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

IX. An Evaluation of Medical, Social, and Public Health Benefits,
With Suggestions for Future Field Study

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Initially, all three study villages had poor environmental sanitation, little medical care, high mortality, and frequent malnutrition. In one village supplemental feeding of the preschool population without other intervention gave an appreciable but limited improvement in disease incidence and physical growth. A program of preventive medicine and medical care in a second village had no effect on frequency of illness and led to no improvement in physical growth; deaths were fewer. Comparison was to a control village with no added services. Collateral studies increased the usefulness of the basic study and enlarged the results.

The broader contribution of the study was bet-

ter definition of the general health of young children. Most usefully, the size of the problem became measurable by case incidence instead of by the usual dependence on number of deaths. Quantitative information on morbidity revealed a burden of illness on preschool children beyond most estimates; it was greatest in the second year. A public health approach based on concerted action against major factors, social as well as biological, can be expected to give better results than measures against any one singly, or in succession, even those as important as malnutrition or infectious disease.

THIS FIELD study of nutrition and infection began almost ten years ago. The thought and planning antedated that. As a consequence, this final summary of results warrants something more than the usual listing of conclusions derived from the collected data.

In any research the primary obligation is

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to state those additions to knowledge derived from meeting originally stated objectives. A second responsibility, especially with long-term studies, is to bring together separately published collateral findings. Some had their origin in a demonstrated need for more facts about features directly related to the main theme. One or two were of general interest, made possible by the existing organization for field study. Another group, although less directly related, rather clearly came from the stimulus of the original study. Some were by the staff of the project itself, others by members of the parent institute directing the study, and still

others by workers in other places and other institutions, influenced to an extent by formal and informal exchange of results as the study progressed.

We also present what we call "missed opportunities." They are really undeveloped possibilities coming from investigational leads projected by the data of the study. They await a day when their independent exploration becomes practicable. They are included for the benefit of others who may find them useful.

All concerned with this study have an interest extending beyond an explicit search for scientific knowledge, although admittedly that is a driving motivation. We would be remiss if we did not express a view on how the findings may be put to the practical benefit of public health in developing countries; and, thereby, to the aid of social and economic progress.

We end with a brief review of new field studies within the general area of nutrition and infection; some proposed, others underway; some by staff members of this institute, and an encouraging number by others in diverse regions where the need approximates that of Central America. We also identify independent areas in nutritional research where the method of long-term prospective field study is advantageous.

Contributions of the Definitive Study

We began this field study with a realization that disease among young children of less developed regions has an individuality setting it apart from illness at equivalent ages in industrialized areas. Case incidence and death rates were much greater. The diseases themselves were not, in the main, peculiar to these regions. Most were the same kinds of illness present everywhere: acute diarrheal diseases, upper respiratory infections, the common communicable diseases of childhood, and nutritional disorders. The greater numbers might be attributable to no more than an adverse environment, but the explanation was not that simple.

With some identifiable exceptions, disease was also more severe in these situations, more exacting in deaths, in length of disability, and with strong suspicion that aftereffects were also more deeply seated and frequent. This was particularly true of the infectious diseases, which outnumber all others. The reasons seemingly rested in host characteristics more than in qualities of the physical environment, and nutritional status stood out prominently.

It would be convenient to settle on the state of host nutriture as the decisive element, but the explanation is still more complicated. We believe it to lie mainly in the synergism between malnutrition and infectious disease, to give an effect beyond summation of the two. This is expressed in the title of this series, where nutrition and infection are designated an entity, not to be viewed as a simple association of the individually active elements.

The synergism between malnutrition and infectious disease is but one expression of the basic ecologic interaction between a host and its environment. Inevitably, other features of both elements were drawn into evaluation of any particular combination, notably the social environment. Social attributes were a determinant of nutritional deficiencies, and equally of infectious diseases; sometimes the same ones, sometimes wholly different, but all having to do with the habits, the customs, and the prejudices of people.

Granted, then, that the objectives of the study called for obtaining detailed information about two highly active influences on child health in developing regions—nutrition and infection—and that this objective was conscientiously adhered to, the ultimate concern was how these two conditions fitted into the broad pattern of general health and well-being of child populations. Quantitatively, how much did they influence it? The specific gains in knowledge have been recorded in the several papers of the series.¹⁻⁸ The issue here is: what were the broad contributions to child health through study of these two selected influences?

The Stressful Age.—Public health activities among children centered initially in school health because school children were a captive audience readily assembled. Infant mortality was always an independent problem. It became increasingly apparent that in less developed countries the more serious problems were among preschool children. That age group is now appropriately accorded first priority almost everywhere.

In this connection two outstanding facts have emerged from the present study, both so strongly supported by evidence from other less privileged countries as to identify them as principles. In all regions, although in developing areas far more than in industrialized ones, the highest death rates between ages 1 and 4 years are in the second year—among children who are over 1 and under 2 years. This holds true to such extent that in some countries the second year accounts for one half or more of fatalities within these four years.

The second point is that the pattern of infant mortality in developing countries is not characteristic of that in industrialized regions. The main reason that death rates of the first year are so high is that deaths in the postneonatal period exceed those of the first month, in contrast to industrialized areas where the concentration is in the neonatal first month, commonly in a proportion of 2:1. Furthermore, in less developed countries death rates in the postneonatal period of the first year and in the second year are often of the same general magnitude. The same kinds of disease predominate and the excess mortality relates to the same general pattern of causes. The two periods constitute a unit.

