

## ***Recommendations***

### **IAP Guidelines 2006 on Management of Acute Diarrhea**

#### ***Writing Committee***

**Shinjini Bhatnagar\***

**Rakesh Lodha\***

**Panna Choudhury\*\***

**H.P.S. Sachdev\*\*\***

**Nitin Shah†**

**Sushma Narayan††**

**Nitya Wadhwa\***

**Preeti Makhija\***

**Keya Kunnekel\***

**Deepak Ugra‡**

#### **Background**

*IAP National Task Force for framing Guidelines on the Management of Diarrhea, August 2003.*

The Indian Academy of Pediatrics National Task Force for framing Guidelines on the Management of Diarrhea in children convened a meeting at the All India Institute of Medical Sciences under the chairmanship of Professor MK Bhan in August 2003, 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

\* All India Institute of Medical Sciences, New Delhi.

\*\* Maulana Azad Medical College and LNJP Hospital, New Delhi.

\*\*\* Sitaram Bhartiya Institute of Science and Research, New Delhi.

† National President IAP 2006

†† Kasturba Hospital, New Delhi.

‡ Secretary General IAP 2006.

*Correspondence to: Dr. Shinjini Bhatnagar, Center for Diarrheal Disease and Nutrition Research, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110 029,  
E-mail: shinjini\_bhatnagar@rediffmail.com.*

young infant and severely malnourished subjects. Several important developments had been made in the field of management of diarrhea in children as a result of research done in India and globally. The objective of this meeting was 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 meeting was convened to achieve a consensus on these issues based on careful review of the literature and keeping in mind the requirements of treatment of individual children as well as the needs of Diarrheal Diseases National Control Program. As individual studies are often too small to yield precise estimation of effect size, the recommendations were largely based on pooled data or meta-analysis of randomized placebo controlled trials. These recommendations were published in the official journal of the Academy, Indian Pediatrics in April 2004(1). Based on these recommendations some policy changes took place at the National level.

#### **IAP National Task Force for Framing Guidelines on the Management of Diarrhea, May 2006 held under IAP Action Plan 2006**

The Indian Academy of Pediatrics decided under IAP Action Plan 2006 in 2006 that it would further consolidate the above recommendations and take steps to increase awareness amongst pediatricians and other physicians for the revised guidelines for management of diarrhea. A core committee was formulated to review all the relevant literature based on pooled data or meta-analysis of randomized placebo controlled trials for oral rehydration solutions, zinc, probiotics and antisecretory drugs in acute diarrhea, drug treatment of dysentery, and management of severely malnourished subjects. New data, if any, published after the last consensus meeting was reviewed. The data was presented at a workshop to the members of the Task Force (Members are listed in annexure) at the IAP National Consensus

Meeting on Acute Diarrhea held on 6th May 2006. We summarize below the revised consensus recommendations (and wherever relevant the rationale) of the group. For sections on reduced osmolarity ORS and zinc the literature presented is similar to the earlier report with some minor modifications.

### A. 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(2). 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

#### (a) Children with acute non-cholera diarrhea

The published meta-analysis of trials of reduced osmolarity ORS was reviewed(3). It 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 L (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.

**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

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

Adapted from reference 2 and 3

### Analysis of ORS efficacy stratified for sodium content

An analysis of all studies was conducted (2), 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 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 that of ORS solution containing sodium less than 75 mEq/L, even on unidirectional tests of significance.

#### (b) Children with acute cholera diarrhea

In the pooled data(3) 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 multicenter

study (sodium 75 mEq/L, glucose 75 mmol/L, osmolarity 245mosm/L). In the other two studies, however, stool output was reduced by about 30% in children with cholera who were treated with reduced osmolarity ORS.

