Several important developments have been made in the field of management of diarrhea in children as a result of research done in India and globally. It is important to take follow-up steps to ensure that the benefits of new knowledge reach affected children in India and at the same time ensure that new products are not inappropriately used.

The Indian Academy of Pediatrics Committee For Framing Guidelines On The Management Of Diarrhea In Children (members listed in Annexure 1) convened a meeting at the All India Institute of Medical Sciences, New Delhi, to revise the guidelines for management of diarrhea in children. The focus of this review was oral rehydration solutions, zinc and probiotics in acute diarrhea, drug treatment of dysentery, and management of diarrhea in the young infant and severely malnourished subjects.

Reduced osmolarity ORS in acute diarrhea

The current standard WHO ORS has a sodium concentration of 90 mEq/L (glucose 110 mmol/L, osmolarity 311 mOsm/L), which corresponds to the stool electrolyte composition in toxin-mediated diarrhea. However, it has worked well even in young children with non-cholera diarrhea when used according to the recommended guidelines with ready access to plain water during oral rehydration.

Several considerations lead to the clinical evaluation of reduced osmolarity oral rehydration salts solutions and they have been examined by WHO(1). Initially, one main concern was the potential risk of hypernatremia with standard WHO-ORS in children with non-cholera diarrhea. There was also the recognition that the standard WHO-ORS may provide too much sodium to edematous children. In later years, there were reports of recurrent dehydration in young infants treated with standard WHO-ORS on a weight to volume basis as replacement of ongoing stool losses that was promptly reversed when...
patients were kept nil orally and on intravenous fluid regimens. Finally, laboratory experiments showed that reduced osmolarity solutions (sodium 60 mmol/L, glucose 80-120 mmol/L, osmolarity 240 mOsmol/L) promote water and sodium absorption more efficiently than the WHO-ORS.

**Review of clinical trials of reduced osmolarity oral rehydration salts solutions**

*Children with acute non-cholera diarrhea*

A recently published meta-analysis of trials of reduced osmolarity ORS was reviewed(2). The meta-analysis included all randomized trials in which a reduced osmolarity ORS containing glucose, maltodextrin or sucrose (total osmolarity 210-268 mOsmol/L) and a sodium concentration ranging from 50 to 75 mEq/L was used. These studies were conducted mainly in developing countries and included well-nourished and malnourished children aged 1 month to 5 years with acute diarrhea of duration <7 days with dehydration. Four of the studies were done in India, two as part of large multi-center trials.

Results of the meta-analysis were as follows: *(i)* Use of reduced osmolarity ORS was associated with a significant 39% reduction in need for IVF; need for IVF was considered an important outcome measure as in many peripheral health facilities, where IV therapy is often unavailable, reducing the need for unscheduled IV therapy would reduce the risk of death from dehydration, *(ii)* 19% reduction in stool output and *(iii)* 29% lower incidence of vomiting *(Table I)*. The incidence of hyponatremia (serum sodium <130 mEq/L) at 24 hours, evaluated in 3 clinical trials was greater among children given reduced osmolarity ORS. 51 children treated with reduced osmolarity ORS and 36 children treated with standard WHO ORS developed hyponatremia *(OR = 1.45, 95% CI: 0.93 to 2.26)*. None of these children were symptomatic. This difference was not statistically significant but could be as much as twice that associated with standard WHO ORS.

**Analysis of ORS efficacy stratified for sodium content**

An analysis of all studies was conducted (1), stratifying them according to the sodium content of the reduced osmolarity ORS: *(i)* reduced osmolarity ORS containing less than 75 mEq/L of sodium (range 60 to 70 mEq/L), and *(ii)* reduced osmolarity ORS containing exactly 75 mEq/L of sodium. *Table II* shows the comparison of each of the two types of reduced osmolarity ORS with standard WHO

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**TABLE I**—Summary of The Results of the Published Meta-Analysis of All Randomized Clinical Trials Comparing Reduced Osmolarity ORS With Standard WHO ORS in Children With Acute Non-Cholera Diarrhea

