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INFECTIONS AND INFECTIOUS DISEASES IN A MALNOURISHED POPULATION: A LONG-TERM PROSPECTIVE FIELD STUDY

by Leonardo J. Mata[1] and Juan J. Urrutia[2]

INTRODUCTION

The importance of infectious disease and its role in the shaping of the history of mankind has been recognized since Biblical times. Pestilences were recorded in many classical books, while most religions developed concepts and traditions pertaining to the prevention of certain communicable diseases. It is in the last 20 years, however, that the role of malnutrition in determining the behavior of infectious diseases has become fully recognized. The most obvious manifestation of the interaction is the exceedingly high case fatality ratio of many infectious diseases as compared with the behavior of societies living under better conditions (Scrimshaw et al., 1968). Infection in underdeveloped populations is an unavoidable event and hits all individuals regardless of their nutritional status. Therefore, infection is an important" component in the complex causality of malnutrition. The present observations were derived from the files of a long-term prospective study, the "Cauque study", carried out in a typical Mayan Indian village in the Guatemalan highlands (Mata et aI., 1967) (Fig. I).

COLLECTION OF OATA

Descriptions of the study design and methodology have appeared elsewhere (Mata et aI., 1967; Mataetal., 1971; Mata et aI., *1972b. c).* Methods to assess infection and infectious disease will be summarized here. Surveillance of illness and disability of pregnant women and of cohort children was favored by excellent relations between field workers and villagers (Fig. 2).

Maternal illness was recorded at the time of regular visits to homes. Data of infection and morbidity of children were collected for a cohort of 45 children observed from birth to at least 3 years of age. Infection with viruses, bacteria and parasites was established by examination of feces every week for every child. Stool specimens were collected in cardboard boxes with the aid of wooden spatulas and were transported to the village laboratory for processing within 30 to 60 minutes of evacuation. Examination of stools by standard procedure was described elsewhere (Mata et al., *1969a;* Mata et aI., 1972a. *c).*

Discovery of morbidity was made through weekly home visits incident to routine collection of dietary data or of fecal specimens. The type of illness was established by a staff physician who examined each child preferably in the home (Fig. 3). Thereafter, the child was examined on alternate days until the disability ended in recovery or death. If the disease was serious, daily visits were made. Such close supervision favored prompt recognition of disease and complications as well as prescription of therapeutic measures. The physician classified each indi-

1 Instituto de Investigaci6n en Salud , Universidad de Costa Rica, San Jose, Costa Rica.
~ Division de Biologia Arnbiental, lnstituto de Nutrici6n de Centro America y Panama. Guatemala, Guatemala.

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Fig. 1. A typical Indian home in Santa Marfa Cauque. The mother prepares maize in a stone *metate* while she breast-feeds her child. Maize is the staple food; it provides more than 60 % of the total food intake of adults and about 40-50 % of supplementary food for weanlings. Water is stored in a large earthen jar (background right corner). One single *lapel-co* (bed) serves for the whole family (background left comer). The *fog6n* (fireside) is on the floor.

vidual case according to a code that summarized entities recognized during several years of field experience. When the clinical manifestations of the child were interrupted by one or more days of apparently good health, two episodes of illnesses were assumed.

Anthropometric measurements of all infants were made shortly after birth (Mata et al., (975) and at frequent intervals thereafter. Weight was determined shortly after onset of disease and at frequent intervals during the course of illness.

CHARACTERISTICS OF THE STUDY POPULATION

A background of childhood malnutrition and frequent infections extending through pregnancy are presumably responsible for more than 40% of low birth weight infants (Mata et al., 1975).

All children are breast-fed in the village. No failures were recorded in 9 years of observation providing infants survived the first 48 hours. Breast milk is the only food given during the first 2 or 3 months. Then, weaning begins with fluids (rice water) and gruels (cereal, starch) and by 9-12 months. solid foods are given. Definitive weaning is accomplished between IS and 48 months; the mode is about 22 months.

Mortality among infants and children was strongly influenced by foetal maturity and by the infectious environment. Postnatal physical growth was adequate for all groups of children in the first months of life, but with

Fig. 2. A typical street scene in Santa Maria Cauque. The physician and nurse chat with a village midwife.

Fig. 3. Most clinical examinations were made in the home. The child was placed in an infant meter for determination of body length.

Table I. *Incidence of infectious diseases among 82 women observed from conception to delivery, Santa Marfa Cauque, /972-1973*

Trimester of pregnancy	Respiratory infection		Diarrhoea and dysentery	Urinary tract bacterial infection"	Other illnesses"
	Upper	Lower			
lst	37 (45)'	5 (6)	7 (9)	8 (10)	7 (9)
2nd	26 (32)	6 (7)	9 (II)	8 (to)	5 (6)
3rd	41 (SO)	14(17)	13(16)	6 (7)	8 (10)
Total per 100 pregnacies:	104(127)	2.5(30)	29 (36)	22 (27)	20 (25)

~ ...100000bacterial colony forming units per ml urine.
b Conjunctivitis, otitis media, stomatitis, skin infection.
~ Number of attacks (rounded percentage).
Adapted from Urrutia et at. (1975).

the onset of the protracted weaning process (at 3 to 6 months of age) stunting began and became marked by one year of age. This was the result primarily of the interaction of malnutrition and infection and appeared to be of similar nature in all groups of infants as defined by fetal maturity. Thus, deficits in growth evident at birth and observed in the first 3 months of life continued throughout preschool age.