In developing regions the emphasis on prevention and control is therefore within the general range of 4 to 24 months. Faltering of physical growth and development is then at its height. With breast feeding close to universal, this corresponds to the period of weaning, defined as beginning with the first consistent introduction of a food supplement and ending with complete transfer of the child to a general diet.

The growing consideration of mental as well as physical aftereffects of disease and injury makes even more important a recognition of this time of life as the period of greatest stress. If brain growth is permanently impaired, the evidence is that it occurs before 3 years of age. Still more, if the period of greatest brain growth is the decisive factor, the stated period of major risk may have to include fetal life, not necessarily because maternal malnutrition is then the likely major concern, but because of other pathologic conditions prevailing at that time.

Size of the Problem.—This study provides one of the few sources of information on general morbidity among rural child populations in less developed regions over an appreciable length of time. Almost without exception, the usual dependence for direction of health activities is on numbers of deaths.

While the first year of life maintained its usual position of highest death rates, the outstanding demonstration in this study was a peak incidence of illness in the second year, considering all preschool years including the first. Infectious disease provided the main contribution, in regular combination with malnutrition. If the period of 4 to 24 months is taken as a unit, morbidity was relatively constant during that time. The morbidity rates themselves, the closer spacing of episodes of illness, and their longer duration support a conclusion that this period is of major consequence in preschool years past the first neonatal month. This feature acquires added importance as improving medical care curbs death rates. Children who formerly might have died now live, and the quality of survival becomes pertinent.

Public Health Measures.—More information on prevention and control, particularly that suited to public health programs in developing regions, was of natural interest to the study. The sharper definition of age of greatest effect, and its relation to weaning, was a real gain. To be able to express the size of the problem by the number of persons ill, instead of the number who died, was of practical value. Although new and useful procedures for public health action became evident, the principles established decades ago remained unchanged. The demonstration of a multifactorial causality had brought recognition that a program for control necessarily includes measures against a variety of factors. Eventually had come understanding that prevention and control, based on ecological grounds and directed toward a multifactorial causative complex, attained maximal effectiveness only when all indicated measures were applied concurrently. To single out individual elements for special attention, or to apply them in succession or indiscriminately, is to fail of full achievement. A truly integrated health program is required, with a common approach to diseases having an interlocking and interacting effect.

The results of this study reinforced that concept. The provision of a food supplement to a population produced a measurable, although not a striking, result in promoting physical growth and development and a lesser disease incidence. Similarly, the program for medical care, when it was the sole endeavor, had its gains in fewer deaths than ordinarily expected but not in lesser morbidity, or in better growth and development.

The principle of concurrent implementation of major procedures applies equally to areas of human interest as diverse as business, agriculture, government, and education. It goes by the currently popular name of systems analysis and management; that is, bringing along a project through concerted attention to all features. Thus, in agriculture progress requires concern with more than seed alone, or fertilizer, or insecticides; or with machinery, water, agricultural extension, or credit. Improvement results when all advance together. Despite its new and imposing title, the principle is no more than applied ecology.

The concern with general community health just presented was implicit in the stated objectives of the study: to see what effect a feeding and a medical care program had on frequency of illness among preschool children, and the influence thereby exerted on their growth and development. Malnutrition and infectious disease were the items specially investigated because they account for the bulk of childhood illness in developing regions. The study also produced its share of more specific contributions to the two main classes of disease, some of which are now summarized.

Collateral Studies

The definitive series of papers¹⁻⁸ covered specifically defined objectives of the study. Other contributions arising from study data, or stimulated by results of those investigations, were in greater number. They were of three general classes: (1) those by staff members of the study group, based on collected data of the study; (2) those by members of the INCAP staff other than project

personnel, or continuing studies by former staff members after field work ended, sometimes using the same facilities; and (3) theoretical concepts arising from field experiences, methods for prevention and control based on study findings, and review and analytical articles drawing heavily on those observations.

Arising From Study Data.—As special parts of field operations were completed, the results were published individually. So were a few progress reports as accumulated results warranted. Some appeared as formal publications, others as abstracts.

Weanling Diarrhea.—As the cause of death among preschool children and the commonest precipitant of kwashiorkor in already malnourished children, acute diarrheal disease had special and continued attention.9-23 Irrespective of season, cases were consistently present in the villages. Minor fluctuations in frequency were usual, but, in common with the general region, the endemic situation was disturbed from time to time by extensive outbreaks, having a broad periodicity of about three outbreaks each decade. In their long duration, they differed from the usual sharply rising and rapidly subsiding outbreaks of more favored areas; almost invariably they lasted a year, often two years, and in rare instances three years.

The disease in its acute manifestations was clinically characteristic, although conforming to no specific etiology. It is a syndrome due to a variety of infectious agents, some specifically identified with the diarrheas and the dysenteries, the majority undifferentiated; agents other than microbial occasionally cause diarrhea but not the typical syndrome. Shigella was most often identified, in 20.7% of cases. Salmonella was decidedly rare; and, in contrast to urban and especially industrialized regions, enteropathogenic Escherichia coli in these rural, less developed communities, was relatively scarce.

No less than 15% of cases among this population of malnourished preschool children were of a chronic recurrent type, presenting a succession of acute episodes interspersed with brief periods, of days to a week or more, of lesser or absent clinical activity. Duration was long; by definition cases ex-

ceeded two weeks, often they lasted a month or more, and in rare instances five or six months.

The relation to malnutrition of acute diarrheal disease of the more usual clinical form was also evident in a progressively greater frequency of attack the greater the retarded weight for age; and also a greater clinical severity the more definite that finding.

