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Is diarrhoea a major cause of malnutrition among the under-fives in developing countries? A review of available evidence

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To evaluate whether, at the community level, diarrhoea is a major cause of malnutrition or inversely whether the association between diarrhoea and growth retardation can be explained by a higher susceptibility of malnourished children to diarrhoea, all recent studies examining the relationship between diarrhoea and malnutrition in the community were reviewed. It was determined, for each of these two hypotheses, to what extent four standard causality criteria were met, viz., (i) lack of temporal ambiguity, (ii) consistency of findings, (iii) strength of association and (iv) biological plausibility. That malnutrition predisposes to diarrhoea seems likely: this is supported by a series of studies which adequately fulfil the examined causality criteria and seems biologically plausible. On the other hand, it is not clear whether diarrhoea is a major cause of malnutrition. Some studies examine the effect of diarrhoea on nutritional status over short time intervals and it cannot be determined whether diarrhoea-induced growth faltering is transient or sustained. Other studies examining this effect over longer periods do not show clearly that diarrhoea precedes malnutrition. Inconsistencies between studies and lack of evidence supporting a biologically plausible mechanism also question the importance of diarrhoea as a cause of malnutrition.

The association between diarrhoea and malnutrition is so frequent in the developing world that the existence of a self-reinforcing diarrhoea malnutrition cycle, with diarrhoea leading to malnutrition and malnutrition itself predisposing to diarrhoea is an attractive concept. There is considerable evidence that, in terms of prognosis, malnutrition and infections may mutually aggravate each other (Scrimshaw, Taylor & Gordon, 1968). This has often been interpreted as evidence that diarrhoea is a major cause of malnutrition (Grant, 1984; WHO/UNICEF, 1985). As a result, control of infections, and in particular of diarrhoeal disease, is often presented as

an important component in the prevention of malnutrition in developing countries.

There is no doubt that repeated attacks of diarrhoea in the same child may lead to a reduced weight gain or even weight loss and the assumption that diarrhoea may cause malnutrition in some individual children is definitely correct. This does not necessarily mean, however, that diarrhoea is a major cause of malnutrition at the community level. First, the prevalence of diarrhoea in the community and its quantitative effect on growth must be consistent with this hypothesis. Then the causality of the relationship at the community level between diarrhoea

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and malnutrition has to be established.

Determining whether two events occurring in association are causally related is one of the most difficult tasks of epidemiology. In the case of the association between diarrhoea and malnutrition, this task is particularly difficult since it has been claimed that diarrhoea and malnutrition may be, at the same time, cause and consequence of each other.

In this article, community studies from developing countries published in the last 20 years and giving some quantitative information on the strength of the association between diarrhoea and malnutrition were critically reviewed. It was then determined to what extent diarrhoea or malnutrition may be considered as a cause or a consequence of each other by using four criteria, which have been proposed to determine the causality of an observed association (Table 1) (Lilienfeld & Lilienfeld, 1980; Kleinbaum, Kupper & Morgenstern, 1982). Presence of all these criteria is necessary to show that a relation is causal but is not sufficient to prove it.

Does malnutrition predispose to diarrhoea?

Fifteen studies examining whether malnutrition predisposes to diarrhoea are listed in Table 2. The studies suggest that malnutrition does predispose to diarrhoea: when these studies are considered together, causality criteria seem to be adequately met.

Table 1. Criteria used to test the causality of an association between diarrhoea and malnutrition.

1. Lack of temporal ambiguity:
The postulated cause must precede the occurrence of the consequence.
2. Consistency of the findings:
All studies dealing with the same association should give similar results.
3. Strength of the association:
The stronger the association, the less likely it is to be due to various sources of errors which may influence the results.
4. Biological plausibility:
The cause and effect relationship should make sense in view of accepted facts and current understanding regarding the physiopathology of diarrhoea and malnutrition.

Lack of temporal ambiguity

All studies examining whether malnutrition predisposes to diarrhoea have a similar design. At the beginning of the study, nutritional status is assessed in terms of weight-for-age, height-for-age or weight-for-height in a group of children which are then followed-up for a variable period of time during which diarrhoea morbidity is monitored. This common design has the advantage of almost eliminating the problem of the temporal ambiguity since diarrhoea observation always follows nutritional assessment.

It may be argued, however, that nutritional status at the beginning of these studies may already have been influenced by diarrhoea and that malnutrition does not necessarily always precede diarrhoea in all these studies. Yet, in two studies (El Samani, Willett & Ware, 1988; Sepulveda, Willett, & Munoz, 1988), previous history of diarrhoea is included among the potential confounding variables and the results are not markedly altered when this correction is made. Moreover, the association between previous history of diarrhoea and malnutrition is not strong enough to affect markedly nutritional status measured in terms of weight-for-age, height-for-age or weight-for-height (also next) as measured at the beginning of follow-up in all these studies. Finally, this could be a problem for interpreting these studies only if diarrhoea episodes were strongly clustered and occurred repeatedly in the same children, which, to our knowledge, has never been shown. Hence, previous history of diarrhoea does not seem to explain this association.

Children with low birth weight have apparently more frequent diarrhoeal episodes, even beyond the first year of life (Mertens, Cousens & Feachem, 1987). This observation is also consistent, without any temporal ambiguity, with the hypothesis that growth retardation predisposes to frequent diarrhoea.

