

Technical

Discussions



Washington, D.C. September-October 1974

Provisional Agenda Item 19

CSP19/DT/5 EN

31 July 1974

ORIGINAL: SPANISH

STUDIES AND STRATEGIES TO REDUCE MORBIDITY AND MORTALITY FROM ENTERIC INFECTIONS

THE SIGNIFICANCE OF FEEDING AND NUTRITION
IN THE PATHOGENY AND PREVENTION
OF DIARRHEIC PROCESSES

bу

Dr. Moisés Béhar

Director of the Institute of Nutrition of Central America and Panama (INCAP)
Guatemala, C.A.

THE SIGNIFICANCE OF FEEDING AND NUTRITION IN THE PATHOGENY AND PREVENTION OF DIARRHEIC PROCESSES

In most of the countries of Latin America diarrheic processes constitute one of the most serious health problems, especially for small children. They have a dual relationship with feeding and nutrition: on the one hand, diarrhea is an important factor which precipitates and aggravates malnutrition; on the other, feeding practices and the nutritional state play their part in the pathogeny of diarrheic processes. This interrelationship, which we may describe as synergetic, and the very magnitude of the problem, explain why in the Estudio de Mortalidad en la Niñez, sponsored by the Pan American Health Organization, (1) it was found that in the whole sample diarrhea was the most important basic cause of death. It was also observed that in 60.8 per cent of the deaths caused by diarrhea, malnutrition was a related cause.

Accordingly, we would like to analyze first in what way food, in itself and not as a vehicle of specific pathogenic agents, can intervene in the pathogeny of diarrheic processes. For this purpose, there are two periods of infancy which must be studied: the breast-feeding period and the weaning period.

Protective Role of Breast-feeding

During the breast-feeding period, the first point to consider is the protection which this type of feeding provides against the environmental factors which cause diarrheic processes. Since the introduction of artificial feeding with cow's milk, clinical and epidemiological observations in general have revealed that in bottle-fed babies the frequency and severity of diarrheic processes has been greater than in breast-fed babies. Today it is known that human milk plays a protective role against enteric infections, at least through the following processes.

Specific Activity of Antibodies

It has been proved that colostrum and human milk, during the first weeks, contains high concentrations of immunoglobulins, especially IgA,(2) among which antibodies and antigens of enterobacteriaceae have been isolated.(3)

Figure 1 shows the concentration of IgA found in the colostrum and milk of women from a village in Guatemala. As may be seen, the concentration is high in colostrum and, although it drops sharply, still maintains appreciable levels during the first year of lactation. Undoubtedly, these antibodies do not pass through the intestinal wall, but it has been observed that they pass almost intact through the whole gastrointestinal tract. It is therefore felt that they can play a part in the defense of the host acting within the intestinal lumen. This has been proved in the case of the poliovirus.(4,5)

Eifid Factor

It is well known that the feces of breast-fed children are different from those of children fed with cow's milk: the former do not have a disagreeable smell and are of acid reaction; the latter are alkaline and have a putrid smell. This is because the intestinal flora are completely different. In breast-fed children the flora consist almost exclusively of gram-positive anaerobic bacilli (bifid-bacteria); in bottle-fed children the predominant components are gram-negative anaerobic organisms which constitute also the predominant flora of adults. This difference is due to the presence in human milk of a substance which favors the development of bifid-bacteria, the "bifid factor,"(6) which is not found in cow's milk. The bifid-bacteria metabolize the sugars which have not been absorbed in the upper parts of the intestine, producing large quantities of acetic and lactic acid which are responsible for the low pH of the feces of breast-fed children. The environment thus created in the intestinal lumen is unfavorable to the growth of pathogenic enterobacteriaceae and intestinal protozoa. These observations have been confirmed by Mata et al(7) in Guatemala. They proved that in breast-fed children with characteristic intestinal flora, infections with Shigella were transitory and did not produce disease, While in older children these infections were associated with diarrhea. In breastfed children it has also been observed that the Entamoeba histolytica passes through the intestine and does not colonize.

In a longitudinal study, carried out in a village of Guatemala, (8) of intestinal colonization by pathogenic enterobacteriaceae in small children, the prevalence of infection by Shigella was found to be as shown in Figure 2. As may be seen, this infection is minimal during the first nine months of life, increases rapidly, especially after the first year when the children are receiving a fair amount of other food besides their mother's milk, and reaches a maximum in the third year when practically all the children have been completely weaned.