MATERNAL INFECTION AND INTRAUTERINE ANTIGENIC STIMULATION

Infection and infectious diseases in the pregnant woman are a common occurrence (Mata et aI., 1975). Table I illustrates the frequency of disease detected by a prospective clinical study of 82 village women. It is illustrative that the incidence of disease was so high (127 per 100 pregnancies) with an important component of bacteriurias (27 per 100 pregnancies), of severe respiratory tract infection and of diarrhoea (30 per 100, respectively). In contrast, albuminuria was very rare and no cases of toxemia or severe oedema were discovered (Urrutia et aI., 1975).

The high infectious morbidity among pregnant women probably resulted in greater opportunities for foetal antigenic stimulation as revealed by the common finding of elevated values of immunoglobulin M (IgM) in umbilical cord serum (Mata et aI., 1971). Because cord blood is easily admixed with maternal blood, venous blood from consecutive neonates of four lowland Guatemalan villages was examined within 3 to 4 days of birth. This was possible through the collaboration of Dr Hernan L. Delgado of the INeAP's study of Nutrition and Mental De-

Table 2. *Incidence of elevated values of immunoglobulin M (...0.20 mg/ml) among neonates of four Guatemalan villages, 1972-1973*

Village	Number of infants	Number (%) with elevated IgM"	Range of elevated values
S.D.O.	48	to (21)	0.22-0.48
S.I.S.	52	4 (8)	0.20-0.54
E.S.	40	6 (IS)	0.27-0.74
C.	67	II (16)	0.23-0.55
Total	207	31 (IS)	

" Established in 3-4 day blood from the femoral vein.

Table 3. *Parasites in meconium and feces of the first week of life, Santa Marfa Cauque, 1964-1966*

Number of child	Age (days)	Parasitic forma
12		*E. histolytica* (c); *E. nana* (c)
	4	*E. histolytica* (c); *E. nana* (c)
	5[b]	*E. coli* (c)
23	1	*E. coli* (c); *E. nana* (c); *E. hominis* (l)
186	3	*E. coli* (c, t); E. *nana* (c, t): C. *mensnlli* (t); G. *Lamblia* (c, t)
	5	*E. nan a* (c, t)
42	4	G. *Lamblia* (t)
172	4	*E. nana* (c)
175	4	G. *Lamblia* (c)
80	4	G. *Lamblia* (c)
9	6	*E. coli* (c); *E. nana* (c)
49	6	*I. biitschlii* (c)

a c=cyst; t=trophozoite.
b This child had diarrhoea in the 2nd week of life, but the cause remains unknown. The other infants were free of gastrointestinal symptoms.

velopment. Fifteen per cent of infants (Table 2) had concentrations of IgM in excess of the borderline level of presumptive intra-uterine infection (Alford et aJ., 1969). Actually, many infants had concentrations above 0.25 mg/ml, while several had more than 0.5 mg/ml. Since IgM is not normally transported across the placental barrier, these findings are interpreted as indicative offetal antigenic stimulation. The origin of the fetal IgM could be through an increased incidence of intra-uterine infection (Mata et aI., 1972*b)* or a response to antigens available during the course of maternal infection, or the response to maternal immunoglobulins synthesized during pregnancy as a result of infectious processes.

Maternal infection and intra-uterine infection are important determinants of deficient growth. Other relevant factors are the short stature of village women (average 148 ern) and their background of malnutrition that extends throughout pregnancy.

EARL Y INFECTION WITH PATHOGENIC ORGANISMS

The phenomenon of colonization of the intestinal tract of breast-fed village infants has been described elsewhere (Mata and Urrutia, 1971). A predominant flora of anaerobic gram-positive bacilli (bifidobacteria) is formed under the influence of breast milk. This bacterial flora is firmly maintained as long as the child is primarily breast-fed; the flora evolves with the initiation of supple-"?" mentary feeding, admitting progressively greater concentrations of gram-negative anaerobes. When weaning is completed, the child's bacterial flora is quite similar to that of the adult (Mata and Urrutia, 1971; Mata et al., *1972a).*

Infectious agents with pathogenic potential appeared in the feces of infants shortly after life. Nine infants among 192 (4.7%) excreted protozoa (Table 3) two as early as the first day of life; some of these were recognized pathogens. *Shigellae* and entero-

Table 4. *Injection with ShigeLLand enteropathogenic Escherichia coli in the first week of life, Santa Marfa Cauque, 1964-1966*

