

## CHAPTER 6

# WEANLING DIARRHEA — A SYNERGISM OF INFECTION AND NUTRITION

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### Introduction

The preceding chapter presented the principles of field epidemiology as they apply to interactions of nutrition and infection. The present one shows how these principles were put to use in India and in Guatemala, the results that were obtained, and the bearing that the findings have on practical prevention and control.

The attempt to understand and control the acute diarrheas has broad significance, with implications beyond the direct morbidity and mortality these diseases cause. The attendant disability has important economic consequences.

In less developed countries where diarrheal disease is highly prevalent and a major cause of death, it is recognized that the synergism between diarrhea and malnutrition seriously affects the general health of young children, at the same time exerting a lasting effect on growth and development. The deterioration in nutritional state after an episode of diarrhea frequently results in patent malnutrition. As already brought out, this, in turn, commonly impairs resistance to other infections and also precipitates specific nutritional disease, notably kwashiorkor. Consequently, the community control of diarrheal disease is intimately tied to general health activities, with a proper balance between specific measures and the general procedures that relate to nutrition and environmental sanitation. Control of diarrheal disease is not an isolated effort, whether at national, state, or local level.

### The Diarrheas of a General Population

The commonest communicable diseases of man are not always the best understood. For example, the ordinary acute infections of the upper

respiratory tract, the common colds, give rise to more disability than any other known disease, and yet their etiologic agents remain much of a mystery, their clinical management is ineffective, and community control scarcely exists. Globally, the diarrheas and the dysenteries may not have equal rank in resulting morbidity, but in many localities they come close to it. As a killing disease, the diarrheas far overshadow upper respiratory illnesses. In large parts of the world deaths from diarrheal disease in the general population outnumber those from any other single cause (World Health Organization, 1964a). In all areas, they are a regular and prominent feature of deaths among infants and young children.

In most of the more highly developed countries, acute diarrheal disease has lost much of the significance it had no longer than fifty years ago. Many factors are responsible, including a favorable economy, improved environmental sanitation, technical gains in human nutrition and communicable disease control, and the development of modern pediatrics. The common disregard of the diarrheal diseases in regions where nutrition and sanitation are good gives a false idea of the significance these diseases have in technically less developed areas of the world. Furthermore, low as the death rate now is in countries with advanced sanitation and public health services, acute diarrheal disease still ranks among the five principal causes of death of young children, even in the USA (US Public Health Service, 1964).

“Acute diarrheal disease” has become the usual term to denote the general syndrome, for this is indeed a group of diseases that are not clearly distinguished one from another, either clinically or etiologically (Cvjetanović, 1962). Although something is lost in discarding the agreeably alliterative name of “the diarrheas and the dysenteries”, the substitute may promote appreciation of the broad epidemiologic unity of these acute intestinal illnesses.

The major endeavor in basic research on diarrheal disease is to distinguish further etiologic entities, which surely exist. In the management of patients, the clinician must make such divisions as are possible on the basis of microbial cause and separate the remaining cases into broad disease patterns susceptible to individual methods of management. Because of present limitations in clinical and laboratory differentiation (Higgins, 1956), a program for community control, which is here the main consideration, is preferably based on epidemiologic distinctions within the general syndrome—distinctions made possible by differences in behavior according to age of patients or social and ecologic characteristics of a population (Gordon, 1965). This procedure is especially indicated in developing countries in which control facilities are limited and much diarrheal disease exists. To attempt control by attention to individual diseases is currently impractical. To do so is to leave the bulk of the problem untouched.

Viewed thus, in its entirety, “acute diarrheal disease” is understood to include well-defined entities as well as intestinal disorders of unknown etiology. This is diarrheal disease as defined in the Hippocratic writings:

those conditions in which the main presenting sign is "an abnormal frequency and liquidity of fecal discharges". Typhoid and other enteric fevers, cholera, and food poisoning, each with its individual epidemiologic characteristics, are excluded.

The ordinary diarrheas and dysenteries have many common characteristics. They occur everywhere; in certain environmental situations, repeated attacks are frequent and usual at all ages, disability is great, and deaths are inordinately frequent. Group epidemiologic characteristics such as reservoir and source of infection, modes of transmission, period of communicability, and incubation time are common to the indeterminate acute diarrheas and to those caused by specific pathogens. Despite failure to isolate infectious agents from most patients, the spread of the disease in families and other groups of persons and the decline in incidence with advancing age clearly suggest that most cases are of infectious origin.