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies reporting</th>
<th>Reduction in odds (95%CI) for children receiving reduced osmolarity ORS when compared to those receiving standard WHO ORS (311 mosmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unscheduled IV</td>
<td>9</td>
<td>39% (19%, 53%)</td>
</tr>
<tr>
<td>Stool output</td>
<td>12</td>
<td>19% (12%, 26%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6</td>
<td>29% (8%, 45%)</td>
</tr>
</tbody>
</table>

Adapted from reference 1 and 2
ORS and not a direct comparison with each other. ORS solution with a sodium concentration of 75 mEq/L and sodium concentration of less than 75 mEq/L are both more effective than standard WHO ORS with regard to need for unscheduled IV therapy and occurrence of vomiting and that the incidence of hyponatremia, while not significantly higher than for standard WHO ORS, could be up to double its incidence. Although the effect size suggests a trend that is consistent with greater reduction in stool output in the ORS with sodium concentration of less than 75 mEq/L, the test for interaction could not differentiate between the efficacy of ORS solution with a sodium concentration of 75 mEq/L and and that of ORS solution containing sodium less than 75 mEq/L, even on unidirectional tests of significance.

**Children with cholera diarrhea**

In the pooled data (1) of all studies with cholera diarrhea in children there was a small, but statistically significant reduction, in mean serum sodium at 24 hours in patients receiving reduced osmolarity ORS (sodium 70-75 mEq/L, glucose 75-90 mmol/L, osmolarity 245-268 mOsm/L) when compared with those given standard WHO ORS [(mean difference 0.8 mEq/L, 95% CI: 0.6 to 1.0). The children receiving reduced osmolarity ORS did not have a higher risk, than those receiving standard WHO ORS, of developing hyponatremia (serum sodium <130 mEq/L) at 24 hours (RR = 1.8, 95% CI: 0.9 to 3.2), but a possible doubling of the incidence cannot be ruled out based on the confidence intervals. None of these children with hyponatremia were symptomatic. Stool output at 24-hours was not different between treatment groups in children with cholera in the multicentre study (sodium 75 mEq/L, glucose 75 mmol/L, osmolarity 245 mOsm/L). In the other two studies, however, stool output was reduced by

<table>
<thead>
<tr>
<th>Table II—Pooled Analysis Stratified According to the Sodium Content of the Reduced Osmolarity ORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced OSM ORS with &lt; 75 mEq/L of sodium in comparison to standard WHO ORS</td>
</tr>
<tr>
<td>Odds ratio (95% CI) for unscheduled IV therapy for patients given RED OSM ORS when compared to those given standard WHO ORS</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Ratio of geometric means (95%CI) for stool output in children given RED OSM ORS when compared to those given standard WHO ORS</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Odds ratio (95%CI) for vomiting for patients given RED OSM ORS when compared to those given standard WHO ORS</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Odds ratio (95%CI) for hyponatremia (&lt;130 mEq/L) for patients given RED OSM ORS when compared to those given standard WHO ORS</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Reproduced from Reference 1
about 30% in children with cholera who were treated with reduced osmolarity ORS.

Reduced osmolarity ORS in adults with cholera

The combined analysis of three studies(1) that compared the efficacy and safety of reduced osmolarity ORS (osmolarity 245-249 mOsm/L) to that of standard WHO ORS in adults with cholera showed a minimal, and statistically insignificant, mean reduction of 0.5 ml/kg (95% CI: –14.6 to +15.6) in stool output during the first 24 hours among patients given reduced osmolarity ORS. A small, but statistically significant reduction in mean serum sodium of 1.3 mEq/L (95% CI: 0.3 to 2.3) was observed at 24-hours in patients treated with reduced osmolarity ORS when compared to those given standard WHO ORS. None of these patients who developed hyponatremia became symptomatic.