As may be seen in Table 1, it was also found that even when, in the same community, Shigella bacteria were those most commonly associated with diarrhea, this is not true during the initial months of life. For example, during the first six months Shigella bacteria were isolated in 1.2 per cent of the diarrheic processes, while in the third year of life they were isolated in 55 per cent of the cases. It may therefore be concluded that the intestinal flora of breast-fed children protect them against enteric infections.

These two processes and others that are not yet clear—such as the high concentration of lysozyme (of bacteriolitic action) in human milk and in the feces of breast—fed babies—explain the lesser frequency and sever—ity of diarrhea in these children compared with those who are bottle—fed. This may be seen even in communities with a high degree of environmental hygiene and, of course, is more common in communities where environmental hygiene is precarious and hygienic education is poor. In these latter communities the disadvantage of artificial feeding is accompanied by the

equally serious one of having a high degree of contamination of formulas prepared at home and of the utensils used to prepare them, especially feeding bottles.

We therefore consider that the early weaning and artifical feeding of babies in towns with poor socioeconomic and cultural conditions are dangerous. They limit the natural defenses of the child against enteric infections and expose him much more to an unhealthy environment. The result is the occurrence of frequent and serious diarrheic processes. The Estudio de Mortalidad en la Niñez of PAHO, already referred to, confirms the relationship between mortality from diarrhea and the feeding practices used for babies.

"Weaning Diarrhea"

For breast-fed children living in an unhealthy environment the introduction of other foods to complete their nutritional requirements and, finally, the total elimination of mother's milk, are accompanied by a marked increase in the incidence of diarrheic processes. This is observed independently of the age at which weaning occurs and explains why in certain towns the greater prevalence of diarrheic diseases is observed in the first months of life, while in others this occurs only towards the end of the first year or during the second year of life. This situation has been clearly described by Gordon, (9) who characterizes it epidemiologically as a phenomenon called "weaning diarrhea." This does not seem to be associated with a specific agent but with the high contamination by common bacteria involved in the feeding of small children in an unhealthy environment.

Indeed, careful bacteriological studies carried out in this field reveal the presence of pathogenic organisms in the feces of these children only in 25 per cent of the cases; nor is there sufficient evidence to prove that these organisms are really the agents responsible.

Epidemiological evidence indicates, however, that this syndrome is of an infectious nature and is probably related to a great variety of germs to which children eventually become resistant.

Table 2 summarizes the incidence of diarrhea by age groups in four rural communities of Guatemala, carefully studied over a period of three years.(10)

It may be observed that the incidence is relatively low in the first six months of life during which children are almost exclusively breast-fed; it increases considerably in the ages six months to two years—the weaning period—and drops rapidly after this age.

The important point about these observations is that we must consider at what age supplements to breast-feeding should be recommended in communities with a very low level of environmental sanitation. The possible nutritional advantages of the introduction of solid foods must be weighed

against the risks of infection to which the child is exposed. We believe that the early introduction of other foods in the diet of the nursing baby, so fashionable in some countries regardless of whether it is necessary from the nutritional standpoint, is not desirable in communities where the health environment is poor. In the latter case, breast-feeding only must be encouraged during the first three or four months of life, and should be continued for as long as circumstances permit.

Diarrhea and Nutrition

The second point we will consider is the possible role of malnutrition in the pathogeny of diarrheic processes. In the course of epidemiological studies it has been observed that diarrhea is more common and more severe in malnourished children. Table 3 shows the results of such studies in a village of Guatemala.(10) As the figures show, the rate of attack among children classified as well-nourished was 86.6 cases per 100 children, per year, a rate which increases with the severity of malnutrition; it reaches 274.5 among children with third-grade malnutrition. At the same time, the percentage of severe cases was greater among malnourished children than among well-nourished children. We admit that it is not easy to conclude from these observations whether children had more diarrhea because they were malnourished or were malnourished because they had more diarrhea. In any case, the interrelationship between these two phenomena is obvious.

At the clinical level also it is commonly observed that severely malnourished children entering hospital often have diarrhea. In most of the cases it is impossible to identify a specific agent associated with the diarrhea and the diarrhea yields to dietetic treatment as the child recovers from the severe malnutrition, without any specific medication. It is also known that even when these severely malnourished children do not have diarrhea, they always suffer from intestinal malabsorption, mainly of fats.