To ignore the accepted principle of specific control of communicable diseases, and to view acute diarrheal disease as a syndrome, brings no great loss. Current control practice is largely empirical; it depends on general measures for limiting the spread of infection and reinforcing host defense. Even for acute intestinal disorders of known etiology, such specifically directed measures as exist have minor usefulness.

The simplest and most natural division of the acute diarrheas epidemiologically is to separate those regularly and consistently present in a community, endemic diarrheal disease, from those whose typical occurrence is in frank epidemics. Three general situations are recognized as endemic and two others, as characteristically epidemic (Gordon, 1964). They are sufficiently distinct to profit from individual programs for control.

Endemic diarrheal disease may exist in a community at high or low levels, commonly distinguished as endemic or hyperendemic. The typical distribution of cases in a general population is sporadic or in family groupings, although there may be occasional waves of increased incidence or even true outbreaks. This is the classical fluctuating endemicity of many common infectious diseases of man, especially those of childhood, such as measles and chickenpox.

Of endemic diarrheal diseases, the group involving young children of ages less than five years outweighs all others in numbers of cases and deaths (Richard & Moinet, 1965). Special conditions distinct from those active in later life govern its presence (Ponnampalam & Musa, 1965; Gomez & Berria, 1965). A second general division includes the diarrheas of a general population other than young children; and the third, the diarrheas experienced by travelers, has its origin in abrupt changes in ecologic situations incident to change of residence.

Two primarily epidemic manifestations of acute diarrheal disease are recognized, although in both instances the reservoir of infection is in the prevailing endemic acute diarrheal disease of the regions where they occur.

The distribution of cases, however, is typically epidemic; and the outbreak subsides as the conditions responsible for its presence either end or are brought under control.

One example of this is epidemic diarrhea in nurseries for the newborn, a disease geographically limited to areas where babies are born in hospitals and housed together in the first weeks of life. The condition arises from this social circumstance and is therefore chiefly encountered in the developed countries. Among total diarrheas of the communities where it occurs, it is an inconsequential part; but fatality is regularly great, and infection occasionally spreads to general populations outside the hospital (Greengard et al., 1962), ordinarily to older pre-school children.

The second general class of epidemics results from a variety of circumstances, having the common denominator of a newly aggregated population, in large part strangers to each other and abruptly exposed to an unfamiliar environment. The attendant situations range from natural disasters—wind, fire, and flood—to the presence of migrant labor for seasonal agricultural activities or the construction of roads, buildings, or other improvements.

An outstanding feature of acute diarrheal disease in less developed areas is the concentration of cases among infants and young children during and immediately after weaning (Durand & Pigney, 1963). Malnutrition is especially common at this time. The two conditions are so interrelated that we have adopted the term "weanling diarrhea" as singularly descriptive of the existing synergism. A poor environmental sanitation contributes importantly to spread of the disease. The descriptions of this epidemiologic entity that now follow draw heavily on field studies in India and Guatemala as representative of areas where diarrheal disease is frequent and malnutrition prevails at a high level.

### **Acute Diarrheal Disease of Early Childhood (Weanling Diarrhea)**

As with most public health activities, epidemiologic understanding and the drafting of a control program demand first of all familiarity with the clinical nature of the disease. The syndrome of weanling diarrhea includes several specific bacterial diseases as well as a variety of infections due to irregularly pathogenic bacteria, enteroviruses, helminths, and protozoa. More often than not, no definable infectious agent can be identified. Clinical manifestations of diarrhea are invariably present, often accompanied by fever. (Looseness of the bowels may also be due to a variety of causes other than microbial or parasitic, including psychological factors.)

#### **Clinical characteristics**

In a particular locality, the specific diarrheal diseases cannot be distinguished clinically from each other, nor from the mass of microbiologically

undifferentiated diarrheas (Tuckman et al., 1962). Highly distinctive differences in general clinical behavior and severity exist, however, between the acute diarrheal disease of young children in less developed regions and that experienced by infants and toddlers in technically advanced countries (Hardy, 1959).