Case number	Pathogen	Day of life isolated"	Clinical manifestation
297	*S. flexneri* 2	I	none
170	*S. flexneri 4*	2	none
265	*E. coli* 0119: B 14	3	none
258	*S. flexneri 4*	3,5	none

" All infections were detected on this day only. except that of child No. 258 who excreted the organisms for 3 days .

pathogenic *Escherichia coli* were found also in the first days of life (Table 4) to give a rate of 1.6 and 0.5 per 100 infants, respectively, for the first week of life. With viruses, excretion rate was also very high as compared with any industrialized population living under better conditions (Table 5). Some of the protozoa may have represented "spurious" infections. *Shigella* likely represented transient infections. Due to the highly lytic and rapid replication cycle of enteroviruses, shedding could begin 24 hours after infection, as with attenuated polioviruses, but the larger incubation period of echoviruses and the high dose in which they were found are suggestive of true infections, some probably of congenital origin. Early infections usually were asymptomatic unless the practice of breast-feeding became complicated or altered (Mata et al., *1969b).*

INTESTINAL INFECTION DURING WEANING

During exclusive breast feeding, infections with *Giardia. Entamoeba histolytica, Shigella* and *Salmonella* were very low. With weaning, infection increased to attain high rates by the end of the first year and particu-

Table 5. *Enteroviruses in meconium and feces in the first three days of life. Santa Maria Cauque, 1964-1966*

Day of life	Number of children tested	Number and percent positive children	Case no.	Virus isolated	Viral concentration log., $TCID_{.0}$ per gram
lst	79	I (1.3)	264	Echo 7	2
2nd	54	4 (7.4)	66	Echo 6	3
			70	Echo 6	3
			82	Echo 6	3
			166	Polio I	5
3rd	61	5 (8.2)	63	Polio I, Echo 6	4
			162	Echo 9	5
			171	Echo II	5
			251	Echo 7	5
			296	Echo 6	5

larly during the second and third years of life. Multiple and chronic infections were more often seen at those ages.

With enteroviruses, resistance was less effective but still evident as shown in Fig. 4 for 18 children cultured weekly (Mata et al., *1972c).* Virus shedding increased in the second semester of life and in the second and third years children virtually had a persistent "viral flora".

The marked intestinal resistance to infection exhibited by the breast-fed child seemed related to the intestinal bifidus flora that developed with maternal milk and to the presence in milk of complement, immune cells, immunoglobulin A, lyzozyrne and lactoferrin (Mata and Urrutia, 1971; Wyatt et aI., 1972; Goldman and Smith, 1973; Hanson et al., 1975; Reiter et al., 1975).

The implications for the host of excessive infections are: *(a)* precocious development of the serum immunoglobulins with IgG and IgM attaining very high concentrations in the first year of life (Caceres and Mata, 1974; McGregor et al., 1970); and *(b)* damage to the intestinal mucosa resulting in malabsorption (Rosenberg et al., 1974) and an accentuated inflammatory "physiologic" mucosal lesion (Schenk et aI., 1972). The most important implication, however, is an increased risk of clinical manifestations, particularly because the population undergoes progressive deterioration of the nutritional status.

INFECTIOUS DISEASE

The high rates of moribidity are quite obvious by examining the life history of a typical child in the first 3 years of life (Fig. 5). Infectious disease virtually occurs in a continuum and is very often associated with weight loss. Rates of infectious disease as shown in Table 6 are expressed as cases per 100 person-months, by 6-month intervals.

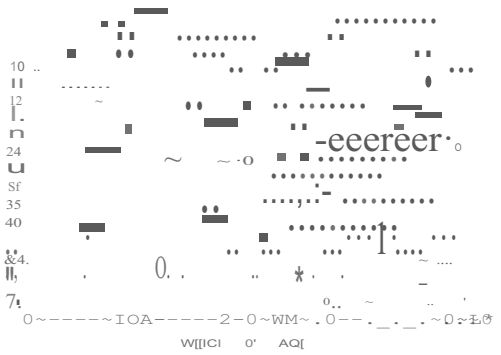

Fig. 4. Viral excretion by 80 infants from birth to one year. Weekly examination of feces was performed in three cell culture systems. A circle represents a week positive for enterovirus and triangle a week positive for adenovirus.

Clinical manifestations are common from birth onwards. Some illnesses increased in frequency with age to reach high values in the second year of life, as was the case of diarrhoea and dysentery. Other illnesses exhibited less variation with age. Among the total clinical experience, the diarrhoeas accounted for 43 % of all episodes, followed by respiratory infections (35 %) and diseases of the eye, ear and nose (10%).

Disease is not only frequent but complex with several clinical entities complicating the initial episode. To illustrate this. the experience of identical twins No. 124 and No. 125 during the first 5 years of life is shown in Table 7. Twin No. 124, born with 98%ofthe weight of Twin No. 125, showed the more complex morbidity of the pair. Cornplications became more common in the second half of the first year and in the second year of life. Duration of disease is another important feature. Table 8 shows days of disease for the same period. Of interest is that Twin 124 with the more complex morbidity had fewer days of disease during the first year, although still extending over a third of the total life experience of the first year; Twin 125 was ill for a half of the first year.

