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21 Breast Feeding, Diarrheal Disease, and Malnutrition in Less Developed Countries

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1. Introduction

It has been known for centuries that non-breast-fed infants have a higher probability of dying prematurely than do breast-fed infants under conditions of underdevelopment. On the other hand, artificial feeding is more risky when carried out by persons other than the mother. The fact was documented in the exceedingly high mortality of infants who, in the past, were taken away from their mothers and placed in foundling homes or "baby farms" under the care of "professional foster mothers" [1]. Furthermore, infants born with abnormalities such as cleft palate, or infants unable to suck, invariably die from diarrhea and starvation in villages where there is no access to treatment and alternative forms of feeding.

Prospective observation of traditional societies reveals the remarkable resistance of breast-fed infants to infection, especially diarrhea, otitis, and respiratory disease. Epidemiologic studies consistently show that diarrhea and infant mortality are more frequent in weaned infants than in weanlings, and more in these than in wholly breast-fed infants [2-5]. Such behavior is characteristic in less developed countries, but it is also observable in modern societies.

In exclusively breast-fed infants of a typical traditional Guatemalan village of low socioeconomic condition (Santa María Cauqué), infections with *Shigella* and enteroviruses were generally asymptomatic and transient, and intestinal protozoa were rare [2,6-8]; also, the attack rate of diarrhea was lower during exclusive breast feeding than thereafter [7]. In this village the adverse effect of diarrhea and other infectious diseases on nutrition and growth was well documented. Diarrhea was often associated with reduced food intake, weight loss, stagnation of height, and chronic wasting and stunting [6-9]. Furthermore,

studies conducted by our institute in a different rural dispersed population, in Puriscal, Costa Rica, also showed that diarrhea is more frequent in infants in the process of weaning or in those totally weaned than in breast-fed infants [10], despite the fact that children were relatively well nourished as they grew above the 25th percentile of the National Center for Health Statistics reference curves [11].

The PAHO Interamerican Study of Childhood Mortality had already revealed a strong association between diarrheal disease and malnutrition and between these and infantile death in representative cities of the Americas [12]. Thus diarrhea is the main cause of chronic malnutrition in tropical regions where famine and natural disaster are not usual problems; also, diarrhea is the commonest precipitating factor of acute protein-energy malnutrition and premature death in less developed countries.

II. Anti-Infectious Properties of Human Milk

Infection and colonization of the intestine with pathogens is much less common during exclusive breast feeding than at later ages [2,4]. As supplementary foods are introduced around 4-6 months of age, invasion by pathogens becomes important [13], especially if personal hygiene, education, and environmental sanitation are deficient [2].

The beneficial effect of colostrum and milk stems from its capacity to prevent diarrheal disease, respiratory infection, otitis, and other infectious and non-infectious processes. Although this effect has been recognized since ancient times, it was only recently that scientific research characterized some of the principles capable of reacting against enteric noxae and their harmful products. Table 1 summarizes the main factors related to antimicrobial activity in human milk. Table 2 compares the composition of human and cow's milk.

A. Immunoglobulins

These appear to be the most important, of which secretory immunoglobulin A (SIgA) stands out for its high concentration in colostrum (500 mg per 100 ml), its wide range of antibodies against infectious agents experienced by the mother, and its resistance to digestive juices [15]. SIgA is synthesized in duct epithelial cells of the mammary gland and then secreted with milk. Its high concentration (Fig. 1) declines abruptly as colostrum evolves into mature milk [16], but the total contents remain high, as revealed once the volume is taken into account [15]. Practically all antibodies sought for have been encountered in SIgA of colostrum and milk [15-17], including activities to rotaviruses and bacterial enterotoxins [18-21], antibodies that neutralize or destroy infectious agents or that interfere with their attachment to or invasion of the mucosa [15-22]. It is also possible that antibodies against local foods such as beans and rice exert

Table 1 Anti-Infective Factors in Human Milk

Factor	Capacity
Secretory IgA,	Specific activity against microorganisms
IgM, and IgG	Specific activity against allergens
Lactoferrin	Bacteriostasis
Lysozyme	Bacterial lysis
Complement (C3, C4)	Opsonization
Lactoperoxidase	Bacterial lysis
Antistaphylococcal factor	Inhibits systemic staphylococcal infection
Bifidus factor	Promotes growth of bifidobacteria
Antiviral RNAase	Inhibits viral activity
Interferon	Inhibits viral infection
Lymphocyte	Synthesis of immunoglobulins
Macrophage and polymorph	Bacterial killing and phagocytosis

Table 2 Composition of Mature Human and Cow's Whole Milk

Concentration per 100 ml	Human milk	Cow's milk
Fat (g)	3.0	3.7
Lactose (g)	7.2	4.8
Protein (g)	0.9	3.4
α -Lactalbumin (mg)	150.0	90.0
β -Lactoglobulin (mg)	0	300.0
Serum albumin (mg)	50.0	30.0
Lactoferrin (mg)	150.0	?
Lysozyme (mg)	50.0	0.01
Secretory IgA (mg)	100.0	3.0
Potassium (mg)	55.0	138.0
Sodium (mg)	15.0	58.0

Source: Refs. 4 and 14.

an antiallergenic capacity, which would explain, at least in part, the very low rate of asthma and allergies among breast-fed infants [2,4,8].

