

Child Health

ARE DIARRHOEA CONTROL PROGRAMMES LIKELY TO REDUCE CHILDHOOD MALNUTRITION? OBSERVATIONS FROM RURAL BANGLADESH

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Summary Growth of rural Bangladeshi children aged 6–35 months was examined in relation to the history of diarrhoea in 1772 3-month intervals. Weight gain and linear growth were lower in intervals with a history of diarrhoea than in intervals without diarrhoea. However, comparison of weight and height gains in intervals during which diarrhoea occurred at the beginning or at the end showed that after non-bloody diarrhoeas children catch up and that deficits in weight gain and linear growth were no longer apparent a few weeks later. These findings suggest that the effect of diarrhoea on growth is transient and that efforts to control diarrhoea are unlikely to improve children's nutritional status in the long term.

INTRODUCTION

THE association between diarrhoea and malnutrition is so common in poor communities that the concept of a diarrhoea-malnutrition cycle, with diarrhoea leading to malnutrition and malnutrition predisposing to diarrhoea, is appealing. Several studies have shown that in malnourished children, diarrhoeas have a higher incidence,¹ or prevalence,² last longer,^{3–6} are more severe,^{6–9} and have a higher case-fatality rate^{8–10} than in well-nourished children. There is little doubt that malnutrition leads to diarrhoea or that malnutrition aggravates diarrhoea.

The opposite hypothesis—that diarrhoea is a major causative factor in malnutrition—has never really been questioned; however, it is now endorsed by the most influential international health organisations¹¹ and diarrhoea is often presented as the major cause of malnutrition in poor countries.¹² Yet, this hypothesis is based on weak evidence; it relies on a limited number of studies, which examined the relation between weight gain and diarrhoea over short periods of time,^{13–17} and assumes that the effect of diarrhoea on growth is cumulative over time. However, even in healthy children, growth occurs in spurts and weight gain over short times is extremely variable.¹⁸ The low or negative weight gain associated with diarrhoea is likely to have a lasting effect on nutritional status, measured by weight-for-age or height-for-age, only if it is not followed by catch-up growth.

In this study, we have re-examined the relation between diarrhoea and malnutrition in a rural community in Bangladesh, giving special attention to the growth of children recovering from diarrhoea, to determine whether diarrhoea is really a major cause of malnutrition.

SUBJECTS AND METHODS

This analysis is based on data collected for the evaluation of a water and sanitation project near the town of Mirzapur, in rural Bangladesh.¹⁹ To assess the effect on health of handpumps and latrines, information on diarrhoea morbidity and nutritional status

of children under 5 years old was collected in an area with water and sanitation intervention and in a similar area with no intervention. Children in both areas received oral rehydration therapy if diarrhoea occurred and were referred to a nearby hospital if they were seriously ill. This analysis was done on data from the intervention area.

Baseline demographic information was collected in January, 1984, and then updated monthly until December, 1987. Height and weight were measured quarterly from October, 1984, to December, 1987 (fourteen rounds) by trained female community health workers. Naked or lightly clothed children were weighed to the nearest 0.1 kg on a Salter scale, which was regularly checked against standard weights. Recumbent length, for children under 2 years old, was measured to the nearest 1 mm on a locally made wooden platform with a sliding footboard. For children over 2 years a height scale was used.

Anthropometric measurements were compared with the National Center for Health Statistics (NCHS) standards.^{20,21} The mean time between measurements was 87 days but it varied substantially since the area was inaccessible in some seasons. The analysis was restricted to intervals of 60–120 days. Weight and height gains were standardised to an interval of 30 days by means of the actual number of days between two visits. To allow comparisons of growth rates among children of different ages, weight gains and height increments were expressed in percentages of the increment of the NCHS median for children of the same age.

From March, 1984, onwards, detailed information on diarrhoea morbidity was collected by means of weekly recall by the children's mothers in interviews conducted by female community health workers. Exact dates of onset and recovery and whether the stools were watery and/or bloody were recorded. Dysentery was defined by the presence of blood in the stool at least once during an episode of diarrhoea. An increased frequency of unformed soft stools without blood was classified as non-bloody, non-watery diarrhoea.