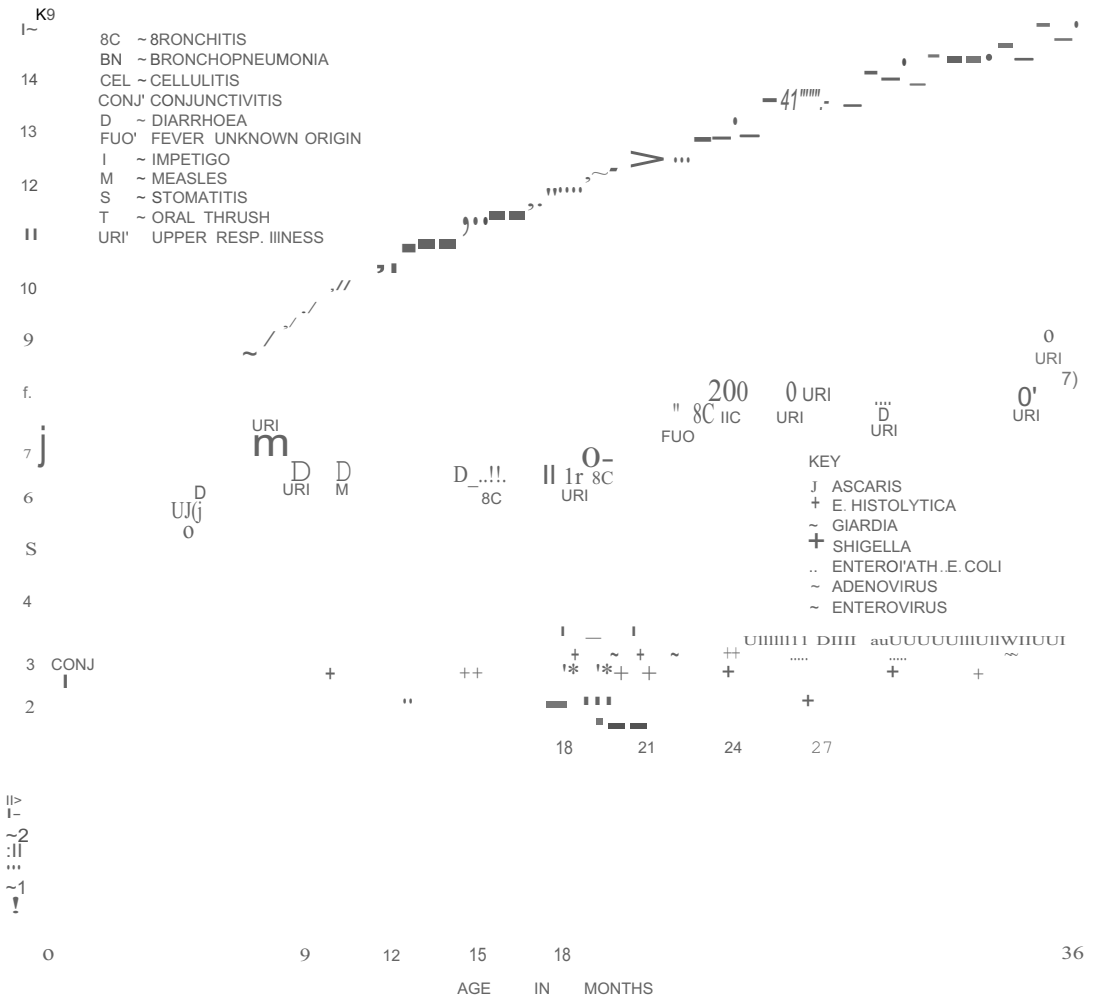

Fig. 5. Weight, infections and infectious diseases, male child of Santa Maria Cauque, Top: -, weight of child; ---, median of the Iowa standard. Length of each horizontal line indicates duration of infectious disease. Each mark shows a week positive for the particular infectious agent. Bottom: observed weight increments (vertical bars) and expected median increments (dots) of the standard.

Later on, Twin 124 experienced more days of illness and of greater severity than Twin 125.

Infectious disease has a marked effect on the nutritional status as evidenced with a case of whooping cough in a village girl (Fig. 6). Onset of the infection at 39 weeks of age set off a weight loss that persisted throughout the prolonged recuperation that required approximately 38 weeks. The slow convalescence was a result of this persistent weight loss and other infectious diseases. To illustrate this further, Table 9 shows that 50 % of the whooping cough cases lasted for 13 weeks or more, while 41 % lasted 17 weeks or more and 25 % at least 25 weeks.

Allergies were rarely seen.

