

Original Articles

Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964

I. Study Plan and Experimental Design

Nevin S. Scrimshaw, MD; Miguel A. Guzmán, PhD; and
John E. Gordon, MD, Guatemala City

MALNUTRITION and communicable disease are the two ranking health problems of developing countries. Traditionally, their prevention and control have been independent public health activities. Communicable diseases have had the higher priority: Clinical effect is more direct and obvious; measures for case management and community control are better established; and, for many, case report to official health agencies is a legal requirement.

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With a few exceptions, and those in only an occasional country, nutritional diseases are not reportable. The deficiencies in case report of most communicable diseases are well known. The result is a principal reliance on notified deaths to determine priorities and the extent of public health action against both conditions. In developing countries the information on deaths, although much better than for cases, has serious limitations.

Background

Death Rates.—Recording of deaths rarely approaches completeness; the discrepancy between deaths which occur and deaths reported is often large. The greater difficulty

is inexactness of assigned causes of death. Physicians are few in rural regions of developing countries, and, yet, the greater part of the population lives there. Large areas often have no direct public health or medical service. As a result, most deaths are reported by lay officials.

Deaths from infectious disease are likely to be reported so that their origin is suggested, although fever or cough¹ poorly identifies the event. Cause becomes wholly uncertain when stated as "the evil eye" or as due to eclipse of the sun or moon. Deaths from nutritional disease are usually ascribed to some other cause, especially to intestinal parasites. As a consequence, malnutrition is seriously underrated when stated causes of death are the index. That deaths from all causes are regularly far more in developing regions than in industrialized parts of the world is supported by experience where reporting is good, particularly in urban areas² or through special surveys in rural districts.³

Infant mortality is high, and, at the inclusive ages of 1 to 4 years, deaths in Latin American countries range from 10 to 30 times as many as in North America or Europe.² Infectious diseases are strongly represented. Rates for the five common communicable diseases of childhood—measles, chickenpox, rubella, mumps, and whooping cough—are sometimes 200- to 300-fold greater than in industrialized countries with good health services. Acute diarrheal disease is frequently the leading cause of death for a country as a whole, and is regularly so for preschool children. Fatalities from infections of the respiratory tract have their usual prominent place.

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From the Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala.

Reprint requests to Building E18-479, Massachusetts Institute of Technology, Cambridge, Mass 02139 (Dr. Gordon) or to INCAP, Apartado 1188, Guatemala City (Dr. Guzman).

Recorded deaths from nutritional disease are few and many times are absent from official lists, despite a prevailing malnutrition at childhood ages of such an extent that as many as 85% of village children aged 1 to 4 years have a deficiency in weight for their age more than 10% below the mean for middle-class families of the region.⁴ A field study of deaths among children of four rural Guatemalan communities⁵ showed that two fifths of those dying at ages 1 to 4 years had the signs and symptoms of kwashiorkor. Nevertheless, only one death at any age up to 15 years was listed officially as due to malnutrition, a patient who died in a hospital and whose cause of death was medically certified. The usual certified cause was intestinal parasites, especially worms.

A further limiting factor to use of the number of deaths in determining of public health significance is that both infectious and nutritional disorders include numerous conditions with characteristically low death rates. Many are highly prevalent in developing regions; for example, upper respiratory disease, the acute diarrheas, and early malnutrition. The part they have in determining the health and productivity of general populations through their influence on the growth and development of young children is increasingly recognized.

Disease Incidence.—A natural alternative in the face of these restraints is to turn to frequency of disease occurrence, case incidence. Although knowledge of cases is theoretically more satisfying than that of deaths, the practical difficulties in acquiring that information are great, whatever the disease. Individual case reports are legally required only for some of the infectious diseases—and justifiably so, for the primary purpose of notification is to restrict transmission and assure prompt diagnosis and treatment. The relative completeness of reporting is also conditioned by these two factors, with the consequence that some diseases are well reported and others scantily. A number are reportable only as they occur in epidemics. Still others, and these include many of the commonest infections, are not reportable at all for the evident reason that little is to be gained in more effective control.⁶

As stated, official case reports of nutritional diseases are not required in world practice. As with many infections, both reportable and nonreportable, a large part of the nutritional disorders occurring in rural regions of developing countries are not

sufficiently severe to warrant the excessive effort necessary to obtain medical services from the next city, if indeed that is possible. Knowledge of both groups of diseases therefore remains indefinite and yet when they occur in young children they have presumptive long-term after-effects.⁷ Deaths are reportable but medical care for patients in urgent need is often unavailable, and relatively few among seriously ill patients are admitted to hospitals. The general result is that causes of death also remain highly indefinite.