This analysis was made by child-intervals, each child being entered as a new individual for every interval between two anthropometric measurements. Intervals were included in this analysis provided no diarrhoea information was missing from the weekly records and that the child's age was between 6 and 35 months. On average, 230 children in this age range were seen at each survey. 40.7% of intervals were excluded because of incomplete morbidity information or inadequate duration between two anthropometric rounds.

Comparisons of means were made by a *t* test or one-way analysis of variance.²² Relative risk and its 95% confidence interval were calculated by the Miettinen test²³ and attributable risk and its confidence interval according to Walter.²⁴

RESULTS

Altogether, 1772 3-month intervals had complete diarrhoea information and complete anthropometric data at their beginning and at their end. On average, children enrolled in this study were underweight, wasted, and stunted: mean (SD) weight-for-age, weight-for-height, and height-for-age were, respectively, 73.4% (9.3%), 88.0% (7.5%), and 90.3% (4.1%) of NCHS medians. They had an average of 0.29 episodes of diarrhoea every month, equivalent to 1 episode for each child every 3.4 months. The mean duration of an episode was 11 days, but the distribution of the duration of episodes was skewed (median 6 days), with a high number of short episodes. Non-bloody, non-watery diarrhoea was the most common, in terms of both incidence and percentage of time with diarrhoea (table 1).

Altogether, 821 intervals (46% of the total) were free from diarrhoea. During these intervals, children gained on average 155 g and grew 7.8 mm per month, which corresponded, respectively, to 74.5% and 80.1% of the NCHS medians. In 435 intervals (25% of the total, on average 1 interval per year), there were 10 days or more of

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TABLE I—INCIDENCE, PERCENTAGE OF DAYS WITH DIARRHOEA, AND MEAN DURATION OF EACH EPISODE FOR DIFFERENT TYPES OF DIARRHOEA

Type of diarrhoea	Monthly incidence (episodes per child per mo)	% of days with diarrhoea	Mean (SD) duration of episodes (days)
All	0.29	9.6	11.1 (14.8)
Watery	0.06	1.3	6.3 (9.2)
Dysenteries	0.04	1.7	14.2 (15.8)
Non-watery, non-bloody	0.19	6.7	11.3 (15.2)

diarrhoea. For these intervals, the weight and height increments were significantly lower than for intervals without diarrhoea ($p < 0.01$, table II).

To determine whether the effect of diarrhoea on growth persisted for longer than a few weeks, we compared intervals which had at least 10 days of diarrhoea at the beginning of the interval but the last 45 days free of diarrhoea with intervals which had at least 45 days of diarrhoea in the last 45 days but no diarrhoea at the beginning. Weight gain was similar in intervals with more than 10 days of diarrhoea only at the beginning and in those without diarrhoea. In contrast, intervals with more than 10 days of diarrhoea in the last 45 days were associated with a significantly lower weight gain than diarrhoea-free intervals. Intervals with diarrhoea at both the beginning and the end had a weight gain similar to the average for all intervals with at least 10 days of diarrhoea (table II).

The same approach was used to determine whether diarrhoea had a durable effect on linear growth. The increments were similar for intervals with diarrhoea at the end and intervals without any diarrhoea. On the other hand, intervals with diarrhoea at the beginning were associated with a significantly smaller height increment. Intervals with diarrhoea at both the beginning and the end had height increments similar to the average for all intervals with at least 10 days of diarrhoea (table II).

If we included in the analysis intervals with at least 5 days of diarrhoea at the beginning or at the end of the interval, the number of intervals with diarrhoeas was large enough to repeat the analysis by type of diarrhoea (figure). No type of diarrhoea occurring in the first part of the interval had a significant effect on weight gain over the interval. Watery diarrhoea had a highly significant effect when it occurred at the end of an interval, but no effect at all when it occurred in the first part of an interval. Dysenteries and non-bloody, non-watery diarrhoeas also had a greater effect on weight gain when they occurred in the last part of the interval, but the effect was less pronounced than that of watery diarrhoea. For all types of diarrhoea combined, the difference in weight gain between intervals with at least 5 days of diarrhoea at the