Recommendations by the WHO Task Force, New York, July 2001

The WHO Meeting of Experts(1) concluded that there are programmatic and logistic advantages of using a single solution around the world for all causes of diarrhea in all ages. After reviewing the data the group of experts proposed that reduced osmolarity ORS with 75 mEq/L of sodium and 75 mmol/L of glucose is effective in adults and children with cholera and that reduced osmolarity ORS solution with 60 mEq/L of sodium does not seem to be significantly better than reduced osmolarity ORS solution containing 75 mEq/L of sodium. They concluded that safety data in patients with cholera, while limited, are reassuring.

The WHO Meeting of Experts(1) further recommended that this formulation falls within the ranges defined by the WHO’s Program for the Control of Diarrheal Diseases (CDD) in March 1992 for a safe and efficacious oral rehydration solution, which, therefore, remain unchanged. The recommended ranges were that the total substance concentration (including that contributed by glucose) should be within the range 200-311 mmol/L. The individual substance concentration of glucose should at least equal that of sodium, but should not exceed 111 mmol/L and that of sodium should be within the range of 60-90 mmol/L. The concentrations of potassium, citrate and chloride should be within the range of 15-25 mmol/L, 8-12 mmol/L and 50-80 mmol/L respectively as shown below (1).

Recommendations of the IAP National Task Force for use of ORS in diarrhea, August 18-19, 2003

1. All doctors should prescribe ORS for all ages in all types of diarrhea.
2. The group noted that the new improved universal ORS recommended by the WHO containing sodium 75 mmol/L and glucose 75 mmol/L, osmolarity 245 mOsmol/L is acceptable for all ages and may be made freely available by the Government. However it was proposed that a pediatric ORS containing sodium 60 mmol/L, glucose 84 mmol/L, osmolarity 224

(1) WHO recommended range for safe and efficacious oral rehydration solution

The total substance concentration should be within the range 200-311 mmol/L (including that contributed by glucose).

The individual substance concentration of:

- Glucose should be equal to or less than that of sodium, but should not exceed 111 mmol/L.
- Sodium should be within the range of 60-90 mmol/L.
- Potassium should be within the range of 15-25 mmol/L.
- Citrate should be within the range 8-12 mmol/L.
- Chloride should be within the range 50-80 mmol/L.
mOsmol/L is the most suitable solution for children and the industry should be encouraged to produce such a formulation.

3. The current formulations ORS A and ORS citrate allowed in the Indian Pharmacopia, 1996\(^2\) should no longer be used and only the above recommended formulations be in the market. Consideration should be given to a different color code for the two formulations so that the formulation containing sodium 60 mmol/L, glucose 84 mmol/L, osmolarity 224 mOsmol/L is identified as more suitable for children. This can be further symbolized by sporting a child’s picture.

4. The powder packet to make 1 liter of solution should be continued. Since mothers tend to use ORS a glass at a time, a measuring device should be included inside to measure the required amount of powder accurately for 200 ml of fluid.

5. The group was deeply concerned that ORS was not available free of cost at public institutions. It recommended that measures should be taken by the Government to improve its availability and reduce its cost.

6. The group did not currently recommend marketing of ORS with additives (probiotics, minerals). They should only be permitted after demonstrating benefit in studies carried out in Indian patients as breastfeeding rates, dietary habits and intestinal flora varies from European and North American children.

**Zinc in the Treatment of Acute Diarrhea**

The rationale for use of specific nutrients as treatment of acute diarrhea is based on their effects on immune function or on intestinal structure or function and on the epithelial recovery process during diarrhea.

Zinc deficiency has been found to be widespread among children in developing countries, and occurs in most of Latin America, Africa, the Middle East and South Asia. Zinc has been identified to play a critical role in metallo-enzymes, polyribosomes, the cell membrane, and cellular function, leading to the belief that it also plays a central role in cellular growth and in the function of the immune system. Intestinal zinc losses during diarrhea aggravate pre-existing zinc deficiency. Convincing evidence for its clinical importance has come from recent randomized controlled trials of zinc during acute diarrhea.

