

PERSISTENT DIARRHOEA

Persistent diarrhoea is becoming recognised as an important child health problem in developing countries, although its control and prevention have received less attention than acute diarrhoea. This special *DD* insert reports on the main conclusions of a meeting held in Mombasa, Kenya in 1991, which presented an overview of the problem and an update on research about appropriate treatment.

Persistent diarrhoea is an important cause of illness and death in children in developing countries. Moreover, as acute diarrhoea is more widely and successfully treated with oral rehydration therapy (ORT), the proportion of diarrhoea deaths associated with persistent diarrhoea will probably increase. In the mid-1980s the World Health Organization recognised that efforts to control persistent diarrhoea were inadequate. Several studies have since been carried out, aimed at formulating strategies for its management and control.

What is persistent diarrhoea?

Acute and persistent diarrhoea are not two separate diseases but form a continuum. Most episodes of diarrhoea last less than one week, but a small proportion of episodes last for two or more weeks. The definition of persistent diarrhoea has varied, but it is helpful to have a standard one so that different studies can be compared, and recommendations made for treatment. In 1987, a meeting sponsored by WHO defined persistent diarrhoea as an episode which starts acutely but which lasts at least 14 days. This definition has been adopted by most investigators and programmes.

Is it a serious problem?

In 8 community based studies in Asia and Latin America (see table 1), persistent diarrhoea accounted for between 3 per cent and 23 per cent of all cases of diarrhoea. In 7 studies (see table 2), the incidence of persistent diarrhoea varied greatly. For every 100 children aged 4 years or less, 7 cases of persistent diarrhoea were seen per year in India, and 150 cases in north-eastern Brazil. In all studies the incidence was much higher in children under 2 years than in older children.

Persistent diarrhoea may account for a large proportion of all deaths due to diarrhoea. WHO and UNICEF estimated that

in 1991 persistent diarrhoea accounted for only 10 per cent of diarrhoeal episodes, but as many as 35 per cent of diarrhoeal deaths in children under 5 years of age. Evidence from studies in Bangladesh, India, Peru and Brazil indicated that approximately 45 per cent (range 23 per cent to 62 per cent) of diarrhoea associated deaths were due to persistent diarrhoea.

Although findings from some studies indicate that persistent diarrhoea most often occurs in children below 2 years of age,

most persistent diarrhoeal deaths occur in children aged 1 to 4 years old when malnutrition is most common, because deaths from persistent diarrhoea are frequently associated with malnutrition.

What causes persistent diarrhoea?

A number of studies have tried to find out if particular pathogens are associated with persistent diarrhoea. This information

Table 1: Duration of diarrhoeal episodes

Country	Age (years)	Total episodes	Percentage of episodes by duration		
			1-7 days	8-14 days	15+ days
Indonesia	0-1	618	83%	14%	4%
Guatemala	0-1	262	53%	27%	19%
Peru	0-1	1,299	79%	14%	7%
Peru	0-2	5,302	88%	9%	3%
Bangladesh	0-4	941	66%	21%	14%
Bangladesh	0-4	2,609	71%	22%	7%
Bangladesh	0-5	1,074	50%	27%	23%
India	0-5	471	35%	55%	10%

Table 2: Incidence (per 100 child-years) of persistent diarrhoea by age group

Country	Age group					
	<1 year	1 year	2 years	3 years	4 years	Overall (0-4 years)
India	31	9	6	2	0	7
Nepal	15	17	12	10		14
Peru	31	22	16	—	—	26
Bangladesh	72	25	29	28	6	34
Bangladesh	58	57	55	39	33	48
Bangladesh	64	74	67	43		59
Brazil	171	216	160	90	60	150

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could help to predict the course of the disease and help decide whether to use an antibiotic. However, most cases of persistent diarrhoea seem to be associated with the same pathogens that cause acute diarrhoea.

Four studies in India, Bangladesh and Peru found that rotavirus, *Aeromonas*, *Campylobacter*, *Shigella* and *Giardia lamblia* were equally common in acute and persistent diarrhoea. *Cryptosporidium* was more common in persistent than acute diarrhoea in Bangladesh, but the reverse was true in Peru. Evidence from several studies suggests that the enteroadherent *Escherichia coli* (so called because of their ability to adhere to intestinal cells in tissue culture) may be particularly associated with persistent diarrhoea. However, these organisms may be responsible for only a small proportion of all episodes.

Even though most pathogens seem to be equally common at the onset of acute episodes that do or do not become persistent, different pathogens are found if cultures are taken from the same individual during the course of persistent diarrhoea. Studies in Bangladesh and Peru showed that it was not common to find the same pathogen in samples taken at different times during a persistent episode. The current evidence therefore suggests that no single pathogen is responsible for the persistence of episodes. Moreover, successive infections with different pathogens often occur in children with persistent diarrhoea.