#### (c) Reduced osmolarity ORS in adults with cholera

The combined analysis of three studies(2) 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(2) 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(2) 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

**TABLE II**—Pooled Analysis Stratified According to the Sodium Content of the Reduced Osmolarity ORS

	Reduced OSM ORS with < 75 mEq/L of sodium in comparison to standard WHO ORS	Reduced OSM ORS with 75 mEq/L of sodium in comparison to standard WHO ORS
Odds ratio (95%CI) for unscheduled IV therapy for patients given RED OSM ORS when compared to those given standard WHO ORS	N = 4 studies N = 678 children 0.65 (0.41 to 1.00)	N = 4 studies N = 1175 children 0.56 (0.39 to 0.80)
Ratio of geometric means (95%CI) for stool output in children given RED OSM ORS when compared to those given standard WHO ORS	N = 8 studies N = 771 children 0.69 (0.49 to 0.98)	N = 4 studies N = 1049 children 0.88 (0.71 to 1.06)
Odds ratio (95%CI) for vomiting for patients given RED OSM ORS when compared to those given standard WHO ORS	N = 3 studies N = 270 children 0.49 (0.27 to 0.91)	N = 3 studies N = 1031 children 0.74 (0.58 to 0.95)
Odds ratio (95%CI) for hyponatremia (<130 mEq/L) for patients given RED OSM ORS when compared to those given standard WHO ORS	N = 3 studies N = 139 children Not analyzed	N = 3 studies N = 1120 children 1.45 (0.93 to 2.26)

Reproduced from reference 2.

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 in below<sup>(1)</sup>.

### Recommendations of the IAP National Task Force for use of ORS in diarrhea, August, 2003

The IAP National task Force<sup>(1)</sup> recommended that all doctors should prescribe ORS for all ages in

<sup>(1)</sup> 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 at least equal 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

all types of diarrhea. 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 was acceptable for all ages and measures should be taken by the Government to improve its availability and reduce its cost. However it was proposed that two formulations could be recommended so that the formulation containing sodium 60 mmol/L, glucose 84 mmol/L, osmolarity 224 mosmol/L is identified as more suitable for children. The group suggested that formulations ORS A and ORS citrate allowed in the Indian Pharmacopoeia, 1996<sup>(2)</sup>

<sup>(2)</sup>The two ORS formulations in the IP, 1996 are:

	ORS-A	ORS-citrate (the current WHO formulation)
Sodium chloride	3.5g	3.5g
Potassium chloride	1.5g	1.5g
Sodium citrate	2.9g	2.9g
Anhydrous dextrose	27g	20g
or		
Dextrose monohydrate	29.7	20g

ORS-A contains glucose in very high concentrations.

should no longer be used and only the above recommended formulations be in the market<sup>(3)</sup>. 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. The group did not recommend marketing of ORS with additives (probiotics, minerals). They should only be permitted after demonstrating benefit in studies carried out in Indian patients as breast-feeding rates, dietary patterns and etiology of diarrhea are different from the west.

### **Recommendations by the Government of India, 2004**

Based on the WHO/UNICEF and the IAP recommendations a National Expert Group formulated by the Ministry of Health, Government of India recommended that a single universal ORS solution containing sodium 75 mmol/L and glucose 75 mmol/L, osmolarity 245 mosmol/L was acceptable for all ages and all types of diarrhea. The revised formulation was approved by the Drug Controller of India and the Government formally launched it in June 2004.

### **Revised Recommendations of the IAP National Task Force for Use of ORS in Diarrhea, May 2006**

1. ORS should be prescribed by all physicians for all ages in all types of diarrhea.
2. The group noted that the new improved ORS recommended by the WHO/UNICEF containing sodium 75 mmol/L and glucose 75 mmol/L, osmolarity 245 mosmol/L is the universal solution for all ages and all types of diarrhea.

<sup>(3)</sup> Composition of Currently WHO/IAP/GOI Recommended Reduced Osmolarity ORS

Component	Concentration (mmol/L)
Sodium	75
Chloride	65
Potassium	20
Citrate	10
Glucose	75
Osmolarity	245

3. 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 use rates continued to be very low in several regions across the country. The group decided that efforts will be made by the IAP to increase awareness among pediatricians and other physicians for use of ORS by organizing regional meetings and workshops. It recommended that measures should be taken by the Government to improve ORS availability and reduce its cost. There should be provision for ORS to be available with the ASHA and the anganwari workers.
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 they had different breast-feeding rates, dietary patterns and diarrhea etiology from the west.

