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The Santa María Cauqué Study: Health and Survival of Mayan Indians Under Deprivation, Guatemala

Leonardo Mata

Editor's note:
Although many references to published papers of this author are cited, most of the material in this chapter can be found in the book *The Children of Santa María Cauqué. A Prospective Field Study of Health and Growth* by Leonardo Mata which is highly recommended for persons desiring more detailed information on this remarkable study.

Introduction

The study discussed in this chapter is described in detail with multiple photographs, figures, tables and references in the book *The Children of Santa María Cauqué: A Prospective Field Study of Health and Growth* (Mata, 1978a). The study was carried out from 1963 through 1972 in Santa María Cauqué, a Maya Cakchiquel Indian village in the central Guatemalan highlands (Figure 1). Prior to this study, the community was the "infection control" in the pioneer three-village study of nutrition and infection interactions in 1959–1962 (Scrimshaw et al., 1967a,b). The other villages were Santa Catarina Barahona (the nutrition control) and Santa Cruz Balanyá (the nonintervened control). The Health Clinic in Santa María Cauqué, supported by the Ministry of Health and the Institute of Nutrition of Central America and Panama (INCAP), was expanded in 1963 to facilitate more detailed epidemiological observations, laboratory studies, and medical therapy. The primary data management was carried out directly at the village; final editing, filing, and analysis of data were performed at the Division of Environmental Biology of INCAP in Guatemala City and the Division of Biostatistics of the School of Public Health and Community Medicine of the University of Washington in

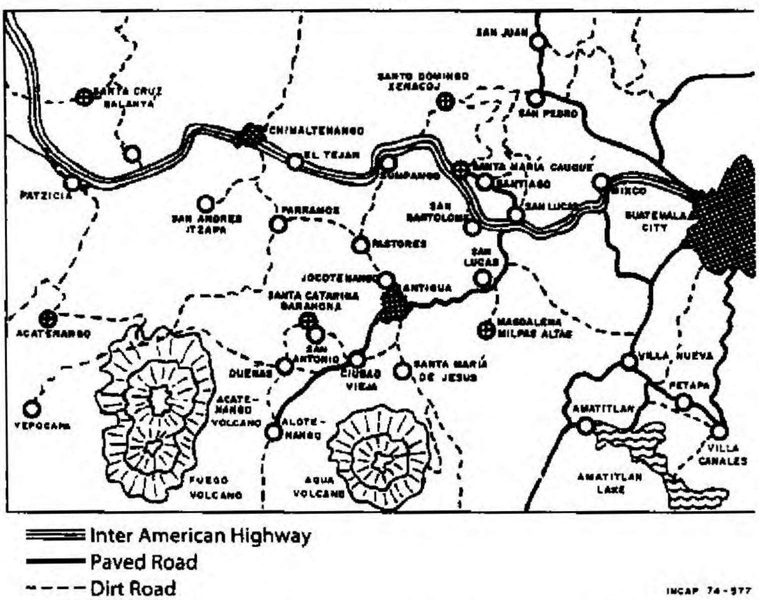
Seattle. The conceptual idea, objectives, results, and significance of the study have been published in book form. This article summarizes the main scientific results of the study, and their implications for modern public health and human development.

Methodology

The Human Laboratory

The study consisted of a long-term prospective observation of all cohorts of mothers and infants of the village from 1963 through 1972. Such a "human laboratory" permitted biological and sociological data to be gathered on all child cohorts during the study period, although virtually every other person in the community contributed data at one time or another. Most treatments were prescribed in accordance with Western medical guidelines and ethics. The study favored observation of the natural

FIGURE 1



Map of central Guatemala showing the distribution of highland Indian villages where INCAP carried out field studies. Santa Cruz Balanyá, Santa Catarina Barahona, and Santa María Cauqué were involved in the field study of nutrition and infection (1959–1963). Santa María continued as the village for detailed studies of infectious diseases and malnutrition (Cauqué Study) (1963–1972) and later for the maize fortification study (1972– 1975). Additional research on diarrheal diseases was recently pursued in Santa María de Jesús.

course of infectious disease with little disturbance, a situation difficult to replicate today.

The Health Clinic

The first year (1963) was devoted to getting acquainted with authorities, leaders, and village folk. The treatment protocol and standard operation procedure for field and laboratory were produced and tested. Virtually every pregnant woman was included in yearly cohorts for studies at the clinic or in their homes when there was illness. Smallpox had been eradicated in Guatemala before the study began. Expanded immunization for bacillus Calmette-Guérin (BCG) and diphtheria-pertussis-tetanus (DPT) was nonexistent. These vaccines were often rejected by villagers, but coverage improved through the study period. Vaccines against measles, rubella, and mumps were not available. The first one-shot national measles immunization campaign was conducted in 1972, the year the Cauqué study ended (Mata et al., 1974). More than 95% of children under five developed significant measles antibody titers according to pre- and post-vaccination representative samples. Measles mortality fell from the precampaign rate of 59 to 4.7 per 100,000 one year after the campaign. Lives were saved by measures of Western medicine. Penicillin was used to treat complicated respiratory infections and other suspected bacterial diseases. Sulfonamides were given for urinary tract infections and other illnesses. Continued breast-feeding was encouraged during attacks of infectious disease and convalescence. Traditional home beverages and intravenous fluid therapy were used to treat dehydrating infectious diseases. Implementation of Western medicine at the clinic was favored by the absence of an Indian shaman at the time of the study. Two pediatricians (Carlos Beteta, 1963–1965; Juan Urrutia, 1965–1974) contributed importantly to the improved health and reduced mortality attained during the study.

Cohorts of Pregnant Women

Pregnant women were the most assiduous in visiting the clinic. Although speaking the local Cakchiquel, they knew sufficient Spanish to communicate with the staff. Vaginal examinations were excluded from the protocol because they were not culturally acceptable. Blood pressure, urinalysis (including bacterial culture and test for pregnancy hormone), and diagnosis for sexually transmitted diseases were carried out. Dietary studies by recall and direct measurement were conducted each trimester.

Examination for intestinal parasites, bacteria, and viruses were performed during pregnancy on most women.

The date of birth was approximated from the date of the last menstruation and uterine height. Frequent contact between women, midwives, and staff favored identification of impending deliveries. These were assisted by two experienced folk midwives from the village, who collaborated as if they were members of the study team. Auxiliary nurses, posted at the Health Clinic around the clock, observed most of the deliveries during the study period.

Cohorts of Children

The nurses recorded the characteristics of each birth and newborn baby. Babies were examined by the pediatrician soon after birth, and within 14–15 hours if born at night. The physician also examined the mothers. All yearly cohorts of children were studied from 1964 through 1972. All the newborns were measured at birth (weight, length, circumference of head and thorax), then daily (weight) for one week, and weekly (weight, length) for one month. Most clinical, dietary, and anthropometric appraisals and collection of laboratory specimens were conducted in the homes. Onset and duration of breast-feeding and weaning were recorded for all. Colostrum and milk were collected from a series of women to determine concentrations of secretory immunoglobulin A (S-IgA) and antibodies to selected pathogenic agents. Hemoglobin and other limited parameters were studied in only a small group of children, because drawing of blood was not readily accepted by villagers. Most newborns appeared healthy and almost all were quite protected from disease during the first weeks of life.

Intensive Cohort

A cohort of 45 children was retrospectively and randomly selected from the children born in the first two years of the study, when the oldest was 18 months of age. Clinical examination and anthropometry were carried out at birth (as above), fortnightly (weight, length, head and thorax circumference) from one month to one year of age, monthly up to age two years, and thereafter at three-month intervals until termination of the study, when the oldest child was nearly eight years old. Weekly dietary investigations by recall were conducted from birth to age three years. All acute and chronic episodes of infectious diseases were recorded for the first three years of life. Fever was measured by thermometer, and anorexia was deduced from the interview with the mother. Illnesses were diagnosed according to standard criteria. This included number of bowel movements per day, duration, recurrence of episodes, and appearance of blood and mucus in stools. Fecal specimens were obtained daily for the first week of life, and weekly thereafter until the end of the third year of life. Stools were brought to the clinic by nurses and relatives within one hour of evacuation. Cultures and other procedures were performed at the clinic's field laboratory.

Cultures taken at the village were processed in the field laboratory, and aliquots were refrigerated or suspended for processing at INCAP's laboratories. Most enteric viruses, bacteria, and parasites known in that epoch were investigated. The indigenous anaerobic and facultative microflora was quantified at weekly intervals, in the field, for 12 randomly selected infants, from birth to age one year. All epidemics of infectious disease in the village were studied.

Remaining Children

The rest of the children were examined and measured with the same technique as the 45 cohort, as follows: at birth, weekly for one month, monthly for one year, and at six-month intervals until termination of the study.

Data were recorded in the field in precoded questionnaires and were edited at the clinic and headquarters for computer processing. Approximately 5 million data points were accumulated for analysis.

Main Results

Many of the findings of the Cauqué study were either new, poorly understood, controversial, or unbelievable when communicated to the scientific community. Some found it difficult to accept that calories were more limiting than protein in the village diet, that 40% of village newborns had low birth weight (LBW), that the high concentration of S-IgA in human colostrum and milk protected against enteric infection, that children averaged seven or more attacks of diarrhea per year, and that children had enteric pathogens during more than one-half of their first three years of life. The most difficult postulate to understand was that the force of infection and infectious disease was the main determinant of poor health, growth retardation, malnutrition, and death of infants and young children. Such ideas conflicted with prevailing dogma, despite previous studies that pioneered the field (Scrimshaw et al. 1959, 1968). The main findings of the Cauqué study follow.

Maternal Health and Nutrition

Courtship began at 14–17 years for girls and at 17–20 years for boys. Stable couples by common-law union or marriage were the rule; the few unaccompanied pregnant women were engaged. Motherhood started two or three years after union of the couple. Pregnancies usually occurred before age 20 and were spaced by two-year intervals as a result of prolonged breast-feeding and sexual restraint. The number of pregnancies averaged 12 for women 40–43 years old; the total span of fertility was 25 years. Birth intervals strongly correlated with gestational age: short birth intervals (9–17 months) led to more premature births than longer birth intervals (18 months or more), a highly significant difference. The association probably reflected a more limiting maternal nutrition and health when there was shorter spacing between pregnancies. It may also reflect the social practices in this group. Child-rearing expertise was acquired from older women.

Most young women were slim and stunted, although weight for height was adequate for most when they approached reproductive age; some became stocky at the end of their obstetric experience (Table 1). Stunting was the result of early synergism between infectious diseases and nutritional deprivation. Almost all pregnant women were barefoot, did not observe adequate personal hygiene, and lived in an unsatisfactory sanitary

TABLE 1

Anthropometric Values of 171 Women[a] of Santa María Cauqué, 1963–1971.

Age (years)	Number of women	Weight (kg)	Height (cm)	Tricipital Skinfold (mm)
14	1	58.4	142.2	14.0
15–19	80	52.2 (0.7)[b]	142.5 (0.5)	10.7 (0.4)
20–24	117	52.7 (0.6)	143.5 (0.4)	9.5 (0.3)
25–29	66	52.8 (0.7)	144.3 (0.6)	8.5 (0.4)
30–34	75	52.8 (0.8)	142.8 (0.5)	9.4 (0.4)
35–39	50	53.1 (0.9)	141.9 (0.6)	10.0 (0.5)
40–44	21	56.8 (1.6)	143.5 (0.9)	9.6 (0.8)
Mean		52.9	143.1	9.6

[a] Contributing 410 pregnancies to the study
[b] Mean (standard error)

Source: Mata (1978a)

environment. Therefore, a high proportion harbored enteric pathogenic parasites, bacteria, and viruses (Table 2).