The relationship of feeding practices to incidence of diarrheal disease among infants and toddlers was highly characteristic. Cases were relatively few while children were wholly breast-fed; they increased as weaning began and other foods were added to the diet. Peak incidence was at the time of completed weaning (median, 25 months); it was of lesser degree in the three subsequent months, and thereafter dropped sharply to relatively low levels. This behavior was not a function of age but of the weaning pattern, determined primarily by the time it began and ended, to such extent that the disease was called weanling diarrhea. It accounted for the bulk of diarrheal disease in the study: it occurred at a highly critical age in childhood growth; and attacks were repetitive, two or three per year and sometimes a good many more.

Weanling diarrhea was established by these studies as a classical example of synergistic interaction of malnutrition and infectious disease and, in developing countries, as probably the most important single factor in growth and development of children in their most formative years.

Bone Maturation.—Wrist roentgenograms were taken to assess the effects of the two treatments, feeding and medical care, on bone maturation.²⁴⁻²⁹ These measurements paralleled determinations of height and weight in appraisal of physical growth.⁷

A score of each child for bone maturation was obtained through comparison of findings with corresponding values for age-and sex-specific distributions of ossification centers present in well-nourished Ohio children. It was not surprising that children of the three villages initially scored much lower, and that differences among the villages were insignificant. The steady increase in size of the scores with the feeding program, and also parallel differences in mean cortical bone thickness of the second metacarpal,

were findings supporting the value of the dietary supplement.

Comparison of ossification scores and cortical bone thickness of usual village children with those hospitalized for kwashiorkor showed surprisingly few differences. This confirmed the concept that kwashiorkor in Guatemala ordinarily is an acute disease of short duration, superimposed upon a long-standing malnutrition. Ordinarily it ends promptly in death unless energetically treated. Children with marasmus had a much wider spread of ossification scores, indicating that preceding undernutrition in some instances was more severe and prolonged than for most village children.

The wrist roentgenograms were also compared with those of children in Costa Rica and Panama subsisting on diets with a much lower calcium intake than in Guatemala where tortillas are made from lime-soaked corn. The higher calcium diets in Guatemala were of no advantage, as judged by roent-genographically measured bone density.

Dietary Surveys.—Two studies, 30,31 one made during the pilot investigation, were the basis for calculating the amount and kind of dietary supplement for the feeding village. The surveys continued at regular intervals during the definitive study. The results from the treatment village showed that program had no effect in improving dietary intake; and for the control population there was no secular trend. The remarkable feature of these periodic examinations was the uniformity of diets among children and adults in individual villages from season to season and from year to year. The children of the feeding village initially had a slightly better diet than those of the other two. This entered into the interpretation of results but, fortunately, the bias was in the proper direction.

A particularly poor diet during the second year of life was a distinctive finding. Previous surveys in the region had followed the general practice of tabulating diets of 1- to 4-year-old children as a unit. This obscured two facts: that the greatest inadequacy was in the 12- to 23-month period, and that diets improved steadily thereafter. The intake of breast milk was not measured nor taken into account in the calculations. While this introduced a bias, total protein intake, even al-

lowing for breast milk, was lowest in the second year relative to requirements. The mean protein intake per kilogram of body weight for preschool children beyond the second year met estimated minimum requirements for healthy children of equivalent weight.

The detailed data on diet made possible calculation of protein scores for children by year of age.³² The predominantly corn diets contained only about one half of the tryptophan required for optimal protein quality. Consequently, protein scores of 50 prevailed, and they varied little with age of the child.

Common Communicable Diseases of Childhood.—In less developed regions these universally prevalent diseases of early life have a significance in deaths and disability beyond any experience derived from industrialized areas. All five (measles, whooping cough, rubella, mumps, and chickenpox) occurred at one time or another as scattered cases; all three villages had epidemics of measles and the control village an outbreak of chickenpox.

An attack of any of these diseases regularly resulted in loss of weight, or, at best, a failure to show any growth increment.³³ In general, the result was exaggerated when the specific disease occurred within a short interval of another acute infection, a common circumstance in the first and second years. Attacks of these specific communicable diseases were relatively more numerous early in life than in industrial communities.

Case fatality in epidemic measles was invariably great, on the order of 6% to 7%; and disease-specific mortality exceeded that of industrialized nations by as much as 400 times.³⁴ Diarrhea was the commonest complication, centering almost wholly in the prodromal period or at the time of the eruption, with a frequency of 67% in one epidemic.³⁵ In this respect, measles in these less developed communities was like the measles of a hundred years ago in now more favored regions.

An epidemic of 50 cases of chickenpox among preschool children of the control village was an outstanding event.³⁶ Severity of infection and a high fatality are more or less expected with measles and whooping cough, but chickenpox is usually lightly regarded. In this outbreak, diarrhea occurred as a

complication in 58% of the cases, again centering in the prodromal period as with measles. Children in a less satisfactory nutritional state were most involved, although the incidence of chickenpox itself was unrelated to state of nutrition. No less than five cases of kwashiorkor developed among the 50 patients, in each instance after a complicating diarrhea, and, in general, among patients with an existing malnutrition of at least moderately severe degree as indicated by weight for age.

From clinical experience in this region, an epidemic of whooping cough would be expected to exceed other diseases of this group in frequency of complications, in duration of illness, and in deaths. No epidemic occurred during the study; such events are not unknown, however, for immunization in the villages is irregular. Much of the diarrheal disease in later years of the preschool period, past the time of weanling diarrhea, was attributable to these specific communicable diseases of early childhood.