Recently, a mechanism of exchange of local immunity between the human intestine and the breast has been described. Basically, B lymphocytes from Payer's patches sensitized to antigens ingested by the mother migrate through lymphatics and blood vessels to "home" in exocrine glands such as the breast. Then blastic transformation results in synthesis of antibodies to antigens ingested by the mother. Furthermore, lymphocytes may translocate and fall in the alveoli to appear in colostrum and milk. The mechanism may be of great significance in natural defense and offers opportunities for eventual protection of the infant through active immunization of the lactating mother [23].

Lactoferrin is very important because it binds free iron, making it unavailable for bacterial multiplication, remaining bioavailable to the host. Lactoferrin seems to be the most potent inhibitor of bacterial growth in milk, being effective within the intestinal milieu [24]. Bacterial inhibition is so marked that

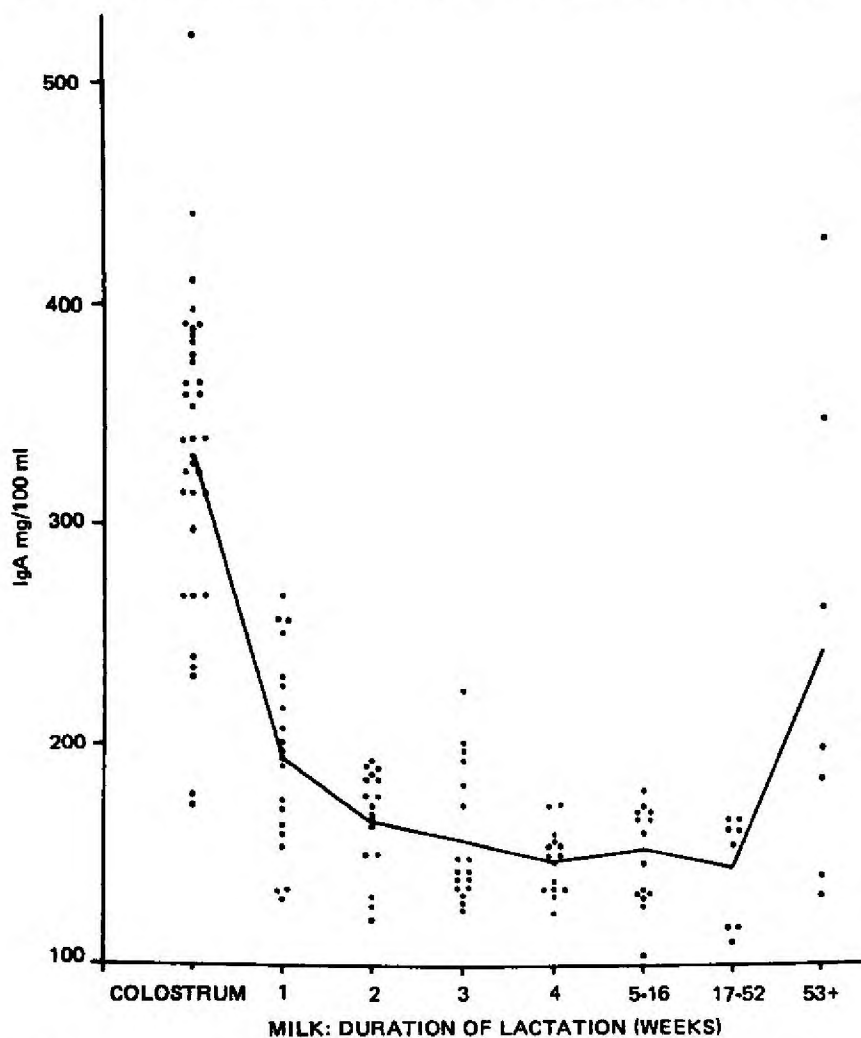


Figure 1 Concentrations of secretory immunoglobulin A in colostrum and milk of village Indian women of Santa Maria Cauqué. Determinations were by radial immunodiffusion of 133 specimens from 43 women [2,16]. (From Ref. 2, reprinted with permission of the MIT Press.)

human milk can be stored at room temperature for 2-3 hr in tropical environments (Mata, unpublished data, 1980).