The relationship of infectious disease with nutrition and growth becomes evident from the study of identical twins living in the same microsystem (Fig. 7). As with other pairs of

Table 6. *Infectious diseases, rates per 100 person-months, by 6 month intervals, 45 cohort children, birth to 3 years, Santa Maria Cauque, /964-/969*

Class	Age. months 0-5	6-11	12-17	18-23	24-29	30-35
	270·	270	270	270	255	250
Upper respiratory tract	25.6	34.1	33.3	31.1	30.1	35.7
Lower respiratory tract	15.9	23.0	23.7	27.4	24.3	14.0
Intestinal tract	33.3	63.0	77.8	87.4	78.0	55.0
Eye	21.9	18.5	13.7	14.4	8.9	5.0
Ear	0.7	0.4	1.5	0.4	1.9	0.8
Mouth	9.3	6.3	8.2	4.1	7.0	3.9
Skin, scalp	1.9	3.3	2.2	6.3	2.7	4.7
Common communicable	1.9	10.0	8.2	9.6	7.7	7.4
Other"	0.7	1.1	2.2	4.1	1.2	1.9
Total	111.1	159.7	170.7	184.8	161.8	128.3

~ Number of person-months.
6 Genito-urinary tract; fevers; ringworm; tenosynovitis.

identical village twins, the smaller twin at birth usually lags in growth, and eventually, growth differences become manifested by a greater severity of infections and more complications in the twin with poorer growth. This, however, may not always be true; it is conceivable that a particular twin at a certain moment receives a larger infectious dose than the other twin, even under the same environmental conditions. Twin 125 grew better especially after the third year and fared better in type of response to infections; or conversely, due to less morbidity his growth was better. Disease episodes associated with outstanding weight loss have been identified (Fig. 7). Numeral I indicates marked weight loss at age 49 weeks after diarrhoea with mucus (Twin 124) and diarrhoea with rnoderated dehydration (Twin 125). Numeral 2 marks whooping cough at age 78 weeks in both twins; weight loss was more pronounced in Twin 124. At 3 years, Twin 124 had laryngotracheobronchitis of 7 days duration; 3 weeks later Twin 125 had an acute diarrhoeal disease of 11 days. These events are marked with numeral 3; while weight loss was more severe in twin 125, recuperation was better. Numeral 4 identifies 10 days of bronchitis and diarrhoea in twin 124 at 4 years of age, with marked weight loss and slow recuperation. The other twin had 3 days of diarrhoea with mild weight loss. In the course of time, differences in weight became progressively divergent. Although both twins shared the same environment. variations in clinical features were noted, conceivably related to varying host susceptibility and dosage. More accentuated clinical response correlates well with large deficits in weight and height.

The role of infection on metabolism and nutrition has been well established. With infectious disease there is anorexia and vomiting, and impaired digestion and absorption. all actions resulting in reduction of intake and food wastage (Scrimshaw et aI., 1968). Furthermore. infection induces alterations in body nitrogen and in lipid. vitamin and electrolyte metabolism which result in increased losses of these nutrients (Beisel. 1972). Other effects of infection are nutrient

Table 7. *Illnesses in identical twins, birth to* 3 *years, Santa Marfa Cauque, 1966-1969*

Key: BP::bronchopneumonia; Br=bronchitis; C=conjunctivitis; Ds=diarrhoea; Dbrn=diarrhoea with blood and mucus; Dm=diarrhoea with mucus; OOH=diarrhoea and dehydration; Imp=impetigo; Lar=laryngitis; R::rubella; URI=upper respiratory tract infection; UTI=urinary tract infection; Yom:: vomiting; WC=whooping cough

	First year		Second year		Third year	
Quarter	Case 124	Case 125	Case 124	Case 125	Case 124	Case 125
	C· Imp O URI dm+URI	C Imp O URI O	URI URI O	URI Om	URI O Yom	URI+O
2	C C URI Ovom	C URI C O	Herpes URI+C URI	URI	Br+Irnp+C	URI+C+Ov
3	URI Om+C+URI URI+C Exanthem BP	URI+C Br+C+O	WC+BP+ Stom+ URI+O	O WC+BP+O	Obm+C+ Imp+ URI+O	Imp
4	URI R+SP Om+Exanthem	R URI OOH+ UTI+ URI	None	URI+Vom	Imp Yom Sr Lar	Br Yom

wastage or sequestration of minerals such as iron; synthesis of foreign proteins, lipids and carbohydrates (as in viral replication) and of host molecules of no apparent need for the host economy, a phenomenon referred to as nutrient diversion (Beisel, 1972). Finally. infection induces alterations of the intestinal flora and of the immune system (Mata et aI., *1972a:* Faulk et al., 1975).

Malnourished children exhibited an in-

Table 8, *Days of infectlous diseases, identical twins, birth to* 3 *years, Santa Marfa Cauque, 1966-1969*

	First year		Second year		Third year	
Quarter	Twin 124	Twin 125	Twin 124	Twin 125	Twin 124	Twin 12S
I	43	48	24	21	12	12
2	29	60	44	28	13	8
3	44	30	IOS	87	34	8
4	24	37	0	S	34	12
Total	104	I7S	173	141	93	38

Total days in 3 years: Twin 124=406 days; Twin 125=354 days.