In less developed regions, the onset of clinical disease is acute and rapidly progressive, with liquid or semi-liquid stools, varying from three to as many as twenty a day. A proportion of patients, commonly about one-fourth, have blood or mucus in the stools and, frequently, pus. Fever may be absent, but low-grade fever is usual, along with malaise, toxemia, intestinal cramps, and tenesmus. The usual clinical course is four to five days. In malnourished children, a low-grade indisposition often continues for a month or more, sometimes as long as three months, with irregularly recurring loose stools, a progressively depleted nutritional state, and occasional recurrent acute episodes. The chronic recurrent form often constitutes as much as 15% of cases, and is limited essentially to malnourished children (Wittmann & Hansen, 1965). In infants with diarrhea and severe malnutrition, the biochemical disturbance is of a different nature from that in dehydrated infants without malnutrition (Metcoff et al., 1957). Dehydration and electrolyte imbalance are common and often difficult to correct, sometimes because of climatic factors and often because of the advanced stage of the disease when the patient is first seen. During an acute attack, mothers commonly restrict an already deficient diet, which aggravates the situation. Kwashiorkor or other nutritional deficiency disease is a frequent aftermath.

Case fatality for patients in the first and second years of life in general populations of less developed regions ranges from 1% to 4% (Gordon et al., 1963). At later ages, deaths are far less frequent (World Health Organization, 1964a). Infants less than one year old, especially those prematurely born (Lasbrey et al., 1963), are more likely to develop a serious illness than are older children (Goodwin et al., 1960). For hospitalized patients (Pérez Navarrete & Jan Robledo, 1961; Bevan, 1962), case fatality in these regions is often much greater (Athavale, 1963), sometimes as much as 30% to 40% for young children (La Torre, 1956).

By contrast, acute diarrheal disease in economically favored regions is a mild indisposition (Spence et al., 1954; Dingle et al., 1956) and usually more a cause of discomfort than of serious morbidity. The duration is as short as one or two days, although loose stools may continue for a week. Fever is far more likely to be absent than present. Deaths are few, although their number is often incompletely appreciated.

Relatively, acute diarrheal disease continues in high rank among the ten leading causes of death in early childhood (World Health Organization, 1964b; Zijl, 1966). Fifty years ago, case incidence and mortality rates were as high in now advanced countries (New York City Department of Health,

1962; Great Britain, Registrar General, 1902) as in developing regions today, and in some instances measurably greater.

### Agents of disease

The designation of acute diarrheal disease as a clinical syndrome in no way excludes specific disease entities. A few disease syndromes, such as infectious mononucleosis, have no demonstrated infectious agent, although they are evidently communicable. Other syndromes are composed almost wholly of specific infectious diseases of a wide variety, e.g., aseptic meningitis. Still others are a mixture of the known and the unknown, e.g., the common cold.

The diarrheal syndrome in its broad epidemiologic characteristics resembles the common cold. Both are clinical syndromes that include a minority of known disease entities, a predominating bulk of undifferentiated, presumably infectious, processes, and an indefinite number of non-infectious illnesses. The proportions are by no means fixed; the pattern is dynamic, frequently changing and with no characteristic distribution of elements, in either local or general areas (Olarie et al., 1964; Rao & Murti, 1965).

The recognized specific infectious diarrheas within the diarrheal syndrome include shigellosis, salmonellosis, enteropathogenic *Esch. coli* infections, and amebiasis. Cruickshank (1963) states that in Great Britain an etiologic agent can be identified in not more than 15% to 20% of all cases of diarrhea in a community, and perhaps in 30% of severe cases in hospitals (Landsman & Bell, 1965). In less developed regions where rates of incidence are high, one or other of the three bacterial agents is often present in less than 20% of cases in the general population: from recent reports, 11.4% in India (Sen, 1962; Prakash et al., 1963), 18.5% in Jamaica (Back & Brooks, 1962), and 9.4% in Malaya (Chan & Lucas, 1964). The usual frequency among young children is slightly in excess of those levels, for example, in Guatemala (Mata et al., 1965), in Argentina (Lubin et al., 1963), and in Romania (Wisner et al., 1963). During the recent epidemic of classical and El Tor cholera in India, twice as many hospital patients were reported to be suffering from an associated cholera-like diarrhea as from cholera itself (Lindenbaum et al., 1965; Carpenter et al., 1965; McIntyre & Feeley, 1965). With rare exceptions, no recognizable intestinal pathogen could be demonstrated (McIntyre et al., 1965; Mukerjee, 1965). A proportion of 40% of diarrheas of early childhood associated with one of the recognized bacterial pathogens is rare, and 50% is highly exceptional.

