Epidemiology & management of persistent diarrhoea in children of developing countries

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Diarrhoea that begins acutely but lasts longer than two weeks is defined to be persistent. Revised estimates in developing countries including India showed that acute diarrhoea accounts for 35 per cent, dysentery 20 per cent and non-dysenteric persistent diarrhoea (PD) for 45 per cent of total diarrhoeal deaths. PD also often changes marginal malnutrition to more severe forms. Factors that increase the risk of acute diarrhoea becoming persistent have been identified in India and other developing countries. These include antecedent malnutrition, micronutrient deficiency particularly for zinc and vitamin A, transient impairment in cell mediated immunity, infection with enteric aggregative Escherichia coli and cryptosporidium, sequential infection with different pathogens and lack of exclusive breast feeding during the initial four months of life particularly use of bovine milk.

Several issues regarding the management of persistent diarrhoea in hospitalized children in India have been resolved. Diets providing modest amounts of milk mixed with cereals are well tolerated. In those who fail on such diets providing carbohydrate as a mixture of cereals and glucose or sucrose hasten recovery. The role of antimicrobial agents and individual micronutrients in PD is currently being investigated. A management algorithm appropriate for India and other developing countries has been developed and found to substantially reduce case fatality in hospital settings to about 2-3 per cent. Recent epidemiological and clinical research related to persistent diarrhoea is also reviewed.

Key words Impaired immunity - incidence - lactose intolerance - mortality micronutrient deficiency - persistent diarrhoea

Although the majority of episodes of acute diarrhoea are self limiting, a small proportion last several weeks1. These episodes persistent diarrhoea are important because of a substantially higher case fatality rate than in acute diarrhoea, impact on nutritional status and the fact that these adverse outcomes may not be prevented by oral rehydration therapy alone67.

The distribution of the duration of diarrhoeal episodes is a continuum8. As such, delineating a subgroup of diarrhoeal episodes as persistent by any cut-off is arbitrary. The World Health Organization (WHO) has now defined persistent diarrhoea as an episode that begins acutely and lasts for at least 14 days1. The use of 14 days cut-off to partition acute and persistent episodes seems justified. In India for instance, in a longitudinal study the case fatality rates were similar for diarrhoeal episodes of 1 and 2 wk duration (0.61 and 0.8% respectively) and this increased to 14 per cent as the duration exceeded two weeks7. The term persistent diarrhoea does not include specific disorders, such as hereditary syndromes, celiac disease or surgical conditions and these are not considered in this review1.
Incidence of persistent diarrhoea

Estimates indicate that 3-20 per cent of episodes of acute diarrhoea become persistent. The incidence of persistent diarrhoea obtained in several longitudinal studies varied considerably from 7-150 episodes per 100 child years. In most settings the incidence of persistent diarrhoea peaked between 7 months and 2 yr of age; in countries with very high diarrhoea attack rates, the incidence was as high even in the first six months of life. The incidence of persistent diarrhoea declined rapidly after the fourth year. This high variability in attack rates across countries may be due to differences in disease definitions and intensity of household surveillance, apart from true geographical differences.

Mortality and growth faltering related to persistent diarrhoea

Recent research has led to a revision of the earlier estimates of the contribution of different types of diarrhoea to diarrhoea related mortality. In an international study that compared clinical patterns of diarrhoea among diarrhoea related deaths in India, Bangladesh, Brazil and Senegal, a similar pattern was observed; acute diarrhoea accounted for 35 per cent (range 25 to 46%), dysentery 20 per cent (range 8 to 24%) and non-dysenteric persistent diarrhoea 45 per cent (range 23 to 62%) of the total diarrhoeal deaths. The dysenteric deaths included those related to acute as well as persistent illness. In India the cause specific mortality rates (per 1,000) in children aged less than five years for acute watery diarrhoea, dysentery and non dysenteric persistent diarrhoea were similar (Table 1). While efforts to promote oral rehydration therapy and antibiotic treatment of dysentery must be sustained, persistent diarrhoea needs greater attention than at present.

Antecedent malnutrition, lack of breast feeding, and associated systemic infection increase the risk of death during persistent diarrhoea. In a community based study in north India, nearly a third of fatal cases of persistent diarrhoea had associated pneumonia.