It appears, therefore, that malnutrition per se conditions or favors the development of diarrheic processes. We shall now consider some of the possible processes likely to explain this situation.

Morphological Alterations of the Intestinal Mucus

Consistently, it has been observed that in severely malnourished children there are marked morphological alterations in the intestinal mucus; these are characterized mainly by considerable atrophy of the villi, which appear flattened and joined together, giving the mucus a cerebroid appearance. The thickness of the mucus, the height of the epithelial cells and the width of the brushed edge are also diminished. These changes are similar to those found in cases of sprue and other syndromes of intestinal malabsorption. Recent studies in INCAP(11) have proved that these alterations are more severe in malnourished children with diarrhea. On the other hand, it has been observed that they are not completly restored after nutritional rehabilitation. Indeed, they have been found among

children living in the same environment but not suffering from severe malnutrition. The question remains therefore as to what is the real cause of these alterations.

Functional Alterations

In the severely malnourished child the time of intestinal passage is markedly increased. This intestinal stagnation could not in itself explain the diarrhea but it does favor the development of other alterations which result in diarrheic processes, such as the changes in the intestinal flora referred to above.

In children with severe malnutrition there also occurs poor intestinal absorption of various nutrients, especially fats. These children have poor ability to solubilize fats. Apparently, this is not associated with lipase deficiency since this enzyme has been found in normal concentrations in most of them. (12)

The problem seems to be more related to a decline in the concentration of conjugated bile acids and an increase in the concentration of free bile acids, with a consequent reduction in the ability to solubilize fats. (13) The high concentration of free bile acids might be due to the breaking down of the conjugated acids by bacterial action in the upper parts of the intestine. The free bile acids thus produced may irritate the intestinal mucus and cause diarrhea.

Alterations of the Flora

Two important changes are observed in the intestinal flora of malnourished children. The first is a marked increase in the flora, both
anaerobic and facultative in the jejunum, duodenum and stomach, (14) i.e.,
upper parts of the gastrointestinal tract where flora normally is scarcer.
This invasion of the upper parts of the gastrointestinal tract by the flora
that is normal in the lower areas may be related to the diminution of intestinal motility referred to earlier or to a decrease in the acidity and
bacterial action of the gastric secretions; in its turn, it may be the
factor responsible for the breaking down of the conjugated bile salts. All
these developments contribute to malabsorption and diarrhea.

The other important microbiological alteration which has been found in malnourished children is a change in the relationship between anaerobic and facultative bacteria in the feces, with an increase in the proportion of the latter. This situation also appears to favor the development of diarrhea in malnourished children.

To sum up, even though we cannot explain clearly some of the physiopathological processes, it is obvious that malnutrition favors the development of diarrhea while, on the other hand, we must stress that diarrhea in its turn precipitates and aggravates malnutrition. Children living on a marginal diet, which barely covers their minimum caloric and nutritional needs, fall into a state of malnutrition as a result of frequent infections, particularly diarrhea. This not only reduces the ingestion of food but also increases nutritional requirements and results in a loss of nutrients ingested.

The result of the synergism between inadequate and unsuitable diet and the presence of frequent infections is illustrated in Figure 3. This summarizes the history of a child studied longitudinally by Mata et al(15) in INCAP and is representative of what occurs among the large majority of children in poor communities.

As may be seen, the child made good progress in terms of weight during his first six months of life. During this period his mother's milk was enough to satisfy his needs and the infections he suffered were relatively few. From then onwards, he did not receive the foods necessary to supplement breastfeeding and he began to suffer frequent attacks of infectious diseases, especially diarrhea. The result was a rapid deterioration in his nutritional state which is reflected in a complete flattening of the weight curve for a whole year, up to the age of 18 months, and an inadequate and irregular growth after that age.

We believe that this figure illustrates very clearly the sad story of millions of children in our Latin America. A large proportion of them die as a result of the synergetiic action of malnutrition and diarrhea and the survivors do not attain their full genetic potential for growth and physical and functional development. The control of diarrheic infections alone would greatly improve their nutritional situation. On the other hand, better feeding after the lactation period, with essentially breast-feeding during the early months duly supplemented later and followed by a sound diet after weaning, would considerably reduce the danger and damage caused by diarrheic infections.

