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STUDIES OF DIARRHEAL DISEASE IN CENTRAL AMERICA*

VIII. MEASLES, DIARRHEA, AND NUTRITIONAL DEFICIENCY IN RURAL GUATEMALA

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Measles in tropical and other less developed parts of the world is a killing disease. Death rates in industrialized countries of Europe and North America in 1962 varied between 0.1 and 0.5 per 100,000 population.[1] In the same year the rates were 85 times greater in Mexico than in the United States, 268 times in Guatemala, and 274 in Ecuador.[2]

The reasons for these striking differences assuredly are multiple; expectedly they vary from place to place; and some are peculiar to less developed regions, notably a prevailing impaired nutritional state of low weight for age among young children. Under these conditions the quality and availability of medical care have more than usual significance as an influence on mortality. A greater virulence of the measles virus and an adverse effect of the tropical climate have been advanced as factors but with little supporting evidence. Deaths from measles are universally most frequent during the first three years of life; regions with an average early age at attack have high death rates.

Field investigations of the Institute of Nutrition of Central America and Panama (INCAP) on the interaction of nutrition and infection, so commonly synergistic, provided information on the behavior of measles in epidemiological situations where malnutrition was prevalent and other infectious diseases common. Evidence is presented of the nature and frequency of complications, the effect of nutritional state on clinical course and fatality, and the role of measles in precipitating severe protein deficiency.

MATERIALS AND METHODS

The studies were in rural Mayan Indian villages of the mildly temperate Guatemalan highlands, and they extended through five years. The region is almost wholly agricultural but with the population aggregated in villages, as in most developing countries.

In one community, Santa Catarina Barahona, (population 851) children from six months to five years of age, together with pregnant and nursing mothers, were offered a daily dietary supplement of a protein-rich vegetable mixture (Incaparina) with added powdered milk and sugar, and banana. This provided 15 grams of good quality protein and approximately 450 calories.

The proportion of village children who participated in the feeding program and the extent to which they consumed the prescribed supplement was variable and sometimes sporadic. About 27% received the supplement more than three-fourths of the time, 13% from three-fourths to a half, and 15% from a half to a fourth of the time. About 22% had less than a fourth of the prescribed amounts, and essentially the same proportion had none at all.

Another village, Santa Cruz Balanyá, (population 1459) served as a control. No food or nutritional advice was supplied. In both communities each family was visited every two weeks by resident health workers who recorded all illnesses of children under five years of age, and measles among those older. Illnesses reported or suspected to be measles were verified by a physician. Diarrheal disease was defined for infants as more than five liquid or semiliquid stools within 24 hours, and for children more than one year old as three or more. No medical care or other health measures were provided in either village except those educational efforts directly related to the feeding program.

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Preschool children were measured for height, weight, and skinfold thickness each three months and received a complete physical examination annually. For some measles patients weight was determined at short intervals through early convalescence. By fortunate coincidence, one of the annual examinations in Santa Cruz Balanyá immediately preceded a measles epidemic so that current nutritional status of subsequent measles patients was accurately known, including one who died.

RESULTS

Measles appeared among school children of Santa Cruz Balanyá in July, 1960, and spread rapidly to the preschool population. The epidemic ended in December. Total cases were 136, 57% within preschool ages. Another outbreak of 70 cases between May and July of 1963 followed the pattern of the first.[3]

The proximity of Santa Catarina Barahona to Antigua, an important market center, resulted in a more frequent invasion of the community by measles, five times within the five years of observation, but with total attack rates that were essentially the same, 99 cases in the smaller population. In industrialized countries, the age of greatest incidence of reported cases is six years, on entering school.[4] In the Guatemalan villages, it was during the second year of life, with a greater proportion of cases in the preschool years in Santa Catarina because the community was invaded more frequently; 80% of all cases compared with 58% in Santa Cruz.

An acute diarrhea was a prominent and early complication of measles. During an epidemic period in Santa Cruz Balanyá, the incidence of diarrheal disease among patients with measles less than five-years-old was approximately eightfold that for children of the same age without measles (Table 1). For older children, mainly of school age, the diarrhea rate during measles was half that for the younger group and yet 86 times the incidence for those without measles. The clinical severity in the two groups was indistinguishable. Onset of diarrhea was mainly during measles prodromes, as shown in Figure 1, either four days before or coincident with the first appearance of the exanthem, corresponding in general to the period of measles viremia. Similar observations in neighboring villages and in later epidemics of the study villages substantiated these findings. Indeed, the incidence of diarrhea was somewhat greater than here recorded; of 190 measles patients less than five years old, two-thirds developed diarrhea. The frequency was in direct relation to the extent of malnutrition; diarrhea in patients less than 75% of normal weight for age was three times that for patients within 10% of normal weight.[5] Occurrence of diarrhea among preschool measles patients in the feeding village was 39%.