Childhood Growth and Development.— The impact of such ordinarily mild diseases on the growth of children in developing regions showed clearly that field study of general childhood populations was requisite to full understanding. The specific need was information on the complete continuum of both malnutrition and infectious disease, from their inapparent presence to a lethal outcome. Studies of hospital patients do not give this information.

Observations confined to marasmus and kwashiorkor lose sight of the bulk of prote-in-calorie malnutrition. These two clinical conditions are a small proportion of the childhood morbidity due to this nutritional complex.

The situation holds equally for infections. Shigellosis among malnourished children had an inapparent form, the carrier state, with exaggerated frequency; and, still more important from the standpoint of communicability, a long duration, occasionally five months, in contrast to the usual week or so in the well-nourished host. At the other extreme of the biologic gradient, clinically manifest shigellosis averaged 7.7 days duration in place of the usual two or three. Chronic recurrent shigellosis was a special

feature. All forms have the potential capacity to impair growth and maturation.

The findings of the study included information on height and weight for age at close intervals over a long period, as well as illnesses of all degrees of severity according to number of attacks, interval between them, and days of disability. This permitted estimates for the acceleration and deceleration in height and weight during the first year of life, forces that reach an equilibrium at about 10 months of age. Thereafter, through ages 1 to 4 years, rates of growth for children of developing regions are essentially linear. Departures from linear growth at those ages, as well as exaggerated deceleration in the first year, may prove a sensitive means to detect and measure the impact of episodes of illness on growth. The study of estimated rates of growth through fitting them to appropriate mathematical models gives more information of greater reliability and versatility than does the traditional method of calculating series of increments.

Several publications, in the form of presentations to symposiums and international congresses, gave progress reports on various features of retarded physical growth³⁷⁻⁴⁰ before the results were formally summarized.⁷

Studies by Other INCAP Staff Members.
—Staff members of the institute other than those directly concerned with the three-village study sometimes used its facilities or employed data partially drawn from it in related or allied investigations.⁴¹

Weaning and the weaning period were recognized early as critical to understanding malnutrition and the growth process. Detailed investigations by a social anthropologist,42 in one of the study villages and in neighboring communities, enlarged that viewpoint. Information on the time weaning began and ended, the foods given, and the cultural attitudes influencing these decisions gave a good description of traditional Mayan Indian practices. More importantly, it confirmed the direct relation to malnutrition and infectious disease at this time of life. Subsequently, the studies were extended to prenatal practices and customs, delivery of the child, and child rearing.43 Attempts to measure amounts of breast milk received by infants of different ages, by weighing the child before and after each feeding over a period of days, proved hopeless. Breast-fed Indian babies are not nourished according to schedule; for much of the time the breast serves rather as a pacifier, with irregular ingestion of small amounts of milk too little to measure with any accuracy. These investigations were one of the few specific efforts to quantitate social factors.

Review Articles, Books, and Monographs.—Theoretical concepts frequently were derived or enlarged from the findings of the field study and incorporated in special monographs. 44-57 Also, several reviews of diseases indigenous to the study region were based in large measure on study data, especially acute diarrheal disease.

Two comprehensive publications provided the ground work for the study. The first⁴⁴ presented the conceptual idea of synergism and antagonism between malnutrition and infectious disease. The second⁴⁵ outlined technical methods and procedures in long-term prospective field study, with emphasis on those used in this investigation. The third, a book,⁵⁶ included added ideas and factual observations on interactions of nutrition and infection arising from the study.

An international conference on malnutrition, learning, and behavior in 1967 made use of the experiences and methods of the three-village study in formulating plans for field investigation, a main objective of the conference. The proceedings⁵⁷ present evidence from animal experiments and clinical observation strongly suggesting that synergism between nutrition and infection is a factor in the retarded learning and behavior common among children of less developed countries.

Missed Opportunities

To label the items that follow as missed opportunities is really unwarranted. The leads recognized but of necessity left untouched, or postponed to another day, are one of the challenges of research; and so is the certainty that further work is needed to fill in the pattern of proof, that knowledge remains incomplete. Many opportunities became evident in the course of the study which could, at little extra cost, be incorporated into future longitudinal studies of this general character.

Weaning Practices in Developing Countries.—The evidence from this study strengthened the view that where breast feeding is as universal and long-continued as in most developing regions, the problem of nutrition and infection centers in the weaning period, approximately the 4th to the 24th month, is sometimes longer. The anthropological surveys by González and Béhar⁴³ reinforced that conclusion. Difficulties continue in later preschool years but to far lesser extent.

Precise knowledge of breast milk intake is woefully lacking for representative developing regions. The value and the necessity of breast feeding in most developing regions for the first 6 months is firmly established, in some places to such extent that it is almost a matter of "nurse or die." Is excessively long breast feeding, however, actually harmful because of the assumption that the child is being well-fed in later months when in reality he is not? Or is it a saving grace because of social and economic inability to provide a better substitute? These are questions largely unanswered.

Maternal Nutrition During Pregnancy.— Enough information on food supplementation for pregnant women was collected to stimulate more intensive study. This becomes increasingly pertinent as the concern about malnutrition of infants and young children extends to inhibition of mental as well as physical growth. The highly critical time in brain growth is the latter part of intra-uterine life and the immediate postnatal period. Just as the critical period in physical growth and development has been pushed back from the five preschool years to the first two, the increasing attention to brain growth may extend the time back into fetal life.

Congenital Anomalies.—The ecological field methods employed in the present work could readily provide information about developmental malformations in man. Fragmentary information suggests a relation to nutrition and infection, sufficient to warrant building that interest into the experimental design of an appropriate future investigation. The required population would need to be large, because the readily determined events are relatively uncommon. Present studies on malnutrition, learning, and be-

havior from birth through adolescence would appear especially suited to recognition of the many late-appearing and less recognized defects.