TABLE II—WEIGHT AND HEIGHT GAIN IN RELATION TO HISTORY OF DIARRHOEA IN PREVIOUS 3 MONTHS

History of diarrhoea during interval	n	Mean (SEM)			
		Weight gain		Height increment	
		g/mo	% NCHS	mm/mo	% NCHS
None	821	155 (6)	74.5 (0.3)	7.8 (0.2)	80.1 (1.6)
10 days or more					
At any time	435	124 (6)*	58.6 (4.4)*	7.2 (0.3)	70.3 (2.0)†
At beginning	106	153 (6)	72.7 (9.5)	6.6 (0.4)*	68.3 (4.2)*
At end	91	100 (6)*	47.7 (5.1)*	7.6 (0.5)	77.7 (4.8)
At both beginning and end	238	121 (6)*	56.5 (5.8)*	7.3 (0.4)	68.4 (2.6)†

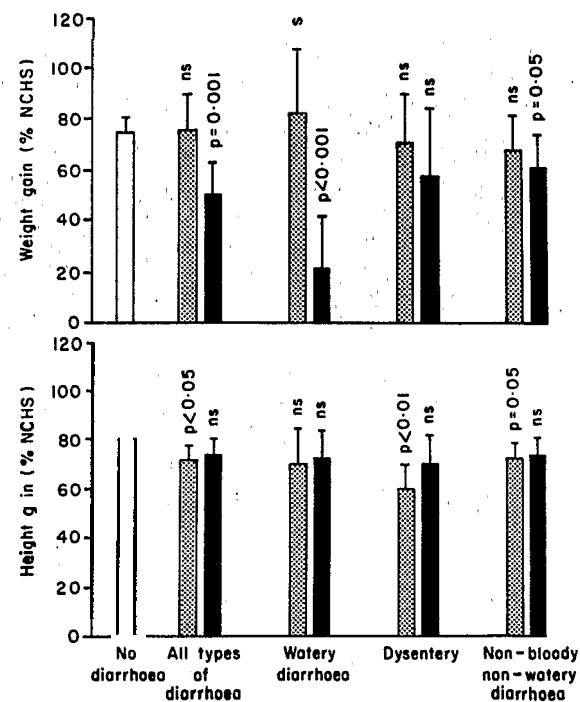
For comparisons with intervals without diarrhoea * $p < 0.01$; † $p < 0.001$.

beginning and intervals with at least 5 days of diarrhoea in the last 45 days was significant ($p < 0.01$).

The different types of diarrhoeas had no significant effect on height increment when they occurred at the end of an interval (figure). Dysentery, if present at the beginning of the interval, was associated with a significantly smaller height increment. Intervals with non-bloody, non-watery diarrhoea were also associated with a smaller height increment than intervals without diarrhoea when diarrhoea occurred at the beginning of the interval.

To determine whether the effect of diarrhoea on growth in height was sustained or transient, intervals which were followed 3 months later by another height measurement were examined. The growth in height over 6 months did not differ between 106 children who had at least 5 days of non-bloody, non-watery diarrhoea at the beginning of the 6-month period and 475 children without diarrhoea. In contrast, 31 children who had dysentery at the beginning of the 6 months had significantly smaller height increments over 6 months than the 475 children who had no diarrhoea (62.7 [SD 26.0] vs 76.8 [25.0]% of NCHS standard; $p < 0.01$).

The hypothesis that malnutrition leads to diarrhoea was tested by examining the relation between nutritional status at the beginning of an interval and the percentage of days with diarrhoea during the interval. This indicator combines the effect of incidence and duration of diarrhoea, which are both reported to be higher if there is pre-existing malnutrition.¹⁻⁶ The percentage of days with non-watery, non-bloody diarrhoeas was significantly higher among children who were stunted (table III). There was no significant association between wasting or stunting and other types of diarrhoeas.



Weight and height gain (% NCHS, with upper 95% confidence limit) in intervals with at least 5 days of diarrhoea at either the beginning or the end.

p values refer to comparisons with intervals without diarrhoeas.