As an example, in a Guatemalan highland village (Gordon et al., 1964b), at least one of the three bacterial pathogens known to cause diarrhea was present in 24% of 578 patients under five years of age observed during a period of 17 months (Table 22). A single specimen of feces, usually obtained by rectal swab, was cultured on three different bacteriologic media.

TABLE 22. BACTERIAL PATHOGENS PRESENT IN 578 CASES OF ACUTE DIARRHEAL DISEASE OF CHILDREN, 0-4 YEARS OLD, IN A RURAL GUATEMALAN VILLAGE\* BETWEEN FEBRUARY 1961 AND JUNE 1962

Bacterium	No. of cases	% of all cases of acute diarrheal disease
<i>Sh. dysenteriae</i> 1	10	1.7
<i>Sh. dysenteriae</i> 2	4	0.7
<i>Sh. flexneri</i> 1	2	0.3
<i>Sh. flexneri</i> 2	23	3.8
<i>Sh. flexneri</i> 3	32	5.5
<i>Sh. flexneri</i> 6	36	6.2
<i>Sh. boydi</i>	5	0.9
<i>Sh. sonnei</i>	9	1.6
<i>Salmonella</i>	1	0.2
<i>Esch. coli</i>	17	2.9
None	439	76.0

\* Santa María Cauqué.

An additional 115 cases were subjected to intensive examination, by methods beyond ordinary practical field application. Specimens included material from both rectal swabs and stools. A minimum of five serial examinations were made on successive days, and two augmented lines of culture media were employed. The result was isolation of a bacterial pathogen in 35% of cases, the gain being mainly in *Salmonella* and *Esch. coli*, the less frequent members of the group. The demonstration of *Shigella* was not significantly increased.

Isolation of a pathogen from the stools of a patient does not, of course, establish an etiologic relationship between this pathogen and the diarrhea. Diarrhea due to other causes can occur in a bacterial carrier. Furthermore, in no less than 12% of patients with a demonstrated pathogen in the Guatemalan experience, two infectious agents were present concurrently, with no certainty which, if either, was the responsible agent. This experience has been duplicated in many places (Kareva et al., 1962; Banta et al., 1964; Young et al., 1962; Guardiola-Rotger et al., 1964). Enteroviruses were frequently associated with bacterial agents; and more often than not, a pathogenic bacterium when present was accompanied by a protozoon or other intestinal parasite. High or low incidence of diarrhea was not a determining factor in these observations. The usual order of frequency (Nehaul, 1960; Ingram et al., 1966) of the three pathogens in most countries is *Shigella*, *E. coli*, and *Salmonella*.

Every serotype of the four broad groups of *Shigella* has been isolated in some place at some time from child patients with diarrhea. No particular *Shigella* characterizes the disease. From a world standpoint, however, the Flexner or B group is most common in pre-industrial areas (Gordon & Babbott, 1959; Goodwin et al., 1960; Fossaert et al., 1961; Sen et al., 1963; Akman, 1965), whereas *Sh. sonnei*, or group D, tends to predominate in Britain (Taylor, 1957; Cruickshank, 1963) and other countries of Europe

(Madjarić & Zdravković, 1963). Group A is of lower frequency. The classical type 1 of this group, the original Shiga bacillus, appears in relatively few places (Antia et al., 1961; Davey, 1962). Types of *Sh. boydii*, group C, are least common, except in the Middle East. In general, *Shigella* seldom accounts for more than 10% to 15% of childhood diarrheas in most developing countries and is of still less consequence in general child populations of advanced societies, although exceptions are known (Nelson et al., 1967). Cases are relatively few before six months of age. In all situations, in less developed regions (Roux et al., 1963; Donoso, 1964) and in the USA (Rosenstein, 1964), *Shigella* is usually responsible for more than its expected proportion of severe cases, as judged by the presence of blood or mucus in the stools.