**Clinical efficacy of zinc as an adjunct to oral rehydration therapy in acute diarrhea**

The results of pooled analyses\(^3\) of zinc treatment trials in children with acute diarrhea and the findings of subsequent studies are summarized in *Table III*. The main features of these trials include the randomized placebo controlled design subjects’ aged between 6 months and 3 years, and daily elemental zinc dose ranging from 10 to 30 mg per day.

In the trials subjected to pooled analysis, zinc supplemented children had 16% faster recovery (95% CI 6% to 22%). Zinc treatment also resulted in a 20% reduction (95% CI –2% to 22%)
STATEMENT

TABLE III—Results of Pooled-Analysis and Subsequent Randomized Controlled Trials in Children with Acute Diarrhea Comparing Impact of Zinc with that of Placebo.

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of subjects</th>
<th>Effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of continuation of diarrhea</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled analysis (3)</td>
<td>1252/1194</td>
<td>0.85 (0.76 to 0.95)</td>
</tr>
<tr>
<td>Subsequent studies in South-East Asia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strand et al. (4)</td>
<td>442/449</td>
<td>0.79 (0.68 to 0.93)</td>
</tr>
<tr>
<td>Bahl et al. (5)</td>
<td>404/401</td>
<td>0.89 (0.80 to 0.99)</td>
</tr>
<tr>
<td>Bhatnagar et al. (6)</td>
<td>132/134</td>
<td>0.76 (0.59 to 0.97)</td>
</tr>
<tr>
<td>Diarrhea lasting &gt;7 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled analysis</td>
<td>1252/1194</td>
<td>0.78 (0.56 to 1.09)</td>
</tr>
<tr>
<td>Subsequent studies in South-East Asia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strand et al.</td>
<td>442/449</td>
<td>0.57 (0.38 to 0.86)</td>
</tr>
<tr>
<td>Bahl et al.</td>
<td>404/401</td>
<td>0.61 (0.33 to 1.12)</td>
</tr>
<tr>
<td>Bhatnagar et al.</td>
<td>132/134</td>
<td>0.09 (0.01 to 0.73)</td>
</tr>
<tr>
<td>Stool output</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roy et al. (7)</td>
<td>57/54</td>
<td>–91 g</td>
</tr>
<tr>
<td>Dutta et al. (8)</td>
<td>44/36</td>
<td>–900 g (–1200 to –590)</td>
</tr>
<tr>
<td>Bhatnagar et al.</td>
<td>132/134</td>
<td>0.69 g/kg (0.48, 0.99)</td>
</tr>
</tbody>
</table>

Reproduced from Reference 1.

to 38%) in the odds of acute episodes lasting >7 days. The findings of the subsequent trials are consistent with the conclusions of the meta-analysis. The study by Bhatnagar et al. is of interest as it was hospital based, involved cases of acute diarrhea with dehydration and measured impact on stool output. In the zinc treated children, the total stool output was reduced by 31% (95% CI 1% to 52%) than in the placebo group.

The effect of zinc did not vary significantly with age, or nutritional status assessed by anthropometry. The effects were not dependent upon the type of zinc salts: zinc sulfate, zinc acetate or zinc gluconate. The optimal dose is yet to be determined but there seems to be little gain in efficacy when the commonly used 20 mg daily dose of elemental zinc was increased to 30-40 mg daily. Majority of the studies so far were conducted in South East Asia, where zinc deficiency is common. Finally, there is relatively little data on children aged less than 6 months to allow any conclusions about efficacy in this age group.

Another study conducted in Bangladesh(9) used a cluster randomized design to evaluate the effect on mortality and morbidity of providing daily zinc for 14 days to children with diarrhea as part of the diarrhea treatment programme in the community. The intervention and the comparison clusters were both given ORS and advice on feeding during diarrhea. The children in the zinc cluster had a shorter duration (hazard ratio 0.76, 95%CI 0.65 to 0.90) and lower incidence of diarrhea (rate ratio 0.85, 95% CI 0.76 to 0.96) than children in the comparison group, lesser
admission to hospital of children with diarrhea (rate ratio 0.76; 95% CI 0.59 to 0.98), and lower mortality due to non injury deaths, notably diarrhea or pneumonia (rate ratio 0.49; 95% CI 0.25 to 0.94) in the zinc treated cluster. The data are consistent in showing a beneficial effect of zinc in acute diarrhea.