Stillbirths and Abortions.—The information about deaths in early childhood in developing countries has contributed to better understanding of child health, notably the disproportion of postneonatal to neonatal fatalities, and the significance of the second year death rate. The long-recognized and yet ill-defined question of stillbirths, more pertinently perinatal deaths, under conditions of a developing technology and the changes incident to an altered rural social structure, add interest. The rising rate of induced abortions in many developing regions compounds the inherent problem of spontaneously occurring events. The technical difficulties in field study of these matters are themselves serious enough; the social and cultural inhibitions that hinder acquisition of good data are greater. Long-term prospective investigations that cultivate the confidence and understanding of the people and have other and more appealing primary objectives may well provide the best means of obtaining such information.

Field Studies in Progress

Investigations of nutrition and infection in less developed countries are being extended and expanded by several workers. Procedure in each instance is epidemiologic, and the viewpoint ecologic. Two further studies under the auspices of the institute began shortly after the present field work ended.

Cohort Study of Infection and Nutrition. -This investigation began in February 1964 in one of the villages of the earlier study, using a part of its facilities. The unique feature of the study is its experimental design. Mata has employed the principle of small group epidemiology in place of the large numbers of people more usual in community studies. For two years newborn babies of a Mayan Indian village were selected on a cohort basis. The small numbers in the eventual study population, about 45, permit more frequent and more intricate examinations.58-63 Emphasis is on microbial colonization of the intestine, and thus on the natural history of intestinal infection and malnutrition. The first child born during the study is now past 4 years old. The intent is to follow all until they enter school at age 7 years.

Malnutrition, Learning, and Behavior.— The late phases of the three-village study included some exploration of nutritional deficiencies in early childhood in causal relation to mental retardation. In August 1965 Canosa began a thorough field study of the effect of malnutrition on mental growth and development in comparable Ladino villages of Guatemala. 64-66 The approach is likewise ecologic, an attempt to distinguish the effect of malnutrition within the intricate complex of causality that includes infectious disease, lack of education, social deprivation, poverty, inadequate medical services, climatic stress, genetic inheritance, and more.

Only one other known field study on any subject rivals this one in ambition or in comprehensiveness, that one being the Framingham study of heart disease. The present plan is for a definitive study of children until they enter school at age 7 years. If the results then warrant, the intent is to extend the observations through adolescence, or until age 21 years.

The problem is more complex than that of the three-village study, with its limitation to physical growth. This investigation includes that and, in addition, mental performance. Field methods applicable to the specialized part of the investigation, mental development, were not available. The seven-year definitive study began after three years of perfecting technical procedure and a pilot study, a highly commendable allotment of time and energy. Without accuracy of measurement and a consistent ability to count similar things, the search for cause has no reality.

Malnutrition and Mental Development.—Cravioto was a pioneer in field study of this aspect of nutrition. After exploratory studies in Mexico, he came to Guatemala in 1962 to develop an informative pilot investigation. Returning to Mexico in 1964, he undertook a definitive ecologic study in Mexican villages, measuring levels of attained intelligence, mental capacity, and cultural behavior.⁶⁷ The contribution of multiple factors was recognized, but concentration is on the role of nutrition.

Nutritional Effect in General Community Disease.—The investigations thus far noted are by nutritionists with the direct purpose of measuring the role of nutrition in human health, particularly in relation to growth and development, physical and mental. Many field studies have found nutrition an essential feature in assessment of community diseases which are not of direct nutritional origin. The Framingham heart study probably affords the best example, but this is also true of field studies of diabetes, rheumatic fever, chronic arthritis, and a number of others. In India, Taylor in the Punjab, and Wyon in the Hyderabad State, have included nutrition, with good reason, in their field studies of population dynamics and population control.

Field study has great usefulness in bringing nutrition into the general fabric of public health activities, and in recognition of the extent to which it enters into most problems. The method applicable to other specific problems of nutrition beyond those to which it has been applied. Worthwhile possibilities include: (1) the complex causality of anemias associated with nutritional defects; (2) food mycotoxins and the incidence of primary liver carcinoma; (3) dietary intervention in atherosclerosis; and (4) consequences of malnutrition in pregnancy in less developed countries.

Comment

Commitment to a long-term prospective field study requires fortitude and dedication. Five years of data collection usually means at least two years of organization, fund raising and preparation, and an equal or greater time afterwards in the analysis and reporting of findings. The present study followed this pattern. Whether an investigator is engaged fulltime or not, a study of this kind dominates his professional activities and commitments for a goodly portion of an active scientific life. The initial selection of objectives and decisions on method and procedure are, therefore, of crucial importance personally, as well as mandatory for scientific productiveness. Once they are accepted, their specific test outranks all other considerations, although the research is likely to

turn in varied directions. A study develops a philosophy and a personality of its own. In that spirit, the present study has been evaluated.

The first of the two main objectives was to see whether dietary supplementation could of itself lead to a better result in terms of physical growth and incidence of disease. It did, but not outstandingly. The program for preventive medicine did not bring less disease or better physical growth among preschool children. The community benefited from the medical treatment provided.

Long observations on weanling diarrhea demonstrated an existing synergism between malnutrition and infectious disease as one reason for the small result. An adequate practice of prevention and control necessarily considers the two conditions as a clinical and epidemiological unit, with measures appropriate to each part applied concurrently. The biological interaction must not, furthermore, discount appreciation that weanling diarrhea and other such associations are fundamentally sociomedical problems. Multiple social factors enter into the pattern of causality of both elements and, consequently, into the observed synergism. The findings in weanling diarrhea led naturally to expanded effort in measuring clinical and epidemiological modifications of other prevailing infectious diseases under influence of a malnourished host. This led to questions of the interpretation of malnutrition itself.