In Bangladesh, malnourished children had a 68 fold higher risk of death from persistent diarrhoea than those who were better nourished and residing in the same communities.

### Table 1. Cause specific mortality rate* among children under five years of age

<table>
<thead>
<tr>
<th>Type of diarrhoea</th>
<th>No. of deaths</th>
<th>Cause specific mortality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute watery</td>
<td>8</td>
<td>5.6</td>
</tr>
<tr>
<td>Acute dysentery</td>
<td>3</td>
<td>2.1</td>
</tr>
<tr>
<td>Dysenteric PD</td>
<td>4</td>
<td>2.8</td>
</tr>
<tr>
<td>All dysentery</td>
<td>7</td>
<td>4.9</td>
</tr>
<tr>
<td>Non-dysenteric PD</td>
<td>8</td>
<td>5.6</td>
</tr>
<tr>
<td>All persistent diarrhoea</td>
<td>12</td>
<td>8.5</td>
</tr>
</tbody>
</table>

* (number of deaths in a year/mid population) x 100

PD, Persistent diarrhoea

The contribution of dehydration to persistent diarrhoea associated deaths is uncertain but available data indicate that it is much less important than in acute watery diarrhoea.

Role of enteric pathogens in persistent diarrhoea

Several theoretical models for the role of microbial agents in the genesis of persistent diarrhoea can be conceived. Firstly, an acute enteric infection may result in non infectious complications e.g., lactose intolerance which leads to prolonged symptoms. Secondly, persistent diarrhoea may occur as a result of sequential acute infections with different pathogens. Lastly, prolongation of diarrhoea may result from persistence of intestinal infection; the failure to eliminate the organisms from the intestinal tract may be related to the characteristics of the pathogen, to host factors or to both.

Across various studies, one or more pathogens were detected in half to two-thirds of children with persistent diarrhoea during the initial few days of illness. The interpretation of these isolations is difficult because the pathogens were also commonly excreted by asymptomatic children. In general, the pathogens excreted during persistent diarrhoea were the same as those reported in acute diarrhoeal episodes with the exception of rotavirus, which was often detected in acute episodes, but rarely in those that became persistent. To identify enteric pathogens which may have a predilection for causing prolonged diarrhoea, the approach commonly adopted has been to compare their initial excretion rates in...
episodes that last less than 14 days with those that last for a longer period (Table II). Among the many pathogens examined, enteroaggregative *Escherichia coli* and cryptosporidium were isolated with a significantly greater frequency in persistent episodes in some studies.\textsuperscript{14}

Enteroaggregative *E. coli* infection may be particularly important given a high rate of isolation in one-third to half the cases of persistent diarrhoea in India, Bangladesh and Mexico; these rates were higher than in acute diarrhoea\textsuperscript{12-15}. However, this pathogen was excreted with a similar frequency in persistent and acute episodes in some studies\textsuperscript{11,12}. Notably, enteropathogenic *E. coli*, diffusely adherent *E. coli*, shigella and *Giardia lamblia* were detected with a similar frequency in acute and persistent diarrhoea in most reported studies. The importance of shigella infection in persistent diarrhoea may have been masked by the timely and appropriate antibiotic treatment of acute dysentery.

Studies in Bangladesh and Peru where sequential stool cultures were obtained, suggest that persistent infection with the same organism is an uncommon phenomenon\textsuperscript{12-13}. A more frequent occurrence was the isolation of different pathogens at various phases of the persistent episode. In persistent diarrhoea associated with AIDS, *Cryptosporidium parvum*, *Isospora belli*, *Enurocytozoa bieneusi* and *Mycobacterium avium - intracellulare* are the most frequently identified pathogens\textsuperscript{16}. The importance of these pathogens in persistent diarrhoea among HIV negative children has not been well investigated.