**Zinc fortified ORS**

The efficacy of 40mg elemental zinc mixed with a liter of standard WHO ORS solution was compared with ORS without zinc and with zinc syrup administered separately from ORS(5). While zinc-ORS was superior to ORS alone, it was less efficacious in reducing duration of the episode than zinc supplements given separately from the ORS solution. The data are currently too limited.

The therapeutic benefits in acute diarrhea may be attributed to effects of zinc on various components of the immune system and its direct gastrointestinal effects. Zinc deficiency is associated with lymphoid atrophy, decreased cutaneous delayed hypersensitivity responses, lower thymic hormone activity, a decreased number of antibody forming cells and impaired T killer cell activity. Zinc deficiency has also been recently shown to effect the differentiation of CD4 response towards Th1 rather than Th2 pathway. The direct intestinal effects of zinc deficiency include decreased brush border activity, enhanced secretory response to cholera toxin, and altered intestinal permeability, which is reversed by supplementation.

**WHO constituted a Task Force consisting of a group of experts, which met in New Delhi in May 2001(10). They reviewed all the studies done till 2001 and concluded that:**

1. Zinc supplementation, given at a dose of about 2 RDA per day (10 to 20 mg per day) for 14 days, is efficacious in significantly reducing severity of diarrhea as well as duration of the episode.

2. They recommended effectiveness studies to assess different strategies for delivering zinc supplementation to children with diarrhea. These studies should investigate the feasibility, sustainability and cost effectiveness of different zinc delivery mechanisms, and monitor variables such as ORS solution consumption, antibiotic use rate, non diarrhea morbidity and overall mortality. They recommended further research to determine the effect of zinc supplementation in young infants.

**Recommendations of the IAP National Task Force for use of Zinc in Diarrhea, August 18-19, 2003**

1. Based on studies in India and other developing countries there is sufficient evidence to recommend zinc in the treatment of acute diarrhea as adjunct to oral rehydration. However, ORS remains the mainstay of therapy during acute diarrhea and zinc has an additional modest benefit in the reduction of stool volume and duration of diarrhea as an adjunct to ORS. Under all circum-stances, oral rehydration therapy must remain the main stay of treatment.

2. Treatment of acute diarrhea with zinc may have benefits on morbidity and mortality from other childhood infections and these should be further investigated.

3. A uniform dose of 20 mg of elemental zinc should be given during the period of diarrhea and for 7 days after cessation of diarrhea to children older than 3 months. Recommendations for below 3 months must await further research.

4. Based on all the studies the group proposed that zinc salts e.g., sulphate, gluconate or acetate may be recommended.
5. The industry should be encouraged to prepare a zinc formulation, which contains only zinc. Until these are available, the group proposed that formulations providing vitamins together with zinc may be used provided doses of former are within 1 RDA. Iron containing formulations should not be used with zinc as iron interferes with zinc absorption.

**Probiotics in the Treatment of Diarrhea**

Probiotics are nonpathogenic microorganisms that, when ingested exert a positive influence on the health or physiology of the host. They consist of either yeast or bacteria, predominantly Bifidobacterium and Lactobacillus. There is some preliminary evidence that ingestion of probiotics offers therapeutic benefit in the treatment of acute gastroenteritis in children. There are several possible mechanisms by which probiotics may exert their clinical effects. They can protect the intestine by competing with pathogens for attachment, strengthening tight junctions between enterocytes and enhancing the mucosal immune response to pathogens.

The group reviewed the available published randomized controlled studies on therapeutic benefits of probiotics in acute diarrhea. Most of the studies are small in size except for a single large multicentre trial and have been done in developed countries. None of the studies are from India. Some inferences are possible from the recently published meta-analyses.

