who returned for subsequent treatment after discharge, all were successfully treated with ORT alone. There were no significant differences among the children with respect to age, etiology or initial degree of dehydration.

The authors concluded that ORT, given *ad libitum*, was highly efficacious regardless of etiology. Weight gains in moderately and se-

verely dehydrated cases were due to the net retention of the ORT solution, they felt, but net losses in those not visibly dehydrated may have resulted from insufficient caloric intake.

145. Varavithya, W., et al., Comparison of oral rehydration with electrolytes solution and soy milk in acute diarrea, *J Med Ass Thailand*, 63(11):593-597, 1980.

Hypothesizing that accompanying disaccharidase deficiency may interfere with intestinal absorption of nutrients during acute diarrheal dehydration, and that lactose-containing formulae may complicate treatment, the authors compared the efficacy of lactose-free soy milk to either breastmilk or "humanized" infant formula as an adjunct to sucrose-electrolyte solution in ORT.

Forty-six patients under the age of two years were admitted to hospital with acute diarrhea and divided alternately into two equal groups of 23 each. Weights and mean serum electrolyte values were assessed at admission and at 24 and 48 hours. Stool samples were also examined. Group I patients, of which one was moderately and the rest mildly dehydrated, were treated with 200 ml/kg of diluted soy milk (ie., 100 ml. of full strength soy milk plus 100 ml of a simple salt/sugar (SSS) solution containing: Na^+60 mEq/l, Cl^-60 mEq/l, sucrose 5%) over the first 24 hours. The milk concentration was gradually increased to full-strength by the third day. The second group, which included four moderately and 19 mildly dehydrated cases, received 200 ml/kg of the same SSS solution on the first day and either infant formula (15) or breast milk (8) in gradually increasing concentrations on the second and third days. Rehydration fluids were administered to both groups by nasogastric drip on the first day and by mouth afterwards.

Pre-admission weight for age and serum electrolyte values at admission, 24 and 48 hours were nearly identical in both groups. The authors found 30% of Group I and 27% of Group II patients had sugar malabsorption, as indicated by stool pH of less than 6 and stool glucose concentrations of "more than 1^+ on the Labstix scale". There were no significant differences between the groups with respect to total fluid intake or weight gain. Recovery time, however, was significantly shorter in the group given breastmilk from Day 2 onwards compared to either the dilute-soy or humanized formula groups (p less than 0.05).

The authors concluded there was no advantage to using the dilute soy formula and recommended that a sucrose-based ORT solution be given, followed by breastfeeding.

Although the breastfed group appeared to respond best, the data do not support either the initial hypothesis or the recommendation that sucrose *vis-à-vis* glucose-electrolyte solution should be used.

Finberg, L., et al., The role of oral electrolyte-glucose solutions in hydration for children—international and domestic aspects, *J Pediatr* 96(1):51-54, 1980.

Islam, M. R., et al., Use of low and high sodium containing oral rehydration solution in paediatric diarrhea. (*Presented at The 21st Conference of the Indian Society of Gastroenterology, Calcutta, 1980.* Reprints: MRI, Chief Physician, ICDDR,B, GPO Box 128, Dacca-2, Bangladesh).

146. Kahn, A., et al., Hyperkalemia and UNICEF type rehydration solutions (letter), *Lancet* 1:1082, 1980.

The authors reported finding serum electrolyte abnormalities in seven Belgian infants treated for diarrheal dehydration with WHO-recommended ORT solution.

On admission, 2 of the 7 patients were hypernatremic (serum sodium concentrations of 155 and 158 mmol/l) and 5 were normonatremic. *Campylobacter* was isolated from two stool samples, *E. coli* from one. All were well nourished.

The patients were given an average of 140 ml/kg ORT solution in 24 hours. In all cases, they reported, ORT had to be stopped after a mean period of 41 ± 9 hours because of "high levels of plasma potassium" in 6 cases and "aggravation of preexisting hypernatremia" with development of seizures in one.

Mean serum potassium concentrations rose from 4.1 ± 0.2 mmol/l before treatment to 5.1 ± 0.2 mmol/l after 24 hours. Peak K^+ values were 6.1 ± 0.2 mmol/l; 24 hours after ORT had been discontinued, mean K^+ had fallen to 4.7 ± mmol/l. They observed the highest plasma K^+ levels in those presenting with no or few stools during treatment.

Serum sodium concentration had risen from 155 mmol/l to 161 mmol/l in the patient who had seizures, they noted.

In well-nourished children below one year of age, concluded the authors, ORT based on the WHO-recommended composition should not last more than 24 hours. Besides the known risk of hypernatremia, they stated, potassium loading also seems to be a problem. Beyond 24 hours, they stated, "no scheme of treatment has been proposed" except for use in underdeveloped countries where breastfeeding is advocated. They felt a guide for therapy is therefore needed in cases where mothers do not breastfeed.

These observations are at variance with those of other investigators, most of whom have shown serum electrolyte inbalances are corrected, even in neonates, when the WHO-recommended ORS composition is used.

The authors did not state whether the children were given other fluids or foods during the initial 24 hours. Neither were presenting levels of dehydration nor time to achieve initial rehydration described. In small children the WHO recommends that ORT solution be accompanied by free water, breastmilk or diluted cow's milk and that ORT be discontinued once dehydration has been corrected and purging has stopped.

(See also abstract No. 148.)

147. Clements, M. L., et al., Oral therapy with glucose electrolyte solution (letter), *Lancet* 2:34, 1980.

The authors questioned the findings of Kahn, et al. (see preceding abstract), in which hyperkalemia and hypernatremia were reported to be risks of using the WHO-recommended ORT solution.

They noted that important factual and methodological details (e.g., total number of patients seen, initial degree of dehydration, stooling rates, exact treatment regimen followed) were not described in the article. If anything, hypo-, rather than hyperkalemia was seen by many investigators as an improbable but possible complication of using the WHO-recommended ORT solution. For this reason, the authors reported, the amount of potassium in ORS now used in Costa Rica has actually been increased to yield 30 vs. 20 mmol/l of K^+. After treating thousands of essentially well-nourished, mainly bottlefed babies, no hyperkalemia has been reported in Costa Rica. Neither has hypernatremia been found to be a significant problem. In fact, they stated, the WHO-recommended regimen has been shown to correct hypernatremia. Moreover, the Costa Rican treatment regimen beyond 24 hours has been shown successful and, contrary to what Kahn, et al., recommended, serum electrolytes need not be routinely monitored.

The hyperkalemia reported by Kahn, et al., may have resulted from administering excessive amounts of ORT without a source of free water to infants having few diarrhoeal stools. Falsely high K^+ values may also have resulted from haemolysis, they added.

Nalin, D., et al., Rice powder and electrolyte solutions (letter), *Lancet* 2(8290):155-156, 1982.

Islam, M. R., et al., Labon-gur (common salt and brown sugar) oral rehydration solution in the treatment of diarrhoea in adults, *J Trop Med Hyg*, 83,41-45, 1980.

Walker, S. H., Hypernatremia from oral electrolyte solutions in infantile diarrhea (letter), *N Eng J Med*, 304:1238, 1981.

Santosham, M., et al., Oral electrolyte solutions for infantile diarrhoea (letter), *N Eng J Med* 305(10):581, 1981.

Cleary, T. G., et al., The relationship of oral rehydration solution to hypernatremia in infantile diarrhea, *J Pediatr*, 99(5):739-741, 1981.

148. Kahn, A., et al., Glucose electrolyte solutions in a European context (letter), *Lancet* 2:361-362, 1981.

The authors reported their clinical observations on the use of ORT to treat diarrheal dehydration among 50 children less than 2 years of age presenting to a hospital in Brussels, Belgium.

Having earlier encountered hyperkalemia and hypernatremia when using WHO-recommended ORT (see abstract No. 146), the authors halved the K^+ and Na^+ concentrations to yield the following ORT solution (in mmol/l): Na^+ 57, K^+ 9.6, Cl^- 40.5, HCO_3^- 30 and glucose 111.

Upon admission, all the infants were "about 10% dehydrated". Thirty-nine (78%) of the 50 infants were from immigrant families; 13 (33%) of these had recently returned to Belgium after extended stays in North Africa or Turkey. No child had been previously breastfed and 36% had been on "low solute", 64% on "high solute" feeds. Sixteen (32%) of the 50 children presented with hypernatremia (not defined).

Over the first 24 hours, those presenting with hypernatremia ingested an average of 120 ml/kg of the ORT solution; those with normal or low serum electrolyte values received 150 ml/kg. Nasogastric administration was used "if necessary". On the second day, the bicarbonate was omitted from the solution. This lowered the Na^+ concentration to 30 mmol/l. Normal milk feeds were then reintroduced.

In contrast to the findings of their first study, the 16 cases presenting with hypernatremia recovered without sequelae. However, 9 infants presenting with normal or low serum Na^+ (130 mmol/l) and K^+ (2.7 ± 0.3) values required oral K^+ supplementation. These 9 were all immigrant children who had histories of recent, prolonged diarrhea (mean 15 days) and were significantly underweight compared to the others (88% of weight for age). These 9 did not differ from the other 25 presenting with normal or low Na^+ values as regards age, sex, nationality, feeding history, vomiting, associated illness or previous antibiotic treatment.

Oral rehydration was judged successful in all 50 infants. However, after 24 hours, plasma K^+ remained significantly lower (p less than 0.001) in the 9 who had presented with hypokalemia.

The authors concluded their modified ORT solution was safe and efficient, did not require alternation with other fluids and did not cause either hypernatremia or hyperkalemia.

The fact that 9 children required K^+ supplements, however, would seem to contradict this conclusion. The data do not show the author's modified solution to be superior to that recommended by WHO; on the contrary, they indicate the K^+ concentration should not have been reduced.

149. McLean, M., et al., Etiology of childhood diarrhoea and oral rehydration therapy in northeastern Brazil, *Bull Pan Am Hlth Org* 15(4):318-326, 1981.

To determine the epidemiological characteristics of diarrheal diseases in northeastern Brazil and to assess the efficacy of ORT in this setting, the authors performed microbiological studies and a controlled clinical trial from 8 March to 24 April, 1978, in Fortaleza, Brazil.

Fifty-three children over three months of age presenting with uncomplicated, acute diarrhea to a Fortaleza treatment center were selected for study. All but one were less than five years old. None had been given antibiotics during the previous 2 weeks. Case histories were obtained from the mothers, clinical assessments made, stool specimens collected, and all patients were given initial intravenous therapy.

Upon initial improvement, the children were randomly divided into either intravenous only (24) or intravenous and ORT (29) groups. While the former continued receiving IV therapy (according to the local, standard regimen) those in the latter group were switched from IV to oral therapy. The mothers administered the fluid, which was prepared using WHO-recommended ORS. The ORT was considered successful if the signs of dehydration had diminished, the patient's state of conciousness had

improved, urination had ensued and weight was gained.

Results from 20 of 37 (54%) stool cultures were positive. Enterotoxigenic *E. coli* was identified in 27%, ST-producing *E. coli* in 26%, and LT-producing *E. coli* in the remaining 5.4%. *Salmonella*, *Shigellae*, *G. lamblia* or rotavirus were found in 10 (27%) of the samples.

All patients responded well to therapy. However, one ORT patient had to be switched back to IV therapy due to persistent vomiting. During initial IV treatment there were no differences in duration, fluid intake, weight gain or level of consciousness. Age, stooling rates, duration, presence of vomiting, serum specific gravities and degree of dehydration were comparable between the two treatment groups. The ORT group, however, required significantly less fluid (mean 237 ml vs. 545 ml) and significantly less treatment time (mean 3.8 vs. 8.6 hrs.) than the IV group. No significant differences in weight gain were noted. Adjusting for body weight, the ORT group required an average of only 32.3 ml of fluid per kilogram body weight while the IV group needed 67.3 ml/kg to achieve full rehydration.

The authors concluded that ORT was effective in treating diarrheal dehydration of varied etiology, was well accepted and could provide an inexpensive alternative to IV therapy.

150. Manfredi, L., et al., Informe preliminar sobre un esquema de rehidratación oral en la deshidratación por diarrea aguda (Preliminary report on a scheme for oral rehydration in acute diarrheal dehydration), *Rev Hosp de Niños (Bs As)*, 23(96):169-174, 1981, (Article in Spanish).

The authors reported the results of an uncontrolled clinical trial of ORT in a large Buenos Aires hospital.

Thirty-seven children below 2 years of age (mean 8.3 months) were selected for study. After admission, histories were taken, initial physical and biochemical examinations performed and the children were administered ORT by their mothers using WHO-recommended ORS. Normal feeds were resumed once initial rehydration was achieved. Serum electrolytes were measured at admission, upon initial rehydration and at 24 hours.

Fifteen (41%) children were eutrophic, 14 (38%) were mildly, 7 (19%) moderately and one severely malnourished (Gomez classification). Dehydration was judged mild in 6 (16%), moderate in 28 (76%) and severe in 3 (8%) children.

Thirty-seven (95%) children were successfully rehydrated using ORT alone. Vomiting was observed in 48% of cases. Nasogastric tubes were used briefly in 13 (37%) of these. The average time to achieve initial rehydration was 3 hours (range 1-7 hours). Hypernatremia was not seen. In 8 children whose serum electrolytes were measured, sodium, potassium and pH values tended towards normal over the initial 24 hours. Patients were discharged after a mean of 2.5 days (range 1-8) in hospital.

There were two treatment failures. One, a seriously malnourished five-month-old who had presented with 8% dehydration, had been initially given ORT but later had to be switched to IV therapy. The presumed cause was intestinal malabsorption secondary to severe malnutrition. The second failure, a four-month old with no malnutrition and 5% dehydration, consistently refused ORT and, after 20 hours, was switched to IV therapy.

The authors concluded ORT was simple, effective, rapid and reduced hospitalization stay dramatically. They recommended its use on the primary care level as a means of avoiding the risks that accompany hospitalization and involving mothers directly in treatment.

151. Ashley, D.E.C., et al., Oral rehydration therapy in the management of acute gastroenteritis in children in Jamaica, In: Holmes, F., et al., (eds.): *Acute Enteric Infections in Children. New Prospects for Treatment and Prevention*, Amsterdam, Elsevier/North-Holland Biomedical Press, 389-394, 1981.

The authors described the results of a one-month, uncontrolled sequential clinical trial of ORT in the Casualty Ward of the Bustamante

Hospital for Children in Kingston, Jamaica in March, 1979.

After they had received appropriate training, auxiliary hospital staff selected for study 552 children presenting to the Casualty Ward with uncomplicated acute diarrhea and mild to moderate dehydration. The auxiliaries examined the children, assessed fluid needs and instructed the mothers on how to give ORT. Under their supervision, the mothers successfully treated 496 (89.9%) of the children with ORT alone on an outpatient basis.

After initial rehydration, the mothers were given WHO-recommended ORS packets and instructed to continue ORT at home.

Of 136 children later followed up, 119 (87.5%) were found to have been successfully managed by ORT alone; 6 (4.4%) required IV therapy and 34 (6.1%) required subsequent hospitalization.

During the previous month, 304 of 559 (55%) presenting cases had required IV therapy and 94 (16.8%) had been admitted to hospital. Thus, use of ORT on an outpatient basis led to a fifteen-fold reduction in IV usage and a four-fold reduction in hospital admissions.

By November 1979, ORT was sufficiently established to justify the conversion of a pediatric ward previously devoted to gastroenteritis into a general medical ward.

After the training of selected health personnel and the preparation of ORT guidelines, the routine use of ORT was established in two hospitals and four health centers in the greater Kingston area. A nationwide diarrheal disease control program is now being phased in through health centers throughout the island.

152. Sunakorn, P., Oral electrolyte therapy for acute diarrhea in infants, *J Med Ass Thailand* 64(8):401-404, 1981.

Noting that ORT has come into routine use worldwide, the author summarized three recent (1980) clinical trials, the results of which indicated the method is equally efficacious in Thailand.

In the first study, 30 children below 2 years of age were successfully rehydrated by means of WHO-recommended ORT solution given *ad libitum*. Transient edema was seen in 3 patients. The second trial, also using the WHO-recommended ORS, compared an *ad lib* ORT regimen to a "dilute" ORT dosage schedule (9% glucose alternated with full-strength ORT solution) in children below 6 months of age. Again, edema was seen in 5/80 of the "*ad lib*" and 2/80 of the "dilute ORT"-scheduled patients. There was one treatment failure. Edema was correlated with total fluid intake, noted the author, not with Na^+ content. The third study again compared ORT to "dilute" ORT regimens in children under 6 months of age. This time, however, fluid intake was matched to stool losses. No edema was seen.

The author endorsed use of WHO-recommended ORS but concluded the third, controlled ORT regimen should be used.

153. Sugijanto, et al., Edema in oral rehydration, *Paed Indones* 21:229-234, 1981.

As early as 1971 ORT was commonly practiced by Indonesian clinicians, reported the authors. At that time two ORS formulations were in use, one for cholera and another for other kinds of diarrhea. In 1974, Indonesian experts suggested a single ORS formulation be adopted countrywide for use in all types of diarrhea. The ORS formula then endorsed yielded (in mEq/l): Na^+ 85, K^+ 15, HCO_3^- 30 and glucose 120 mOsm/l. In 1978, home administration of ORT was endorsed, using the same formula but with orange flavoring added.

Observing that transient edema was an occasional, undesirable side effect of the recommended ORS formula, some clinicians were reluctant to accept the home use approach. The authors therefore carried out an uncontrolled sequential clinical trial, using the recommended formula, to assess to what extent edema was a problem in ORT.

One hundred-sixty children, ages 5 days to 12 years (mean 10.4 months), presenting to an Indonesian hospital with moderate diarrhoeal dehydration, were selected for study. Sixty-four percent of the children were moderately to severely malnourished. Feeding histories and

breastfeeding information were not given. Patients were given ORT *ad libitum* (those over one month of age) or by nasogastric drip (neonates) over the first 24 hours using one of 3 local ORS formulations, all of which conformed to the composition described earlier. If dehydration persisted beyond 24 hours, ORT was continued. If edema was noted, ORT was stopped and boiled water or sweetened tea were substituted. No further treatment details were given.

Treatment was apparently successful in all 160 cases. Fluid intake ranged from 200-4400 ml (mean 898 ml) over 1-4 days (mean 1.5 days). Seven of the 160 (4.4%) patients developed periorbital edema, with or without pretibial edema. Their ages ranged from 2 to 16 months; mean body weight was 6.6 kg. The 7 had ingested a mean volume of 1,743 ml (range 800-4400) of the ORT solution over a mean period of 2 days. Edema disappeared gradually within 9.5 to 48 hours.

Based on age, body weight, initial degree of dehydration and duration of diarrhea, the authors estimated the daily Na^+ requirements of the 7 dematose cases. To do this, they used standard age-adjusted estimates of daily stool sodium losses. (Neither serum nor stool sodium levels were actually measured in any of the patients.) Comparing their estimated requirements to actual sodium intake (mean 151.8 mEq Na^+) the authors calculated that 5 of the 7 dematose patients had received excessive sodium, 1 had been given the correct amount and 1 had not been given enough.

The authors concluded the edema observed was not directly related to total sodium intake, nor could it be associated with age, sex or nutritional status.

Although methodological factors (e.g., no comparison group, no actual Na^+ measurements) and incomplete information (i.e., on feeding histories or dietary intake during ORT) limit the usefulness of these data, of interest is the fact only 7 of the 160 patients manifested edema even though none, apparently, had received free water, breastmilk or other feeds during the ORT.

154. Rohde, J. E., et al., Therapeutic interventions in diarrhoea, *Food Nutr Bull (United Nations Univ.)*, 3(4):34-38, 1981.

Distilled from the proceedings of an international workshop entitled "Interactions of diarrhoea and malnutrition," held in Bellagio, Italy in May, 1981, this report was prepared by five distinguished scientists in the field of enteric diseases.

A brief review of ORS composition was presented. The authors felt that, whenever possible, the WHO-recommended "complete" ORS formula should be used but that greatest emphasis should be placed on replacing fluid and salt losses as early and rapidly as possible before the onset of clinical dehydration. The authors presented an interesting review of the prospects for including hypo-osmotically active substrates, such as cereals, rice powder, starch and other calorie-rich glucose sources, in ORS to improve its energy content.

The importance of continued feeding during diarrheal episodes was stressed. Better weight gain, shortened duration and avoidance of malabsorption syndromes were the key reasons identified by the authors.

Increasing food intake immediately after diarrheal episodes was also strongly recommended by the authors. Summarizing the results of several balance studies, they recommended that children recovering from acute diarrhea be fed 25-50% more than the recommended daily allowance within a period no longer than two to four times the duration of diarrhea.

The risks of using drugs and other anti-diarrheal agents were discussed. For a physician deciding solely on clinical grounds, the most useful indicator for the use of antibiotics is bloody dysentery with fever. Even then, varying resistance patterns in *Shigella* may necessitate culturing and sensitivity tests for antibiotic therapy to be effective.

Wong, H. B., Rice water in treatment of infantile gastroenteritis, (letter) *Lancet*, 2: 102-103, 1981.

155. Pizarro, D., et al., Treatment of 242 neonates with dehydrating diarrhea with an oral glucose-electrolyte solution, *J Pediatr (in press)* 1982.

This retrospective study summarized four years' experience (1978-1981) with glucose-electrolyte solutions (GES) for treatment of diarrheal dehydration in neonates in a controlled hospital setting in San José, Costa Rica.

Over the study period, a total of 257 neonates (28 days of age or less) were admitted to hospital with diarrheal dehydration. Of these, 242 neonates were treated with a GES formula that contained (in g/l): NaCl 3.5, KCl 2.25, $NaHCO_3$ 2.5, and anhydrous glucose 20. In one litre of water, the formula, which closely resembled that of WHO-recommended ORS, provided (in mmol/l): Na^+ 90; K^+ 30, Cl^- 90, HCO_3^- 30 and glucose 111.

The mean age of the neonates was 19 days. The mean duration of diarrhea prior to admission was 3.5 days. Most cases were brought to the hospital within the first 3 days. Eighty-seven neonates (40%) presented with mild dehydration (less than 5% loss of body weight), 113 (52%) suffered dehydration of 5-10% loss of body weight, and 17 (8%) had over 10% loss of body weight.

Mothers administered oral GES by baby bottle under close supervision. Two bottles of GES, followed by one of plain water, were given to 36% of cases while 61% were given all the calculated GES requirement at one time, followed by all the free water in a ratio of 2:1.

Oral rehydration was successful in 234 of the 242 neonates (96.7%). Eight were rehydrated by intravenous therapy. No deaths were reported.

Preadmission vomiting was recorded in 69% of the neonates but this was not an obstacle to complete rehydration. The average time needed to rehydrate patients was 7.44 ± 3.51 hours. The mean quantity of total fluids ingested was 424 ± 13 ml and the rate of ingestion was 26 ± 1.0 ml/kg/hr.

Of 78 cases whose blood chemistries were analyzed, 19 (24%) presented with hypernatremia (serum sodium greater than 150 mmol/l) and 5 (6%) presented with hyponatremia (serum sodium less than 130 mmol/l). All were successfully rehydrated. However, two of the hypernatremic patients had seizures, one occurring 18 hours after admission (serum Na^+ 163 mmol/l) and the other 6 hours after admission (Na^+ 181 mmol/l). Expressed as a rate, the occurrence of seizures (10.5%) was lower than that during 1977 (13.9%) when only intravenous rehydration was used. Severe acidosis, found in 18 of 57 (32%) neonates tested, was corrected in all cases within 48 hours.

The authors concluded ORT is the method of choice for the treatment of neonates with diarrheal dehydration.

(See also abstracts No. 44, 141.)

156. Dugdale, A., et al., Refeeding after acute gastroenteritis: a controlled study, *Arch Dis Child*, 57:76-78, 1982.

To determine the effects of rapid refeeding during acute diarrhea, the authors studied 59 children, 6 months to 5 years of age, presenting to a Brisbane, Australia hospital with uncomplicated acute diarrhea.

Informed consent was obtained and children were matched for age and sex and initial degree of dehydration. After initial "unstandardized" treatment (either oral or I.V. therapy, according to hospital routine) they were randomly assigned to either "gradual" or "immediate" refeeding groups. The former were given half-strength whole milk for 24 hours, then normal feeds, while in the second group, normal feeds were immediately reintroduced. Food and fluid intake and body weights were monitored in all children. In both groups, if signs of dehydration reappeared or vomiting or diarrhea "markedly worsened" children were given clear fluids again. Within the first week after discharge, home visits were made of all children.

In the rapid refeeding group, 7 of 28 (25%) were at some time put back on clear fluids; however, only one of these lost weight, while five continued to gain weight and one's weight was unchanged. In the gradual refeeding

group, 3 of 32 (9%) required additional fluids; 2 of these lost weight while that of the third remained stationary. The rapid refeeding group lost less weight and was discharged, on the average, a half-day sooner compared to the gradual refeeding group. Neither difference, however, was statistically significant. Home visits showed that recurrences of vomiting or diarrhea had occurred in 2 (7.1%) of the rapid and 4 (12.9%) of the gradual refeeding groups.

The authors concluded that rapid refeeding during acute diarrhea does not entail any risk of worsening a child's condition and may, in fact, result in less weight loss and shorter hospital stays.

Although of interest, small sample sizes and unclear methodology limited the extent to which the study's findings can be generalized.

157. Soeprapto, et al., Feeding children with diarrhea, *Trop Ped Env Chld Hlth*, 25(4):97-100, 1982.

According to some observers, diarrheal dehydration may be viewed as fluid-electrolyte malnutrition. A second nutritional consideration is the fact that recurrent diarrhea often leads to, or exacerbates, protein-energy malnutrition. Whereas the former can be relatively easily and rapidly repaired using intravenous or oral rehydration, only early and rapid refeeding can forestall the latter.

To measure the effects of dietary intake on weight gain following acute diarrhea, the authors placed forty babies less than 2 years of age into two groups, A and B. The groups were similar with respect to sex, nutritional status, degree of initial dehydration (all but 3 cases were moderately to severely dehydrated) and presence of reducing substances in stools. Stools were tested for reducing substances using the "clinitest" method. Following initial rehydration by either oral or intravenous routes, (ie, until urine specific gravity fell to or below 1.020) within 4-6 hours refeeding was begun and fluids continued as needed.

Group A children were refed according to a "classic" schedule, which started with dilute formula and returned to a full diet nine to eleven days later. Thirteen cases in Group A whose stools were positive for reducing substances were begun on low-lactose formula, with "ordinary milk formula" gradually substituted by Day 8. Solid food was re-introduced on the ninth day. The remaining 7 cases without reducing substances received dilute ordinary milk formula, increasing to full-strength by Day 6, and were given solid food beginning on Day 7.

In contrast, Group B children were given dilute formula the first day, increased to full-strength by Day 2. Solid foods were also introduced the second day and a normal diet was restored by Day 4. As in Group A, a low-lactose formula was given to those cases with stool reducing substances (12) while the others (8) received ordinary milk formula.

Not surprisingly, there were highly significant differences in mean daily weight gain (Group A: 6g/day; Group B: 49g/day), and duration of hospital stay (Group A: mean 9.9 days, range 9-14; Group B: mean 4.6 days, range 4-10). Duration of diarrhea (mean: 3 days), however, did not differ significantly. In view of these findings, the authors recommended a high calorie diet be given as early as possible as part of treatment.

These results agree with those of many other investigators, illustrating the obvious nutritional benefits of rapidly restoring dietary intake during bouts of acute diarrhea.

Finberg, L., et al., Oral rehydration for diarrhoea (Editorial), *J Pediatr* 101(4):497-499, 1982.

158. Nalin, D., Oral therapy for dehydration due to infantile diarrhoea, *Postgrad Doc—Middle East*, February, pp. 60-68, 1982.

The author presented detailed, practical guidelines on ORT and other aspects of diarrheal case management.

There are 2 goals to treatment, felt the author: reduction of mortality rates to less than one percent and teaching mothers how to effectively manage diarrhea at home using ORT.

Over 90% of cases are mild and self-limiting, he observed. These can be managed easily

by mothers, using the episode as an opportunity to instruct them. A useful table, entitled "Essential instructions to the mothers", was included in the article.

Moderately dehydrated cases can also be managed by the mother, using the 2:1 ORS to free water regimen. It is important not to mix them, however, because this will lower the glucose concentration and impair intestinal absorption. Once initial rehydration is achieved, normal milk feeds should be reintroduced. Using this method, a third of all such cases can usually be discharged from hospital (with continued home ORT) within 6 hours, felt the author.

Severely dehydrated cases (over 10% dehydration) require initial IV therapy but usually can be switched to ORT within one to two hours. The author also recommended ORT (using the WHO-recommended ORS formula) to correct hypo- and hypernatremia, using the 2:1 regimen. Because of the risk of hypokalemia (too little potassium) the author advised against using SSS solutions.

Even in severe cases, ORT is successful 93-96% of the time, stated the author. Causes of ORT treatment failure may include congenital malabsorption syndromes, excessive vomiting and improperly prepared solutions. Most commonly, however, failure is due to not giving enough ORT fluid.

The author concluded there is no present justification for any therapy other than ORT in uncomplicated cases of diarrhea. Many factors militate against using antibiotics and numerous researchers have conclusively shown ORT is equally efficacious in diarrheas of all etiologies.

159. Santosham, M., et al., Oral rehydration therapy of infantile diarrhea: A controlled study of well-nourished children hospitalized in the U.S. and Panama, *N Eng J Med* 306(18):1070-1076, 1982.

To assess the safety and efficacy of the WHO-recommended ORS formula in treating well-nourished children in a developed-world setting, the authors conducted a controlled clinical trial comparing two different oral rehydration solutions to standard IV therapy among 146 well-nourished children, aged three months to two years, hospitalized with acute diarrhea.

The study population consisted of 52 U.S. children (non-Indian) admitted to four hospitals over a three-year period (July 1977-March 1981) and 94 Panamian children hospitalized at the Social Security Hospital in Panama City, Republic of Panama, during a five-month period (Dec. 1979-March 1981). Diarrhea was considered present when the stools took the shape of their containers. The decision to hospitalize was made by the hospital house officers, based on clinical assessment of five percent or more dehydration. Only uncomplicated cases were studied.

Fifty patients randomly assigned to Group A received the standard WHO ORS formula (i.e., containing 90 mEq/l Na^+) with a strawberry flavoring. Forty-eight patients in Group B received a solution containing only 50 mEq/l Na^+ without flavoring (Solution B concentrations in mmol/l: Na^+ 50, K^+ 20, Cl^- 40, HCO_3^- 30 and glucose 111). The 48 patients in Group C, the control group, received conventional intravenous therapy (0.45% saline with 5% glucose and 20 mEq/l of KCl) for rehydration and maintenance. Patients in Group C were also given oral "Pedialyte" (in mmol/l: Na^+ 30, K^+ 20, Cl^- 30, glucose 277 and citrate 31) for 12 hours after the diarrhea stopped.

Patients who were mildly to moderately dehydrated (58%) on admission were both initially rehydrated and maintained with either ORT given *ad libitum* (Groups A and B) or with IV fluids (Group C). Eleven (11%) patients in Groups A and B who were admitted with severe dehydration were given initial IV therapy, then switched to ORT. In the U.S. children, no additional free water was given for the first 24 hours unless the diarrhea stopped within that time. Sera and stools were examined at admission. Follow-up sera examinations were performed at 8, 24 and 48 hours after admission and two weeks after discharge.

All 98 children receiving ORT were success-

fully rehydrated with the exception of one who later required additional IV therapy because of an exceptionally high stooling rate (11 ml/kg/hr). Ninety percent of the children received no IV therapy during hospitalization. Six patients were hypernatremic on admission (serum solution greater than 150 mEq/l) and three were hyponatremic. Mean serum electrolyte values for all three groups were normal at 8, 24 and 48 hours. No children developed hypernatremia or hyponatremia during therapy. The duration of diarrhea after hospitalization was similar in all three treatment groups.

Observing that treatment begun with ORT was successful in 97/98 cases, the authors concluded that both (50 mmol/l and 90 mmol/l sodium) oral rehydration solutions were safe and effective for use in well-nourished children with acute watery diarrhea. They also noted both oral solutions rapidly corrected presenting hypernatremia, a finding which discounts the suggestion by others that the WHO-recommended formula contains too much sodium for use in children from developed countries.

These findings, and the obvious operational and economic advantages, led the authors to recommend use of a single ORT solution, preferably that endorsed by the WHO, in well-nourished children in developed countries.

Patra, F. C., et al., Can acetate replace bicarbonate in oral rehydration solution for infantile diarrhoea? *Arch Dis Child*, 57:625-627, 1982.

Ho, T. F., et al., Rice water and milk: effect on ileal fluid osmolality and volume, *Lancet* 1:169, 1982.

Molla, A. M., et al., Rice-powder electrolyte solution as oral therapy in diarrhea due to *V. cholera* and *E. coli, Lancet*, 2:1317-1319, 1982.

Nalin, D., et al., Rice powder and electrolyte solutions (letter), *Lancet* 2(8290):155-156, 1982.

Kjellman, B., et al., Oral solutions for gastroenteritis—Optimal glucose concentration, *Arch Dis Child*, 57:313-315, 1982.

Chapter 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, H. N., Control of vomiting in cholera and oral replacement fluid, *Lancet* 2:1063, 1953 (see No. 2).

Harrison, H. E., The treatment of diarrhea in infancy, *Pediatr Clin North Am* 1:335-348, 1954 (see No. 4).

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

Hirschhorn, N., Decrease in net stool output in cholera during intestinal perfusion with glucose containing solutions, *N Engl J Med* 279:176-181, 1968 (see No. 12).

Nalin, D. R., et al., Oral maintenance therapy for cholera in adults, *Lancet* 2:370-372, 1968 (see No. 13).

Pierce, N. F., et al., Oral maintenance of water-electrolyte and acid-base balance in cholera, a preliminary report, *Ind J Med Res* 56:640-645, 1968 (see No. 15).

Pierce, N. F., et al., Replacement of water and electrolyte losses in cholera by an oral glucose-electrolyte solution, *Ann Intern Med* 70:1173-1181, 1969 (see No. 18).

Nalin, D. R., et al., Oral therapy for cholera (letter), *Ann Intern Med* 72:288-289, 1970 (see No. 19).

Pierce, N. F., et al., Oral electrolytes in cholera (letter), *Ann Intern Med* 72:959, 1970 (see No. 20).

Nalin, D. R., et al., Reduction of maintenance intravenous fluid needs in cholera by means of an oral therapeutic solution, *J Pakistan Med Assoc* 19:373-379, 1969 (see No. 60).

Pierce, N. F., et al., Oral replacement of water and electrolyte losses in cholera, *Ind J Med* 57:848-855, 1969 (see No. 21).

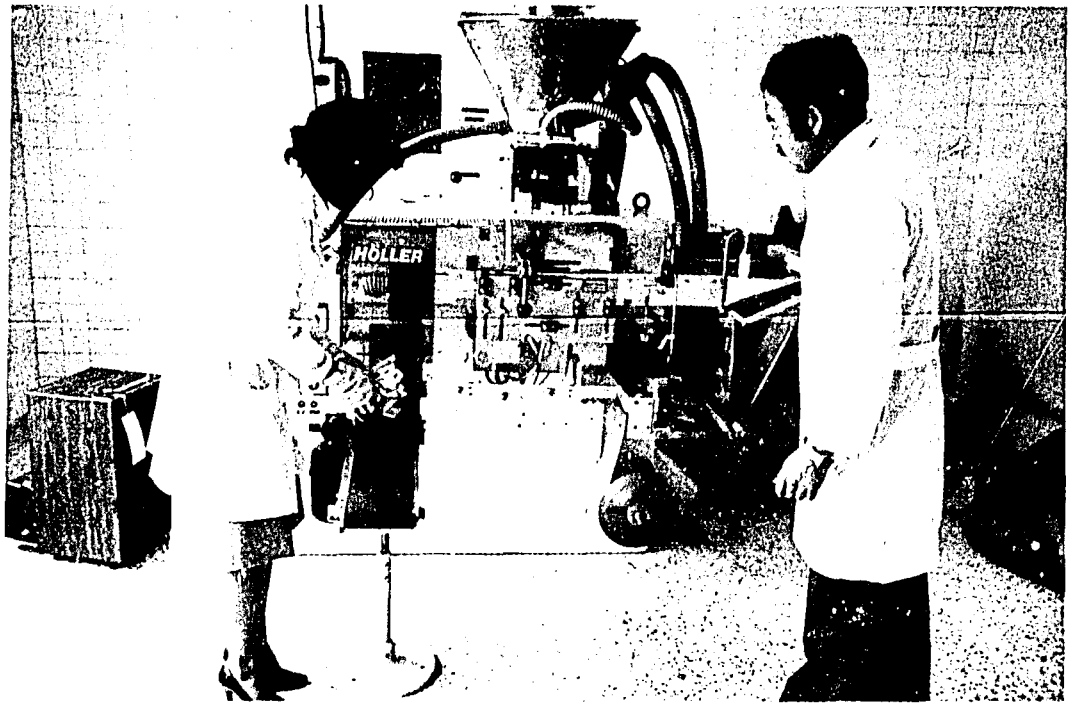
Bart, K. J., Pediatric cholera, Pathophysiology and treatment, *Pak Pediatr J* 1:45-53, 1970 (see No. 22).

Cash, R. A., et al., A clinical trial of oral therapy in a rural cholera-treatment center, *Am J Trop Med Hyg* 19:653-656, 1970 (see No. 23).

Mahalanabis, D., et al., Water and electrolyte losses due to cholera in infants and small children, a recovery balance study, *Pediatrics* 45:374-385, 1970 (see No. 24).

46. Nalin, D. R., et al., Oral (or nasogastric) maintenance therapy for cholera patients in all age groups, *Bull WHO* 43:361-363, 1970.

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



Many countries are undertaking large-scale automatic production of ORS packets. (Photo: B. P. Wolff, UNICEF)

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, HCO_3^--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.

47. Nalin, D. R., Oral or nasogastric maintenance therapy for diarrhoea of unknown aetiology resembling cholera, *Trans Roy Soc Trop Med Hyg* 64:769–771, 1970.

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, HCO_3^--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.

48. Nalin, D. R., et al., Effect of glycine and glucose on sodium and water absorption in patients with cholera, *GUT* 11:768-72, 1970.

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, HCO_3^--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, D. R., et al., Oral or nasogastric therapy for cholera, *WHO Public Health Paper No. 40*, Chapter 11, pp. 73-76, 1970 (see No. 25).

Sack, R. B., et al., The use of oral replacement solutions in the treatment of cholera and other severe diarrhoeal disorders, *Bull WHO* 43:351-360, 1970 (see No. 26).

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

49. Nalin, D. R., et al., The optimal oral therapy formula for cholera and cholera-like diarrheas, In: *Proceedings of the Sixth Annual International Epidemiologic Association Scientific Meeting*, Belgrade, Savremena Administracya, pp 1048-1057, 1971.

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 authors noted, with the 48 mEq of 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.