**Nutritional status, immune mechanisms and persistent diarrhoea**

An increased diarrhoeal incidence in malnourished children has not been consistently observed\textsuperscript{25-31}. On the other hand studies have consistently shown that malnutrition is associated with a substantial increase in the average duration of diarrhoea and the incidence of persistent diarrhoea\textsuperscript{12-24}.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Persistent episode culture</th>
<th>Persistent episode culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 7 days</td>
<td>≥ 14 days</td>
</tr>
<tr>
<td></td>
<td>India (n=42)</td>
<td>Bangladesh (n=251)</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>2.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Aeromonas sp.</td>
<td>0</td>
<td>4.8</td>
</tr>
<tr>
<td>Campylobacter sp.</td>
<td>4.7</td>
<td>7.1</td>
</tr>
<tr>
<td>EAEC-AA</td>
<td>34.9</td>
<td>77.4</td>
</tr>
<tr>
<td>EAEC-DA</td>
<td>0</td>
<td>9.6</td>
</tr>
<tr>
<td>EAEC-LA</td>
<td>2.3</td>
<td>4.0</td>
</tr>
<tr>
<td>ETEC</td>
<td>9.3</td>
<td>4.8</td>
</tr>
<tr>
<td>Salmonella sp.</td>
<td>4.7</td>
<td>0.4</td>
</tr>
<tr>
<td>Shigella sp.</td>
<td>2.3</td>
<td>5.6</td>
</tr>
<tr>
<td>Vibrio sp.</td>
<td>0</td>
<td>0.4</td>
</tr>
<tr>
<td>Cryptosporidium</td>
<td>5.6</td>
<td>0.8</td>
</tr>
<tr>
<td>Entamoeba histolytica</td>
<td>2.3</td>
<td>0</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>2.3</td>
<td>1.6</td>
</tr>
</tbody>
</table>

EAEC, enteropathogenic *Escherichia coli*; AA, aggregative; DA, diffuse adhering; LA, localized adhering; ETEC, enterotoxigenic *Escherichia coli*. Superscript no. indicates the reference no.
Malnourished children are more likely to have subclinical deficiency of individual micronutrients and the deficiency of some of these may explain, at least partly, the increased risk of persistent diarrhoea in the undernourished. In a recent Indian study, children 6-36 months of age attending a community clinic with acute diarrhoea were supplemented with zinc gluconate or placebo during the enrollment episode and for a 6 months period thereafter; zinc supplementation resulted in a significant reduction in the average duration of the acute enrollment episodes and in the proportion that became prolonged. Over the ensuing 6 months the incidence of persistent diarrhoea was reduced by 49 per cent in zinc supplemented children older than 11 months but there was no such effect in those below this age. Zinc supplementation was previously shown to reduce the duration and severity of acute diarrhoea by others.

A positive association between vitamin A deficiency and diarrhoeal morbidity has been reported in only some studies. In Brazil, routine administration of vitamin A (200,000 IU) at 4 monthly intervals to children aged 1-5 yr reduced the incidence of severe diarrhoea by 20 per cent and diarrhoea prevalence by 23 per cent; the incidence of persistent diarrhoea was not reported. Micronutrients such as zinc and possibly vitamin A reduce the severity and duration of diarrhoea either by a rapid and effective repair of the intestinal epithelium following an acute enteric infection due to its role in the regulation of cell division or by enhancing the immune response.

Immuno incompetence, particularly decreased cell mediated immunity is one of the likely underlying mechanisms for the increased incidence of persistent diarrhoea among malnourished children. In Peru and Bangladesh, however, reduced delayed hypersensitivity responses (DHR) to several skin antigens were found to be associated with an increased risk of persistent diarrhoea, even after controlling for nutritional status. The impairment in DHR was often transient. Transient cell mediated immunosuppression may be the result of acute viral infections. Anergy has also been reported following bacterial infections such as tuberculosis and pneumonia. Diminished cell mediated immunity could also be related to decline in micronutrient status.

Recent morbidity and persistent diarrhoea

It has been seen that children are at an increased risk of persistent diarrhoea following an episode of measles or acute diarrhoea but not acute lower respiratory tract infection. The basis for an increased risk of persistent diarrhoea over the 2 to 3 months period following an acute diarrhoeal episode is unclear. A possible explanation may be that children who develop persistent diarrhoea are a subgroup with a high overall diarrhoea burden. Alternatively, an acute diarrhoeal episode may induce alterations in the intestinal epithelium or in immune responsiveness that renders the subsequent diarrhoeal episodes to be more severe or prolonged. Acute diarrhoea is characterized by excessive faecal zinc losses. It has been postulated that the impaired epithelial cell renewal and immuno incompetence associated with subclinical zinc deficiency may be the basis for the increased susceptibility to persistent diarrhoea following acute diarrhoea. These hypotheses need to be examined in future studies.