▨ At least 5 days of diarrhoea in the first part of the interval

■ At least 5 days of diarrhoea in the last part of the interval

TABLE III—PERCENTAGE OF DAYS WITH DIARRHOEA IN RELATION TO HEIGHT-FOR-AGE AT BEGINNING OF INTERVAL

Height-for-age	Total intervals	Mean (SEM) % days with			
		All diarrhoeas	Watery diarrhoeas	Dysenteries	Non-bloody, non-watery diarrhoeas
Less than 85%	137	13.5 (1.7)	2.2 (0.9)	2.3 (0.9)	9.0 (1.3)*
85%–89.9%	618	10.4 (0.7)	1.3 (0.2)	1.2 (0.2)	8.0 (0.7)
90% or greater	1017	8.6 (0.5)	1.2 (0.2)	1.9 (0.3)	5.6 (0.4)

* $p < 0.01$ between nutritional categories by one-way analysis of variance.

For 1464 child-intervals, diarrhoea information was available for the 3 months before and the 3 months after nutritional assessment. The risk of having at least 1 episode of diarrhoea was greater when there had been a history of diarrhoea in the previous interval (relative risk 1.32, 95% confidence interval [CI] 1.19–1.46). This risk was significant for watery diarrhoea (2.04, 1.50–2.76) and non-watery, non-bloody diarrhoeas (1.35, 1.19–1.54) but not for bloody diarrhoea. For all non-bloody diarrhoeas, the proportion of episodes which could be related to a previous history of diarrhoea (the attributable risk) was 9.3% (95% CI 3.7–14.9%). The correlation of percentage of days with diarrhoea in 2 consecutive 3-month intervals was 0.094 ($p < 0.001$).

DISCUSSION

Our findings are consistent with previous studies in that growth (in both weight and height) was lower during intervals with diarrhoea than during intervals without diarrhoea.^{13–17} As shown previously,¹⁶ differences in weight gain were more pronounced for watery diarrhoea than for other types of diarrhoea, and dysentery had almost no effect on weight gain but mainly affected linear growth.

Our findings are, however, incompatible with the hypothesis that diarrhoea is a major cause of malnutrition (measured by weight-for-age or height-for-age) in this community; episodes of diarrhoea occurring at the beginning of a 3-month interval had virtually no effect on weight gain averaged over the whole interval. The effect of diarrhoea on weight gain was transient and could not be detected after a few weeks. The effect on linear growth was delayed but, with the exception of dysentery, was also temporary. These findings suggest that diarrhoea episodes produce short depressions on the growth curve without greatly affecting its general shape.

Our data also show that children are free from diarrhoea for 90.4% of the time. Hence, their nutritional status, defined in terms of attained weight-for-age, depends more on growth during intervals without than intervals with diarrhoea. Yet, in intervals without any diarrhoea, weight gain was equivalent to only 74.5% of the NCHS median. This finding suggests that, in this community, any diarrhoea control intervention, however successful, will have little effect on the overall level of malnutrition, given the extent of growth retardation taking place between episodes of diarrhoea.

It may be argued also that temporary growth faltering by itself is an indication of malnutrition; by this definition, our data would show that diarrhoea results in malnutrition. There is growing evidence, however, that in young children, transient growth faltering is associated with a much lower risk of dying than is malnutrition defined in terms of a low weight-for-age.^{25,26} To determine the nutritional consequences of diarrhoea in a public health perspective, the

nutritional impact of diarrhoea has to be assessed on malnutrition defined in terms of low weight-for-age.

Catch-up growth between diarrhoea episodes could explain the weak association between diarrhoea and weight gain found when the relation is examined over long periods of time.^{5,16,27,28} This contrasts with the strong association between diarrhoea and growth faltering observed when the relation is assessed over short times.^{15,16,28} Presumably, the association reported in previous studies would have been smaller, or even absent, had it been corrected for episodes taking place at the end of intervals or had account been taken of the tendency for malnourished children to have diarrhoea more often.