What increases the risk of persistent diarrhoea?

Several factors have been identified as possibly increasing the risk of persistent diarrhoea.

• Previous diarrhoea infection

A relatively small proportion of children have many episodes of diarrhoea, and it is predominantly these children who develop persistent diarrhoea. This observation is supported by studies which show that a recent diarrhoeal illness is often associated with the occurrence of persistent diarrhoea. More studies are required to find out whether these high-risk children are in an environment where there is greater trans-



Studies have shown that breastfed babies are less likely to have persistent diarrhoea.

mission of enteric pathogens, or if they have greater susceptibility to illness. Studies are also needed to find out if the frequency of diarrhoea infections affects the child's immune status and ability to resist subsequent infection.

• Nutritional status

Evidence from Bangladesh, India and Brazil shows that malnutrition is strongly associated with persistent diarrhoea. Researchers have found a small increased risk of diarrhoea incidence in malnourished children, but a large increased risk of prolongation of the episode. In Bangladesh, for example, among persistent diarrhoea deaths, 81 per cent were associated with malnutrition. These findings suggest that malnutrition significantly increases the risk of dying in children suffering from persistent diarrhoea.

• Feeding practice

Studies have shown that breastfeeding shortens the duration of diarrhoeal episodes, and that lack of breastfeeding is associated with persistent diarrhoea. In Peru, for example, infants aged from 9

months to 11 months who were not breastfed had average diarrhoeal durations that were 49 per cent longer than those of infants who continued to receive some breastmilk. One reason for this is that diarrhoea infections can reduce a child's capability to digest lactose, a sugar found in milk. When this happens, drinking animal milk can cause diarrhoea to worsen or be prolonged.

• Other factors

Research is continuing on the relation of several other factors to persistent diarrhoea. These include deficiency of vitamin A, zinc, iron and other micronutrients; behaviours related to water source and use, food preparation and consumption and hygiene; presence of other diseases such as measles; suppression of immunity; and the interaction of these factors.

Other studies have attempted to find out whether clinical characteristics during the initial days of diarrhoeal illness can predict which episodes are likely to persist. Results from Peru and Bangladesh show that the initial phases of what became persistent episodes were more likely to be accompanied by fever, vomiting, high stool frequency, dehydration and reduced activity in children. However, these associations were not sufficiently strong to be able to precisely predict which episodes would persist.

Treatment

The same general principles apply for treating acute diarrhoea and persistent diarrhoea. Stool losses should be replaced with appropriate fluids, feeding should be continued and unnecessary medicines avoided.

Dietary management is especially important in persistent diarrhoea because of the association of persistent diarrhoea with malnutrition, lactose intolerance and (probably) micronutrient deficiency, and because the diet of children with persistent diarrhoea should be modified so that the intake of animal milk is reduced.

• Oral rehydration therapy

The principle of replacing water and electrolyte losses is well established for acute diarrhoea and is no different for persistent diarrhoea. The aim of treatment is to re-

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place initial and ongoing fluid losses until the diarrhoea stops. In nearly all cases of persistent diarrhoea ORT is all that is required for fluid replacement.

• Dietary management

The association between persistent diarrhoea and malnutrition means that appropriate feeding is very important during and after the diarrhoea episode. There are two key principles of dietary management of persistent diarrhoea:

(a) Reduce lactose by decreasing the amount of non-human milk in the diet

Persistent diarrhoea is less common in children who are breastfed than in those who are given cow's milk or other non-human milks.

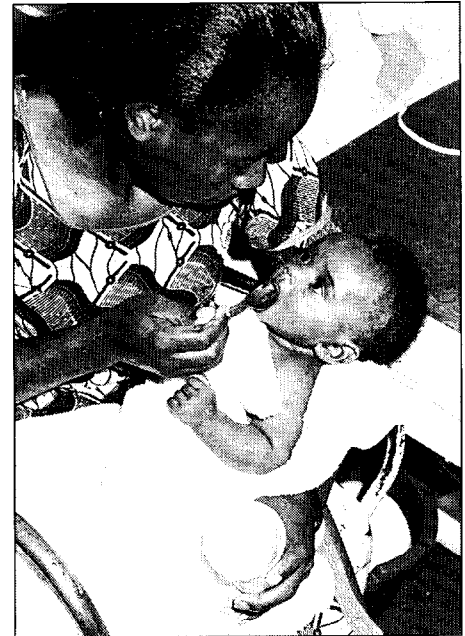
Lactose intolerance occurs especially in children who are severely malnourished or who have severe diarrhoea. Lactose is a sugar providing about 35 to 45 per cent of the calories in non-human milks used for feeding children. Once in the gut, it must first be broken down by an intestinal

enzyme called lactase, before it can be absorbed by the gut wall cells. During the early phase of a diarrhoeal episode lactase production may decline, slowing down digestion of lactose.