Ideally, the application of both these measures at the same time, i.e., improved feeding and improved environmental sanitation, would result in the best possible advancement for our peoples, through the application physical and functional damage, and, consequently, in a more promising future for the new generations of citizens of the Americas.

TABLE 1

Percentage of Cases of Diarrhea, by Age, Associated with Shigella in Children 0-3 Years of Age (Santa María Cauqué, Guatemala, 1964-67)

Age (months)	% of Diarrhea Cases Associated with Shigella
0-5	1.2
6–11	9.2
12–17	19.0
18-23	39.0
24–29	41.6
30–35	55.5

TABLE 2

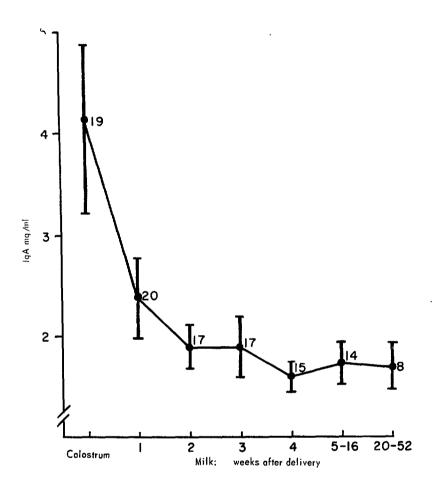
Rates of Attack of Acute Diarrhea per 100 Persons, by Year and by Age-groups, in Four Rural Communities of Guatemala, 1956-59

Age	Number of Persons	Cases of Diarrhea	Rate of Attack (Cases/Year/100)
0-5 months	92	43	46.7
6-11 months	79	87	110.7
1 year	135	162	120.0
2 years	122	129	105.7
3 years	119	66	55.4
4-6 years	406	86	21.2
7-14 years	839	69	8.2
15+ years	2,390	109	4.6
All ages	4,182	751	18.0

TABLE 3

Incidence and Severity of Diarrhea in Relation to the Nutritional
State in Children Under Five Years of Age (Santa María Cauqué, 1961-62)

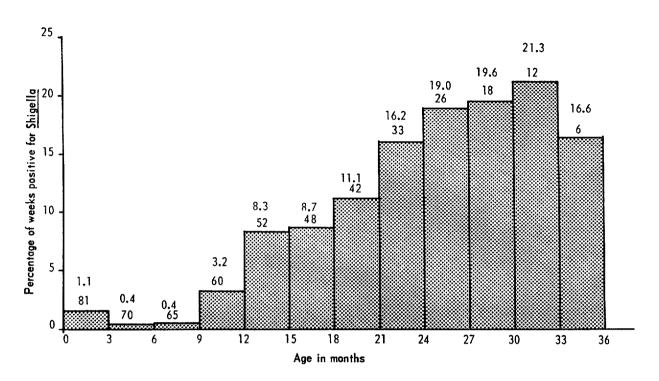
Nutritional State	Rate of Attack (Cases/Year/100)	% of Severe Cases
Normal	98.8	22.9
1st grade malnutrition	164.1	37.8
2nd grade malnutrition	252.5	29.1
3rd grade malnutrition	274.5	40.0



Incap 74-747

Concentrations (average - 1 S.E.) of IgA in colostrum and milk of Indian women of Santa María Cauqué, Guatemala, 1968. The numbers above the curves indicate the number of women studied.

FIGURE 2

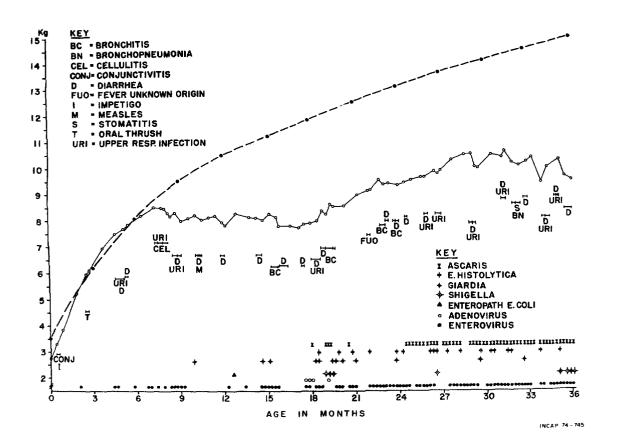


The figures with decimal points express the percentage of weekly cultures that resulted positive for Shigella. Whole figures show the number of children studied during the period indicated.