Hirschhorn, N., et al., Oral fluid therapy of Apache children with acute infectious diarrhoea, *Lancet* 2:15-18, 1972 (see No. 28).

50. Hirschhorn, N., et al., Ad libitum oral glucose-electrolyte therapy for acute diarrhea in Apache children, *J Pediatr* 83:562-571, 1973.

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): Na^+-81, K^+-18, Cl^--17, 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 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.

Ludan, A. C., The efficacy of oral electrolyte fluid in the therapy of diarrhea, *J Philip Med Assoc* 49:243-252, 1973 (see No. 29).

Mahalanabis, D., et al., Oral fluid therapy of cholera among Bangladeshi refugees, *Johns Hopkins Med J* 132:197-205, 1973 (see No. 71).

Mahalanabis, D., et al., Use of an oral glucose-electrolyte solution in the treatment of paediatric cholera—a controlled study, *J Trop Pediatr Environ Hlth* 20:82-87, 1974 (see No. 31).

De, S., et al., Oral fluid therapy for cholera and non-choleraic diarrhoeas in children, *J Com Dis* 7:124-128, 1975 (see No. 32).

De, S., Oral glucose-electrolyte solution in the treatment of cholera and other diarrhoeas, *J Ind Med Assoc* 65:230-232, 1975 (see No. 33).

Aballi, A. J., Single solution not ideal for oral therapy of diarrhoea (letter), *Lancet* 2:513-514, 1975 (see No. 91).

51. Editorial, Feeding sick babies, *Brit Med J* 4:539, 1975.

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.

52. Moenginah, P. A., et al., Oral sucrose therapy for diarrhoea, (letter) *Lancet* 2:323, 1975.

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 solu-

tion 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.

53. Nalin, D. R., Sucrose in oral therapy for cholera and related diarrhoeas, *Lancet* 1:1400-02, 1975.

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.

54. Bart, K. J., et al., Single solution for oral therapy of diarrhoea, (letter) *Lancet* 2:633-34, 1976.

The authors 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.

55. Nalin, D. R., et al., Sodium content in oral therapy for diarrhoea, (letter) *Lancet* 2:957, 1976.

Responding to the letter of Bart and Finbey (see preceding abstract), 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.

56. Naik, N. V., et al., Oral rehydration in acute gastro-enteritis in young children, *Ind Pediatr* 13:127-133, 1976.

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 within 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 in rural Nigeria, *Pediatr Nurs* Sept/Oct:32-33, 1976 (see No. 97).

57. Rahilly, P. M., 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* 51:152–4, 1976.

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

One-hundred-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 treatment 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.

Ware, S., Hypernatremia and glucose water (letter), *Lancet* 1:494, 1976 (see No. 100).

58. Chatterjee, A., et al., Evaluation of a sucrose/electrolyte solution for oral rehydration in acute infantile diarrhoea, *Lancet* 1:1333–1335, 1977.

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 (50 mmol/l), bicarbonate (15 mmol/l), and sucrose (130 mmol/l), had an osmolarity 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 effi-

cacy of this therapy versus glucose oral rehydration or no oral rehydration at all.

Gracey, M., et al., ROSE system for treatment of cholera dehydration (letter), *Br Med J* 1:839-840, 1977 (see No. 104).

International Study Group, A positive effect on the nutrition of Philippine children of an oral glucose-electrolyte solution given at home for the treatment of diarrhoea. Report of a field trial by an international study group. *Bull WHO* 55:87-94, 1977 (see No. 75).

59. Palmer, D. L., et al., Comparison of sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrheas, *N Engl J Med* 297:1107-1110, 1977.

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 purging rates. The clinic staff had no difficulties preparing the solution from premixed packets and administering it under standard rural hospital conditions, a point of great practical importance.

60. Field, M., New strategies for treating watery diarrhea, (Editorial) *N Engl J Med* 297:1121-1122, 1977.

This is a companion editorial to the paper by Palmer (see preceding abstract), 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 theoretical 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.

61. Sandle, G. I., et al., Oral therapy in cholera, (Letter) *N Eng J Med* 298:797-798, 1978.

In light of certain findings by Palmer, et al, (see abstract No. 59) 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, N. F., et al., Oral fluid—a simple weapon against dehydration in diarrhoea, *WHO Chron* 31:87-93, 1977 (see No. 26).

62. Chatterjee, A., et al., Oral rehydration in infantile diarrhoea. Controlled trial of a low sodium glucose electrolyte solution, *Arch Dis Child* 53:284-289, 1978.

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 hypernatrema 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.

63. Moenginah, P. A., et al., Sucrose electrolyte solution for oral rehydration in diarrhea, *J Trop Ped Env Child Hlth* 24:127–9, 1978.

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 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.

64. Nalin, D. R., et al., Comparison of sucrose with glucose in oral therapy of infant diarrhoea, *Lancet* 2:277–279, 1978.

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.

As an editorial note, the higher intraluminal, post-hydrolysis osmolarity of the sucrose solution may partly account for the difference in performance when compared to the glucose solution.

65. Sack, D. A., et al., Oral hydration in rotavirus diarrhoea: A double-blind comparison of sucrose with glucose electrolyte solution, *Lancet* 2:280-283, 1978.

Oral rehydration solutions containing glucose and sucrose were compared to intravenous therapy for the treatment of hospitalized Bangladeshi children aged 5 months to 2 1/2 years with rotavirus-associated diarrhea.

Eighty-nine males with uncomplicated watery diarrhea of less than one week duration who would normally have been admitted for IV hydration were randomly assigned in a double-blind fashion to groups receiving one of 4 coded oral solutions; 2 contained glucose (111 mmol/l) and 2 contained sucrose (111 mmol/l). In addition, all solutions contained the WHO-recommended electrolyte concentrations, orange flavoring, and orange color. Serial intake and output measurements were recorded and weights, complete blood count, serum electrolytes and serum specific gravities were monitored. Feedings of water, breast-milk, and food (without free sugar) were continued and no antibiotics were given. A control group consisted of 44 other children (males and females) with rotavirus infection treated intravenously.

Of the 89 children initially selected, 57 had rotavirus infections. Twenty-eight of these received the sucrose solution while 29 were treated with the glucose solution. All the treated children recovered without incident, and no children receiving oral therapy required IV's. The major difference between the IV and oral treatment groups was that a lower serum specific gravity was seen after 4 hours of treatment in the IV group. There was no statistical difference in the purging rate, concentration of reducing substances, or duration of diarrhea between the glucose and sucrose groups.

This study showed that children with considerable dehydration caused by rotavirus diarrhea can be rehydrated and maintained on oral therapy. Although absorption and digestion of carbohydrates is probably impaired in ro-

tavirus diarrhea, adequate hydration with a glucose or sucrose oral solution was obtained. The higher osmotic load of the sucrose solution (40 g/l sucrose vs 20 g/l glucose) did not result in significantly greater purging rates or duration of stools. Although the 90 mEq/l sodium concentration in the oral solution is approximately twice as high as the sodium concentration in rotavirus stools, no hypernatremia was encountered. This may be related to the encouragement of water and breastmilk consumption during therapy.

Seriki, O., Management of moderately severe dehydration by continuous intra-gastric infusion of electrolyte solution. *Trop Doc* 8:134-136, 1978 (see No. 38).

Hutchins, P., et al., Comparison of oral sucrose and glucose electrolyte solutions in the outpatient management of acute gastroenteritis in infancy, *J Hyg (Camb)* 82:15-19, 1979.

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 plastic 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 had 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, concurrent 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.

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.

67. Kuberski, T., et al., Coconut water as a rehydration fluid. *New Zeal Med J*, 90:98-100, 1979.

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 glu-

cose 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.

Nalin, D. R., et al., Oral rehydration and maintenance of children with rotavirus and bacterial diarrhoeas. *Bull WHO* 57:453-459, 1979 (see No. 40).

Rahaman, M. M., et al., Diarrheal mortality in two Bangladeshi villages with and without community-based oral rehydration therapy. *Lancet* 2:809-812, 1979 (see No. 78).

Hirschhorn, N., The treatment of acute diarrhea in children: An historical and physiological perspective. *Am J Clin Nutr* 33:637-663, 1980, (see No. 132).

International Study Group: Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea: Part 1) Studies in two ambulatory care clinics *J Trop Ped* 27(2):62-67, 1981, (see No. 79).

International Study Group: Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea: Part 2) Studies in seven rural villages *J Trop Ped* 27(3):136-139, 1981, (see No. 80).

68. Nalin, D. R., et al., Comparison of low and high sodium and potassium content in oral rehydration solutions, *J Pediatr* 97(5):848-853, 1980.

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/1 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.

Taylor, P. R., et al., Oral rehydration therapy for treatment or rotavirus diarrhea in a rural treatment center in Bangladesh *Arch Dis Child* 55(5):376-379, 1980, (see No. 45).

Second Edition Abstracts

Although by 1980 the WHO-recommended ORS composition had been widely accepted, some clinicans continued to question its 90 mEq/l sodium concentration on the grounds it predisposes to hypernatremia, particularly among developed world children. Numerous studies have since shown this is not the case. Party to assuage these fears, however, the use of a 2:1 ratio of ORT solution to free water in very young children was endorsed by WHO.

A host of more recent field studies continued to evaluate the use of SSS solutions on the field level. Others examined alternative ORS ingredients such as rice powder, acetate and glucose polymers.

160. Eiseman, B., Intravenous infusion of coconut water, *AMA Arch Surgery*, 68:167-178, 1954.

This article presented laboratory and clinical data on coconut water in order to assess its suitability as an intravenous fluid for treating dehydration.

Fresh coconut water was found to be a sterile, pyrogen-free fluid containing, on the average, 2.1 and 3.8 gms./100 ml of glucose and fructose, respectively. Chemical analysis of 20 coconut water specimens, however, showed that the electrolyte composition varied according to the age of the coconut. Coconut water was found to contain high concentrations of chloride (mean: 63 mEq/l), potassium (mean: 49 mEq/l), magnesium (mean: 17 mEq/l) and calcium (mean: 12 mEq/l), but only traces of sodium and bicarbonate.

After toxicity and sensitivity tests in animals proved negative, the authors administered from 300 to 550 ml of filtered coconut water intravenously to some 21 "non-acutely" ill patients. No serious reactions occurred.

Noting the limitations of their small sample size, the authors concluded water from unripe coconuts may be suitable as a source of intravenous fluid and should be considered when no other sources of pyrogen-free intravenous fluids are available. However, they added, the risk of bacterial contamination and the fluid's high potassium concentration make it less than desirable.

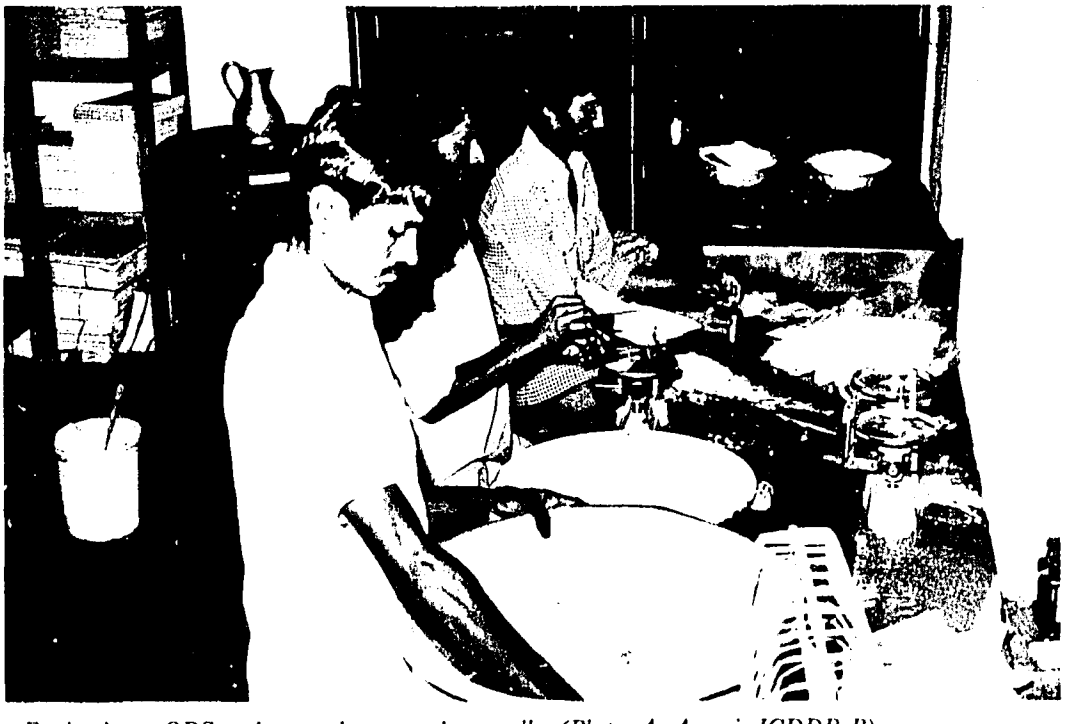
Thirugnanasambandam, C., Prevention of dehydration in infants with gastroenteritis, *The Antiseptic*, 72:3, 125-128, 1975.

161. Sack, D. A., et al., Sucrose or glucose: which sugar to use in oral rehydration solution? A summary of four clinical trials, In: Takeya, K. and Zinnaka, Y. (eds), *Symposium on Cholera*, Karatsu (Japan) 1978. (*Proceedings of 14th Joint Conference, U.S.-Japan Cooperative Medical Science Program*, Cholera Panel, Tokyo, Japanese Cholera Panel), pp. 154-164, 1979. (Also reported in: *Lancet* 2, 280, 1978).

Realizing there may be significant operational and economic advantages to using sucrose *vis-à-vis* glucose, the authors performed three double-blind controlled trials and one "before-after" trial comparing the clinical efficacy of sucrose and glucose ORT solutions in patients hospitalized for both bacterial and viral dehydrating diarrheas at the ICDDR,B ORT centers in Matlab and Dacca, Bangladesh. The authors wished to determine: (a) whether higher stooling rates (as reported elsewhere) or excessive intake of the sweeter-testing, sucrose-based solution were significant problems, and (b) whether the decreased intestinal disaccharidase levels and impaired glucose-facilitated transport in the intestinal mucosa known to result from rotavirus diarrhea would adversely affect ORT using either of the two solutions.

The first two study groups consisted of 148 adults and 111 children (ages 5 months-4 years) with at least 7.5% dehydration due to "cholera-like" diarrhea. Patients were stratified according to degree of dehydration and then randomized to either glucose- or sucrose-based treatment groups. Except for the substitution of sucrose, both fluids conformed to the WHO-recommended composition. Treatment failures were defined as all those cases requiring unscheduled intravenous therapy.

The overall success rates were 75% for sucrose and 84% for glucose in the adult groups and 73% and 77%, respectively, in the children. Oral fluid intake rates were similar for the two comparison groups in each trial, as were the purging and vomiting rates. The primary determinant of ORT success was the



For local use, ORS packets can be prepared manually. (Photo: A. Ansari, ICDDR,B)

purging rate in that the two were inversely related. Although none of the differences between sucrose and glucose groups were significant, slightly better results were shown with glucose.

The third double-blind trial involved 57 children, aged 5 months to 2.5 years, with stools positive for rotavirus and greater than 5% dehydration. They were randomly divided into either sucrose or glucose groups. All cases were successfully treated using ORT alone. Purging rates were somewhat higher in the sucrose group but, again, the difference was not significant.

Fortuitously, a similar group of rotavirus cases, which were treated with intravenous therapy (IV) as part of another, concurrent study, was available for comparison. Purging rates in the IV group were found to closely approximate those in the sucrose group.

The above findings led to the eventual replacement of glucose with sucrose-based ORS in the ICDDR,B treatment centers.

The fourth trial was a retrospective comparison of clinical outcomes of rotavirus cases attending the Matlab treatment center before and after the switch to sucrose-based ORS. Among children with either no or mild initial dehydration, the overall success rates were 88% in the sucrose group and 92.6% in the glucose group. For those moderately to severely dehydrated who were initially given IV therapy, then switched to ORT, the success rates were 84.3% and 88.1% in sucrose and glucose groups, respectively. The differences were not significant.

In summary, all 4 clinical trials indicated a relatively but not significantly higher success rate for glucose-electrolyte solution, the difference being most apparent in severe, cholera-like diarrhea. The authors therefore recommended that glucose continue to be used in pre-packaged ORS but that the decision to substitute sucrose should be made on the local level in light of availability, cost and logistic factors.

Cutting, W.A.M., Management of diarrhoea in children at the primary care or peripheral level, *Ann Soc Belge Med Trop*, 59:221-235, 1979.

162. Phichaipat, V., et al., Oral rehydration with three different electrolyte solutions, *Siriraj Hosp Gaz* 31(9):1413-1422, 1979, (Article in Thai).

The authors compared three oral electrolyte solutions of varying compositions for treating moderate dehydration in infants.

Twenty-five infants (ages not given) were divided into three groups, each of which received a different ORT solution. Prior to treatment, patients were weighed and hematocrits and serum electrolyte values measured. Eight children were given solution I (Na^+ 30, K^+ 120, HCO_3^- 20, Cl^- 30 mEq/l, sucrose 5%); 9 received solution II (WHO-recommended ORS: Na^+ 90, K^+ 20, Cl^- 80, HCO_3^- 30 mEq/l, glucose 2%); and 8 were given solution III (SSS: Na^+ 60, Cl^- 60 mEq/l, sucrose 5%). Each patient received 200 ml/kg of electrolyte solution via nasogastric drip the first day and a mixture of 75 ml/kg cow's milk formula and 75 ml/kg of the respective ORT solution during the second day.

Dehydration was successfully repaired in all 25 patients. Although not significant, relatively higher mean serum sodium and transient edema were observed in Group II patients (WHO-recommended solution) as were lower serum potassium levels in Group III (SSS solution).

As indicated by weight gain, the disappearance of clinical signs of dehydration and reduction of haematocrit and serum urea nitrogen, the authors concluded ORT was successful using all 3 solutions. Noting that ORT solutions containing sodium levels ranging from 30-90 mEq/l could be used with apparently equal effectiveness, they recommended the use of SSS solution (number III), which can be easily prepared and administered in the home.

The transient edema observed in 4 of the 9 Group II children may have been due to the forced, nasogastric route of administration and the withholding of either foods or free water over the initial 24 hours.

Roberts, A. B., Cholera in the Gilbert Islands II. Clinical and laboratory findings, *Am J Trop Med Hyg* 28(4):685-691, 1979.

163. Djoeanda, P., et al., Oral rehydration of infants and children in the Dr. Hasan Sadikin General Hospital, Bandung, *Paed Indones* 19:72-78, 1979.

In this early study (1975) the authors performed a simple clinical trial comparing the effectiveness of two glucose-electrolyte solutions of differing compositions.

Fifty-nine patients under the age of 5 years admitted to a Bandung, Indonesia, hospital with gastroenteritis and moderate dehydration (range 5-10% volume depletion) were alternately divided into two groups. The first group (29 patients) was treated with an ORT solution developed in Indonesia, which contained a relatively high sodium concentration (composition in g/l: NaCl 4, $NaHCO_3$ 4, KCl 1.2 and glucose 10). The second group (30) was treated with the "Hirschhorn" formula, lower in sodium, which more closely resembled the ORS formula later recommended by WHO (composition in g/l:NaCl 2.5, $NaHCO_3$ 1.25, KCl 1.5, and glucose 30).

There were no significant differences in age, sex, body weight, nutritional status or grade of dehydration between the two groups. Oral rehydration was successful in all patients. Of the 59 cases, 41 (70%) were rehydrated in 12 hours or less; 14 (23.7%) in 12-24 hours; and only 4 (6.7%) required more than 24 hours. The latter 4, observed the authors, were all malnourished. Duration of treatment prior to achieving initial rehydration did not significantly vary between the groups. Pre-admission hyper- or hyponatremia were found in 9 cases; plasma sodium levels returned to normal in each once rehydration was achieved.

The authors concluded both ORT regimens were highly effective.

Cutting, W.A.M., et al., Can village mothers prepare oral rehydration solution?, *Trop Doc* 9, 195-199, 1979.

Anonymous, Oral rehydration therapy (ORT) for childhood diarrhoea. *Population Reports, Series L, No. 2, (75 pages), Nov-Dec 1980*, (available in several languages from the Population Information Program, the Johns Hopkins University, Hampton House, 624 N. Broadway, Baltimore, Md. 21205, USA).

164. Cutting, W.A.M., et al., Oral rehydration in diarrhoea: Applied pathophysiology, *Trans Roy Soc Trop Med Hyg* 74(1):30-35, 1980.

The authors presented a careful review of absorption physiology in the gut with emphasis on ORT. Use of the WHO-recommended ORS composition was endorsed. In considering the practical implications of delivering ORT, the authors favored a combination of approaches—widespread distribution of ORS packets and early home use of simple salt/sugar solutions (SSS).

During acute diarrhea, secretion by small bowel enterocytes exceeds the capacity of both small and large intestines to reabsorb the fluid, resulting in a net loss of water and electrolytes. Despite this hypersecretion, the gut's ability to absorb water and electrolytes remains largely intact throughout the diarrheal episode. This permits rapid ongoing replacement of the losses by means of an oral isotonic glucose-electrolyte solution, the basis for ORT.

The composition of such an oral replacement solution rests on several factors. First, the solution must be isotonic (of the same concentration as the serum and intercellular fluid) or the intestinal mucosa will secrete additional water (if the solution is hypertonic) or electrolytes (hypotonic) in an effort to reduce the osmotic gradient between lumen and blood serum. Second, the presence of glucose in the solution enhances sodium transport into the intestinal mucosal cells. This, in turn, permits the passive transport of water, sodium and other electrolytes into the mucosa by the resulting osmotic gradient. Third, the addition of bicarbonate and potassium allows correction of acidosis and hypokalemia, respectively.

After introducing some clinical guidelines

for ORT, the authors discussed the advantages of using a single ORS formula, stating that the WHO-recommended composition is optimal.

While distributing ORS packets presents a challenge, the authors concluded, for the vast majority of diarrheal cases which are mild and self-limiting, SSS solutions alone would prove satisfactory for early ORT in the home. In order to ensure accurate home mixing, health education must be an essential part of any ORT program, added the authors.

Parker, R. L., Oral fluid therapy in diarrhea and dehydration: Current concepts and practical considerations, (*Unpublished Document available from*: Dept. of International Health, Johns Hopkins Univ. School of Hygiene and Pub Health, Baltimore, Maryland, USA), July 1980.

Anonymous, Training manual on treatment and prevention of diarrhea, *Publication No. 12*, International Center for Diarrheal Disease Research, Box 128, Dacca-2, Bangladesh, 1980.

165. Kasemsarn, P., et al., Oral rehydration in diarrheal infants and children, *J Med Ass Thailand*, 63(12):646-650, 1980.

Concerned about the high sodium concentration in the WHO-recommended ORS (i.e., Na^+ 90 mEq/l) the authors had earlier reported good results using a simple salt/sugar (SSS) solution containing 60 mEq/l Na^+ in treating diarrheal dehydration (Varavithya, Y. A., et al., 1978). To determine the effect of adding potassium to SSS, the authors performed a trial comparing the clinical efficacy of SSS with and without added K^+ to that of the WHO-recommended ORS.

Forty patients, ages 2 months to 14 years, were admitted to hospital with mild to moderate diarrheal dehydration and were divided into three groups. Eleven patients in Group I were treated orally with an SSS solution containing potassium (in mEq/l: Na^+ 60, K^+ 34, Cl^- 94, in 5% sucrose solution); 20 patients in Group II were treated with an SSS solution without K^+, (in mEq/l: Na^+ 60, Cl^- 60 in 5% sucrose solution); 9 Group III patients were given WHO-recommended ORT solution, but with 40 grams of sucrose substituted for 20 grams of glucose. All patients were given 150 ml/kg of fluid at the rate of 10-20 ml/kg/hr over the first two hours, the remainder being given over the succeeding 24 hours. Dilute formula, breastmilk or soft foods were given after 24 hours.

Dehydration was corrected in all patients within 24 hours. Serum sodium amd potassium levels were corrected within 48 hours and did not vary among the groups. No hypernatremia or hypokalemia was reported. Persistent acidosis, however, was noted in Group I. Edema was observed in two of the nine (22%) patients who had been given the WHO-recommended ORT solution.

Although the results indicated the two SSS formulations and WHO-recommended ORS were equally effective in correcting dehydration, the authors postulated the persistent acidosis in Group I was due to high chloride and/or potassium levels. They also attributed the edema in Group III patients to the high ORS sodium concentration. In any case, the data do not support these last two assertions and the edema probably resulted from both fasting and the absence of free water during the first 24 hours of treatment.

166. Islam, M. R., et al., Use of low and high sodium containing oral rehydration solution in paediatric diarrhea, (*Presented at The 21st Conference of the Indian Society of Gastroenterology, Calcutta, 1980.* Reprints: MRI, Chief Physician, ICDDR,B, GPO Box 128, Dacca-2, Bangladesh).

In a one-year clinical study (Sept. 1976 to Oct. 1977) at the the Cholera Research Lab treatment center in Dacca, Bangladesh, the efficacy and safety of two types of ORT solutions with varying sodium levels were compared.

Sixty-five children, aged 6 months to 2 years, with a history of acute watery diarrhea and dehydration, were studied. After initial in-

travenous therapy was given to all patients, 40 children received an ORT solution containing low sodium (composition, in mmol/l: Na^+ 60, K^+ 25, Cl^- 55, HCO_3^- 15, citrate 15, glucose 111; total mOsm/l 281) while the remaining 25 children were given an oral solution containing high sodium concentration (composition in mmol/l: Na^+ 120, K^+ 25, Cl^- 95, HCO_3^- 25, citrate 25, glucose 111; total mOsm/l 401). Mothers were instructed to administer ORT and continue feeding every 4 hours.

Blood samples were drawn on admission and at 4, 24, and 48 hours after ORT was begun. Catheter specimens of stools and urine samples were sent simultaneously for sodium determinations.

The study groups were comparable with respect to age, duration of diarrhea and serum and stool laboratory values. As indicated by weight gain, follow-up serum specific gravity, haematocrit and urination, no significant difference in rate of rehydration was observed between the groups. Fluid and electrolyte balances were successfully maintained in all children. No differences were observed in fluid or dietary intake, purging rates or duration of hospitalization.

Although a significant rise in mean serum sodium was observed in the high-sodium fluid group, hypernatremia was observed in only 2 cases. These two cases, in which sodium concentrations increased from 146 to 161 and 152 mmol/l, were taken off the high sodium solution. Both stool and urinary sodium excretion were significantly higher after 24 and 48 hours of therapy in children receiving the high-sodium solution. The authors felt use of sodium citrate, combined with an equal proportion of sodium bicarbonate, was effective in correcting acidosis.

The authors concluded that ORT solutions with sodium concentrations ranging from 60 to 120 mmol/l are safe and effective in managing diarrheal dehydration in a clinical setting but that further studies are necessary to evaluate their use in the home. They also noted sodium citrate may be a viable substitute for sodium bicarbonate. Advantages to such a substitution, they pointed out, would include improved palatability and longer ORS shelf life.

167. Carrazza, F. R., et al., Reidratacao oral em pediatria, *Arq Gastroent, Sao Paulo*, 17(3):168-172, 1980, (Article in Portuguese).

Writing to Brazilian colleagues, the authors reviewed the major studies leading to the development of ORT and the refinement of the current WHO-recommended ORS formula.

The authors questioned the suitability of the 90 mEq/l sodium concentration in the WHO formula, however, reflecting the concerns of other investigators who felt such a high sodium concentration could lead to increased risk of hypernatremia, particularly in infants. They cited a 1979 WHO-sponsored study group meeting which recommended that a second ORS solution be used, one containing 50 mEq/l of sodium (for infants) to complement the current WHO-recommended composition. Due to the operational problems using more than one ORS formula would entail, this recommendation was not accepted. Instead, a compromise regimen, tested in Costa Rica, was endorsed by WHO. It recommended giving two parts WHO-recommended ORS solution followed by one part water.

The authors also questioned this "2:1" regimen, preferring instead a simple, 1:1 ORS to free water regimen developed by another group of investigators. This, they reasoned, would lower the sodium concentration to 45 mEq/l but, in the process, the potassium concentration would also be halved, from 20 to 10 mEq/l. The authors favored giving additional potassium to bring the concentration back to 20 mEq/l and called for more detailed balance studies to further refine this regimen.

Noting that several ORS formulations were available, the authors analyzed four commercial ORS products found in Sao Paulo. Although all had sodium concentrations of approximately 50 mEq/l, two had potassium contents of less than 20 mEq/l and two were hypertonic. Nearly all investigators agree ORT is best accomplished with isotonic solutions, stated the authors.

Although ORT may be a valid alternative for treating diarrheal dehydration, the authors felt more research is needed to develop the ideal ORS composition.

168. Finberg, L., et al., The role of oral electrolyte-glucose solutions in hydration for children—international and domestic aspects, *J Pediatr* 96(1):51-54, 1980.

The author traced the development of ORT, contrasting the WHO "global" point of view to that of North American pediatricians.

In essence, the WHO position favors the use of a single, universal solution (ORS, which yields, *inter alia*, 90 mEq/l Na^+) for treating dehydration in all age groups regardless of etiology. The authors, however, felt First World clinicians should have oral solutions of varying compositions to choose from. The WHO formula, they contended, is well suited to children in developing countries, especially where cholera, which causes high sodium losses, is prevalent. However, the absence of cholera and typically high-sodium diets in developed world children, they felt, rule out the use of the WHO-recommended ORS in that setting, largely due to the risk of hypernatremia.

The authors heralded a "compromise" ORT regimen developed by Costa Rican investigators which calls for two parts ORS followed by one part free water, but only for use in developing regions. There is no reason, they concluded , why private industry cannot produce a range of different solutions, thereby allowing North American clinicians to better "individualize" treatment along purely physiologic lines.

169. Woodward, W. E., Oral rehydration for diarrhoea (letter), *J Pediatr* 97(3):515-516, 1980.

Referring to an editorial by Finberg (see preceding abstract), the author objected to Finberg's call for three ORT solutions of varying compositions rather than use of a single, universal ORS composition as advocated, *inter alia*, by WHO.

Although theoretically attractive, to introduce 3 separate solutions would add unneeded complexity, the author wrote. The vast majority of cases will invariably recover regardless of which solution is used and, in very ill patients, careful hospital monitoring is needed in any event. The use of 3 different ORT solutions in an inpatient setting would be "asking for trouble".

As stool volume rises, so does Na^+ concentration and in profund cases stool sodium losses may exceed 120 mEq/l, stated the author. To lower the Na^+ concentration from the 90 mEq/l recommended by WHO could entail the risk of hyponatremia in such serious cases. Use of a single ORT solution obviates the risk and, because fluid intake decreases with stool volume, any risk of hypernatremia is further minimized by giving 2 parts ORS followed by one part free water.

170. Finberg, L., Oral rehydration therapy for diarrhoea (letter), *J Pediatr* 97(3):516-517, 1980.

Responding to Woodward's comments (see preceding two abstracts) on his earlier editorial, the writer clarified his views on ORT.

The writer agreed that stool sodium concentrations do rise with stooling rates but only in cholera and "probably" enterotoxigenic *E. coli* infections. In rotavirus and other nonspecific, presumed viral diarrhoeas, however, stool Na^+ losses are low. Because of diet, cultural, climatic and architectural factors, the writer felt that use of the WHO-recommended ORS, containing 90 mEq/l Na^+, will lead to hypernatremia in urban and suburban North American children. He acknowedged, however, that no systematic, controlled study had been done to substantiate this.

The WHO-recommended ORT solution works so well in the developing world, felt the author, because, in effect, to give breastmilk and plain water in addition to ORS (as recommended by WHO) is to use 3 different solutions. Secondly, enterotoxigenic diarrheas predominate in these areas.

The author reiterated his call for three separate ORS formulations for use in comparatively advanced North America. One (containing 50 mEq/l Na^+ and 20 mEq/l K^+), could be used for maintenance and for mild cases. A second solution (containing 75 mEq/l Na^+ plus 15 mEq/l K^+) would be used for achieving rehydration and a third (25 mEq/l Na^+ and 25 mEq/l K^+) for treating known hypernatremic cases. (The latter two, felt the author, should be available by prescription only.)

For patients with even "mild circulatory compromise", ORT should not be used initially, only IV therapy, stated the author. Nevertheless, the author added that use of the WHO-recommended solution, based on the 2:1 regimen, should be continued in "underdeveloped" areas.

171. Sack, D. A., Oral rehydration for diarrhoea (letter), *J Pediatr* 97(3):517-518, 1980.

Continuing the debate occasioned by Finberg's editorial (see abstract No. 168), the writer referred to an earlier study he had performed (see abstract No. 65), which showed that, as Finberg had stated, stool Na^+ concentrations in rotavirus diarrhea are low, ranging from 30 to 50 mEq/l, and are indeed independent of purging rates. However, the same study also showed that, following the 2:1 regimen, serum sodium levels not only did not increase when the WHO-recommended ORT solution was used but actually decreased in patients who had presented with initially high serum Na^+ levels (i.e., 145 to 154 mEq/l). During the first 48 hours, the rotavirus patients drank an average of 51 ml/kg water (plus breastmilk) and 223 ml/kg of ORT solution. This would effectively reduce the Na^+ concentration to less than or equal to 73 mEq/l, stated the author, a value not far from the 60 mEq/l Na^+ concentration recommended by Finberg.

The writer agreed with Finberg that a 60 mEq/l Na^+ solution would probably be ideal for the U.S. but felt the WHO-recommended ORT solution would achieve the same results when additional free water or breastmilk are offered. Parenthetically, the writer felt the "2:1" regimen may be unnecessarily rigid and that the basic thirst mechanism is "quite good in regulating fluid intake".

In conclusion, the author observed that what is missing from medical practice in North America is the acceptance of the basic premise of ORT: that hydration can be accomplished with an oral solution and that IV use can be minimized and usually eliminated in the treatment of dehydrating diarrhea. He called on pediatricians and nurses to gain confidence in ORT, to instruct parents on its routine use and, in so doing, avoid IV therapy and hospitalization altogether.

Pizarro, D., et al., Oral rehydration of infants with acute diarrhoeal dehydration: a practical method, *J Trop Med Hyg*, 83, 241-245, 1980.

172. Sack, D. A., et al., Oral therapy in children with cholera: A comparison of sucrose and glucose electrolyte solutions, *J Pediatr*, 96(1):20-25, 1980.

To compare the relative efficacy of sucrose as a substitute for glucose in oral rehydration solutions, the authors studied 111 children below five years of age presenting to hospital with uncomplicated, cholera-like diarrhea and moderate (greater than or equal to 7.5% fluid deficit) to severe (greater than or equal to 10%) dehydration. Patients were matched by age, sex, duration of symptoms prior to admission, degree of dehydration and admission laboratory values and were then assigned in double-blind fashion to either sucrose or glucose treatment groups.

Exhaustive biochemical and etiological determinations were performed for each patient. *Vibrio cholera* was isolated from the stools of 102/111 patients. Severely dehydrated cases (89/111) were given intravenous (IV) fluids for the first two hours until 70% of their estimated fluid deficits were replaced, then switched to oral therapy. Those moderately dehydrated (22/111) were immediately begun on ORT. In addition to *ad libitum* ORT, patients were of-

fered plain water continuously, bread and butter on the first day, and a general diet on subsequent days.

Treatment was considered successful if no further IV fluids were given. Although not significantly different, the glucose- and sucrose-group success rates, 77% and 73%, respectively, were relatively lower than reported elsewhere. There was one death and 28 failures. All but one failure had diagnosed cholera and all but two were severely dehydrated on admission. Treatment failures were attributed to very high purging rates, (significantly higher than in those successfully treated orally) which are characteristic of cholera.

In contrast to other reports regarding the use of sucrose-based fluids, there were no significant differences between the groups in either purging rates, presence of stool reducing substances or carbohydrate malabsorption (found in only 3 cases). Secondly, the authors attempted to introduce ORT in severely dehydrated cases as early in the rehydration phase as possible following rapid initial IV therapy, (e.g., 70% fluid deficit replacement within the first two hours). Under uncontrolled conditions, noted the authors, full IV-therapy is the method of choice for severely dehydrated cases presenting in shock. The authors concluded sucrose may be safely substituted for glucose in ORT for cases of enterotoxigenic bacterial diarrhea.

173. Levine, M. M., et al., Variability of sodium and sucrose levels of simple sugar/salt oral rehydration solutions prepared under optimal and field conditions, *J Pediatr* 97(2):324–327, 1980.

Alternatives to prepackaged ORS have been widely advocated, particularly for use in underdeveloped areas not covered by health services. In this article, the authors reported the results of a comparative trial to evaluate three such alternatives for preparing simple homemade oral rehydration solutions.

Five U.S. nurses in Baltimore, USA and 14 Honduran mothers in a rural health center prepared a series of oral rehydration solutions using three methods: 1) "pinch and scoop"; 2) household teaspoon and glass and 3) special double-ended plastic spoons. Each method was tested using both exact and approximate volumes of water (either 200 ml or 500 ml). Both U.S. and Honduran subjects were asked to bring their own household teaspoons and glasses. In both places locally purchased salt and sugar were used. The U.S. nurses were asked to prepare four samples, with both exact and approximated volumes of water, using each of the three methods. After both collective and individualized instruction, the Honduran mothers were asked to estimate 500-ml volumes using household glasses, and then to mix two SSS solutions, one by "pinch-and-scoop" and the second using household spoons.

Results showed that, among the U.S. nurses, the special plastic, double-ended spoons gave the most consistent results in that sodium and sucrose concentrations most closely approximated the intended values of 75 mEq/l and 2.0 gm/dl, respectively. (Sodium concentrations ranged from 64 to 93 mEq/l.) Using the pinch-and-scoop technique, however, 2 of the 5 nurses prepared hypernatremic solutions (i.e., Na^+ greater than 150 mEq/l). The greatest variation occurred with the pinch-and-scoop method using approximate volumes of water. Greater variation occured among nurses rather than among methods, indicating each tended to be consistent in their estimations.

In contrast, 5 of the 14 Honduran mothers produced hypertonic solutions using one or the other method, despite intensive training beforehand. The household "teaspoons" were of variable volume; eight were standard sized (4 to 6 ml), four were much larger (15–20 ml.) and two were demitasse spoons (2.5 ml). Household glasses also varied greatly, ranging from 150 to 500 ml in volume.

The authors concluded that the inherent variability of the pinch-and-scoop and household teaspoon/glass methods are too great to permit their promotion in an ORT program without health worker supervision. More eval-

uation research of the special double-ended spoon method is also needed, the authors felt.

Poudayl, L., et al., Home-made oral rehydration solutions: feasibility study in Nepal, *WHO Chron*, 34(12):496-500, 1980.

Hendrata, L., et al., Sodium concentration of home mixed rehydration solutions, *Paediatr Indones* 20:91-92, 1980.