The diet consisted of maize — the staple food — prepared as tortillas (flat pancakes of ground lime-treated kernels), black beans, and greens, with little animal protein and an occasional fruit. It was deficient in calories, animal protein, iron, and some vitamins. Food intake during pregnancy did not meet the increased need. Women did not gain enough weight during gestation (mean 6.8 kg) and experienced several disease episodes during pregnancy. Caloric intake, but not protein intake, during pregnancy correlated with birth weight and length. Thus, mothers had been affected by infectious diseases and poor diets and were stunted. Stunting correlated with fetal growth retardation and premature birth.

Birth at Home

Data were obtained by nurses for 297 natural births occurring from February 1964 through 1973; additional data were furnished by relatives

TABLE 2

Pathogenic Viruses, Bacteria, and Parasites and Antibodies to Selected Pathogens, Santa María Cauqué Mothers of Cohort Children, 1964–1965

	Number	Infectious Agents Diagnosed	Prevalence (%)
Enteric Infections	32	Enteroviruses	25
		Adenoviruses	3
	116	*Shigella* spp.	9
		Salmonella spp.	5
	24	*Entamoeba histolytica*	54
		Dientamoeba fragilis	8
		Giardia intestinalis	8
		Ascaris lumbricoides	83
		Trichuris trichiura	58
Significant Antibodies	50	Poliovirus type 1	100
	93	Coxsackievirus type B1	55
	93	Echovirus type 3	27
	93	Reovirus type 1	14
	48	Rubella agent	50
	200	*Brucella* spp.	0.5
	200	*Treponema pallidum*	0
	22	*Toxoplasma gondii*	50

Source: Mata (1978a)

for another 111 deliveries (Mata, 1978a). The midwife, relatives, and friends were present at the deliveries. Women gave birth on their knees (90%), squatting (8%), or in the supine position (2%). Traditional obstetrics did not include shaving, disinfection, analgesics, episiotomy, or forceps. Enemas were not given, and in all but two deliveries, passage of maternal feces occurred with soiling of the newborn. External maneuvers were the rule, with an occasional vaginal or rectal exploration, without handwashing or gloves. The main role of the midwife was to support the delivering woman with words, prayers, and massage of the back, abdomen, and limbs. The nurse assumed obstetric roles on few occasions, by specific invitation of the midwife or a relative.

Rupture of membranes was spontaneous in all deliveries, and birth ensued within 10 to 20 minutes (85.5%), 20 to 60 minutes (4.4%), one to 2 hours (3.4%), or 3 to 98 hours (6.6%). The duration of labor ranged from a few minutes to 19 hours (mode, four hours). The midwife cut and cauterized the umbilical cord with a hot sickle or machete, and in 72% of the cases dressed the stump with gauze and treated it with alcohol. These practices likely accounted for the virtual absence of tetanus neonatorum. Oxytocin, antibiotics, and other drugs were unknown or not available. Over 10 years, births were uncomplicated, 99.3% cephalic and 0.7% with breech presentation. No maternal deaths in puerperium were recorded. Puerperal fever and other diseases were not observed. One mother had cellulitis in the elbow and one developed psychosis — both while nursing — and they died within six months postpartum. Their infants were nursed by foster mothers and survived.

The success of natural birth was remarkable when compared with hospital delivery before the sanitary revolution initiated by Semmelweis in Europe in the nineteenth century or the advent of asepsis, antisepsis, and modern obstetrics (Table 3). There were no cesarean sections or nosocomial infections and no recorded puerperal fever or similar infections, despite the lack of asepsis in childbirth. In contrast, abnormal delivery and puerperal infections are common in modern societies. In Costa Rica, more than 95% of the births are in clinics and hospitals, with 36% spontaneous deliveries, 15% cesarean sections, and 15% maternal infections (Mata, 1982a). Cesarean section was found to be associated with shorter periods of breast-feeding (Mata et al., 1988) and an increased risk of neonatal death (Bobadilla et al., 1991). More complications and deaths would occur with such sections if it were not for the wide use of broad-spectrum antibiotics and other medical resources.

Mother-Infant Interaction

The newborn baby was immediately placed naked on a mat or cloth on the dirt floor, without removing the *vernix caseosa*. After a few minutes, the baby was wrapped in clothes. Maternal colostrum was given to only one-third of the babies. If the mother had been nursing an older child throughout the present pregnancy, she offered the breast to the newborn without delay. In many instances the mother gives colostrum to her baby. Under other circumstances a foster mother, generally a friend or relative, the grandmother of the infant as recorded in a few instances, serves in this capacity. In the first two days postpartum, the mother and baby had a 30- to 45-minute bath in the *temascal* (traditional sauna) accompanied by the midwife and perhaps a friend. She resumed her domestic, agricultural, and market duties within three days postpartum, carrying the baby wrapped on her front or back in intimate contact with her body. She slept with the baby to keep him warm and nursed him on demand (day and night) for months or years.

Optimal mother-infant contact promoted exchange of pheromones and odor, eye-to-eye contact, and verbal communication (Klaus and Kennell, 1976). It also stimulated breast-feeding, which is crucial for

TABLE 3

Delivering Babies in Contrasting Ecosystems
Vienna (1850), USA (1926), Santa María Cauqué (1964–72), and Puriscal (1979–81)

	Place and Date			
Variable	Vienna 1858 (%)	USA 1979 (%)	Cauqué 1964–72 (%)	Puriscal 1979–81 (%)
Type of Delivery				
Spontaneous	90	–	100	36
Conduced	0	–	0	45
Cesarean	0	15	0	14
Other[a]	10	–	0	5
Puerperal Complications				
Maternal infection	High	7	0	8
Maternal mortality	12[b]	0.04[c]	0	0.04
Source	Haggard, 1929	Cohen and Estner, 1983	Mata, 1982b	Mata, 1983c

[a] Induced, forceps, manual maneuvers, combinations

[b] Reduced to 1.2% by hand washing of attendants

[c] 40% by puerperal fever

optimal intake of nutrients, maternal hormones, and immune factors. The bifidus factor of human milk, along with S-IgA and lactoferrin, favored colonization of the child's intestine with bifidobacteria. The peaceful environment of home and village was supportive of such mother-infant interaction. Bonding contributed to the universal success of efficient breast-feeding for months and years, the absence of child abandonment, and the very low rate of corporal punishment of children in the village. The quietness of the home was occasionally altered by a quarrel, perhaps preceded by a fiesta accompanied by *guaro* (local hard liquor).

Breast-Feeding and Weaning

Breast-feeding was considered a natural event. Approximately one-half the mothers continued to nurse while pregnant. Among women not lactating during gestation, one-third offered colostrum to their infants. Although 33% of the families owned cows (the 1971 census showed 45 cattle), there was no bottle-feeding in the village. Few families had refrigerators, and milk formula was not available. An absence of urban life, low levels of modernity, and no organized labor for women outside the home were contributing elements. Soiling of the babies with maternal feces during birth resulted in infections with pathogenic viruses and bacteria during the first days of life, which generally were asymptomatic. About one-half the mothers gave sweetened water and infusions to their newborns with the aid of a piece of cloth, but this practice did not result in diarrhea. Colostrum and milk had large concentrations of S-IgA, which, together with the bifidus flora and lactoferrin, provided an effective defense against infection (Wyatt et al., 1972; Yolken et al., 1978). Antibodies in S-IgA are resistant to digestive enzymes and remain active after transit through the alimentary canal (Hanson et al., 1975).

Most women produced sufficient milk (an average of 686 g/day at three months) to nurse satisfactorily for three to six months, but quality and quantity were lower when compared to values for well-nourished Swedish women (776 ml/day) (WHO, 1985). This volume, however, may not be enough to satisfy the needs in the second trimester (Waterlow, 1981). Women experienced infectious diseases and low food intake since childhood, but most had adequate weight for height, and all lactated for two to four years. The intimate contact between the bodies of the mother and child, as it is carried constantly, the heat of the *temascal* baths, and frequent exposure to sunshine were factors counteracting the hypothermia of small newborns in this cool climate.

The weaning foods, normally introduced at three to five months of age, were tortillas, broths, beans, and other foods of the adult diet. They were bulky, of low caloric density, and a source of microbes (Mata et al., 1976a). For instance, tortillas, relatively sterile soon after cooking, became contaminated with *Escherichia coli, Bacillus cereus*, and *Clostridium perfringens* within 24 hours of storage under a moist cloth, a traditional practice (Capparelli and Mata, 1975). Lack of refrigeration and limited firewood were contributing factors.

Recurrent infections during and after weaning contributed to the marked reduction in calorie consumption (Table 4). The main nutritional deficit was in calories and not in protein, as was thought in the past (Gopalan et al., 1974; Valverde et al., 1975). Dietary deficiencies were assumed to be due to low food availability in the community, until it was shown that Cauqué children had marked caloric deficits ("dips") during attacks of infectious disease, and adequate caloric intake during good health (Mata et al., 1977; Mata, 1978b, 1979).

No change in onset of definitive weaning was noticed in five yearly cohorts, reflecting the stability of this deeply rooted tradition (Figure 2) (Mata et al., 1982). Weaning age was conditioned by the interplay of maternal factors: a new pregnancy (main cause of abrupt interruption of

TABLE 4

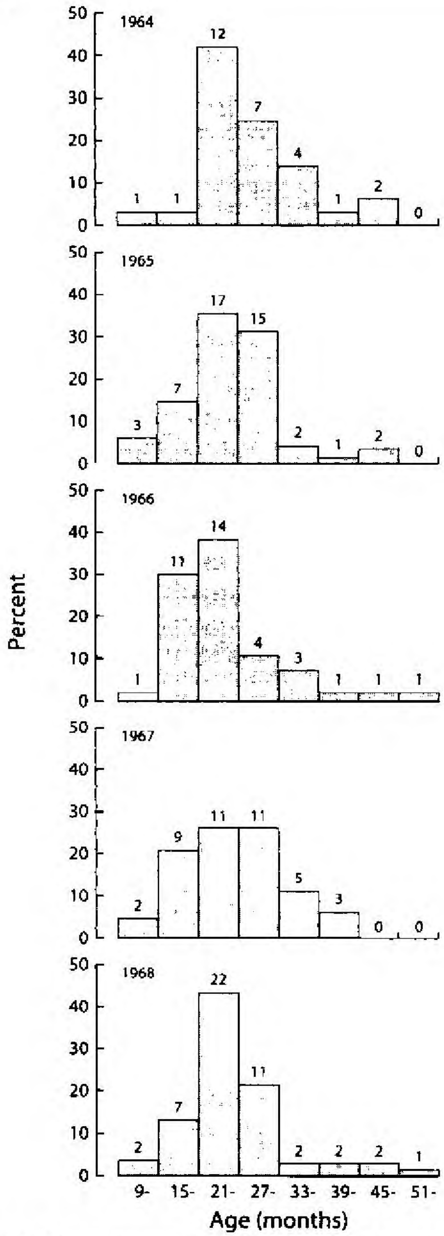
Nutrient Value of Food Supplements Consumed by Fully Weaned Children One to Three Years Old.