Other factors are complement; lysozyme; lactoperoxidase, active in bacterial lysis; antistaphylococcal factor; antiviral RNAase substance; and interferon [4,14,16,17]. Lymphocytes and macrophages and their immunocompetent expression may be more important than recognized at present [25,26], but this is discussed by others in this volume.

B. Bifidus Factor

This hitherto poorly described substance is present in large concentrations in human milk and determines in part the composition of the intestinal flora, especially that of the colon [27]. Its effect is quite specific, particularly for the development of bifidobacteria; no milk other than that of humans seems to have this capacity. There is no doubt that the indigenous and autochthonous flora of animals exert profound anatomic, physiologic, and immunologic influences on the intestinal mucosa and on host nutrition [28]. Similarly, the indigenous flora of the child acts in the defense of the intestine against enteric pathogens.

The fetus is virtually sterile at birth, but soon thereafter the infant becomes colonized by microorganisms from the mother if delivery is at home, or from hospital attendants and the environment if mother-infant separation has been effected. The development of the indigenous fecal flora of infants was studied in the Indian village of Santa María Cauqué. Deliveries are at home in the kneeling and squatting position, and because mothers do not undergo any special preparation, heavy fecal contamination of the newborn is a common occurrence [7]. *Escherichia coli* colonizes in all breast-fed infants in the first 24 hr after birth, but by the end of the first week of life it has been restricted and most infants have a flora of predominant bifidobacteria in concentrations of about 10^{11} colony-forming units per gram of wet feces [13]. Clostridia and streptococci, commonly found shortly after birth, also decrease in the first few weeks as bifidobacteria rise. In the village, weaning begins at 3-6 months, but it is complete only by the end of the second year of life [2] (Table 3).

The bifidobacterial flora evolves in a subtle manner as the protracted weaning process takes hold. The gram-positive bifidobacterial flora decreases slightly, while the gram-negative anaerobes, such as fusobacteria and bacteroides, and the facultatives, such as the Enterobacteriaceae, increase significantly [13]. Eventually, the flora of children becomes like that of adults of the same environment [29].

Recently, similar results have been obtained for a traditional society in Nigeria [30], where contamination with feces at birth also occurs (Table 3). However, colonization of infants born in hospitals in industrial societies is

Table 3 Fecal Bacterial Flora of Infants Born and Reared Under Different Conditions

Fecal exposure, birth:	Country:	Guatemala ^a	Nigeria ^b	England ^c	
	Delivery:	Home	Home	Hospital	
	Feeding:	Heavy	Heavy	Very low	
	Age:	Breast	Breast	Breast	Bottle
		5-8 weeks	1 year	6 weeks	6 weeks
Bifidobacteria		9-10 ^d	9.1	4.5	6.5
<i>Bacteroides</i>		8	8.1	9.3	8.8
<i>Clostridia</i>		8	4.3	6.4	6.3
<i>Veillonella</i>		8	Nil	7.3	6.8
Enterobacteriaceae		6	5.9	9.5	9.4
Enterococci		7	8.0	7.7	9.1
Staphylococci		6	7.2	8.0	8.4

^aAfter Ref. 13.

^bAfter Ref. 30.

^cAfter Ref. 31.

^dLog₁₀ of bacterial count per gram of wet feces.

markedly different from the one just described, regardless of type of feeding. The effect of breast milk is not as apparent in hospital-born infants, probably because they acquire bacteria from attendants and the hospital environment [31]. Thus the bifidobacteria do not develop as easily in infants born in hospitals as in village infants, even if they are breast fed.

III. Resistance of Village Breast-Fed Infants to Enteric Infection

By monitoring excretion of enteric agents in feces, it was possible to document the marked intestinal resistance to invasion and colonization by pathogens. Studies were conducted in a cohort of 45 children of Santa Maria Cauqué observed from birth to at least 3 complete years. Examination of feces collected every week from each child [2] included all intestinal parasites, all intestinal pathogenic bacteria known at the time of the study (1962-1969), and entero- and adenoviruses [2,6-8].

As indicated above, infants have many opportunities for exposure to feces: during childbirth, and later as fingers of attendants and small amounts of fluids and foods are introduced into the infant's mouth [2]. There is evidence that infection with enteric viruses infect frequently early in life, as indicated by their isolation from meconium and feces [2,7,8]; also, shigellae and protozoa are found in neonates [6]. However, these infections generally are asymptomatic and transient [6,8] as long as infants are at the breast exclusively. But if infants receive other foods, *Shigella* infections are accompanied by clinical manifestations.