**Results of meta-analysis of RCTs comparing probiotics with placebo in hospitalized children aged 1-48 months with diarrhea <7 days**

**Overall effect size of probiotics on diarrheal duration**

The first meta-analysis reported details of 10 treatment studies involving hospitalized children aged 1-48 months with diarrhea less than 7 days(11). All studies were conducted in developed countries from the West except for one from Thailand. The probiotics used were Lactobacillus GG, Lactobacillus reuteri, Saccharomyces boulardii, Streptococcus thermophilus lactis, Lactobacillus acidophilus and Lactobacillus bulgaricus. Rota-virus was the cause of diarrhea in more than 75% cases in studies from Finland, 28% in Russia, 48% in Thailand and 35% in the multicentre trial. Figure 1 summarizes the pooled effect of probiotics on duration of diarrhea in 7 trials involving 679 children. Probiotics significantly reduced the duration of diarrhea compared with the placebo by 21 hours (the pooled weighted mean difference assuming the random–effect model was –20.1 (95% CI –26.1, –14.2).

The second meta-analysis included most of the studies from the first analysis and one small study from Pakistan, which enrolled only 36 subjects(12). The results were consistent with the earlier meta-analysis reporting a reduction in diarrheal duration of 0.7 days (95% CI 0.3 to 1.2) in subjects who received lactobacillus compared with those who received the placebo.

**Effect size by type of Lactobacillus strains**

The first meta-analysis(11) further reported subgroup analysis for different probiotic strains (Fig. 1). Both LGG (pooled weighted mean difference assuming the random-effect model was –22 (95% CI –31.3, –21.8) and L. reuteri (pooled weighted mean difference assuming the random–effect model was –25.3 (95% CI 40.7 to –9.95) significantly reduced the duration of diarrhea as compared to the placebo. There was only one study with Lactobacillus acidophilus which reported a trend in the reduction of diarrheal
duration but this was not statistically significant –13.6 (95% CI –28 to 0.83) . Only LGG (data not shown) showed a consistent effect on the reduction in risk of diarrhea lasting >3 days (pooled estimate RR 0.4 95% CI 3 to 9).

Effect size by different types of Lactobacillus strains on types of diarrhea; viral or invasive

LGG and L. reuteri significantly reduced duration of diarrhea as compared with the placebo in 297 children with rotavirus diarrhea (weighted mean difference –24.8h (95% CI –31.8 to –17.9) while a similar effect was not seen in a small sub-group of subjects with invasive diarrhea 1.3h (95%CI –15.3 to 17.9) (Fig. 2).

Probiotics available in the Indian market

Lactobacillus GG is not available in the Indian market. The other commonly available probiotics are Lactic Acid bacillus, Lactobacillus acidophilus and Saccharomyces boulardii.

Recommendations of the IAP National Task Force for Use of Probiotics in Diarrhea, August 18-19, 2003

The group recommended that based on the above studies there is presently insufficient evidence to recommend probiotics in the treatment of acute diarrhea in our settings as:

1. Almost all the studies till now were done in developed countries except for one very small study from Pakistan. It may not be possible to extrapolate the findings of these

Fig. 1. Results of meta-analysis of RTCs comparing problems with placebo in hospitalized children aged 1-48 months with diarrhea <7 d. Adapted from Reference 12.
studies to our setting where the breast feeding rates are high and the microbial colonization of the gut is different.

2. The effect of probiotics is strain related and there is paucity of data to establish the efficacy of the probiotic species (namely *L. acidophilus*, Lactic Acid Bacteria) available in the Indian market. To recommend a particular species it will have to be first evaluated in randomized controlled trials in Indian children.

3. The earlier studies have documented a beneficial effect on rotavirus diarrhea which was present in >75% of cases in studies from the west. Rotavirus constitutes about 25% of diarrhea in hospitalized children and 15% in outpatient practice in India.