	26 months (14 children)	36 months (31 children)	International Recommendation, 1- to 3-year-olds[a]
Energy (kcal)	619 (176)[b]	992 (272)	1300
Protein (g)	17 (4.9)	27 (6.6)	16
Iron (mg)	6 (1.8)	10 (3.6)	10
Retinol (μg)	90 (95)	111 (77)	250
Thiamin (mg)	0.4 (0.2)	0.6 (0.1)	0.6
Riboflavin (mg)	0.3 (0.1)	0.4 (0.2)	0.9
Niacin (mg)	3.4 (1.1)	5.8 (1.5)	10.2
Ascorbic acid (mg)	16 (8.0)	24 (10)	20

[a] NAS/NRC (1989)
[b] Mean (SD)

Source: Mata (1978a), adapted

FIGURE 2



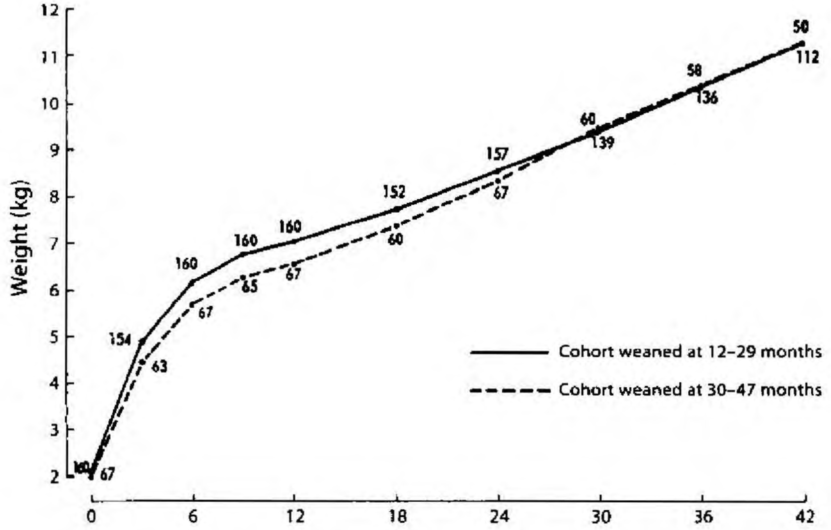
Percent distribution of weaning age, in months, of five cohorts by year of birth, Santa María Cauqué, 1964–1972. Figures above bars indicate the number of girls and boys weaned at given ages. Most children were weaned late, from 21 to 32 months of age. The slight increase in length of breast-feeding for the 1966 and 1968 cohorts may not be significant in view of the relatively small number of children in each cohort (Mata et al., 1982).

breast-feeding), prepregnancy nutrition, and working, economic, and emotional conditions. Such child factors as size and maturity at birth, growth velocity, and health status also have an influence. Infants who grew faster in the first months of life were weaned earlier; those who grew more slowly were weaned at a later date (Mata, 1978a) (Figure 3).

Force of Infection and Infectious Disease

Infectious diseases in the 1940s were very common and devastating, according to the Registry kept in the village Town Hall since 1936. Simultaneous epidemics of dysentery, respiratory disease, whooping cough, and measles ravaged the village, killed as many as 7% of the total village population in a given year (Mata, 1978a). The Cauqué study revealed a formidable pressure of infection on pregnant women and children. Most women of reproductive age harbored intestinal pathogens, which infected newborns at delivery (see Table 2). In pregnancy, 31% of the women had one episode of infectious disease, 22% had two, 16% had three, and 2%

FIGURE 3



Weight curves of two cohorts of children defined by different weaning ages, from birth to age 42 weeks, the stage of growth deceleration. Top curve: children weaned earlier, at 12–29 months. Lower curve: children weaned later, at 30–47 months. Children who grew faster in the first months of life tended to be weaned later. A similar relation occurred with body length, Santa María Cauqué, 1964–1972 (Mata, 1978a).

had four or five (Table 5) (Mata, 1978a). Diarrheal disease, lower respiratory infection, cystitis, pyelonephritis, and febrile bacterial infections often had deleterious effects on maternal health. Infection in the mother likely contributed to the frequency of elevated fetal IgM (Mata, 1978a; Mata and Villatoro, 1977), but no correlation was found between this and fetal growth retardation.

Intestinal colonization of newborns with indigenous microorganisms was rapid and efficient and originated in perinatal contamination with microflora of maternal feces and tegumenta (Mata and Urrutia, 1971). The bifidus flora, S-IgA, and lactoferrin provide a natural barrier against many intestinal pathogens that invade the neonate (Table 6). Enteroviruses and pathogenic bacteria were found in the intestinal tract of several neonates, but such infections often were asymptomatic, reflecting the effective defense conferred by immune principles in maternal colostrum and milk (Mata and Wyatt, 1971; Cruz et al., 1977).

Breast-fed infants were markedly resistant to *Giardia* and *Shigella* during the first semester or longer (Figure 4). As they grew older, however,

TABLE 5

Incidence of Infectious Diseases and Syndromes
365 Pregnancies, by Trimester

	Trimester		
Illness or Syndrome	**1st**	**2nd**	**3rd**
Upper respiratory disease	18.9[a]	26.3	30.9
Bronchitis	1.9	2.5	3.0
Laryngotracheobronchitis	0.3	1.6	1.6
Otitis media	0	0.8	0.8
Pneumonia	0	0.6	0.3
Conjunctivitis	0.3	0	0.3
Fever of unknown origin	0.3	0	0
Diarrhea	4.9	4.9	8.2
Dysentery	1.4	1.1	1.1
Cystitis, pyelonephritis	1.9	1.9	1.4
Hepatitis	0	0.5	1.1
Skin infection[b]	3.0	0.8	3.0
Tenosynovitis	0	0.3	0

[a] Percentage of pregnancies
[b] Impetigo, cellulitis, abscess
Source: Mata (1978a), adapted

TABLE 6

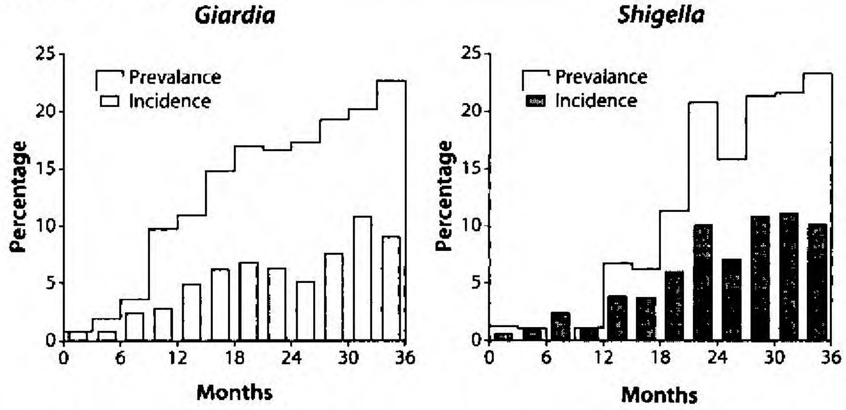
Early Neonatal Infection with Pathogenic Viruses, Bacteria, and Parasites

Age of Child	Number of Children Tested (% positive)	Pathogenic Agent (Number of Children)
1 day	79 (1.3)	Echo 7 (1)
2 day	54 (7.4)	Polio 1 (1) Echo 6 (3)
3 days	61 (8.2)	Polio 1 + echo 6 (1) Echo 6 (1) Echo 7 (1) Echo 9 (1) Echo 11 (1)
3 weeks 4 weeks 12 days 28 days	109 (3.6)	*Sh. flexneri* type 1 *Sh. flexneri* type 3 *Sh. flexneri* type 2 *Sh. sonnei*
1 day 3 days 4 days 4 days	191 (2.6)	*E. histolytica* c[a] (1) *G. intestinalis* c t (1) *G. intestinalis* t (1) G. intestinalis c (2)

[a] c = cysts; t = trophozoites

Source: Mata (1978a); Mata et al. (1969)

FIGURE 4



Incidence and prevalence of *Giardia intestinalis* and *Shigella* spp., by age of child, cohort children from Santa María Cauqué, examined weekly from birth to age three years. Marked differences in incidence and prevalence were noted, reflecting the chronicity of infection with both pathogens (Mata et al., 1971; Mata, 1982a,b). Note the significantly lower rates of infection during the period of exclusive breast-feeding. With weaning, children became more readily infected, and if they were malnourished, they often had persistent infection.

they became infected with pathogenic enteric viruses (Table 7), shigellae (Table 8), and intestinal parasites (Table 9). The indigenous flora were less protective at older ages when children were exposed to larger infectious doses acquired from weaning foods, water, and attendants (Mata, 1983a).

Infection with rotavirus was investigated by an antigen-capture enzyme-linked immunosorbent assay (ELISA) in 5,891 weekly specimens from the 45 cohort children, which had been kept frozen since

TABLE 7

Prevalence of Infection with Pathogenic Enteric Viruses
45 Cohort Children of Santa María Cauqué, Birth to Age Three

Age (months)	Number of specimens	Enteroviruses	Adenoviruses
0–5	1,116	230 (20.6)[a]	34 (3.1)
6–11	1,162	483 (41.6)	46 (3.9)
12–17	917	481 (52.5)	33 (3.6)
18–23	953	438 (45.9)	60 (6.3)
24–29	908	446 (49.1)	58 (6.4)
30–35	867	530 (61.1)	48 (5.5)

[a] Number of fecal specimens (percentage positive)

Source: Mata (1978a)

TABLE 8

Incidence of *Shigella* Excreted in Feces
45 Cohort Children, Birth to Age Three Years

Age (weeks)	Number of children	Weeks at risk[a]	Prevalence
0–25	81	1,783	1 (0.06)[b]
26–51	65	1,546	11 (0.7)
52–77	52	1,192	20 (1.7)
78–103	46	1,096	37 (3.4)
104–129	44	1,100	39 (3.6)
130–155	43	1,075	40 (3.7)
Total		7,792	148 (1.9)

[a] Weeks at which children were examined clinically and bacteriologically
[b] Number of new infections (rate per 100 child–weeks)

Source: Mata (1978a)

1964–1969 (Mata et al., 1983). Rotaviruses were uncommon during exclusive breast-feeding. When they entered the village, however, they rapidly infected as many as 50% of the children, particularly those 6 to 18 months old (Figure 5). Rotavirus diarrhea often was accompanied by fever, dehydration, and weight loss (Wyatt et al., 1979; Mata 1983a).

Enteroviral and rotaviral infections were short-lived. In contrast, many adenoviral, bacterial, and parasitic infections were prolonged, either due to failure of the host defense to repel them or due to repeated infections. One striking example were the shigellae, with more than 50% of the infections lasting two weeks or more, and 10% lasting two months or more (Table 10) (Mata et al., 1984). The use of the immunomagnetic separation/polymerase chain reaction might increase these rates by two- to threefold, as shown for Costa Rican children (Achí et al., 1995). Prolonged infections with *Giardia* also had a deleterious effect on nutrition and growth of Cauqué children (Farthing et al., 1986).