174. Clements, M. L., et al., Potassium supplements for oral diarrhoea regimens (letter), *Lancet* 2(8199):854, 1980.

The authors referred to an earlier double-blind trial they had conducted in Honduras which had compared the safety and efficacy of a simple salt/sugar (SSS) solution to that of WHO-recommended ORS solution (see abstract No. 186). In that study the authors found SSS solution corrected dehydration and acidosis but that persistent hypokalemia was a problem.

In Honduras, the authors tested the potassium content of various local foods which might serve as a potassium-rich dietary supplement to the SSS. Data were presented for bananas, coconut water, lemon and orange juice, papaya and tomatoes.

Of all foods tested, bananas provided the highest potassium content. The authors estimated each infant receiving SSS would have required at least 280 ml of pureed banana (about 2 whole bananas) per day to approximate the potassium level provided by the WHO-recommended ORS. Both lemon and orange juices were found to be remarkably low in potassium.

The authors concluded bananas could provide a suitable supplementary source of potassium but that further evaluation is required to assess childrens' ability to digest such relatively large volumes of banana while receiving SSS solutions.

Kahn, A., et al., Hyperkalemia and UNICEF type rehydration solutions (letter), *Lancet* 1:1082, 1980.

Clements, M. L., et al., Oral therapy with glucose electrolyte solution (letter), *Lancet* 2:34, 1980.

175. Greenough, W. B., III, Oral replacement therapy in diarrhea: consensus and controversy, In: Field, M., et al., (eds), *Secretory Diarrhea*, Bethesda, MD, American Physiological Society, 1980.

In this essay the author, who is Director of the International Centre for Diarrhoeal Disease Research (ICDDR,B) in Dacca, Bangladesh, reviewed several ORT-related research topics of current interest and considered their practical implications.

After briefly discussing the importance of diarrheal diseases and the initial development of ORT, the author highlighted several issues requiring further research. Noting that hyper- and hyponatremia are seen at approximately equal frequency in children admitted to hospital with no prior history of ORT, the author called for studies to determine if this is true in areas with standardized ORT programmes. Before such programmes can succeed, he felt, the people must be taught the most appropriate means of measuring the ingredients for ORT in the house.

In addition to glucose, other "carrier molecules" (i.e., any actively absorbed organic solute) which facilitate water and sodium absorption during ORT may exist. They may be derived in the gut from certain foods. In view of local cultural practices, ICDDR,B investigators are now comparing ORT solutions containing refined sucrose, raw cane sugar and rice starch as possible alternatives to glucose in the WHO-recommended ORS formula.

Addressing the efficacy of simple salt/sugar solutions (SSS) the author noted an ICDDR,B field study has shown persistent acidosis in diarrheal patients who were treated with SSS *vis-à-vis* those who had been treated with the complete ORS formula. The clinical consequences of such acidosis need further investigation. They may be linked to higher purging rates, which, in turn, can lead to ORT treatment failure. Finding a means of controlling high purg-

ing rates, therefore, may be the underlying challenge.

Speculating on the prospects of affecting the secretory process in the gut epithelia, the author mentioned a good deal of research is now underway on the gut's local immune systems and on toxin-receptor interactions. Recent ICDDR,B research has demonstrated the common antiemetic chlorpromazine causes a substantial decrease in fluid loss in severe cholera cases. Further research on chlorpromazine and other antisecretory agents, the author felt, could solve the problem of high fluid volume loss in diarrhea without resorting to large volumes of I.V. fluids.

In conclusion, the author felt the field of diarrheal diseases research reflects a uniquely successful marriage between the theoretical concerns of scientists and the often dramatic application of their research findings.

176. Islam, M. R., et al., Labon-gur (common salt and brown sugar) oral rehydration solution in the treatment of diarrhoea in adults, *J Trop Med Hyg*, 83,41-45, 1980.

Reasoning that delivery of intravenous therapy or even pre-packaged ORS containing glucose is prohibitively expensive in Bangladesh, the authors performed a controlled clinical trial on 50 adult Bangladeshi patients (age 16 to 50 years) with moderate dehydration due to acute diarrhea in order to observe the efficacy of an oral rehydration solution containing only common salt (labon) and unrefined sugar (gur). The experimental "labon-gur" group was then compared to a control group of 24 moderately dehydrated adult patients who were treated with a sucrose-based oral replacement solution (WHO-formulation, in mEq/l: Na^+90, K^+20, HCO_3^- 30, Cl^-80, and sucrose 40g/l). The groups were comparable with respect to age, duration of diarrhea prior to admission and initial serum specific gravity.

Results in the two groups were comparable. In the "labon-gur" group, volume losses were corrected in less than eight hours after beginning oral therapy. Oral fluid alone was sufficient in 41/50 cases. Nine cases, however, were initially rehydrated intravenously due to persistent vomiting, then switched to oral fluid. Acidosis in the labor-gur group was not corrected in nine (18%) of the patients, even after 48 hours of therapy. In those patients, failure of plasma bicarbonate correction was significantly related to their purging rates (greater than 50ml/kg/24 hours).

Despite the acidosis problem, the authors concluded adult patients with diarrheal dehydration can be successfully rehydrated by means of a labon-gur solution. The labon-gur solution, they observed, is almost seven times cheaper per liter than commercially-produced glucose-based oral rehydration packets. Additionally, gur contains enough potassium to yield a mean of 7.6 mEq/l K^+ (the WHO-recommended value is 20 mEq/l). The authors cautioned that the consequences of sustained acidosis may be more serious in children and severely affected adults.

177. Steinhoff, M. C., Oral rehydration therapy for diarrhoea (letter), *J Pediatr* 97(3): 515, 1980.

The author reported favorable results over the previous 8 years using a locally prepared ORT solution (designed to resemble that originally proposed by Hirschhorn, et al.) for treating diarrheal dehydration in a Rochester, New York, USA hospital. Composed of 450 ml of isotonic saline (0.95% NaCl), 500 ml of 5% glucose (D_5/W), 10 ml of potassium chloride (2 mEq/l) and 30 ml of 8.4% sodium bicarbonate (1 mEq/ml) solutions, the homemade fluid yields (in mEq/l): Na^+ 99, K^+ 20, Cl^- 89, HCO_3^- 30 and glucose 138 mmol/l. In addition to the ORT solution, breastmilk or clear liquids are routinely given to mildly or moderately dehydrated cases. Despite close monitoring, hypernatremia has never been observed.

Prior to 1973, most of these cases would have been given IV therapy, the author observed. Since then, patients, parents and ward staff have come to appreciate the simpler and equally effective alternative of ORT. Until in-

dustry provides an acceptable solution, the author stated, other clinicians may wish to utilize the above composition for ORT.

178. Munir, M., et al., Coconut water as one of the optimal oral electrolyte solutions, *Paed Indones* 20:38-46, 1980.

While the concept of ORT is sound, alternatives to fixed rehydration centers and the used of pre-mixed ORS are needed for remote rural areas, reasoned the authors. To test one alternative approach the authors performed a clinical trial to compare the efficacy of a coconut water/salt mixture to that of a manufactured ORS packet called "oratrolit" in treating diarrheal dehydration.

To assure replicability at the village level, the authors prepared the coconut water/salt solution by mixing 200 cc. plain water with 200 cc. coconut water, then adding 6 thumb-and-index finger pinches of salt, (mean total: 1.3 grams).

Forty-three children, all under 5 years of age, with diarrhea and mild to moderate dehydration were randomly divided into two groups and treated with either the coconut water/salt solution (mEq/l: Na^+ 57; K^+ 22.6; Cl^- 90.7; HCO_3^- 2.9; and "sugar" 27.5 g/l) or the commercial "oratrolit" solution (composition not described). Tetracycline was given to all children, although etiological determinations were not performed.

The results indicated the stooling rate and duration of diarrhea in the coconut water/salt group were less than in the "oratrolit" group. No side effects were reported in the group treated with the coconut water/salt solution.

The authors observed a "better response" in the coconut-water group which, they hypothesized, may have been due to the presence of amino acids in the coconut water, which are known to enhance intestinal sodium and water readsorption. The findings, however, do not support this hypothesis.

Several methodological and operational problems limit the extent to which these results can be generalized. Among them are the small study population, lack of serum electrolyte findings, (which may have verified the "better response"), and the wide variability in composition and measurement of coconut water and common salt.

179. Sommer, A., Vitamin A, xerophthalmia, and diarrhoea (letter), *Lancet* 1, 1411-1412, 1980.

Xerophthalmia, a serious visual disorder caused by Vitamin A deficiency, is most commonly found among children suffering from protein-energy malnutrition (PEM). Such children are most at risk of xerophthalmia not only because of inadequate dietary Vitamin A intake but also because their liver stores of the vitamin are low. Any insult to the body, such as recurrent diarrheal episodes, may upset this precarious metabolic balance, triggering onset of the disease.

Once detected, xerophthalmia is treated with large doses of Vitamin A injected intramuscularly and/or given orally. The parenteral-plus-oral regimen is traditionally preferred over oral treatment alone, however, because metabolic response is more rapid and because intestinal absorption of Vitamin A has been shown to be impaired by both PEM and diarrheal disease. Nevertheless, some experts have suggested the addition of Vitamin A to ORS packets might constitute a feasible xerophthalmia control measure (Nalin, et al., 1980).

In an earlier study of 114 Indonesian children with xerophthalmia, the author had shown clinical responses to parenteral-plus-oral vs. oral-only Vitamin A regimens were equivalent, even in the presence of PEM and diarrhea (ref: Sommers, A., et al., "Oral versus intramuscular vitamin A in the treatment of xerophthalmia", *Lancet* 1, 557-559, 1980). Noting its practical advantage, the author recommended that high potency oral Vitamin A therapy be administered to suspected cases by teachers and mothers as well as medical workers.

Responding to readers' enquiries on the ear-

lier report, in this letter the author presented more detailed data which showed that oral administration of 200,000 IU Vitamin A on two successive days was as clinically effective as a massive intramuscular dose followed by an oral dose the next day. This was true even if the analysis was limited to those children who presented with concurrent diarrhea (55) and/or PEM (77), he added.

Since children with diarrhea are at increased risk of xerophthalmia, the author felt, any method for increasing their Vitamin A intake, including its addition to ORS, should be investigated.

180. Raghu, M. B., et al., Oral rehydration for diarrhoeal diseases in children, *Trans Roy Soc Trop Med Hyg* 75(4):552-555, 1981.

Given that stool sodium concentrations usually vary from 40 to 60 mmol/l in infantile diarrhea, the authors reasoned an oral electrolyte solution containing less sodium than that recommended by WHO (i.e., 90 mmol/l) would be optimal.

To test this hypothesis, a four-week study was conducted at the University Teaching Hospital, Lusaka, Zambia. Eighty-eight children, ages 2-36 months, with watery diarrhea and mild to moderate dehydration, were divided into two groups. Group A consisted of 60 children who were treated with a low-sodium oral solution ("Rehydrant": composition in mmol/l: Na^+ 50, K^+ 20, Cl^- 50, HCO_3^- 20, citric acid, 9, and sucrose or glucose, 188). Group B included 28 children who were treated with the WHO-recommended ORS solution (in mmol/l: Na^+ 90, K^+ 20, Cl^- 80, HCO_3^- 30, glucose 111). Thirty percent of the study patients had some degree of malnutrition; six with frank kwashiorkor were included in Group A. Otherwise, the groups were similar with respect to age, sex, degree of dehydration and initial serum biochemical values.

Children judged mildly dehydrated were given either of the ORT solutions at the rate of 50-60 ml/kg until initial rehydration was achieved, after which the rate was lowered to give a total of 100-120 ml/kg (maintenance therapy) over the next 24 hours. Moderately dehydrated children received an initial 100 ml/kg (deficit therapy), then a total of 100-120 ml/kg. Neither free water nor breastmilk were given for the first 24 hours. In "a few cases" metochlorpromide was used to suppress vomiting.

All of the children were successfully orally rehydrated and none required intravenous therapy. Although by 24 hours serum sodium levels had risen significantly in both groups (mean variations, Group A: 131.6-137 mmol/l; Group B: 130.5-135 mmol/l), they did not significantly vary and none of the children in either group developed hypernatremia. Sodium levels in the six kwashiorkor cases, however, remained unchanged. There was no difference in the recovery rates; 85% of the cases in both groups were fully rehydrated within the first day of treatment.

The authors concluded the low-sodium (50 mEq/l) solution was as effective as the WHO-recommended solution (90 mEq/l) in treating diarrheal dehydration.

181. Walker, S. H., Hypernatremia from oral electrolyte solutions in infantile diarrhea (letter), *N Eng J Med*, 304:1238, 1981.

The author described as inappropriate a recently introduced commercial ORS preparation ("Hydra-lyte") which contains, *inter alia*, 84 mmol/l of sodium. The advertising for the product cited favorable findings when similar home ORT solutions were used in "underdeveloped communities". The author felt this sodium concentration was too high, however, referring to earlier studies which stated hypernatremia was frequent in the U.S. when ORT solutions containing 50 mEq/l of sodium were used but has declined in Great Britain since the introduction of low-solute milk containing less than 20 mmol/l of sodium. Large amounts of water must be ingested to counteract the risk of hypernatremia if oral solutions with higher sodium concentrations are given, he stated. Such solutions are inappropriate for use in the U.S., concluded the author. Instead, he recommended solutions containing either

no sodium or less sodium than is found in cow's milk.

182. Santosham, M., et al., Oral electrolyte solutions for infantile diarrhoea (letter), *N Eng J Med* 305(10):581, 1981.

Responding to a letter by Walker, (see preceding abstract), which stated that fluids used for treating acute diarrhea should contain less than 17 mmol of sodium per liter, and that solutions containing more than 80 or 90 mmol of sodium per litre should only be administered in a hospital setting, the authors cited studies among American Indian and middle-class children in Arizona and in Baltimore that refute these recommendations.

Over a nine-year period, over 1,500 Indian and 100 middle-class urban children were treated with WHO-recommended ORS without encountering a single case of hypernatremia, reported the authors. Use of solutions with less than 17 mmol of sodium per litre in diarrheal patients would be inappropriate, they felt, and could lead to hyponatremia. Commonly used solutions in the U.S., such as Pedialyte (Ross Laboratories) and Lytren (Mead Johnson), are not ideal for diarrheal management, the authors wrote. They recommended instead that the WHO-endorsed ORS formula be used universally.

183. Cleary, T. G., et al., The relationship of oral rehydration solution to hypernatremia in infantile diarrhea, *J Pediatr*, 99(5):739-741, 1981.

To determine whether or not use of WHO-recommended ORS predisposes to hypernatremia, the authors studied 100 children less than one year of age who were admitted to an Egyptian hospital during June, 1980 with diarrheal dehydration. Seventeen percent of the infants were hypernatremic on admission (serum Na^+ greater than 150 mEq/l), 27% were hyponatremic (serum Na^+ less than 130 mEq/l) and 56% isonatremic. The mean age was 6.7 months (range 1 to 12 months). The infants were treated with "Rehydran", a prepackaged form of ORS produced and available in Egypt, which is based on the WHO-recommended composition. Each "Rehydran" packet contains 0.7 gm sodium chloride, 0.5 gm sodium bicarbonate, 0.3 gm potassium chloride, and 4.0 gm dextrose and is to be dissolved in one glass (approximately 200 ml) of water.

Of the 100 children, 8 had been given Rehydran at home prior to admission. Four of these presented with hypernatremia.

Infants were given ORT *ad libitum*. A 2:1 regimen was used: 200 ml Rehydran were given, followed by 100 ml of water in frequent, small feedings. When clinical signs of dehydration disappeared the children were given human milk or half-strength formula, increasing to full-strength after 24 hours.

Of the 17 hypernatremic infants, ORT alone was successful in 16. One patient was too lethargic on admission to take oral fluids and was given IV therapy. Of the remaining 16 infants, one developed a brief focal seizure after 24 hours of therapy. At discharge, however, this infant, like all others, appeared neurologically normal. In 63% of the infants who had presented with hypernatremia, serum sodium values returned to normal within 6 hours of therapy. Within 24 hours, 94% of them were normonatremic. One patient required 48 hours of ORT before serum sodium concentration returned to normal. All other initially hypernatremic infants were discharged after 24 hours of therapy.

These results agreed with those reported by others, indicating that following the 2:1 ratio of ORT solution to free water, hypernatremia is successfully corrected in all cases using the WHO-recommended ORS.

The authors pointed out that the incidence of seizures in the infants rehydrated orally with the WHO-recommended ORS is comparable to the best clinical results reported with intravenous therapy. (Seizures and other severe neurological abnormalities reportedly occur during intravenous therapy in about 30% of infants, although some authors report rates ranging from 6% to 46%.) The authors also noted the risk of hypernatremia appeared

higher in those children given Rehydran *a priori* in an unsupervised setting, apparently because Egyptian mothers fail to give free water or to continue breastfeeding along with the ORT solution.

184. Pizarro, D., et al., Tratamiento oral de la deshidratación hipernatremica (Oral treatment of hypernatremic dehydration), *Act Med Cost*, 24(4):341-346, 1981, (Article in Spanish).

To determine the efficacy of ORT in correcting hypernatremia secondary to diarrheal dehydration, the authors studied 21 Costa Rican children presenting to a San José hospital with acute diarrhea and serum Na^+ values greater than 150 mEq/l. Eleven of the 21 patients were less than 28 days of age, 5 were between 1 and 3 months, and another 5 were between 5-22 months.

The twenty-one hypernatremic patients were given an ORT solution based on the WHO-recommended formula but with 10 mmol/l more potassium. Mothers were trained to administer two parts ORT solution followed by one part free water (2:1 regime). Following initial rehydration, patients were given breastmilk, half-strength formula or fruit or vegetable purees. Mothers were then instructed to continue the regimen at home.

Oral rehydration therapy alone was successful in 95% of the patients. One patient developed abdominal distension and was switched to intravenous therapy. Another experienced convulsions 4-1/2 hours after rehydration commenced but had developed no neurological sequelae at the time of discharge. There were no deaths. Of the original 21 patients, 6 were rehydrated in less than 6 hours, 9 patients were rehydrated between 6 and 9 hours, and 6 between 9 and 14 hours. After the first 24 hours of ORT only 2 patients had serum sodium levels above 150 mEq/l.

The authors concluded ORT is both safe and effective for correcting hypernatemic dehydration and, they noted, it provides a simpler alternative to the classic method of slow intravenous infusion of hypotonic fluids.

Kahn, A., et al., Glucose electrolyte solutions in a European context (letter), *Lancet* 2:361-362, 1981.

Sugijanto, et al., Edema in oral rehydration, *Paed Indones* 21:229-234, 1981.

185. Black, R. E., et al., Glucose vs. sucrose in oral rehydration solutions for infants and young children with rotavirus-associated diarrhea, *Pediatrics*, 67(1):79-83, 1981.

The efficacy of two oral rehydration solutions of equal osmolality containing essential electrolytes and either glucose or sucrose was compared in a double-blind sequential trial of 784 children under five years of age with rotavirus-associated diarrhea treated at a center in rural Bangladesh. The glucose oral rehydration solution (GORS) group and the sucrose oral rehydration solution (SORS) group were matched by age, sex, frequency of vomiting, duration of diarrhea and vomiting before hospitalization, admission specific gravity, frequency of stool pathogens and nutritional status. The data generated from the (GORS) and the (SORS) groups were analyzed according to the patients' dehydration status: none-to-mild, and moderate-to-severe.

Oral therapy failure were determined by hospital staff who decided the patient was unable to consume enough oral fluid to match continuing fluid losses because of persistent vomiting and/or high purging rates. The ORT failure rate was 11.5% for the SORS group and 7.3% for the GORS group; the difference was not significant.

Vomiting was a significantly more common cause of failure for the group treated with SORS and was associated with an increased rate of intake of the sweeter sucrose-containing solution. However, the presence of vomiting in 88% of the successfully treated children in both groups showed that vomiting *per se* is not a contraindication to ORT. The purging rates were not different for the two groups. As assessed by purging rate and initial degree of dehydration, failure rates for the most malnourished children (less than 60% of expected weight for age) did not differ either between the groups or

when compared to the better nourished children as a whole. This was true even though the stool losses of this group constituted a greater proportion of their body weight.

The authors concluded that, although glucose is preferable, sucrose-based ORT solutions can be used safely and effectively for the treatment of diarrhea regardless of etiology.

These findings closely agreed with those of earlier studies, including some which examined ORT efficacy in non-rotavirus diarrhea.

186. Clements, M. L., et al., Comparison of simple sugar/salt verus glucose/ electrolyte oral rehydration solutions in infant diarrhoea, *J Trop Med Hyg* 84:189-194, 1981.

The authors performed a double-blind clinical trial to compare the efficacy of a homemade simple salt/sugar (SSS) solution to that of one based on the "complete" WHO-recommended ORS composition (GES). Sixty-one infants, aged 3-18 months, were admitted to hospital with mild to moderate diarrheal dehydration, were randomly assigned to one of the two treatment groups and were rehydrated orally. The SSS solution contained 3.5 grams of table salt and 30 grams of table sugar in one liter of water (in mmol/l: Na^+ 60, Cl^- 60, sucrose 83).

Moderately dehydrated infants (6-9% loss of body weight) received 25 ml/kg of either solution hourly for 4 hours (total 100 ml/kg). This was followed by 50 ml/kg of free water ("complete" formula group) or continued SSS over the next 2 hours. Mildly dehydrated infants (4-5% loss of body weight) received one-half the above volumes during the initial six-hour rehydration period.

All 32 infants in the complete formula group and 27 of the 29 infants (93%) in the SSS group were successfully rehydrated. Improvements in metabolic acidosis and rapidity of rehydration were similar in the two groups. Two infants in the SSS group, however, were withdrawn from the study due to persistent, severe acidosis and focal seizures. They later recovered. After six hours of therapy, 57% of SSS- and 56% of complete-formula treated infants were completely rehydrated. By 12 hours, the figures were 88% and 94% respectively, and by 18 hours, they were 93% and 100% rehydrated. No statistically significant differences were observed between the groups at 0, 4, 6, 12, 18, and 24 hours with respect to mean weight gain, serum urea, haematocrit, plasma specific gravity, total fluid intake (320 vs. 302 ml/kg), estimated insensible loss (250 vs. 259 ml/kg), or total stool output (152 vs. 166 ml/kg) over the 24-hour period.

Vomiting was observed in 22 SSS-group patients (76%) and in 19 of the complete formula group (59%), a nearly significant difference ($p = 0.07$). The mean volume of fluid vomited, however, was significantly greater in the SSS- (25 ml/kg/24 h) than in the complete-formula group (6 ml/kg/24 h), (p less than 0.001). In spite of the association between vomiting and SSS intake, all children who vomited were successfully rehydrated orally.

Significantly more SSS-group patients developed hypokalaemia after admission than did those in the complete formula group (13 vs. 6, p less than 0.02). Subsequently, banana puree, which is rich in K^+, was given to patients in both groups as an adjunct to ORT. Eleven of the SSS and five of the complete formula patients remained hypokalaemic at discharge.

On admission, 5 of 29 (17%) SSS patients and 3 of 32 (9%) complete formula patients were hypernatraemic (serum Na^+ more than 150 mmol/l). By discharge, 2 SSS- infants and 1 complete-formula infant remained mildly hypernatremic (range Na^+ 152-156 mmol/l).

The findings suggested SSS solutions, when correctly prepared, constitute a safe and effective alternative to the WHO-recommended glucose-electrolyte solution. As reported elsewhere, however, their use is associated with slightly more severe vomiting. Until the critical problem of hypokalaemia accompanying SSS therapy is resolved, contended the authors, the WHO-recommended formula (containing NaCl, KCl, $NaHCO_3$ and glucose or sucrose) must remain the composition of choice for ORT.

(See also abstract No. 174).

187. Islam, R., Common salt and sugar with and without sodium bicarbonate as an oral rehydration solution in diarrhea of children, *Scientific Publication, (undated) ICDDR,B,* (Reprints available from MRI, Chief Physician, ICDDR,B, GPO Box 128, Dacca-2 Bangladesh).

To determine the extent to which sodium bicarbonate prevents acidosis when a simple salt/sugar (SSS) solution is used for ORT, the author carried out a comparative clinical trial at the ICDDR,B treatment centre in Dacca, Bangladesh.

One-hundred-and-one children, aged one to twelve years, presenting to the treatment center with acute watery diarrhea and moderate dehydration, were randomly assigned to one of two ORT study groups. After all patients had been given initial intravenous therapy to restore electrolyte deficits, 57 children were switched to an SSS oral solution (containing mmol/l: Na^+ 87, Cl^- 87, K^+ 10, and glucose 111) while the remaining 44 children received the same solution with sodium bicarbonate added (containing mmol/l: Na^+ 90, Cl^- 60, HCO_3^- 30, K^+ 10, and glucose 111). ORT was continued until diarrhea stopped.

The study groups were similar with respect to age, sex, body weight, duration of diarrhea prior to admission, etiology and severity of diarrhea (as measured by admission serum specific gravity and serum electrolyte values).

The authors reported an overall success rate of 65%. Hydration was successfully maintained in 41 out of 57 patients (72%) in the SSS group, and in 26 out of 44 children (59%) in the SSS-plus-bicarbonate group. The difference was not significant. Over the initial 48 hours, sustained acidosis was observed in all patients in the SSS group. In contrast, acidosis was corrected in all patients successfully treated with the SSS-plus-bicarbonate fluid. Comparing treatment successes to treatment failures, the authors observed no significant difference in acidosis correction within the SSS-plus- bicarbonate group.

Although the crude sugar (gur or molasses) which had been used in both ORT solutions contributes some natural potassium, the author noted that potassium balances were not maintained in any of the children during the period of observation. After 48 hours, in fact, severe hypokalaemia was found in the SSS treatment failures.

When stooling rates are very high, concluded the author, neither solution is completely effective. Secondly, without bicarbonate, SSS solutions do not correct acidosis. Thirdly, potassium depletion develops in children treated with either SSS or SSS-plus-bicarbonate and is most severe in those with highest purging rates.

188. Harland, P.S.E.G., et al., Composition of oral solutions prepared by Jamaican mothers for treatment of diarrhoea, *Lancet* 1:600-601, 1981.

To estimate the accuracy with which Jamaican mothers prepare home ORT solutions, the authors studied 44 mothers attending the University of the West Indies Hospital Casualty Department who had previously used a homemade ORT solution to treat their children with diarrhea.

Using a standardized questionnaire the authors first determined the type of homemade solution each mother used and her source of information on how to prepare and administer it. The mothers were then asked to bring samples of their solutions to the hospital. If samples were not available, the mothers were shown a tray with a jug of water, salt, sugar, glucose and a standard (250 ml) cup and were asked to prepare a solution exactly as they had done at home. Locally common, partially refined, dark sugar was used. Mothers who had prepared simple salt/sugar (SSS) solutions were given standard two-ended plastic spoons (popularized by TALC, Institute of Child Health, London) and, after instructions, were asked to prepare a second sample solution. To assess the variability of the sugar itself, the authors prepared and analyzed solutions using both dark and white, refined sugar as measured by the

two-ended spoon. All sample solutions were analyzed for sodium concentration (by flame photometer), for osmolality (Fiske osmometer) and for sugar concentration (refractometer).

The 44 mothers reported using a variety of home solutions. Sucrose water was used by 15, SSS solutions by 13, herbal teas with lime or orange juice by 9, and glucose water by 7. Of the 13 SSS users, 6 had obtained their information from the radio and 3 had been so advised by doctors. Seven of the 11 physicians they had consulted, however, had advised the mothers to give "sugar water".

Mothers' estimates of fluid volume given the 24 hours prior to admission varied from 176 ml. to 2,280 ml.

Analysis showed the mean osmolality of the 7 glucose solutions was very high (mean 1216, range 212-3000 mOsm/l); that of the 15 sucrose solutions was lower (mean 809, range 401-2397 mOsm/l). Of 7 SSS samples prepared without using a double-ended spoon, the sodium concentrations of 5 exceeded 150 mmol/l and the solutions were hyperosmolar (mean 844 mOsm/l). When double-ended spoons were used, 6 of 7 SSS samples had a satisfactory osmolality (less than 300 mOsm/l). Using the double-ended spoon, the authors determined that one spoonful of white, refined sugar—compared to 4 or 5 of dark, unrefined sugar—was needed to attain a concentration of 5%.

The authors concluded the compositions of home-made ORT solutions prepared by mothers without adequate training and supervision are often dangerously wrong, most likely because the mothers prepared the solutions to taste. The use of a double-ended spoon may improve the precision with which homemade ORT solutions are prepared. However, the wide variability of crude vs. refined sugar demands that each be locally analyzed and that instructions given to mothers be adjusted and standardized accordingly.

Levine, M. M., et al., A practical, reliable method for preparing simple sugar/salt oral rehydration solution, *J Trop Med Hyg* 84:73-76, 1981.

Shields, D. S., et al., Electrolyte/glucose concentration and bacterial contamination in home-prepared oral rehydration solution: A field experience in Northeastern Brazil, *J Pediatr* 98(5):839-841, 1981.

189. Wong, H. B., Rice water in treatment of infantile gastroenteritis, (letter) *Lancet*, 2:102-103, 1981.

The author reported the results of a sequential clinical trial comparing WHO-recommended ORS to rice water for ORT.

One-hundred-thirty babies with gastroenteritis who were admitted to the Department of Pediatrics, National University of Singapore, were alternately assigned to either WHO-recommended ORS or rice-water groups. There were 63 patients on oral electrolyte solution and 67 on rice water.

Milk was withheld the first 24 hours, then gradually reintroduced in dilute form, reaching full concentration by Day Five. Oral therapy was begun immediately. More severely dehydrated children were initially given IV therapy, then switched to one or another of the oral solutions. Serum electrolyte and urea values were measured for all patients upon admission and at Day Three of treatment. The groups were similar with respect to age, sex, race, duration of diarrhea prior to admission, severity of dehydration and serum electrolytes.

Stooling rates were higher in ORS than in rice-water subjects, observed the author. Serum values differed significantly in only three cases, at Day Three, but this might have been due to the effects of the IV therapy. There were no deaths or complications.

Given its universal availability in many parts of the developing world, rice water may be a more practicable alternative to ORS, concluded the author. He also suggested rice water may be superior because its lower osmolality reduces the role of intestinal secretion and because in infantile gastroenteritis, glucose absorption is disrupted more than starch absorp-

tion. The few data presented, however, do not substantiate these hypotheses.

190. Kleevens, J.W.L., Rice water for infant gastroenteritis (letter), *Lancet* 2:306, 1981.

Observing that the use of rice water for treating diarrheal dehydration is evidently a popular folk remedy throughout island Southeast Asia, the writer described the regimen used in his native Indonesia.

First, rice is boiled with a deliberate excess of water. The excess water is then drained off, seasoned with a few drops of soy sauce and given to the patient to drink. No other food or fluids are given the first day. The second day, a diet of soft, cooked rice, chicken broth and mashed vegetables, seasoned with salt or soy sauce, is given.

The writer later used this regimen, with good results, while practicing pediatrics in Indonesia. Although he regretted never performing clinical trials, his impression was that the rice water regimen seemed to shorten the duration of diarrhea in adults.

191. Izgü, E., et al., The solid state stability of oral rehydration salts, *J Clin Hosp Pharm*, 6, 135-144, 1981.

This highly technical article presented the results of a series of laboratory tests on stability and other physical properties of ORS.

The main indicator of stability was discoloration. A reflectometer was used to measure color changes when the ORS was subjected to dry heat (50°C oven) to heat and humidity (50°C, 70% relative humidity) and to room temperatures (22°C). The WHO-recommended ORS composition was used.

Results showed the ORS tended to discolor after one week at 50°C and high humidity and after 4 weeks at room temperature. When mixed in varying aqueous concentrations and analyzed spectrophotometrically, decomposition of the glucose component was observed. This decomposition was more rapid in the presence of sodium bicarbonate.

The authors concluded that bicarbonate hastens the decomposition of glucose and that ORS mixtures should ideally be prepared extemporaneously.

192. Patra, F. C., et al., Can acetate replace bicarbonate in oral rehydration solution for infantile diarrhoea? *Arch Dis Child*, 57: 625-627, 1982.

Unless packaged under ideal conditions, ORS packet shelf life can be shortened due to a chemical reaction that may occur between glucose and bicarbonate. A more stable buffer, acetate, has been proposed as a substitute for bicarbonate. To compare the clinical efficacy of ORT solutions containing either bicarbonate or acetate, the authors performed a double-blind, clinical trial on forty children presenting to a Calcutta hospital with acute, uncomplicated diarrhea and signs of moderate to severe dehydration.

After initial examinations, the children were weighed and randomly assigned to either treatment or control groups. The groups were similar with respect to age, sex, nutritional status, presence of vomiting and duration, severity and etiology of diarrhea. Both stool and blood samples were drawn and complete serum biochemical examinations performed at admission and at 6, 24 and 72 hours. The 20 control group children were given WHO-recommended ORS solution as were the 20 children in the treatment group, except that 30 mmol/l of acetate was substituted for the 30 mmol/l of bicarbonate.

Due to signs of hypovolumic shock, 5 children in the acetate and 9 in the control group had to be given one to two hours of I.V. therapy before being switched to ORT. Tetracycline was given to all patients.

Enteropathogens were isolated in 78% of cases. All were successfully rehydrated orally. All but one of the patients recovered uneventfully within 72 hours; diarrhea continued in one child in the control group until Day 5. The authors concluded acetate can be substituted for bicarbonate in the WHO-recommended

ORS formula without affecting either palatability or clinical efficacy.

Santosham, M., et al., Storing oral rehydration solution (letter), *Lancet* 1:797, 1982.

193. Ho, T. F., et al., Rice water and milk: effect on ileal fluid osmolality and volume, *Lancet* 1:169, 1982.

Observing that others have found it efficacious as an oral rehydration solution, the authors evaluated the effect of rice water on ileal osmolality and volume in two infants who had had ileostomies created for reasons unrelated to diarrheal disease.

The infants, who weighed 2.05 kg and 2.45 kg at 4 and 5 weeks of age, respectively, were given total parenteral nutrition (TPN) for a week, then gradually weaned to oral humanized milk. In between milk feeds, the rice water was infused to both infants at 150 ml/kg body weight over a two-day period. Daily ileal fluid volume and ileal fluid osmolality, (measured by an Advanced Osmometer Model 3W. Advanced Instruments, Massachusetts) were monitored.

When compared with milk, rice water produced significantly lower ileal fluid osmolality (p less than 0.02) and lower ileal fluid volume. When compared with TPN, milk, but not rice water, produced a significantly higher ileal fluid osmolality (p less than 0.01) and a higher ileal fluid volume (p equal to 0.05). These findings agreed with recent experimental evidence of osmoregulation of luminal content in rat duodenum and ileum, observed the authors, and provided circumstantial evidence that low osmolality is responsible for the efficacy of rice water in the treatment of acute infantile diarrhea.

Providing ethical considerations could be satisfied, a carefully controlled balance study in children with acute, uncomplicated diarrhea, would be needed to confirm the authors' observations.

194. Molla, A. M., et al., Rice-powder electrolyte solution as oral therapy in diarrhoea due to *V. cholera* and *E. coli*, *Lancet*, 2:1317-1319, 1982.

Because it is cheaper, more readily available and has been used for centuries as a traditional dietary therapy for diarrhea, the authors wished to compare rice powder to sucrose as the carbohydrate constituent in ORS.

Rice powder, the authors noted, is easily hydrolized, yielding 80-86% glucose by weight. It also yields amino acids, including glycine, several of which, like glucose, are known to promote intestine sodium transport as well. Secondly, these constituents are released slowly during intraluminal digestion, avoiding any additional osmotic load. A third possible advantage to using rice powder could be nutritional, due to its higher caloric density.

To evaluate rice-powder ORS, the authors carried out a controlled clinical trial, comparing it to sucrose-based ORS.

One-hundred-and-twenty-four adults and children with acute diarrhea and moderate to severe dehydration were divided into two groups. Fifty-nine patients were treated with rice-powder electrolyte solution while 65 patients, matched for age, sex, etiology and severity of dehydration, served as controls and were treated with a standard sucrose-electrolyte solution. For practical reasons, small children with rotavirus were excluded from the study.

The electrolyte content of both solutions met the WHO recommendations (in mmol/l: Na^+ 90, Cl^- 80, K^+ 20, HCO_3^- 30). Because *in vitro* hydrolysis converts 80-86% of rice powder into glucose, sucrose (40g) was replaced by 30g of rice powder. Plain water was allowed on demand. The efficacy of this cereal-based therapy was assessed by the rate of purging, change in body weight, serum specific gravity, urine output and post hydrolysis sugar content in the stool. Recourse to IV therapy once ORT had begun was considered treatment failure.

The majority of patients had cholera. Among adults with cholera, stool output, oral fluid intake and urine output after the first 24 hours of treatment were comparable in both groups. Over the first 24 hours about 80% of

these patients gained weight. Serum specific gravities returned to normal levels and the success rates were the same for both groups (81%).

Results in cholera patients below 10 years showed that patients in the sucrose-electrolyte group consumed more oral solution than did those receiving the rice-powder solution (p less than 0.05). Stool output was higher, urine output lower, and post-hydrolysis glucose content in the stool was less in the sucrose group compared to the rice-powder group, but these differences were not significant. Weight gain and success rates in both groups were similar (85% success in the sucrose group, 80% in the rice-powder group).

Among *E. coli* patients, both groups gained body weight within 24 hours and the success rates were identical.

Among patients of all ages, the average success rate in the rice-powder group was 80% for cholera patients and 88% for *E. coli* patients, no different from those receiving the sucrose-electrolyte solution. Failures were due to purging rates that exceeded the patients' ability to drink enough replacement solution and were not related to the type of solution used.

The authors concluded that a cereal-based, rice-powder electrolyte solution is efficient and safe to use in ORT for acute diarrhea.

195. Nalin, D., et al., Rice powder and electrolyte solutions (letter), *Lancet* 2(8290): 155-156, 1982.

Commenting on a study by Molla, et al., (see preceding abstract) regarding the use of rice powder as a replacement for glucose in ORT, the authors pointed out a number of studies have shown treatment failure rates increase whenever other carbohydrates are substituted for glucose. The effect is most pronounced in severely dehydrated cases, primarily because of decreased absorption rates but also due to the osmotic effect of non-absorbed molecules.

Treatment failures occur with rice-powder ORT solutions, the authors postulated, because gut transit is too rapid to permit hydrolysis of the starch, which would then reduce the resulting concentration of glucose. However, the authors added, in the majority of cases which are mild and can be treated in the home, rice-powder solutions may be perfectly acceptable.

196. Patra, F. C., et al., Is oral rice electrolyte solution superior to glucose electrolyte solution in infantile diarrhoea? *Arch Dis Child* 57, 910-912, 1982.

Noting that rice, when hydrolyzed, yields glucose, amino acids and oligopeptides, all of which have been shown to enhance water and sodium absorption in the small intestine, the authors performed a controlled clinical trial to evaluate rice powder as a substitute for glucose in ORS.