Changes in weight during measles and in convalescence were measured weekly for 12 children aged six to 10 years. As summarized in Figure 2,

TABLE 1

Cases and case incidence of acute diarrheal disease per 100 person-weeks, in Santa Cruz Balanyá during an epidemic of measles, April 7 to August 5, 1963, by age and by presence or absence of an attack of measles

Age in years	Total children	Children with measles			Children without measles		
		No. of children	Cases of diarrhea*	Cases per 100 person-weeks	No. of children	Cases of diarrhea†	Cases per 100 person-weeks
Under 1	18	3	3	50.0	15	23	9.0
1	52	15	10	33.3	37	34	5.4
2	60	7	3	21.4	52	15	1.7
3	42	7	2	14.3	36	23	3.8
4	43	9	3	16.7	34	8	1.4
0–4	215	41	21	25.6	174	103	3.5
5–11	295	29	8	13.8	266	7	.16

* Within 2 weeks (7 days before to 7 days after) of appearance of measles rash.

† Cases of diarrhea in children who did not have measles during the 17 weeks of the epidemic.

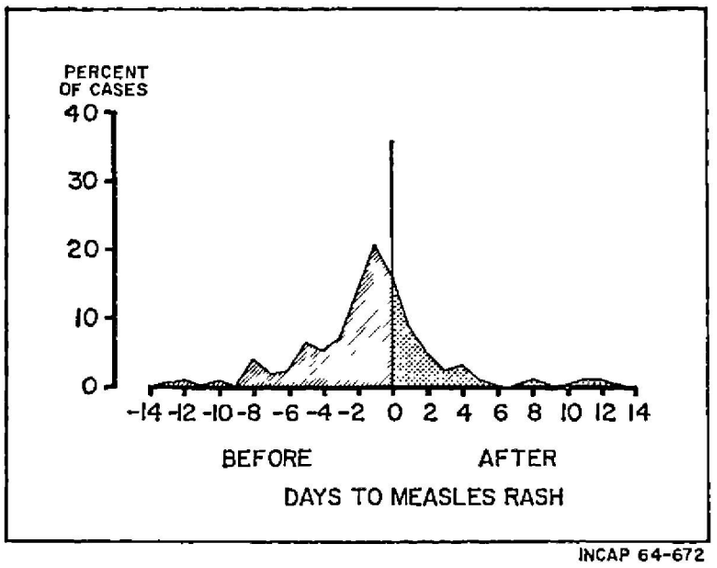

FIGURE 1. Percent distribution of 127 cases of diarrhea complicating measles, patients less than 5 years old, by day of onset before and after first appearance of measles rash, Santa Cruz Balanya, 1960–63.

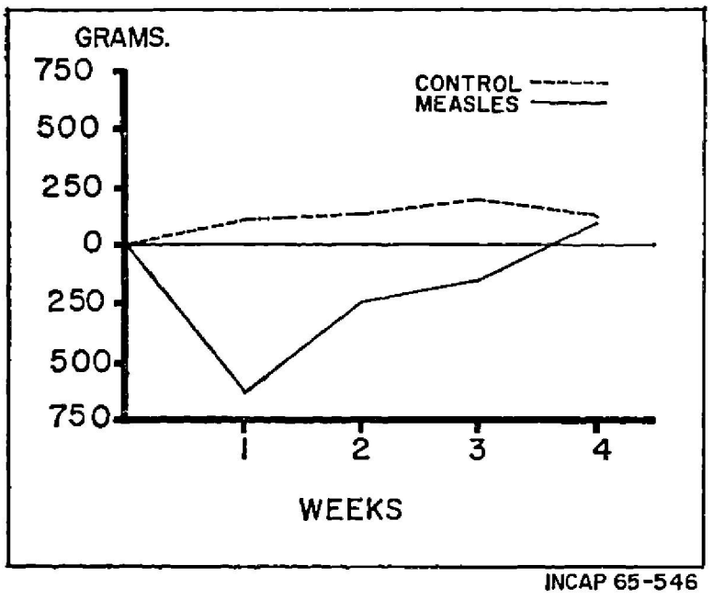

FIGURE 2. Average weekly variation in weight of 61 children without measles and 12 with measles, ages 5 to 12 years, Santa Cruz Balanya, epidemic of 1963.

these children lost about a half kilogram of weight during the week of active measles, while 61 children aged five to 12 years without measles averaged a small but consistent gain.