The 45 cohort children harbored one or more intestinal pathogens in one-half of their infant period. These were found in two-thirds during the second and third years of life. Consequently, most children had recurrent diarrhea during most of their early years of life. With regard to etiology,

TABLE 9

Incidence of Pathogenic Parasites

45 Cohort Infants, Birth to Age Three Years, by Six-Month Intervals

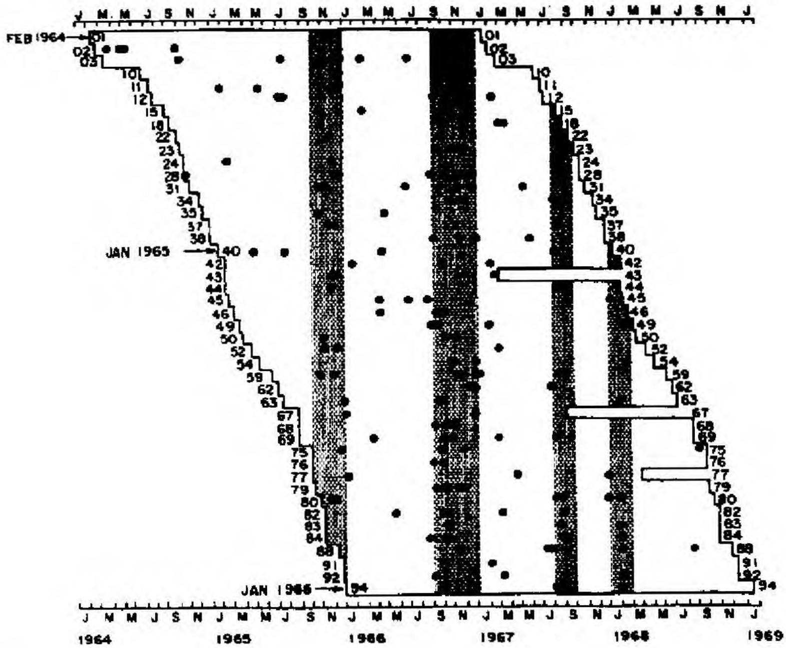
	Months					
Parasite	**0–5**	**6–11**	**12–17**	**18–23**	**24–29**	**30–35**
E. histolytica	5[a]	0 (5)[b]	6 (11)	9 (20)	12 (32)	5 (37)
D. fragilis	0	3 (3)	1 (4)	1 (5)	1 (6)	5 (11)
G. intestinalis	8	13 (21)	14 (35)	4 (39)	1 (40)	2 (42)
A. lumbricoides	4	9 (13)	14 (27)	14 (41)	1 (42)	0 (42)
T. trichiura	2	2 (4)	4 (8)	6 (14)	3 (17)	3 (20)
H. nana	0	0	0	1	3 (4)	2 (6)

[a] Number of children with parasite

[b] (Accumulated number of children with parasite)

Source: Mata (1978a); Melvin and Mata (1979)

FIGURE 5



Incidence of rotavirus infection in 45 cohort children sampled weekly from birth to age three years. Each dot represents a week positive for rotavirus antigen by ELISA. The vertical shaded bands represent the periods in which rotaviruses spread across all age groups. Such events immunized most of the susceptible population, until new individuals accumulated to face new entrances of these viruses (Mata et al., 1983).

TABLE 10

Duration of *Shigella* Infection (Cases and Carriers)

45 Cohort Infants, Birth to Age Three Years

Shigella Subgroup	No. of Episodes[a]	Weeks of Duration					
		1	2–4	5–8	9–12	13–16	17–38
dysenteriae	29	7 (24)[b]	10 (34)	4 (14)	3 (10)	2 (7)	3 (10)
flexneri	5	18 (24)	21 (28)	18 (24)	9 (12)	5 (7)	4 (5)
boydii	21	14 (67)	6 (28)	1 (5)			
sonnei	7	7(100)					
Total	132	46 (35)	37 (28)	23 (14)	12 (9)	7 (5)	7 (5)

[a] Two isolations were considered independent if separated by more than 2 weeks.
[b] Number of events (percentage within *Shigella* subgroup)

Source: Mata (1978a)

more than 50% of the diarrheas were associated with known pathogens (Table 11) , an underestimate because in that epoch many agents had not been discovered or rediscovered. For instance, by retrospective testing, rotaviruses were found associated with 10% of the diarrheas of the 45 cohort children (Mata et al., 1983) (Table 12). Also, in the Mayan village of Santa María de Jesús, located in the same geographic region and similar

TABLE 11

Enteric Pathogens in 381 Cases of Diarrhea Experienced by 22 Cohort Children from Birth to Age Three Years.

Agent[a]	Number Positive (%)
Giardia intestinalis	92 (24.1)
Shigella spp.	89 (23.3)
Rotaviruses[b]	44 (11.5)
Entamoeba histolytica	44 (11.5)
Adenoviruses (cultivatable)	29 (7.6)
Salmonella spp.	11 (2.9)
Enteropathogenic *Escherichia coli*	6 (1.6)
Dientamoeba fragilis	3 (0.8)
One or more of the above	227 (59.6)

[a] Strains of *Escherichia coli* [enterotoxigenic (ETEC), enteroinvasive (EIEC), enterohemorrhagic (EHEC), and enteroaggregative (EAggEC)], *Campylobacter*, *Cryptosporidium*, diarrhea adenoviruses, and small round structured viruses were not investigated at the time of the Cauqué Study.

[b] Rotaviruses were studied in stored frozen specimens (Mata et al., 1983).

Source: Mata et al. (1984)

TABLE 12

Incidence of Rotaviruses in Diarrhea of Children Living in Contrasting Ecosystems

Population	Child-Years	All Diarrhea	Rotavirus Diarrhea	Rotavirus Infection	% Diarrhea Due to Rotavirus
Cauqué[a] 1964–1969	132.5	1,050 (7.9)	109 (0.8)	166 (1.2)	10.4
Matlab[a] 1978–1979	120	727 (6.1)	34 (0.3)	—	4.7
Winnipeg[b] 1976–1979[c]	139	165 (1.2)	40 (0.3)	50 (0.4)	80.0

[a] Rural poor, adjusted to account for uncollected or unavailable specimens (Mata et al., 1983)

[b] Recalculated from Black et al. (1982a)

[c] Adapted from Gurwith et al. (1981)

in many respects to Cauqué (see Figure 1), adenovirus types 40 and 41 were incriminated in the acute diarrheas of childhood (Cruz et al., 1990).

Diarrhea morbidity, which is low during exclusive breast-feeding, increased with weaning to attain the highest rates from the second to the fifth semesters (Mata, 1975). There were, on the average, seven attacks of diarrhea per child per year in the first three years of life. The incidence was greater during weaning ("weanling diarrhea"; Gordon et al., 1963), from 6 to 26 months of age (Figure 6). Other infections were less frequent than diarrhea, but added together they were very important as causes of disease, disability, and death (Table 13): namely, tonsillo-pharyngitis; bronchitis and bronchopneumonia; thrush, herpes simplex, glossitis, and cheilitis; impetigo, abscess, and furuncle; measles, rubella, and varicella; and undifferentiated febrile illness. These illnesses were found in greater frequency during weaning ("weanling morbidity"). Complications of measles (Urrutia and Mata, 1974) and whooping cough (Mata 1978a) were common.

In sum, children were ill with infectious diseases during much of their infancy and preschool years. Such a force of infection contributed to an early increase in serum immunoglobulins. By the age of one year, 95% of children had acquired the village adult level of IgG, and 99% had reached the adult value of IgM. With regard to IgA, 73% of the children had adult levels of this immunoglobulin by the age of five to nine years (Cáceres and Mata, 1974).

Effect of Infection on Food Intake and Growth

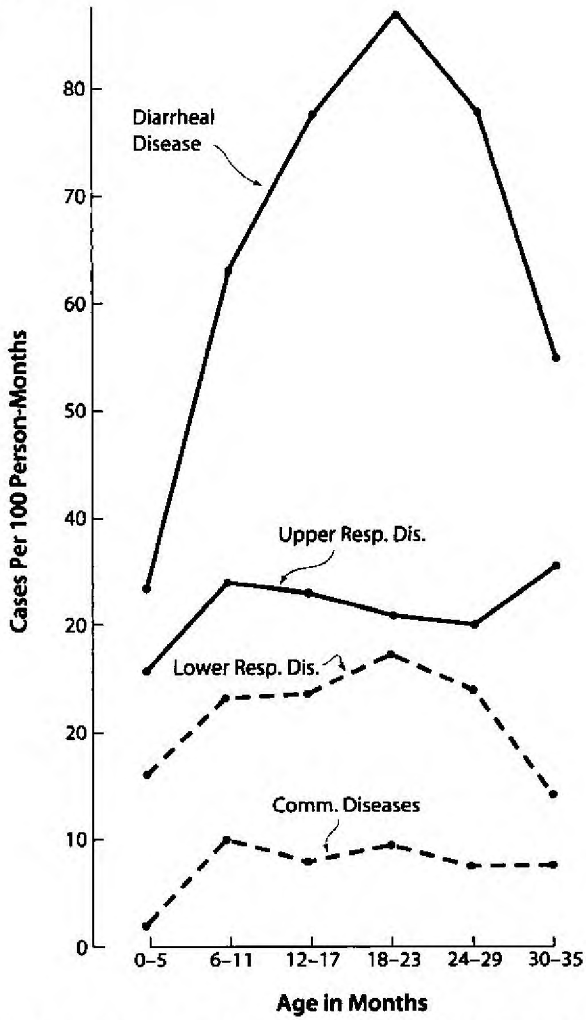
Frequent symptoms and signs in children were despondency, prostration, fever, anxiety, and anorexia. These are common manifestations of stress triggered by interleukins and tumor necrosis factor released by macrophages in response to infection (Beisel 1977; Dinarello, 1984). The main nutritional consequences of infection are reduced consumption of calories; loss of ingested foods; increased transit of food through the alimentary canal; altered digestion and absorption; protein-losing enteropathy; loss of electrolytes, vitamins, and other nutrients; altered metabolism; sequestration of trace elements; and nutrient diversion (Beisel, 1977).

Cauqué children ate less food during episodes of infectious diseases, regardless of etiology, severity, or target organ. The effect was more pronounced with fever, sepsis, diarrhea, and lower respiratory infection. Thirty-three percent of children with whooping cough consumed only one-half of the customary amount of tortilla in the first month of illness;

maize intake was also significantly depressed in the second and third months of the disease (Table 14).

Fully weaned children consumed an adequate amount of food when they were free of disease. However, intake fell below recom-

FIGURE 6



Incidence of infectious diseases, per 100 person–months, in a cohort of 45 children observed from birth to age three years, Santa María Cauqué, 1964–1972. Diarrheal diseases predominated, with rates as high as 80/100, about eight cases per child per year. Upper and lower respiratory infections, combined, were almost as frequent as diarrhea. Note that infectious morbidity tended to accumulate in the weaning months (Mata, 1978a).

mendations when they acquired enteric, skin, and lower respiratory infections (Figure 7) (Mata et al., 1977; Mata, 1979). The average decrease attributed to diarrhea alone was 24% for total protein and 21% for calories (Mata, 1983b). In Uganda, the mean reduction of intake in children consequent to infection was 48% (Whitehead, 1981). Food restriction is worsened by the traditional custom of withholding food during illness (Scrimshaw et al., 1968). Fortunately, much of the absorp-

TABLE 13

Incidence of Selected Infectious Diseases and Symptoms Experienced by 45 Cohort Children, Birth to Age Three Years

Diseases, Symptoms[a]		Cases	Percent of All Cases	Rate per 100 Person-Years[b]
Diseases	Respiratory			
	Bronchitis	256	10.5	193.9
	Bronchopneumonia	70	2.9	52.0
	Tonsillo–pharyngitis	10	0.4	7.6
	Enteric			
	Diarrhea	640	26.1	484.8
	Diarrhea with mucus	313	12.8	237.1
	Dysentery	97	4.0	73.5
	Mouth			
	Herpes simplex, primary	20	0.8	15.1
	Stomatitis	23	0.9	17.4
	Thrush	28	1.1	21.2
	Glossitis, cheilitis	14	0.6	10.6
	Skin, scalp			
	Impetigo	31	1.3	23.5
	Abscess, furuncle	16	0.7	12.1
	Common communicable			
	Measles	32	1.3	24.2
	Rubella	15	0.6	11.4
	Chicken pox	26	1.1	19.7
	Febrile exanthem	25	1.0	18.9
	Whooping cough	10	0.4	7.6
	Other			
	Fever of unknown origin	14	0.6	10.6
Symptoms	Fever, 37.5+ C	1,148	25.7	869.7
	Diarrhea, all	1,205	27.0	912.7
	Vomiting	235	5.3	178.0
	Anorexia	823	18.4	623.5
	Despondent, irritable	1,008	22.6	763.6

[a] Twenty–four diagnoses had fewer than 10 cases each and were omitted from the table.
[b] 132 person-years of experience, taking attrition into account

tive capacity of the mucosa remains intact during enteric infection, permitting feeding during illness and convalescence (Molla et al., 1982).