Malnutrition is a term readily used by everyone, but usually without definition. From the beginning we recognized that physical growth alone was an inadequate criterion for evaluation of that state, but we had none better. Physical examination for

clinical signs proved virtually useless. Biochemical measures under field conditions were not feasible, because the necessary blood samples were unobtainable without coercion of the people and loss of cooperation. Analysis of bone maturation added some precision. That the effects of malnutrition on mental development, learning, and behavior might be even more significant for less developed countries than physical growth was well appreciated, but neither the means, the staff, nor proven methods of measurement were available.

Our acceptance of an ecological interpretation of malnutrition is reflected in the manner in which the many collateral studies developed. Because of their diverse nature and because reports have appeared in a variety of places, they have been collected for ready reference in the bibliography of this paper. A half dozen or so others are completed and in the course of publication.

As the study ends, our own evaluation is that the major benefits from the three-village study are in knowledge gained of the number and nature of illnesses among young children in a typical underdeveloped area, the ages at which the problem centers, and the indicated public health approach. The findings, specific in some respects as they are, have an important bearing on the general health of people whose status desperately needs improvement. Their application through public health programs in less developed countries can aid in promoting social and economic progress.

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References

- 1. Scrimshaw, N.S.; Guzmán, M.A.; and Gordon, J.E.: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: I. Study Plan and Experimental Design, *Arch Environ Health* 14:657-662 (May) 1967.
- 2. Scrimshaw, N.S., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: II. Field Reconnaissance, Administrative and Technical; Study Area; Population Characteristics; and Organization for Field Activities, Arch Environ Health 14:787-801 (June) 1967.
- 3. Scrimshaw, N.S., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: III. Field Procedure, Collection of Data and Meth-

- ods of Measurement, Arch Environ Health 15:6-15 (July) 1967.
- 4. Ascoli, W., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: IV Deaths of Infants and Preschool Children, *Arch Environ Health* 15:439-449 (Oct) 1967.
- 5. Scrimshaw, N.S., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: V. Disease Incidence Among Preschool Children Under Natural Village Conditions, With Improved Diet, and With Medical and Public Health Services, Arch Environ Health 16:223-234 (Feb) 1968.
- 6. Gordon, J.E., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: VI.

- Acute Diarrheal Disease and Nutritional Disorders in General Disease Incidence, *Arch Environ Health* 16:424-437 (March) 1968.
- 7. Guzmán, M.A., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: VII. Physical Growth and Development of Preschool Children, *Arch Environ Health* 17:107-118 (July) 1968.
- 8. Béhar, M., et al: Nutrition and Infection Field Study in Guatemalan Villages, 1959-1964: VIII. An Epidemiological Appraisal of its Wisdom and its Errors, *Arch Environ Health* 18:814-827 (Nov) 1968.
- 9. Gordon, J.E.; Béhar, M.; and Scrimshaw, N.S.: Acute Diarrhoeal Disease in Less Developed Countries: I. An Epidemiological Basis for Control, *Bull WHO* 31:1-7, 1964.
- 10. Gordon, J.E., et al: Acute Diarrhoeal Disease in Less Developed Countries: 2. Patterns of Epidemiological Behaviour in Rural Guatemalan Villages, *Bull WHO* 31:9-20, 1964.
- 11. Gordon, J.E.; Béhar, M.; and Scrimshaw, N.S.: Acute Diarrhoeal Disease in Less Developed Countries: 3. Methods for Prevention and Control, *Bull WHO* 31:21-28, 1964.
- 12. Gordon, J.E.: Weanling Diarrhea: A Synergism of Nutrition and Infection, *Nutr Rev* 22:161-163 (June) 1964.
- 13. Mata, L.J.: Agentes Causales de las Diarreas, Rev Cot Méd Guatemala 15:64-71 (June) 1964.
- 14. Mata, L.J.; Lüttman, R.; and Sánchez, L.: Microorganismos Enteropatógenos en Niños con Diarrea Severa, *Rev Col Méd Guatemala* 15:176-184 (Dec) 1964.
- 15. Gordon, J.E., et al: Studies of Diarrheal Disease in Central America: VI. An Epidemic of Diarrhea in a Guatemalan Highland Village, With A Component Due to Shigella dysenteriae Type 1. Amer J Trop Med Hyg 14:404-411 (March) 1965.
- 16. Mata, L.J., et al: Prevalence of Shigella, Salmonella and Enteropathogenic Escherichia coli on Six Mayan Villages, Amer J Public Health 55:1396-1402 (Sept) 1965.
- 17. Gordon, J.E., and Scrimshaw, N.S.: "Nutrition and the Diarrheas of Early Childhood" in Acheson, R.M. (ed.): Comparability in International Epidemiology, New York: Milbank Memorial Fund, 1965, pp 233-239.
- 18. Catalán, M.A.; Mata, L.J.; and Fernández, R.: Estudio sobre Portadores de Shigella, Guatemala Pediátrica 5:55-66 (Sept) 1965.
- 19. Gordon, J.E.: Weanling Diarrhea: Synergism of Nutrition and Infection, *Pediatrics Dig* 7:146, 1965.
- 20. Mata, L.J.; Catalán, M.A.; and Gordon, J.E.: Studies of Diarrheal Disease in Central America: IX. Shigella Carriers Among Young Children of a Heavily Seeded Guatemalan Convalescent Home, Amer J Trop Med Hyg 15:632-638 (April) 1966.
- 21. Ascoli, W., and Mata, L.J.: Studies of Diarrheal Disease in Central America: VII. Treatment of Preschool Children with Paramomycin and Sulfamethoxypyridazine Under Field Conditions in a Guatemalan Highland Village, Amer J Trop Med Hyg 14:1057-1061 (June) 1965.
 - 22. Gordon, J.E., and Scrimshaw, N.S.: Nutrition