Consistency of findings

Among the 15 studies listed in Table 2, 12 find some association between initial nutritional status and subsequent diarrhoea morbidity. The effect is either on incidence or on duration or on prevalence of diarrhoea,

which combines the effect of incidence and duration of episodes.

The negative findings of two studies (Chen, Huq & Huffman, 1981; Mathur *et al.*, 1985) can presumably be explained by the length of the follow-up period. In these two studies, diarrhoea morbidity is monitored for 2 years and 1 year, respectively, following nutritional assessment, and changing nutritional status among some children may have affected the strength of the association between nutritional status and subsequent diarrhoea morbidity. Sepulveda *et al.* (1988) provide evidence in favour of this interpretation by showing that when a 1 year follow-up is simulated with their own data set, the association between initial nutritional status and risk of diarrhoea disappears.

The third negative study by Glass *et al.* (1989) examines the effect of initial nutritional status on incidence and duration of diarrhoea among secondary cases of cholera. This very specific objective may explain why the findings are at odds with those of other studies in which cholera cases were probably rare.

Strength of the association

Although fairly consistent from study to study, the association between initial nutritional status and subsequent history of diarrhoea is not strong. Since malnutrition and diarrhoea can both be considered to be consequences of poverty, the possibility that their association could be indirect and non-causal should also be considered. Yet, in four studies (Bairagi *et al.*, 1987; El Samani *et al.*, 1988; Tomkins, Dunn & Hayes, 1989; Sepulveda *et al.*, 1988) the association between initial nutritional status and subsequent diarrhoea morbidity is controlled for different socio-economic indicators and this does not significantly alter the strength of this association. This is also in favour of its causality.

Biological plausibility

An impaired immunity, a slower turnover of intestinal cells and reduced levels of intestinal enzyme activity are the mechanisms most frequently put forward to explain the

higher prevalence of diarrhoea among malnourished children (Scrimshaw, Taylor & Gordon, 1968; Palmer *et al.*, 1976; Black, Brown, & Becker, 1984a; Sepulveda *et al.*, 1988; Black, Lanata & Lazo, 1989). The hypotheses are: (i) malnourished children have a depressed immunity and therefore are more easily infected or, when infected, take a longer time to eliminate pathogens; (ii) when enterocytes are damaged, by direct invasion by a pathogen or by adherence of a toxin, more time is needed to replace them in malnourished children; (iii) lower levels of digestive enzyme activity, and especially of lactase, may prolong diarrhoea. These hypotheses are supported by clinical (Brunser *et al.*, 1966; Knudsen *et al.*, 1968; Chandra & Newberne, 1977; Roediger, 1986) and community studies (Koster *et al.*, 1987; Black *et al.*, 1989). Mechanisms postulated to explain a longer duration of diarrhoea during malnutrition could be reproduced in experimental studies (Guiraldes & Hamilton, 1981; Butzner *et al.*, 1985; Butzner & Gall, 1988; Young & Levin, 1990a, b).

These different mechanisms are not mutually exclusive and may be viewed as consequences of protein metabolism alteration occurring during malnutrition. Despite its small mass, intestinal epithelium protein turnover represents about one-quarter of the whole body protein turnover (Waterlow, Garlick & Millward, 1978). Protein-energy malnutrition depresses whole body protein turnover (Golden, Waterlow & Picou, 1977) and is likely also to affect intestinal epithelium metabolism. Intestinal epithelium cells use mainly glutamine as fuel for their metabolism (Felig, 1981). Glutamine comes mainly from the muscle pool of free amino acids and seems also to be involved in the regulation of muscle protein synthesis (Jepson *et al.*, 1988). Glutamine also seems to play a key role in lymphocyte proliferation during the immune response (van den Berg, 1974). Muscle mass is reduced during malnutrition (Reeds *et al.*, 1978). It seems plausible that the reduction of muscle mass and of protein turnover observed during protein-energy malnutrition may at the same time have an effect on immune response, enterocyte turnover and levels of digestive activity by

Table 2. Studies examining whether malnutrition predisposes to diarrhoea.