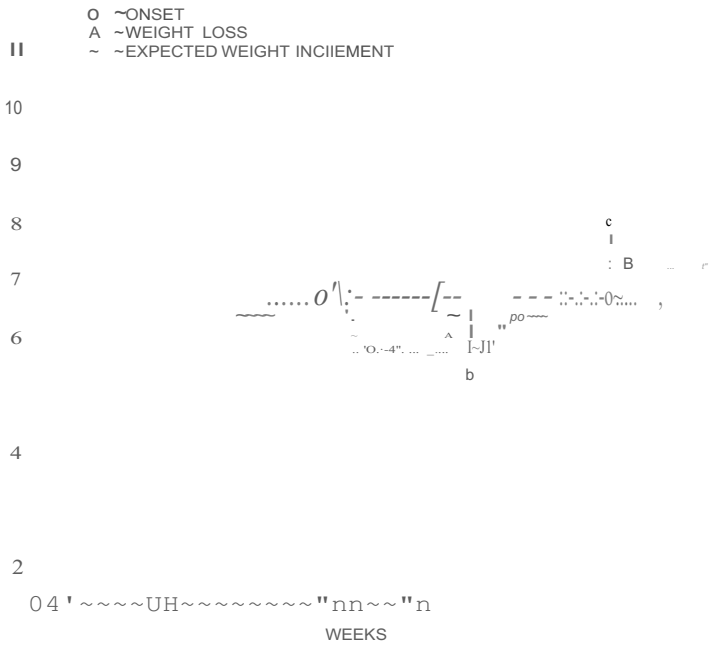

Fig. 6. Deterioration of nutritional status in a female child from Santa Maria Cauque after an attack of whooping cough. Top: -- -, corresponds to the Iowa standard; -, the mean weight of village children. Bottom: weight of child. O=onset of disease; A=weight loss; B=weight gain expected in period equivalent to the length of recuperation. To estimate this amount. the mean weight curve for Cauque children was used: the curve of the child was assimilated-at the time of onset-to such curve.

creased susceptibility to infectious disease demonstrable by longer duration of the carrier state of certain agents like *Shigellae* (Mata et aI., *1969a)* or prolonged persistance of measles virus in giant cells (Scheifele and Forbes, 1972). On the other hand a greater attack rate of diarrhoea has been shown in malnourished as compared with well nourished children (Gordon et aI., 1964). Weight loss during measles is more pronounced in children who already have a large deficit in weight for age (Table 10). In general, well nourished children had the smaller weight loss and had a tendency to recover from it in a more efficient way. Malnourished children are more prone to develop complications during disease, as evidenced in Table 11; and practically all cases became complicated with diarrhoea, or bronchopneumonia or both.

The greater susceptibility to infectious disease, a prolonged carrier state for certain

Table 9. *Elapsed time, onset of whooping cough to return to original weight.* 44 *children, Santa Marfa Cauque, 1968*

Time. weeks	Number of cases	Percent	Accumulated percent
0-4	6	14	100
5- 8	8	18	86
9-12	8	18	68
13-16	4	9	50
17-24	7	16	41
25+	11	25	