Intestinal resistance is demonstrable against microorganisms that replicate and do their harm within the small intestine (*Giardia*, enterotoxigenic *Escherichia coli*) or in the colon (*Shigella*, *Entamoeba histolytica*). The period of resistance afforded by breast feeding varies with the agent. It is more prolonged for *Shigella* and a bit shorter for *Giardia* (Fig. 2), although the results are inevitably influenced by the diagnostic techniques [7].

It should be remembered that contacts with the sources of infection are fewer in breast-fed infants because of their greater limitation to the nipple. Furthermore, the absence of allergenic proteins in human milk, contrasted with the high concentration of β -lactoglobulin in cow's milk, indirectly reduces the incidence of secondary infection in respiratory and skin diseases. Also, the lower content of protein and the lower concentration of potassium and sodium ions in human milk as opposed to cow's milk reduces the need for extra water and consequently, the risk of waterborne infection [4,14].

Finally, because of the unique biochemical composition of human milk [4], optimal growth and development is attained for at least 3-6 months, as revealed by prospective observation of poor village infants in their ecosystem [2]. The fact that growth is normal in the first months of life, even for preterm and small-for-gestational age infants [2], under conditions of poverty is a good indication of the protective role of breast milk against prevailing infections in village settings [2,8,9] (Fig. 3).

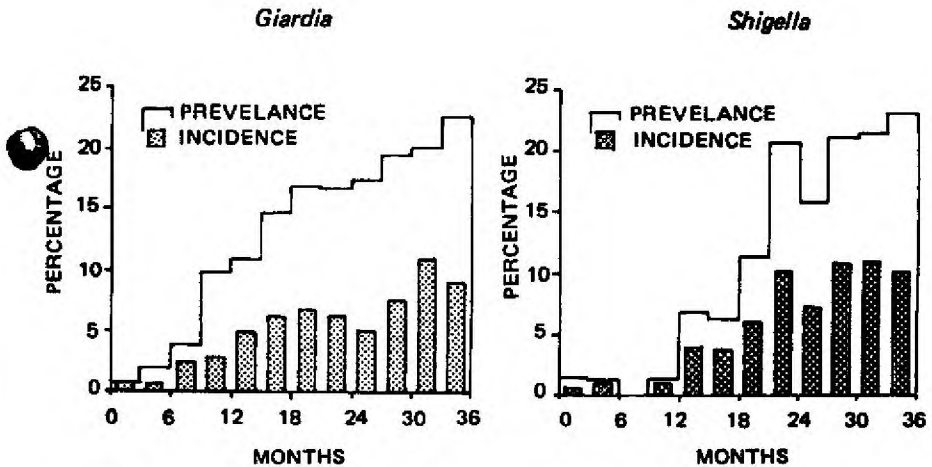


Figure 2 Prevalence and incidence of *Giardia* and *Shigella* in fecal specimens of village children, collected each week from each child from birth to 3 years of age [7]. Note the very low rates of organisms during the period of exclusive breast feeding (birth to 9 months).

IV. Weaning, Diarrheal Disease, and Malnutrition

The decrease in intake of anti-infectious factors and the good food of breast milk as the child is weaned result in the progressive acquisition of enteropathogens and onset of recurrent diarrheal disease. The earliest weaning begins, the sooner changes in flora and diarrhea are detected. The transition from maternal milk to other foods is marked by "weanling diarrhea" in humans and other animal species [32]. In the past, the phenomenon was thought to be the result of nutritional and dietary deficiencies, but the discovery of enterotoxigenic