4. The primary outcome analyzed in all the studies was the duration of diarrhea. The more objective parameter of stool output was not evaluated.

### Treatment of Acute Diarrhea in the Young Infant (< 2 months)

The IAP group suggested that for assessment of diarrhea in young infants (up to age 2 months) recommendations by the Integrated Management of Neonatal and Childhood Illnesses, which is an adapted version of Integrated Management of Child-hood Illnesses for India, should be followed. The following additional recommendations were made:

1. Infants who are breastfed and have no dehydration do not need ORS and mothers should be advised to increase breast feeds. Young infants with dehydration should be treated as has been recommended for other children with dehydration.

2. Low osmolarity ORS (Pediatric ORS of glucose 80 mmol/L, sodium 60 mmol/L and osmolarity 224 mOsmol/L) should be used. If this ORS is not available the new WHO recommended ORS (glucose 75 mmol/L, sodium

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**Fig. 2. Efficacy of probiotics in reducing duration of rotavirus diarrhea. Adapted from Reference 12.**

Weighted mean difference (h) in duration of diarrhea between probiotics and placebo

- LGG–Lactobacilli GG; LR–Lactobacilli reuteri; LA–Lactobacillus WMD weighted mean difference

**Favours treatment**

- Finland, n=71 (LGG)
- Finland, n=39 (LGG)
- Multicentre, n=101 (LGG)
- Russia, n=40 (LR)
- Finland, n=46 (LR)
- Overall random

**Favours placebo**

- Multicentre n=53 invasive bacterial diarrhea (LGG)

**WMD 95% Confidence Interval**

-24.8 (-31.8, -17.9)

1.3 (-15.3, 17.9)

---
sodium 75 mmol/L and osmolarity 245 mOsmol/L) may be used. There is no need to
give extra plain water during rehydration
with ORS.

3. Third generation cephalosporins (intravenous ceftriaxone, cefotaxime, oral
cefixime) or intravenous ciprofloxacin
should be given for treatment of dysentery.
Where hospitalization is not possible, the
drugs can be used orally.

**Antibiotic Use in Acute Dysentery**

The issue of indiscriminate use of
antibiotics as well the increasing incidence of
antibiotic resistance is causing great concern.
The national diarrheal disease control program
currently recommends the use of
cotrimoxazole as the first line drug for the
management of acute bloody diarrhea.

Recent studies from India and other Asian,
as well as non-Asian developing nations have
shown high rates of resistance of shigella to
cotrimoxazole, ampicillin, chloramphenicol
and tetracyclines. Resistance rates to nalidixic
acid and quinolones are still low.

The following consensus was reached on the
issues of antibiotics:

1. Antibiotics are indicated only for acute
bloody diarrhea.

2. Antibiotics are not indicated for children
with acute diarrhea and no visible blood in
stools, with pus cells on stool microscopy
because of poor specificity of the test.
Routine stool examination or stool cultures
have no useful role in the management of
usual cases of acute bloody diarrhea.

3. Data on resistance of shigella and other
enteric pathogens to antibiotics is still limited
and is inadequate to make a uniform single
recommendation for the entire country.
Therefore, a concerted attempt needs to be
made to produce data regarding resistance
patterns from all over the country.

4. In areas where resistance rates to
cotrimoxazole exceed 30%, nalidixic acid
should be used as the first line drug for
the treatment of acute bloody diarrhea. In
case of poor response, norfloxacin,
ciprofloxacin or a third generation cephalo-
sporin must be used as second and third line
drugs.

5. In areas where such data does not exist or
rates of resistance have been demonstrated to
be lower than 30%, cotrimoxazole should be
the first line drug to manage acute bloody
diarrhea in all but high-risk cases; these
include infants who have not been breastfed
and severely malnourished children. In these
high-risk groups nalidixic acid or nor-
flaxacin should be the first line drug.