Under these conditions the preferred method is the direct survey of cases and deaths, using the principles and techniques of field epidemiology.

Synergism of Infection and Nutrition.—A further need for better information on these two groups of disease, as they exist in developing countries, comes from the resurgence in recent years of a concept which dates from the beginning of modern nutrition; namely, that infectious disease and malnutrition have interlocking relationships and do not act as wholly independent processes.⁸ A synergism frequently exists whereby infectious disease has the capacity to precipitate an acute nutritional disease in persons of borderline nutritional state; and conversely, individuals with manifest nutritional deficiency commonly experience a severity and frequency of infection beyond ordinary expectation.

A report of a World Health Organization expert committee⁹ stresses these interactions, and a new WHO monograph documents the subject extensively.¹⁰ The evidence suggests that much of the excess morbidity and mortality among preschool children in developing countries, so often ascribed individually to either infectious disease or malnutrition, is, in reality, the result of the combined effect of the two conditions, acting in concert and enhanced by synergism.¹¹

Age at Attack.—In nearly all less-developed countries, the incidence of both infectious disease and malnutrition is greatest among children under 5 years of age. Breast feeding is a regular and close-to-universal practice, often well into the second year of life and frequently longer. Malnutrition occurs because breast milk fails to provide sufficient protein and calories beyond about 6 months of age and the necessary supplementary feeding is grossly inadequate.

The weanling child, living in an insani-

tary environment, lacking the specific immunity to be acquired by eventual experience with infectious agents, and with susceptibility enhanced by malnutrition, is singularly vulnerable to infectious disease, of which acute diarrheal disease¹² is a main component. The health problems associated with nutrition and infection are common to all ages in developing countries, but the young child, still partially dependent on breast milk, suffers most often and most seriously.

Exploratory Studies of Nutrition and Infection.—The Institute of Nutrition of Central America and Panama (INCAP) during a decade or more has documented the nutritional problems of the Guatemalan highlands as they pertain to protein deficiency and retardation of physical growth and development of young children. Dietary surveys measured the sometimes startling food deficiencies;¹³ failures to attain expected levels of weight and height were correlated with insufficient food intake,¹⁴ and kwashiorkor was identified as an important cause of death.¹⁵

A series of studies on diarrheal disease established a high prevalence of *Shigella* among general populations of preschool children,¹⁶ demonstrated an excessively high incidence of diarrheal disease;¹⁷ showed that relatively few cases of diarrhea, about 20%, could be related to the usually recognized bacterial and parasitic agents of that disease syndrome,¹⁸ a finding substantiated in other less developed countries;¹⁹ and further showed that infection was usually by personal contact rather than through agency of food or water.²⁰

A striking feature of these two lines of investigation, nutritional surveys and diarrheal disease studies, was the extent to which the findings converged. From a community standpoint, poor environmental sanitation and a lack of medical care were rather clearly identified among determinants of excess cases and deaths. Both, however, are continuing conditions, impinging on all fractions of the general population, while diarrheal disease centers in early childhood. Dietary deficiency also was active at older ages, and yet, like diarrheal disease, the greatest incidence and severity were in the first 3 years of life. This behavior was not altogether surprising. Nutritional demands are heavy during the early period of active growth, although breast feeding meets the usual requirements of the initial 6 months. The finding that the peak incidence of both

diseases coincided within the general period of 6 to 24 months suggested a connection between the two, with weaning¹⁰ as the common factor.