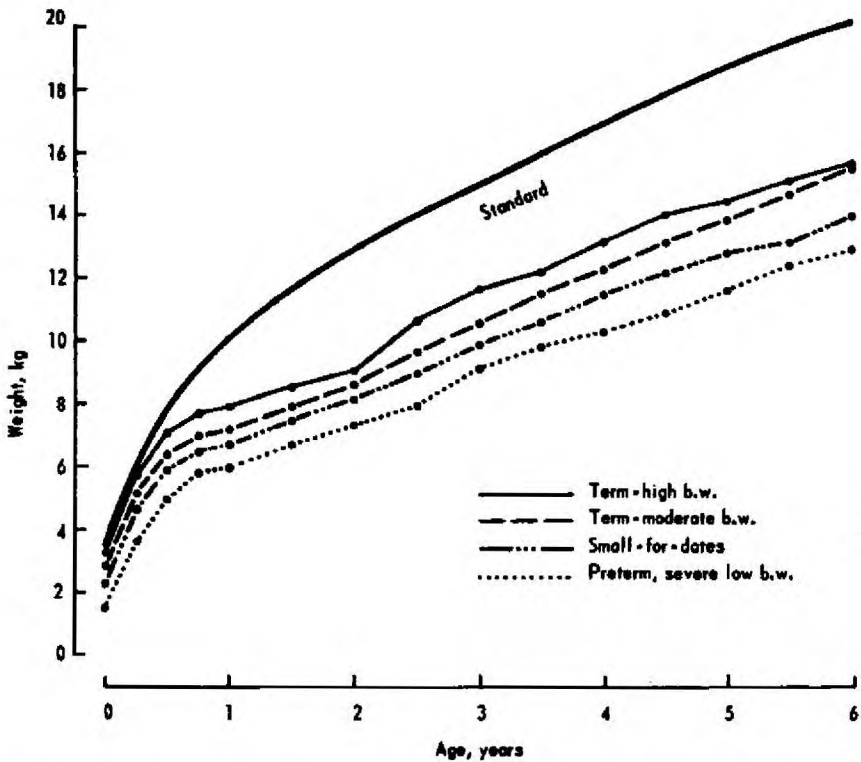


Figure 3 Mean weight curves of village Indian children studied prospectively from birth to 6 years of age (b.w., birth weight). Cohorts of children were set by computer according to fetal maturity. Comparison is with the Boston-Iowa reference growth curve [2,38]. Note that infants grow at a normal velocity during the first months of life, that is, during exclusive breast feeding, regardless of the presence of prematurity or fetal growth retardation. (From Ref. 2, reprinted with permission of the MIT Press.)

bacteria, rotaviruses, and other agents showed that weaning diarrhea is of an infectious nature and that environmental sanitation, personal hygiene, and deficiencies in maternal technology [9] play a part in the complex web of causality [33]. Agents are acquired by the oral route (although diarrhea viruses may have a respiratory phase), by person-to-person contact, or by ingestion of contaminated food and water. The demonstration that common village foods, even those that need cooking, are contaminated after storage for consumption at a later date [34,35] broadens the dimensions of epidemiology of diarrheal disease in the community.

Diarrhea in the village increases with age and depends strongly on the pattern and duration of weaning; it peaks in the second year of life in countries where breast feeding is prolonged and weaning is late; and it peaks in the first year in nations where weaning occurs in the first year of life. Consequently, severe malnutrition follows a typical epidemiologic occurrence: in the second year of life if weaning is late; in the first year if weaning is early and abrupt. This relationship often reflects the type of malnutrition observed and is definitely related to the degree of transition in a given society. Whereas in traditional societies kwashiorkor is observed in the second year of life or even later, in transitional countries marasmus predominates, particularly in young infants [36]. Actually, the decline in breast feeding in many countries in transition has been followed by a relative increase in marasmus at younger ages [3,4,14].

The strong epidemiologic correlation between diarrheal disease and malnutrition has been clarified by field studies in poor villages in various parts of the world. Diarrhea interferes with nutrient consumption in a significant way [37]. Since dietaries of village children are about 80% of the recommended levels [38], a further reduction of intake places the child in a restricted calorie intake incompatible with adequate growth. Otherwise, village intakes are adequate for maintenance and growth, as confirmed by another prospective study in the rural area of Puriscal, Costa Rica [39]. Observations in other rural areas have also documented this effect [40].

The first encounters of the host with pathogenic agents, once weaning has begun, almost invariably result in the appearance of diarrhea. Figure 4 shows 1 of 45 children observed prospectively from birth to 2 years of age, by weekly studies of etiologic agents, fortnightly measurement of weight and height, weekly assessment of clinical conditions, and other detailed studies [2]. This case illustrates a phenomenon described for most children of the cohort [2,6-10,38,41,42]. The child experienced nine episodes of acute diarrheal disease during the first 2 years of life. Four of the episodes were not associated with any of the agents investigated. The remaining were associated with rotavirus, *Shigella*, *E. histolytica*, *Giardia*, and *Dientamoeba*. During the study period (1963-1972) no investigation was made of enterotoxigenic bacteria, *Campylobacter*, or other vibrios. Rotaviruses were retrospectively investigated in frozen specimens