Figure 3 illustrates patterns of weight change during the epidemic as observed in routine quarterly examinations of preschool children. Patient A received supplementary food; patient B was from the control village. Both children had measles at 38 months of age. The first child showed no change in quarterly weight; the second lost over a kilogram (nearly 10% of body weight) which was only slowly regained. Cases C and D illustrate the impact of measles in children of 44 and 13 months, more or less the age extremes of the series. Much of the acute effect expectedly is obscured by measurements as far apart as three months. Patient E chanced to be weighed during active measles, with weight loss thus more accurately detected. In Case F measurement was again during active measles, in a child 12 months old but with a preceding malnutrition of six months duration. Weight loss was extreme, almost two kilograms, or 25% of body weight. Measles was a precipitating cause of kwashiorkor in two of 41 preschool children with measles in the control village and in none of 55 in the village with supplementary feeding.

Significant differences in measles mortality before and after institution of supplementary feeding are shown in Table 2. In the ten years immediately preceding the study, age-specific measles mortality for children up to 10 years of age was statistically the same in the two villages, being slightly in excess of 550 deaths per 100,000 children of those ages per year. In Santa Catarina Barahona where the feeding program was introduced, deaths among the zero to four year group had been more frequent than in the village subsequently serving as a control. During the five years of feeding, only two deaths from measles occurred, a rate of 163 deaths per 100,000 per year. One child who died had never participated in the supplementary feeding program; the other was a sibling long malnourished and participating only irregularly. Both were preschool children. Death rates for measles for all children in the control population remained the same during the trial period; indeed they were numerically, although not significantly, greater than previously. For preschool children of the test village, even though the feeding program did not reach all of them, the mortality from measles was less than half that in the control village. The greater proportion of cases in Santa Catarina in the early years of life, already mentioned, would have made likely a higher rate than in the control village; it had been so during the preceding 10 years.

Of necessity, deaths are expressed in terms of mortality rather than fatality, because only deaths and not cases were known for the years antedating the study. For preschool children, case fatality during the study period was 6.8%