### **B. 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(4) 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 38%) in the odds of acute episodes lasting >7 days. A combined meta-analysis of all the studies (all studies included in the pooled analysis and the subsequent trials) done till now showed that zinc supplemented children had 16% faster recovery (95% CI 11% to

22%) and resulted in a 34% reduction (95% CI 17% to 48%) in the odds of acute episodes lasting >7 days (Bahl, Bhan and Bhatnagar, personal communication). The study by Bhatnagar *et al*(5) 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. Studies have shown that there seems to be little gain in efficacy when the commonly used 20mg daily dose of elemental zinc was increased to 30-40mg daily. Majority of the studies so far were conducted in South East Asia, where zinc deficiency is common. Finally, there are relatively few data on children aged less than 6 months to

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

Study	No. of subjects	Effect size (95% CI)
<b>Risk of continuation of diarrhea</b>		
Pooled analysis (3)	1252/1194	0.85 (0.76 to 0.95)
Subsequent studies in South East Asia Strand <i>et al</i> (6)	442/449	0.79 (0.68 to 0.93)
Bahl <i>et al</i> (7)	404/401	0.89 (0.80 to 0.99)
Bhatnagar <i>et al</i> (5)	132/134	0.76 ( 0.59 to 0.97 )
<b>Combined estimate (Meta-analysis)</b>	<b>5614</b>	<b>0.84 (0.78 to 0.89)*</b>
<b>Diarrhea lasting &gt;7 days</b>		
Pooled analysis	1252/1194	0.78 (0.56 to 1.09)
Subsequent studies in South East Asia		
Strand <i>et al</i>	442/449	0.57 (0.38 to 0.86)
Bahl <i>et al</i>	404/401	0.61 (0.33 to 1.12)
Bhatnagar <i>et al</i>	132/134	0.09 (0.01 to 0.73)
<b>Combined estimate (Meta-analysis)</b>	<b>4362</b>	<b>0.66 (0.52 to 0.83)*</b>
<b>Stool output</b>		
Roy <i>et al</i> (8)	57/54	-91g
Dutta <i>et al</i> (9)	44/36	-900g (-1200 to -590)
Bhatnagar <i>et al</i>	132/134	0.69 g/kg (0.48, 0.99)
<b>Stool output per diarrhoea</b>		<b>Ratio of GM (95% day of CI) of geometricmeans</b>
Bhatnagar <i>et al</i>	266	0.76 (0.59, 0.98)*

allow any conclusions about efficacy in this age group.

Another study conducted in Bangladesh(10) 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 program 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. There was 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 40 mg 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(7). 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. Results of a large randomized controlled trials are awaited.

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 affect 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(11). They reviewed all the studies done till 2001 and concluded that:**

1. Zinc supplementation, given at a dose of about 2 RDA per day (20 mg per day for >6 months and 10 mg per day for younger than 6 months) 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 circumstances, oral rehydration therapy must remain the main stay of treatment. Treatment of acute diarrhea with zinc may have benefits on morbidity and mortality from other childhood infections and these should be further investigated. 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.

Based on all the studies the group proposed that zinc salts *e.g.*, sulphate, gluconate or acetate may be recommended.

The industry should be encouraged to prepare a zinc formulation, which contains only zinc. Iron containing formulations should not be used with zinc as iron interferes with zinc absorption.

#### **Addition of zinc to current case management strategy in primary health setting in India**

Since the earlier recommendations addition of zinc to current case management strategy in primary health setting has been evaluated in developing country settings including in India. Antibiotic use was less (70% (95% CI 65 to 75) in areas where 20 mg zinc was introduced with ORS and the ORS use rates increased by 50% ( $P < 0.01$ ) in comparison with the group which did not receive zinc(12). Similar results were seen in a large multicentre study done across India, Brazil, Ethiopia, Egypt, and the Philippines(13). Bhandari et al showed that ORS use rates increased and use of injections and antimicrobials decreased significantly from the baseline six months after zinc was added to ORS in the management of diarrhea(14).