- and the Diarrheas of Early Childhood in the Tropics: Milbank Mem Fund Quart 43:233-239 (April) 1965.
- 23. Mata, L.J.: Importancia Biológica de la Biota (Flora) Normal, Rev Col Méd Guatemala 18:95-100 (June) 1967.
- 24. Garn, S., et al: Compact Bone Deficiency in Protein-Calorie Malnutrition, Science 145:1444-1445 (Sept) 1964.
- 25. Garn, S.M., et al: Catch-up Bone Development During Treatment of Kwashiorkor, Fed Proc 23:338 (March-April) 1964.
- 26. Rohmann, C.G., et al: Osseous Development of Guatemalan Children on Low-Protein Diets, Fed Proc 23:338 (March-April) 1964.
- 27. Guzmán, M.A., et al: Osseous Growth of Guatemalan Children Fed a Protein-Calorie Supplement, Fed Proc 23:338 (March-April) 1964.
- 28. Béhar, M., et al: Osseous Development in Children With Kwashiorkor, Fed Proc 23:338 (March-April) 1964.
- 29. Garn, S.M., et al: Continuing Bone Growth Throughout Life: A General Phenomenon, Amer J Phys Anthrop 26:313-317 (May) 1967.
- 30. Flores, M., et al: Annual Patterns of Family and Children's Diet in Three Guatemalan Indian Communities, *Brit J Nutr* 18:281-293, 1964.
- 31. Flores, M.; Flores, Z.; and Lara, M.Y.: Food Intake of Guatemalan Indian Children, Ages 1 to 5, J Amer Diet Assoc 48:480-487 (June) 1966.
- 32. Flores, M., et al: Evaluation of the Protein Quality of Diets of Rural Guatemalan Children (By Calculation and Biological Trials), Proceedings of the Sixth International Congress of Nutrition, Edinburgh, 9-15 August 1963, Edinburgh: E. & S. Livingstone, Ltd., 1964, p 554.
- 33. Salomon, J.B.; Mata, L.J.; and Gordon, J.E.: Malnutrition and the Common Communicable Diseases of Childhood, *Amer J Public Health* 58:505-516 (March) 1968.
- 34. Gordon, J.E.; Jansen, A.A.J.; and Ascoli, W.: Measles in Rural Guatemala, *J Pediat* 66:779-786 (April) 1965.
- 35. Scrimshaw, N.S., et al: Studies of Diarrheal Disease in Central America: VIII. Measles, Diarrhea, and Nutritional Deficiency in Rural Guatemala, Amer J Trop Med Hyg 15:625-631 (April) 1966.
- 36. Salomon, J.B.; Gordon, J.E.; and Scrimshaw, N.S.: Studies of Diarrheal Disease in Central America: X. Associated Chickenpox, Diarrhea, and Kwashiorkor in a Highland Guatemalan Village, Amer J Trop Med Hyg 15:997-1002 (June) 1966.
- 37. Guzmán, M.A.; Béhar, M.; and Scrimshaw, N.S.: The Conditioning Effect of Illnesses on the Rates of Gain in Height and Weight in Chronically Malnourished Children, *Proceedings of the Seventh International Congress of Nutrition*, abstracts, Hamburg, Aug 3-10, 1966, pp 49-50.
- 38. Viteri, F.; Arroyave, G.; and Béhar, M.: Estimation of Protein Depletion in Malnourished Children by Creatinine Height Index, *Proceedings of the Seventh International Congress of Nutrition*, abstracts, Hamburg, Aug 3-10, 1966, pp 46-47.
- 39. Guzmán, M.A.: Impaired Physical Growth and Maturation in Malnourished Populations, in