Authors	Number of child intervals	Age range (months)	Length of follow-up (mo)	Results by type of diarrhoea	Confounding factors examined	Association between malnutrition at the beginning of the study period and risk of diarrhoea
Ghai & Jaiswal (1970) (India)	11005 child-weeks	0-59	3-6	No	None	When weight-for-age was below 85% of reference median incidence of 7.7 episodes of diarrhoea for 100 weeks versus 3.3 episodes when weight-for-weight age above 85%.
James (1972) Costa Rica	137	0-60	12	No	None	No relation between nutritional status and incidence of diarrhoea under 36 months of age. After 36 months, incidence of diarrhoea doubled among low weight-for-age children. Episodes lasted 3 d longer in low weight-for-age children after 1 year of age.
Chen <i>et al.</i> (1981) Bangladesh	2109	12-23	24	No	None	No association between nutritional status and risk of hospital admission.
	207	0-59	12	No	None	No relation between initial nutritional status and incidence of diarrhoea.
						No relation between weight gain in the preceding month and monthly incidence of diarrhoea.
Tomkins (1981) Nigeria	343	6-32	3	No	None	Wasted children had 47% more diarrhoeal episodes.
Black <i>et al.</i> (1984a) Bangladesh	859	2-24	2	Yes	None	Among them, episodes lasted 79% longer.
Mathur <i>et al.</i> (1985) India	674	0-59	12	Yes	None	Duration of diarrhoea 56% longer in children below 80% weight-for-height compared to those above 90% with a dose-effect relationship.
						No relation between malnutrition and diarrhoea incidence.
Bairagi <i>et al.</i> (1987) Bangladesh	1466	12-59	2	No	Age, socio-economic status, maternal education	No association between nutritional status and incidence or duration of diarrhoea.
						Severe dehydration more frequent and Enterotoxigenic <i>E. coli</i> more frequently isolated in children less than 60% weight-for-age
						Duration of diarrhoea 45% higher in low weight-for-age or low weight-for-height groups with a dose-effect relationship.
						No relation between malnutrition and diarrhoea incidence.
Henry <i>et al.</i> (1987) Bangladesh	1496	5-24	2	Yes	None	No association between nutritional status and incidence of diarrhoea.
Koster <i>et al.</i> (1987) Bangladesh	225	0-120	6	No	None	Duration of non-watery diarrhoea 52% longer in stunted children.
El Samani <i>et al.</i> (1988) Sudan	1684	0-59	2	No	Age, socio-economic indicators, season	In children older than 36 months, longer duration of diarrhoea in children with low weight-for-height. No effect in younger children. No effect in multiple regression when cellular immune response was taken into account
Sepulveda <i>et al.</i> (1988) Mexico	1089	0-35	3	No	8 socio-economic indicators and previous history of diarrhoea	Relative risk of having diarrhoea was 1.7 (95%, CI: 1.1-2.8) in children with weight-for-age below 90% if diarrhoea present in preceding interval.
						If not, relative risk was 1.2 (95%, CI: 0.9-1.6).
Glass <i>et al.</i> (1989) Bangladesh	412	12-96	0.3	Yes	None	Yearly incidence of diarrhoea was 3.3 episodes for well-nourished children, 3.7 episodes for mildly malnourished children and 6.0 episodes for moderately malnourished children: dose-effect relationship.
Tomkins (1989) Gambia	647	6-35	4	No	Type of housing, maternal education	Among cholera contacts, children below 70% of Harvard standard had the same number of cholera episodes, with the same severity and duration than well-nourished children
Briand <i>et al.</i> (1989a) Bangladesh	5316	6-35	3	Yes	None	During the rainy season, the prevalence of diarrhoea in children below 3 s.d. of height-for-age was on average twice that of children with Z-score higher than 0: dose-effect relationship.
Black <i>et al.</i> (1989) Peru	1872	6-26	6	No	None	No association during the dry season.
						Non-watery non-bloody diarrhoea prevalence 60% higher in children with height-for-age below 85% compared to those above 90%: dose-effect relationship.
						Incidence of diarrhoea significantly higher in children with low height-for-age. No effect of malnutrition on duration of diarrhoea.

Table 3. Studies examining whether diarrhoea leads to malnutrition.

Authors and country	Number of child intervals	Age (months) (months)	Length of study periods (months)	Technique used to estimate the impact of diarrhoea	Results by type of diarrhoea	Confounding factors examined	Association diarrhoea-nutritional status
Mata <i>et al.</i> (1971) Guatemala	43	0-35	30	Regression model and comparison low/high diarrhoea groups	No	None	Non-significant with the regression model. Significantly better growth in low infection group. Size of the difference not mentioned.
Martorell <i>et al.</i> (1975) Guatemala	1343	0-84	6	Comparison low/high diarrhoea groups	No	Age, sex, food supplement	Weight gain lower by 18 g/month in high diarrhoea group.
Condon-Paolini <i>et al.</i> (1977)	1083	0-35	12	Comparison low/high diarrhoea groups	No	Sex, growth failure	Weight gain lower by 17 g/month in the highest diarrhoea quartile compared to lowest diarrhoea quartile.
Mexico Rowland <i>et al.</i> (1977) Gambia	1210	6-36	1	Regression model	No	None	Weight gain reduced by 102 g/month on average as a result of diarrhoea. The model suggests a 770 g weight loss if diarrhoea present for a month.
Cole & Parkin, 1977 Uganda	1062	6-36	1	Regression model	No	None	Monthly weight gain reduced by 161 g when diarrhoea present.
Baumgartner & Pollitt (1983) Taiwan	236	0-12	6	Regression model	No	Sex, sibling order, treatment	No association between diarrhoea and growth between 0 and 6 months. Diarrhoea explained 3% of variance of weight gain between 6 and 12 months.
Guerrant <i>et al.</i> (1983) Brazil	482	0-71	3.5	Regression model	No	Nutritional status at beginning of interval	Height gain reduced by 41% when diarrhoea in the interval.
Black <i>et al.</i> (1984b) Bangladesh	859	2-48	2	Regression model	Yes	Age, weight, height at beginning of interval	Weight gain reduced by 33% in 2-month intervals with diarrhoea prevalence higher than 30%. On 12 months intervals, no relation between diarrhoea and weight gain, effect of dysentery visible only on height gain.
Bairagi <i>et al.</i> (1987) Bangladesh	1466	12-59	2	Comparison of intervals with no diarrhoea and low and high diarrhoea prevalence	No	Socio-economic status, maternal education interval	Weight gain lower by 56 g/month in high diarrhoea group. Evidence of catch-up growth after diarrhoea; no more visible effect of diarrhoea on weight or height gain 6 months after the end of the interval.
Franks & Jurgensen (1985) Abemama atoll, Central Pacific	50	6-12	6	Regression	No	None	No correlation between centile drop for weight-for-age and frequency of diarrhoea.
Zumrawi <i>et al.</i> (1987) Soudan	cohort of 439 children	0-6	1	Regression and comparison of diarrhoea in well-nourished and underweight children at 6 months	No	None	Regression model on monthly intervals showing weight gain reduced by 80 to 90 g/month as a result of diarrhoea. At 6 months, diarrhoea explained 41 g (1.7%) of the 2360 g weight difference observed between the top and the bottom growth quartiles.
Rowland <i>et al.</i> (1988) Gambia	1863	0-24	1	Regression model	No	No	Weight deficit of 610 g attributed to diarrhoea when summing monthly deficits from 0 to 12 months. No significant effect of diarrhoea in exclusively breastfed children.
Briand <i>et al.</i> (1989a) Bangladesh	1772	6-35	3	Comparison of intervals with and without diarrhoea	Yes	None	Weight gain reduced by 31 g/month in intervals with diarrhoea. No difference in weight gain when the last 45 d of the interval were without diarrhoea. After 6 months, only dysentery had a persisting effect on height gain.