#### **Revised recommendations of the IAP National Task Force for use of zinc in diarrhea, May 2006**

The group reviewed the literature again and concluded that adequate evidence was available to show that zinc supplementation reduced the duration and severity of diarrhea. ORS remains an essential component of the management of childhood diarrhea. The consensus recommendations of the group were:

1. All cases of diarrhoea should receive zinc in addition to ORS. A uniform dose of 20 mg of elemental zinc should be given to all children older than 6 months and should be started as soon as diarrhea starts and continued for a total period of 14 days. Children aged 2 months to 6 months should be advised 10 mg per day of elemental zinc for a total period of 14 days.
2. Based on all the studies the group proposed that zinc salts e.g. sulphate, gluconate or acetate may be recommended.
3. The industry should be encouraged to prepare dispersible tablets that are reasonably priced, can be stored and transported easily. They can be dissolved in breast milk or water before use.
4. Iron containing formulations should not be used with zinc as iron interferes with zinc absorption.
5. The group recommended that both zinc and ORS be made available at all parts of the country including remote areas. This will facilitate early initiation of treatment and also reduce the family's expenditure on irrational therapy during diarrhea.
6. IAP would organize workshops and seminars to increase the awareness for this intervention amongst pediatricians, and other health care providers.

#### **Recommendations by the Government of India, 2007**

Based on the WHO/UNICEF and the IAP recommendations and the data available on the evaluation of addition of zinc to current case management strategy in primary health setting [(14) and personal communication of a larger study by Bhandari, *et al.*] the Ministry of Health, Government of India has recommended that 20 mg of elemental zinc should be given to all children with diarrhea, older than 6 months, and should be started as soon as diarrhea starts and continued for a total period of 14 days. Children aged 2 months to 6 months should be advised 10 mg per day of elemental zinc for a total period of 14 days.

#### **C. Probiotics and Antisecretory Agents in the Treatment of Diarrhea**

##### *Conclusions of the IAP National Task Force for use of probiotics in diarrhea, May 2006*

The group recommended that there is presently insufficient evidence(1) 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. It may not be possible to extrapolate the findings of these 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*,



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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.
5. There is an urgent need to study the following issues before probiotics may be considered for treatment of diarrhea:
  - Strain standardization
  - Product regulation
  - Evaluation of more than one strain for therapeutic effect
  - Evaluation of probiotics in subgroups
  - Dose and duration of therapy
  - Carrier substances
  - Interactions with other medication
  - Interactions with other enteropathogens

### Antisecretory Drugs in Diarrhea

There is presently not enough evidence on either safety or efficacy of antisecretory drugs like racecadotril for its routine use in the treatment of diarrhea. There is no data from our settings. Methodology of most of the published studies is questionable in addition to them being sponsored by the drug company. More importantly all results are not made available after another large multicentre study evaluating efficacy and safety of the same drug(15).

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### Annexure

#### **Members of the Task Force**

Advisers:	M.K. Bhan, H.P.S. Sachdev
Chairperson:	Nitin Shah
Conveners:	Shinjini Bhatnagar, Panna Choudhury
Co-conveners:	Rakesh Lodha
Members:	Naveen Thacker, Raju Shah, Deepak Ugra, S.C. Arya, Shiela Aiyer, Seema Alam Tarun Gera, Surjit Singh, Ajay Gaur, Siddhartha Gogia, Keya Kunnikel, Preeti Makhia Jitender Nagpal, G.B. Nanda, Sushma Narayan, Sangita Subudhi, Nitya Wadhwa
UNICEF:	K. Suresh, Anjana Gulani, Yogesh Jain, Asish Sen, Gaurav Arya, Raman Atkuri, Sherin Varkey
WHO:	Harish Kumar

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