In terms of energy balance, catch-up growth between diarrhoea episodes seems plausible, even in this poor community. A previous community survey from rural Bangladesh did not show a significant reduction in food intake in children suffering from diarrhoea.²⁹ The energy needed to recover from diarrhoea, calculated on the basis of the weight loss³⁰ or of the reduction of the food intake,³¹ is very small compared with total energy needs. In this age group, doubling the rate of weight gain requires an increase of only about 5% of the energy intake.¹⁸ Presumably, an even smaller increase in energy intake would be needed to recover the weight deficit we found in this study.

Watery diarrhoea had the greatest effect on weight gain, probably owing to the loss of water that occurs during diarrhoea, even in the absence of clinical dehydration. Since carbohydrate intake and absorption are commonly reduced during diarrhoea,³² this water loss may also be aggravated by the loss of water and minerals accompanying sudden reductions in carbohydrate intake.³³ This weight loss is likely to be quickly recovered after the end of diarrhoea at a low nutritional cost. Yet, although the rapid weight gain of children after watery diarrhoea is known,³⁴ it is usually overlooked when the nutritional cost of diarrhoeas is estimated.

Dysenteries had an effect on linear growth which did not become visible immediately after the beginning of the episode but was still present 3 months after its appearance. However, catch-up growth in height is known to be a much slower process than that in weight.¹⁸ We do not know whether the height deficit caused by dysentery is sustained and whether catch-up growth can take place between 2 episodes, although this seems plausible, since a child in this community has an average of 1 episode every 2.5 years.

If, in individual children, diarrhoeas occur very frequently, full recovery between 2 episodes might not be possible. The incidence of dysentery was, however, unrelated to previous history of dysentery. For non-bloody diarrhoeas, the risk of having an episode of diarrhoea was higher if there was a history of previous diarrhoea, suggesting the possibility of a diarrhoea-diarrhoea cycle. The low attributable risk associated with a history of diarrhoea and the low correlation between the percentage of days with diarrhoea for 2 consecutive intervals suggests, however, that such a cycle would affect only a limited number of children and should have little effect on the overall nutritional status of the community.

Only non-bloody, non-watery diarrhoeas were related to the nutritional status of children, as measured by height-for-age at the beginning of the intervals, which is consistent with previous studies.²⁴ Hence, only this type of diarrhoea might theoretically be involved in a diarrhoea-malnutrition cycle. However, its effect on linear growth was temporary; since

height increments over a few weeks are small compared with attained height, the existence of such a cycle seems unlikely. We suggest that the frequent association of diarrhoea and malnutrition seen in poor communities is due to the higher prevalence or severity of diarrhoea in malnourished children and not to the existence of a diarrhoea-malnutrition cycle.

Diarrhoeas, in particular dysenteries and prolonged diarrhoeas, are associated with a high risk of dying.³⁵ Their prevention and treatment (especially by oral rehydration therapy) are a high priority. Improving feeding practices during diarrhoea is also important, since there is strong evidence that a high proportion of deaths from diarrhoea are related to hypoglycaemia.^{36,37} However, our study suggests that efforts to control or treat diarrhoea should not be expected to reduce the prevalence of malnutrition. In this respect, an intervention which achieved a substantial reduction in diarrhoea morbidity could show no effect on children's nutritional status.³⁸ In our study, no improvement in nutritional status was seen in the area with improved water and sanitation facilities.¹⁹

In conclusion, we suggest that in poor communities, children are malnourished mainly because they do not get enough food, and not because they suffer from diarrhoea. A food consumption survey in another community in rural Bangladesh showed that the average intake of energy in this age group was grossly inadequate (63–71 kcal/kg daily, representing about 55% of estimated energy needs of children of the same age).³⁹ Ensuring that deprived children have enough food to eat still seems the best approach to alleviating the problem of malnutrition.