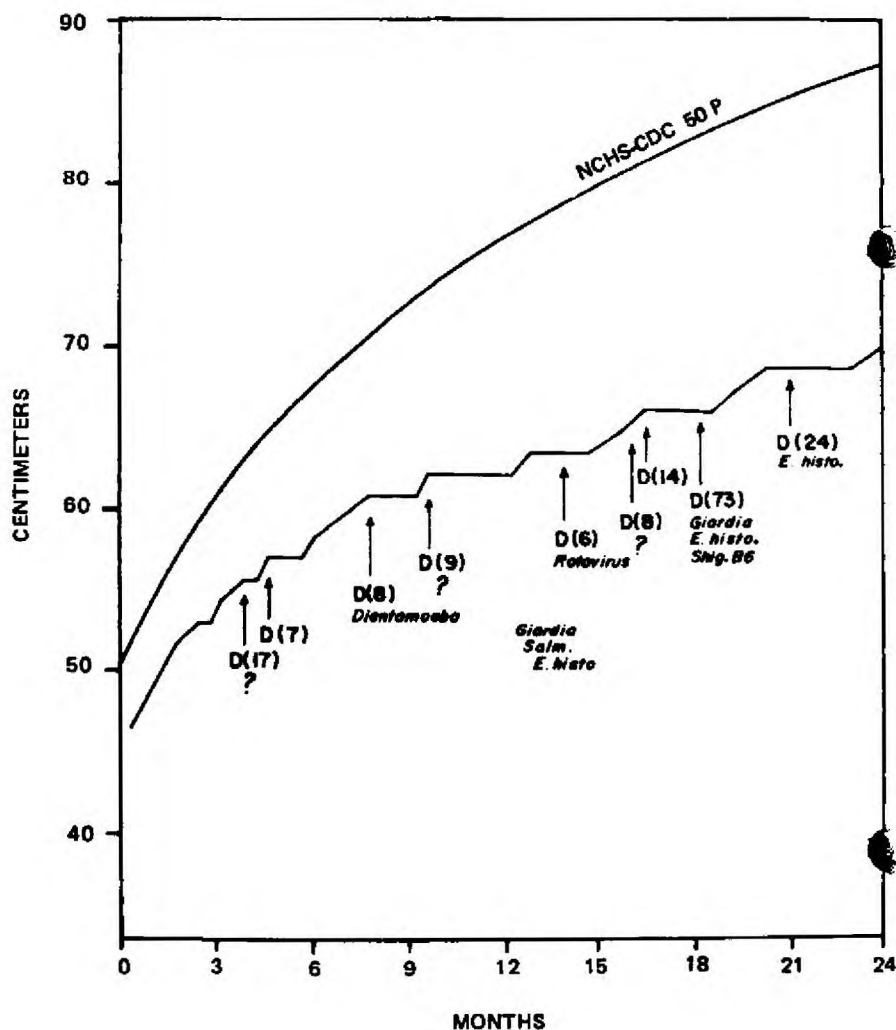


Figure 4 History of growth (height) and acute diarrheal episodes of a child of Santa Maria Cauqué studies prospectively from birth to 2 years of age. Growth was adequate during the first 3 months of life, as compared with the 50th percentile of the NCHS-CDC reference curve. Five of the nine acute diarrheal episodes were associated with one or more infectious enteric agents. Diarrheas coincided with periods of growth arrest of varying duration [10].

by ELISA [10]. It is quite evident that most diarrhea attacks were associated with periods of growth arrest, as shown by stagnation of the height curve in comparison with the 50th percentile of the NCHS-CDC reference curve [11]. Most diarrheas were associated with weight loss and growth (height) arrest, as evidenced in the figure.

In another population, Puriscal of Costa Rica, enjoying a much better nutritional status [10,39], rotavirus diarrhea had a more serious nutritional effect in weaned children than in those receiving breast milk (Table 4). The outcome of diarrhea was benign in wholly breast-fed infants. Also, incidence of diarrhea was lower in breast-fed than in non-breast-fed babies [10].

To summarize, diarrhea seems to be the main cause of reduced food intake, weight loss, wasting, and stunting of village children. Breast-fed infants are significantly protected against diarrhea and other infectious diseases, even if they thrive in impoverished environments.

V. Diarrheal Disease, Malnutrition, and Survival

If diarrhea is the main contributor to wasting, stunting, and premature death in less developed countries, one would expect that a decrease in diarrhea will be associated with a concomitant reduction in malnutrition and infant mortality. This association is difficult to document because data-collecting systems in less

Table 4 Nutritional State After Rotavirus Diarrhea in Relation to Type of Feeding

Feeding	Age of child (months)	Number of diarrhea cases	Number of cases		
			Weight loss ^a	Weight faltering	Weight gain ^b
Breast milk	0-2	4	0	0	4
	3-5	0	0	0	0
Breast milk + supplements	0-2	0	0	0	0
	3-5	3	2	0	1
Weaned	0-2	3	1	0	2
	3-5	4	1	1	2
Total		14	4	1	9

^a5% or more.

^bExpected gain.

Source: Ref. 10.

developed countries are imperfect and are not originally set to establish this kind of relationship. On the other hand, experimental field interventions are complex, difficult to analyze, and have not conclusively established the association.