*Salmonella* accounts for relatively few cases of early childhood diarrhea, whether in pre-industrial regions or otherwise. This finding is not universal; for, in some areas, such as Argentina (Lubin et al., 1963), Tunisia (Huet, 1962), and Costa Rica (Moore et al., 1966b), patients with salmonellosis outnumbered those with shigellosis.

Next to *Shigella*, the ten or more serotypes of enteropathogenic *Esch. coli* are the commonest organisms found among bacteriologically differentiated cases in early childhood. These infections are recognized with greater frequency in industrialized regions than in developing countries, one likely reason being that they receive more attention there. In Goodwin's series (1960) of clinic and hospital patients in Arizona, *Esch. coli* was demonstrated in about 34% of patients less than one year old, mainly from three to six months of age. They constituted 89% of cases at all ages attributable to that agent. Russian experience (Kagan et al., 1961; Kareva et al., 1962) showed an even greater proportion among diarrheas of infants. Cases also occur in the second and third years, and evidence increases (Kagan et al., 1961) that their significance at these immediately older ages has been somewhat underrated. Diarrhea of this origin accounts for the larger part of severe infant diarrheal disease in Great Britain.

As reports accumulate from less developed countries, similar findings are reported for hospitalized children: in the Philippines (Briones et al., 1963), in Indonesia (Lie et al., 1960), India (Prakash, 1962), Chile (Rodríguez-Leiva, 1960), and western Alaska (Brenneman & Fortuine, 1966). The importance of these infections in general populations, especially when the distribution of the disease is sporadic and endemic, is less well determined. Unusually careful studies in a Guatemalan village, where children were visited at twice-monthly intervals from birth until the age of two years (Mata et al., 1967) gave only a single case of *Esch. coli* infection among 262 cases of acute diarrheal disease. The results support the general observation that incidence is lower in rural developing areas than in industrial areas. They agree with studies of diarrheal disease in native New Guinea infants (Lawson & Curtis, 1967).

There is general agreement that clinical disease due to *Esch. coli* is uncommon among older children and adults; but infection, as distinguished from infectious disease, is another matter. Carriers are recognized fairly frequently: often among both household and neighborhood contacts in epidemic situations (Boris et al., 1964); among 5% of pediatric patients with no intestinal disease (Solomon et al., 1961); among hospital staff members and family members associated with child patients (Minck et al., 1962); and in general populations of children (Cooper et al., 1957; Gamble & Rowson, 1957; Thomson, 1955) and adults (Cooper et al., 1959; Barua, 1963; Perepelkin et al., 1963). A single examination of stools showed that 11% of 657 pregnant women had various serotypes (Schaffer et al., 1963).

The existence of carriers in appreciable numbers bears directly on modes of transmission and on the origin of diarrheal disease in early childhood. It also emphasizes that concurrence of symptoms and an associated infectious agent is not itself evidence of pathogenicity. Solomon and co-workers (1961) have stressed this point, and Ewing and associates (1963) have warned that many reports of the bacteriology of infantile gastro-enteritis are based on inadequate serologic methods, and that slide agglutination tests alone are inadequate beyond presumptive diagnosis. These findings emphasize a need for intensive investigations and an exact evaluation of *Esch. coli* infection in diarrheas of early childhood to give information beyond the present generalizations.

The viruses now known do not provide the answer to the etiologic enigma of the acute diarrheal disease of early childhood in general populations. The main reason to suppose that they might be responsible (Higgins, 1956) is that most cases are clearly of an infectious nature and yet often no bacterial or parasitic agent can be demonstrated. The case for an etiologic role of viruses has been presented by a number of workers (Dodd, 1959; *Lancet*, 1963; Sabin, 1963; Melnick, 1965).

Studies of healthy children (Gelfand et al., 1957; Honig et al., 1956; Ramos-Alvarez & Sabin, 1956; Galbraith, 1965) show enteroviruses to be commonly present in the feces. They transiently inhabit the gastro-intestinal tract, are most frequently isolated before the age of four years, and vary in number with time and place. In the INCAP studies in Guatemala, enteric viral agents were isolated with equal frequency from about a half of the rectal swabs from children with and without diarrhea.