altering inter-organs exchanges of amino acids. It seems also plausible that some of these effects may be compounded by associated vitamin or mineral deficiency.

Does diarrhoea cause malnutrition?

Thirteen studies examining whether diarrhoea leads to malnutrition are listed in Table 3. Causality criteria are poorly met even when these studies are considered together.

Temporal ambiguity

To demonstrate without any temporal ambiguity that diarrhoea, in the community, is a major cause of malnutrition, one has to show, from longitudinal data, that a large proportion of initially well-nourished children have their nutritional status deteriorating after each episode of diarrhoea, that they do not recover between episodes and that they are malnourished at the end of the follow-up. Longitudinal data of this kind, taking into account the whole history of children, are scarce. Mata, Urrutia & Lechtig (1971) show how the growth curves of 2 children are influenced by intercurrent infectious diseases and in particular by diarrhoea; Eccles, Cole & Whitehead (1989a) do the same for 7 children from rural Gambia. Examination of these growth curves shows that infectious episodes, and especially diarrhoea, are frequent in these children during the weaning period and that each episode is associated with a transient depression of the growth curve. These results, however, do not give clear evidence that diarrhoea precedes the growth retardation observed on the long term among these children.

All studies listed in Table 3 examine the effect of diarrhoea on nutritional status by comparing growth in standard time intervals with and without diarrhoea or with low and high prevalence of diarrhoea. This is made either by directly comparing mean weight or height gain during these intervals or by using multiple regression models. This approach leads to temporal ambiguity: in these studies, growth is measured on the same time interval during which diarrhoea morbidity is monitored and they do not

clearly indicate whether diarrhoea or growth faltering comes first.

Examining growth of children at standard intervals of time leads to two other problems. First, in most studies, but especially in those with short observation periods, the same children are observed during several intervals and the statistical assumption that the different observations are independent is not strictly correct. This, however, may have little effect on the overall results (Cole, 1989). Second, interpretation of these studies is ambiguous. Large differences in weight gain between intervals with and without diarrhoea may be due to (i) either a major effect of diarrhoea on growth during the interval with diarrhoea or (ii) an important catch-up growth in intervals without diarrhoea in the absence of long-term effect of diarrhoea on growth. Hence, unless the duration of study intervals is considerably larger than the time needed to recover from a diarrhoea episode, this approach cannot make the difference between a transient or a sustained effect of diarrhoea on growth; differences in growth rates between intervals with and without diarrhoea tend even to be exaggerated when there is no long-term effect of diarrhoea on growth (Fig. 1).

Examining the effect of diarrhoea on attained height is especially difficult; seasonal variations of growth (Brown, Black & Becker, 1982; Briend *et al.*, 1989b) and growth curves of children recovering from various illnesses (Prader, Tanner & von Harnack, 1963) suggest that it may take several months to catch up from temporary linear growth faltering. Hence, in terms of linear growth, studies that examine the effect of diarrhoea even over intervals of 6 or 12 months may not be suitable for long-term projections.

Studies listed in Table 3 fall into two broad categories according to the length of the intervals during which the relation between diarrhoea and growth is examined: intervals may be short, 1–2 months, or long, from 6 to 12 months. These two categories of studies have different strengths and weaknesses (Table 4).

Studies on short intervals. All these studies show that weight gain is markedly reduced

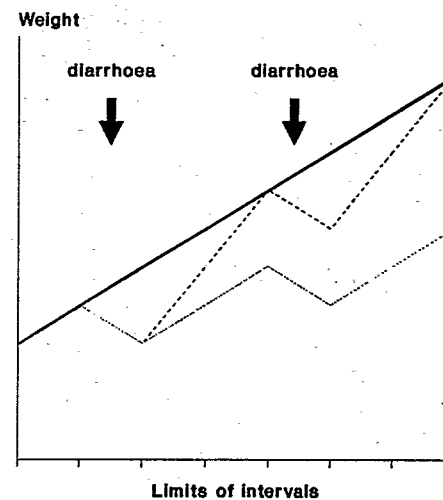


Fig. 1. Effect of diarrhoea on growth in the absence (model 1) or presence (model 2) of catch-up growth between diarrhoeal episodes. Although diarrhoea would have a sustained effect on growth only in model 1 (.....), differences in weight gain for intervals with and without diarrhoea are higher in model 2 (---); (—, no diarrhoea).