Type of feeding and persistent diarrhoea

It is important to identify feeding practices that increase the risk of persistent diarrhoea as these are potentially modifiable.

Factors that increase the overall risk of diarrhoea are also likely to cause more persistent diarrhoea. In infants under 3 months of age by feeding mode at the age of 1 wk; reference group: exclusively breast-fed.
Brazil, breast feeding was protective against persistent diarrhoea even after controlling for socio-economic status\(^1\). In early infancy, use of milk supplements in addition to breast feeding increased the risk of persistent diarrhoea by three fold. The risk was even greater among the non breast-fed (Fig. 1).

Once an acute diarrhoeal illness has occurred, the mode of feeding during the acute phase may influence the severity and duration of symptoms. Breast feeding during acute diarrhoea reduces the severity and duration of the episode\(^5\).

A highly contentious issue is whether the use of bovine milk or infant formula during acute diarrhoea increases the episode duration and severity. Several factors may influence the response to milk feeding during acute diarrhoea; the source of milk, amount, type of processing, other foods consumed during the illness, severity of the infection and factors related to the host\(^5\). The lack of consistency in the findings on this issue across studies is therefore understandable.

There is evidence that feeding of non human milk as the sole or predominant nutrient source during acute diarrhoea may increase the episode severity and duration\(^5\). In many of the studies where milk intake during acute diarrhoea was moderate, or when milk was offered as a part of a mixed diet containing cereals, a significant increase in the episode duration or severity was not observed\(^5,5\). Lactose malabsorption is dose dependent and it is likely that milk in moderate amounts particularly when mixed with other foods is well tolerated by most children with acute diarrhoea.

In an Indian study, the risk of persistence of acute diarrhoea was more with bovine milk than with an infant formula\(^5\). This seems plausible as bovine milk has a higher lactose content and osmolarity and the sensitization capability of milk protein in the infant formula is reduced due to spray drying during the manufacturing process.

Fermented products of milk such as yoghurt have been shown to be better accepted by lactose intolerant subjects and by children with persistent diarrhoea\(^5\). In a recently completed trial however, the feeding of yoghurt instead of milk to malnourished children during acute diarrhoea was not associated with a reduction in the episode duration or the risk of persistent diarrhoea (Singh et al unpublished data).

When viewed together, the reported data indicate that the use of mixed diets including low to moderate amounts of milk during acute diarrhoea promote weight gain without increasing the episode duration.

Type of oral rehydration salts (ORS) solution and persistent diarrhoea

Rice-based ORS was shown to substantially reduce the stool output in cholera in comparison to standard ORS, but its effect on stool output and episode duration in non cholera acute diarrhoea has been relatively small\(^6\). In a study from Bangladesh, the use of rice ORS during acute diarrhoea was reported to have reduced the proportion of episodes that became persistent\(^6\).

In recent clinical trials, where feeding was carefully standardized, there was no significant difference in the outcome of episodes treated with rice-based ORS than with standard ORS\(^6\). Thus, in the presence of optimal feeding, rice-based ORS during acute diarrhoea is unlikely to substantially reduce the risk of development of persistent diarrhoea.

In a recent multi-centre WHO sponsored clinical trial including India, the effect of a reduced osmolarity ORS (224 mmol/litre) on the stool output and episode duration was examined in comparison to the standard WHO ORS (311 mmol/litre). Stool output was reduced by 30 per cent and the average episode duration by 22 per cent in the children treated with reduced osmolarity ORS\(^6\). Data on the proportion of episodes that became persistent were not reported.

There are few community-based reports on the risk of development of persistent diarrhoea in relation to antibiotic use during the first week of diarrhoeal illness. In a study from India, antibiotic use during the initial days of illness was equally common in episodes that were eventually classified as acute or persistent\(^7\). In another study, initial antibiotic treatment was significantly less common in the episodes that became persistent, raising the possibility of a beneficial effect\(^1\). Nevertheless it is important to recognize that unwarranted antibiotic treatment for acute diarrhoea could lead to Clostridium difficile associated pseudo membraneous colitis and hasten the emergence of antibiotic resistant pathogens.