Clinical study of the weanling child provided further evidence. Age, of itself, was not the deciding element; instead, this was the time at which weaning began and ended. Early weaning gave an early peak incidence of diarrhea, late weaning a postponed peak. Diarrheal incidence increased with progressive dietary deficiency and greater complexity of diet. It decreased as weaning and the adjustment to conventional food were completed. Intensive studies of kwashiorkor, a form of acute protein-calorie deficiency disease, showed that disease to be precipitated with much regularity by an acute infection two or three weeks before the attack. It regularly involved an already malnourished child.

These investigations were instituted primarily to define the magnitude of nutritional disease in less developed areas. The suggestion that a synergistic interaction existed between infection and nutrition enlarged the scope of the problem and yet simplified the issue. Information was wanted on the extent to which differing degrees of malnutrition influenced clinical severity of an infectious disease, the duration of attack, and case incidence. Moreover, how general was the interaction, beyond the observations on acute diarrheal disease?

Conversely, if infectious disease exaggerates the nutritional deficiency incident to an inadequate diet, how broadly active are infections in this regard; and, more specifically, does the effect derive from some infectious diseases more than from others? What is the effect of differences in interval between illnesses, and do numbers of episodes or total days of illness have the greater impact?

Study Plan

A Longitudinal Investigation.—The brief duration and mild disability of many of the illnesses of childhood are such that knowledge of their infrequency and broad significance depends necessarily on cases, on morbidity rather than mortality. Deaths have their place in this decision but with causes better defined than by official reports. These reasons dictate the need for field study; and, for maximal reliability, a prospective rather than retrospective investi-

gation, continuous over an appreciable time. Minor illnesses are suggestively important. They are usually promptly forgotten; at best, the details quickly become hazy, as is also the case for major illnesses if they are sufficiently remote.

The traditional methods of the cross-sectional nutritional survey and the prevalence study of infectious disease do not suffice. Malnutrition, and most nutritional disease, is a slowly developing process, and the significance of infectious disease often rests not so much in the immediate event as in the number and progression of preceding episodes and in their relation one to another. Measurement of a postulated synergistic action between infectious disease and malnutrition requires their concurrent study by the epidemiological method of long-term observation of repeated illnesses as they occur under natural conditions. For operational as well as theoretical reasons, the study is best restricted to children less than 5 years old. A cohort observation is highly desirable, and the fullest value is from cohorts initiated at birth and continued to school age.

The practical objective of such studies, granted proof that the synergism of malnutrition and infectious disease is of meaningful proportions, was the accumulation of facts upon which to base a new kind of public health activity, where nutrition and infection are approached as a single concern, in contrast to control activities based on the individual elements. This endeavor is justified by a growing appreciation that malnutrition and the associated infections of childhood have a long-range effect on the health and productivity of the general populations of technically underdeveloped areas.

Programs for prevention and control must maintain an appropriate relationship to the whole of national public health activities and the effort toward economic development. The lag of food production behind population increase²¹ now present in most of the pre-industrial countries makes it urgent that the full significance of malnutrition be recognized and that programs for prevention receive appropriate priority.

Experimental Design.—The principles upon which to base the study offered less difficulty than decision on how best to implement them. The central question was the nature and extent of existing synergism. A practical consideration was the most promising course of action to produce a definite answer within the facilities and staff permitted

by a budget which was liberal and yet not limitless. In pursuit of the sequential objective of an improved program for prevention and control, a main consideration was whether the aim should be a system fitted to the current economic and professional capabilities of the study region and others like it or should represent the potential attainable with ideal facilities and resources.

The first thought was of a long-term investigation conducted so as not to introduce any intentional modification of the communities observed. The methods of descriptive epidemiology would apply, with the main purpose being characterization of the synergism of nutrition and infection. The nutritional state of young children would be determined by periodic survey and all illnesses followed for their relation to changes in that state and to subsequent growth and development.

The evidence to be had by this method would identify an association between infection and nutrition but not necessarily establish a causal relationship. This approach had the practical limitation of a known poor nutritional status among the general preschool population of the area, so great as to exclude any possibility of a representative sample of well-nourished children within a village with which to contrast the malnourished group.

An alternate plan was to introduce experimentally health measures currently nonexistent in these village populations in order to further such comparisons. The design in its basic form was a feeding program in one population and an integrated medical service of preventive measures and medical care in a second with a third population as a control. Field operations under such a plan were more involved, the expense was greater, and analysis of the collected data more complicated.