Table 4. Strengths and weaknesses of studies examining whether diarrhoea leads to malnutrition according to their design.

	Short intervals	Long intervals
Temporal ambiguity	Yes, but little ambiguity regarding the direction of the cause-effect relationship.	Yes
Assessment of long-term association	Not possible	Possible

when diarrhoea is present in the interval. Although these studies do not show that diarrhoea precedes the growth faltering, this interpretation is the most likely; dietary inadequacy which is the other common cause of growth faltering (Behrman & Vaughan 1983) does not occur suddenly. It does not seem likely, although it is not strictly impossible, that inadequate food intake could have been the common cause

of both sudden growth faltering and diarrhoea. These studies, however, examine a fragment of the growth curve which is not large enough to draw conclusions on the long-term effect of diarrhoea on weight gain. Estimates of the overall effect of diarrhoea on growth obtained from these studies by summing growth differences in intervals with and without diarrhoea should be regarded with caution.

Studies on long intervals. These studies also show that weight or height gain is lower in intervals with a high prevalence of diarrhoea but it is not clear from them whether growth faltering precedes, accompanies or follows diarrhoea. Hence, these studies may suggest either (i) that diarrhoea is a cause of growth faltering or (ii) that an inadequate dietary intake, suggested by the low weight gain, predisposes to diarrhoea. Both interpretations are plausible: enterocytes use mainly free amino acids from muscle for their metabolism and these amino acids may also regulate growth (see preceding section, biological plausibility). An association between rate of growth and susceptibility to diarrhoea seems quite plausible.

Consistency of findings

Studies examining whether diarrhoea is a cause of malnutrition do not give the same results when they are done on short or on long intervals. Studies using long intervals suggest an impact of diarrhoea on growth which is considerably less than indicated from studies using short intervals (Table 3). This is quite the opposite of what should occur, had repeated attacks of diarrhoea a cumulative impact on growth. This lack of consistency is even present in studies in which data were analysed both on the short term and the long term (Black *et al.*, 1984b; Bairagi *et al.*, 1987; Zumrawi, Dimond & Waterlow, 1987). The most likely explanation is that the impact of diarrhoea on growth is only transient and that most children exhibit catch-up growth after diarrhoea (Briend *et al.*, 1989a). Hence, studies on short intervals are likely to overestimate the impact of diarrhoea on nutritional status since catch-up growth has not time to take place during the short observation period.

Studies on intervals lasting more than 6 months give a more realistic picture of the relationship between diarrhoea and malnutrition on the long term. Yet, presence of children with diarrhoea at the end of the interval and who have no time for catch-up before nutritional assessment may also lead to an overestimation of the effect of diarrhoea on growth. It is also possible that some of the apparent long-term effect of diarrhoea on growth is due to the higher susceptibility to diarrhoea of children with inadequate growth.

Strength of the association

All studies listed in Table 3 use weight gain or height gain to measure the impact of diarrhoea on nutritional status. Among all nutritional indices, weight gain is the most sensitive to rapid nutritional change but is only poorly related to attained weight (Briend *et al.*, 1989b; Henry, Briend & Cooper, 1989). None of the studies listed in Table 3 shows that diarrhoea has a significant effect on nutritional status measured by weight-for-age, height-for-age or weight-for-height. This distinction is important since the risk of dying is more closely related to attained weight-for-age than to weight variations (Briend & Bari, 1989). This also suggests that, in absolute terms, the effect of diarrhoea on nutritional status is rather small since, apparently, it can be detected only by the most sensitive nutritional indices. This also almost eliminates the problem of temporal ambiguity in studies suggesting that malnutrition predisposes to diarrhoea, since in all these studies initial nutritional assessment was made in terms of weight-for-age, height-for-age or weight-for-height and there is so far no evidence that these indices could have been markedly affected by previous history of diarrhoea.

Biological plausibility

The hypothesis that diarrhoea is a major cause of malnutrition implies either (i) that nutrient losses in the stools are very high or (ii) that food intake is markedly depressed during diarrhoea and (iii) that nutritional losses resulting from diarrhoea are too important to be made up during con-

valence. Adequate evidence is still lacking to confirm these assumptions.

Absence of evidence regarding the existence of important nutrient faecal losses during diarrhoea. There is hardly any information, from community studies, on the amount of nutrient lost in the stools during diarrhoea. Available evidence from developing countries is mainly derived from hospital studies (Molla *et al.*, 1983a). Current understanding, however, is that energy faecal losses are small during diarrhoea and cannot explain the observed weight loss (Briscoe, 1979). This seems to be also the case even in protracted diarrhoea (Tomkins, 1983) and in coeliac disease (Gent & Creamer, 1968).

The scarcity of information regarding nutrient losses in the stools during diarrhoea is unfortunate; these losses are really lost for the child and represent an economic loss for the family since they can be made up only at extra cost during the recovery of the child. This is in contrast with food not eaten during diarrhoea as a result of anorexia or of cultural beliefs. In this case, food is available to other members of the family or for delayed consumption during recovery by the sick child (Briscoe, 1979).

Lack of adequate evidence supporting the existence of a major anorexia during diarrhoea. The effects of diarrhoea on food intake have also been mainly examined in hospital studies (Hoyle, Yunus & Chen, 1980; Molla *et al.*, 1983b; Khan & Ahmad, 1986). These results cannot be extrapolated to the community since diarrhoeal episodes leading to hospital admission are not representative of those occurring in the community. Moreover, hospital admission may by itself interfere with the food intake measurements.