Although no epidemic of acute diarrheal disease in a general population is known with certainty to have been due to an enterovirus, filterable agents have been demonstrated on numerous occasions in selected cases (Jordan et al., 1953; Gordon, 1955; Abraham & Cheever, 1963). Moreover, several outbreaks under the special conditions of the newborn in nurseries have been related to ECHO viruses, notably type 18 (Eichenwald et al., 1958), type 14 (Lépine et al., 1960) and also other types (Bergamini & Bonetti,

1960; Cramblett et al., 1962). Finally, infection has been induced experimentally in volunteers (Buckland et al., 1959) with enteroviruses isolated from patients, and has occurred accidentally in laboratory workers (Klein et al., 1960; Cramblett et al., 1962).

Dingle et al., (1965) have emphasized the common occurrence in Cleveland of childhood illnesses with both respiratory and diarrheal symptoms. Among Guatemalan pre-school children, the seasonal peaks of diarrheal disease and of acute respiratory infections coincide in the rainy months from June to September, and clinical association of the two sets of symptoms occurs with an indefinite frequency at all seasons (Gordon et al., 1968). In Scotland, Stott et al., (1967) compared viruses isolated from the nose and throat of 113 pre-school children admitted to hospital for respiratory illnesses with viruses from a second group having diarrheal disease. Patients were matched for age (mean age 18 months) and for time of admission. Sixteen per cent of those with respiratory infections harbored an enterovirus, as did 19% of patients with diarrheal disease. Adenoviruses were equally prevalent in both groups: 8%. The authors suggest a low pathogenicity of both infectious agents, or an ability to cause both respiratory and diarrheal symptoms. In another study of viruses among hospital patients with respiratory and other diseases, Holzel et al. (1965) found enteroviruses less frequently among patients with respiratory disease than did Stott; throat secretions of a control group of patients with gastroenteritis gave few isolations of enterovirus: 4%. These viruses were an inconsequential finding in acute respiratory infections studied by Clarke et al. (1964).

Controlled virologic studies of groups of patients with sporadic diarrhea in England (Sommerville, 1958), Canada (Walker et al., 1960; McLean et al., 1961; Joncas & Pavilanis, 1963), the USA (Ramos-Alvarez & Sabin, 1958), and Mexico (Ramos-Alvarez & Olarte, 1964) have given varying results, with a preponderance sometimes of ECHO viruses (Ejercito et al., 1966) and sometimes of Coxsackie group B viruses (Pelon et al., 1966).

Yow et al. (1963) have compared the results of several investigations with those of their own three-year experience in Houston, Texas. The conclusions reached are generally representative of current opinion. There was no evidence that poliovirus or any of the group of Coxsackie viruses causes the diarrheal syndrome alone. There was some indication that ECHO viruses may cause sporadic cases of diarrhea in young children; but, as a group, the enteroviruses could not be shown to play a significant role in the production of infantile diarrhea. There was no evidence of a bacteria-viral synergism; peak incidence of the two was seasonally different. Workers from the same laboratory (Parks et al., 1966, 1967) extended their studies to Pakistan and obtained results in general agreement with the earlier findings. Viruses were isolated from about 80% of patients with diarrheal disease and in equal proportion from controls, with no significant differences in respect of age, sex, or socioeconomic status.

Although proof is lacking that ECHO and other enteroviruses are an important cause of primary diarrhea, the potential pathogenic role of these and other viruses cannot be dismissed lightly, if only because of the early ages at which they are found and the observed recurrent waves of diarrheal disease at about three-year intervals observed in several less developed regions (Bruch et al., 1963).

In addition to the varying proportions of commonly recognized intestinal pathogens, the intestinal flora in health as well as in acute diarrheal disease contains large numbers of commensal organisms, both aerobic and anaerobic, that are normal inhabitants of the intestinal tract, without accepted pathogenicity. Between these extremes is a group of infectious agents of indeterminate and irregular pathogenic power (Ramacciotti et al., 1962; Fulton, 1965), poorly evaluated as to numbers and of diverse kinds (Poindexter, 1953). They include certain serologically distinct *Esch. coli* other than those commonly recognized in diarrheal disease, other bacilli, enteroviruses in profusion, coagulase-positive staphylococci, occasional fungi, and intestinal protozoa and helminths. As a group, they are of low-grade pathogenicity, with evidence to suggest that, if they attain disease-producing power, it is mainly through favorable host or environmental factors, of which malnutrition is a major consideration. Observations by Dammin (1964, 1965) at INCAP suggest a mechanism of pathogenicity analogous to that in cholera, in which an overgrowth of micro-organisms in malnourished persons produces huge numbers at all levels of the intestinal tract.