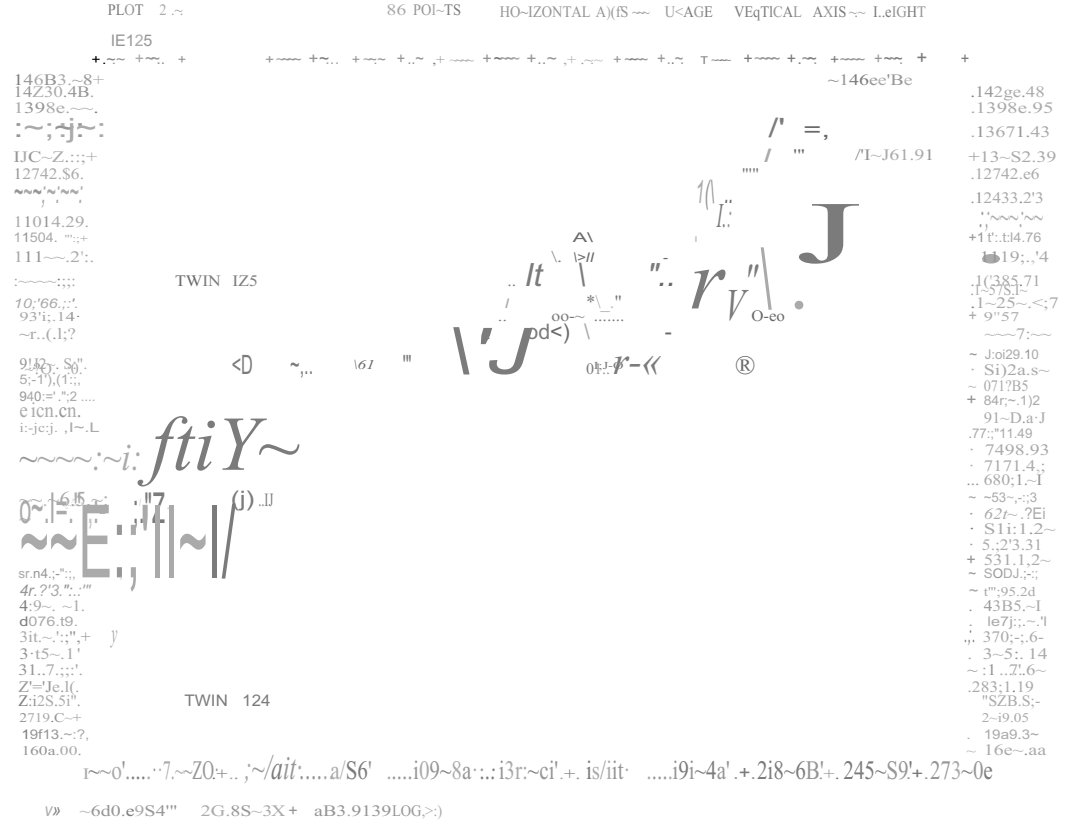

Fig. 7. Growth curves of monozygotic twins, cases 124 and 124, Santa Maria Cauque, for the first 5 years of life. *Ordinate:* grams; *abscissa:* weeks. Numeral represent events involving weight loss (see text).

infectious agents, frequent complications as well as longer convalescence and increased lethality of infectious disease in malnourished children are all indicators of a deficiency in the immune system and in amplification of the immune response. Profound alterations in antibody synthesis, cell-mediated immunity, complement levels and endocrine function have been demonstrated in children suffering from protein-calorie malnutrition (Brown and Katz, 1966; Harland and Brown, 1965; Chandra, 1972; Sirisinha et aI., 1973; Schonland et al., 1972; Hansen, 1975). The data presented here are indirect evidence of an impaired amplification of the immune response to infection.

PUBLIC HEALTH IMPLICATIONS OF MALNUTRITION AND INFECTIOUS DISEASE

Malnutrition-infection interactions have great public health implications (Scrimshaw et aI., 1968; Taylor and DeSweemer, 1973; Gopalan and Srikantia, 1973). Intra-uterine malnutrition-infection interaction could explain the high incidence of low birth weight infants in the Indian village; it accounts for the high rate of neonatal mortality. This mortality, however, was not significantly greater than that observed in urban societies once birth weight was taken into account (Table 12). Small babies had a greater risk of death than large ones, but the risk was quite similar

Table 10. *Weight loss during measles as a function of the degree of weight deficit at onset, Santa Marfa Cauque, 1965-1972*

Weight deficit"	Number of children	Percent patients with weight loss oP 2%	2-4%	5+%
None	8	63	38	0
1()"25	35	43	34	23
26-40%	60	35	43	22
40%	19	21	32	47

" As compared with weight of the standard, by age.
6 As percent of the weight at onset of illness.

in the village and in the urban population (Table 12). Fetal maturity is a good predictor of survival in infancy and also seems to influence survival in the remaining of preschool age (Table 13). Term small-for-gestational age children exhibited greater mortality in the period 1 to 4 years as compared to children born at term with adequate weight. This finding could be the result of impaired immune function or could be due to a greater deficiency in the socio-economic level of homes of small-for-date children. The important consideration is that an improvement in fetal growth would result in decreased infant and preschool mortalities.

Malnutrition-infection interactions are also primarily responsible for the "stunting" observed in the village population (Fig. 8). Most children show marked deficits in weight and height in infancy and early childhood. The effect is similar for all children irrespective of the degree of fetal growth retardation evident at birth. The implication is that children retain their growth rates as defined by birth weight and gestational age (fetal maturity). Since the present environmental conditions seem quite stable in this and most Guatemalan Mayan Indian villages, girls expectedly will be significantly stunted by the time they reach reproductive age. Many will be at risk of delivering small-for-dates. thus initiating a new cohort of handicapped infants who will eventually become stunted. High rates of childhood mortality are accompanied by elevated birth rates; the repetition of the cycle inevitably leads to saturation of the land with a stunted population (demographic explosion) unless the cycle is altered by socio-economic development and improvement of the quality of human life.

COMMENTS

An important observation derived from prospective studies of malnourished human

Table 11. *Complications of measles, percent by age, Santa Maria Cauque, 1965-1971*

Age (years)	Number of measles cases	Diarrhoea" only (1)	Broncho-pneumonia only (2)	Diarrhoea and broncho-pneumonia (1+2)	Total (1+2+3)
<1	50	50	12	28	90
1	37	27	8	54	89
2	34	29	18	41	88
3	16	6	19	63	88
4	14	43	14	43	100
S+	23	26	30	30	87
Total	174	33	16	41	90

" Dysentery excluded.