There is no doubt that the diarrheal disease death rate is one of the main correlates of infant mortality: both declined dramatically in Costa Rica, particularly after 1964 (Fig. 5). The first significant reduction (1942-1948) coincided with a period of substantial social and economic reform. In the following years (1949-1963) no significant change occurred in the rates; this period began with a civil war followed by social instability, migration, and marked population growth. Thereafter, the mortality due to diarrhea and infant mortality decreased to the low figures of 12 per 100,000 and 22 per 1000, respectively, in 1978 [42,43]. The correlation between diarrheal disease death rates and infant mortality rates was quite strong (a large proportion of diarrhea deaths occur among infants). Thus it was clear for both the neonatal and the postneonatal infant mortalities until 1965 [43]. Thereafter, the neonatal mortality was not so strongly influenced by diarrhea deaths, because these had already been reduced and other causes of neonatal death acquired greater relevance. The regression equations for the various portions of the mortality curves are illustrated in Fig. 6. Significant values of r were noted for all data and for the specific portions of the curves after 1939. The lack of correlation for the first portion of the curve (1926-1939) could have been influenced by inaccuracies in the registration of deaths and by other communicable diseases and malnutrition, which caused many more deaths in the past.

If diarrheal disease is the main determinant of wasting and stunting in populations not suffering from recurrent food shortages and natural or human-made disasters, one should expect that a decrease in diarrhea must necessarily induce an improvement of the nutritional status, as seems to be the case in Costa Rica. The first nutritional evaluation in this country was made in 1966 [44]. Surveys in 1975 and 1978 using similar sampling procedures [45] revealed an important decrease in stunting in the urban and rural population [36,38]. Furthermore, the malnutrition ward of the National Children's Hospital was closed 5 years ago because of the marked reduction in incidence of severe protein-energy malnutrition [46]. Thus the nutritional improvement documented in Costa Rica appears to have followed the sharp reduction in diarrheal disease mortality.

VI. Summary

There is no doubt that infants breast fed by well-nourished mothers grow normally for several months without the need of supplementary feedings. Furthermore, prospective studies in developing nations show that poor village infants also grow adequately for periods ranging from 4 to 7 months, even if

their mothers are malnourished. The normal growth velocities observed in village infants contrast with the highly deficient sanitary conditions under which they dwell, and attest to the anti-infectious protective role of human milk. In fact, newborns and young infants are constantly exposed to contamina-