Combining supplementary feeding with observations on morbidity from infectious and nutritional diseases and comparing the findings with those of a control population would, however, give direct proof of postulated benefits from better nutrition. The provision of medical services in a second population with no feeding program would permit measurement of such effects on nutritional state as might come through partial relief from the burden of infection. The two individual approaches could be compared with each other and each with a control as

to the frequency and severity of disease. This was the operational scheme selected.

The underlying question of how elaborate the two programs should be led to the decision that both should fit within reasonable probabilities of how much public health activities would expand in this and similar regions within the succeeding 10 years. This imposed the following secondary considerations on selection of the field staff: that they should be people of the country, of good but not unusual competence, and clearly not foreign experts; and that the food supplied should be from indigenous sources rather than imported, be within local economic feasibility, and in amounts and quality reasonably appropriate.

The smaller the number of subjects, the easier it would be to manage the experimental program. The longer the required period of observation to attain statistical significance, the greater was the possibility of uncontrolled changes affecting the community; for example, a chance epidemic in one of the populations and not in the others. On the other hand, to obtain sufficient information within a year or two required an unmanageably large sample and staff. The compromise was to choose populations of such size that the effect of experimental manipulations, as judged by physical status and disease incidence, might reasonably be apparent within 5 years.

The likelihood of obtaining statistically significant differences in mortality was discarded; that aim would require either a larger sample or a still more extended period of observation. A study of 5 years gave reasonable expectation that fluctuations in disease incidence in the three villages would even up during that time. The experimental design finally adopted combines the advantages of long-term epidemiological observation of a natural population (the control) and those of a direct controlled experiment to test specific hypotheses.

Study Objectives.—The formally stated objectives of this long-term, prospective epidemiological study of malnutrition and infectious disease in rural Guatemalan communities were as follows:

1. To observe and describe the interactions of malnutrition and infectious disease among infants and young children through the fifth year of life in a rural population of a developing country where both classes of disease were highly prevalent.

2. To measure the changes in nutritional

state which result from addition of supplementary food to the diet of breast-fed children during weaning and thereafter, and to determine the effect of such changes on the characteristic incidence and behavior of common infectious diseases at those ages in that locality.

3. To measure the results of an integrated medical service, combining preventive and curative measures, on the frequency and behavior of infectious diseases among preschool children and to determine the effect of observed changes on nutritional status at those ages.

4. To identify and evaluate the relative influence of other broad ecological factors involved in the frequency and severity of infectious and nutritional diseases of early childhood in rural populations of a developing country, primarily those inherent in environmental sanitation and in the cultural pattern of the community.

In terms of the high case incidence and excessive death rates associated with malnutrition and infectious disease, the Guatemalan highlands were broadly representative of most rural regions in technically underdeveloped areas in Latin America and in much of the world.

The next two papers to be published deal with the organization and administration of this long-term field project under the difficult conditions of rural and rather primitive communities. The first describes the choice of methods and procedures and the action taken in pretesting their reliability and application to field work. It gives details of the study area and presents the population characteristics of these highland Guatemalan villages. The second outlines field procedure, collection of data, and methods of measurement. Subsequent contributions are concerned with the specific results of various parts of the study, with conclusions derived from the findings—in particular as they apply to public health action now and in the immediate future, and, finally, with the implications for future research.

Summary

Malnutrition and infectious disease are the leading causes of death among preschool children of developing countries. They have a deleterious effect on growth and development which is profound, long continued, and potentially an influence on social and economic progress of the general population.

Accumulating evidence indicates a synergistic interaction between nutrition and infection, and, consequently, the need for a unified public health program for prevention and control in place of the conventional independent action. Officially reported causes of death in the regions most affected are so ill-defined as to be useless in evaluation; case incidence, the preferred means, is virtually unknown. A prospective 5-year epidemiological field study of nutrition and infection in children less than 5 years old is

described. The essential features are a feeding program in one Guatemalan village, provision of an integrated medical service in another, with a third as a control. Cases of disease and injury and deaths from all causes are determined by fortnightly home visits. Nutritional state and food intake are measured periodically.

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MARRIAGE LICENSE TEST?

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