Fifty-two children, ages 3 months to 5 years, presenting to a Calcutta, India hospital with acute diarrhea and moderate to severe dehydration, were admitted to the study. Children were weighed and randomly assigned to either control or treatment groups. In both groups the WHO-recommended ORS composition was used except that in the treatment group, 50 g/l of 'pop rice' powder was substituted for the 20 g/l glucose.

'Pop rice' is prepared by popping unhulled rice on heated sand and is a traditional snack throughout the Indian subcontinent. Cooked pop rice was bought in a local market, ground to a powder and 50 g of it were added to the study-group ORS.

The ORT solutions were given *ad libitum*, free water was offered and breastfeeding was continued. Fluid intake and stool output were monitored and body weight and serum electrolytes were measured at 0, 6, 24 and 48 hours. Protein content of the rice powder was determined by the micro-Kjeldahl method.

The groups were similar with respect to age, duration of diarrhea prior to admission, history of vomiting, nutritional status and presence of pathogens. Two patients in each group had to be switched to IV therapy due to excessive vomiting and purging rates; these were excluded from analysis. All remaining patients

responded well to ORT, recovering within 72 hours. The 24-hour and the total stool outputs, however, were significantly lower in the study group, as was total fluid intake (234 ± 30 ml/kg vs. 366 ± 54 ml/kg in the control group, p less than 0.05) and duration of diarrhea (30 ± 4 hrs. vs. 43.5, p less than 0.05).

The pop rice was found to contain 87 g/kg of protein and, upon hydrolysis, it liberated 700 g/kg glucose. The authors calculated that study-group children ingested an average of 40 ± 5.3 calories and 1.02 ± 0.13 grams of protein per kilogram body weight over an average treatment period of 30 hours.

The authors concluded the rice-based ORS was superior to the glucose-based formula, based on the clinical criteria of fluid intake, stool output and duration of diarrhea. Powdered rice may also be nutritionally more advantageous than glucose-based ORS, they added.

197. Sandhu, B. K., et al., Oral rehydration in acute diarrhoea with a glucose-polymer electrolyte solution, *Arch Dis Child* 57, 152-160, 1982.

Recognizing that increasing the caloric content of isotonic ORT solutions could provide "nutritional support" during diarrhea, the authors conducted an uncontrolled clinical trial to assess the efficacy of a glucose-polymer ORT solution.

Seven normally nourished children (mean age 12.8 months) presenting to a London hospital with mild to moderate dehydration were studied. Rotavirus was found in 4, enterovirus in one and no agent in 2 cases. The children were given between 100 and 150 ml/kg of an isotonic oral solution (supplemented by breastfeeding in 2 cases) and water *ad libitum* until symptoms abated. Dietary intake was not described.

Besides electrolytes (in mmol/l: Na^+ 90, K^+ 19, Ca^{++} 4.5, Mg^{++} 5, Cl^- 40 and citrate 30), the ORT solution contained 125 g/l caloreen, a commercial glucose-polymer product which yielded 730 mmol/l free glucose on complete hydrolysis (110 mOsm/l).

Fluid intake during the first 24 hours was 989 ± 78 ml (129.2 ± 18 ml/kg) of which 845.7 ± 83 ml (114 ± 20 ml/kg) was ORT solution.

Transient increases in blood sugar above 7.5 mmol/l occurred in one child only. No sugar was detected in this child's stools but diarrhea resolved uneventfully when the child was taken off the glucose-polymer solution on Day 5. In another child whose diarrhea worsened over the first 48 hours, sugar was found in the stools and severe hypernatremia (serum Na^+ 162 mmol/l) led to a convulsion; the child recovered with IV therapy.

On admission, all children were normonatremic (mean 140 ± 0.4 mmol/l). Within 48 hours, stated the authors, mean serum sodium had risen (146.2 ± 3.3 mmol/l, range 137-162). Blood urea and bicarbonate values, however, improved significantly (p less than 0.005 and 0.002 respectively). In the 5 cases entirely treated with the glucose-polymer ORT solution, body weight increased only moderately; body weights fell in the two who had to be taken off the solution.

Observing the successful outcome in 5 of the 7 cases, the authors concluded a glucose-polymer ORT solution, which has a caloric content 3 and 6 times greater than those of isotonic sucrose- and glucose-based solutions, respectively, could be useful in ORT. However, they felt the 90 mEq/l Na^+ concentration (recommended by WHO) was too high, as evidenced by the rise in serum Na^+ in 5 of the seven cases studied.

From a logical viewpoint, the authors' conclusions are not supported by the data. There was no evidence of any nutritional benefit and evidence of glucose malabsorption was seen in the one hypernatremic case. Methodologically, the absence of a comparison group and lack of information on dietary intake, purging rates and other clinical parameters also compromise these findings. Finally, the children were not given free water or breastmilk in a 2:1 ratio with the ORT solution, as recommended by WHO.

198. Kjellman, B., et al., Oral solutions for gastroenteritis—Optimal glucose concentration, *Arch Dis Child*, 57:313-315, 1982.

Noting that ORT solutions in use primarily in developed countries often contain 4-5% glucose, compared to 2% as recommended by WHO and widely used in developing countries, the authors performed a sequential clinical trial to determine the effects of varying glucose concentrations on intestinal absorption.

Sixty-seven Swedish children below 4 years of age with uncomplicated acute diarrhea were studied. The first 31 children (Series A) were given an ORT solution containing 225 mmol/l of glucose (4.6%), 35 mmol/l sodium, and 20 mmol/l potassium. After 36 hours, increasing amounts of a milk-based formula and decreasing amounts of the ORT solution were given. A second series (B-1) of 20 children was given the same ORT solution while a third series (B-2) was given a solution containing 2.3% glucose. Stool samples were periodically collected from each patient and examined for glucose concentrations (using the Rediatest method). Any stool samples with 0.3% glucose or greater were considered positives.

Examination of 198 fecal specimens in Series A showed 13 of 27 children (48%) had positive stool glucose. Testing 96 specimens in Series B-1, the authors found 9 of 20 (45%) children positive while 6 of 16 (38%) in Series B-2 were positive. There were no significant differences among the groups with regard to hospital stay, treatment failure or stooling rates. Most positive specimens contained 0.5% or more glucose. One child begun on the 4.6% glucose solution developed hyperosmolar dehydration (serum sodium of 152 mmol/l) and had to be switched to I.V. therapy.

The authors concluded that, although generally well tolerated, use of 4-5% glucose ORT solutions is of questionable value. Given that much of the glucose is excreted, there can be little of the hypothetical caloric value in the high concentration solutions and, referring to earlier studies, optimal absorption may take place when the glucose concentration is as little as 1%.

Although the findings do not support the assertion, the authors also stated that use of high-glucose solutions could induce more severe diarrhea.

199. Finberg, L., et al., Oral rehydration for diarrhoea (Editorial), *J Pediatr* 101(4):497-499, 1982.

A distinguished group of 35 pediatricians, epidemiologists and public health workers met in March, 1982 at Johns Hopkins University in Baltimore, Maryland, USA to review findings to date regarding ORS composition, use of ORT, feeding during diarrhea and techniques for disseminating ORT, particularly in developing countries. The editorial summarized their findings on all but the latter topic.

The participants discussed the evolution of ORT from the early studies of Darrow and Harrison through the work of Phillips, et al., studies which first demonstrated *in vivo* that glucose actively promotes sodium absorption. Working with cholera, Phillips, et al., found the optimal ORS composition contained, *inter alia*, 2% glucose and 90 mmol/l of sodium.

However, other investigators were reluctant to endorse an oral solution containing 90 mmol/l of sodium for non-cholera diarrheas, particularly in children, because stool sodium losses are much lower and relatively high insensible water losses in infants could predispose to hypernatremia. On the other hand, stated the editorial, the advantages of a single ORS formula would be manifold from a public health point of view. Such a universal ORS formulation would have to be equally effective for rehydration and maintenance therapy in all ages regardless of etiology.

Taking into account these and other points, the participants agreed on the following recommendations: 1) the WHO-recommended ORS composition is a suitable *rehydrating* solution for infantile dehydration with hyponatremia, regardless of cause or specific physiologic disturbance; 2) *maintenance* of hydration during diarrhea may be accomplished utilizing the WHO-recommended ORS solution, provided additional free water (in the form of breast-

milk, plain water or juices) is given to infants; 3) alternatively, in those regions such as the United States where it may be economically and logistically feasible, a separate oral maintenance solution may be prepared and used, one which contains no more than 111 mmol/l of glucose, about 40-60 mmol/l of sodium; 20-30 mmol/l of potassium and anions such as chloride (30-50 mmol/l) and base (e.g., bicarbonate or citrate, 30 mmol/l).

The authors pointed out several commercial ORS formulations are currently available which do not conform to either the WHO-recommended ORS formula or to the guidelines proposed in the third recommendation above; many of these contain up to 8% carbohydrate.

It is important to realize, the authors noted, that glucose is essential in ORT in order to promote optimal sodium (and, passively, water) absorption and not as a source of calories *per se*. Rather, continued feeding will ensure caloric intake because, evidence suggests, many digestive and absorptive processes in the intestine are normal or near normal during an episode of diarrhea. Fasting, therefore, is not indicated and may be detrimental.

Breastfeeding should always be continued, recommended the authors. For unknown reasons, however, cow's milk and lactose-containing formulas may not be well tolerated. In non-breastfed infants these feeds should be suspended the first day or two of diarrhea, then gradually reintroduced. Once initial rehydration has been accomplished, the authors recommended resuming a normal diet as soon as the child will accept it.

The authors concluded ORT is effective, safe and inexpensive and that its widespread use should dramatically reduce hospitalizations, mortality and the deleterious effects of acute diarrhea on nutritional status.

Santosham, M., et al., Oral rehydration therapy of infantile diarrhea: A controlled study of well-nourished children hospitalized in the U.S. and Panama, *N Eng J Med* 306(18):1070-1076, 1982.

Clements, M. L., Oral rehydration therapy, In: "*New Developments in Tropical Medicine*," pp. 63-68, National Council for International Health, 2121 Virginia Ave NW, Washington, D.C. 20037, USA, 1982.

Booth, I. W., et al., Oral rehydration therapy: An issue of growing controversy, *J Trop Pediatr* 28, 116-123, 1982.

CHAPTER 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.

Chatterjee, H. N., Control of vomiting in cholera and oral replacement fluid, *Lancet* 2:1063, 1953.

Harrison, H. E., The treatment of diarrhea in infancy, *Pediatr Clin North Am* 1:335-348, 1954 (see No. 4).

Phillips, R. A., Water and electrolyte losses in cholera, *Fed Proc* 23:705-712, 1964 (see No. 9).

Hirschhorn, N., Decrease in net stool output in cholera during intestinal perfusion with glucose-containing solution, *N Engl J Med* 279:176-181, 1968 (see No. 12).

Nalin, D. R., et al., Oral maintenance therapy for cholera in adults, *Lancet* 2:370-372, 1968 (see No. 13).

Pierce, N. F., et al., Oral maintenance of water-electrolyte and acid-base balance in cholera: A preliminary report, *Ind J Med Res* 56:640-645, 1968 (see No. 15).

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

69. **Nalin, D. R.**, et al., Reduction of maintenance intravenous fluid needs in cholera by means of an oral therapeutic solution, *J Pakistan Med Assoc* 19:373-379, 1969.

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, HCO_3^--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 vomitus output.

Twenty-nine 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.

Pierce, N. F., et al., Oral replacement of water and electrolyte losses in cholera, *Ind J Med Res* 57:848-855, 1969 (see No. 21).

Bart, K. J., Pediatric cholera: Pathophysiology and treatment, *Pak Pediatr J* 1:45-53, 1979 (see No. 22).

70. Cash, R. A., et al., Rapid correction of acidosis and dehydration of cholera with oral electrolyte and glucose soiution, *Lancet* 2:549-550, 1979.

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.

Cash, R. A., et al., A clinical trial of oral therapy in a rural cholera-treatment center, *Am J Trop Med Hyg* 19:653-656, 1979 (see No. 23).

Mahalanabis, D., et al., Intraperitoneal fluid therapy in cholera and non-cholera diarrhoea, *WHO* 42:837-846, 1979 (see No. 83).

Biddulph, J., Standardized management of diarrhoea in young children, *Pediatr Indones* 11:37-46, 1971 (see No. 85).

Ludan, A. C., The efficacy of oral electrolyte fluid in the therapy of diarrhea, *J Philip Med Assoc* 49:243-252, 1973 (See No. 29).

71. Mahalanabis, D., et al., Oral fluid therapy of cholera among Bangladeshi refugees, *John: Hopkins Med J* 132:197-205, 1973.

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, HCO_3^--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.

During the 8 weeks of the outbreak, 3703 persons were treated 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.

72. Levine, G. M., et al., Role of oral intake in maintenance of gut mass and disaccharide activity, *Gastroent* 67:975-982, 1974.

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 (44%) 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.

Mahalanabis, D., et al, Use of an oral glucose-electrolyte solution in the treatment of paediatric cholera—a controlled study, *J Trop Pediatr Environ Hlth* 20:82-87, 1974 (see No. 31).

73. Barker, W. H., Perspectives on acute enteric disease epidemiology and control, *PAHO Bull* 9:148-156, 1975.

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.

Barzgar, M. A., et al., Evaluation of the effectiveness of oral rehydration in gastroenteritis in children under 3 years of age, West Azerbaijan, Iran, 1977. (Presented to the Regional Scientific Meeting on the Epidemiology of Enteric Infections of the International Epidemiological Association, Alexandria, May 27-31, 1978) *WHO Document: Ent Inf WP No. 18* (see No. 37).

De, S., Oral glucose-electrolyte solution in the treatment of cholera and other diarrhoeas, *J Ind Med Assoc* 65:230-232, 1975 (see No. 33).

74. Hirschhorn, N., et al., Oral glucose-electrolyte therapy for diarrhea: A means to maintain or improve nutrition, *Am J Clin Nutr* 28:189-192, 1975.

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.

Brotowasisto, et al., Rehydration programme in Indonesia, *Proceedings of the 5th Asian Pacific Congress of Gastroenterology*, Singapore, 1976, pp 488-490 (see No. 95).

Bollag, U., Cup and spoon rehydration of children with acute diarrhea, *J Trop Ped Env Child Hlth* 23:268-270, 1977 (see No. 101).

Field, M., New strategies for treating watery diarrhea, (Editorial), *N Engl J Med* 297: 1121-1122, 1977 (see No. 60).

Gracey, M., et al., ROSE system for treatment of cholera dehydration (letter), *Br Med J* 1:839-840, 1977 (see No. 104).

75. International Study Group, A positive effect on the nutrition of Philippine children of an oral glucose-electrolyte solution given at home for the treatment of diarrhoea, Report of a field trial by an international study group, *Bull WHO* 55:87-94, 1977.

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 abstract No. 79).

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.

Kielmann, A. A., et al., Home treatment of childhood diarrhea in a Punjab village, *J Trop Ped Env Child Hlth* 23:197-201, 1977 (see No. 106).

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

76. Pal, S. C., Promotion of oral rehydration therapy in India, *WHO Chron* 31:470-71, 1977.

Oral therapy for cholera patients has saved over $50,000 in parenteral fluid costs annually at the Infectious 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, N. F., et al., Oral fluid—a simple weapon against dehydration in diarrhoea. *WHO Chron* 31:87-93, 1977 (see No. 36).

McCord, C., et al., A successful programme for medical auxiliaries treating childhood diarrhea and pneumonia, *Trop Doc* 8: 220-225, 1978 (see No. 117).

Sack, D. A., et al., Oral hydration in rotavirus diarrhea: A double-blind comparison of sucrose with glucose electrolyte solution, *Lancet* 2:280-283, 1978 (see No. 65).

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

77. Cash, R. A., Oral therapy for diarrhea, *Trop Doc* 9:25-30, 1979.

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 breastfed 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.

Nalin, D. R., et al., Oral rehydration and maintenance of children with rotavirus and bacterial diarrhoeas, *Bull WHO* 57:453-459, 1979 (see No. 40).

Nalin, D. R., et al., The problem of emesis during oral glucose-electrolyte therapy given from the onset of severe cholera, *Trans Roy Soc Trop Med Hyg* 73:10-14, 1979 (see No. 41).

78. Rahaman, M. M., et al., Diarrheal mortality in two Bangladeshi villages with and without community-based oral rehydration therapy, *Lancet* 2:809-812, 1979.

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-à-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).

Hirschhorn, N., The treatment of acute diarrhea in children: an historical and physiological perspective, *Am J Clin Nutr* 33:637-663, 1980, (see No. 132).

79. International Study Group, Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea, Part 1) Studies in two ambulatory care clinics *J Trop Ped* 27(2):62-67, 1981.

In a continuation of a previous study of the effect of oral therapy on the nutrition of Fili-

pino 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 (see abstract No. 75) 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 was 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 supervision with intensive follow-up can be used safely and widely. The long-term effects on nutrition are difficult to assess and may be influenced by general economic conditions, unemployment, food shortages, natural disasters, and the quality of nutritional instruction. The impact of oral therapy on hospitalization and mortality rates may be greater when family-based home treatment programs are instituted emphasizing early use of oral therapy.

80. International Study Group, Beneficial effects or oral electrolyte-sugar solutions in the treatment of children's diarrhea, Part 2) Studies in seven rural villages *J Trop Ped* 27(3):136–139, 1981.

The final portion of this study on the effectiveness of an oral rehydration program measured the acceptance, understanding, and use of oral therapy on the part of the mother and its impact on children in 7 comparable, rural Philippine villages.

ORS packets were distributed directly by trained health workers to people in the community, by-passing the government health centers. Information about oral therapy was initially disseminated at community meetings, and several community members received on-the-job training to dispense the solution and related information. Packets of the WHO-recommended solution were used. Several types of bottles were used as standard containers for volume measurements. Surveys detailing demographic information and knowledge, attitudes, and practices concerning treatment of diarrhea were carried out before and after the study. During the study, mothers whose children reported to the community worker were interviewed with regard to their child's diarrhea and oral rehydration treatment.

No comparable comparison villages were available to measure the impact of oral therapy on hospitalization rates. Use of oral therapy, both by episode and in total, by community increased during the study while the practice of fasting children during diarrheal episodes decreased. The surveys showed that the overwhelming majority of mothers accepted oral therapy and almost all could repeat the directions for mixing the oral solution correctly. One-third of the children with diarrhea were not seen by village workers but some of these received oral therapy through neighbors. Half of all episodes were treated with antimicrobials and non-specific drugs.

Oral rehydration therapy was well accepted in these communities, and the village mothers

With a modicum of training, mothers can give life-saving ORT in the home.
(Photo: D. Mack, Save the Children)

demonstrated the ability to prepare the solution properly.

Several obstacles to an effective oral rehydration program were identified. Program impact, as measured by usage rate and volume of intake, may be related to the level of enthusiasm and interest displayed by the primary health care worker. Local factors such as access to medical therapeutic agents may also play a role in acceptance of oral therapy.

Nalin, D. R., et al., Comparison of low and high sodium and potassium content in oral rehydration solutions *J Pediatr* 97(5):848-853, 1980, (see No. 68).

Taylor, P. R., et al., Oral rehydration therapy for treatment of rotavirus diarrhea in a rural treatment center in Bangladesh *Arch Dis Child* 55(5):376-379, 1980, (see No. 45).

Second Edition Abstracts

By 1980, many workers were reporting dramatic decreases in hospitalization and intravenous therapy as a result of the routine use of ORT. On the field level, less precise impacts were observed in refugee settings. Some early studies also showed ORT improved nutritional status when used on the village level.

Although much work remains to be done, over the past three years an explosion of studies has more clearly revealed positive impacts of large-scale ORT use on diarrhoeal mortality and nutritional status. Additionally, some investigators have considered the cost-effectiveness of ORT, the use of alternative delivery and promotional strategies and have examined the extent of ORT use worldwide.

200. Lozoff, B., et al., Infection and disease in south Indian families: Beliefs about childhood diarrhea, *Human Organization* 34(4), 1975.

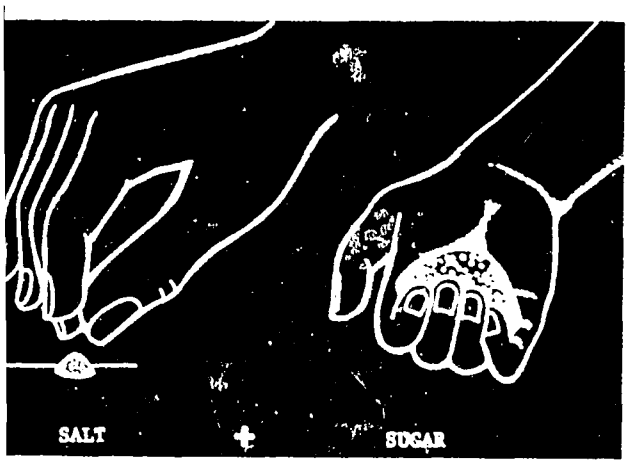
This interesting article contrasted the allopathic, biomedical notions of diarrheal diseases and dehydration to those of a tradition-directed culture in south India.

After observing the reticence of the local population (Tamil) to seek hospital treatment for dehydrating diarrhea, the authors interviewed fifty-six families in Vellore, India in order to better understand their beliefs about childhood diarrhea and dehydration. Diarrhea, they found, is thought to be a problem of individual physiology that can be cured by dietary manipulation. Vellore families commonly believe that diarrhea is caused by the excessive ingestion of foods classified as "hot". Excess "heat in the body" is therefore countered by eating "cold" foods. Diarrhea resolves when the proper balance of "hot" and "cold" is restored.

Local Western-trained physicians frequently use "sugar water" for treating diarrhea, a practice antithetical to the families' beliefs because, in south India, sugar is thought to be a "hot" food. In order to make ORT culturally acceptable, the authors suggested substituting honey, a "cold" food, for sugar.

The survey also disclosed that the people do not believe dehydration to be a complication of diarrhea. Instead, it is felt to indicate a state of pollution that requires ritual purification. The cure for dehydration is through chants (matram) recited by traditional medical practitioners (vaidyars) or special chanters (manthramkaran) and by means of a special thread-tying procedure.

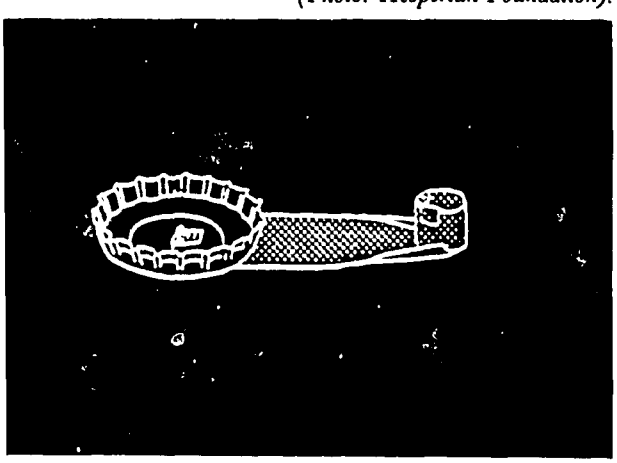
In light of these findings the authors suggested the most effective way to achieve rehydration would be through the vaidyars or manthramkaran, who are generally the first to see the severely dehydrated child. An ORT regimen could be prescribed and administered by the vaidyar or manthramkaran in addition to his purifying chant.

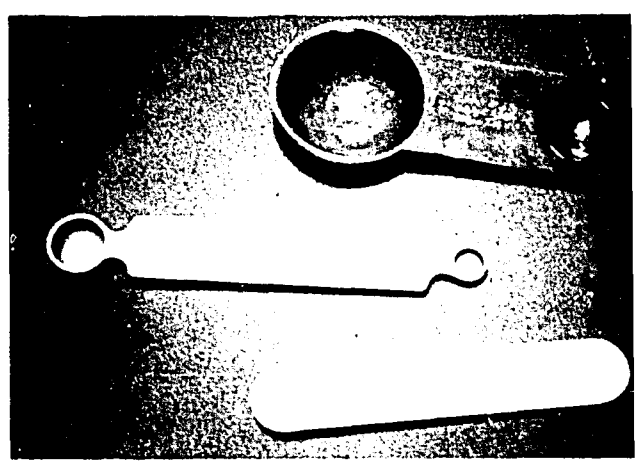


"Pinch-and-scoop." (Photo: WHO).

Household measures. (Photo: M. L. Clements, U. Md. Medical School).

Locally-made spoon. (Photo: Hesperian Foundation).





Double-ended plastic spoons. (Photo: TALC).

Simple salt/sugar (SSS) solutions can be prepared using various techniques.

Prepackaged "complete formula" ORS. (Photo: WHO).

Home preparation of ORT solution. (Photo: PAHO).

This study demonstrated that although both south Indian families and Western medicine recognize that diarrhea and dehydration are problems, they differ on their understandings of causation and therapy. The authors suggested therapeutic combinations be found which satisfy the requirements of both Western medicine and the prevailing local cultural beliefs.

Shyamsunder, P., Oral hydration therapy in the management of cholera and other diarrhoeal diseases, *Antiseptic (India)*, 74(10):633-638, 1977.

201. Cutting, W.A.M., et al., Can village mothers prepare oral rehydration solution?, *Trop Doc* 9, 195-199, 1979.

To determine the accuracy with which mothers prepare oral rehydration solutions in the home, the authors conducted two field studies in India and Trinidad comparing "pinch-and-scoop" and standard ORS packet methods.

In the first study, mothers whose children had diarrhea were shown how to take a two-finger-and-thumb pinch of salt. Multiple pinches of salt were weighed on standard laboratory scales to find their average weight. Three grades of salt were used in India—crude salt, crushed crude salt and refined salt. In Trinidad, two varieties of refined salt were used.

In India, a total of 358 salt pinch samples were weighed. The mean pinch size was (in grams) 1.63 with crude salt, 1.97 for crushed crude and 2.27 for refined. In contrast, the mean pinch size for Trinidadian mothers using both varieties of refined salt was 0.96 grams (97 samples). The range of weights was very wide as were variations between and within subjects. The authors hypothesized factors such as type of salt, granule size, relative humidity, perspiration on the hand, finger size, personality traits and cultural differences regarding the use of hands explained the variability.

In the standard ORS packet study 78 rural Indian mothers were instructed to fill a common household water pot ("chembu": volume 906 ml.) with water and to add to it the contents of one ORS packet. Twelve mothers who prepared the solutions under supervision served as "controls".

When the packets were correctly dissolved in the "chembu", the sodium concentration was about 102 mmol/l. The mean sodium concentration of solutions prepared by the 66 unsupervised mothers was 120 mmol/l with a range of 39-510 mmol/l. By comparison, the solutions prepared by the supervised "controls" had both a lower mean (105 mmol/l) as well as a reduced range of sodium concentration (61-163 mmol/l). Overall, 83% of the unsupervised mothers mixed the solution to within 40 mmol/l of the "correct" value.

The authors concluded that, with proper training, rural Indian mothers were able to prepare oral rehydration solutions within reasonable limits using pre-packaged ORS packets and domestic vessels. The simple hand measurement technique for measuring salt, however, was too inaccurate to be recommended for field use. In any case, the authors added, careful practical training in a culture-specific manner is a *sine qua non* for home ORS preparation.

(Note: This study was reported earlier in a letter to *Lancet*. See abstract No. 103.)

202. Roberts, A. B., et al., Cholera in the Gilbert Islands II. Clinical and laboratory findings, *Am J Trop Med Hyg* 28(4):685-691, 1979.

The authors described a 1977 cholera epidemic which caused 585 hospital admissions and about 300 outpatient consultations over a two-month period in Tarawa, Gilbert Islands. ORT was used extensively.

Upon presentation, all cases were examined and their degree of dehydration assessed. All those with clinically evident dehydration as well as all children below 5 years of age were admitted to hospital. The rest were treated as outpatients. Nutritional status was assessed in

all children below 5 years of age. Forty-two percent of those admitted were normally hydrated, 31.4% mildly (up to 5% loss of body weight), 18.4% moderately (between 5 and 10% loss of body weight) and 8.3% severely dehydrated (more than 10% loss of body weight).

Both outpatients and mildly dehydrated inpatients were treated with ORT alone. Others were begun on IV therapy, then switched to ORT once initial rehydration was achieved. Oral tetracycline was administered routinely.

ORT consisted of alternate volumes of a homemade salt/sugar solution (2.5% table sugar and 0.3% table salt) and "moimoto"—water from a seven-month old, immature coconut. Moimoto is a hypotonic solution containing high concentrations of potassium (about 4 mmol/l), and carbohydrates (mainly glucose about 220 mmol/l), in addition to low concentrations of sodium, calcium, magnesium and amino acids. All patients were encouraged to drink the maxium amount of fluid they could tolerate every hour. Fluid balance charts were kept for each patient. Once formed or semi-formed stools were passed patients were discharged.

One hundred and eighty-three (31.3%) patients required IV fluids. Adults received an average of 8.1 litres IV over 1.6 days; children below 12 years were given a mean of 4.2 litres over 1.5 days. There were 8 deaths, all among hospitalized cases (case-fatality rate = 1%). Six of the deaths were due to unresponsive circulatory failure, one to renal failure and one to probable fluid overload. No deaths were specifically reported among the exclusively orally rehydrated patients. Of 61 cases below 5 years admitted to hospital, 28 (46%) had weight-for-age values below the 80th percentile (Harvard standard). According to a recent survey, however, only 15% of Gilbertese underfives fell below the 80th percentile, leading the authors to assume malnourished children were 3 to 4 times more likely to suffer cholera.

The authors concluded coconut water, alternated with a salt/sugar solution, comprised a successful ORT regimen. Among the Gilbertese, noted the authors, coconut water (moimoto) was not only universally acceptable but was used as a reward for drinking an equal volume of the less palatable sugar-electrolyte solution.

Finally, ORT was judged safe and efficacious, even when delivered by hastily trained volunteer and paramedical workers receiving a minimum of supervision.

203. Isaza, P., et al., A diarrheal disease control program among Nicaraguan refugee children in Campo Luna, Honduras, *Bull Pan Am Hlth Organ* 14(4):337-342, 1980.

In this uncontrolled field trial, 71 mildly to moderately dehydrated Nicaraguan refugee children with acute diarrhea were treated with the WHO-recommended oral rehydration solution (ORS) by mothers trained and supervised by nurse auxiliaries in a refugee camp in Honduras.

Fifty-two of the 66 (79%) patients finishing the study were discharged completely asymptomatic and fully rehydrated. Thirteen (20%) were discharged completely rehydrated but with diarrhea or vomiting persisting. One patient, who presented with severe dehydration, was referred to hospital for IV therapy. An average of 1.3 liters of ORS were consumed by each patient. The mean duration of treatment was 3.1 days. The duration of treatment and the duration of diarrhea before admission were significantly associated with the number of dehydration symptoms identified by the auxiliary at initial presentation, (p less than 0.05).

The results indicated that health auxiliaries, with a minimum of training, can reliably diagnose diarrheal dehydration and that mothers can successfully deliver ORT to their children in emergency field settings when given proper instruction and adequate supervision.

204. Chen, L., et al., Village-based distribution of oral rehydration therapy packets in Bangladesh, *Am J Trop Med Hyg*, 29(2): 285-290, 1980.

The authors studied a rural Bangladesh population over a four-month period to assess the short-term impacts of a community-based ORT program. The study area, served by the ICDDR,B treatment center at Matlab, was divided into two groups: an experimental population of about 157,000 received ORS packets through some 160 female village workers while a neighboring area of about 134,000 served as an comparison group.

The village workers in the experimental area were given two half-days of training on diarrheal diseases and ORT and were supplied one-litre size ORS packets and one-litre volume bottles to ensure accurate mixing. The packets, which cost approximately US$0.05 to produce locally, conformed to the WHO-recommended formula except that sucrose was substituted for glucose in a 2:1 ratio.

During routine, daily household visits, the workers explained ORT to the mothers, showed them how to obtain one-litre volumes using household measures and distributed the ORS packets free of charge. Workers in both experimental and comparison areas maintained log books. Those of the workers in the experimental area included number of ORS packets received, number of diarrheal cases encountered and number of packets used per episode.

Log books, packets and samples of oral solutions prepared by both village workers and mothers were examined on a random-sample basis throughout the study. Additionally, records at nearby Matlab hospital were screened to identify any diarrheal admissions from either the experimental or comparison populations.

Periodic village-level interviews indicated acceptability of the packets, and of ORT in general, was high. Over 33,000 packets were distributed over the four-month period. During the peak months of July and August, each worker delivered an average of 70 packets per month, about 1.26 packets per episode for all ages.

Although variations by weight of the locally packed ingredients were found to be within acceptable limits, the electrolyte concentrations of solutions prepared in the villages tended to vary. The workers prepared solutions which, on the average, had satisfactory compositions but those prepared by the mothers were significantly more dilute. None of the samples were markedly hyper-concentrated.

Compared to the same period a year previous, the experimental group had a substantially lower rate of hospital visits (8.2/1000 population in 1977 vs. 4.5/1000 in 1978) but so did the comparison group (14.3/1000 vs. 12.0/1000). Adjusting, the authors found the reduction was significantly greater (29%) in the experimental group ($z = 2.66$, p less than 0.01). Secondly, by comparing the ORS distribution data to hospital admissions over the peak months of July and August, the authors estimated that for every case presenting to the Matlab hospital, 47 cases had been treated in the field. They also noted that 56% of hospitalized patients had previously received ORT in the field, a figure they interpreted as "actual coverage". Coverage may have been higher, however, because many hospitalized patients may have bypassed the village workers and come directly to the hospital.

The authors concluded that a village-based ORS distribution program, with local ORS production and a minimum of training for primary care workers, can achieve relatively high effective coverage and substantially reduce diarrheal hospital admissions over the short-term.

Recognizing the limitations of this study, the authors called for other longer, more detailed investigations that would examine other expected program outcomes, such as improved child feeding practices and nutritional status and reduced diarrheal mortality.

205. Rahaman, M. M., et al., A review of findings on the impact of health intervention programmes in two rural areas of Bangladesh, *Special Publication No. 11*, International Centre for Diarrhoeal Disease Research (ICDDR,B), Box 128, Dacca, Bangladesh, November, 1980.

In this paper the authors provided a useful overview of the major health problems in Bangladesh, briefly reviewed the history of the ICDDR,B and described some selected village-level PHC interventions recently undertaken by the Centre.

It was principally to combat diarrheal diseases, the major cause of death in Bangladesh, that the ICDDR,B was created in 1960. The Centre's mission has since evolved from testing cholera vaccines to providing facility-based treatment for diarrheal cases and, most recently, evaluating various approaches to delivering selected PHC services on the village level. Throughout the 1960's and 1970's the Centre played a pivotal role in the development of ORT. At the Centre's two field stations at Matlab and Teknaf, the problems of delivering ORT to the country's largely inaccessible rural population have also been systematically addressed. The findings indicate that case prevention will be difficult until overall socioeconomic development and massive improvements of water and sanitation infrastructures take place but that improved case treatment now provides a feasible strategy for controlling diarrheal diseases.

Reliance on fixed facilities to deliver ORT, however, limits coverage due to geographic factors. Figures from the Centre's Teknaf field station, for example, showed diarrheal mortality was significantly reduced only in the population living within a four-mile radius of the facility. Alternative outreach schemes, therefore, aimed a distributing locally made ORS packets at the household level, have been systematically evaluated. Delivery approaches have included female PHC workers, traditional healers, family "depot holders" and "bari" (extended family compound) mothers.

The findings to date in Matlab and Teknaf have led the authors to conclude: 1) that diarrheal cases can be successfully managed by basically-trained lay persons with little or no medical supervision, and 2) permanent facilities are not essential for case treatment. Based on these and other experiences, the Bangladesh Ministry of Health and Population Control, in consultation with ICDDR,B, launched a nationwide ORT programme in 1979.

Further impacts on diarrheal diseases, stated the authors, will depend on educational efforts which are carefully adapted to social and cultural factors. The Centre plans to develop better survillance and evaluation techniques which will allow the impacts of such efforts to be more precisely measured.

206. Rohde, J. E., et al., Elementary-school pupils as health educators: role of school health programmes in primary health care, *Lancet* 1:1350–1352, 1980.

Observing that most developing countries devote more resources to education than to public health, the authors carried out an action-oriented health education program aimed at modifying health-related behavior in rural villages in Central Java, Indonesia. Among other topics, five half-hour lessons on diarrhea were given to rural schoolteachers by local health center staff as the first step of the training program. After the lessons, the teachers used illustrative posters, stories and lesson guides to teach their pupils. As homework, the pupils then used aides found close to the school to "demonstrate" the lessons to their parents and neighbors.

To assess the impact of the lessons on modifying health-related behavior, a knowledge-attitude-practices (KAP) survey on diarrhea was administered before and six months after the program to 10% of the population served by the participating rural schools. A comparison of the survey results indicated a substantial improvement in knowledge, both of appropriate treatment and of when diarrheal cases should be referred. In the pretest it was found that only 3% knew extra fluid was needed for diarrheal patients; after education, the post-test indicated this had increased to 70%. Where none initially knew how to prepare oral rehydration fluid, after the program the figure was 70%.

The authors concluded that elementary school teachers and pupils are an effective conduit for community health education efforts.

A possible threat to the validity of these findings, however, was the fact that the number pretested was much larger than the number post-tested (47); those who were not interested or who learned nil may have dropped out of the program.

207. Rowland, M.G.M., et al., The effect of early glucose-electrolyte therapy on diarrhoea and growth in rural Gambian village children, *J Trop Ped* 26(2):54-57, 1980.

To examine the effects of ORT on height and weight gain and on prevalence of acute diarrhea, the authors performed a three-month controlled study in a rural Gambian village.

Twenty-one children, ages 4-1/2 to 24 months, were arbitrarily divided into study and control groups by a road bisecting the village. The mothers of the ten study subjects were visited each day by a village field worker to ascertain the prevalence of diarrhea. When diarrhea was detected, the mother was given a one-liter supply of glucose-electrolyte mixture for her child (composition, in mEq/l: Na^+ 119.4, K^+ 24.1, Cl^- 95.9, HCO_3^- 47.6 and glucose 111 mmol/l). This was replaced as necessary on a daily basis. No attempts were made to influence mothers' decisions to seek treatment at a nearby clinic. When the 11 children in the control group attended the clinic for diarrhea, they received the same treatment as the study children.

The authors examined the effect of ORT on height and weight gain and on prevalence of diarrhea in the two groups. Although no sex differences were noted, the two groups were significantly different in age (study group mean = 10.8 months, control group mean = 16.9 months); an age-correction factor, based on past local surveys, was utilized to compare age-specific diarrheal prevalence between the two groups.

No significant differences were noted between the groups with respect to either length or weight increases. However, the study group suffered fewer "clinic days" of diarrhea than did controls (p less than 0.05). Mean daily consumption of ORS among cases in the study group was 285 ml. (standard deviation ± 185 ml).