6. *Entamoeba histolytica* and helminths rarely
ever cause acute diarrhea in children.
Metronidazole and antihelmintics therefore
have no role in the routine management of
acute bloody diarrhea. Metronidazole
should be used when cases of acute
dysentery fail to respond to second line drugs
for dysentery such as norfloxacin or when a
stool examination has confirmed tropho-
zoites of *Entamoeba histolytica*.

7. Aminoglycosides like gentamicin and
amikacin have a poor spectrum of activity
against shigella species and therefore they
are ineffective in the management of acute
bloody diarrhea.

8. Antibiotic Use in Acute Dysentery (*Table
IV*).

**Antiemetics in Acute Diarrhea**

Vomiting is the commonest symptom
associated with acute diarrhea in children.
Often vomiting is particularly distressing to
the parents and therefore, antiemetics are
frequently prescribed. Concerns were raised
by members, on their use, in view of the
serious side effects these drugs can produce.
Low osmolarity ORS is expected to reduce the
incidence of vomiting in children with acute
gastroenteritis. Most children with vomiting can be managed with frequent small sips (5-10 ml) of ORS.

1. Antiemetics should be reserved for children in whom the vomiting is severe, recurrent and interferes with ORS intake.

2. Among the available antiemetics in use for children domperidone is the safest with no central nervous system side effects. Therefore, the group recommended a single dose of domperidone in children with severe vomiting. Continued use is not recommended. Domperidone should be used at a dose of 0.1-0.3 mg/kg/dose.

Management of a HIV Positive Patient with Acute Diarrhea

In children who are HIV positive or are immunocompromised due to other immunodeficiency states the management of acute diarrhea varies from the management in the immunocompetent. The causative organisms of diarrhea differ and the consequences of diarrhea are more severe in these children, particularly in those with Cryptosporidiosis(13). The primary determinant of the organisms and consequences is whether the child is receiving antiretroviral therapy and its intensity. A HIV positive child with acute diarrhea must have a stool culture, stool examined for ova, cysts and atypical protozoa (includes isospora, microspora and cryptospora on at least three occasions) and CD4 counts determined.

Children with optimum antiretroviral therapy and CD4 counts >500

Children on intense retroviral therapy and CD4 counts greater than 500 can be managed like normal children with diarrhea.

Children on inadequate or no antiretro-viral therapy or CD4 counts <500

1. Children with low CD4 counts (<500) or not on antiretroviral drugs and those children who have failed to respond to standard first line therapy of acute diarr-hea must be started on a combination of ciprofloxacin and metronidazole along with adequate amounts of ORS.

2. In cases where the response is poor despite 5-7 days of therapy repeat stool examination for ova, cysts and atypical protozoa (includes isospora, microspora and cryptospora on at least 3 occasions) should be done and oral cotrimoxazole should be added.

3. Children who do not respond to the above therapy by a week should be referred to a higher center for investigations and treatment. These include flexible sigmoidoscopy with a biopsy of mucosa for typical pathological changes as in cytomegalovirus and culture of rectal tissue for bacteria

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Drug</th>
<th>Dose/Kg body wt/ day</th>
<th>Divided doses</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nalidixic acid</td>
<td>55 mg/kg / day</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>Norfloxacin</td>
<td>20 mg /kg /day</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>Cotrimoxazole</td>
<td>5-8mg/kg/day</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>Ciprofloxacin</td>
<td>&lt; 20 kg: 125 mg</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 20 kg: 250 mg</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>
(especially campylobacter).

4. Oral Nitazoxanide (200 mg doses in children aged 4-11 years and 100-mg doses in children aged 1-3 years given in two divided doses for a total of three days), azithromycin (10 mg/kg/ once daily for 10 days), clarithromycin (15 mg/kg/day in two divided doses) or paramomycin can be tried for management of Cryptosporidium. Gancyclovir (12 mg/kg in two doses per day IV) is recommended for 6 weeks when pathological evidence of Cytomegalovirus infection is established.

Acknowledgements

We acknowledge Ministry of Health, Government of India and the WHO for providing technical support and CMS for their support for the meeting.

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