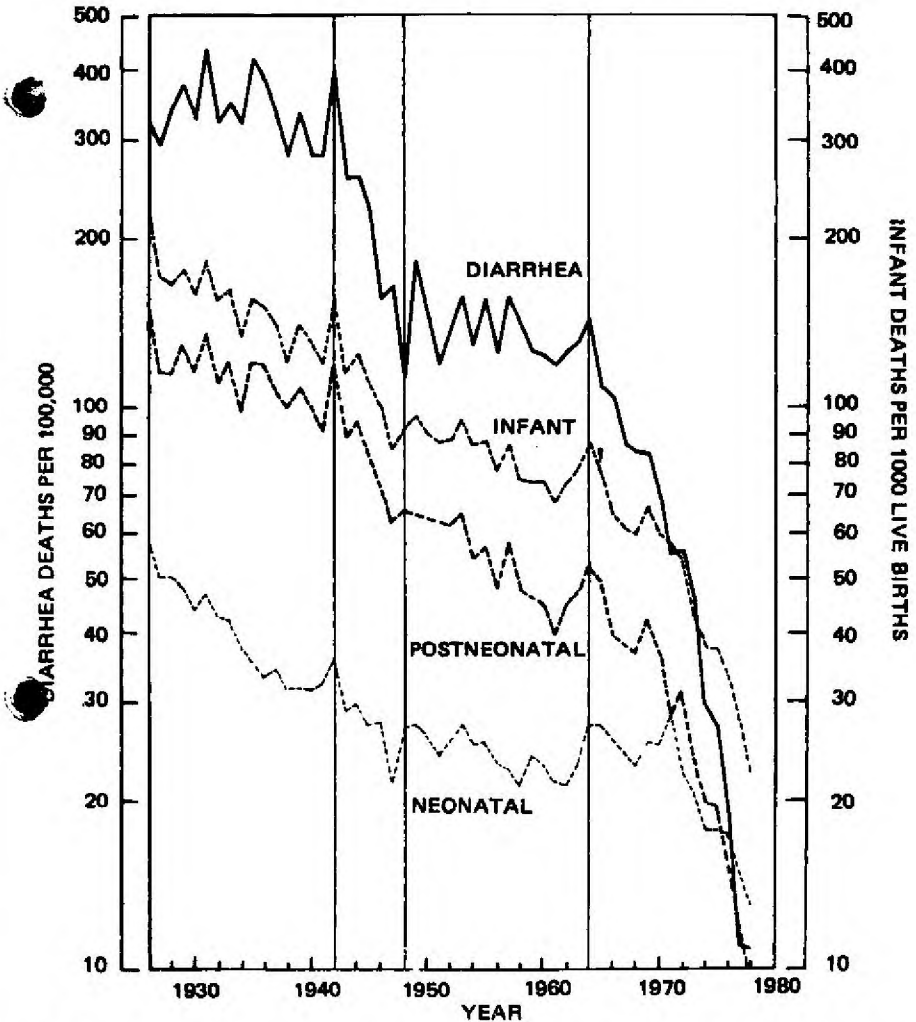


Figure 5 Decline of diarrheal disease deaths and infant mortality in Costa Rica, 1926-1978. Diarrhea deaths decreased to a very low figure of 12 per 100,000 population. Infant mortality decreased to a low 23 per 1000 live births in 1978. The dramatic reduction in diarrhea deaths resulted in a neonatal mortality larger than the postneonatal infant mortality after 1976.

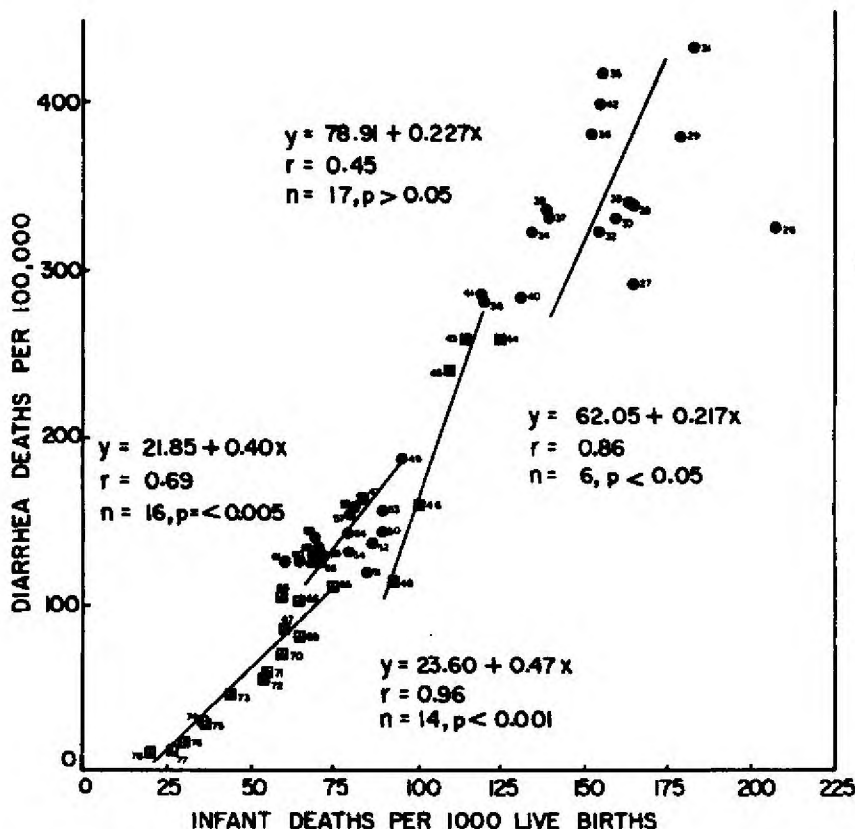


Figure 6 Correlation between diarrheal disease death rates and infant mortality rates in Costa Rica, 1926-1978. Four regressions were calculated, corresponding to the four sections of the curves arbitrarily selected and shown in Figure 5. (From Ref. 43.)

tion with feces, as evidenced by the common demonstration of enteric viruses, enteropathogenic bacteria, and intestinal parasites during the early months of life. Such infections generally are transient and asymptomatic, but as the child begins the protracted weaning process, infections are more frequent and persist for longer periods. Diarrhea then becomes a frequent manifestation of infection, often associated with periods of weight loss and stunting. While village children are exclusively at the breast, their nutritional states are adequate; thereafter, diarrhea begins the process of malnourishment. It is quite apparent that an improved nutrition can be attained by lowering the occurrence of diarrhea and/or diminishing or correcting the deleterious effects of diarrhea on

the host. Consequently, the control and prevention of diarrhea in a given society inevitably leads not only to a reduction in the rate of premature death, but to a reduction in the prevalence of severe and chronic malnutrition.

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