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REFERENCES

1. El Samani EFZ, Willett WC, Ware JH. Association of malnutrition and diarrhea in children aged under five years: a prospective follow-up study in a rural Sudanese community. *Am J Epidemiol* 1988; 128: 93–105.
2. Tomkins AM, Dunn DT, Hayes RJ. Nutritional status and risk of morbidity among young Gambian children allowing for social and environmental factors. *Trans R Soc Trop Med Hyg* 1989; 83: 282–87.
3. Black RE, Brown KH, Becker S. Malnutrition is a determining factor in diarrhoeal duration, but not incidence, among young children in a longitudinal study in rural Bangladesh. *Am J Clin Nutr* 1984; 39: 87–94.
4. Henry FJ, Alam N, Aziz KMS, Rahaman MM. Dysentery, not watery diarrhoea, is associated with stunting in rural Bangladesh. *Hum Nutr Clin Nutr* 1987; 41C: 243–49.
5. Bairagi R, Chowdhury MK, Kim YJ, Curlin CT, Gray H. The association between malnutrition and diarrhoea in rural Bangladesh. *Int J Epidemiol* 1987; 16: 477–81.
6. Tomkins A. Nutritional status and severity of diarrhoea among preschool children in rural Nigeria. *Lancet* 1981; i: 860–62.
7. Mathur R, Reddy V, Naidu AN, Ravikumar Krishnamachari KAVR. Nutritional status and diarrhoeal morbidity: a longitudinal study in rural Indian preschool children. *Hum Nutr Clin Nutr* 1985; 39C: 447–54.
8. Scrimshaw NS, Taylor CE, Gordon JE. Interactions of nutrition and infection. Geneva: World Health Organisation, 1968. WHO Monogr Ser 57.
9. Ryder RW, Reeves WC, Sack RB. Risk factors for fatal childhood diarrhea: a case-control study from two remote Panamanian islands. *Am J Epidemiol* 1985; 121: 605–10.
10. Briand A, Dykewicz C, Graven K, Mazumder RN, Wojcyniak B, Bennis M. Usefulness of nutritional indices and classifications in predicting death of malnourished children. *Br Med J* 1986; 293: 373–75.
11. The management of diarrhoea and use of oral rehydration therapy. A joint WHO/UNICEF statement. Geneva: World Health Organisation, 1985.
12. Grant JP. The state of the world's children. Oxford: Oxford University Press, 1984.
13. Mata LJ, Urrutia JJ, Lechtig A. Infection and nutrition of children of a low socioeconomic rural community. *Am J Clin Nutr* 1971; 24: 249–59.
14. Martorell R, Habicht JP, Yarbrough C, Lechtig A, Klein RE, Western KA. Acute morbidity and physical growth in rural Guatemalan children. *Am J Dis Child* 1975; 129: 1296–301.
15. Rowland MGM, Cole TJ, Whitehead RG. A quantitative study into the role of infection in determining nutritional status in Gambian village children. *Br J Nutr* 1977; 37: 441–50.
16. Black RE, Brown KH, Becker S. Effects of diarrhea associated with specific enteropathogens on the growth of children in rural Bangladesh. *Pediatrics* 1984; 73: 799–805.
17. Rowland MGM, Goh Rowland SGJ, Cole TJ. Impact of infection on the growth of children from 0 to 2 years in an urban West African community. *Am J Clin Nutr* 1988; 47: 134–38.
18. Energy and protein requirements. Report of a joint FAO/WHO/UNU expert consultation. Geneva: World Health Organisation, 1985. WHO Tech Rep Ser no 724.
19. Aziz KMA, Hoque BA, Huttly S, et al. Mirzapur Handpump Project. Final report. Dhaka: World Bank and International Centre for Diarrhoeal Disease Research, Bangladesh, 1989.
20. Hamill PVV, Drizd TA, Johnson CL, Reed RB, Roche AF, Moore WM. Physical growth: National Center for Health Statistics percentiles. *Am J Clin Nutr* 1979; 32: 607–29.
21. WHO Working Group. Use and interpretation of anthropometric indicators of nutritional status. *Bull WHO* 1986; 64: 929–41.
22. Armitage P. Statistical methods in medical research. Oxford: Blackwell Scientific Publications, 1971.
23. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiological research: principles and quantitative methods. Belmont: Lifetime Learning Publications, 1982.
24. Walter SD. Calculation of attributable risk from epidemiological data. *Int J Epidemiol* 1978; 7: 175–82.
25. Bairagi R, Chowdhury MK, Kim YJ, Curlin GT. Alternative indicators of mortality. *Am J Clin Nutr* 1985; 42: 296–306.
26. Briand A, Bari A. Critical assessment of the use of growth monitoring for identifying high-risk children in primary health care programmes. *Br Med J* 1989; 298: 1607–11.
27. Condon-Paolini D, Cravioto J, Johnston FE, de Licardie ER, Scholl TO. Morbidity and growth of infants and young children in a rural Mexican village. *Am J Publ Health* 1977; 67: 651–66.
28. Zumrawi FY, Dimond H, Waterlow JC. Effect of infection on growth in Sudanese children. *Hum Nutr Clin Nutr* 1987; 41C: 453–61.
29. Brown KH, Black RE, Robertson AD, Becker S. Effects of seasons and illness on the dietary intake of weanlings during longitudinal studies in rural Bangladesh. *Am J Clin Nutr* 1985; 41: 343–55.
30. Waterlow JC. Observations on the suckling's dilemma—a personal view. *J Hum Nutr* 1981; 35: 85–98.
31. Martorell R, Yarbrough C, Yarbrough S, Klein RE. The impact of ordinary illnesses on the dietary intakes of malnourished children. *Am J Clin Nutr* 1980; 33: 345–50.
32. Fomon SJ. Infant nutrition, 2nd ed. Philadelphia: WB Saunders, 1974.
33. Lewis SB, Wallin JD, Kane JP, Gerich JE. Effect of diet composition on metabolic adaptations to hypocaloric nutrition: comparison of high carbohydrate and high fat isocaloric diets. *Am J Clin Nutr* 1977; 30: 160–70.
34. Black RE, Brown KH, Becker S. Influence of acute diarrhoea on the growth parameters of children. In: Bellanti JA, ed. Acute diarrhoea: its nutritional consequences in children. New York: Raven Press, 1983: 75–84.
35. Briand A, Wojcyniak B, Rowland MGM. Arm circumference and other factors in children at high risk of death in rural Bangladesh. *Lancet* 1987; ii: 725–28.
36. Hirschorn N, Lindenbaum J, Greenough WB, Alam SM. Hypoglycaemia in children with acute diarrhoea. *Lancet* 1966; ii: 128–33.
37. Jones RG. Hypoglycaemia in children with acute diarrhoea. *Lancet* 1966; ii: 643.
38. Stanton BF, Clemens JD, Khair T. Educational intervention for altering water-sanitation behavior to reduce childhood diarrhea in urban Bangladesh: impact on nutritional status. *Am J Clin Nutr* 1988; 48: 1166–72.
39. Brown KH, Black RE, Becker S, Nahar S, Sawyer J. Consumption of foods and nutrients by weanlings in rural Bangladesh. *Am J Clin Nutr* 1982; 36: 878–89.