Table 12. *Infant deaths per 1000 Live births, Santa Marfa Cauque and the United States, by birth weight"*

Birth weight (grams)	Neonatal			Post-neonatal		
	S.M.C.	U.S.	*rb*	S.M.C.	U.S.	*r*
I 501-2000	273	210	1.3	303	26	11.7
2001-2500	34	45	0.8	34	13	2.6
2501-3000	10	10	1.0	43	7	6.1
3001-3500	0	5		23	5	4.6

~ S.M.C.~data for 1964-1972;U.S. data of Chase (1962).Figures rounded to nearest integer.
b r=ratio S.M.C./U.S.

populations is the exceedingly greater rates of infection as compared with industrial societies; this appears to be quite independent of the state of malnutrition *per se*. Responsible factors are poverty, crowding and deficient sanitation and education, which favor the spreading and transmission of infectious agents. Malnutrition in turn accounts for differences in disease manifestation, with prolonged clinical course and carrier state, frequent complications and an increased fatality ratio.

Infections result in diminished food intake through the mechanism of fever, malaise and debility; food wastage through vomiting, increased peristalsis and mucosal damage; nutrient wastage due to metabolic alterations such as mobilization of muscle amino acids, abnormal lipid synthesis and loss of nitrogen, vitamins and electrolytes; sequestration of zinc, iron and other minerals; and nutrient diversion by synthesis of foreign and host proteins of no apparent relevance to the host economy and defense. Bodily reserves are low or depleted in malnourished states; the input demanded for the anabolic phase of infection is not readily available.

While repetitive infection in developing

Table 13. *Childhood mortality by foetal maturity, 416 infants.* *a* *Santa Marfa Cauque, 1964-1972*

Class of infant	Neonatal «29 d)	Post neonatal (29d to II mol	Total «I yr)	Second year	Third year	Fourth year
Pre-term	10(323)6 *n=31*	6 (286) *n=21*	16(516) *n=31*	0 *n=15*	0 *n=13*	0 *n=8*
Term small-for-gestational age	4 (28) *n=143*	8 (58) n=139	12(84) *n=143*	8 (76) *n=105*	3 (39) *n=78*	3 (50) *n=6O*
Term	2 (8) *n=242*	10(42) *n=240*	12(50) *n=242*	9 (44) *n=204*	5 (33) *n=153*	I (8) n=122
Total	16(39) n=416	24 (60) *n=400*	40 (96) n=416	17(52) *n=324*	8 (33) *n=244*	4 (21) n=l90

~ Prospective study; attrition with age explained because cohorts of infants were recruited beginning in 1964at a rate of about 50 per year. The last cohort was recruited in 1971.
b Number of deaths (deaths per 100children alive when the period started). *n* =initial population.

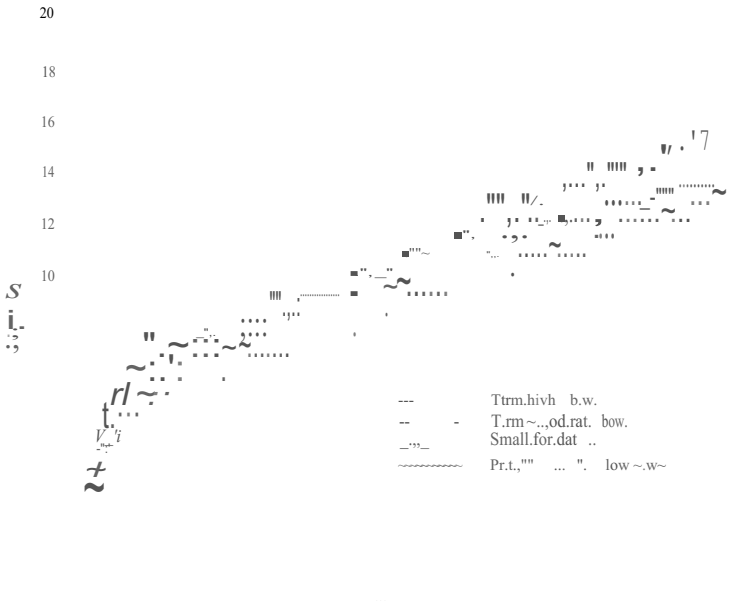

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Fig. 8. Mean weight curves, birth to age 6 years, cohorts of children observed prospectively and defined by fetal maturity, Santa Maria Cauque,

areas of the world accounts for a precocious development of high levels of serum immunoglobulins, other defense mechanisms such as the skin and intestinal indigenous flora may become altered. It is not known if recurrent intestinal infection alters synthesis of secretory IgA nor if mucosal injury will decrease opportunities for sensitization to food and bacterial antigens. Levels of food antibodies have not been established in malnourished populations, particularly in the acutely malnourished child who has marked alterations of the intestinal mucosa. Breast milk offers an efficient protective barrier against infection and probably against sensitization to food and other environmental allergens. In the village, deficient weaning practices, decreased milk production after 2 or 3 months and very poor sanitation are responsible for progressive deterioration of the nutritional status, high childhood mortality and deficient growth and development.

Ideally, improvement in education, sanitation and economic status should be effected simultaneously, with an equal emphasis in preservation of breast feeding.

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