The deleterious effect of infection on nutrition is reflected in lower body weight and height. Male child No. 12, born with some weight deficit, had normal growth velocity during exclusive breast-feeding (Figure 8). Enteroviral infections and mild respiratory illnesses in that period had no apparent clinical impact. But with increasing morbidity from 6 to 27 months (weaning), the curve flattened, particularly from the second to the fifth semesters. Most cohort children behaved like child No. 12: they became malnourished in the second semester until the end of the second

TABLE 14

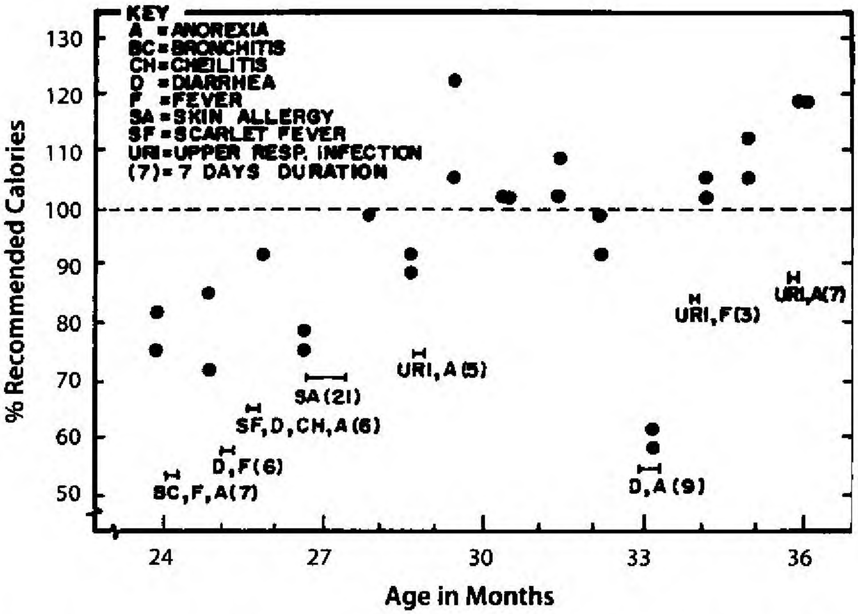
Consumption of Tortillas During Whooping Cough by 21 Cauqué Children Two to Three Years Old

Child Number	Age (months)	Percent Consumed[a] by Month Ill		
		1st	2nd	3rd
22	41	43[b]	84	108
54	36	93	79	82
37	38	41	94	94
52	35	108	109	149
59	35	130[c]	200	200
76	31	94	90	92
11	44	133	111	102
16	44	110	122	142
35	39	98	45	105
24	41	52	109	105
23	41	95	54	90
31	41	96	122	117
69	31	99	91	97
83	29	55	39	103
91	26	100	100	60
49	36	78	80	69
34	38	139	57	80
88	27	98	89	98
80	29	100	91	100
94	27	113	154	224
18	42	33	36	74

[a] Percent consumption in relation to intake before onset, considered as 100%
[b] Reduction by more than 50% of usual intake
[c] Increase by at least 25% of usual intake

Source: Mata (1978a)

FIGURE 7



Calorie consumption and infectious diseases after cessation of breast-feeding in child No. 37. Intakes were measured at weekly intervals, and adequacy was expressed as percentage of recommended calories per day. Low caloric intakes were observed during illnesses, and adequate intakes during periods of good health. A considerable calorie deficit ("dip") of approximately 40% of the recommended calories was noted at about 33 months of age, coinciding with diarrhea with anorexia. A similar response was observed in the remaining fully weaned children (Mata et al., 1977).

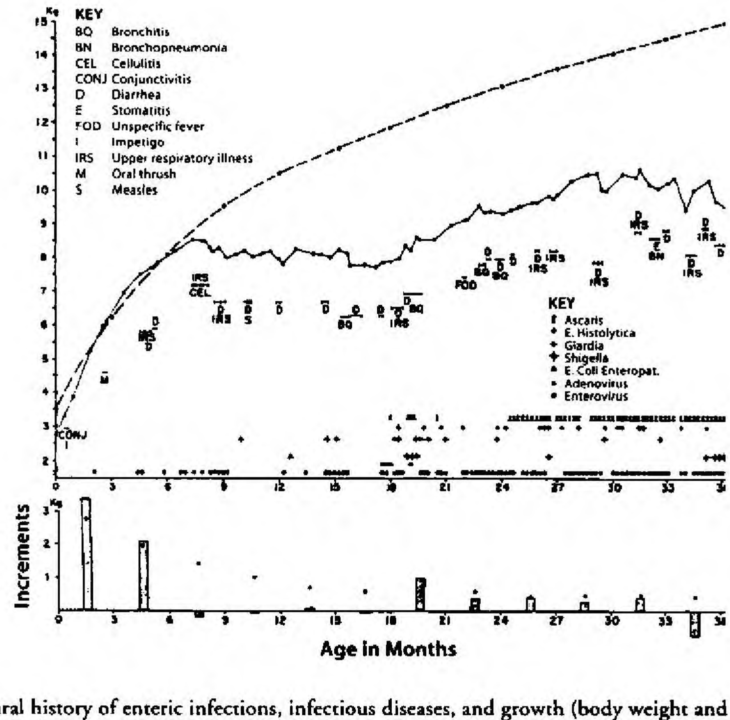
year or longer. Weight increments improved in the third year of life for some, but not all, children.

The age of the child and the type of feeding influenced the effect of infection on growth. For instance, whooping cough was of less nutritional consequence during exclusive breast-feeding (Figure 9, children No. 214 and 216) than in the protracted weaning period (Figure 9, children No. 172, 177, and 181). Girl No. 177 lost almost 2 kg in two weeks, which she could not recover until 16 weeks later. She caught up to preinfection weight after about 36 weeks, but was still further below the mean weight for village children by this time.

The nutritional effect of infection was worse if there was underlying fetal growth retardation or prematurity, illustrated for two children with different birth weights (Figure 10). All diarrhea episodes in the first two years of life were associated with some stagnation of linear growth, and this was greater and more prolonged in the child who had been born with greater fetal growth deficit (Mata, 1982b).

Infectious diseases were efficient killers of infants who were either born small-for-gestational age or prematurely. For instance, female child No. 19, born with deficient weight but growing satisfactorily under exclusive breast-feeding (Figure 11), developed respiratory infection and anorexia at 9 weeks of age and meningitis at 13 weeks, which lasted 6 weeks. These events were associated with 12 weeks of weight faltering. The child

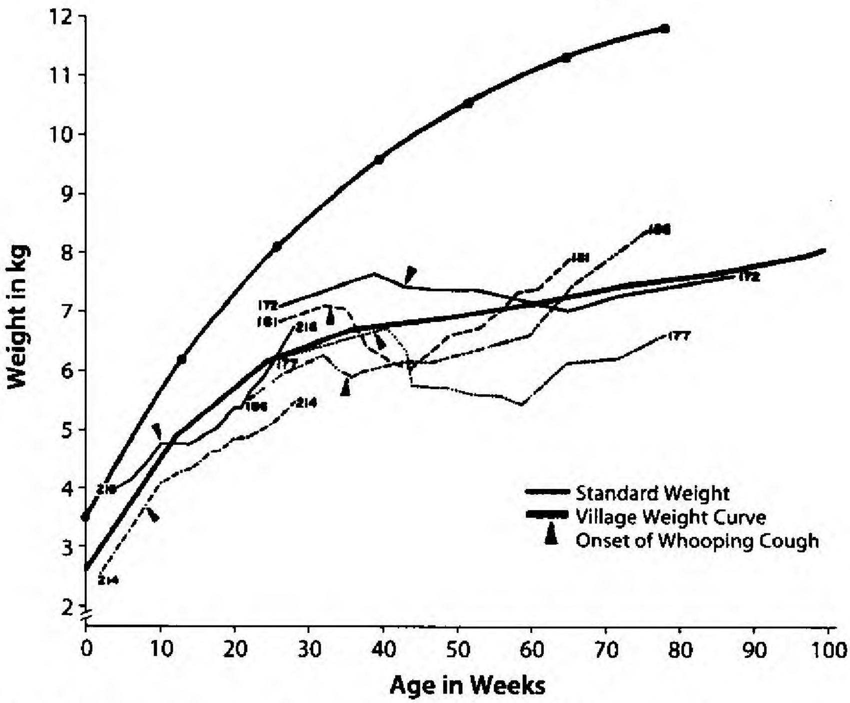
FIGURE 8



Natural history of enteric infections, infectious diseases, and growth (body weight and increments) of village child No.12 during his first three years of life. Good protection against infection was observed during exclusive breast–feeding (7 months in this case). Infections appeared early in life but were most common after the first year. Diarrhea increased with weaning, to reach maximum rates in the second year of life. Growth was adequate during exclusive breast–feeding, but thereafter, there were recurrent periods of acute weight loss or growth faltering in conjunction with emerging infectious diseases. The child became overtly malnourished by age one year (Mata et al., 1971; Mata, 1978a).

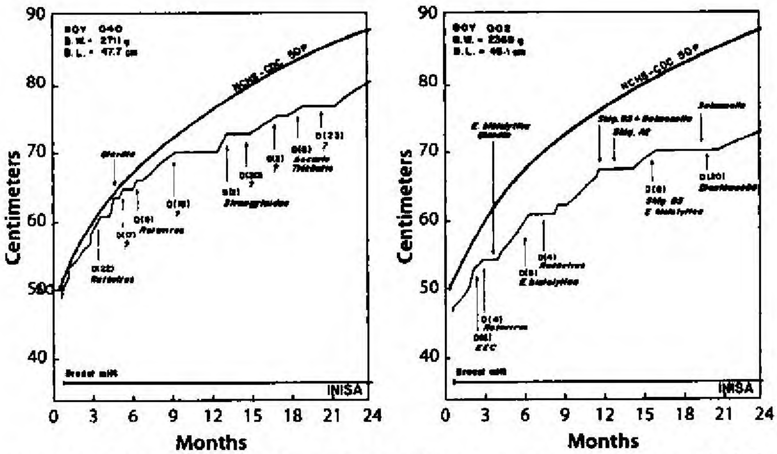
continued at the breast, with supplementary food, and caught up somewhat (oddly, after diarrhea and varicella). However, growth deteriorated shortly thereafter, coinciding with attacks of stomatitis, diarrhea, and respiratory infection. The child developed severe psychomotor retardation and malnutrition, and died at the end of her second year of life. The infection-malnutrition complex can kill children who have survived the perilous weaning period. For instance, child No. 44, discussed above (see Figure 8), reached school age but succumbed to typhoid fever at seven years of age. Other examples of infection-nutrition interactions in the 45 cohort children were described elsewhere (Mata, 1975, 1978a, 1982b, 1983a,b,c, 1985, 1990, 1992; Mata et al., 1971, 1972a,b, 1975, 1976b, 1977, 1982, 1984).