There are three reports of community studies that examined whether food intake is decreased during diarrhoea (Table 5) by comparing food intake during a diarrhoeal episode with periods when the child had no diarrhoea. Two of these studies (Mata *et al.*, 1977; Martorell *et al.*, 1980) estimate food intake by 1 or 7 days recall respectively, a method known to be fairly inaccurate. In these two studies there is no attempt to

Table 5. Comparison of community studies estimating the reduction of food intake associated with diarrhoea.

Authors, country	Number of days of dietary survey	Age (months)	Dietary survey technique used to estimate food intake	Diarrhoea prevalence (%)	Reduction of food intake during diarrhoea
Mata <i>et al.</i> (1977) Guatemala	cohort of 30 children (number of surveys not stated)	24-36	7 d-recall survey limited to non-breastfed children	Not stated	Negative correlation between diarrhoea prevalence and food intake. Regression coefficient between diarrhoea prevalence and food intake not given. Reduction of energy intake: 160 kcal/d of diarrhoea. Reduction of protein intake: 3 g/d of diarrhoea.
Martorell <i>et al.</i> (1980) Guatemala	total: 3439	15-60	24-h recall. No estimation of breast milk intake	Not given. Most data on diarrhoea pooled with those of common illnesses which included 'apathy with anorexia' 13%	Non-significant reduction of energy intake of 2.68 kcal/kg body weight per day of diarrhoea.
Brown <i>et al.</i> (1985) Bangladesh	no diarrhoea: 883 diarrhoea: 131	5-18	Food eaten during the whole day weighed; plate waste measured. Breast milk intake measured by test-weighing during the day. Night feeds estimated.		

measure breast milk consumption among children under observation, although breast milk seems to be an important component of the diet in children with diarrhoea (Hoyle *et al.*, 1980). In the study of Martorell *et al.*, data on prevalence of diarrhoea are pooled with those of other common illnesses, including 'apathy' which had anorexia in its definition, and this makes impossible the assessment of the overall effect of diarrhoea on food intake. Conclusions of these two studies must be taken with caution. In the third study by Brown *et al.* (1985), food intake, including breast milk, is actually measured. This study, however, shows only a non-significant reduction of food intake of 2.68 kcal/kg for days with diarrhoea, suggesting that food withdrawal and anorexia are quite small for most mild diarrhoeal episodes occurring in the community. Since diarrhoea prevalence in this study is 13 per cent, overall impact of diarrhoea on food intake can be considered as negligible. Thus, the only study that actually measures food intake in the community is not consistent with the hypothesis that diarrhoea is a major cause of malnutrition.

A major effect of diarrhoea on the child food intake is essential not only to validate the hypothesis that diarrhoea is a major cause of malnutrition but also to explain in nutritional terms the specific effect of diarrhoea on growth. In all previous studies from developed countries, the effect of diarrhoea on growth is consistently found to be more pronounced than that for other infections (Martorell *et al.*, 1975). The same observation was also made in several studies from developing countries (Martorell *et al.*, 1975; Rowland, Cole & Whitehead, 1977; Cole & Parkin, 1977; Zumrawi *et al.*, 1987) with the exception of one study in the Gambia (Rowland, Goh & Cole, 1988). Martorell *et al.* explained this finding by postulating that diarrhoea resulted in a decrease of food intake which was more serious than in other infections even when these infections are associated with fever. A similar interpretation was proposed by Briscoe (1979) who calculated that weight loss during diarrhoea is largely superior to that expected from the quantity of energy lost in the stools, whereas in diseases associ-

ated with fever it corresponds roughly to that expected to result from the increased metabolism. This hypothesis, however, is not consistent with the study of Brown *et al.* (1985), which shows that fever is associated with a greater reduction of food intake than diarrhoea.

The effects of different types of diarrhoea on weight gain are also inconsistent when explained in nutritional terms; weight gain is depressed less during dysentery, which is often accompanied with fever and anorexia, than during watery diarrhoea (Black *et al.*, 1984; Briend *et al.*, 1989a). This last finding suggests, as speculated in an early study from Jamaica (Miall, Desai & Standard, 1970), that weight changes observed during diarrhoea are related more to dehydration than to variations of food intake, and should not be interpreted only in nutritional terms. Few studies, however, examined the effect of watery diarrhoea separately when assessing the effect of diarrhoea on weight gain (Table 3) and none eliminated the effect of dehydration.

Lack of evidence in favour of a nutritional mechanism explaining a sustained effect of diarrhoea on growth. Even if present, a reduction of food intake during diarrhoea compared to periods without diarrhoea would not be sufficient to prove that diarrhoea is a major cause of malnutrition. One has to show also that the child is unable to recover from the temporary nutrient losses. If food which is not given to him during diarrhoea is given during recovery, overall cost of diarrhoea is just equivalent to the cost of mobilising nutrient reserves during diarrhoea and storing these nutrients again during recovery. This cost is bound to be markedly lower than the difference of food intake of children with and without diarrhoea (Briscoe, 1979). This factor, not taken into account in previous studies, further limits the conclusions that can be drawn from food consumption surveys during diarrhoea.

Catch-up growth of children recovering from severe protein malnutrition is mainly limited by energy intake (Ashworth *et al.*, 1968) and one may speculate that energy is also the main factor limiting catch-up growth after diarrhoea-induced growth faltering.