In retrospect, the authors questioned the use of a glucose-electrolyte solution with such a high sodium content, although no cases of hypernatremia occurred. They attributed this to the overall low nutritional status of the children and to the almost complete absence of reconstituted milk formulas in this community. They further speculated that malabsorption may result from the poor nutritional status and may have precluded any differences in weight gain.

Because referral rates and the treatment given in the clinic were equivalent for both groups, the authors concluded domicilary ORT use did not affect growth but did reduce diarrheal prevalence as indicated by "clinic days". However, a household survey showed study children had experienced "numerous short episodes of diarrhea," lasting only one or two days, for which home ORT had been provided. It may be, therefore, that early ORT use reduced the severity and duration of diarrhea but not the number of episodes *per se*.

Although this study was interesting and well carried out, larger sample sizes and a longer period of observation may be required to measure growth impacts due to early use of ORT.

208. Egemen, A., et al., A study of oral rehydration therapy by midwives in a rural area near Ankara, *Bull WHO* 58(2):333-338, 1980.

To determine the effectiveness and acceptability of ORT on the village level, the authors performed a controlled operational trial over a sixteen-month period in Etimesgut, Turkey.

Twenty-three villages, each served by a government health station, were selected for study. The villages were matched for various socioeconomic variables and divided into experimental and control groups. After appropriate training, nurse-auxiliary midwives, one of whom was assigned to each health station, instructed mothers in both groups about the seriousness of diarrheal diseases and the importance of continued breastfeeding and

administration of liquid feeds, especially "ayran" (mixed yoghurt and water) during diarrhea. Mothers in both groups were asked to report all cases of diarrhea in their children to the midwives. In both groups, the midwives measured weight for age of all children 0-4 years of age both before and after the 16-month study.

Although all the midwives were trained to recognize and treat diarrheal dehydration, only those in the experimental group were provided WHO-recommended ORS packets. They were then asked to instruct the mothers on how to prepare and use ORT when they brought their children with diarrhea to the health stations or when they detected cases during monthly home visits, which were made by the midwives in both study areas. Cases in the control group were not given ORT. In both groups, midwives took rectal swabs for laboratory analysis and, using WHO treatment guidelines, diagnosed and referred all moderate or severe cases to the physician in the nearest health centre.

Over the study period, 62.3% of the 1,237 children studied experienced one or more diarrheal episodes; 39.1% had 1 or 2 episodes, 15.7% had 3 or 4 and 7.5% had 5 or more. The midwives detected 65.3% of these during the home visits while the rest were reported by the mothers. There were no significant differences in age distribution, duration before reporting, etiology or severity of cases between the groups. In the experimental group, however, the midwives referred only 3.8% (14/369) of the diarrhea cases to health centers while the figure in the control group was 33.8% (98/290). Duration of diarrheal episodes was also significantly shorter in the experimental group—2.6 days vs. 5 days in the control group. Thirdly, children in the experimental group were found to have gained significantly more weight for age over the 16 months. Another significant difference was found in antibiotic use; in 76.5% (222/290) of detected cases, mothers in the control group had given their children antibiotics compared to only 8.9% (33/369) of the experimental mothers.

The authors concluded home use of ORT is both safe and feasible when carried out under a PHC worker's supervision. Field observations also led them to state that ORT had achieved widespread acceptance by mothers and that its efficacy may have led to the drop in habitual antibiotic use among experimental group mothers. They attributed the greater weight gain observed in the experimental group to improved appetite which, in turn, resulted from earlier water and electrolyte replacement.

Several methodological questions must be clarified before these results can be generalized. The treatment modality used by midwives in the control group was not clearly described. Because the only cases recorded were those reported by the mothers or actually encountered by the midwives during monthly visits, the validity of the incidence figures is questionable. Children's heights and weights, the authors stated, were measured only twice—before and after the 16-month study period—and not on a monthly basis. The reliability of these measurements cannot be assessed from the available data. The author's assertion that the experimental children, on the average, gained more weight per month is therefore unsubstantiated. Also, the reliability with which either the midwives or the mothers prepared the oral solutions was never determined. Finally, acceptability of ORT is difficult to assess without knowing the number of ORS packets used by both midwives and mothers at the domiciliary level.

209. Oberle, M., et al., Diarrheal disease in Bangladesh. Epidemiology, mortality averted and costs at a rural treatment center, *Intern J Epid*, Oxford Univ Press, 9(4):341-348, 1980.

In this careful study the authors analized 1975 data from the ICDDR,B treatment centre in Matlab, Bangladesh to determine the cost-effectiveness of rehydration therapy for treating diarrheal diseases. In addition to hospital records, the authors reviewed routine demographic surveillance data collected by ICDDR,B village health workers serving the

catchment area. Based on this information, they prepared both minimum and maximum estimates of the mortality averted by the hospital, the cost of averting this mortality, and the effect of the hospital in reducing both the general and diarrhea-specific mortality in the surrounding population. The cost per death averted was reported for each type of pathogen isolated and by age groups.

According to the center's 1975 criteria, only patients judged to have lost 5% or more of their body weight were admitted to hospital, where they were treated with intravenous and oral fluid therapy and with selected antibiotics. Less dehydrated patients were treated with ORT in the outpatient department.

The authors estimated both the minimum and maximum numbers of deaths averted by rehydration therapy based on a combination of historical observations and clinical indices at admission. The minimum, or conservative, estimate assumed that 80% of all patients who were in shock at admission (i.e., no obtainable blood pressure) or whose degree of dehydration involved loss of 10% or more of normal body weight, would have died without hospital treatment. The maximum estimated was made by adding to these other patients whose risk of death increased with degree of dehydration at admission and with increasing purging rates.

Taking into account the costs of personnel, oral and intravenous fluid, other medicines, speedboat and auto transport and maintenance, the authors estimated the daily inpatient treatment cost at US$11.00. Amortization of equipment, the village-based surveillance system and outpatient department costs were not included in the calculations. By multiplying number of hospital days by the cost per day, total costs were then calculated according to age group and, when isolated, type of enteric pathogens. The cost per death averted was then calculated for each age and etiological category.

A total of 1,964 acute diarrheal cases from Matlab were admitted to the field hospital in 1975. Enteric pathogens were isolated in 33.7% of these. The authors estimated between 435 and 924 deaths were averted by rehydration therapy at a cost of $38-$81 (min-max) each. Mortality from cholera was the least costly to avert while that caused by shigellosis was the most expensive. Cost breakdown by age ranged from $30-$53 per death averted for those between 5-14 years of age to $41-$244 per death averted for children less than one year of age.

Overall crude mortality in the treatment center's catchment area was lowered by approximately 7%-15% thru rehydration therapy. For all types of diarrhea, between 26% and 42% of expected deaths in Matlab were averted; for "acute watery diarrhea" the range was 81%-90%.

The cost of operating the Matlab center was approximately US$125,000 in 1975 or US$0.14 per capita.

The authors concluded that simple rehydration therapy is a highly cost-effective means of reducing diarrheal mortality. They further speculated that a community-based rehydration programme could be even more cost-effective.

Although highly impressive, these findings cannot be easily applied to other area because the method is based on clinical prognoses which necessarily would vary with diarrheal incidence and etiology, geographic and host factors as well as with different types of health care systems.

210. Mobarak, A. B., et al., Diarrheal disease control study, May through October 1980, Cairo, Egypt, *Ministry of Health Rural Health Dept., Strengthening Rural Health Delivery Project*, (51 pages) 1980 (available through Westinghouse Health Systems, Inc., Columbia, MD, USA).

The authors reported the results of a six-month study (May-October, 1980) in Egypt on the use of oral rehydration therapy to reduce child mortality from diarrhea. The six-cell design study (two control and four "treatment" cells) included 11 villages with a total population of 200,000. WHO-recommended ORS in

sealed packets was distributed to homes and made available commercially in two cells, while sugar/salt was given for home preparation and in prepackaged mixtures in the other two treatment cells. Data were collected from household surveys, ingredient and utensil surveys, laboratory analysis of home-prepared ORS solutions, mortality surveys, verbal autopsy reports and treatment and referral records.

Results indicated that accuracy of measuring salt, sugar, and water improved during the study and the sodium content of homemade ORT solutions in all treatment cells closely approximated expected concentrations. Mortality rates of children between one month and five years of age in the two control cells and in those where ORS was available mainly from commercial sources did not change significantly between 1976-79 and in 1980. Where ORS was distributed to homes, mortality fell from 18.9 to 11.2 per 1,000 population below 5 years. Where sugar and salt was prepared at home, mortality fell from 17.7 to 10.3 and where prepackaged sugar and salt was distributed to homes, mortality declined from 23.4 to 9.3. These three drops in mortality of 40-60% were statistically significant (p less than 0.05). Diarrheal deaths were 50% lower in the ORS home distribution and in the two sugar/salt cells than in the two control cells. Eighty-three percent of a sample of the deaths (50) consulted physicians but only 42% were given fluids; 76% received too small a quantity of ORT. The cost per death averted ranged from $52 in the sugar/salt home prepared cells to $691 in the control cells. In the ORS home-distributed cells it was $104.

These results were impressive but monitoring over a longer period would yield a better sense of ORT program impacts.

211. Black, R. E., et al., A two-year study of bacterial, viral and parasitic agents associated with diarrhea in rural Bangladesh, *J Infect Dis* 142:660-664, 1980.

Over a two-year period, the authors conducted an exhaustive etiological study of diarrheal cases presenting to the ICDDR,B's field hospital in Matlab, Bangladesh. The frequency, severity, and seasonality of disease associated with enterotoxigenic *Escherichia coli* (ETEC), rotavirus, *Vibrio cholera*, *V. parahaemolyticus*, *Shigella*, *Salmonella*, *E. histolytica*, *G. lamblia* and other, non-specific organisms, were described.

In Years 1 and 2, respectively, 43% and 41% of all patients were children less than two years of age; 22% each year were children 2 through 9 years old and 35% and 37% were over 10 years of age.

Regardless of etiology, patients with no or mild dehydration were treated with the WHO-recommended oral electrolyte solution. Other patients, judged to have moderate or severe dehydration upon admission, were given initial IV treatment to replace fluid deficits and then switched to the WHO-recommended oral solution for maintenance therapy. In Year 2, 40 g. sucrose/liter was substituted for 20 g. of glucose in the oral electrolyte solution.

The overall case-fatality rate for patients of all ages with watery diarrhea associated with identified pathogens was a very low 0.3% (37/14,499). Case-fatality rates by pathogen ranged from 2.6% (1/38) for *Salmonella* to 0 (0/2,279) for ETEC. Furthermore, the authors reported no significant difference in fatality rates between Year 1, when glucose-electrolyte solution was used, and Year 2, when sucrose was substituted for glucose.

The authors cited the low case-fatality rates, using either glucose- or sucrose-electrolyte solutions, as further documentation of the efficacy of both ORS formulations.

212. Poudayl, L., et al., Home-made oral rehydration solutions: feasibility study in Nepal, *WHO Chron*, 34(12):496-500, 1980.

In this brief report, the author described the results of an uncontrolled, comparative trial to determine the accuracy with which Nepalese mothers could prepare homemade SSS solutions.

In the first study, 56 mothers were divided into small groups of six to eight and were asked

by local village health workers (VHWs) to bring a pot, spoon and "mixing" utensil from their homes. Using a local measure ("mana") of approximately 580 ml., the VHW measured the volumes of the 4 mothers' pots and demonstrated to each group three different methods of SSS preparation: "pinch-and-scoop", use of domestic spoons and use of the double-ended "Morley spoon". Each method called for mixing the ingredients in one mana of water. After each mother had prepared solutions using the three methods, 100 ml. samples of each were collected for later laboratory analysis.

The experiment was repeated with a second group composed of 51 mothers from 3 other, more distant villages. This time, however, the VHWs showed the mothers the correct volumes of one *mana* of water, 1.75 grams of salt and 20 grams of sugar and asked them to prepare one *mana* of SSS solution.

Results showed the solutions prepared by mothers in the first group were more variable than those of the second group. Using the pinch-and-scoop method, sodium concentrations in the first group ranged from 32 to 91 mmol/l; the ranges for domestic and "Morley" spoons were 20-69 and 22-81 mmol/l, respectively. While sodium concentrations exceeded 90 mmol/l in 25% of samples prepared using the "pinch-and-scoop" method, they were less than 50 mmol/l in 49/55 domestic-spoon and 13/55 Morley-spoon samples.

No data were presented from the second group.

The authors concluded the additional training given the second group produced "better results" but there were no data to show this. However, it was also found that less than 50% of the homes in some areas had either sugar or spoons of any kind and that the volumes of the few teaspoons that were found varied from 3.2 to 6.5 ml. The concept of a *mana* appeared to be universal.

Until ORS packet distribution becomes feasible on a widespread basis, the authors reported, further evaluation of the pinch-and-scoop method as an interim measure will be undertaken by the Nepalese authorities.

213. Hutchins, P., et al., Oral solutions for infantile gastroenteritis -variations in composition, *Arch Dis Child*, 55, 616-618, 1980.

To examine the accuracy with which home-mixed ORT solutions are prepared in the developed world, the authors tested the sodium concentrations and osmolalities of four commercially available ORT solutions mixed by parents in London, England whose children were acutely ill with diarrhea.

Parents were instructed to prepare the solution at home and to bring samples to the hospital for testing.

The solutions consisted of: a) a concentrated electrolyte mixture, to which water and either glucose (18 samples) or sucrose (25 samples) was to be added; b) a prepackaged glucose-electrolyte mixture requiring only water (25) and; c) an already diluted electrolyte solution to which sucrose was added (23). None of these mixtures were based on the WHO-recommended formula.

The authors found a wide range of osmolality in all four types of home-mixed solutions. In general, osmolality was higher in glucose than in sucrose solutions. Although there was a wide range of sodium concentrations, in none of the samples did it exceed 43 mmol/l. Mean osmolalities and mean Na^+ concentrations were most nearly correct in the prepackaged samples. They varied more widely in this group, however, when compared to the other 3 groups which had to add either glucose or sucrose.

Noting that the highest osmolality achieved when sucrose was added to the electrolyte solution hardly exceeded that of the "correctly formulated" glucose solution, the authors concluded prepackaged mixtures based on sucrose rather than glucose would be most appropriate for use in developed countries.

The data do not support this conclusion, however. When compared to the "correct" concentrations, there were no significant differences between mean osmolalities of either glucose or sucrose-based samples.

214. Hendrata, L., et al., Sodium concentration of home mixed rehydration solutions, *Paediatr Indones* 20:91-92, 1980.

The authors reported the results of an uncontrolled trial to determine the reliability of ORT solutions prepared by Indonesian women using packet and double-ended spoon methods.

Sixty literate Indonesian women, "drawn from high, middle and lower classes", were divided into two equal groups. Women in Group A were given one-liter size ORS packets first, those in Group B the double-ended spoons. No verbal instructions were given. The women were simply asked to follow the instructions on the packets (for mixing in one liter) or the spoons (for mixing salt and sugar in one glass). After doing so, the women were then asked to prepare solutions using the alternate technique.

Of the 120 samples tested, five in the packet group and two in the spoon group had sodium concentrations in excess of 120 mmol/l. Of those who had erred in the packet group, 3 had done so before seeing the spoon. This fact, reasoned the authors, showed the differences in volume did not cause the errors. None of the "high class" women prepared hypernatremic solutions. Excluding the 7 hypernatremic solutions, mean sodium concentrations were 96 mmol/l for packets (range 35-119) and 47 (range 27-63) for spoons.

The authors concluded the danger of preparing hypernatremic solutions using plastic spoons is no greater and may be less than that of using packets.

Anonymous, Oral rehydration therapy (ORT) for childhood diarrhea, *Population Reports, Series L, No. 2*, (75 pages), Nov-Dec 1980, (available in several languages from the Population Information Program, the Johns Hopkins University, Hampton House, 624 N. Broadway, Baltimore, MD 21205, USA).

Parker, R. L., Oral fluid therapy in diarrhea and dehydration: Current concepts and practical considerations, (*Unpublished Document* available from: Dept. of International Health, Johns Hopkins Univ. School of Hygiene and Pub Health, Baltimore, Maryland, USA), July 1980.

215. Ellerbrock, T. V., Oral replacement therapy in rural Bangladesh with home ingredients, *Trop Doc* 11:179-183, 1981.

Concerned that reliance on packets, special spoons or any other "outside" technology for ORT would not be feasible in rural Bangladesh the author described a program to promote early home use of sugar/salt solution to orally treat diarrheal dehydration.

The program was implemented by the Bangladesh Rural Advancement Committee (BRAC) in 8,359 rural households in four isolated villages (thanas) of Sylhet District in Bangladesh. Teams of "oral replacement workers" (ORWs) systematically provided household training to village women on how to prepare the "labon-gur" mixture (one three-finger pinch of salt, (labon) and two four-finger scoops unrefined sugar ("gur") added to 1/2 "seer" (467 ml) of tube-well or boiled water). In addition, the village women were taught "ten points to remember", which covered when to use the mixture, how much of it to give, when the mixture can be dangerous, when a doctor should be consulted, and what nutritional advice should be given to a person suffering from diarrhea.

An interesting aspect of the program was its system of salary incentives. The ORWs were paid according to how well they trained the village women. This was assessed by monitors on a sample basis a few weeks after the training. The monitors visited 1,079 randomly selected households, interviewed village women and collected samples of homemade ORT solutions for later analysis.

Women were graded "A" if they could reiterate all 10 "points" as well as correctly prepare the solution; a grade of "B" was given to those who remembered 7, 8 or 9 points but made the solution correctly. "C" indicated less than 7 points were remembered but that the solution was correctly prepared, while those unable to prepare the solution correctly were graded "D".

Results showed that only 4 of 996 (0.4%) women sampled prepared dangerously concentrated solutions (i.e., Na^+ greater than 120 mEq/l). Of the 1,079 women interviewed, 336

(34%) were given grade "A"; 692 (64%) grade "B"; 21 (2%) grade "C", and none grade "D".

The ORWs received 4 taca (15 taca = US$1.00) for each "A" household, 2 taca for B's, 1 for C's and none for D's. This worked out to an average monthly salary of 600 taca (US$ 40) per ORW; the total program cost was approximately 6 taca (US$0.40) per household visited.

The author concluded that village women can learn oral therapy, including how to make oral solutions correctly from locally available substances using finger measurements. The study also provided an example of a workable approach to supervision and monitoring of a rural health program in a developing country which is based on intensive household-level training and the achievement of specific educational objectives.

216. Levine, M. M., et al., A practical, reliable method for preparing simple sugar/salt oral rehydration solution, *J Trop Med Hyg* 84:73-76, 1981.

Based on the findings of an earlier study (see abstract No. 173), the authors performed a controlled field trial to assess the accuracy with which rural Honduran mothers can prepare SSS ORT solutions in the village using only home measures.

Because of their wide availability, 5 ml teaspoons and 1.0 liter containers were chosen as standard measures. After laboratory analysis to determine optimal dosages, 5 U.S. nurses and 20 rural Honduran mothers were asked to prepared SSS by the identical method of mixing one level teaspoonful of salt and four heaping teaspoonsful of sugar in 1.0 liter of water. The Honduran mothers had been asked to bring their own teaspoons and one-liter measures to a nearby health center where they were provided both group and individualized instructions and were supervised by a local health auxiliary.

Although all 20 mothers brought appropriate one-litre volumes, only 16 brought correct (i.e., 5 ml) teaspoons; one mother brought a 20 ml tablespoon and 3 had slightly small (4 ml) teaspoons. The latter 4 mothers were given correctly-sized teaspoons to use in the trial.

Subsequent laboratory findings showed the mean Na^+ and sucrose concentrations of quadruplicate solutions prepared by the U.S. nurses were 74 ± 8 mmol/l and 3.3 ± 0.3 gm-%, respectively. The "recommended" values were 60-95 mmol/l Na^+ and 2-4 gm-% sucrose. By comparison, the mean sodium concentration of the solutions prepared by the Honduran mothers was 86 ± 20 mmol/l, with a range of 60-145 mmol/l. Sodium in only one solution exceeded 115 mmol/l; in 16 of 20 solutions, Na^+ concentrations were between 60 and 95 mmol/l. Sucrose concentrations, however, were more variable, ranging from 1.3 to 3.7 gm-%. Sixteen of 20 solutions were in the optimal range of 2-4%. Potassium levels did not exceed 0.7 mmol/l in any solution.

The authors concluded rural mothers in developing countries can be taught to mix SSS solutions with acceptable concentrations of sucrose and Na^+. However, at least one person in the village should be formally trained to assure utensils of the correct size are used and to supervise the actual preparation of the SSS solutions. In addition to preparing SSS solutions, the authors stated, mothers must be taught to give their infants adequate amounts of free water (in the form of breastmilk, plain water or other low solute fluids) to lessen the risk of hypernatremia as well as to give potassium-rich foods (banana, citrus fruits, coconut water) to prevent the development of hypokalaemia.

As neither the method of selection nor the characteristics of the 20 Honduran mothers (e.g., age, parity and literacy, etc.) were described, it is difficult to generalize the authors' conclusions.

217. Shields, D. S., et al., Electrolyte/glucose concentration and bacterial contamination in home-prepared oral rehydration solution: A field experience in Northeastern Brazil, *J Pediatr* 98(5):839-841, 1981.

The authors conducted un uncontrolled, comparative study in two northeastern Brazil-

Results of field studies show ORT programs can dramatically reduce diarrheal mortality. (Photo: WHO)

ian villages to determine the accuracy of mixing and levels of bacterial contamination of homemade ORT solutions. Three groups of ten persons each were compared: local traditional healers, village health volunteers and parents of children with acute diarrhea. To adjust for socioeconomic and environmental influences, participants were divided into those with in-house running water and those without.

Participants were given packets and were instructed to boil more than one liter of household drinking water for five minutes, to allow the water to cool until tepid, and, using their own measures, to mix one liter of the water with one ORS packet. Those without running water obtained it from one of two sources: a cement-encased, eleven-meter deep well or a small, nearby river. Twelve to 18 hours after mixing, the samples were collected, transported on ice to a laboratory and cultured within one to two hours for fecal coloforms (using the most probable number technique). Samples of the water from both the well and the river were also collected and cultured, both with and without ORS mixed in. Sodium levels were determined by flame photometer.

None of the participants prepared hypernatremic solutions. The traditional healers, results showed, prepared solutions with the smallest standard deviation and narrowest range of sodium concentrations (mean 75 ± 11, range 61–94 mEq/l). The authors attributed this reliability to the presence of a commonly available, widely recognized one-liter local measure in the communities. River water was found to be consistently more contaminated than well water. However, when mixed with ORS, both supported bacterial growth (greater than 10^7 fecal coloform colonies/deciliter within 16 hours at 37°C).

Solutions prepared by participants using river water were consistently more contaminated than those prepared with well water, (p less than 0.05). Taken together, solutions prepared by participants without running water in

their homes were significantly more contaminated than were solutions prepared by those with (p less than 0.05).

The ten participants whose solutions were most heavily contaminated were given autoclaved water and asked to prepare the solutions again in their homes. Nine of the 10 solutions were again found to be contaminated (i.e., greater than 10^7 FC/dl).

The authors concluded that villagers in Northeastern Brazil can measure and prepare homemade ORT solutions with acceptable reliability. However, in the absence of running water, bacterial contamination to "potentially significant" levels is nearly certain on the home level. Moreover, such contamination results whether or not water is boiled beforehand. These findings, the authors suggested, could justify the addition of a bacteriostatic or bacteriocidal agent to the WHO-recommended ORS formula.

218. Rahman, A.S.M.M., Village practitioners of Bangladesh: Their characteristics and role in an oral rehydration programme, *Thesis and Dissertation No. 2*, ICDDR,B, Dacca, Bangladesh, 1981.

The author reported the findings of a one-year study to assess the feasibility of delivering ORT through traditional health practitioners in rural Bangladesh.

Twenty-two villages with a total population of about 29,000 were chosen for study. A census was performed, after which the study area was divided into five equally-sized zones. Following this, a baseline "knowledge-attitudes-practice" (K-A-P) survey was made of every tenth house. Based on the findings, the investigator chose 3 groups for training in ORT and diarrheal diseases: village practitioners, selected volunteers and adult family members (mainly mothers).

In each zone a different combination of ORT providers was trained. One zone, in which only educational materials and double-ended spoons (for home mixing of SSS solutions) were distributed, served as a comparison group. The traditional practitioners received intensive theoretical and practical training over a seven-day period. Village volunteers, who were at about the same educational level as the practitioners, were given slightly less intensive training. Family members were trained in the home by project staff during surveillance home visits.

Surveillance and follow-up of cases began immediately after training. Each home was visited weekly and detected cases were followed for up to 2 weeks. Village practitioners submitted weekly written reports. After one year, the sample K-A-P survey was repeated.

Of 169 village practitioners living in the study area, 105 (62%) were trained during the project. Of these, only about 12% had received any sort of institutional health training prior to the study; 41% had been apprenticed to other village practitioners. A total of 5,923 mothers and 102 village volunteers also received training.

Prior to the study, 76% of the practitioners had reported treating an average of less than 10 diarrheal cases per month. According to the author, none of the 105 who received training had correct ideas about either the epidemiology or treatment of acute diarrhea.

A total of 5,385 diarrheal episodes were detected over the one-year study. More than 50% of cases were in children less than 5 years of age. Ninety-one percent of cases had no dehydration at all and only 7% had mild dehydration. Age-specific attack rates were comparable in the 5 study zones.

Surveillance data showed the practitioners had treated about 17% of all cases, trained family members had treated 50% and other, untrained providers had treated 23%. Seventeen percent of cases had not received any treatment. Less than 1% received treatment from the village volunteers. The practitioners, many of whom were versed in I.V. therapy, reported using ORT alone in 72–92% of all cases. However, only about one-half of their monthly reports were actually submitted. The reporting practitioners claimed to have treated nearly five times as many cases as were detected through house-to-house surveillance in their catchment areas.

Of 10,084 cases the practitioners reported, 9,975 (99%) were "cured", 100 (1%) had to be referred and 9 (0.08%) died. By comparison, of 5,898 cases detected by surveillance, 3,970 (67%) were treated by one or more of the trained groups, 3,464 (87%) with ORT. Only 12 (2%) cases had to be referred to hospital and, among all cases recorded, there were 23 deaths (0.38%).

Comparing the 5 zones, relatively more cases were detected and treated in the 3 zones where treatment was offered by 2 or more of the 3 trained groups. The proportion of cases treated by "untrained" groups, however, did not vary by zone, except in the comparison zone where it was lowest (17%). Patients were also most likely to receive only ORT in the comparison group (78%).

Although it would be best to train all family members, the author concluded traditional practitioners offer the next most robust alternative for introducing ORT on the community level. Because the public seeks their services, the author reasoned, the practitioners can provide ORT to a larger population than could trained family members, thereby reaching more diarrheal cases. The author therefore recommended that the Bangladesh national diarrheal diseases control program make use of traditional practitioners as an interim strategy for increasing ORT coverage.

Although the overall findings were impressive, they did not necessarily support the author's conclusions. Clearly, home treatment was preferred by a three-to-one margin and the average number of diarrheal cases treated by the practitioners did not measurably increase as a result of the intervention. Training the practitioners may have improved their case management techniques and may have had a promotional effect but it was the public demand for ORT which most increased ORT coverage.

Harland, P.S.E.G., et al., Composition of oral solutions prepared by Jamaican mothers for treatment of diarrhoea, *Lancet* 1:600-601, 1981.

219. Mata, L., Diarrhoeal diseases—How Costa Rica won, *WHO Forum*, 2 (1):141-145, 1981.

Major improvements in social welfare, water supply, and education were cited by the author as reasons why the diarrheal disease death rate in Costa Rica has fallen from about 400 per 100,000 population in 1930 to the present rate of less than 15 per 100,000.

However, he pointed out, there are still an estimated 200 diarrheal deaths annually in Costa Rica, occurring mostly in infants. In response, the Ministry of Health has embarked on an ambitious two-year program to train mothers to treat diarrhea with ORT using the WHO-recommended ORS formula.

An operational problem was identified when surveys revealed a scarcity of one-liter size containers (needed for mixing the standard-size UNICEF/WHO ORS packet. A smaller sized ORS packet was subsequently designed which contains the correct amount of salts for mixing in 8 oz. bottles which were found in over 98% of the homes. The health authorities estimated each episode requires 6 of the smaller packets. Several million ORS packets, along with clear, written instructions on their use, have been distributed to households *a priori* by the social security services.

Unfortunately, the author pointed out, breastfeeding has declined in Costa Rica in recent years. Nutrition surveys in 1975 and 1978 revealed 30% of newborns were not put to the breast at all and by 5 months of age, 61% of Costa Rican infants had been weaned. In contrast, in rural, mountainous areas 95% of infants are breastfed at 1 month of age, 84% at 3 months and 68% at 8 months. The diarrheal attack rate in these isolated rural children is far less than their urban and periurban counterparts: less than 1 episode per year *vis-à-vis* 2 per year in the primarily bottlefed children. The author attributed this difference to the antibodies and "anti-rotavirus factors" found in most colostrum and breastmilk specimens.

The total cost for the national ORT program will be approximately US$232,000. The program is expected to produce a minimum 50%

reduction in hospital admissions and consultations which will, in turn, result in an annual savings of US$1.7 million.

220. Mata, L., Epidemiologic perspective of diarrhoeal disease in Costa Rica and current efforts in control, prevention and research, *Rev Lat-amer Microbiol* 23:109-119, 1981.

In this wide-ranging article, the author presented a variety of data on diarrheal diseases in Costa Rica over the past 50 years (see preceding abstract).

Fairly reliable data on diarrheal diseases are available from about 1925 to the present, the author stated, and they clearly show a decrease in diarrheal mortality; by 1945, with social and economic reforms underway, it had fallen to about 200 per 100,000. The rate stagnated over the following 15 years, however, a period characterized by civil war, migration and high population growth. From 1964 to the present, the decline has been even more dramatic: from about 110 to only 12 per 100,000. The author felt that improved water supply, personal hygiene, sanitary facilities and rising per capita income (US$1690 in 1979) were some of the factors to which the decrease can be attributed. Infant mortality trends, observed the author, closely mirror those of diarrheal mortality.

Although data on diarrheal diseases morbidity are limited, acute diarrheal diseases remain an important cause of hospital admissions in Costa Rica today. Their etiologic and epidemiologic characteristics have been well described, with highly seasonal patterns correlating closely with rotavirus and enterotoxigenic *E. coli* peak prevalences.

The author described important research and cited the now widespread use of ORT as the chief reason the diarrheal case-fatality rate has decreased at the National Children's Hospital in San Jose from 3.0 deaths per 1,000 cases in 1977 to only 0.5 per 1,000 in 1979, an 83% reduction.

An estimated 150 diarrheal deaths, mostly in infants, still occur each year in Costa Rica. The author described the national ORT program, which seeks to eliminate these deaths by introducing ORT in the home.

The home-based strategy was adopted after research at the Children's Hospital demonstrated mothers could easily master ORT, even without medical supervision. When it was found one-liter size containers were not common in Costa Rica homes but that 8-ounce bottles were, the national Social Security System bought and distributed millions of 250-ml-size ORS packets nationwide. The packets are accompanied by instructional materials. A "communications scheme for the educational component", aimed at professionals, has been developed and is also being implemented by the national ORT program.

In 1977, hospital consultations and admissions for diarrheal diseases cost the government at least US$3.5 million, wrote the author. By placing ORT in the hands of mothers, the program is expected to reduce diarrheal hospitalizations by 80% and hospital consultations by 50% at an annual cost of US$232,000 (1977 dollars). Besides reducing mortality and benefitting overall nutritional status, he estimated the program could therefore save the country as much as US$1,958,000 per year.

In addition to continuing research in diarrheal diseases, nationwide efforts are underway to promote breastfeeding. Surveys in 1975 and 1978 found that about 30% of Costa Rican newborns were not put to breast at all and that, by one month of age, 24% of rural infants had been weaned into infant formula schedules. The author reported preliminary results from a careful cohort study in a rural area which showed that encouraging mother-infant stimulation after delivery and promotion of breastfeeding by hospital staff have apparently led to dramatic improvements. Ninety-five percent of infants were exclusively breastfed at age one month, 84% at 3 months and 68% were being at least partially breastfed at 8 months. During their first six months of life, the author noted, these infants experienced far less diarrhea than had been expected.

Ashley, D.A.E., et al., Oral rehydration therapy in the management of acute gastroen-

teritis in children in Jamaica, In: Holmes F, et al, (eds.): *Acute Enteric Infections in Children. New Prospects for Treatment and Prevention*, Amsterdam, Elsevier/North-Holland Biomedical Press, 389-394, 1981.

Anonymous, Manual for the planning and evaluation of national diarrhoeal diseases control programmes, (*WHO Unpublished Document*, WHO/CDD/SER/81.5, WHO Programme for the Control of Diarrhoeal Diseases, 20 Avenue Appia, 1211 Geneva 27, Switzerland) 1981.

221. Kumar, V., et al., The introduction of oral rehydration in a rural community in India, *Wld Hlth Forum* 2:364-366, 1981.

The authors described how ORT was made part of the health services in a rural area of India. Three-hundred-and-fifty community health workers serving a rural community development "block", consisting of 158 villages with a total population of about 112,000, were trained both in health education techniques and the use of ORT. Using locally prepared pamphlets, puppet shows and presentations at local festivals and village fairs, they then instructed mothers and school teachers on the correct use of ORT, the importance of continuing feeding during diarrheal episodes and how to prevent the diarrhea from recurring.

Adhering to the WHO-recommended ORS composition, ORS was locally prepared in one-kg. size polythene bags using carefully marked plastic measures. To prolong shelf life the sodium bicarbonate was packaged separately. From these, village-level volunteers later measured, mixed and packaged smaller, 12.5-gram doses of the ORS for dilution in 500 ml of water in the home. As before, the sodium bicarbonate was separated but packaged with the other 3 ingredients. Using this approach, the authors calculated, the cost of delivering ORT was approximately US$0.04 per liter. Up to 2,000 500-ml size ORS packets were required monthly for the entire block.

As a result of the program, case-fatality rates in the six villages tested were about 0.4% *vis-à-vis* 2% in villages where ORT had not yet been introduced. Additionally, medical referrals for acute diarrhea were "dramatically reduced".

Although not substantiated by discrete data, the authors further stated knowledge and attitudes of the rural mothers regarding diarrheal diseases had improved. Most had accepted ORT and were now continuing breastfeeding throughout diarrheal episodes whereas before the program the reverse had been the case. Similarly, a questionnaire showed "significantly increased" knowledge of the management of diarrheal diseases among 168 schoolteachers and 218 pupils. Repeated retraining of the community health workers on the use of ORT was judged important by the authors.

The authors concluded ORT was acceptable, affordable, and accessible to rural villagers in this "block". They attributed the program's success to: (1) the use of the existing health infrastructure; (2) the involvement of the community, (3) the use of appropriate technology, relying on local village volunteers to package and deliver ORS; (4) the repeated reorientation and retraining of health workers, and (5) the use of folk media and other culture-specific educational materials to spread the word about ORT.

222. Morrison, P. S., et al., How is gastroenteritis treated? *Brit Med J* 283:1300, 1981.

To verify the findings of a recent survey, which had shown that improvements were needed in the diarrheal case management techniques used by British physicians, the authors reviewed the case histories of 181 children admitted with acute diarrhea to a London hospital over an eight-month period.

Representing about 15% of all pediatric admissions, virtually all the 181 children had been initially seen and later referred to hospital by general practice physicians. Once admitted, patients were given ORT (IV therapy if severely dehydrated) and no drugs.

Eighty-one (45%) of the children were less than one year of age. Prior to admission, 90 (50%) had been given drugs—54 antidiarrheal agents, 41 antiemetics and 39 antibiotics. The

parents of 14 of the children said they had been advised to stop solid foods and give "fluids" only. None of the children had been prescribed a glucose-electrolyte solution for oral rehydration.

Once hospitalized, IV therapy was needed for 30 (17%) cases; of these, 19 (63%) had been previously given one or more drugs at home. Fifty (29%) children were well enough to be discharged after 24 hours; of these, 24 had been given drugs at home. Eighty-three percent of the children "quickly" recovered without sequelae using ORT alone. Although pathogenic bacteria were isolated from the feces of only seven patients, 39 (22%) had been prescribed antibiotics. One 22-month old child with severe dehydration died a few hours after admission. This child had been ill for three days prior to admission and had been treated with Lomotil (diphenoxylate and atropine). No pathogenic bacteria were isolated from either the feces or blood cultures.

The authors pointed out that antidiarrheal drugs such as Lomotil and Kaolin, which had been given to 30% of the children, served no purpose and were potentially harmful. They also advised against using either antiemetics (given to 23%) or antibiotics (22%), particularly in Great Britain where most diarrheal cases are viral in origin. Proper diarrheal case management, the authors stressed, consists solely of replacement and maintenance of fluid and electrolytes. The popular demand for some kind of "medicine" can be met by prescribing ORS, they felt.

The authors concurred with the findings of the previous survey and noted there was room for improvement in the way British physicians treat acute diarrheal diseases.

223. Cutting, W.A.M., et al., A worldwide survey on the treatment of diarrhoeal disease by oral rehydration in 1979, *Ann Trop Pediatr* 1, 199–208, 1981.

To determine prevailing treatment patterns for acute diarrhea, the authors conducted a worldwide survey of health workers in 1979.

Five-hundred eighty-six health workers in 81 countries were surveyed (the actual survey questionnaire was annexed). Nearly all were on the mailing lists of, or had been postgraduate students at, the Ross Institute of the London School of Hygiene and Tropical Medicine or the Tropical Child Health Unit of the Institute of Child Health, also in London.

A total of 338 (58%) responded. Of these responses, 283 (84%) were analyzed either manually or by computer. Of those analyzed, 50% were from Africa, 36% from Asia, 7% from Europe, Austrialia or North America and the rest from Latin America and the Middle East. Forty-six percent worked for voluntary agencies, 40% for governments and 4% in private practice.

When asked to describe local beliefs regarding the causes of diarrhea, the respondees most frequently answered diet or "bad food" (30%), "teething and teeth" (15%), infection (12%), breastmilk (10%), "evil eye" (8%), weather (3%) and "God's will" (2%).

To assess the popularity of different treatment methods, the authors devised a simple scoring system. The methods judged most common were given 4 points, the next most common 3 points, and so on. The scores were totalled, compared to the maximum score attainable and expressed as a percentage. Respondees were asked to describe treatment modalities at the time of the survey (1979) as well as 3 years previous.

The authors found ORT had been widely used (50%) in 1976 and that its use had increased (to 74%) by 1979. The comparative scores for intravenous therapy were 46% for 1976 and 58% in 1979. Kaolin received 36% of the maximum score in 1976 but declined to 19% in 1979. The use of sulfonamides and antispasmodics also had declined over the 3 years (from 31% to 18% and from 13% to 5%, respectively) but that of antibiotics remained about the same (28% in 1976, 27% in 1979).