FIGURE 9



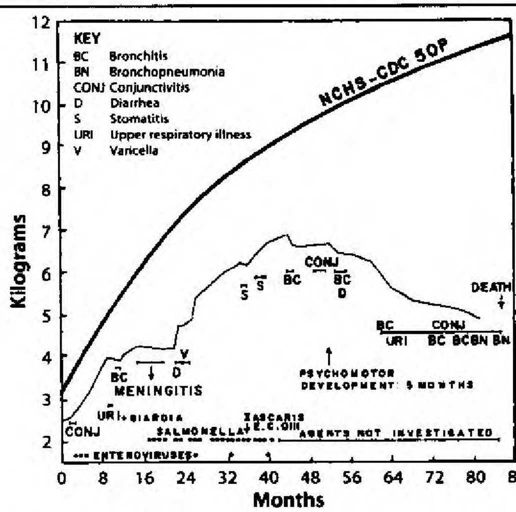
Effect of whooping cough on the weight curve of children at the breast or undergoing weaning. This disease had a negative effect on growth. Exclusively breast–fed infants showed moderate weight loss and better recuperation (children Nos. 214 and 216) than weanlings and fully weaned children. These lost more weight and took several months to make up the loss (children Nos. 177, 172, 181, and 186) (Mata et al., 1972a,b,c; Mata, 1978a).

FIGURE 10



Growth in body length during the first two years of life, two typical village boys with different grades of intrauterine growth (IUGR). The child at the left (No. 40) had moderate IUGR; the one at the right (No. 2) had marked IUGR. Most episodes of diarrhea in both children were associated with growth retardation of varying duration, regardless of the etiology of the diarrhea. Stunting (deficit in length) was noticeable in both children, but it was more evident in the child born with the lower birth weight.

FIGURE 11



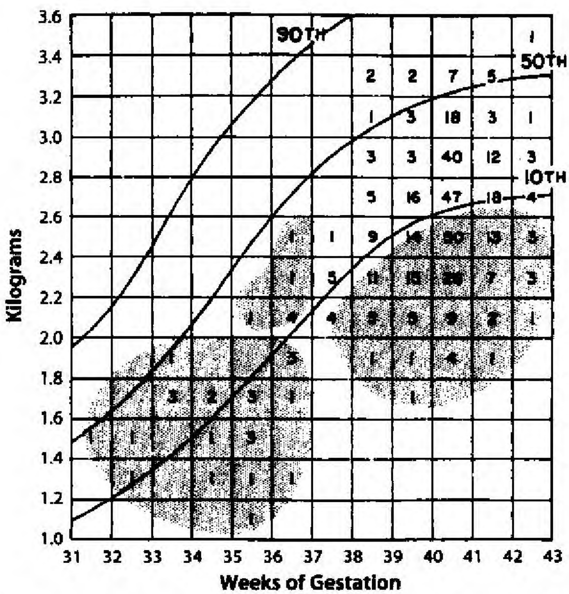
Elimination of village child No. 19 by the interaction of infectious diseases and malnutrition. Growth velocity of this low–birth–weight girl was adequate during the first nine weeks of life when she was fed exclusively at the breast. At that point she developed bronchitis with growth faltering and, soon after, an episode of *Streptococcus* meningitis, followed by diarrhea and varicella. For 12–14 weeks, the child hardly grew. Later, she caught up somewhat but still could not attain the village average growth curve. A new series of infections affected the girl, who already had evident psychomotor retardation. Eventually, the child died prematurely at the end of the second year of life (Mata et al., 1975; Mata, 1978a).

Growth and Development of Under-Fives

The distribution of 430 Cauqué singletons, by birth weight and gestational age in the Lubchenco grid, revealed fetal growth retardation for all types of newborns (Figure 12). The large shaded area in Figure 12 identifies small-for-dates infants (33% of the total). The smaller area (7%) identifies premature babies (Mata, 1978a). The total of these subpopulations equaled 42% of the singletons. The remaining infants were adequate-for gestational age, although of smaller size than newborns from well-nourished women. The relative distribution of low birthweight and small-for-dates infants did not vary over the nine years of study.

This population of small and malnourished neonates evolved into small and stunted children, as seen in the mean weight curve of Cauqué girls and boys, during the first three years of life, in comparison with the standard (Figure 13) (Mata, 1978a). Weight gain was stereotyped: it was adequate during exclusive breast-feeding, departed from the reference curve there-

FIGURE 12

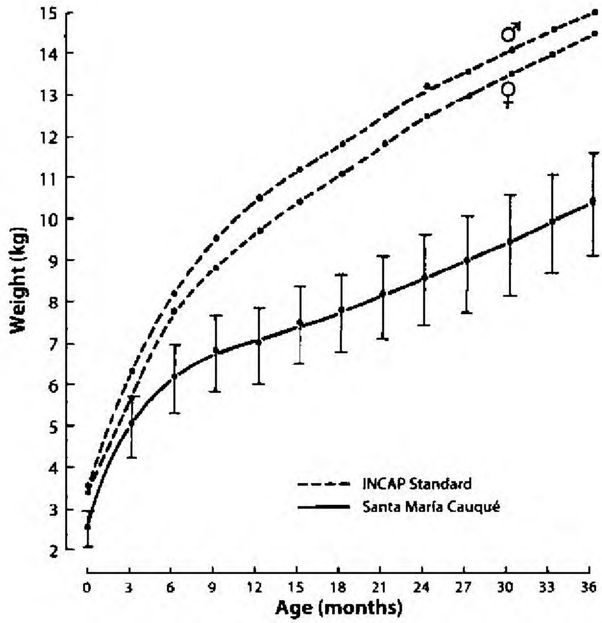


Distribution of 430 singleton infants by birth weight and gestational age, in the Lubchenco grid. Figures are the number of infants within each compartment. Three shaded areas are marked: two of infants less than 37 weeks of gestation (premature, of which the largest (less than 2 kg) were the most immature. One large area brackets the babies born at term, with less than 2.5 kg, namely, the "small–for–gestational age." These two groups of babies accounted for 42% of the total delivered during the study period (Mata, 1978a).

after, and showed marked deficits from one to three years of age. The same behavior was seen for height and for circumference of head and thorax. Children tended to remain within growth tracks defined at birth, with the largest children growing better postnatally, and the smallest ones growing more slowly during infancy and preschool age (Figure 14) (Mata, 1978a). The same was seen with the other anthropometric variables.

There was a significant correlation between birth parameters and postnatal growth, but only a small part of the variance of physical growth was explained by weight and height at birth. Small girls grow into stunted women, who deliver small babies. The interruption of the intergeneration cycle would require breakage of the infection-malnutrition interaction in childhood, through control and prevention of infections.

FIGURE 13

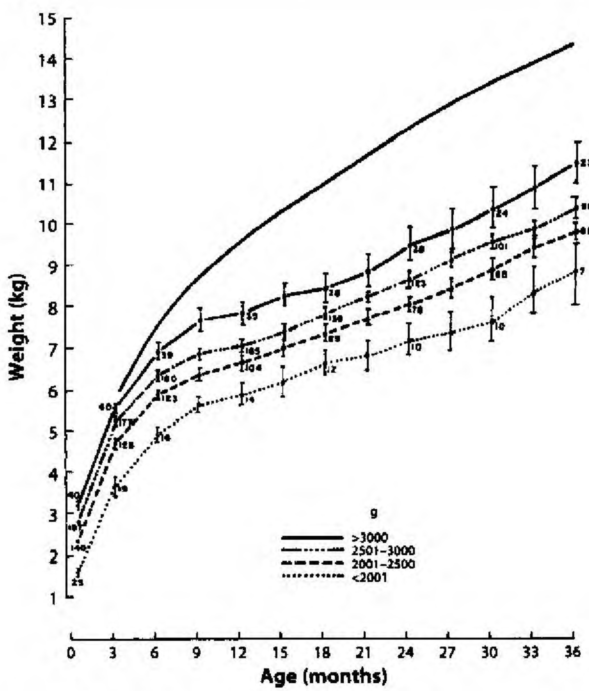


Average weight curve for Cauqué children (boys and girls together), compared with the Jackson–Kelly standard. There were individual variations in growth, but children in general experienced some degree of wasting and stunting after they entered into the protracted weaning period. By one year of age, all had nutritional deficit of some sort. On average, boys were slightly larger than girls, but malnutrition was similar in both sexes. Surviving children were adapted to the deficient environment, and wasting tended to disappear after preschool age. In contrast, stunting persisted through adolescence (Mata, 1978a).

Individual growth curves were fitted by the regression equation $y = a + bx + c \log x$ used to fit cross-sectional data (Malcolm, 1970), where a is the intercept, an estimate for age 0; b is the linear parameter, reflecting most of the growth after growth deceleration; and c is the parameter of growth in the first months. The fitting gave R^2 values as high as 0.99. Stepwise regression analysis of fitted physical growth showed that higher maternal weight, lower maternal age, fewer deliveries, lower weaning age, and smaller number of days with respiratory infections correlated with faster growth in the first months of life (Mata, 1978a).

By stepwise regression for parameter c (child growth in early months), days of respiratory disease, maternal weight, young maternal age, number of deliveries, weaning age, and fewer days of respiratory infection were positively correlated. In a multivariate analysis, days of respiratory infection in infancy were negatively correlated with growth in the first months,

FIGURE 14



Mean weight curves and standard errors for all village children separated into four subcohorts defined by birth weight. Numbers on the curves represent the number of children measured. On the average, infants with higher birth weight grew better, and those with the lowest birth weight grew poorly. Children tended to remain within their growth tracks. A similar behavior was noted for body length and for circumferences of head and thorax (Mata, 1978a).

explaining 19% of the variance. Maternal age was negatively correlated, adding 14.5%. Birth length and maternal weight also explained part of the variance. These four variables accounted for 48.7% of the total variance of early child growth (Mata, 1978a). Young women had infants who grew faster in the first months, whereas older mothers had infants who grew more slowly. Premature infants, as a whole, had adequate growth velocities while they remained at the breast.

Regarding parameter *b*, weaning age accounted for 16.3% of the variance of linear growth by stepwise multivariate analysis. Other variables contributing significantly to explaining delayed linear growth were short birth interval, maternal height, rate of *Entamoeba histolytica* infection, fewer deliveries, and rate of infection with *Shigella flexneri*. This evidence indicated the need to improve the condition of the mother and the sanitary environment, in order to boost nutrition of young girls, pregnant women, and other women of reproductive age.

With regard to psychomotor development, most Cauqué newborn infants appeared adequate at birth, as noted for other Cakchiquel infants (Wug de León et al., 1964). With adapted scales (Cravioto et al., 1966), Cauqué infants showed adequate psychomotor development in the first semester of life. Thereafter, deficits became evident, and an evaluation of six- to seven-year-olds of the 1964 and 1965 cohorts, aided by the bilingual teacher of the village, showed a lower performance as compared to urban children. The lack of marked individual variation among children suggested that deficits probably reflected the influence of the "village environment" on all children. As adolescents and adults, Cauqué Indians used a rich vocabulary to describe and interpret the weather, agriculture, handicrafts, health, and other aspects of village life, a vocabulary in some ways richer than that of Spanish-speaking mestizo and caucasians of Central America.