Non-invasive diarrhoea, the most common type of diarrhoea, does not seem to have any effect on energy requirements except those needed for growth; in the absence of fever, basal metabolism is not increased during diarrhoea (Eccles, Cole & Whitehead, 1989b) and energy needed for physical activity is more likely to be reduced than increased. Hence, energy needed to recover after successive episodes of diarrhoea is equivalent to the energy needed for repeated spurts of catch-up growth. Even if food withdrawal, which may occur during diarrhoea as a result of anorexia, is regarded as a loss for the child, overall impact of diarrhoea in energy terms seems rather small. Energy needed for repeated growth spurt after diarrhoea has been calculated by Waterlow (1981) from the data of Rowland *et al.* (1977) from the Gambia and is equivalent to 2 kcal/kg/d for 6- to 36-month-old children. Although this study shows the greatest impact of diarrhoea on growth (Table 3), this quantity of energy is quite low and, in terms of energy, diarrhoea cannot be considered as a major cause of malnutrition. In this age-group, the energy needed for growth represents only a few per cent of total energy needs (Joint FAO/WHO/UNU Expert Consultation, 1985; Prentice *et al.*, 1988) which explains the low energy cost of diarrhoea (Waterlow, 1981). In fact, most of the weight lost during diarrhoea is likely to be due to dehydration; large quantities of water are lost in the stools and reduction of carbohydrate intake or absorption may, by itself, cause additional water loss (Lewis *et al.*, 1977). Hence, the energy cost of diarrhoea must be even lower than previously calculated by Waterlow (1981), assuming that the energy cost of growth after diarrhoea was equivalent to the energy cost of catch-up growth after malnutrition (Spady *et al.*, 1976).

During the first 6 months of life, when nutritional cost of growth represents an important fraction of total nutritional needs, diarrhoea may, in theory, represent an important energy cost. In poor communities of the developing world, however, most infants are breastfed, and among them diarrhoea is infrequent and seems to have little effect on growth (Rowland *et al.*,

1988). Artificially-fed young infants with repeated attacks of diarrhoea in the first few months of their life may be the only children for which diarrhoea-induced energy deficit may be plausible.

The same approach, which was used to show that energy is unlikely to limit recovery after diarrhoea, can be used to show that any nutrient which has low requirements for tissue deposition compared to body maintenance is unlikely to limit growth following diarrhoea. Diarrhoea-induced growth retardation would be plausible only if growth were limited by a nutrient needed in high quantities for catch-up growth but in small quantities for body maintenance and if this same nutrient were lost in high quantities in the stools during diarrhoea.

Height measurements are not confounded by dehydration and are more reliable to assess the nutritional effects of diarrhoea. The observation that dysentery has a delayed effect on linear growth which was still visible several months after weight went back to normal (Black *et al.*, 1984b; Briend *et al.*, 1989a) suggests that some nutrients lost during dysentery or used during weight recovery may limit linear growth for several months. To some extent, the same remark may apply to other non-watery diarrhoeas which also seem to have a delayed but transient effect on linear growth (Briend *et al.*, 1989a). A relationship between individual nutrient deficiencies and linear growth seems plausible (Golden 1988), yet data on micro-nutrient losses during diarrhoea are limited (Castillo-Duran, Vial & Uauy, 1988).

Lutter *et al.* (1989) in Colombia recently reported that the negative correlation between diarrhoea prevalence and attained height disappears when giving a food supplement containing iron, vitamin A and dried skimmed milk. This finding is compatible with the hypothesis that growth of un-supplemented children in that community is limited by a nutrient deficiency caused by diarrhoea which could be corrected by nutrient supplementation. This study does not prove formally, however, that diarrhoea is a cause of linear growth retardation in that community. Alteration of protein metabolism may predispose to diarrhoea (see earlier section, biological plausibility)

and maybe also some vitamin and mineral deficiencies. Moreover, enriching the diet of weanlings with skim milk may promote growth (Brown *et al.*, 1980). In other words, results of this study could also be explained by a nutrient deficiency being the common cause of linear growth retardation and high prevalence of diarrhoea among some of the unsupplemented children.

Potassium is lost in large quantities in the stools during diarrhoea (Molla *et al.*, 1981) and is also needed for growth (Golden, 1988). Potassium is abundant in most diets but is low in cereal flour (Michaelsen & Clausen, 1987) which is used for preparation of traditional weaning food. Low potassium diets such as consumed by children weaned on cereal flour may never have occurred in man's history since during most of its evolution, it used to have a diet of unprocessed potassium-rich food (Eaton & Konner, 1985) and the organism seems more adapted to cope with potassium overload than with potassium deficiency (Silva, Brown & Epstein, 1977). An effect of diarrhoea on growth as a result of potassium deficiency seems plausible. It has been speculated that its replacement by oral rehydration therapy may have nutritional benefits (Nalin, 1983).

Data from the Philippines suggest that the use of oral rehydration solution with potassium for home treatment of diarrhoea is associated with higher weight gain (International Study Group, 1977) but this early finding, however, has not been confirmed in other settings (Watkinson & Watkinson, 1982).