If the sick child continues to ingest milks containing lactose, any undigested lactose passes into the lower intestine, where it can draw fluid from the gut wall cells into the intestinal lumen, thereby increasing the severity of diarrhoea. Fortunately, clinically significant lactose intolerance occurs in only a very small proportion of children with acute diarrhoea.

In a child with persistent diarrhoea, adverse effects can usually be avoided by reducing lactose intake to about 2 to 3g/kg/day (about 30 to 50ml/kg/day of whole cow's milk) and mixing the milk with cereal. Replacement of cow's milk by fermented milk products, such as yoghurt, which contains less lactose, is another way to reduce the intake of lactose.

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As with acute diarrhoea, giving ORT during a persistent diarrhoea episode is the best way to prevent dehydration.

Evaluating the benefits of giving nutritious food with a low lactose content

Two studies in Pakistan evaluated the use of: (a) a traditional diet – *khitchri* (rice and lentils cooked with oil) – for treating children with acute diarrhoea, and (b) *khitchri* and yoghurt for children with persistent diarrhoea. *Khitchri* is commonly given to sick children in Pakistan.

The first study was carried out to assess the efficacy of *khitchri* along with half-strength cow's milk in the treatment of severe acute diarrhoea¹. This study involved boys aged between 9 months and 4 years old who had had acute diarrhoea for 72 hours or less, moderate or severe

dehydration and no previous antibiotic treatment.

After initial rehydration the children were randomly assigned to two groups. One group received only glucose ORS for 24 hours. The other was given *khitchri* as well as glucose ORS. The intake of food, fluid and glucose ORS and the output of stool and urine were measured and recorded: 44 children were successfully treated, 21 with ORT and 23 with *khitchri*. After 24 hours there were no significant differences between the two groups in mean stool output, frequency of stools or weight gain. These data indicate that the *khitchri* diet was well tolerated and did not cause increased stool output in young children with acute diarrhoea.

Successful local diet

The second study evaluated *khitchri* combined with yoghurt in the management of persistent diarrhoea². The study compared soy formula milk (which has no lactose) with a *khitchri*-yoghurt mixture in boys aged between 6 months and 3 years old. Yoghurt is widely used as a dietary supplement in Pakistan and is well absorbed, mainly because the lactose content of milk is reduced by half by fermentation. Soy milk was used in the control group because a diet low in lactose

is often advised during persistent diarrhoea.

Children with persistent diarrhoea were randomly allocated to the two treatment groups: *khitchri* with yoghurt, or soy formula. During the first week of the study, despite a comparable intake of calories, children fed the *khitchri*-yoghurt diet had lower stool volume, lower stool frequency and greater weight gain than children on soy formula.

Children on soy formula were switched to *khitchri*-yoghurt during the second week. Their weight gain during this week was significantly greater than during the first week.

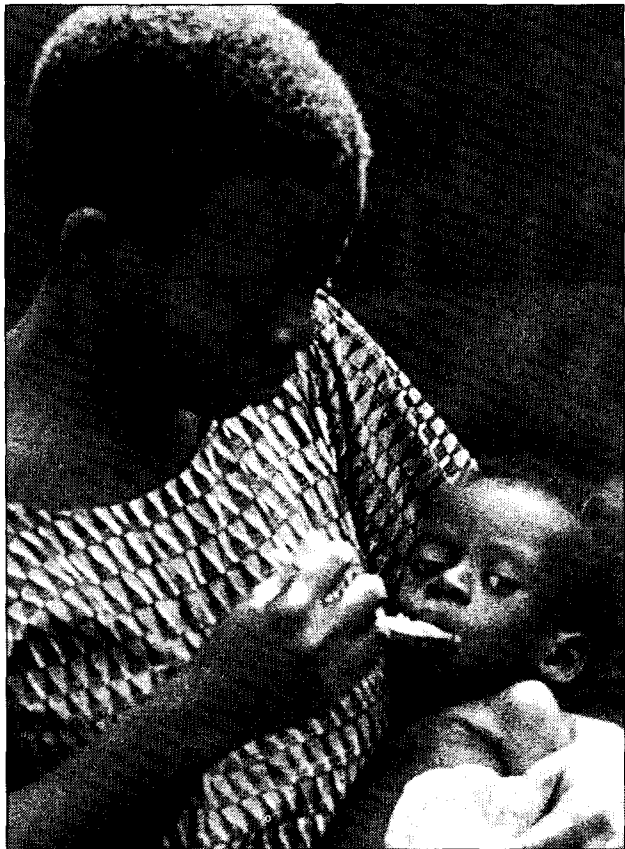
In addition to the advantages of clinical efficacy and convenience, the potential financial benefits of a diet based on local foods are also great. The weekly cost of the soy formula (which is mostly imported) is about \$14.00 for a 5kg child compared with only \$2.00 for *khitchri*-yoghurt. The difference, when multiplied by the many episodes of persistent diarrhoea treated each year, could result in large financial savings for the whole country. These studies provide one example of a local diet using rice, lentils and yoghurt which can be successfully used for the dietary management of both acute and persistent diarrhoea.