Specific causes and their role in the pathogenesis

The common causes of persistent diarrhoea as seen in developing countries are persistent infection
with one or more enteric pathogens, sequential enteric infection, disaccharide and rarely monosaccharide malabsorption and dietary protein intolerance [5, 14, 22, 63-70]. The hallmark of the disorder is persistent mucosal damage which may result from failure to eliminate the causative agent or delayed and ineffective mucosal restoration. Protein energy malnutrition and micronutrient deficiency in humans are known to be associated with abnormalities in intestinal structure and function. Delayed regeneration of the epithelium with reduced crypt cell multiplication and ineffective maturation of cells during their migration up the villi following an enteric infection has been demonstrated in experimental malnutrition [67]. Pathogenic bacteria cause mucosal damage and diarrhoea through mucosal effacement or invasion and action of enterotoxins or cytotoxins; malnutrition in the host prolongs the healing of the injured mucosa, the state of malabsorption and diarrhoea. In a proportion of cases, an immunological response to luminal, bacterial or dietary antigens has also been proposed as the basis for gut mucosal damage in persistent diarrhoea but the data are still inconclusive [68].

Faltered growth in persistent diarrhoea is not only the result of nutrient malabsorption; inadequate dietary intake due to anorexia, a continuation of faulty pre-illness feeding practices or as a response to diarrhoeal illness itself by the family or the physicians, are all important.

Management

The initial step is to determine the appropriate place for care. Patients with persistent diarrhoea require hospitalization in the presence of dehydration, associated systemic infection requiring intravenous antibiotics or when anorexia is severe. Intravenous fluid therapy may be required initially when dehydration is severe, to correct major electrolyte abnormalities or acidosis, and in extremely cachexic or systemically infected infants who accept oral fluids poorly.

Children with some but not severe dehydration can be effectively treated with oral rehydration salt solutions. It is important to provide additional potassium supplements to those severely malnourished.

When clinical dehydration is not associated, home available fluids are appropriate for replacement of ongoing stool losses.

Basis for dietary management

Several general principles have been established through recent studies in persistent diarrhoea.

In developing countries, the need to use total intravenous nutrition arises very rarely. Optimal oral feeding, based on an appropriately constituted diet is well tolerated and achieves recovery and catch up growth in the vast majority of these patients. Although there is some malabsorption of nutrients in persistent diarrhoea, about 80-90 per cent of carbohydrates and 70-75 per cent of fats and proteins are actually absorbed from mixed diets based on locally available ingredients.

Breast feeding is safe and well tolerated during diarrhoea. Although, a few predominantly breast-fed infants with acute diarrhoea may continue to pass stools with more than the usual frequency or stools of somewhat liquid consistency for more than two weeks, physical growth is well maintained.
Should milk be withdrawn in persistent diarrhoea?

In the non breast-fed babies, an important issue is whether milk should be totally eliminated or simply reduced in amount during persistent diarrhoea.

Brown and colleagues reported increased stool weights on diets predominantly based on whole milk as compared to lactose hydrolysed milk. The milk intakes were equivalent to about 6 g/kg/day or more of lactose; few children in Indian communities take such large quantities of milk. The issue of whether lower intakes equivalent to 2.5 g/kg lactose load per day would also be poorly tolerated has been recently examined in a clinical trial; preliminary analysis showed significantly greater weight gain in the group receiving a mixture of cereals with milk in which the latter provided 35 per cent of the total calories than in the other group consuming isocaloric cereal-based diet without milk. There was only a modest 15 per cent increase in the stool output in the milk group but the treatment failure rates were similar (Table II)73.

Similarly, Bhutta et al74 reported lower stool output and greater weight gain in persistent diarrhoea with curds cereal mixtures than with lactose free soy based diets. Together, these studies make a case for reduction rather than total elimination of milk as the initial step. A modest amount of milk in cereal diets improves their protein quality, trace elements and mineral content. Further, the consistency and palatability ensures higher intakes of these diets than with purely cereal-based diets. The possibility of occasional milk protein allergy is outweighed by the benefits offered by adding modest amounts of milk to cereal based diets.