Incap 74-746

Prevalence of Shigella in children 0 to 3 years old. Santa María Cauqué, Guatemala, 1964-67

FIGURE 3



Weight, infections and infectious diseases in a child studied longitudinally by Mata et al.(15) Solid line represents weight of child; broken line is median of the standard. Length of each horizontal line indicates duration of infectious disease. Each mark shows a week positive for the particular infectious agent.

REFERENCES

- Puffer, R. R. and C. V. Serrano. <u>Características de Mortalidad en la Niñez</u> -Investigación Interamericana de Mortalidad en la Niñez. Pan American Health Organization. Scientific Publication 262, Washington, D.C., 1973.
- 2. Hodes, H. L., R. Berger, E. Ainbender, M. M. Hevizy, H. D. Zepp and S. Kochwa. "Proof that Colostrum Polio Antibody is Different from Serum Antibody". J Pediat. 65:1017, 1964.
- 3. Mata, L. J. and R. G. Wyatt. "Amamantamiento y resistencia del huésped a la infección". En <u>El Valor Incomparable de la Leche Materna</u>. Pan American Health Organization. Scientific Publication 250, Washington, D.C., 1972. p. 14.
- 4. Warren, R. J., Martha L. Lepow, G. E. Bartsch, and F. C. Robbins. "The Relationship of Maternal Antibody, Breast Feeding, and Age to the Susceptibility of Newborn Infants to Infection with Attenuated Polioviruses". Pediatrics 34:4, 1964.
- 5. Katz, M. and S. A. Plotkin. "Oral Polio Immunization of the Newborn Infant; A Possible Method for Overcoming Interference by Ingested Antibodies". J Pediat. 73:267, 1968.
- 6. György, P. "A Hitherto Unrecognized Biochemical Difference Between Human Milk and Cow's Milk". Pediatrics 11:98, 1953.
- 7. Mata, L. J. and J. J. Urrutia. "Intestinal Colonization of Breast-fed Children in a Rural Area of Low Socioeconomic Level". Ann N Y Acad Sci 176:93, 1971.
- 8. Mata, L. J., R. Fernández and J. J. Urrutia. "Infección del intestino por bacterias enteropatógenas en niños de una aldea de Guatemala, durante los tres primeros años de vida". Rev Latinoamer Microbiol Parasitol 11:103, 1969.
- 9. Scrimshaw, N. S., C. E. Taylor and J. E. Gordon. <u>Interactions of Nutrition and Infection</u>. WHO Monograph Series No. 57. Geneva, 1968. Chapter 6 "Weanling Diarrhea A Synergism of Infection and Nutrition". p. 216.
- 10. Gordon, J. E., M. A. Guzmán, W. Ascoli and N. S. Scrimshaw. "Acute Diarrhoeal Disease in Less Developed Countries. 2. Patterns of Epidemiological Behaviour in Rural Guatemalan Villages". Bull Wld Hlth Org 31:9, 1964.
- 11. Schneider, R. E. and F. E. Viteri. "Morphological Aspects of the Duodenojejunal Mucosa in Protein-Calorie Malnourished Children and During Recovery". Am J Clin Nutr 25:1092, 1972.

CSP19/DT/5 (Eng.)
Page 14

- 12. Viteri, F. E., C. Contreras and R. E. Schneider. "Intestinal Malabsorption in Malnourished Children and During Recovery. Duodenal Content of Lipase, Nitrogen, and Micellar Fat After Fat Stimulation". Arch Latinoamer Nutr 22:613, 1972.
- 13. Schneider, R. E. and F. E. Viteri. "Luminal Events of Lipid Absorption in Protein-Calorie Malnourished Children; Relationship with Nutritional Recovery and Diarrhea. I. Capacity of the Duodenal Content to Achieve Micellar Solubilization of Lipids". Am J Clin Nutr, 1974. (In press).
- 14. Mata, L. J., F. Jiménez, M. Cordón, R. Rosales, R. Prera, R. E. Schneider and F. Viteri. "Gastrointestinal Flora of Children with Protein-Calorie Malnutrition". Am J Clin Nutr 25:1118, 1972.
- 15. Mata, L. J., J. J. Urrutia and A. Lechtig. "Infection and Nutrition of Children of a Low Socioeconomic Rural Community". Am J Clin Nutr 24:249, 1971.