When asked what ORS preparations they used, there were 447 responses from 272 respondees. Homemade mixtures were most widely used (43%), followed by packets (31%)

and ready-made solutions (23%). Homemade ORS mixtures were prepared using spoons in 27% of the services responding and by hand measurement in 16%. Of the 31% of services using packets, less than one-third (10%) used WHO/UNICEF packets, 11% used other commercial and 11% used locally-made ORS packets.

Twenty-four percent of services used the "complete" WHO-recommended ORS formula, 41% used simpler (SSS) and 24% other specific or more complex ORS compositions (e.g., Darrow's or Ringer solutions).

In reply to the question "What difficulties have you had using ORT?", 30% responded none, 15% reported patient or parents' rejection, 13% identified irregular ORS supply and 5% excessive cost. Asked to identify any medical difficulties encountered with ORT, 23% reported none, 28% complained patients would not ingest sufficient fluid, and 22% identified vomiting. Other complications identified were failure to respond (8%) and swelling (6%).

Answers to a question about what instructions on ORT are given to patients were ambiguous. In 24%, the matter was left to those who actually gave out the ORS. Some form of "standardized verbal instructions" to teach patients ORT was used in 47% of services. Only about 13% used any written leaflets and few of these (6%) were illustrated.

The authors concluded that ORT had achieved fairly wide acceptance but felt more health education, greater ORS availability and more systematic training of health workers were needed before all understand that rehydration is more important than medication.

Anonymous, Oral therapy for acute diarrhea, (Editorial) *Lancet* 2:615-617, 1981.

Mahalanabis, D., et al., Oral rehydration therapy—Recent advances, *Wrld Hlth Forum*, 2(2):245-249, 1981.

224. Snyder, J., et al., Home-administered oral therapy for diarrhoea: A laboratory study of safety and efficacy, *Trans Roy Soc Trop Med Hyg* 76(3):329-33, 1982.

To determine whether home preparation and use of either prepackaged ORS or simple salt/sugar (SSS) solutions leads to electrolyte abnormalities such as hypernatremia, the authors conducted a one-year controlled trial in rural Matlab, Bangladesh.

A study population of about 40,000 was divided into one comparison and two treatment groups. In the treatment groups, one woman from each extended family unit was selected and trained to store and prepare ORT for her extended family (1-20 nuclear families). In one treatment group, the women were given one-liter size packets containing WHO-recommended ORS, and one-liter bottles for measurement. In the other treatment group, the women were given one-liter bottles, supplies of locally available, unrefined sugar (gur) and salt (labon) and double-ended plastic measuring spoons with which to prepare a SSS solution similar in composition to the packet solution. In both groups, all fluid intake estimates were based on the "seer", a local measure of just under one liter. In the third comparison group no ORT was made available and treatment was by local customs.

Surveillance was maintained and supervision and repeated training were provided to treatment group mothers through bimonthly home visits by female village workers (FVWs), one of whom was assigned to each village (approximately 1,000 population each). In the comparison group, the FVWs carried out only surveillance duties.

As part of another, ongoing study, field assistants (FA's) visited each home in the ORT villages every 2 months. For each diarrheal episode they encountered that had begin within 48 hours before such a visit, the FAs completed a series of questionnaires (Days 1, 3, 7), obtained stool swabs (Day 1) and a capillary blood specimen (Day 3) and followed up the cases.

At the nearly Matlab treatment center all cases presenting with acute diarrhea from any of the three study populations were interviewed and similar specimens were collected.

All blood specimens were centrifuged on the day collected and the sera examined for sodium and potassium by flame photometer. Based on Nelson's *Textbook of Pediatrics*, hypernatremia was defined as Na^+ concentration greater than or equal to 150mEq/l; hyponatremia as Na^+ less than or equal to 130 mEq/l and hypokalemia as K^+ less than 3.0 mEq/l.

In the clinic the criterion for appropriate fluid intake was set at 75% or more of calculated daily requirements. In the villages, it was one-half seer (about 500c) per day for children below two years of age and one seer per day for older persons.

Completed questionnaires and serum electrolyte results were obtained from 81 persons who had received ORT in packet villages and from 75 from labon-gur villages. Mild dehydration (less than 5% dehydration) was found in 153 (98.1%) of these. Five persons (6%) from packet villages and 3 (4%) from lobon-gur villages had electrolyte abnormalities but none of these had ingested appropriate volumes of the oral solutions. The highest serum sodium value was 167 mEq/l, the lowest was 115 mEq/l. The lowest serum potassium value was 2.9 mEq/l. No clinical indications of electrolyte abnormality were noted. The median volume of oral solution ingested was one-third seer per day for each of the first 3 days. There were no differences in mean electrolyte values for those taking appropriate as opposed to less than appropriate volumes.

A total of 489 persons from the 3 study areas were admitted to the treatment center with acute diarrhea over the one-year period. Four hundred-ten (83.9%) of these had mild dehydration. Although 45 (9.2%) had electrolyte abnormalities (including 17 with hypernatremia, 10 with hyponatremia and 18 with hypokalemia) no clinical signs of these electrolyte abnormalities were noted. Seventeen (39%) cases with electrolyte imbalances came from comparison group villages where no ORT was available.

There were no correlations between electrolyte abnormalities and degree of dehydration or amount or type of oral fluid previously ingested. Only about 25% of persons from ORT villages had taken appropriate volumes of fluid. No abnormalities were found in ORT-village patients who had ingested appropriate volumes of either fluid whereas those who had not were significantly more likely to present with hyponatremia or hypokalemia, (p less than 0.015).

The authors concluded that ORT can be safely prepared and administered in the home but pointed out the close supervision and frequent instruction given to the study subjects, the unexpected presence of potassium and bicarbonate in the local lobon-gur mixture, the small sample sizes as well as other intervening factors may have limited the extent to which their findings can be generalized.

Snyder, J. D., From pedialyte to popsicles: A look at oral rehydration therapy used in the United States and Canada, *Am J Clin Nut* 35:157-161, 1982.

225. Chowdhury, A.M.R., The retention of knowledge about home-made oral rehydration solution: A survey in rural Bangladesh, *Sylhet Med J* 6(5):11-15, 1982.

The author described a preliminary field evaluation of a nationwide ORT program, sponsored by a private voluntary organization called the Bangladesh Rural Advancement Committee (BRAC), which promoted home preparation of ORS using the "pinch-and-scoop" method. The program, which reached about 200,000 households its first year, relies on teams of female oral replacement workers (ORWs) who instruct village mothers on diarrhea and ORT using an educational package entitled the "Ten Points to Remember" (see abstract No. 215). Monitors routinely visit randomly sampled households to observe ORT mixing and assess the effectiveness of the teaching. ORW salaries are pegged to the proportion of mothers in each area who have mastered the Ten Points.

To verify the accuracy with which the mothers actually prepared the home ORT solutions

the BRAC research and evaluation division carried out a special sample household survey.

Two 250-household samples were randomly chosen. The first consisted of those that had been visited by an ORW three months prior to the survey. The second sample included homes that had been visited six months before. The field interviewers collected samples of home-made simple salt-sugar (SSS) solutions which were prepared by the mothers using a three-finger pinch of salt (lobon), four-finger scoop of sugar (gur) and one-half seer (a local measure of approximately 467cc volume) of water. The 500 samples were analyzed for sodium concentration at the ICDDR,B laboratory in Dacca.

The survey results showed the sodium concentrations in 89.2% and 89.6% of the solutions in the three- and six-month groups, respectively, were within the "safe and effective", (30-99 mmol/l) range. Mean sodium concentrations were 65.4 mmol/l for the three-month group, and 71.2 mmol/l for the six-month group, a significant difference (p less than 0.01). Of all 500 samples, 8 (1.6%) had sodium concentrations below 30 mmol/l while those of 43 (8.6%) exceeded 100 mmol/l and in 14 (2.8%) were over 120 mmol/l.

Although the range of sodium concentrations found through prior routine surveillance in the same area was nearly identical, the mean surveillance sodium values was relatively lower than that shown by the survey (mean 52.9 mmol/l vs. 68.9; 8.9% vs. 1.6% less than 30 mmol/l; 1.3% vs. 8.6% over 100 mmol/l.).

The fact that nearly 90% of home-prepared SSS solutions were in the safe and effective range, concluded the author, indicated the teaching methodology had been effective. Knowledge had been retained equally well by the two survey groups and compared favorably with those who had been checked by routine surveillance only 15 days after learning the Ten Points.

For several methodological reasons, these findings must be interpreted cautiously. Strictly speaking, there was no comparison group. Subjects in both the routine surveillance and the two survey groups were independently selected, yielding cross-sectional rather than longitudinal observations. Secondly, there were, in fact, significant differences in mean sodium concentrations which appeared to increase over time. Such a trend, however, cannot be validly shown because routine surveillance and survey instruments were not standardized.

226. Conteh, S., et al., A comparison of bottle tops, teaspoons and WHO glucose-electrolyte packets for home made oral rehydration solutions in the Gambia, *Trans Roy Soc Trop Med Hyg* 76(6):783-785, 1982.

The authors performed an uncontrolled field trial to determine the degree of accuracy with which periurban Gambian women could prepare home ORT solutions.

Fifty-eight mothers who brought their children to hospital with acute diarrhea were selected for study. Non-formally trained health auxiliaries instructed the mothers how to prepare ORT solutions using 3 different techniques based on: 1) WHO-recommended, one-liter size ORS packets and local cooking oil bottles of one liter volume; 2) teaspoons, salt, sugar and locally available soft-drink bottles (300 ml volume); and 3) bottle caps, salt, sugar and the same 300 ml soft drink bottles. After instruction, the mothers prepared the solutions in their homes using all 3 techniques. Samples were collected in the homes the following day, frozen and later tested for osmolality (using an osmometer, Wescor, Inc.) and sodium content (flame photometer, Instrumentation Laboratories, Ltd.).

Results showed 51 of 58 (88%) of the ORS packet samples had "safe" sodium levels (80-120 mmol/l). Among samples prepared with teaspoons, 29 of 58 (50%) were in the safe range but 17% had Na^+ levels over 120 mmol/l. Sodium levels in 58 bottle-cap samples were all less than 60 mmol/l.

With respect to osmolality, the concentrations of 51 of 58 (88%) ORS-packet samples were in the acceptable range of 250-350

mOsmol/kg. Of 58 teaspoon samples, however, only 28 (48%) were in the acceptable range and 24% were hyperosmolar. Osmolalities in all 58 bottle-cap samples were less than 250 mOsmol/kg.

Observing that ORS packet delivery is problematic and that both teaspoons and standard one-liter volumes are largely unavailable in the predominantly rural areas, the authors concluded use of the bottle and cap of a widely available soft drink provides the most feasible approach to disseminating ORT technology in the Gambia. They cautioned, however, that simple trials such as this one must be carried out in each area before any one ORT technique can be endorsed.

227. Rahaman, M. M., et al., A diarrhoea clinic in rural Bangladesh: Influence of distance, age and sex on attendance and diarrhoeal mortality, *Am J Pub Hlth*, 72(10): 1124-1128, 1982.

To identify factors which influence attendance rates, the authors monitored the catchment population of a diarrhea clinic in rural Bangadesh during 1977-1978.

A census of the approximately 450,000 population had been conducted in 1975 and each household had then been issued a card with a unique identifying number. Whenever any family members suffered diarrhea, they were instructed to present this card at the clinic. Treatment at the clinic was given free of charge using both ORT and IV therapy. The authors monitored clinic records and weekly home visits were carried out by local health workers with trained assistants in order to determine diarrheal attack rates in the communities within a six-mile radius of the clinic. If acutely ill patients were encountered during the home visits, they were advised to seek treatment at the clinic. Any reported deaths were investigated.

Over the two years, between 60-70% of detected diarrheal cases came to the clinic for treatment. Oral rehydration alone was successful in over 90% of *Shigella* and watery diarrhea and in over 50% of acute cholera cases. For both sexes, over 90% of all detected cases within a one-mile radius sought treatment at the clinic. At two miles radius, however, the attendance fell to 70% for males and 40% for females. On the average, the greater the distance to the clinic, the more severe was the degree of dehydration and larger the amount of intravenous fluid needed to treat each case.

A total of 111 diarrheal deaths were detected over the study period. Mortality was inversely related to clinic attendance. Beyond the two-mile radius, it was 2.5 times higher than among those living nearer to the clinic.

The authors concluded various cultural factors conditioned utilization patterns. It is not permissible, for instance, for young Bangladeshi women to travel freely. The authors, accordingly, questioned the feasibility of any facility-based ORT program in Bangladesh, recommending instead home- or neighborhood-based distribution strategies.

Because many intervening variables were not assessed (e.g., income, type of housing, water source, etc.) the data must be interpreted with caution.

228. Stoll, B., et al., Surveillance of patients attending a diarrhoeal disease hospital in Bangladesh. *Br Med J*, 285:1185-1188, 1982.

The authors studied the records of 3,550 patients presenting with acute diarrhea over a one-year period to the main ICDDR,B hospital in Dacca, Bangladesh.

Sixty-two percent of patients were under 5 years of age. Malnutrition had been found in 34% of those 1-4 years old and in 20% below 1 year of age. Clinical histories showed 58% of all patients had had an acute illness of less than 4 days duration but 21% had been ill for more than a week before presenting to hospital. Overall, enterogenic *E. coli* (20%), rotavirus (19%), *C. jejuni* (14%), *Shigella* (12%), *V. cholera* (6%), *E. histolytica (6%) and G. lamblia* (6%) had been found to be the most common pathogens. Although age-specific infection rates did not vary for enterotoxigenic *E. coli*, rotavirus (27%) and *C. jejuni* (21%) were more frequent

in children below 5 years of age while *Shigella*, *V. cholera* and *E. histolytica* were more common in older ages.

Of those below 5 years, 15.6% had been moderately to severely dehydrated; ORT had been given to 65% of them while 28% had received intravenous therapy. Only 5% of those under 5 years had to be admitted to hospital. Excluding cholera cases in the 1-4 year olds, which tended to be more severely dehydrated, ORT was equally successful in children below 5 years of age, regardless of etiology.

Pointing out that 33% of all patients had received IV therapy, even though only 20% had been moderately to severely dehydrated, the authors felt IV therapy had been overused, perhaps because in this hospital ORT required more staff time to deliver. Nevertheless, the authors concluded ORT was more advantageous than IV therapy in that it was less expensive and provided other, longer-term benefits such as educating mothers on its use in the home.

This study verified earlier findings that ORT is equally successful in all ages regardless of etiology.

Posada, G., et al., Causas de reingreso en un servicio de rehidratación oral (Causes of readmission to an oral rehydration ward), *Bol Med Hosp Infant Mex* 39(2):93-98, 1982.

229. Tekce, B., Oral fluid therapy and diarrhoeal mortality among children in twelve Egyptian villages, (52 pages) *Unpublished report presented at the "Workshop on family planning and health components in community based distribution projects,"* Charlottesville, Virginia, January 12-14, 1982.

The author reported the results of an operational trial to determine the impacts of a community-based ORS distribution program on diarrheal mortality in rural Menoufia, Egypt.

Local female health workers visited a total of 45,000 mothers in 105 villages over the first three months of the trial, distributing WHO-recommended ORS packets, instructing the mothers how to prepare and administer ORT, advising when and where to seek medical assistance and how diarrhea can be prevented. Of the 105 villages, one set of six villages containing about 50,000 inhabitants, was chosen as the treatment area. A similar six-village area, where ORS had not been distributed, served as the control. Births and deaths were recorded through annual surveys. All villages were surveyed twice between March, 1979 and February, 1981.

Doctors and nurses working in government health facilities in and near the study area were given special ORT training and stockpiles of ORS packets were maintained.

The two sets of villages were similar with respect to demographic, socioeconomic and health indicators. To measure mortality impacts, all recorded deaths were investigated by teams of medical interns which, after household interviews, assigned probable causes of death *ex post facto*.

After 10 months no significant differences were found in age-specific diarrheal mortality rates, although the authors had hypothesized the introduction of ORT would reduce diarrheal mortality by one third or more. Moreover, the surveys and subsequent investigations determined that death rates for all causes were equivalent between the treatment and control areas and that diarrheal diseases accounted directly or indirectly for about 50% of all deaths in children below five years of age.

Infant feeding and weaning practices, proximity to health facilities and treatment sought were not significantly different among fatal cases from either treatment or control areas. Over 90% of all fatal cases had received some kind of treatment and over 35% had been hospitalized at least once during the fatal episode. About 30% of fatal cases in both treatment and control areas had been given IV therapy. About 35% of all fatal cases had received ORT; the proportion did not significantly vary between the groups. However, ORT had been given the first day of the episode in only 60% of these fatal cases. Almost none of the fatal cases had been given home ORT.

The authors concluded neither the house-

hold based strategy for introducing ORT nor the ORT training given to health providers had been effective. Single-entry interventions are not likely to produce behavioral change, they reasoned. Reinforcement over time through repeated home visits may be necessary. The fact that anti-diarrheal medicines had been given to at least 85% of fatal cases and that private physicians were first consulted in two-thirds of these cases indicated to the authors a different approach to training health care providers was needed.

From a methodological viewpoint, several factors may have compromised the validity of the study. These included complete reliance on presumptive, retrospective diagnosis of deaths for impact evaluation; failure to assess behavioral factors among the entire population rather than just for households where fatal cases occurred; and the possibility that, due to selection factors, the families of fatal cases may not have been representative of the population at large.

Booth, I. W., et al., Oral rehydration therapy: An issue of growing controversy, *J Trop Pediatr* 28, 116–123, 1982.

Anonymous, Manual for the planning and evaluation of national diarrhoeal diseases control programmes, (*WHO Unpublished Document*, WHO/CDD/SER/81.5, WHO Programme for the Control of Diarrhoeal Diseases, 20 Avenue Appia, 1211 Geneva 27, Switzerland) 1981.

Chapter 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. spoon 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, H. N., 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).

81. Jelliffe, D., Diarrhoea in childhood, In: *Medical Care in Developing Countries*, Maherere, 1966.

This essay 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 ORS 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.

82. Jelliffe, D. B., Rehydration centers in developing countries, (Editorial), *J Trop Ped* 15:1-3, 1969.

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.

Nalin, D. R., et al., Reduction of maintenance intravenous fluid needs in cholera by means of an oral therapeutic solution, *J Pakistan Med Assoc* 19:373-379, 1969 (see No. 69).

Nalin, D. R., et al., Oral therapy for cholera (letter), *Ann Intern Med* 72:959, 1970 (see No. 20).

Pierce, N. F., et al., Oral electrolytes in cholera (letter), *Ann Intern Med* 72:959, 1979 (see No. 20).

Mahalanabis, D., et al., Water and electrolyte losses due to cholera in infants and small children: A recovery balance study, *Pediatrics* 45:374-385, 1979 (see No. 24).

83. Mahalanabis, D., et al., Intraperitoneal fluid therapy in cholera and non-cholera diarrhoea, *Bull World Health Orgn* 42:837-846, 1970.

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

84. Nalin, D. R., et al., Kaolin and cholera, *J Pak Med Ass* 20:177-82, 1970.

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.

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

Nalin, D. R., Oral or nasogastric maintenance therapy for diarrhoea of unknown aetiology resembling cholera, *Trans Roy Soc Trop Med Hyg* 64:769-771, 1970 (see No. 47).

Sack, R. B., et al., The use of oral replacement solutions in the treatment of cholera and other severe diarrhoeal disorders, *Bull WHO* 43:351-360, 1970 (see No. 26).

85. Biddulph, J., Standardized management of diarrhoea in young children, *Paediatr Indones* 11:37-46, 1971.

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 breastfeeding, and by the

A bari mother in rural Bangladesh preparing "labon-gur" ORT solution. (Photo: WHO).

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

Nalin, D. R., et al., The optimal oral therapy formula for cholera and cholera-like diarrheas, In: *Proceedings of the Sixth Annual International Epidemiologic Association Scientific Meeting*, Belgrade, Savremena Administracya, pp 1048-1057, 1971 (see No. 49).

86. Church, M. A., Fluids for the sick child. A method for teaching mothers, *Trop Doc* 2:119-21, 1972.

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 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.

Hirschhorn, N., et al., Oral fluid therapy of Apache children with acute infectious diarrhoea, *Lancet* 2:15-18, 1972 (see No. 28).

87. Hirschhorn, N., et al., Oral rehydration of children with acute diarrhoea, (letter), *Lancet* 2:494, 1972.

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) concentrations (±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.

88. Taitz, L. Z., et al., High calorie/osmolar feeding and hypertonic dehydration, *Arch Dis Child* 47:257-260, 1972.

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 breastfed 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 breastfed 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.

Hirschhorn, N., et al., Ad libitum oral glucose-electrolyte therapy for acute diarrhea in Apache children, *J Pediatr* 83:562-571, 1973 (see No. 50).

Mahalanabis, D., et al., Oral fluid therapy of cholera among Bangladeshi refugees, *Johns Hopkins Med J* 132:197-205, 1973 (see No. 71).

Mazumdar, H., et al., Oral rehydration in gastroenteritis in children, *Indian Pediatr* 10:315-322, 1973 (see No. 30).

89. Rohde, J. E., Rehydration in the field, *Paediatr Indones* 14:148-152, 1974.

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.

90. Rohde, J. E., Training of paramedical personnel. Understanding priorities in treatment of diarrhea, *Paediatr Indones* 14:153-158, 1974.

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.

91. Aballi, A. J., Single solution not ideal for oral therapy of diarrhoea, (letter), *Lancet* 2:513-14, 1975.

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 all infants under all conditions. Studies in many different populations of children are needed to assess the efficacy of oral rehydration, the author concluded.

92. Baral, M. R., Experience with 100 diarrhoea cases treated at Narayani Zonal Hospital Rehydration Therapy Center, Birgunj, *J Nep Med Ass* 13:77-87, 1975.

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.

De, S., et al., Oral fluid therapy for cholera and non-choleraic diarrhoeas in children, *J Com Dis* 7:124-128, 1975 (see No. 32).

Editorial, Feeding sick babies, *Br Med J* 4:539, 1975 (see No. 51).

Hirschhorn, N., et al., Oral glucose-electrolyte therapy for diarrhea: A means to maintain or improve nutrition? *Am J Clin Nutr* 28:189-192, 1975 (see No. 74).

Editorial, Oral glucose-electrolyte therapy for acute diarrhea, *Lancet* 1:79-80, 1975 (see No. 34).

93. Mahalanabis, D., et al., Present and future of oral rehydration therapy for diarrhoeal diseases with special reference to health care delivery, *Ind J Prev Soc Med* 6:286-290, 1975.

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 these techniques.

94. Anonymous, Treatment and prevention of dehydration in diarrhoeal diseases: a guide for use at the primary level, *Non-serial WHO publication, 1976.*

Simple guidelines for treatment and prevention of diarrheal 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.

Bart, K. J., et al., Single solution for oral therapy of diarrhoea (letter), *Lancet* 2:633-634, 1976 (see No. 54).

95. Brotowasisto, et al., Rehydration Programme in Indonesia, *Proceedings of the 5th Asian Pacific Congress of Gastroenterology*, Singapore, 488-490, 1976.

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.

96. Hatcher, G., Diarrhoea, *Brit Med J* 1:571-3, 1976.

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.

As an editorial note, 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.

97. Moran, M., Oral rehydration therapy in home and hospital: experience in rural Nigeria, *Ped Nurs* Sept/Oct, 32-33, 1976.

A missionary nurse working in a rural Nigerian 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 breastmilk, 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.

Naik, N. V., et al., Oral rehydration in acute gastro-enteritis in young children, *Ind Pediatr* 13:127-133, 1976 (see No. 55).

Nalin, D. R., et al., Sodium content in oral therapy for diarrhoea (letter), *Lancet* 2:957, 1976 (see No. 56).

Rahilly, P. M., et al., Clinical comparison between glucose and sucrose additions to a basic electrolyte mixture in the out-patient management of acute gastroenteritis in children, *Arch Dis Child* 51:152-154, 1975 (see No. 57).

98. Rohde, J. E., et al., Taking science where the diarrhoea is, *CIBA Foundation Symposium* 42:339-358, 1976.

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.

99. Sedgwick, J. R., et al., Oral rehydration in rural India, (letter), *Lancet* 1:1194-1195, 1976.

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, averaged 120 mmol/l (versus the 90 mmol/l expected from the packet) with a range of 39 to 510 mmol/l. A mean of 105 mmol/l and a range of 61 to 163 mmol/l were found in the 12 samples produced under supervision.

To reduce the chance of producing hypertonic solutions, the authors suggested designing packets based on the volume of the smallest-size local container. Also, by using smaller volumes, 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.

100. Ware, S., Hypernatremia and glucose water, (letter) *Lancet* 1:494, 1976.

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.

101. Bollag, U., Cup and spoon rehydration of children with acute diarrhea, *J Trop Ped Env Child Hlth* 23:268-270, 1977.

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

Sixteen children (ages 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.

102. Chakraborty, B., Management of infants and children with acute diarrhoea, *J Ind Med Assn* 69:280-283, 1977.

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 after 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.

Chatterjee, A., et al., Evaluation of sucrose/electrolyte solution for oral rehydration in acute infantile diarrhoea, *Lancet* 1:1333-1335, 1977 (see No. 58).

103. Cutting, W.A.M., Rehydration solutions and domestic measurements, (letter) *Lancet* 2:663-64, 1977.

The reliability of the pinch technique for salt measurement was tested using 4 groups of people in 3 countries.

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 can be recommended, they must be carefully tested under local conditions.

104. Gracey, M., et al., ROSE system for treatment of cholera dehydration, (letter), *Brit Med J* 1:839-840, 1977.

This letter reported the success of a simultaneously-administered IV and oral rehydration program in severely dehydrated, hospitalized Indonesian children (ROSE: *R*ehydration, *O*ral, *S*imultaneous IV, and *E*ducation 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, HCO_3^- 30, K^+ 15, and glucose 120). Breastfed children continued breastfeedings 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 $NaHCO_3$ 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.

International Study Group, A positive effect on the nutrition of Philippine children of an oral glucose-electrolyte solution given at home for the treatment of diarrhoea. Report of a field trial by and international study group, *Bull WHO* 55:87-94, 1977 (see No. 75).

105. Jere, A., A little radio goes a long way-...sometimes, In: Shack, K., (ed.): *Teaching nutrition in developing countries*, Meals for Millions Foundation, Santa Monica, California, 87-96, 1977.

The author discussed the use of radio to publicize public health programs and the possible pitfalls in various nutrition education campaigns. For example, radio programs produced at the capital by 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, M. S., et al., Oral rehydration treatment benefits Lao children with diarrhoea, *WHO Chron* 31:421-422, 1977 (see No. 35).

106. Kielmann, A. A., et al., Home treatment of childhood diarrhea in Punjab Village, *J Trop Ped Env Child Hlth* 23:197-201, 1977.

Although effective oral rehydration treatment programs have frequently been carried out in institutional settings, the authors noted that relatively few reports have come from community-based programs. A discussion of the problems in instituting a village-based oral rehydration program in 13 rural Indian villages was presented. Most children were treated with a homemade solution using 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.

107. Nichols, B. L., et al., A critique of oral therapy of dehydration due to diarrheal syndromes, *Am J Clin Nutr* 30:1457-72, 1977.

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 losses 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.

108. Hirschhorn, N., Treatment of diarrheal dehydration, (letter), *Am J Clin Nutr* 31:1967-1968, 1978.

This letter commented on practical, conceptual, physiological, and historical "fallacies" in the review article by Nichols and Soriano (see preceding abstract). 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.

109. Nichols, B. L., Reply to letter by Hirschhorn, (letter), *Am J Clin Nutr* 31:1969-1970, 1978.

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 in developing countries support Hirschhorn's recommendation that a 90/mEq/l sodium solution was used. Whether such a solution would be efficacious in treating children in developed countries has not been determined.

Pal, S. C., Promotion of oral rehydration therapy in India, *WHO Chron* 31:470-471, 1977 (see No. 76).

Palmer, D. L., et al., Comparison of sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrheas, *N Engl J Med* 297:1107-110, 1977 (see No. 59).

Field, M., New strategies for treating watery diarrhea, (Editorial), *N Engl J Med* 297:1121-1122, 1977 (see No. 60).

Sandle, G. I., et al., Oral therapy in cholera (letter), *N Engl J Med* 298:797-798, 1978 (see No. 61).

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

110. Rohde, J. E., et al., Rehydration is everybody's business, (Editorial), *J Trop Ped Env Child Hlth* 23:109-110, 1977.

The efficacy of oral rehydration in the treatment of acute diarrheal disease in children was clearly described, 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 method of health care delivery the hard-sell techniques of private industry must be copied with doctors taking the lead in the campaign.

111. Rohde, J. E., et al., Therapy begins at home: management of acute diarrhea in the developing world, *Proc Int Cong of Ped* (New Delhi, 1977), pp 809-819, 1977.

Diarrhea is a major public health problem, causing an estimated 5 to 18 million child deaths in 1976 alone. 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 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 one-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, this impact could be even greater, felt the authors. Maternal participation is indispensable to the success of the strategies outlined above.

112. Anonymous, Control of diarrhoeal diseases: WHO's programme takes shape, *WHO Chron* 32:369-372, 1978.

This report included a brief review of the epidemiology and public health importance of diarrheal diseases 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 approach of 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.

113. Fortin, J., et al., Dehydration scoring system for infants, *J Trop Pediatr Environ Child Hlth* 24.110–114, 1978.

The authors described a scoring system for grading the 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 children admitted for diarrheal dehydration were undernourished. Outpatients seen at the hospital were often dehydrated while those seen at the MCH center rarely were. Many children with low dehydration scores were admitted to hospitals because of malnutrition, as evidenced by skinfold.

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 rescoring 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 case-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 was used for summer diarrhea, the authors felt the criteria used are independent of etiology and can be used in other circumstances in which dehydration might result, such as diabetes, hyperpyrexia, and "salt-losing" syndromes.

114. Hendrata, L., Spoons for making glucose-salt solution, *Lancet* 1:612, 1978.

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. The 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 of 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 pro-

vider. Studies to determine the accuracy of homemade solutions remain to be done.

Parenthetically, this study utilized a more "culturally available" volume for dilution than the standard one-liter. Such differences in local measures may make worldwide standardization difficult.

115. Hirschhorn, N., Diarrhoeal control: opportunities and constraints as illustrated by development of an oral therapy programme, *WHO unpublished manuscript*, DDC/AGPD/15, 1978.

Alternatives for composition, production, distribution, preparation, and use of oral rehydration solutions were described in this review article. Although many questions remain unanswered, the author felt we should "get on" with utilizing oral rehydration therapy.

116. King, M., et al., *Primary child care—A manual for health workers*, Oxford University Press, Oxford, 1978.

This book included a comprehensive, well-written and concise chapter on diarrhea. Diarrhea was clearly defined and a discussion of its various etiologies (cholera, giardiasis, dysentery, etc.) and specific clinical aspects was included. Breastfeeding throughout the diarrheal episode was strongly encouraged. The authors urged feeding be continued throughout the diarrheal episode because the child has a better chance of maintaining his nutritional state. Clinical signs of dehydration and criteria for determining when to use oral versus intravenous rehydration were reviewed. The section on rehydration covered intravenous and intraperitoneal rehydration as well as 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.

117. McCord, C., et al., A successful programme for medical auxiliaries treating childhood diarrhea and pneumonia, *Trop Doc* 8: 220–225, 1978.

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, continuous monitoring of program effectiveness and in-service training based on the results is essential.

118. Melamed, A., et al., Spoons for making glucose-salt solution, (letter), *Lancet* 1:1317–18, 1978.

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

Using the spoons described by Morley and King (see abstract No. 119), 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 cli-

mate 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 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, therefore, must be taken into account when standardized approaches are advocated.

Moenginah, P. A., et al., Sucrose electrolyte solution for oral rehydration in diarrhea, *J Trop Ped Env Child Hlth* 24:127-129, 1978, (see No. 63).

119. Morley, D., et al., Spoons for making glucose-salt solution, (letter), *Lancet* 1:53-4, 1978.

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 WHO-recommended 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 any given ingredient must be explored.

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

120. Nalin, D. R., "A spoonful of sugar...," (letter) *Lancet* 2:264, 1978.

The author described the vagaries of home preparation of oral rehydration fluid, especially the variabilities in the quality and measurement of the ingredients, including water volume. 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 necessary, high-grade reagents and how the volume of the plastic bag could be calibrated were not addressed.

121. Ransome-Kuti, O., et al., Oral therapy of infant diarrhoea, (letter), *Lancet* 2:471, 1978.

The authors felt that immediate institution of home oral therapy using a salt/sugar solution could decrease diarrheal mortality in preschoolers in the developing world.

A survey of new mothers showed the idea of oral rehydration has spread rapidly in Lago, Nigeria, but less than 1/2 of the women who were 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.

122. Rohde, J. E., Preparing for the next round: convalescent care after acute infection, *Am J Clin Nutr* 31:2258-2268, 1978.

The author 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, effective home-based convalescent care, he feels, is the first important step in preventing future illness in children. Rather than a passive recipient of health services, the mother should be considered a 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.

The author described 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, the author 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.

Sack, D. A., et al., Oral hydration in rotavirus diarrhoea: A double-blind comparison of sucrose with glucose electrolyte solution, *Lancet* 2:280-283, 1978 (see No. 65).

123. Sack, R. B., et al., The current status of oral therapy in the treatment of acute diarrheal illness, *Am J Clin Nutr* 31:2251-2257, 1978.

An evaluation of oral rehydration therapy was presented in this review article. 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.

Seriki, O., Management of moderately severe dehydration by continuous intra-gastric infusion of electrolyte solution, *Trop Doc* 8:134-136, 1978 (See No. 38).

124. Agarwol, A., A cure for a killer—but how to deliver it?, *Nature* 278:389-391, 1979.

The importance of diarrhoeal diseases in the developing world and the historial and scientific antecedents to the development of ORT were reviewed in this feature article. Various approaches to delivering ORT were presented, ranging from the "complete formula" packets advocated by WHO to homemade simple salt/sugar (SSS) solutions mothers can prepare in the home. The pros and cons of each were clearly discussed, highlighting field experiences to date. The overall goal, most observers agree, is to familiarize developing world mothers with ORT so that it becomes a routine home treatment for diarrheal dehydration. To achieve this, observed one advocate, a demystification of medical technology is needed.

The viewpoints of leading experts on how best to "routinize" ORT may be overshadowed by the author's observation that, as in most appropriate technologies, it is difficult to recommend any one method, for each will be viewed from a different perspective according to local cultural, historical and economic conditions.

The ORT debate, concluded the author, is ultimately a political problem, couched within the larger issue of how best to deliver primary health care in general to the peoples of the developing world.

125. Anonymous, The control of acute diarrheal diseases: WHO and UNICEF collaborate in country programmes, *WHO Chron* 33:131-134, 1979.

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.

Cash, R. A., Oral therapy for diarrhea, *Trop Doc* 9:25-30, 1979 (See No. 77).

126. Finberg, L., et al., Oral therapy for dehydration in acute diarrhoeal diseases with special reference to the Global Diarrhoeal Diseases Control Programme, *WHO Unpublished Document*, BAC/DDC/79.1, 1979.

The use of oral rehydration therapy in light of the varying needs of local programs was discussed from the viewpoint of 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, felt the author.

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

The authors recommended use of prepackaged ingredients in amounts which correspond to readily available local measures. 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.

Hutchins, P., et al., Comparison of oral sucrose and glucose electrolyte solutions in the out-patient management of acute gastroenteritis in infancy, *J Hyg (Camb)* 82:15-19, 1979 (see No. 66).

Nalin, D. R., et al., Oral rehydration and maintenance of children with rotavirus and bacterial diarrhoeas, *Bull WHO* 57:453-459, 1979 (see No. 40).

Nalin, D. R., et al., The problem of emesis during oral glucose-electrolyte therapy given from the onset of severe cholera, *Trans Roy Soc Trop Med Hyg* 73:10-14, 1979 (see No. 41).

Rahaman, M. M., et al., Diarrheal mortality in two Bangladeshi villages with and without community-based oral rehydration therapy, *Lancet* 2:809-812, 1979 (see No. 78).

127. McCord, C., Oral fluid treatment for diarrhea in Menoufia governorate, Egypt, *A report from the American Public Health Association, 1979.*

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. Breastmilk and other foods are often withheld from children during bouts of diarrhea.

In this paper the author 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 the governorate (1.7 million inhabitants) within 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 amount and would be preferable to the one-liter packets but local production cannot match the needs of this project. In a field test, 75% of mothers produced acceptable solutions but 25% prepared solutions with hazardous sodium concentrations.

128. Rees, L., et al., Gradual reintroduction of full-strength milk after acute gastroenteritis in children, *Lancet* 1:770-71, 1979.

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. Stooling and vomiting were noted but no determinations of serum electrolytes, stool volume or duration of diarrhea were performed.

Mean length of hospital stay (not given) was not significantly different for any group.

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 did not fully support this conclusion.

129. Anonymous, Report of the Scientific Working Group on Child Care Practices Related to Diarrheal Diseases, *WHO Unpublished Document*, WHO/DDC/79.4, 1979.

In this report of a WHO Expert Scientific Working Group meeting, the "state-of-the-art" regarding the interrelationship of childhood diarrheal disease and what has come to be termed "maternal technology" was reviewed. 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.

130. Anonymous, Report of the WHO Scientific Working Group on Clinical Management of Acute Diarrhea, *WHO Unpublished Document* WHO/DDC/79.3, 1979.

This was a useful review of the key studies that established the theoretical and practical bases for the current WHO-recommended oral rehydration solution composition and implementation scheme. Other medical aspects of the management of childhood diarrhea were discussed, including the importance of continued feedings and indications for 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.

131. Anonymous, Developing an Oral Rehydration Service, *WHO Unpublished Document*

After reviewing the rationale for oral rehydration, the authors 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, designed to permit 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 would be based on field data gathered through a simple recording system. Procedures were outlined which would permit ongoing correction of operational defects through analysis of monitoring data.

132. Hirschhorn, N., The treatment of acute diarrhea in children: an historical and physiological perspective, *Am J Clin Nutr* 33:637-663, 1980.

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 positive impact of oral rehydration on diarrheal disease morbidity and mortality was described 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 and customs.

International Study Group, Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea: Part 1), Studies in two ambulatory care clinics *J Trop Ped* 27(2):62-67, 1981, (see No. 79).

International Study Group, Beneficial effects of oral electrolyte-sugar solutions in the treatment of children's diarrhea: Part 2), Studies in seven rural villages *J Trop Ped* 27(3):136-139, 1981, (see No. 80).

Nalin, D. R., et al,, Comparison of low and high sodium and potassium content in oral rehydration solutions *J Pediatr* 97(5):848-853, 1980, (see No. 68).

133. Pizarro, D., et al., Evaluation of oral therapy for infant diarrhea in an emergency room setting: Utilization of acute episode for instructing mothers in oral therapy method, *Bull WHO* 57(6):983-986, 1979.