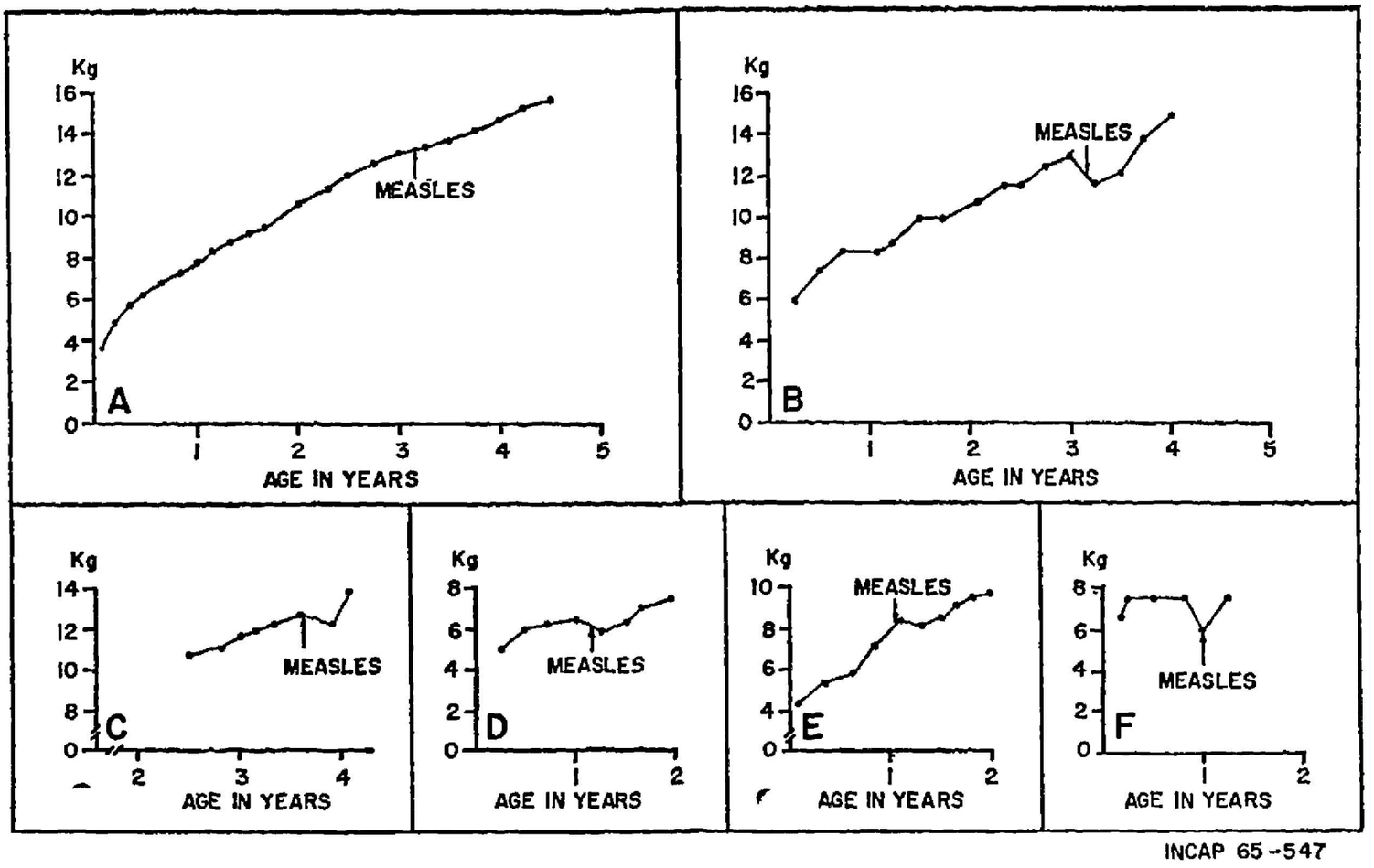

FIGURE 3. Weight change, rural Guatemalan preschool children with measles, measurements approximately each 3 months. A. Measles at age 38 months, supplementary feeding; any weight loss recovered by next quarterly measurement. B. Measles at 36 months of age, no supplementary feeding; body weight was 10% less at next quarterly measurement and regained slowly. C. Measles at 44 months of age, soon after a quarterly weighing, no supplementary feeding; marked weight loss. D. Measles at 14 months, about one month before scheduled weighing, no supplementary feeding; weight loss presumably after measles onset. E. Measles at 13 months and weighed shortly before, no supplementary feeding; weight not regained at the next weighing. F. Measles at 12 months, weighed shortly after onset, no supplementary feeding; long continued malnutrition; body weight loss of 25% barely regained 3 months later.

in the control village and 4.3% in Santa Catarina Barahona. It was zero for children participating in the feeding program 25% or more of the time.

A greater virulence of measles virus seemingly has little place in accounting for the high death rates among village populations. A survey of Guatemalan pediatricians, caring for well-nourished children living under good social and economic conditions, showed no more fatalities than in countries of North America and Western Europe, an observation substantiated by McGregor in the Gambia.[6]

In the highland villages, few patients with measles had the attention of a physician. Most mothers withdrew all solid food and substituted cereal gruels, commonly "tizana", a barley water plus an infusion of seeds from pods of a local tree, *canafistula*, or the skin of a fruit, *tamarindo*. The only other "treatment" was one or repeated 30 gram doses of "Kremor", principally potassium tartrate, purchased in the local pharmacy.

DISCUSSION

Almost everyone in contact with the modern world eventually has measles, whether rich or poor, in industrialized or in developing areas. Only the recent advent of measles vaccines gives any prospect of change. Death rates, on the other hand, have always showed marked differences according to time, place, and person. In the United States they declined from 12.8 per 100,000 populations in 1913, to 0.2 per 100,000 in 1963. Furthermore, rates had reached 1.0 per 100,000 by 1936, well before sulfonamides and antibiotics were available for the respiratory complications which cause most measles deaths. That elements other than medical care greatly influenced past excess mortality in advanced

TABLE 2

Deaths from measles and age-specific death rates per 100,000 population per year in 2 Guatemalan highland villages, 1950–1964

Village	Measles deaths		Measles deaths per 100,000 population per year	
	Pre-study period May 1950–April 1959	Study period May 1959–April 1964	Pre-study period May 1950–April 1959*	Study period May 1959–April 1964†
Santa Catarina Barahona-Feeding program				
0–4 years.....	12	2	973	286
5–9 years.....	0	0	0	0
0–9 years.....	12	2	553	163
Santa Cruz Balanyá-Control				
0–4 years.....	14	8	763	693
5–9 years.....	4	5	289	556
0–9 years.....	18	13	559	633

* Population of 1964, estimated by extrapolation from Guatemalan National censuses of 1950 and 1964.