Children in Pakistan with persistent diarrhoea showed a significant improvement when fed on a traditional diet of *khitchri*.

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Appropriate feeding is very important during and after a persistent diarrhoea episode.

(b) Ensure that the child receives enough nutritious food

A second essential aspect of the dietary management of persistent diarrhoea is to make sure that adequate food intake is maintained.

As most children with persistent diarrhoea are cared for in the community by the family, recommendations for dietary management should be based on foods that are inexpensive, readily available, culturally acceptable, and easy to prepare in the home. Special diets, such as formula milks that are free of cow's milk or lactose, are too expensive for most families in developing countries, and are rarely needed. Recent studies have shown that both acute and persistent diarrhoea can be successfully managed with diets based on local staple foods. But the diet for those with persistent diarrhoea should have the animal milk content reduced or mixed with other foods.

Studies in several countries are evaluating the efficacy of their local diets in managing persistent diarrhoea. A multi-centre study to evaluate a treatment scheme for persistent diarrhoea using local foods is now underway in six countries with the support of the Applied Diarrhoeal Disease Research Project and the World Health Or-

ganization Programme for Control of Diarrhoeal Diseases. These studies are based on the principle of reducing the proportion of lactose in diets to treat persistent diarrhoea. Children in Pakistan are given a diet of *khitchri* (rice and lentils cooked with oil) with yoghurt; children in Peru, India, Vietnam and Bangladesh are given a rice-milk diet; and children in Mexico are given a maize-milk diet. Children who do not recover on the initial diet are switched to a second diet, which contains no milk, such as one diet based on rice mixed with a protein source, for example chicken or egg white.

• Drugs

Antibiotics should not be used in persistent diarrhoea except for certain specific pathogens. *Shigella* is known to cause persistent diarrhoea and can be treated with antibiotics; antibiotics

should be used when *Shigella* is isolated by stool culture or when the stool is bloody. Non-specific antibiotic therapy, given without knowing what is causing the diarrhoea episode, has *not* proved to be effective against persistent diarrhoea and should not be used.

Besides antibiotics, a number of other drugs have been tried in the management of persistent diarrhoea. Cholestyramine and bismuth subsalicylate have shown benefit in some studies, but are not recommended for routine use. Antimotility drugs (codeine, paregoric, tincture of opium, diphenoxylate and loperamide) have serious side effects and should not be used. Adsorbants such as kaolin, smectite and charcoal are also unlikely to be effective.

Why treatment sometimes fails

Although 80 per cent of children with persistent diarrhoea may be managed with proper feeding and ORT, it is important to be able to identify children for whom such treatment is likely to fail or recovery may be delayed. In Pakistan treatment failure was more likely in younger children and those who were vomiting; delayed re-

covery was associated with younger age, malnutrition and severe watery diarrhoea. In Bangladesh children with more severe diarrhoea were also more likely to have delayed recovery.

Key issues for future research

Although many aspects of the development of persistent diarrhoea are unclear, its strong association with malnutrition and high incidence and fatality rates in developing countries, suggest that it deserves much more attention. Information is needed on:

- Locally available diets that can be used for initial treatment and for treatment failures, so that practical treatment schemes can be developed in different settings.
- The role of immune factors in the persistence of some episodes and the recovery from diarrhoea.
- The role of micronutrients in treating persistent diarrhoea and improving growth.
- Care-seeking behaviour during acute and persistent phases of diarrhoea, and the relationship of care-seeking and treatments used to the outcome of the episode.

1. Shaikh S, et al., 1991. A traditional diet as part of oral rehydration therapy in severe acute diarrhoea in young children. *J. Diarr. Dis. Res.* 9:258-263.

2. Bhutta ZA, et al., 1991. Dietary management of persistent diarrhoea: comparison of a traditional rice-lentil based diet with soy formula. *J. Ped.* 88:1010-1018.

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