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 (composition 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, they were sent home to continue giving their babies oral fluid and/or milk. Normal feedings were reinstituted when stools became pasty or semi-formed. Mothers were asked 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 if clinical evidence of shigellosis was seen.

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 mothers accomplishing 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, however, the effectiveness of the program in teaching mothers the techniques of home oral rehydration was difficult to assess.

Second Edition Abstracts

As the major clinical issues have been resolved and large-scale national ORT programs are now becoming operational, attention has focused on various practical, programmatic considerations. Numerous editorials and review articles have advocated wordwide, routine ORT use. Detailed manuals and guidelines have been prepared on ORS production and ORT program planning and evaluation. As with other elements of primary health care, the importance of cultural and behavioral factors has been increasingly recognized as ORT is promoted on the community level.

Egemen, A., et al., A study of oral rehydration therapy by midwives in a rural area near Ankara, *Bull WHO* 58(2):333-338, 1980.

230. Thirugnanasambandam, C., Prevention of dehydration in infants with gastroenteritis, *The Antiseptic*, 72:3, 125-128, 1975.

The author presented guidelines for managing acute dehydrating diarrhea, based on his clinical experience at the Hospital for Children in Madras, India. Diarrheal diseases accounted for 16% of the outpatients, 25% of the inpatients and 21% of hospital fatalities in preschool children, he reported.

After offering a brief review of health and socio-demographic risk factors in diarrheal diseases, the author outlined alternate methods for replacing electrolyte deficits. Continued breastfeeding was advocated. The usefulness of various local weaning foods and medicinal agents was analyzed in terms of their ability to satisfy water and electrolyte requirements.

The author recommended as "ideal" an oral fluid identical to that later recommended by the WHO (ORS) except that it contained an additional 5 g/l of glucose. Various oral fluid preparations ("Electro", "Hydrolyte", and "Lactolyte") locally available in India should not be used, stressed the author, because they do not yield the correct electrolyte concentrations.

Except in the presence of shock or severe vomiting, concluded the author, ORT is the treatment of choice for acute diarrhea.

231. Hirschhorn, N., et al., Logical flow

charts to train and guide health auxiliaries in the treatment of children's diarrhoea, *Trop Doc* (6):33-36, 1976.

Written at a time when the primary health care strategy was still something of a novelty, this article presented a systems analysis approach to training health auxiliaries in the clinical management of acute diarrheal diseases. Three flow charts, or clinical algorithms, were presented which described specific actions to be taken in the diagnosis and treatment of diarrheal dehydration. The first showed how to diagnose and assess degree of dehydration in small children. The second described treatment of mild to moderate dehydration using ORT, while the third outlined treatment for severe dehydration.

The oral glucose-electrolyte solution ("GE-SOL") recommended by the authors closely resembled the later WHO-recommended "complete" ORS composition. For severe cases, the authors recommended Ringer's lactate because of its worldwide availability and low cost. Once initial IV rehydration has been achieved in such cases, the authors advised initiating ORT with Ringer's lactate at a rate sufficient to maintain body weight (approximately 15 ml/kg/hr).

The authors cautioned that flow charts: 1) are not substitutes for proper training in the clinical skills needed in rehydration; 2) can be improved or amended with useful local material and, 3) may not be more effective than current standing orders or formulae in the treatment of acute diarrhea. Provided the flow charts are followed, concluded the authors, 80-90% of all diarrheal cases can be handled by auxiliaries using ORT.

232. **Jain, T. S.**, et al., Diarrhea and dehydration in pediatric practice, *Indian Ped* 14 (5):401-404, 1977.

This relatively early review article outlined recommended guidelines for the clinical management of acute diarrheal diseases. Because most cases are non-specific and self-limiting, the authors identified prevention of dehydration by adequate fluid replacement and maintenance of nutritional status through proper dietary management as the major treatment objectives. Moreover, they stated, dehydration can be successfully prevented or corrected with ORT alone in the majority of cases. The authors suggested using a sucrose-electrolyte solution (in g/l: sucrose 25, NaCl 3, $NaHCO_3$ 2.5 and KCl 1.0, dissolved in one liter of water) *ad libitum* to diarrheal patients. The use of antidiarrheal drugs was judged largely superfluous and IV therapy, while sometimes necessary, can usually be forestalled by adequate oral rehydration. Food should never be withheld longer than 12-24 hours and milk feeds should be reintroduced gradually over a 2-3 day period.

Although the ORS composition recommended is slightly at variance with that later promoted by WHO, this article agreed with most of the current, generally accepted guidelines for the management of diarrheal diseases.

233. **Suharjono, A.S.W.**, et al., Rehydration Centre (R.C.) in the OPD, Department of Child Health, University of Indonesia, during a short cholera outbreak, *Paed Indones* 17:218-222, 1977.

This relatively early study (February, 1976) evaluated the so-called "ROSE" system for treating diarrheal dehydration due to cholera. "ROSE" is an acronym standing for: R-*R*inger's lactate; O-*O*ral electrolyte solution; S-*S*imultaneous administration; E-*E*ducation on continued breastfeeding and home ORT.

During a cholera outbreak in Jakarta, Indonesia, 95 children, aged 6 months to 13 years (median 5 years), suffering from acute diarrhea, dehydratation, shock or pre-shock, were admitted to the outpatient rehydration center of a large general hospital. Twenty-two of 30 (79%) stools examined were positive for cholera El Tor-India. For the first 8 hours, each patient was simultaneously given intravenous Ringer's lactate and an oral glucose-electrolyte solution, followed by 4 hours of oral fluid alone. Continued breastfeeding was encouraged.

The composition of the intravenous Ringer's lactate solution was (in mEq/l): Na^+ 130, Cl^- 109, HCO_3^- 28, K^+ 4, and Ca^{++} 3. The composition of the oral rehydration solution was (in mEq/l): Na^+ 85, Cl^- 70, K^+ 15, HCO_3^- 30, and glucose 120 mmol/l.

Cases were treated in the rehydration center for 12 hours, after which ORT was continued at home. There were no deaths.

The authors concluded home ORT was a useful adjunct to IV therapy in children with acute cholera.

234. Wahed, M. A., et al., Hypernatremia: a complication in the diarrhea in children not receiving oral replacement therapy, 1978, *Scientific Publication available from*: ICDDR,B, Box 128, Dacca-2, Bangladesh.

Responding to the concern of many developing-country pediatricians about the purported risk of hypernatremia due to the 90 mEq/l sodium concentration in the WHO-recommended ORS composition, the authors performed a retrospective review of diarrheal cases presenting to the International Center for Diarrhoeal Disease Research (ICDDR,B) hospital in Dacca, Bangladesh between January, 1977 and December, 1978 in order to determine the incidence of hypernatremia.

Six thousand two hundred and forty-five children, aged 5 years or less, were admitted to hospital with acute diarrhea during the two-year period. Serum sodium levels had been determined (by flame photometer) in those presenting with clinical signs that suggested electrolyte imbalance. Of those examined, serum sodium levels of 145 mmol/l or greater were found in 350, about 6% of all admissions. However, the actual incidence may have been higher because any clinically inapparent cases would have been missed.

Seventy-five percent of detected cases were in children below one year of age. The records showed hypernatremic cases were significantly more dehydrated on admission (p less than 0.01) than were the other cases. Duration of diarrhea, degree of dehydration prior to admission and case-fatality rates were all significantly greater (p less than 0.01) in hypernatremic cases. Only 3 of 195 hypernatremic cases from whom feeding histories were obtained had received any type of ORT prior to admission.

The authors concluded hypernatremia is a significant problem, even without the use of ORT.

Carraza, F. R., et al., Ensaio clinico comparativo sobre aceitacao de duas solucoes hidratantes orais em criancas com diarréia aguda (Comparative clinical trial of the acceptability of two oral rehydration solutions in children with acute diarrhea), *Folha Med (Brazil)* 77(5): 611-614, 1978 (Article in Portuguese).

235. Vinhas, A., et al., Oral rehydration in infantile diarrhoea (letter), *Arch Dis Child* 54(3):243-244, 1979.

Writing from Mozambique, the authors referred to a study by Chatterjee, et al., (see abstract No. 62) in which, although clinical outcomes did not differ, an ORT solution given by nasogastric drip and containing 50 mEq/l Na^+ was found to produce somewhat less periorbital edema than a 90 mEq/l Na^+ solution.

The writers reported that, in treating a large number of children with the WHO-recommended ORT solution (90 mEq/l Na^+) by mouth, no hypernatremia or periorbital edema had been encountered. Only in a relatively few very young children, who for various reasons were given the solution nasogastrically, was periorbital edema observed. It did not appear to influence recovery.

They concluded that oral administration was preferable to the nasogastric route, probably because thirst controls the amount of fluid ingested. Another advantage is that it involves the mother more actively in treatment, opening up greater opportunities for delivering health education.

236. Cutting, W.A.M., Management of diarrhoea in children at the primary care or peripheral level, *Ann Soc Belge Med Trop*, 59:221-235, 1979.

After a brief description of the importance of diarrheal diseases, the author presented some very practical considerations for individual case management and for organizing a diarrheal treatment service at the peripheral level.

The author summarized his guidelines for individual case management as "the five D's": 1) dehydration, 2) diet, 3) disaccharidase, 4) diagnosis, and 5) drugs.

The first and major concern in case management, recognizing dehydration, can be problematic because the most telling signs and symptoms (i.e., apathy, sunken eyes and fontanelle, tachycardia, diminished skin elasticity) often do not appear until a child has lost approximately 10% of its body water. One good criterion is sudden, recent weight loss. Treatment consists of replacing fluid losses as soon as possible. In all but children in shock, the author recommended ORT. The method works because absorptive mechanisms in the small intestine remain intact despite the presence of secretory diarrhea. In the proper ratio, moreover, glucose plus salt and water are absorbed at about 25 times the rate of saline alone. The author felt this optimal ratio is achieved by using the WHO-recommended ORS formula. Except in the most severe cases, he added, a simpler salt/sugar (SSS) solution may be substituted with near equal results. Several methods for calculating fluid needs, based on age, body weight and degree of dehydration, were proposed.

Allowing mothers to give the oral fluid to their own children, using cup and spoon, relieves demands on health workers and also creates an ideal setting for delivering health education.

Proper dietary management includes an adequate intake of nutritious foods during the diarrheal episode as well as continued breastfeeding. Rather than starvation, food should be given as soon as the patient is well enough to take it. There is no benefit in very gradually reintroducing food during diarrheal episodes, stated the author.

Although more usually associated with chronic rather than acute diarrhea, disaccharidase deficiency is a problem in a small proportion of cases. The enzyme most often affected is lactase, which is responsible for splitting milk sugar, lactose, into glucose and galactose. The condition, however, is not a contraindication to continued breastfeeding.

Since diarrheal dehydration is life threatening, therapy precedes diagnosis. Drug or antibiotic therapy is indicated only for patients with *E. coli*, cholera, *Salmonella*, *Giardia lamblia* and *Entamoeba histolytica*. However, definitive diagnosis is problematic and in any event, many cases are viral in origin. The author stressed that routine use of antibiotics—or of any other drugs for that matter—is not warranted.

In organizing an ORT service, the author identified certain administrative and logistical considerations at different levels. First, a standard treatment regimen is needed which is geared to the degree of dehydration. Secondly, there must be a referral system for serious cases. Adequate supplies must be maintained. The continuous delivery of health education to both patients and providers is another essential aspect to be built into every treatment service.

Finally, felt the author, prevention of diarrheal diseases through the traditional strategies of improved water, sanitation, nutrition and overall socioeconomic development can only be achieved if health workers reach outside facilities and make positive initiatives in the community.

237. Khan, S. R., Home management of infantile diarrhoea, Symposium of diarrhoeas and rehydration, *Pakistan Pediatr J* 3(1):77-82, March 1979.

Addressing Pakistani pediatricians, the author reviewed the physiology of acute diarrhea and advocated the early home treatment of diarrheal diseases with ORT, based on the WHO-recommended formula. Pointing out the syndromal relationship of diarrhea and malnutrition, the author stressed the importance of continued feeding, especially breastfeeding, during diarrhea. There is no scientific

A Pakistani father learns how to prepare an ORT solution from a primary health care worker. (Photo: B. Thomas, UNICEF).

basis for "resting the gut" or for the use of antibiotics or other drugs; the sole goals of therapy, he stressed, are to replace fluid and electrolyte losses and to maintain the child's nutritional status.

Although use of WHO-recommended ORS packets is preferable, in their absence the author recommended use of a simple sugar-salt solution. In either event, the fluid should be given *ad libitum* to all but the most serious cases. Home management is feasible, the author felt, citing as proof a recent cholera outbreak in Bangladesh during which the use of ORT by untrained family members under very unfavorable conditions drastically reduced mortality.

In Pakistan, diarrheal diseases account for about one-fourth of all pediatric morbidity and about one-half of all pediatric hospitalizations. This situation could be transformed, concluded the author, if Pakistani physicians would change their emphasis of treatment from the use of drugs to reduce the number of stools to the use of ORT and continued feeding to maintain hydration and nutritional status.

238. Ozorio, P., Las ventajas de la rehidratación oral (The advantages of oral rehydration), *Bol Of Sanit Panam* 86(4):357-359, 1979. (Article in Spanish).

In this editorial aimed at Latin American readers, the writer reviewed the magnitude of the diarrheal disease problem in the region, citing, *inter alia*, a 1972 landmark study which found 28% of all mortality in children under five in the Americas was due to diarrheal diseases. This situation, averred the author, can now be dramatically reversed through the widespread use of ORT.

Although it is simple to prepare and administer, the promised impacts of ORT will only be achieved through deliberate efforts to involve and educate mothers on its use. Experience elsewhere has shown the use of both prepackaged ORS and simple homemade salt/sugar (SSS) solutions should be promoted.

Advantages to using ORT are numerous, stated the author. It not only virtually eliminates mortality but also has a beneficial nutritional effect. By reducing IV needs by 75% or more, it will significantly reduce hospital costs and crowding of pediatric wards. Best of all, he concluded, it need only be put into the hands of the family to have its greatest impact.

239. Sinha, D. P., Oral rehydration in diarrhoeal diseases; A simple solution to a complex problem, *CAJANUS* 12(3):138-148, 1980.

Addressing the journal's primarily West Indian audience, the author briefly reviewed the importance of diarrhea as a public health problem in the Caribbean. After discussing rehydration physiology and citing key studies that led to the development of ORT, the author endorsed the WHO-recommended ORS formula as the most effective oral solution for treating diarrheal dehydration. Noting that some West Indian physicians have expressed concern that the sodium concentration (90 mEq/l) in the WHO formula is too high, the author cited recent studies in Jamaica that showed it to be optimal.

One major advantage of ORT, pointed out the author, is that the ingredients are available at home and so the solution can be rapidly prepared. The importance of accurately measuring the ingredients was stressed, leading the author to recommend using prepackaged ORS whenever possible.

The author described the interrelationship of diarrheal dehydration and malnutrition and called on readers to give high priority to programs to implement ORT.

240. Anonymous, Oral rehydration therapy (ORT) for childhood diarrhoea, *Population Reports, Series L, No. 2*, (75 pages), Nov-Dec 1980, (available in several languages from the Population Information Program, the Johns Hopkins University, Hampton House, 624 N. Broadway, Baltimore, Md. 21205, USA).

Virtually all aspects of ORT were reviewed in this comprehensive report prepared for the lay reader. The authors traced the historial development of ORT and clearly explained its

physiological basis, describing the key studies that led to the refinement of the present WHO-recommended ORS composition. The practical advantages of ORT over traditional I.V. therapy were outlined as were the pros and cons of the various alternatives for packaging or locally preparing ORS. The importance of early home management and continued feeding during diarrheal episodes were also highlighted.

In summarizing the issues regarding delivery of ORT, the authors drew heavily on field data from numerous countries. Actual promotional and training materials were clearly described and the organizational aspects of diarrhoeal disease control programs considered.

A summary table was presented which described design, coverage and impact data from some 45 ORT delivery programs.

The bibliography contains 258 references.

Finberg, L., et al., The role of oral electrolyte-glucose solutions in hydration for children—international and domestic aspects, *J Pediatr* 96(1):51-54, 1980.

241. Anonymous, Oral rehydration therapy supplement, *Unpublished Document available from*: National Council for International Health, 2121 Virginia Ave. N.W., Suite 303, Washington, D.C. 20037, USA, 1980.

To follow up a 1980 seminar on the role of non-government organizations (NGO's) in promoting the use of ORT in the developing world, the authors sent questionnaires to 333 US-based NGO's. The aim was to learn which organizations were using ORT, in which way it was delivered, whether any training or health education materials had been developed and whether any operational research or program evaluations had taken place.

A total of 127 organizations responded. Of these, 52 reported ORT activities were part of their overseas health programs. Forty-nine stated ORT was delivered as a component of basic health services, 19 included it in education programs and two delivered ORT alone. Of 42 reporting their methods, 20 used UNICEF ORS packets, 14 used locally-produced packets, 19 used the "pinch-and-scoop" method and 20 relied on household or plastic spoons. Training materials on ORT had been developed by 42 of 51 respondees, fourteen had conducted ORT operational research and 24 had performed evaluations of their ORT programs.

Geographical breakdowns and thumbnail sketches of each responding organization, as well as a list of financial and technical resource organizations for NGO's interested in ORT, complete this very useful publication.

242. Parker, R. L., Oral fluid therapy in diarrhea and dehydration: Current concepts and practical considerations, (*Unpublished Document available from*: Dept. of International Health, Johns Hopkins Univ. School of Hygiene and Pub Health, Baltimore, Maryland, USA), July 1980.

The significance of diarrheal diseases, the development of ORT, approaches to implementing it and various unresolved related issues are outlined in this thoughtful review. ORT does not reduce the incidence of diarrhea, the author pointed out; rather it prevents death due to diarrheal dehydration. The mechanism by which ORT replaces water and electrolyte losses and promotes recovery of fluid-electrolyte balance is clearly explained. The author endorsed the WHO-recommended composition (containing sodium, potassium chloride, sodium bicarbonate and glucose) as ideal but, where delivery of ORS packets is not feasible, he felt, simple glucose or sucrose and salt (SSS) solutions can also be used to treat diarrheal dehydration with good results. Additionally, the author recommended using the standard mixture containing 90 mmol of sodium per liter; advocated continued feeding despite diarrhea (except in cases of severe vomiting or during the rapid initial rehydration of a dehydrated child); urged that the solution be prepared using the cleanest water immediately available (boiled water is preferred when feasi-

ble); and called for minimal reliance upon packets or kits, given their expense and attendant logistical problems.

The author felt that ORT delivery programs should take a multi-tiered approach, relying initially on early home treatment of diarrhea with SSS solutions and on peripheral health workers to disseminate information, monitor activities and train families on the dosage, preparation and administration of SSS solutions. The system should also include a peripheral rehydration center equipped to provide complete oral fluids (i.e., with potassium and sodium bicarbonate) and intravenous therapy and to reinforce the health workers' training. Thirdly, a referral center should be established to handle the most serious cases and to oversee the overall ORT program.

Unresolved ORT-related issues identified by the author included the ability of families to prepare and administer the solution correctly, the possible limitations of a solution composed solely of sugar and salt and the risk of ORT failure in patients who persistently vomit, are in severe shock, or who have an enzyme deficiency preventing sugar absorption in the small intestine.

Greenough, W. B., III, Principles and prospects in the treatment of cholera and related dehydrating diarrheas, In: *Cholera and Related Diarrheas*, 43rd Nobel Sypm, Stockholm, pp 211-218, Karger Press, Basel, 1980.

Levine, M. M., et al., Variability of sodium and sucrose levels of simple sugar/salt oral rehydration solutions prepared under optimal and field conditions, *J Pediatr* 97(2):324-327, 1980.

243. Anonymous, Guidelines for the trainers of community health workers on the treatment and prevention of acute diarrhea, *WHO Unpublished Document* WHO/CDD/SER/80.1 (*available from*: Program for the Control of Diarrhoeal Diseases, World Health Organization, 1211 Geneva 27, Switzerland, 1980.)

Prepared for adaptation and use on the primary care level, this WHO manual presents trainers of PHC workers with simple methods and approaches now available for the treatment and prevention of acute diarrheal diseases. The material is divided into three parts: a description of the problem of diarrhea, how to treat it, and ways of preventing it. In each part key themes are introduced and pertinent normative information and specific educational objectives are presented in outline form.

A diagnostic guide for assessing diarrheal dehydration is included. The PHC worker is then introduced to three treatment plans and instructed to follow one of them according to the patient's degree of dehydration.

The importance of proper reporting and the need to avoid using any drugs other than ORS are stressed.

Regarding the prevention of diarrhea, guidelines for child feeding and nutritional monitoring are presented as is information on proper food preparation and storage, personal and domestic hygiene and the importance of safe water. Annexes include weight/length for age standards, instructions for preparing simple salt/sugar solutions for ORT, a growth chart and a sample codified reference card for case treatment.

This document, as well as others related to the CDD Programme, is available in several languages free of charge, both through WHO Headquarters and the six WHO Regional Offices.

244. Anonymous, A Manual for the treatment of acute diarrhoea *WHO Unpublished Document* WHO/CDD/SER/80.2 (*available from*: Programme for the Control of Diarrhoeal Diseases, World Health Organization, 1211 Geneva 27, Switzerland, 1980.)

The principles and practices of treating diarrhea of all etiologies in all ages, with special emphasis on the use of oral rehydration therapy in infants, are outlined in this 25-page WHO CDD Programme document. Designed for ready adaptation on the local level, the manual is intended for senior-level, clinical staff. Information on the assessment of dehydration and fluid deficit as well as guidelines for rehydra-

tion (both oral and IV) and maintenance therapy are presented. In addition, child care practices related to the prevention of diarrhea, such as breastfeeding and appropriate weaning, are discussed.

Four annexes are attached which summarize information on common enteric pathogens, composition and physiological considerations of various rehydration solutions, estimation of a child's weight from age or length and the use of a growth chart. Finally, a list of questions most often asked by health workers on diarrheal diseases is included along with appropriate answers.

245. Anonymous, Guidelines for the production of oral rehydration salts, *WHO Unpublished document* WHO/CDD/SER/80.3, (*available from*: WHO Programme for the Control of Diarrhoeal Diseases, 20 Avenue Appia, 1211 Geneva 27, Switzerland, 1980.)

Realizing that increasing worldwide demand for ORS already exceeds current production capacity, WHO prepared these guidelines for countries in which local ORS production may be feasible. In the interest of standardization, the information is based on the WHO-recommended ORS formula.

The document contains primarily technical information on ORS production and quality control procedures. Both automatic (up to 5 million one-liter size packets per year) and semi-automatic (500,000-750,000 per year) processes are considered. Specifications for physical facilities, equipment for both production and quality control, personnel and raw materials are all discussed in detail. Actual production and quality assurance protocols are outlined as well.

A series of annexes is included which outlines planning considerations, criteria for quality control, order specifications, laboratory testing, production control procedures and excerpts from WHO-recommendations on "Good practices in the manufacture and quality control of drugs".

The 58-page document is available upon request, in several languages, both through WHO Headquarters and all six WHO Regional Offices.

246. Anonymous, Training manual on treatment and prevention of diarrhea, *Publication No. 12*, International Center for Diarrheal Disease Research, Box 128, Dacca-2, Bangladesh, 1980.

Prepared by the ICDDR,B for the village-level health worker who will train mothers on the simple treatment and prevention of diarrhea, this manual uses simple, non-technical, concise language to describe four methods of preparing ORS: WHO "complete formula" glucose/electrolyte; simple sugar/salt; sugar/salt/bicarbonate; and molasses/salt using finger measurements. It also emphasizes that the village health workers must explain to village mothers how to administer ORT, the benefits of continuing breastfeeding, and the importance of other measures to prevent diarrheal diseases.

Copies are available upon request and the authors welcome any comments or suggestions for improving the manual.

247. Ramlal, A. M., Administration of oral rehydration therapy, *PAHO Bull*, 14(2):204-206, 1980.

In this abstract of a longer paper entitled "Pathophysiology, therapeutic principles, and local clinical research in diarrheal disease," presented at the WHO-sponsored Caribbean Seminar-Workshop on Diarrheal Disease Control (Kingston, Jamaica, March 1980), the author described the ORT regimen she and her colleagues developed at the University of the West Indies School of Medicine in Kingston for treating children with mild, moderate, and severe dehydration. A simple chart is provided which describes the volume of ORS to administer based on admission weight, approximate age and degree of dehydration. The author endorsed a 2:1 ratio of ORS and either water or breastmilk. Some very useful, practical guidelines on the administration of ORT are included.

This brief article provides a simple but useful guide for all health workers practicing ORT.

248. Voorhoeve, H.W.A., Het wereld diarreeprogramma (The global diarrhoeal disease control programme), *Tijdschrift voor Zieken-verpleging* 33(25):1196-1197, 1980 (Article in Dutch).

Addressed to Dutch clinicians, this brief article reviewed the extent and magnitude of the diarrhea problem in the world and described how to make ORT solutions using either sugar/salt or the WHO-recommended formula.

249. Bennett, F. J., Diarrhoeal disease control (editorial), *East Afr Med J*, 57(5):293-298, 1980.

Highlighting research done in Africa, the author provided an overview of developments which led to the establishment of the WHO CDD Programme. Given the vastness of the problem, new strategies to control diarrheal diseases are sorely needed, felt the author. Not only traditional health facilities but also health auxiliaries, PHC workers, mothers and older syblings must take an active role. A recent breakthrough, the development of ORT, has made feasible the elaboration of vastly improved diarrheal disease control programmes.

After reviewing the various methods of preparing ORS, the author endorsed the use of WHO-recommended ORS packets as the best approach. Depending on logistical considerations, countries may either purchase the ORS packets through UNICEF or establish large-scale, local ORS production. In Africa, proposed the author, ORS production would be feasible on a regional basis.

Eliminating diarrheal mortality through the widespread use of ORT, however, comprises only the immediate and medium-term objectives of the WHO CDD Programme. The long-term objective, recalled the author, is the elimination of diarrhea as a public health problem by improving water supply and sanitation and by promoting better child care practices and generally improved community hygiene.

The author called upon the African countries to begin training programs and for all teaching hospitals to institute ORT both for the systematic training of health workers and to save money. Mothers, too, should be involved, the author felt, as ORT also provides a learning situation for them.

250. Pizarro, D., et al., Oral rehydration of infants with acute diarrhoeal dehydration: a practical method, *J Trop Med Hyg*, 83, 241-245, 1980.

After reviewing previous studies which led to the current, WHO-recommended oral rehydration regime (i.e., one volume of free water for each two volumes of glucose-electrolyte solution (GES), the combined total to equal twice the estimated fluid deficit) the authors evaluated a simplified treatment regimen whereby the total fluid volume administered remains unchanged but all the GES is given at one time followed by all the free water in a ratio of 2:1.

Fifty Costa Rican children, ages 10 days to 24 months (mean 5.2 months), with acute, uncomplicated diarrhea were admitted to the study. All patients were visibly dehydrated (mean 7.5% loss of body weight). Brief clinical histories were elicited, the patients were examined and their weights and serum electrolyte values were measured upon admission, after ingestion of GES, after ingestion of free water, and 24 hours after admission. Because of the hypothetical risk of hypernatremia when using the WHO-recommended solution, patients' serum Na^+ levels were closely monitored. Following instructions, mothers administered both GES (50-200 ml every 15-20 minutes, as tolerated) and free water to their children. After initial rehydration, patients were offered breastmilk or half-strength formula or fruit and vegetable purées (for those over 4 months of age). Mothers were given packets with further instructions to continue the 2:1 regimen at home as needed and to return for follow-up the next day.

Thirty-two (64%) cases were moderately dehydrated (5-10% loss of body weight), 11 (22%) mildly (less than 5%) and 7 (14%) severely dehydrated (greater than 10%) upon admission. None of the patients presented with hyponatremia; 7, however, presented with hypernatremic dehydration. Vomiting was no obstacle to successful rehydration; 26% of the children vomited once, 12% twice, usually at the beginning of treatment. The average time to achieve initial rehydration was 7.9 hours (range 2.3-17 hours) and 50% of the patients spent 12 hours or less in the outpatient ward before discharge. Only three patients required eventual admission to hospital. Of the 94% discharged, only one returned dehydrated and was again given oral GES.

In the vast majority of cases serum Na^+ levels after ingestion of the GES remained unchanged from admission levels. A slight decrease of 2-4 mmol/l typically occurred following ingestion of free water. Of the seven cases presenting with hypernatremic dehydration, serum Na^+ in all but two fell to normal levels (less than 150 mmol/l) after GES ingestion. Following the free water, serum Na^+ returned to normal levels in all cases, where they remained.

The authors concluded the "one-shot" GES/free water regimen does not cause hypernatremia and that health workers now have the simpler option of administering GES as a single dose followed by free water, rather than giving repeated, smaller doses which could lead to confusion in busy or ill-supervised settings.

Varavithya, W., et al., Comparison of oral rehydration with electrolytes solution and soy milk in acute diarrea, *J Med Ass Thailand*, 63(11):593-597, 1980.

Carrazza, F. R., et al., Reidratacao oral em pediatria, *Arq Gastroent, Sao Paulo*, 17(3):168-172, 1980, (Article in Portuguese).

251. Gangarosa, E. J., et al., Global travel and travelers' health. *Aviat Space Environ Med* 51(3):265-270, 1980.

This paper discussed some of the potential health risks associated with international travel. The most common cause of illness identified by the authors is "travelers' diarrhea." Numerous studies have shown that the risk of contracting traveller's diarrhea is highest in those from the more sanitized developed countries while that for travellers from developing countries is lowest. The authors went on to describe major risk factors (e.g., consumption of raw foods, purpose of travel) in travellers' diarrhea.

Misconceptions concerning treatment of travellers' diarrhea abound, stated the authors. Their studies have indicated that over two-thirds of travellers who developed diarrhea required some kind of medication. They were most likely to use antispasmodics (Lomotil) or paregoric in the mistaken belief that arresting the purging process will lead to quick recovery. The authors advised such drugs should not be used because, on the contrary, purging is nature's way of cleansing the gut and should not be interfered with. Kaopectate is also of dubious value for the treatment of diarrhea, the authors stated. They cited the results of a controlled trial which showed no difference in outcome between patients who received Kaopectate and those given only a placebo. Rather than give useless or potentially harmful drugs, stressed the authors, therapy should focus on correcting and preventing fluid and electrolyte imbalances.

In diarrheal diseases water, potassium, bicarbonate, sodium, and chloride are lost. Replacement of these fluid and electrolyte losses comprises the cornerstone of treatment. In many developing countries, prepackaged, WHO-recommended ORS is available at commercial outlets and, in the authors' opinions, constitutes all the medication necessary for travellers' diarrhea. The authors also presented a recipe for homemade ORS should packets be unavailable. Citing current debate on the prophylactic use of antimicrobials to prevent traveller's diarrhea (doxycycline, neomycin, etc.) the authors cautioned against their use until more research is done.

Finally, simple preventive measures were advocated, including adding bleach or iodine or boiling drinking water; avoiding ice made from contaminated water; avoiding green, leafy vegetables or cooked foods that have been store at room temperature, and not swimming in water contaminated by human sewage.

252. Sack, D. A., Management of acute infectious diarrhea, *Comp Ther* (11):50-56, 1980.

This article described the pathophysiological and clinical features of acute diarrhea and reviewed current etiological, epidemiological and therapeutic knowledge on the subject.

The author presented a logical sequence for clinical diagnosis and management of acute diarrheas. The first objective is to distinguish between watery, small-bowel diarrhea and large-bowel diarrheas, often called dysenteries. The first and more common type causes secretory diarrhea while infections of the second type are invasive. The distinction can usually be made on the basis of case histories and clinical signs alone. In children less than three years old, the diarrhea is most likely to be caused by rotavirus. Accurately assessing the degree of dehydration is most important in this youngest age group, felt the author.

The goal of therapy is to replace the excessive water and electrolyte losses caused by the increased stooling. Regardless of etiology, stressed the author, the treatment of choice is the same for all cases: rehydration therapy, which, in all but the most severe cases, can best be accomplished orally. For ORT, the author recommended using the WHO-recommended ORS formula; however, in mild cases a simple sugar-salt-bicarbonate mixture is adequate. Laboratory tests and the use of antibiotics or antimotility drugs such as Lomotil, are usually not appropriate, he felt. Except for cow's milk, plain water and the usual diet should be continued throughout the episode.

The author lamented the fact that ORT has not gained widespread acceptance in the U.S. This, he felt, is because traditional I.V. therapy is highly effective in the U.S. setting. Nevertheless, on the basis of cost and of avoiding the risk of nosocomial infections, which all hospitalizations entail, he felt ORT should replace intravenous therapy as the mode of choice in all but the most severe diarrheal cases.

Greenough, W. B., III, Oral replacement therapy in diarrhea: consensus and controversy, In: Field, M., et al., (eds), *Secretory Diarrhea*, Bethesda, MD, American Physiological Society, 1980.

253. Ransome-Kuti, O., Dependence on commercial oral rehydration preparations (letter), *Lancet* 2:1080, 1980.

ORT has been shown to be highly effective in preventing diarrheal dehydration. Experience throughout the world, including the writer's country, Nigeria, has also demonstrated that mothers, literate and illiterate, can be taught to prepare adequate ORT solutions in the home using locally available salt and sugar. Home use of SSS solutions should therefore be encouraged rather than dependence on commercial ORS preparations. Dependence on commercial ORS should also be avoided, wrote the author, because it violates the ethic of self-reliance, entails the risk of shortages interrupting or preventing ORT, is more expensive and has limited shelf-life. The author drew the analogy of mothers with ample breastmilk being persuaded through advertisements to feed their children with artificial milk.

Clements, M. L., et al., Potassium supplements for oral diarrhoea regimens (letter), *Lancet* 2(8199):854, 1980.

Islam, M. R., et al., Labon-gur (common salt and brown sugar) oral rehydration solution in the treatment of diarrhoea in adults, *J Trop Med Hyg*, 83,41-45, 1980.

Steinhoff, M. C., Oral rehydration therapy for diarrhoea (letter), *J Pediatr* 97(3):515, 1980.

Hutchins, P., et al., Oral solutions for infantile gastroenteritis—variations in composition, *Arch Dis Child*, 55, 616-618, 1980.

254. Watkinson, M., et al., The use of oral

glucose electrolyte solution prepared with untreated well water in acute, non-specific childhood diarrhea, *Trans Roy Soc Trop Med Hyg*, 74:(5):657-661, 1980.

Observing that routine use of ORT is being promoted in rural areas of the developing world but that up to 78% of this population does not have access to safe drinking water, the authors carried out a twelve-week controlled prospective trial comparing the clinical efficacy of an oral glucose-electrolyte solution (GES) mixed in untreated, bacterially contaminated well water to that of an oral GES of the same chemical composition prepared with clean drinking water. The WHO-recommended ORS formula was used.

Forty-eight children between three months and four years of age from a single Gambian village were divided into control and study groups of equal sizes and matched for age and nutritional status. Each child was visited daily, weighed weekly and received complete physical exams at the beginning, middle and end of the 12-week study. Whenever the children had diarrhea, their mothers were given a standard volume (between 100 and 150 ml/kg of the child's weight) of preconstituted GES with instructions for home administration. Continued feeding was encouraged and fresh GES was prepared daily.

The control group's GES was prepared using disinfected water while that of the experimental group was made with untreated water from the single village well. Stool, water and GES samples (both fresh and after 24 hours) were routinely collected, incubated and examined throughout the study.

Compliance with directions for household ORT appeared high; the mean volume of GES consumed in the first 24 hours was 90 ± 36 ml/kg. No significant differences in growth rates, positive stool isolations, clinical outcomes, duration or incidence of acute diarrheal attacks were observed between the two groups. The twelve-week period prevalence of diarrhea was 9.1% in the control group and 8.1% in the experimental group.

No bacterial contamination was found in either the initial "clean" water or the GES prepared from it. Leftover "clean" GES samples, however, were found to be contaminated by coliform bacteria. In contrast, enteric pathogens were isolated from samples of well water and the "well-water" GES throughout the study. After 12 hours of storage at ambient temperatures, bacterial populations were significantly higher (p less than 0.01) in the "well-water" GES than in well water alone, indicating that addition of the ORS enhances bacterial growth in already contaminated water.

The authors speculated that 50% or more of the children given "well-water" GES ingested more than 10^4 *E. coli*/day during diarrheal episodes yet, they noted, the duration and incidence of diarrhea in this group were not significantly different from the control group. They therefore concluded that, despite the presence of bacteria and their toxins in GES, active intestinal absorption of water and electrolytes remains essentially unhindered.

(See also abstract No. 217.)

255. Acra, A., et al., Disinfection of oral rehydration solutions by sunlight, *Lancet* 2:1257-1258, 1980.

Questioning the safety of oral rehydration solutions prepared with contaminated water, the authors hypothesized that exposure to sunlight, using transparent vessels, would render previously contaminated glucose-electrolyte solutions bacteriologically sterile without deterioration of the ingredients.

Fifteen liters of solution were prepared by dissolving WHO-recommended ORS in chlorine-free tap water which had been contaminated with fresh sewage. Fifteen sterile polyethylene bags were then filled with this bacteriologically contaminated ORS solution. Samples of these were placed either in direct sunlight, in a room with artificial or natural lighting or in a dark room.

A zero coliform count was attained within about one hour in the ORS solution exposed to direct sunlight while the other samples remained contaminated. Similar results were ob-

tained in another fifty observations using highly contaminated water in an assortment of transparent glass or plastic vessels of various shapes and colors. Heat was not a factor, as the temperature of the test solutions did not increase by more than 5°C after exposure to sunlight for more than two hours. Neither the pH (8.33) nor $NaHCO_3$ concentration changed, indicating the sodium bicarbonate did not decompose, as would result from heating the solution.

The authors concluded that simple exposure to one hour or more of sunlight is an effective means of sterilizing bacteriologically contaminated glucose-electrolyte solution.

256. Black, R. E., et al., Proliferation of enteropathogens in oral rehydration solutions prepared with river water from Honduras and Suriname, *J Trop Med Hyg* 84:195-197, 1981.

Because unsanitary conditions may lead to bacterial contamination, some observers have cautioned that only boiled water should be used to make ORT solutions in the home and that any solution remaining after 24 hours be discarded. However, these preconditions raise additional obstacles: in many areas the necessary fuel is scarce or expensive and waiting for the water to boil, then cool, entails inordinate delays. Secondly, if more ORS is not readily available, preparing a new batch every 24 hours may be impossible.

In light of these issues, the authors performed laboratory tests to assess the ability of known bacterial enteropathogens to survive and proliferate in solutions made either with distilled water or river water collected in two developing countries.