Conclusions

When all causality criteria are considered together, the causal nature of the pathway leading from diarrhoea to malnutrition, although not certain, seems very likely. There is no clear evidence, on the other hand, that diarrhoea is a major cause of malnutrition (Table 6). No clear pathophysiological mechanism explaining a possible sustained effect of diarrhoea on growth has been shown to be important at the community level. Previous studies examining the effect of diarrhoea on growth overestimated this effect for several reasons: studies on short intervals did not consider the effect of catch-up growth between intervals of diarrhoea; studies on longer intervals could not eliminate the effect of the higher susceptibility of malnourished children to diarrhoea; none of these studies eliminated

the effect of water movement on weight loss during diarrhoea; studies which showed the greatest reduction of food intake during diarrhoea used an unreliable technique to measure food intake; these studies did not eliminate the possible effect of delayed food consumption after diarrhoea episodes. Yet, despite all these causes of overestimation, the effect of diarrhoea on growth is always small in absolute terms and could be detected only by using the most sensitive nutritional indices.

Although there is no doubt that diarrhoea can lead to transient growth faltering in most children, and that in some of them diarrhoea may lead to malnutrition, there is so far no solid evidence to support the hypothesis that diarrhoea may be a major cause of permanent growth faltering in whole communities.

Diarrhoea is a major cause of death in poor communities (Snyder & Merson, 1982).

There is some evidence that diarrhoeal disease-control programmes may have an impact on mortality (Elrafie *et al.*, 1990). Evidence available so far, however, suggests that this type of effort does not reduce childhood malnutrition (Stanton, Clemens & Khair, 1988; Hasan *et al.*, 1989). Programmes aiming at improving nutritional intake during diarrhoea may also prevent deaths from hypoglycaemia, an important cause of death during diarrhoea (Hirschhorn *et al.*, 1966). Nonetheless, they may be poorly effective in improving overall nutritional status of children in poor communities.

Until further evidence is at hand, improving dietary intake of the under-fives remains the most promising approach to reduce childhood malnutrition. This approach may also contribute to the reduction of diarrhoea prevalence and diarrhoea mortality.

Table 6. Comparison of causality criteria for the two possible pathways linking diarrhoea and malnutrition.

	Malnutrition predisposing to diarrhoea	Diarrhoea leading to malnutrition
Lack of temporal ambiguity	Yes	Dubious for studies on long intervals.
Consistency of findings	Good. Negative findings in three studies can be explained by the study design	Poor between studies on short and long intervals.
Strength of the association	Fair; remains unchanged after adjustment for possible confounding factors	Weak, even absent in several studies on long intervals. Association detected only by the most sensitive nutritional indices.
Biological plausibility	Good. Intestinal epithelium represents a large proportion of body protein turnover Enterocytes depend on glutamine from muscle for metabolism Intestinal function likely to be impaired during malnutrition Physiological changes postulated to explain the higher prevalence of diarrhoea during malnutrition can be reproduced in experimental animals	Poor. No nutrient, known to limit growth, lost in large amounts in the stools. No clear evidence that food intake is markedly reduced during diarrhoea. A major effect of diarrhoea on growth is unlikely to involve nutrients needed in small quantity for growth but in high quantity for body maintenance.

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Absorption and retention in acute diarrhoea

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¹⁵N-yeast protein absorption, nitrogen and fat retention and stool reducing substances and lactate were measured in 6 infants who had acute diarrhoea and 15 who had had severe diarrhoea for 4 d. The results were compared with those of previously reported infants, who had had diarrhoea for 8 d. The infants were fed a full cream cows' milk, soy based or low lactose formula. In all cases the losses of nitrogen and energy in stool rose as stool weight increased. In severe diarrhoea, the losses of nutrients in stool were so great that oral feeds did not provide adequate nitrogen and energy. The smallest loss of nitrogen and fat were found in infants who had had diarrhoea for 4 d and who were fed a soy based formula.

Diarrhoeal disease of infancy is usually an acute, self limiting condition and the factors responsible for the development of intractable diarrhoea are not known. Ghadimi, Kumar & Abaci (1973) postulated that intestinal mucosa and digestive enzymes are extremely vulnerable to protein deficiency. They suggested that there is a continuous loss of endogenous nitrogen in protracted diarrhoea resulting in impaired synthesis of mucosa and enzymes. The ensuing vicious cycle may be responsible for precipitating protracted diarrhoea, regardless of aetiology, into an intractable state (Ghadimi *et al.*, 1973). The magnitude and nature of the stool losses of nitrogen found in infants who have had severe diarrhoea for 8 d support this hypothesis (Mann *et al.*, 1982). There is little available information on stool losses in the first few days after the onset of diarrhoea. This paper reports the protein absorption and nitrogen and fat balance of 21 infants in the first week after the onset of diarrhoea. The results are compared with those of 22 infants who had severe diarrhoea for 8 d (Mann *et al.*, 1982).

Patients and methods

All infants had a history of diarrhoea for less than 72 h when they were admitted to hospital for intravenous rehydration. None had monosaccharide intolerance, kwashiorkor, marasmic kwashiorkor (Annotation, *Lancet*, 1970) or any of the skin lesions associated with nutritional deficiencies. Pre-term and small for dates infants who had shown catch-up growth since birth were included in the study even if they were still less than 60 per cent of expected weight for age, but those with a diagnosis of marasmus were excluded. The seven treatment groups are summarized in Table 1 and the feeds used in Table 2.

Six infants (Group 1) were selected for the study 12-15 h after admission to hospital. They were passing frequent large, loose or watery stools and were receiving oral and intravenous half-strength Darrows solution, containing 5 per cent dextrose. Initially while dehydration and acidosis were corrected, all fluids had been given intravenously. The investigations began about

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