- Scrimshaw, N.S., and Gordon, J.E. (eds.): Malnutrition, Learning, and Behavior, Cambridge, Mass: The M.I.T. Press, 1968, pp 43-54.
- 40. Béhar, M.: Prevalence of Malnutrition among Preschool Children, in Scrimshaw, N.S., and Gordon, J.E. (eds.): *Malnutrition, Learning, and Behavior*, Cambridge, Mass: The M.I.T. Press, 1968, pp 30-42.
- 41. Sweeney, E.A., and Guzmán, M.A.: Oral Conditions in Children from Three Highland Villages in Guatemala, *Arch Oral Biol* 11:687-698 (July) 1966.
- 42. de González, N.L.S.: Breast-Feeding, Weaning, and Acculturation, *J Pediat* 62:577-581 (April) 1963.
- 43. de González, N.L.S., and Béhar, M.: Child-Rearing Practices, Nutrition, and Health Status, *Milbank Mem Fund Quart* 44:77-96 (April) 1966.
- 44. Scrimshaw, N.S.; Taylor, C.E.; and Gordon, J.E.: Interactions of Nutrition and Infection, *Amer J Med Sci* 237:367-403 (March) 1959.
- 45. Gordon, J.E.: Field Epidemiology, Amer J Med Sci 246:354-376 (Sept) 1963.
- 46. Gordon, J.E.: Acute Diarrheal Disease, Amer J Med Sci 248:345-365 (Sept) 1964.
- 47. Scrimshaw, N.S.: INCAP Studies on Nutrition and Infection, in Second Far East Symposium on Nutrition (Taipei, Taiwan, China, May 18-25, 1964), sponsored by the Republic of China and the US Interdepartmental Committee on Nutrition and National Development, National Institutes of Health, Government Printing Office, 1965, pp 156-169.
- 48. Gordon, J.E.: "Acute Undifferentiated Diarrheal Disease of Early Childhood," in *Omagiu lui Mihaii Ciuca cu Ocazi Impliniyii a 80 de ani*, Bucuresti, Romania: Editura Academici, 1965.
- 49. Gordon, J.E.: Methods for the Control of Communicable Disease in Man, Report of the First Regional Seminar on the Control of Communicable Disease, appendix 4, Regional Office of the Western Pacific of the World Health Organization, Manila, Philippines, 1965, pp 51-59.
- 50. Scrimshaw, N.S.: "The Effect of the Interaction of Nutrition and Infection on the Preschool Child," in *Pre-School Child Malnutrition*, Washington, DC: National Academy of Sciences-National Research Council, publication 1282, 1966, pp 63-73.
- 51. Gordon, J.E.: Ecologic Interplay of Man, Environment, and Health, *Amer J Med Sci* 252:341-356 (Sept) 1966.
- 52. Gordon, J.E.; Wyon, J.B.; and Ascoli, W.: The Second Year Death Rate in Less Developed Countries, *Amer J Med Sci* 254:357-380 (Sept) 1967.
- 53. Scrimshaw, N.S.: Nutrition and Health, in Proceedings of the Seventh International Congress of Nutrition, Hamburg 1966, Braunschweig, Germany: Pergamon Press, 1967, vol 1, pp 7-11.
- 54. Gordon, J.E.: "Social Contributions to Infectious Disease: Causality, Behavior, Aftereffects," in Eichenwald, H.F. (ed.): The Prevention of Mental Retardation Through Control of Infectious Diseases,

- Proceedings of a Conference on Prevention of Mental Retardation Through Control of Infectious Disease, June 9-11, 1966, Cherry Hill, Public Health Service publication 1692, Government Printing Office, 1968.
- 55. Gordon, J.E.: Social Implications of Nutrition and Disease, *Arch Environ Health*, to be published.
- 56. Scrimshaw, N.S.; Taylor, C.E.; and Gordon, J.E.: Interactions of Nutrition and Infection, WHO Monogr Ser, No. 57, Geneva, 1968.
- 57. Scrimshaw, N.S., and Gordon, J.E. (eds): *Malnutrition, Learning, and Behavior*, Cambridge, Massachusetts: The M.I.T. Press, 1968.
- 58. Mata, L.J., and Beteta, C.: Colonización del Intestino de Niños Lactantes por Virus, Bacterias y Levaduras, *Rev Col Méd Guatemala* 16:127-135 (Sept) 1965.
- 59. Mata, L.J.; Beteta, C.E.; and García, B.: Estudio Longitudinal de las Coloniazaciones Intestinales en el Niño, Salud Pública Méx 7:735-739 (Sept-Oct) 1965.
- 60. Mata, L.J.; Beteta, C.E.; and Urrutia, J.J.: Weight Curves of Infants, Diet, Infectious Diseases, and Microbial Colonization, *Proceedings of the Seventh International Congress of Nutrition*, abstracts, Hamburg, Aug 3-10, 1966, p 289.
- 61. Mata, L.J.; Urrutia, J.J.; and García, B.: "Effect of Infection and Diet on Child Growth: Experience in a Guatemalan Village," in Wolstenholme, G.E.W., and O'Connor, M. (eds.): Nutrition and Infection, Ciba Foundation Study No. 31, London: J. & A. Churchill, Ltd., 1967, pp 112-126.
- 62. Mata, L.J.; Urrutia, J.J.; and Gordon, J.E.: Diarrhoeal Disease in a Cohort of Guatemalan Village Children Observed from Birth to Age 2 Years, *Trop Geogr Med* 19:247-257 (Dec) 1967.
- 63. Dale, D.C., and Mata, L.J.: Studies of Diarrheal Disease in Central America: XI. Intestinal Bacterial Flora in Malnourished Children with Shigellosis, Amer J Trop Med Hyg 17:397-403 (March) 1968.
- 64. Canosa, C.A., et al: Studies on the effects of Malnutrition on Physical Growth and Mental Development, in Proceedings of a Meeting of Organizations Concerned With Studies on Growth and Normal Development of the Normal Child, Stockholm, Centre International de l'Enfance, Bjuv, Sweden: A. B. Findus, 1966, vol 2, pp 135-150.
- 65. Canosa, C.A.: Effecto de la Desnutrición sobre el Desarrollo Mental, Abstracts of Communications Presented at the Eighth Panamerican, First Latin American, and Eleventh Mexican Congresses of Pediatrics, Oct 29-Nov 3, 1966, México, DF pp 131-132.
- 66. Canosa, C.A.: Ecological Approach to the Problems of Malnutrition, Learning, and Behavior, in Scrimshaw, N.S., and Gordon, J.E. (eds.): *Malnutrition, Learning, and Behavior*, Cambridge, Mass: The M.I.T. Press, 1968.
- 67. Cravioto, J.; deLicardie, E.R.; and Birch, H.G.: Nutrition, Growth, and Neurointegrative Development: An Experimental and Ecologic Study, *Pediatrics* 38:319-372 (Aug) 1966.