Two series of 250-ml river water samples were collected from the Paramaribo River in Suriname and the Jutigalpa River in Honduras. In both areas, the rivers were used by local inhabitants for drinking and for preparing food. The samples were then carried in insulated containers to Baltimore, USA, boiled for 10 minutes and plated on blood, easin methylene blue, MacConkey's and thiosulfate-citrate-bile salts sucrose agars. No growth was observed. WHO-recommended ORS was then added (in the recommended concentrations) to the boiled water samples and to distilled water which had been left in an open container for 24 hours (to allow chlorine to dissipate). Approximately 1,000 bacteria in one mililiter of phosphate buffered saline were added to nine mililiter aliquots of the ORS solutions for a final concentration of 100 bacteria/ml. The following enteropathogens were used: *Shigella flexneri* 2a; *Vibrio cholerae* El Tor Inaba; and *Escherichia coli*, strains 851/71 (enterotoxigenic) and B7A (ST and LT). The inoculated solutions were left at room temperature for 48 hours and serial ten-fold dilutions were made of 0.1 ml samples at 0, 6, 12, 18, 24 and 48 hours

The results showed *Shigella* survived very poorly. *V. cholerae* and enterotoxigenic *E. coli*, however, reached concentrations of 10^3-10^4 by 12 hours and 10^4-10^6 by 24 hours in the riverwater samples. The authors concluded that ORT solutions do support proliferation of some enteropathogens. They attributed the more rapid growth rate in riverwater samples to the presence of dead organic matter, which provides a more luxuriant medium than distilled water. Because all samples supported significant bacterial growth, the authors concurred with the recommendation that excess ORT solutions be discarded after 24 hours. However, if logistical or practical considerations make this impracticable, ORT should be continued using the old solution.

257. Anonymous, Use of locally available drinking water for preparation of oral rehydration salt (ORS) solution, *WHO Unpublished Document*, (*available from*: WHO Programme for the Control of Diarrhoeal Diseases, 20 Avenue Appia, 1211 Geneva 27, Switzerland, 1981.)

Responding to enquiries concerning the safety of using non-sterile water to prepare ORT solutions, the authors reviewed current knowledge, made recommendations and identified research priorities related to this issue. The authors considered: 1) the growth of enteric bacteria in ORT solutions prepared from

WHO-recommended ORS; 2) the risk associated with the use of ORT solution that is not bacteria-free; and 3) possible methods of decontaminating either the water used for preparing the ORT solution or the solution itself.

The authors cited eight studies which demonstrated that ORT solutions prepared with untreated water containing organic matter can support the growth of enteric bacteria. ORT solutions made from water that is distilled, boiled, or autoclaved may also support the growth of enteric bacteria, however, as these processes do not remove any nitrogen derived from killed bacteria. Secondly, the use of boiled water for preparing the ORT solution cannot guarantee its sterility as contamination of such water or of the prepared ORT solution can subsequently occur in the home.

Regarding the risk associated with using ORT solution that is not bacteria-free, the author cited one study in the Gambia which found the incidence and duration of diarrhea, as well as growth rates, in two groups of children treated for diarrhea with well water and "clean" drinking water (meeting the WHO standard) were found to be similar. The investigators had estimated that even if "contaminated" ORT solution were given to the children one day out of five, this would account for less than 5% of the total *E. coli* ingested by the children in their local diets.

The authors discussed possible methods of decontamination of water and/or ORT solutions, including adding chemicals to ORS, boiling and exposure to sunlight. At present, no bacteriocidal or bacteriostatic agents are known which could be feasible ORS additives. Although boiling may effectively decontaminate water, it is costly, causes delays and may be invalidated by subsequent re-contamination during mixing, storage and use. Exposure of the solution, or of water, to several hours of direct sunlight in a transparent container may significantly reduce the number of enteric pathogens, one study has shown.

Further research is needed, the authors stated, on the growth of *V. cholerae*, Salmonella and enterotoxigenic *E. coli* in ORT solutions prepared with naturally contaminated water. Epidemiological studies are also needed to determine whether or not using "usual" drinking water for ORT entails additional risks to the patient such as increased severity, duration or susceptibility to subsequent diarrheal episodes. Also, further evaluation of sunlight disinfection and the identification of possible chemical ORS additives is needed.

In conclusion, the authors recommended using water made potable by any method whenever possible until it can be shown there is no relative risk in using "usual" water. However, if potability cannot be guaranteed, the best available water should be used. Once prepared, ORT solutions should be protected against subsequent contamination, stored in a cool, dark place and should never be kept longer than 24 hours.

258. Anonymous, Manual for the planning and evaluation of national diarrhoeal diseases control programmes, *WHO Unpublished Document* WHO/CDD/SER/81.5, *(available from:* WHO Programme for the Control of Diarrhoeal Diseases, 20 Avenue Appia, 1211 Geneva 27, Switzerland, 1981.)

This manual was prepared for health management staff in charge of planning and evaluating national diarrheal disease control (CDD) programs.

Chapter One ("Describing the diarrhoeal disease problem and past control efforts") discusses epidemiological methods for measuring the extent of the diarrheal disease problem. For situations where few or no reported data exist, a relatively simple but reliable sample survey design is described for estimating diarrheal morbidity and mortality. Also included is an outline for describing past and present national diarrheal control activities on which the incipient CDD program will be based.

In Chaper Two ("Developing a plan of operations") a logical framework is presented for developing a national CDD program "plan of action". The steps to be followed include an initial policy review, descriptions of the health

care infrastructure and extent of diarrheal diseases, setting of objectives and targets, identification of CDD strategies and delivery systems and enumeration of proposed activities. Special guidelines are included for preparing a schedule of activities (i.e., chronogram) and a program budget.

The Third Chapter ("Evaluating the programme") considers what types of information are necessary for program evaluation and how means of collecting this information can be built into the program in order to provide for continuous monitoring of ongoing operations. Ultimately, program evaluation depends on the extent to which previously defined objectives and targets have been met.

Chapter Four ("Conducting a comprehensive programme review") contains a checklist for countries wishing to formally review the progress of their national CDD programs.

Although focused on CDD, the manual can easily be adapted for planning and evaluating other types of health interventions as well.

Copies are available in several languages, upon request, from WHO Headquarters and Regional Offices.

259. Anonymous, Management of the diarrheal diseases at the community level, *Unpublished Document*, Committee on International Nutrition Programs, National Research Council, National Academy Press, Washington, D.C., 1981, (22 pages).

This report reviewed two aspects of the management of acute diarrheal diseases, namely, ORT and continued feeding, and recommended that both be implemented at the community level. Citing exhaustive physiological and clinical research findings to date, the Committee endorsed the WHO-recommended ORS formula. The operational realities in delivering ORT favor the use of a single, universal formula as well, agreed the Committee. However, if distributing "complete formula" ORS packets is not feasible, the household use of simple salt/sugar (SSS) solutions for ORT is the next best alternative.

Advantages of pre-packaged ORS were cited: the inclusion of potassium and bicarbonate corrects hypokalemia and acidosis, measuring errors are minimized and the packets constitute a recognizable product which, if desired, can be promoted as a medicine. Packet distribution schemes, whether through the official health care system or through commercial channels, require suitable health education and monitoring and surveillance systems to be successful. Surveillance and education inputs are likewise required for ORT programs based on home-prepared SSS. The Committee suggested that a two-tiered village triage system might be feasible, one in which early home use of SSS is the first intervention. Referrals to the formal health care system, where treatment is based on the WHO-recommended complete formula, are possible for the few cases which don't adequately respond.

In considering the costs of packet-based distribution programs, the Committee pointed out that the investment may be offset considerably by decreased use of IV, antimicrobial and other expensive, non-specific therapies.

Recognizing the relationship between diarrheal disease and malnutrition, the Committee recommended continued feeding throughout the diarrheal episode. Diarrhea predisposes to malnutrition due to the combined effects of negative nitrogen balance, anorexia and the culturally determined withdrawal of food during the diarrheal episode. At all costs, urged the Committee, breastfeeding should be continued, both to assure that lactation is uninterrupted and because breastmilk provides sodium-free water to counteract the already minimal risk of hypernatremia. Feeding also increases net absorption in the small bowel. When feeding is discontinued, however, the bowel's ability to absorb glucose, salt, water and amino acids is rapidly diminished as may be disaccharidase activity. This sets the stage for a malabsorption syndrome, chronic diarrhea and deteriorating nutritional status.

The Committee concluded its recommendations by identifying research priorities. These included operational and evaluative studies on

the impacts, risks and costs of ORT programs; evaluation of educational techniques to promote the programs; culture-specific behavioral studies regarding diarrheal diseases and ORT; development of a simple quality control surveillance system; studies on community organization and the role of community health workers in ORT programs; definition of guidelines for unsupervised use of ORT; and quantitative guidelines for refeeding, including caloric goals and timetables for weight restoration.

260. Anonymous, Oral therapy for acute diarrhea, (editorial) *Lancet* 2:615-617, 1981.

One of a series of *Lancet* editorials on ORT, this article cited studies from Bangladesh, India and Egypt as proof that the potential health benefits of ORT are profound. The results of each study had shown dramatic decreases in diarrheal mortality where ORT has been made available on the village level.

The authors endorsed the WHO-recommended ORS formula, refuting the claims of some workers that the 90 mEq/l sodium concentration could lead to hypernatremia by citing the work of several investigators which has proved otherwise. On the contrary, the authors stated, lowering the sodium concentration to 60 mEq/l, as some have suggested, may entail a risk of prolonged hyponatremia. The success of the WHO-recommended formula, they felt, is due in part to the two-to-one regimen, in which one part of sodium-free water, or breastmilk, is administered to the patient for every two parts of ORT. The levels of both potassium and bicarbonate in the WHO-recommended formula were also endorsed and the possibilities of using sucrose, rice starches and glycine as ORS substrates were discussed.

Where health care infrastructures permit, the authors felt, use of prepackaged ORS is optimal. Where packet supply is problematic, simple salt/sugar solutions are the next best option. Experience has shown measuring accuracy in the home depends most on direct interaction between the health workers and the person who actually gives the treatment.

In addition to correcting and maintaining salt and water balance, the authors stated, ORT has important nutritional benefits in the child. Early initiation of ORT improves appetite and promotes early feeding. This is because mothers are encouraged to continue breastfeeding and to resume the child's regular diet as soon as possible. Numerous studies have shown, in fact, that continued feeding during diarrhea improves nutrition without increasing the severity or duration of the diarrheal episode. The authors called upon European and U.S. pediatricians, who continue a more traditional therapeutic approach—oral replacement of stool loss with low-sodium fluid, limited food intake during diarrhea, and more reliance on intravenous fluid in the moderately dehydrated child—to make more use of experience gained from ORT worldwide.

In closing, the authors identified several ORT-related issues still to be resolved. These included the feasibility of adding other substrates to ORS to increase absorption; the need for better quantitative guidelines for weight restoration and avoidance of milk intolerance; the elaboration of more culture-specific training materials for health workers and mothers; and the evaluation of the full impact of national ORT programs on morbidity and mortality.

Walker, S. H., Hypernatremia from oral electrolyte solutions in infantile diarrhea (letter), *N Eng J Med*, 304:1238, 1981.

Cleary, T. G., et al., The relationship of oral rehydration solution to hypernatremia in infantile diarrhea, *J Pediatr*, 99(5):739-741, 1981.

261. Levine, M. M., Oral therapy for diarrhoea: past, present and future (Editorial), *J Trop Med Hyg*, 84:185-187, 1981.

The author identified some of the key milestones in the development of ORT and highlighted several current issues regarding its use.

As early as the 1950's, Chilean pediatricians (Menenghello, et al.) had shown excellent clinical results rehydrating infants with a glucose/saline solution given by nasogastric tube. The

ORT provides an entry point for teaching mothers ways to prevent diarrhea. (Photo: D. Dowling, PAHO).

following decade, others elucidated the mechanism whereby glucose promotes the active absorption of sodium in the small intestine, even during severe cholera (Philips, Nalin, Pierce, et al.), reducing IV fluid needs by as much as 80%. In the 1970's, it was shown that ORT is efficacious in about 95% of all dehydrated cases, regardless of age or etiology (Hirschhorn, et al.). These findings provided the basis for development of the current WHO-recommended ORS formula.

Neither vomiting nor risk of hypernatremia are obstacles when ORT solutions are properly prepared and administered, stated the author. Recognizing that the sheer number of diarrheal episodes and often weak health care infrastructures in developing countries may limit impact when ORS packets are used, the author endorsed village-level programs to introduce the early use of simple salt/sugar solutions (SSS) to prevent dehydration from developing. Some methods, such as "pinch-and-scoop", may be inherently too variable to safely recommend, he felt, although other practical, reliable methods exist and need only to be carefully adapted to local customs and conditions. The risk of hypokalemia is one drawback to using SSS solutions, the author stated. Further studies are therefore needed to identify locally available potassium-rich foods which can be given as a supplement to home ORT when SSS solutions are used.

The author concluded with the hope that the 1980's will be the decade in which ORT will be applied dilligently and ubiquitously as a cornerstone of pediatric primary care.

262. Cutting, W.A.M., Management of gastroenteritis at home (letter), *Brit Med J* 283:1606, 1981.

The author commented on a recent retrospective study of 181 diarrheal case records in a British hospital (see abstract No. 222) which had shown British physicians often routinely overuse drugs and suspend feeding during diarrhea.

In an Edinburgh hospital, reported the au-

thor, not one of 181 children admitted for diarrhea had been treated with drugs, although at least 134 drugs had been prescribed for these cases prior to admission. Using glucose-electrolyte solution alone, 83% of the cases successfully recovered.

As elsewhere in the world, ORT should be the treatment of choice for diarrheal dehydration in England, the author stated.

263. Mahalanabis, D., et al., Oral rehydration therapy—Recent advances, *Wrld Hlth Forum*, 2(2):245-249, 1981.

The physiological and clinical rationale for ORT were briefly discussed and field experiences to date summarized in this concise review article. Reasons for the 90 mEq/l sodium concentration and the preferability of glucose over sucrose in the WHO-recommended ORS formula were presented. The WHO-recommended composition has been shown to be safe and effective in groups as dissimilar as Costa Rican neonates and Bangladeshi refugees, recounted the authors.

From the public health viewpoint there are manifold advantages to the use of ORT. To illustrate, a 70% decrease in IV fluid expense was reported by two Indian hospitals where ORT was put into routine use. One study in Bangladesh showed household use of ORT reduced health centre consultation rates by 29% and could be successfully performed by mothers without supervision in 85-90% of cases. The authors advanced a final justification for using the WHO-recommended ORS packets: they serve as an ideal vehicle for delivering health-related messages to mothers at their moment of greatest receptiveness.

Kleevens, J.W.L., Rice water for infant gastroenteritis (letter), *Lancet* 2:306, 1981.

264. Rohde, J. E., et al., Oral rehydration: technology and implementation, In: Jelliffee, D. B., et al., (eds.), *Advances in International Maternal and Child Health, Vol. 1*, New York, Oxford Univ Press, pp. 82-97, 1981.

In this comprehensive review the authors described the importance of diarrheal diseases, traced the development of ORT, presented guidelines for diarrheal case management and discussed the myriad operational issues relating to the widespread implementation of ORT.

The authors felt acute diarrheal dehydration can be viewed as a form of malnutrition—fluid-electrolyte malnutrition—which causes at least 6 million deaths annually worldwide.

The early studies leading to the adoption of the WHO-recommended ORS composition were summarized as were the practical aspects of case management. In essence, the discovery that a single ORS composition can lead to universal use of ORT represents the technical solution to an age-old problem, they stated; the remaining problems are largely programmatic.

Where "complete formula" ORS packets are not available, felt the authors, home SSS solutions present the next best alternative. Distilling their experiences promoting ORT in Indonesia, the authors felt the main obstacles to its successful implementation (such as standardization of local household measures, choosing the most appropriate technique for salt/sugar measurement and which local foods are best for supplementing the SSS solution), can only be resolved at the local level.

Highly descriptive, practical and written for the lay reader, this article is recommended for those wishing a concise but wide-ranging overview of ORT-related issues.

There are 60 references.

Clements, M. L., et al., Comparison of simple sugar/salt verus glucose/electrolyte oral rehydration solutions in infant diarrhoea, *J Trop Med Hyg* 84:189-194, 1981.

265. Hendrata, L., et al., Oral rehydration: Where do we go from here?, In: Jelliffe, D. B., et al., *Advances in International Maternal and Child Health, Vol 1*, New York, Oxford Univ. Press, pp. 98-104, 1981.

In this essay the authors proposed that a social marketing strategy be employed for promoting ORT. Traditional approaches to

health education, the authors reasoned, seek to change knowledge and perceptions in order to make them "true", assuming that desired behavioral change will follow as a logical consequence. An effective social marketing approach, on the other hand, is always based on the existing values, beliefs and practices of the potential consumer. Rather than challenging deeply held beliefs, the aim of social marketing is to seek behavioral change by riding on the concepts which already exist.

In the case of ORT, the prevailing cultural beliefs regarding diarrhea should first be examined. A "positioning strategy" can then be tested: the "product" to be marketed is *drinking* during diarrhea. Of secondary importance is the issue of *what* to drink. Once the notion of drinking becomes accepted, the authors felt, it is relatively easy to discuss what is the best drink in the circumstances. The marketing strategy should be aimed at maximizing coverage, even at a slight loss of effectiveness.

Citing experiences in Indonesia, the authors listed seven varying cultural beliefs regarding diarrhea and its treatment and proposed positioning strategies for each (e.g., "diarrhea is a 'hot' disease—drink something 'cold'"; "diarrhea is caused by an imbalance of life forces-restore balance by drinking"; "diarrhea is a cleansing of the body drink water, the cleansing element of the body").

Various techniques can be used to reach difference audiences. As an example of such a "comprehensive" strategy, the authors described a family planning effort on the Indonesian island of Bali. After five years, the authorities realized the classical, facility-based approach was not working. A new positioning strategy was therefore devised, one based on rising population density as a threat to community well-being. Preserving traditional village harmony was the theme. Mass media, local leaders and, most effectively, traditional village meetings of all male heads of households were some of the techniques used. User rates have since climbed from 20 to 60 percent, the authors reported.

If the social marketing approach can produce such dramatic changes in behavior as complex as fertility regulation, the authors reasoned, it should prove even more effective in introducing ORT.

266. Brotowasisto, Diarrheal disease control program in Indonesia: Its constraints and alternatives, In: Holme, F., et al., (eds.): *Acute Enteric Infections in Children. New Prospects for Treatment and Prevention*, Amsterdam, Elsevier/North-Holland Biomedical Press, pp. 395-403, 1981.

The author described the diarrheal disease control (CDD) program of Indonesia as an integral part of the National Health Program which is implemented through the existing health delivery system. From the operational standpoint, the program is under the direction of provincial and regency health services, is integrated with MCH, nutrition and family planning activities and is delivered through health centers.

The CDD program's main control strategy is based on the use of "Oralit", the Indonesian generic name for the locally-produced ORS, which closely resembles the WHO-recommended formula. Oralit packet production is centralized and packets are distributed through the existing system to hospitals, health centers and primary health care units. Oralit packets come in two sizes: a 200-ml size for home use a 1,000-ml size packet for hospitals.

The author identified several managerial, technical and social constraints which currently limit the CDD program's effectiveness. The existing health care delivery system covers only about 25% of the population. Secondly, the integration of health programs has created management problems due to overlapping budgets and activities. Current supplies of Oralit, moreover, cannot meet demand. Also, the product's shelf life is limited by the quality of ingredients, humidity and temperature. Commercially available Oralit is relatively expensive and the high cost, the author felt, limits its utilization. Rural Indonesian mothers commonly consider diarrhea a mild disease of little consequence, another factor the author felt limits Oralit use.

Breastfeeding has been shown to significantly reduce the risk of diarrhea. (Photo: M. McQuestion, PAHO/WHO).

The overall objectives of the CDD program are to get people to accept and practice ORT and to make Oralit available to the community at all times. However, full coverage cannot be assured under the existing health care system, so the use of simple sugar and salt (SSS) solutions on the household level is being considered as well. Results of field surveys indicate that mothers can be trained to prepare SSS, using a special measuring spoon called "the blue spoon", and can successfully treat their children at home. While the author recognized that Oralit is the most effective modality for treating diarrhea, he concluded that SSS can also be used as an early alternative and may provide a means of dramatically increasing the national CDD program's coverage.

Ashley, D.A.E., et al., Oral rehydration therapy in the management of acute gastroenteritis in children in Jamaica, In: Holmes, F., et al., (eds.): *Acute Enteric Infections in Children. New Prospects for Treatment and Prevention*, Amsterdam, Elsevier/North-Holland Biomedical Press, 389-394, 1981.

267. Cutting, W.A.M., et al., Homemade oral solutions for diarrhoea (letter), *Lancet* 1(8227):998, 1981.

Referring to studies in Jamaica and Bangladesh which produced conflicting results on the accuracy with which mothers prepare homemade simple salt/sugar (SSS) solutions, the authors asserted programs with simple, standardized messages and individualized training are most likely to succeed regardless of whether spoons or "pinch-and-scoop" techniques are used. The authors questioned the recommendation made by the Jamaican investigators that local sugar be carefully evaluated before use in home ORT, pointing out that the concentrations at which glucose facilitates sodium absorption range from 14 to 140 mmol/l.

Unfortunately, such flexibility is not the rule with sodium. In preparing SSS solutions, therefore, correctly measuring salt is even more critical than sugar.

Harland, P.S.E.G., et al., Composition of oral solutions prepared by Jamaican mothers for treatment of diarrhoea, *Lancet* 1:600-601, 1981.

268. Nalin, D., Oral rehydration solution (letter), *Trans Roy Soc Trop Med Hyg* 76(2):277-278, 1982.

The author referred to an earlier article in the same journal by W.A.M. Cutting, et al., (see abstract No. 164), which described the 2:1 ORT regimen recommended by the author. He wished to clarify that the WHO-recommended ORT solution should not be diluted with 50% additional water. Rather, the 2:1 regimen calls for giving undiluted ORT solution to moderately dehydrated children, ages 3-15 months, at the ratio of 8 ounces per hour for two consecutive hours followed by 8 ounces of plain water the third hour. (Infants under 3 months of age receive the same regimen, but only 4 ounces per hour). The regimen should be repeated, stated the author, until signs of dehydration have disappeared, after which milk feeds can be resumed.

Intestinal absorption of glucose, electrolytes and water takes place relatively rapidly. However, the rate of absorption is much decreased if the glucose concentration falls below 2%.

Whether by administering free water too quickly after the ORT solution is given or by adding more water to the solution before it is administered, dilution of the ORT solution is to be avoided.

269. Santosham, M., et al., Storing oral rehydration solution (letter), *Lancet* (1):797, 1982.

Responding to concerns that bicarbonate may be lost when ORT solution is stored for 24 hours or more, the authors performed an experiment to assess the effects of bacterial contamination on the stability of bicarbonate in ORT solution.

Twenty one-liter batches of WHO-recommended ORS solution were prepared and ran-

domized into 4 groups. Group A was stored at room temperature (26° Centigrade), Group B was stored at 4°C, Group C was contaminated with 1,000 colonies of *E. coli* and stored at room temperature and Group D was similarly contaminated and stored at 4°C. Samples of each were tested for total CO_2 (using the TCO_2 Analyzer 446, Instrumentation Laboratories) at 24, 48, 72, 96, 156 and 168 hours, while levels of bacterial contamination were assessed for each at 24 hours.

No differences were found in mean CO_2 concentrations among the 4 groups. *E. coli* was not detectable 24 hours after constitution in Group A, B or D samples, while all Group C samples showed contamination (mean 1.1×10^6 colony forming units, range 1.4×10^5 to 2.8×10^6).

The authors concluded that CO_2 remains for at least a week in prepared ORT solution, whether refrigerated or not and regardless of bacterial contamination. They also observed that the solution does not support bacterial growth when refrigerated at 4°C.

270. Snyder, J. D., From pedialyte to popsicles: A look at oral rehydration therapy used in the United States and Canada, *Am J Clin Nut* 35:157-161, 1982.

Although the method has been widely accepted in the developing world, debate continues over the role of ORT and, more specifically, the safety of the WHO-recommended ORS composition in treating children in developed countries, who are generally well-nourished and are often fed high-solute diets.

To better assess the opinions of North American physicians, the author mailed a one-page questionnaire on ORT to the chairpersons of departments of pediatrics of 142 medical colleges. Ninety percent (128/142) of the institutions responded. The results indicated that each uses some type of oral rehydration fluid for treating children with diarrheal dehydration. Commercial sugar/electrolyte solutions are most commonly used (89%), followed by clear liquids (78%) and fruit juices (58%). The compositions of solutions used varied considerably in sugar and electrolyte concentrations and in resulting osmolarity (nearly all were hypertonic). The highest sodium concentration reported was 90 mEq/l (the WHO-recommended value); only 3 of the 142 institutions used these fluids.

Instructions to parents were provided most often (80%) in the form of recommendations given by the doctor or nurse, although many institutions (47%) provided some form of written oral therapy instructions. However, only 29% of the institutions based their plan of therapy on a specific written protocol.

The use of ORT was inversely related to the degree of dehydration. For children with 0-4% dehydration 92% of the institutions routinely used ORT for outpatients, 43% for inpatients. Thirty percent of moderately dehydrated (5-7%) children routinely received ORT in outpatient services compared to 35% of inpatients. Only 7% of the institutions gave ORT in severely dehydrated (8-10%) cases.

The author concluded that the concept of ORT is universally accepted but that fluids with widely differing compositions and concentrations are routinely used. Although this variation may be acceptable for treating mild dehydration, more specific, optimal ORS compositions are necessary before routine use of ORT will be accepted by North American clinicans for treating moderate to severe dehydration.

271. Posada, G., et al., Causas de reingreso en un servicio de rehidratación oral (Causes of readmission to an oral rehydration ward), *Bol Med Hosp Infant Mex* 39(2):93-98, 1982.

The authors analyzed clinical and socioeconomic characteristics of 50 children who had initially presented to hospital with acute diarrhea, had been orally rehydrated and sent home for continued home ORT and were later readmitted to the same hospital for additional treatment.

Between February-June, 1980, the authors treated 1,128 children presenting with acute diarrhea to the emergency room of the National Children's Hospital in San José, Costa Rica. While in hospital, the children's mothers

were given intensive health education which included recognition of the signs of dehydration, preparation and administration of ORT, and causes of diarrhea and ways to prevent it. After initially rehydrating their children under medical supervision, the mothers were given two one-liter size WHO-recommended ORS packets, with an instructional pamphlet, for continued home ORT.

Based on the degree of initial dehydration and the intensity of the diarrhea, the authors explicitly asked more than half the mothers to bring their babies back to the hospital after 24-48 hours. The remaining mothers were advised to do so only if the dehydration worsened or if the diarrhea lasted seven days or more.

Fifty of the 1,128 (4.4%) brought their children back for a second consultation.

The authors then examined and treated these 50 children and compared their clinical findings to those of some 150 randomly selected diarrheal cases which had not returned a second time. In addition, they interviewed the mothers using a detailed questionnaire they had previously designed.

An average of 56 hours (range 4.5-260 hours) had elapsed between the time of initial discharge and readmission. Continued or worsening diarrhea, reappearance of signs of dehydration and vomiting were the principal reasons given by the 50 mothers for returning to the hospital. Thirty percent of the returning mothers had been explicitly asked to do so while the rest returned of their own volition.

The mean age of the 150 comparison group children was 10.7 months (range 2 weeks-67 months), compared to 6.9 months (range 3 weeks-22 months) in the group later readmitted. Upon first admission, the groups were similar with respect to nutritional status and severity of diarrhea (i.e., number of stools per hour); however, at that time the mean degree of dehydration among those who later returned was 7.3%, compared to 4.3% for the controls.

In the 50 children who later returned, initial rehydration was achieved after an average of 10.5 hours (comparable data were not given for comparison group children). At initial discharge from hospital the authors had evaluated the intensity of diarrhea in 21 (42%) of these 50 cases as mild, (less than 6 stools per 24 hours); 28 (56%) moderate (6-12 stools/24 hours) and 1 (12%) severe (more than 12 stools/24 hours). At readmission, however, the values were 13 (26%) mild, 12 (24%) moderate and 25 (50%) severe. Signs of dehydration were found in 44 (88%) of the 50 returning patients. All responded to subsequent hospital treatment.

The results of the interviews showed 90% of the returning mothers lived within a ten-kilometer radius of the hospital, compared to 98.7% of the comparison group mothers. Forty-nine of the 50 (98%) returning mothers reported having received instructions on home ORT during their first visit. The authors determined that 43 (86%) of them clearly understood the information and that 40 (80%) had correctly followed the instructions. Thirty-nine (78%) reported the two ORS packets they had been given provided sufficient fluid for home treatment while 9 (18%) felt the quantity was insufficient and 2 (4%) claimed not to have received any packets. The mean age of the returning mothers was 23.7 years. Although indications were that all came from low socioeconomic levels, only one mother was illiterate. Forty-four percent of the returning mothers reported having breastfed their children, in the majority of cases for less than 2 months.

The data showed that, in broad terms, the fifty mothers seeking a second consultation had good reason to do so. However, no data were given with which to compare these mothers to those who did not return. The returning cases appeared to be younger and their diarrheal episodes were more problematic from the onset compared to the 150 who did not return for a second consultation.

The authors considered the readmission rate to be low and identified improved health education, more generous supply of ORS, longer initial hospitalization of problem cases, promotion of breastfeeding and home visits as possible ways to reduce the rate even further.

Methodologically, the study could have been

strengthened had the comparison group been followed up after initial discharge.

272. Anonymous, Oral rehydration: Is it as good as parenteral therapy? (Editorial) *N Eng J Med* 306(18):1103-1104, 1982.

The author pointed out the immense, global health problem posed by diarrheal diseases and summarized the key research breakthroughs that have led to the refinement of ORT, ".... one of the most dramatic and rapid applications of a basic scientific observation to clinical medicine". Promoting ORT, the author continued, is now the major task of the global WHO Programme for the Control of Diarrhoeal Diseases (CDD).

Nevertheless, the author noted, in certain parts of the world CDD Programme workers have found a major impediment to both ORT and improved dietary management during diarrhea has been Western-trained pediatricians who are reluctant to accept the new approach.

Citing the findings of Santosham, et al. (see abstract No. 159), which proved the WHO-recommended ORS formula was just as safe and effective in well-nourished, Western hemisphere children as in less fortunate developing world children, the author urged that ORT be accepted not only as an equal but perhaps as a superior means of treating diarrheal dehyration, whether in sophisticated, sanitized Western-world facilities or in rural Bangladesh.

Finberg, L., et al., Oral rehydration for diarrhoea (Editorial), *J Pediatr* 101(4):497-499, 1982.

273. Yankauer, A., Oral rehydration and social change; the control of diarrhoeal diseases in the Third World (Editorial). *Am J Pub Hlth*, 72(10):1105-1106, 1982.

The author traced the development of ORT with special reference to early experiences with the method in Latin America. Although ORT had been shown to be efficacious in Mexico and Venezuela as early as 1964, nearly 15 years elapsed before the WHO launched its Programme for the Control of Diarrhoeal Diseases (CDD) in 1978.

As was the case with John Snow and the celebrated Broad Street pump, public health applications of new research findings are often slow to ensue, stated the author, largely due to the resistance of medical "experts" to new ideas. Today, he noted, such resistance to ORT still lingers, particularly among Western trained pediatricians.

Referring to a study in Bangladesh (see abstract No. 227) which demonstrated use of clinic-based ORT is inversely related to distance from treatment centers, the author concurred with the WHO-recommended strategy of promoting home use of ORT. Public health programs to bring this about, the author concluded, will require substantial changes in the *status quo*, both with regard to medical beliefs and practices and in the allocation of scarce health resources.

274. Sack, D. A., Treatment of acute diarrhea with oral rehydration solution, *Drugs*, 23:150-157, 1982.

Writing to a predominantly developed world audience, the author reviewed various aspects of ORT with emphasis on case management techniques. The author explained that even through diarrhea causes hypersecretion of the mucosal cells of the small intestine, the glucose-mediated active transport mechanism by which sodium and water are absorbed remains intact. This provides the physiological basis for ORT. Net absorption is maximized when an isotonic oral solution with approximately the same molar concentration of sodium and glucose is given. Citing numerous studies, the author considered the WHO-recommended ORS formula to be optimal.

After presenting the most common clinical signs, the author outlined a simple means of assessing the degree of dehydration and calculating the amount of oral fluid to be given. Most cases, he stated, require only ORT and

A traditional healer in Northeast Brazil serves as the village ORT provider.
(Photo: D. Shields, U. Va. Medical School)

continued feeding. Antibiotics should be used only when *shigellae*, *campylobacter*, amoebiasis or cholera can be differentially diagnosed.

The importance of instructing the patient or parent was underlined. At a minimum, when leaving the clinic they should understand how to prepare and administer ORT; should realize that the diarrhea may continue for some time and that ORT is not intended to stop it; and should know to return if dehydration recurs, if other complications arise or if the diarrhea lasts longer than five days.

Although especially relevant to developing countries, concluded the author, use or ORT should also be encouraged in developed countries, where it should largely replace IV therapy for treating diarrheal dehydration.

275. Clements, M. L., Oral rehydration therapy, In: "*New Developments in Tropical Medicine*," National Council for International Health, 2121 Virginia Ave NW, Washington, D.C. 20037, USA, pp. 63-68, 1982.

In this article the author reviewed both clinical and public health aspects of diarrheal diseases and ORT. To treat the 10% of all diarrheal cases which lead to dehydration, the author endorsed ORT using the WHO-recommended ORS formula. The contention that the 90 mEq/l concentration of sodium predisposes to hypernatremia, stated the author, has been soundly refuted in numerous studies.

A simplified ORT regimen, based on rapid clinical assessment of the degree of dehydration, was presented. The author stressed the importance of resuming dietary intake as soon as possible after initial rehydration for the following reasons: 1) caloric intake has most likely been decreased due to anorexia or to deliberate withholding of food; 2) vomiting and diarrhea themselves cause increased caloric loss; 3) fever increases catabolism; 4) regardless of etiology, malabsorption in the small intestine may linger for 2-6 weeks after the episode.

Because the problem of childhood diarrhea is most acute in populations least served by health facilities, the author emphasized the importance of training both peripheral health workers and family members, both in ORT and in means of preventing diarrhea. Simple educational materials, such as those developed by WHO using a leaky pot as an analogy for diarrheal dehydration, must be adapted and widely disseminated. However, numerous studies have shown that materials alone cannot accomplish the task. In training health workers and on the primary health care level, there can be no substitute for repeated face-to-face encounters and at least minimal supervision, stressed the author.

The author expressed her preference that, in the village setting, the "complete" WHO-recommended ORS formula be used wherever possible. Where packet supply is not feasible, home-mixing of simple salt/sugar solutions, she felt, is the next best alternative.

Although prevention of diarrheal diseases may be a long-term problem, the author concluded that ORT is an important, highly feasible control measure that should be implemented immediately at all levels of health care.

Dugdale, A., et al., Refeeding after acute gastroenteritis: a controlled study. *Arch Dis Child*, 57:76-78, 1982.

Soeprapto, et al., Feeding children with diarrhea, *Trop Ped Env Chld Hlth*, 25(4):97-100, 1982.

276. Hirschhorn, N., Oral rehydration therapy for diarrhoea in children—A basic primer, *Nutr Rev* 40(4):97-104, 1982.

The author, a noted authority on ORT, presented a concise overview of current ORT-related issues in this thoughtful article.

The historical development and physiological rationale for ORT were summarized and the author endorsed the WHO-recommended ORS composition for use in all types of diarrhea.

The author summarized the findings of six clinical studies that conclusively show ORT is highly effective in adults and children, including neonates; in severely dehydrated (hyponatremic or hypernatremic) patients; in malnour-

ished as well as eutrophic children; and in diarrheas of all known etiologies.

Special attention was focused on the nutrition aspects of acute diarrhea, the need to continue or increase food intake during diarrhea and on the positive nutritional impacts of ORT programs on nutritional status.

Pointing out that access to formal health care systems in developing countries may be only about 10-15% among the predominantly rural populations most in need of ORT, the author identified various alternatives for community-based ORT delivery schemes. Experience to date has shown that careful efforts to educate health workers and families on ORT have led to quick acceptance of the method. Determining optional ORT delivery strategies, concluded the author, could also lead to improvements in other areas of health care delivery.

The article contains 24 key references.

277. Booth, I. W., et al., Oral rehydration therapy: An issue of growing controversy, *J Trop Pediatr* 28, 116-123, 1982.

In this concise, thoughtful review article, the authors summarized the results of numerous key studies and pinpointed several issues of current controversy regarding ORT.

The physiological and biochemical details of glucose-facilitated sodium and water absorption in the small intestine were elegantly summarized. The authors averred that the elucidation of this mechanism probably represents the single most important physiological advance with respect to ORT.

The varying pathophysiological and epidemiological aspects of cholera, *E. coli* and viral diarrheas were described. Comparing stool electrolyte losses and plasma electrolyte disturbances measured by numerous investigators around the world, the authors concluded wide variations exist and that they are probably due to such factors as pathogenicity, climate, age and feeding patterns.

Against this backdrop, they stated, the opposing forces of expediency (represented by the WHO recommendation that a single, universal ORS composition be used) and individualized therapy must be evaluated.

Tracing the development of ORT from its initial success in treating adult cholera to the demostration that it was equally effective in pediatric diarrhea regardless of etiology, the authors highlighted the evidence for and against the use of a single, "high sodium" ORT solution.

Although few dispute the WHO-recommended ORS composition has posited stunning success in developing countries, some experts fear its high sodium (90 mEq/l) concentration may induce hypernatremia in children in the developed world. In the absence of a definitive trial of the WHO-recommended ORS composition among developed world children, stated the authors, pediatricians treating these populations would be well advised to employ ORT solutions containing 25-50 mmol/l Na^+.

Reviewing findings with regard to the potassium content of ORT solutions, the authors cited conflicting results but did not recommend an optimal potassium concentration.

There are equally effective and possibly superior carbohydrate substitutes for glucose in ORT solutions, summarized the authors. Such alternatives include sucrose, starch, rice powder and rice water. Glucose, they felt, should not automatically be preferred; depending on local availability, one or more of the alternatives may be more suitable.

Although ORT certainly has indirect positive impacts on nutritional status, the question of whether ORT *per se* directly ameliorates malnutrition has not been entirely resolved, felt the authors. The rapid restoration of feeding during diarrhea, they observed, may be a much more critical factor.

The authors concluded by stating laboratory and field workers involved with ORT can feel justly proud for what has been achieved over the past 15 years. The success of ORT, however, should not blind us to the fact that much of the world's population lives beyond the reach of clean water, efficient sanitation and adequate food and that many of these problems

are political and economical in nature. The specific controversies regarding ORT, they felt, will surely be resolved through compromise and, in any case, much work in the field remains to be done.

The article is exhaustively documented with 63 references cited.

As an editorial aside, this article was published prior to another study, which showed the WHO-recommended ORT solution (90 mmol/l Na^+) was as safe as one containing 50 mmol/l of sodium among well-nourished "developed world" children with acute diarrhea (see abstract No. 159).

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