Specific recommendations for the initial diet

Once a child is ready for oral feeding after few hours of stabilization, the choice of an initial diet would be milk rice mixtures with added oil, yielding an energy density of about 85-95 kcal/100g with 30-35 per cent calories from milk. The diet provides the ideal minimal 10 per cent energy from a protein source. The composition of one such diet is given in Table IV.

In a small proportion of patients with very severe diarrhoea where some clinicians feel reluctant to use milk even in small quantities, rice sugar oil based diets are appropriate. Egg is well tolerated and provides useful animal protein in such diets.

| Table III. Comparison of milk-based and milk-free diets persistent diarrhoea73 |
|----------------------------------------|--------|----------------|
|                                       | Milk cereal | Milk free cereal |
| Median stool weight in males (g/kg/h) |
| 0-48 h                                 | 1.7     | 1.5            |
| (0.9, 2.5)                             | (0.6, 2.4) |
| 0-120 h                                | 1.6     | 1.3            |
| (0.9, 2.7)                             | (0.61, 2.39) |
| % change in weight at 120 h*           | 2.8     | 2.3            |
| (0.8, 5.9)                             | (0.43)  |

Number with:
- Stool output >200g/kg in any 24 h period: 3
- Reappearance of dehydration during study: 4
- Stool output >60g/kg on day-7: 2
- Weight on day-7 < rehydration weight: 1
- Treatment failures by any of the above (%):
  - Median (range): 17.2 (23.6, 0.67)*
  - Odds ratio (95% CI): 0.24 (1.87)

Superscript no. indicate the reference no

| Table IV. Composition of diet A |
|-------------------------------|--------|
| Ingredients                   | Amount (g) |
| Puffed rice                   | 12.5   |
| Milk                          | 40.0   |
| Sugar                         | 2.25   |
| Oil                           | 2.0    |
| Water to make                 | 100    |
| Energy density (cal/100g)     | 96     |
| Per cent protein              | 10.0   |
| Per cent carbohydrate         | 55.87  |
| Per cent lactose              | 1.73   |
| Per cent fat                  | 33.9   |
| Amino acid score              | 1.0    |
Nearly 25 per cent of hospitalized patients show a poor response to diet A. Useful criteria for defining treatment failure are reappearance of dehydration at any time, passage of 7 or more liquid stools in a day at the end of 7 days treatment and weight loss or poor weight gain despite an oral intake of at least 100 cals/kg/day over the previous three days. Poor oral intake as a result of systemic infection is more often the cause of weight loss than true dietary failure in hospitalized children. In milder cases that are managed at the household level, a common reason for poor weight gain is the offering of only small quantities of thin foods to the child by the family.

The factors related to treatment failure on low lactose (milk) cereal based diets are systemic infection, severe carbohydrate intolerance involving not only lactose but also other disaccharides and starch. Therefore, dietary modification should be made only after effective treatment of associated systemic infection. The second line diet should be milk free with substitution of part of the starch by sucrose or glucose (diet B; Table V). This mixture of sugars achieves the right balance between dietary osmolality, digestibility and energy density. In such a diet, egg or chicken is a suitable protein source. Monosaccharides as the only carbohydrates in the diet should be used for the few patients who are treatment failures on diet B as it is difficult to provide sufficient energy density with the permissible 2-3 per cent glucose concentration; at higher concentrations osmotic diarrhoea may develop.

Until their role in the management of persistent diarrhoea is well established, generous but safe amounts of micronutrients equivalent to 2 times the RDA should be provided. These may include vitamin A, zinc, iron, folate and when feasible others. Severely malnourished children should receive magnesium 1-1.5 ml/kg body weight of a 50 per cent solution, given IM for 2-3 days. Patients on a milk free diet should also receive calcium supplementation.

Several commercial diets are also available. For reasons that are not fully explained, home based low lactose or lactase free diets perform much better than commercial soy based formulations. Semi elemental diets like Nutramigen or Progestimil are useful but expensive. They usually contain protein hydrolysate or calcium caseinate, mixture of disaccharides and oligosaccharides and part or whole of the fats as medium chain triglycerides. Micronutrients and vitamins are already added. The diet B is based on similar principles and is at least as effective. Its advantage is that the concentration of the individual sugars can be tailored to each individual child, it is cheap and can be easily prepared by mothers at home and in small hospitals, the disadvantage is that vitamins and minerals need to be supplemented.