Malnutrition and Adaptation

The main deficiencies of nutrients in the village were calories, good-quality protein, iron, and some vitamins and micronutrients. Iron deficiency in the absence of malaria and hookworm is explained by exceedingly high rates of infection that are associated with sequestering of free serum iron, coupled with the low bioavailability of iron in the predominantly vegetarian diet. Interestingly, most of the anemia disappeared without specific treatment by the fourth year of life, probably when children became immune to the infections prevailing in the village, and when their food consumption improved (Mata, 1978a). No hypoproteinemia was found in Cauqué children except after severe infections (Viteri et al., 1973). Xerophthalmia, keratomalacia, and blindness attributable to vitamin A deficiency were not found during the study. Fruits and vegetables supplied sufficient carotenes and ascorbic acid. There was sufficient exposure to sunlight to prevent vitamin D deficiency. Iodine deficiency had been corrected by the iodination of table salt (Ascoli and Arroyave, 1970). No longitudinal studies of biochemical and endocrine functions were carried out.

Severe infectious diseases diminished food intake, caused nutrient losses, and altered metabolism, aggravating chronic malnutrition or precipitating its acute forms. There were 32 cases of edematous protein-energy malnutrition in children under five during the study period (9 prekwashiorkor, 10 kwashiorkor, and 13 marasmic-kwashiorkor), which appeared a few weeks after the occurrence of diarrhea and other infectious diseases (Figure 15). Most cases appeared from May to September — the rainy season — the period of greater incidence of diarrhea, measles, and other communicable diseases. Paradoxically, this was the period of better supplies of local foods (maize, green leaves, fruits), greater cash income from selling produce, and increased availability of firewood for cooking. There were few or no cases of edematous malnutrition in the drier months (February, March, April, November, and December).

Infant Survival and Mortality

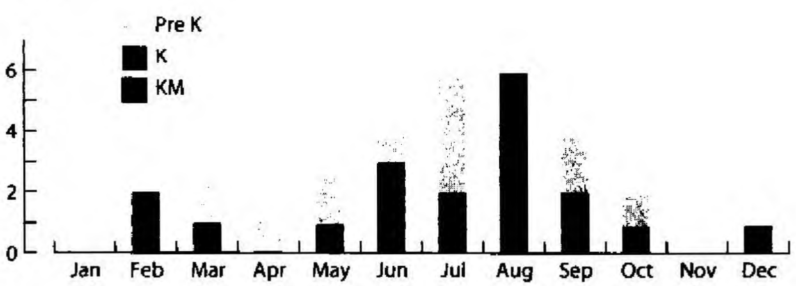
Maternal factors were the main determinants of infant growth and size at birth, and correlated strongly with child survival. Low birth weight infants had lower infant survival than those of normal birth weight. A birth weight greater than 2,750 g correlated with absolute infant survival, regardless of postnatal events, such as measles, dehydrating diarrhea, or deficient diet (Table 15). Exclusively breast-fed infants who weighed at least 2,000 g at birth survived the first week of life; if they weighed at least 2,750 g at birth, they survived the first three months of life; if they weighed at least 3,000 g at birth, they survived the first semester (see Table 16). Similar behavior was seen in cohorts defined by gestational age. LBW accounted for more than 70% of the total infant mortality in Cauqué, just as in modern societies with low infant mortality (Mata, 1982b). Prematurity was the main predictor of low infant survival, but such risk was not evident after the first year of life; that is, premature infants who survived infancy did not die thereafter (Mata, 1978a). Low birth weight infants also had low survival, an effect carried on into the second, third, and fourth years of life (Table 16).

These data show the urgent need to reduce the incidence of low birth weight infants as a necessary step to reduce mortality in children under five. Almost all 18 neonatal deaths occurred in premature babies and were attributed to antenatal causes that are also typical of modern societies. With postneonatal fatalities, all but two "crib" deaths and one undetermined death were attributed to infectious diseases (Table 17). Lower respiratory disease accounted for almost half the deaths in the postneonatal infant period, followed by diarrhea and measles. Whooping cough, pneumonia, measles, and diarrhea were related to two-thirds of the deaths in the second year. The enhanced risk of death due to infection in the second year had been recognized (Gordon et al., 1967). Had the population been vaccinated — a utopian hope at that time — 19 of the 58 deaths (33%) would have been spared. Medical treatment at the Health Clinic most likely averted many deaths from diarrhea and other infectious diseases, as evidenced by the progressive reduction of mortality through the study period.

Paradigm of Infection-Malnutrition

The evidence furnished by the Cauqué study (Mata, 1978a), complemented by observations in Costa Rica (Mata, 1982b, 1983c), identified infections as the main cause of malnutrition, growth retardation, and premature death (Figure 16). This is quite evident for diarrheal disease, unless proper therapy is aggressively implemented, meaning rehydration, proper feeding, and adequate drugs, when indicated. The effect of infec-

FIGURE 15



Accumulated incidence of edematous energy–protein malnutrition, by month of year, Santa María Cauqué, 1964–1972. There were 32 cases, 72% of which appeared from May through September. This is the rainy season, and the months of infectious diseases. Also, they are months of relatively greater availability of food, firewood, and money. Edematous malnutrition was not observed or was infrequent from October through February. Cases were similar for both sexes, and the case fatality ratio was 15.6% (Mata, 1978a).

TABLE 15

Survival During Infancy, by Birth Weight, Among 430 Cauqué Singletons, 1964–1973

Time Survived	No. of Infants	Birth Weight, g 1,000–	1,500–	2,000–	2,250–	2,500–	2,750–	3,000–	3,250–	3,500–	Total
24 hours	430	4/5[a] (80)	25/28 (89)	47/47 (100)	99/99 (100)	125/125 (100)	82/82 (100)	31/31 (100)	11/11 (100)	2/2 (100)	426/43 (99)
7 days	430	4/5 (80)	23/28 (82)	47/47 (100)	99/99 (100)	125/125 (100)	82/82 (100)	31/31 (100)	11/11 (100)	2/2 (100)	424/430 (99)
28 days	429	2/5 (40)	22/28 (79)	45/47 (96)	96/99 (97)	123/125 (98)	82/82 (100)	30/30 (100)	11/11 (100)	2/2 (100)	413/429 (96)
3 months	429	2/5 (40)	18/28 (64)	44/47 (94)	96/99 (97)	123/125 (98)	82/82 (100)	30/30 (100)	11/11 (100)	2/2 (100)	408/429 (95)
6 months	429	1/5 (20)	15/28 (54)	43/47 (91)	96/99 (97)	120/125 (96)	80/82 (98)	30/30 (100)	11/11 (100)	2/2 (100)	398/429 (93)
1 year	428	1/5 (20)	13/28 (46)	41/47 (87)	95/99 (96)	117/124 (94)	78/82 (95)	30/30 (100)	10/11 (91)	2/2 (100)	387/428 (90)

[a] Number of survivors/total cases; below, (percentage surviving)

Source: Mata (1978a)

TABLE 16

Relationship Between Fetal Growth Retardation and One- to Four-Year-Old Mortality, Santa María Cauqué, 1964–1972

Newborn Class[a]	Mortality, Year of Life 1st	2nd	3rd	4th
Normal	12 (50) [242]	9 (44)[a] [204]	5 (33) [153]	1 (8) [122]
Small-for-Gestational Age	12 (84) [143]	8 (76)[b] [105]	3 (39) [78]	3 (50) [60]
Premature	16 (516) [31]	0 [15][a]	0 [13]	0 [8]
Total	40 (96) [416]	17 (52) [324]	8 (33) [244]	4 (21) [190]

[a] By birth weight and gestational age combined (see Figure 11)

[b] Number of deaths (rate per 1,000 children in the class alive at the beginning of the period); below [population at the beginning of the period]. Note: attrition in numbers with age reflects the lower age of younger cohort children. The 1964 cohort contributed more children to the table than cohorts born later on.

Source: Mata (1978a), modified

TABLE 17

Numbers and Relative Percentages of Child Deaths Attributed to Infectious Diseases, Santa María Cauqué, 1964–1972

Age (Years)	Population at Risk[a]	Total Deaths[a]	Acute Diarrhea	Measles, Whooping Cough	Measles, Whooping Cough, Diarrhea
<1	458	41	4 (10)	9 (22)[b]	13 (32)
1	400	19	3 (16)	13 (68)	16 (84)
2	323	8	2 (25)	3 (38)	5 (63)
3	258	4	1 (25)	3 (75)	4(100)
4	198	0			
5	148	0			
6	110	0			

[a] Accumulated during the Cauqué Study, 1964–1972

[b] Number of deaths (relative percentage)

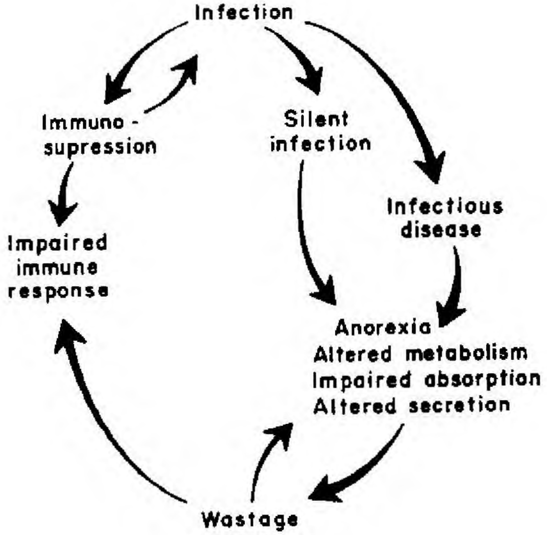
Source: Mata (1978a), modified

tion on nutrition seems stronger than that of the nutritional state on the outcome of infection. In Figure 16, the directions and widths of the arrows illustrate the causality and intensity of the associations.

Recurrent infections progressively lead to wastage and stunting. Severe infectious episodes precipitate acute malnutrition and cause death. In turn, some infections impair delayed hypersensitivity and other immune functions (Scrimshaw et al., 1968). Immunosuppression favors infection, closing the vicious circle. These findings support the conclusion that to improve nutrition it is necessary to control and prevent infections.

The control of environment (water supply, sanitation, personal hygiene) is fundamental to reducing diarrheal disease, and this is a sine qua non to decrease infant mortality (Mata, 1982b).

FIGURE 16
Infection-Malnutrition Interaction



Cycle of infection-nutrition interactions, as seen from the Cauqué experience. Recurrent infectious disease (and asymptomatic infection) reduce consumption of the village diet. Infections alter digestion and absorption and cause nutrient losses and metabolic alterations. The net result is progressive wasting and eventual stunting. Infectious disease precipitates acute energy-protein malnutrition, causes disability, and ends in premature death. Malnourished individuals have an altered capacity to respond to infection and to heal. The cycle can be interrupted by control and prevention of infections acting on the childhood population, to diminish the negative effects of infection and improve nutrition, growth, and survival (Mata, 1990, 1992).

Interventions in Santa María Cauqué

Interventions were minimized during the study, to the extent compatible with ethical principles. Medical services in the clinic conformed with government policies but were better than in most Guatemalan villages. Three programs were were implemented in the village: a) improvement of medical care and hygiene during the three-village study (1959–1963) and the Cauqué study described in this chapter (1964–1972); b) and subsequently improvement of the diet through maize fortification (1972–1976); and c) improvement of housing and income after the 1976 earthquake (1976–1980).

Improvement of Medical Care and Hygiene (1959–1972)[2]

Prior to the study described in this chapter, Santa María Cauqué was the village that received enhanced medical care and some hygiene measures as part of the "three-village study" described in chapter Chapter 1. During the present study, treatment in the clinic was continued and extended to the homes. The quality of the central water supply was improved but not its distribution.