† Population by direct field census, March, 1961.

countries, and continue to act importantly in the less developed regions of today, is consistent with many known facts. In a neighboring village to those studied,[3] a well ordered medical service was provided, along with a comprehensive program of preventive measures which by intent did not include either augmented nutrition or measles immunization. The case fatality for measles in a population of similar nutritional state, and during corresponding years, was still 2%.

In remote island populations and other more or less isolated regions, measles is characteristically a disease of widely spaced epidemics and when they occur, as in the classical Greenland outbreak of 1952,[7] attack is almost universal, striking all ages, adults as well as children. These events are so dramatic and so well known that measles in the usual less developed regions is commonly assumed to behave similarly. The Greenland type of behavior may occur in sparsely populated regions of developing countries, but most developing countries are not sparsely populated.

In this experience, the opposite age distribution was true: more than half of the cases occurred among children less than three years old, much earlier than in most industrialized regions. So far as may be judged by the selected populations of clinic and hospital patients, which are the usual source of information, measles is also a disease of infancy and early childhood in India, Nigeria, Dakar, Chile, Venezuela, and most other developing countries.[8-12]

The high incidence of measles at one to three years coincides with the observed age distribution of acute diarrheal disease[13] in the same localities and with that of malnutrition, the latter well established as due to inadequate supplementation of breast milk and consequent protein-deficient diets during and after weaning.[14, 15] Both diseases bear strongly on the nature and frequency of complications and deaths from measles.[5, 16]

While rarely a part of measles today in well nourished populations, diarrhea was described by Rhazes in 850 A. D. as a common symptom. Creighton found it a usual accompaniment of measles in England a hundred years ago.[17] Diarrhea is currently frequent wherever measles occurs in malnourished preschool children.[10, 18] Inflammatory changes in the jejunal mucosa have been reported for measles and other viral diseases.[19]

Ghosh and Dhatt in India reported complications in less than 17% of well nourished children,[18] compared to 46% among those judged poorly nourished. The findings among hospitalized patients in Caracas were similar.[12]

Under natural conditions a net deteriorating effect of measles on nutritional status is evident in many ways. Loss of body weight occurs during the acute attack. Several weeks are required for weight to return to preceding levels, and still longer to regain expected rates of increase. Urinary nitrogen loss[20] and a decreased nitrogen absorption are exaggerated when diarrheal disease or other infection accompanies measles. Moreover, total food intake is often markedly less because of anorexia and because protein intake is reduced by a change in diet to liquid and starchy foods.

Measles thus has the capacity to precipitate serious nutritional disease in children already suffering from a borderline deficiency. Oomen has described the frequency with which Indonesian children subsisting on diets deficient in vitamin A develop xerophthalmia, keratomalacia

and blindness after measles.[21] Many investigators have emphasized the ability of measles to precipitate kwashiorkor in the protein-deficient child.[22-24] The present observations suggest a three-fold interaction of malnutrition, diarrheal disease, and measles.

Chemotherapy has a place in the management of pyogenic complications. Although rarely required by well nourished subjects, it is often life-saving for the poorly nourished. Under existing conditions in most developing regions, improved nutrition is the most important preventive measure to reduce measles mortality, at least until an effective vaccine becomes universally available.

SUMMARY

Measles in rural populations of Guatemala is a serious disease, mainly affecting children in the first three years of life. The most frequent complication was acute diarrhea, which occurred in half of patients less than five years old. In other communities of the same region, the ratio was as high as two-thirds. Diarrhea contributed to deaths and disability, and the more malnourished the child the more likely the association. Children with measles usually required several weeks to regain their preceding weight. Kwashiorkor was an occasional aftermath.

Within the limitations of small numbers, the age-specific death rate for measles of children under five years in a village where a daily food supplement of 15 grams of protein and 450 calories was offered, declined from 973 per 100,000 during May, 1950–April, 1959, to 286 per 100,000 during the test period, May, 1959–April, 1964. No measles deaths occurred among children receiving the food supplement at least 25% of the time. Death rates in a control village of a similar high order did not change. Neither village population had local medical service.

During the study period, case fatality among preschool children was 6.8% in the control village and 4.3% in the feeding village, despite an earlier average age at attack, and with 22% of eligible children not participating.

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