"In recent months since the approval of intravenous thrombolytic agents in the United States, recombinant tissue plasminogen activator (rt-PA) has been under fire in many peer review medical journal articles. At issue is whether rt-PA, an expensive, elegant product of the molecular biology revolution, is really better than streptokinase, an inexpensive bacterial protein produced by routine laboratory methods . . . The 10-fold price differential between rt-PA and streptokinase is most unfortunate. Tissue plasminogen activator clearly does not open 10 times as many arteries, save 10 times as much heart muscle or save 10 times as many lives. Perhaps never before has a price difference in therapeutic alternatives fueled so much debate and further clinical investigation. Only when the GISSI-2 and ISIS-3 trials are completed will we know for certain whether tissue plasminogen activator's more rapid achievement of coronary artery patency represents a life-saving advantage. Were there no cost differences between fibrinolytic agents, these major trials would probably not have been performed. Thus, the backlash and acrimony over rt-PA has largely been driven by economic issues. The interaction of two powerful streams of medical thought, reperfusion and cost-consciousness, has served the useful purpose of heightening clinicians' awareness of the critical issues confronting modern medicine on both fronts."—Dr E. J. Topol and Dr R. M. Califf. Tissue plasminogen activator: why the backlash? *J Am Coll Cardiol* 1989; 13: 1477–79.