Traditional village infusions and intravenous fluid therapy were used for dehydration from diarrhea, although many mothers refused the latter. Breast-feeding was encouraged for all infants and children still at the breast, even when they were suffering from infectious diseases, especially with dehydration. Invasive diarrhea was treated with broad-spectrum antibiotics. Penicillin was used for complicated bronchitis, pneumonia, and other bacterial infections. Personal hygiene improved somewhat, although it continued to be deficient. The latrine program was stagnant during the study, but usage improved considerably to reach 54% of the families at the end of the study period. In summary, slow progress was evident at the end in personal hygiene, water supply, sanitation, education, and literacy (Mata, 1978a), along with some reduction in mortality.

Improvement of the Diet (1972–1976)

The Cauqué study officially ended on May 29, 1972, in its eighth year. At that time there was still controversy with respect to the relative value of food supplementation versus infection control, despite the fact that the Cauqué study had demonstrated a strong deleterious effect of infection on host nutrition and growth. There was considerable international interest in the implementation of nutrition programs in developing countries, even though they had shown only limited or negligible impact. The experience gained in field work during the Cauqué study justified an intervention consisting of adding a supplement to maize, the staple food, to correct most of its nutrient deficiencies, and "make it like beef." The improved maize supposedly should significantly improve the nutrition of pregnant women, infants, and preschool children, enhance resistance and response to infection, and raise the overall level of health.

The maize fortification study began in June of 1972 and continued for almost four years (Mata, 1971). The fortifying mixture, developed in INCAP by Ricardo Bressani, contained 97.5% soybean flour, 1.5% L-lysine, thiamine, riboflavin, niacinamide, vitamin A, and ferric orthophosphate. When *nixtamal* (maize kernels cooked with lime) was fortified with 8% of this mixture by weight and fed to healthy rats and to children who had recovered from malnutrition, normal nitrogen balances and adequate growth were achieved (Bressani et al., 1976).

Meetings with leaders and villagers were held to discuss the convenience and scope of the intervention. A scale and a set of tin cups were installed in each of the two mills to measure the *nixtamal* and the supplement. The supplement was added at the time of milling to produce the fortified dough for tortillas. Grinding was done almost exclusively at the mills. A literate youngster from the village, posted at each mill, added the supplement in proportion to the amount taken by the women. The operation began as soon as the mills opened early in the morning, to closing time at dawn, every day the mills operated during the study period. The amounts of *nixtamal* and of the fortifying mixture were recorded for each family each time maize was milled.

For the first two days, 95% of the people accepted the supplement. Shortly thereafter, the taste and odor of soy flour led to self-distribution of the families into three groups: a) 40% accepted supplementation at the higher fortification index (FI)[3] of 40–100 (this group contributed 504 newborns to the study); b) 10% accepted a lower FI of 20–39 (43 newborns); c) 50% refused the mixture entirely or allowed an FI no greater than 19 (255 newborns) (Mata et al., 1973; Urrutia et al., 1976).

Fortification was monitored in random samples of tortillas for dietary and chemical analysis, and in random samples of women's urine for riboflavin. Intake was monitored by individual dietary studies. The variables measured and the methods and personnel were those of the Cauqué study (Mata, 1978a). The study of infection and colonization of the intestine could not be repeated. The intervention lasted 45 months, during which there were intermittent problems of acceptance of fortified tortillas, related to odor and taste of soy, previously unknown to the villagers. The perishability of fortified tortillas also was a problem.

At the end of the intervention, no significant changes were noted in mean birth weight and gestational age from previous values of the Cauqué study (Urrutia et al., 1976; Mata 1978a). The supplement which did not affect calorie consumption had no apparent effect on mean weight at six months of age. At 18 months supplemented children actually weighed less. No differences were noted in the mean weight of children when siblings were paired for comparison, in which one sibling was offered the supplement and the other was not (Urrutia et al., 1976; Mata 1978a). The supplement did not influence growth velocity or the development of ossification centers of the hand (Urrutia et al.; 1976).

There were no differences in the rates of infectious diseases among the three groups by FI, but the total number of days ill was larger for children with the lowest FI (Urrutia et al., 1976). Also, infant mortality was lower for children in the group with the highest FI. There was no effect on infant mortality, and an actual increase in one- to four-year-old mortality for the village as a whole during the intervention (Urrutia et al., 1976; Mata 1978a). A plausible explanation for the lower morbidity rates in families with high FI is that acceptance of the supplement by families reflected cooperation with the study personnel. Families with the strongest ties with the clinic would also be likely to have better social development and a greater tendency to seek medical treatment as well as to use the food supplement. Families with a higher risk of infection and malnutrition might have had poorer relations with the staff and have been more likely to reject the supplement.

The Principal Investigator (Leonardo Mata) left Guátemala one year before termination of the maize fortification study, and the Field Director (Juan Urrutia) left two years after its termination. New duties and lack of enthusiasm for publishing negative findings of this intervention delayed release of these data.

Improvement of Housing and Income

At 3:05 a.m. on February 4, 1976, an earthquake (40 seconds, 7 Richter) destroyed homes, mill houses, granaries, mud walls and other structures of the village. Only the clinic, the school, the municipal building, the slaughterhouse, and one private house were left standing, because they had been built with concrete, iron frames, and more adequate materials. The leveled houses had walls made of layers of adobe blocks without supporting frames, with roofs placed on top without enough binding. The structures collapsed while villagers were sleeping. There were 78 deaths (5% of the population), mainly of children and old people (Glass et al., 1977); this number was replaced within 18 months by the 3.6% population growth estimated for 1970–1972.

Immediately after the earthquake, the clinic staff shifted from the maize fortification study to full-time relief activities. In any case, the maize fortification study could not have been continued because the houses, the mills, and the warehouse storing the fortification mixture were destroyed. The local people rapidly rebuilt the village with the aid of national and international organizations. Ulike their former houses, most of the new ones had separate sleeping quarters and improved sanitation. Water toilets became popular and latrines were used more often. A cooperative was organized, widening the opportunities for diversified agriculture, more commerce, and more income. Water quantity and quality increased notably, although the village remained deficient in basic needs. Health services suffered a prolonged attrition and were reduced to sporadic visits by a physician of the Ministry of Health and the services of one or two resident auxiliary nurses.

Infant mortality rate which had been decreasing leveled off or increased after the earthquake. Nevertheless, one-year semilongitudinal data collected 15 years after the Cauqué study (1986–1987) showed moderate increments in maternal body size, breast milk output, and child growth (Delgado et al., 1988). Since no documentation of infectious morbidity and of microbial entities was done on that occasion, no judgment can be made of the force of infection in comparison with the period of the Cauqué study. Nevertheless, it is fair to assume that infections had decreased in the intervening 15 years, consequent to greater availability and usage of latrines, flush toilets, and drinking water. Also, education, communication, personal hygiene, and income had increased in the intervening period.

Determinants of Health

Prior to the Cauqué study, most knowledge of interactions between infection and malnutrition was obtained through clinical and cross-sectional field observations. The background of poverty and deprivation affecting children throughout the world had been mostly ignored or taken for granted, resulting in equivocal interpretation of the origin and nature of the infection-malnutrition complex and its biological and environmental determinants.

The Cauqué study pioneered long-term observation of rural children in their natural ecosystem. The detailed clinical, dietary, microbiological, anthropometric, and epidemiological observations, unique at that time, are still a subject of discussion, because our studies have not been replicated. Different approaches, however, have confirmed or widened the main observations of the Cauqué study. Meantime, paradigms derived from the study have probably influenced changes in policy and management regarding rural health in less developed countries.

In the last 30 years, there has been an emphasis on "primary health care" and "health for all by the year 2000," "growth, oral rehydration, breast-feeding, and immunization" (GOBI), "expanded program of immunization" (EPI), and "improved delivery of medical care." The effort has been more on control and prevention of infection than on improving the diet. Also, more emphasis has been given to holistic strategies to combat poor health than to independent food supplementation and fortification programs. The Cauqué study taught lessons about the positive and negative determinants of health and survival of contemporary less developed populations (Mata and Behar, 1975. Some of these lessons were the following.

Positive Determinants

a. The village population enjoyed a relatively high quality of life, despite the prevailing poverty and underdevelopment. Families were well structured, with strong bonds and low levels of domestic violence. No abandonment or abuse of wives or children was known to the clinic staff during the study.

b. Women had a remarkably low incidence of birth complications. Effective mother-infant interaction contributed to successful breast-feeding and child rearing.

c. Treatment of the umbilical cord stump prevented tetanus neonatorum. There were very few cases of neonatal sepsis, diarrhea, impetigo, and other neonatal infections.

d. Small babies were kept warm at all times by mothers who slept with them from birth through lactation. In the cool climate such a practice was crucial, counteracting hypothermia in very small infants. Since children were exposed to sunlight, neonatal jaundice was corrected. Survival was absolute for infants able to suck the nipple within the first day of life.

e. Exclusive breast-feeding for five to seven months correlated with adequate nutrition, growth, and protection against infection. Prolonged breast-feeding with supplements for two to three years offered an important source of nutrition supplementation and protection against infection.

Negative Determinants

a. The high incidence of LBW infants in Cauqué had a negative effect on village development. More than 70% of the infant deaths were of LBW babies. The priority, then, was to reduce the incidence of LBW infants instead of training more personnel to care for them.

b. Protracted weaning in the village represented a constant risk of enteric infection. Weaning foods had low biological value and were a source of enteric infection.

c. Infections with pathogens of the mucosae and skin were very common during weaning.

d. Stunting was associated with low birth weight, infections, and deficient diets.

e. Deficient health services contributed to the low survival rates.

f. Lack of family planning is resulting in strong demographic pressure in the face of limited land and few opportunities for diversified work.

g. Poor socioeconomic conditions were predominant determinants of biological and environmental deficiencies of the indigenous population and its ecosystem.

h. The most pressing problem is the rapid rise in population density, resulting from greater survival mediated by better public health, and the collateral restricted land, food shortage, inflation, and political unrest. The background of intervention, amply discussed in the early 1970s (Mata, 1978a), remains valid today.

Concluding Comment

In the years of the Cauqué study, we discussed how rapidly improvements should be implemented, or whether it was possible to effect them peaceably. Some decided for revolt, without success. Armed violence in Central America has done great harm. My view of the current situation, resulting from sporadic visits to Santa María Cauqué since I left it in 1974, is of slow progress to correct negative determinants of health, while preserving most of the positive determinants. Village life today continues relatively unaltered from that of the 1960s. Virtually all deliveries today are in the homes, assisted by two younger midwives, one of them the daughter of Doña Juana, the senior midwife of the Cauqué study.

Strong family bonds persist, as in the 1960s, and most families are organized around the family head, usually the father or an elder. There is no evidence of emerging physical or sexual abuse of children or spouses. Vagrancy, drug abuse (including alcohol), street violence, petty theft, and other social pathologies are not evident. In fact, villagers behave now almost as they did during the Cauqué study. Although many new houses now have locks, agricultural plots remain fenceless.

The attitude of the Mayan villagers — stoic, sturdy, hard-working, honest, and smiling — still prevails, as well as their ability to cope with adversity, to survive while enjoying the extended family, friendships, and solidarity. The Mayans are gradually participating in the global transformation that will result in better health for all. My hope is that their unique traditional and societal values will be preserved during that transition.

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Notes

1 At the time of the Santa María Cauqué study Leonardo Mata was the Chief of the Division of Environmental Biology, at the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala City, Guatemala.

2 This program and its results is described in detail in Mata 1978a.

3

$$\text{F.I.} = \frac{\text{days of attendance at the mill}}{\text{six days of the week}} \times \frac{\text{amount of fortifying mixture added to nixtamal}}{\text{pounds of cooked nixtamal}}$$