The role of antimicrobial agents against enteric pathogens in terms of improved nutrient absorption, decreased stool output or shortened illness duration is undecided. In a recent Indian study large doses of nonabsorbable, broad spectrum antibiotic were administered based on the hypothesis that it would eradicate aerobic bacterial overgrowth. There was no improvement in purge rates or weight gain with massive doses of oral gentamicin as compared to a placebo, despite clearance of stool pathogenic organisms including adherent E. coli. It was conceivable that systemic antibiotics may be of greater benefit in persistent diarrhoea. However, a recently concluded double blind field trial done to evaluate the efficacy of metronidazole given alone or in combination with nalidixic acid in comparison to a placebo has shown no significant clinical benefit (Behl et al, unpublished data). Metronidazole was evaluated for its action against anaerobes. Other controlled trials with co-trimoxazole have shown similar results. It appears that when the mucosa is already severely damaged, whatever the initiating factors, nutritional support is the key to its rapid repair.

### Table V. Composition of diet B

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Amount (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>13.50</td>
</tr>
<tr>
<td></td>
<td>11.0</td>
</tr>
<tr>
<td></td>
<td>3.50</td>
</tr>
<tr>
<td></td>
<td>3.50</td>
</tr>
<tr>
<td></td>
<td>100</td>
</tr>
<tr>
<td>Energy density (cal/100g)</td>
<td>95.22</td>
</tr>
<tr>
<td>Per cent protein</td>
<td>9.51</td>
</tr>
<tr>
<td>Per cent carbohydrate</td>
<td>56.9</td>
</tr>
<tr>
<td>Per cent fat</td>
<td>33.29</td>
</tr>
<tr>
<td>Amino acid score</td>
<td>1.00</td>
</tr>
</tbody>
</table>
An effective antishigella agent should be used in the presence of blood or numerous pus cells in the stools. Treatment for giardiasis and amoebiasis is indicated when a stool examination reveals trophozoites. Currently, there is no suitable treatment for cryptosporidium infection.

Cholestyramine, which binds unconjugated bile salts or bacterial toxins, has not proved to be useful. There is also little evidence of clinical benefit when lactobacilli are administered to replace intestinal microflora.

Systemic antibiotics are required to treat associ-
ated pneumonia, septicemia, meningitis or urinary tract infection in patients with persistent diarrhoea. These infections are detected in nearly 60 per cent of patients with associated severe malnutrition usually seen in a hospital setting, they are much less common when malnutrition is only of moderate severity, as is likely with those being treated as outpatients. The search for such infections should be vigorous, even in the absence of fever; useful indicators are persistent anorexia, refusal of liquids and breast milk and dehydration despite modest stool losses.

These recommendations are summarised in a treatment algorithm (Fig. 2). This algorithm was evaluated in an international study including the group at the All India Institute of Medical Sciences (AIIMS), New Delhi. The success rate for the evaluated 460 children with persistent diarrhoea while on diet A was 70 per cent (95% CI 65%, 75%) and it was 84 per cent (95%CI 76%, 93%) for those evaluated while on diet B. Weight gain was achieved in over 90 per cent and associated illnesses requiring antibiotics were found in 61 per cent of the children. The children at greatest risk were the youngest, those severely malnourished, with highest initial purging rates and associated infection.

As diarrhoea is common in children residing in poor communities where family feeding habits contribute to malnutrition, an interaction with health care providers during the illness offers a good opportunity to improve the nutrient intake through purposeful nutritional counselling. Mixtures of milk and cereals or of cereals and legumes fortified with oil are well tolerated during acute and persistent diarrhoea. They have the required energy density and palatability. About 30-40 per cent of calories can be derived from fat sources without any deleterious effect. Mothers must receive nutritional counselling from health care providers that is practical and takes into account the family views and realities and includes clear instructions on the frequency of meals, the amounts to be fed at each and the solutions to problems of the individual child and family. This is currently the weakest link in the sick child - health care provider interaction.

The vast majority of patients with persistent diarrhoea are unable to avail of hospital care due to physical and situational constraints of the family. Therefore, it is the outpatient care of patients with persistent diarrhoea that needs strengthening instead of the current over focus on sophisticated treatment of the few patients who actually get to hospitals.

References


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