Infections of other systems (Bloch, 1962; Lelong, 1963), principally of the respiratory tract and its appendages (McCorkle et al., 1956; Ryan, 1962; Lawson & Curtis, 1967), have the ability to cause intestinal disorders to flare up. Measles has a prominent place among general systemic infections (Morley et al., 1963), as has chickenpox (Salomón et al., 1966).

Certain foods of themselves can induce acute diarrhea. Some act through their content of roughage or condiments; and a few are directly poisonous (Eichenwald & Kotsevalov, 1960)—for example, some varieties of mushrooms and fishes. Diarrhea is also commonly associated with a number of specific nutritional diseases, including pellagra, beriberi, and kwashiorkor (Hansen et al., 1962).

Toxins formed in foods by growth of staphylococci and other bacteria are a common source of epidemic diarrhea in the form of food poisoning (Cockburn et al., 1962) and, to an ill-defined degree, contribute to sporadic disease.

### Epidemiology

The universal occurrence of acute diarrheal disease in all populations of the world suggests innate host characteristics conducive to the illness, and common to all mankind. It is also reasonable to assume that features in

human behavior, in cultural practices, and in the social environment of aggregates of man will influence propagation and presence of the diarrheas.

Considered as a group, and despite indefinite and diverse infectious agents, the reservoir of infection of the infectious diarrheas is apparently almost wholly confined to man. A few intestinal infections, notably salmonellosis, may be spread by animals, but this disease is also transmitted from man to man. In all recognized specific diarrheal disease, carriers have a significant place in the community reservoir of infection (Gordon et al., 1964b). In Guatemalan villages, for example, carrier rates in the general population of children without diarrhea under five years of age were 7.8% for *Shigella*, 0.1% for *Salmonella*, and 4.2% for enteropathogenic *Esch. coli* (Table 23). Epidemiologic evidence strongly supports the probability that diarrheas of indeterminate etiology have appreciable carrier rates. The immediate source of infection in most transmissible diarrhea is probably feces.

TABLE 23. CARRIERS OF ENTERIC BACTERIAL PATHOGENS AMONG CHILDREN WITHOUT DIARRHEA, BY AGE, IN THREE GUATEMALAN HIGHLAND VILLAGES\* 1959-1962

Age in years	No. of children	<i>Shigella</i>		<i>Salmonella</i>		<i>Esch. coli</i>		Total	
		No.	%	No.	%	No.	%	No.	%
Under									
1	647	10	1.5	1	0.2	31	4.8	42	6.5
1	690	61	8.8	0	—	38	5.5	96	13.9
2	678	71	10.5	1	0.1	25	3.7	93	13.7
3	676	69	10.2	0	—	24	3.6	90	13.3
4	459	35	7.6	2	0.4	14	3.0	47	10.2
Total	3150	246	7.8	4	0.1	132	4.2	368	11.7

\* Santa Cruz Balanya, Santa María Cauqué, and Santa Catarina Barahona.

Infectious diarrheas, whether etiologically distinct or undifferentiated, have common modes of transmission, although noteworthy differences exist regarding distribution in time and place. Endemic and sporadic diarrheal disease is transferred predominantly by direct contact (Scott, 1953), by hand-to-mouth infection. Usually, indirect contact through objects freshly contaminated with feces has minor significance, although it is more likely to occur with intestinal infections than with most others. Flies are generally not the main mode of transmission, although, wherever environmental sanitation is poor, they contribute at certain seasons.

The classical picture of epidemic diarrheal disease is one of an infection derived from a common source (Belikova & Kolosov, 1960), such as water, milk, or solid foods, with the outbreak rising and falling abruptly. Such epidemics are no feature of weanling diarrhea nor of diarrheas in early childhood, except where infants and toddlers are involved in a general community outbreak. Nevertheless, epidemics due to contact spread are

frequent among young children in less developed areas. Characteristically, these outbreaks are of slow evolution; they fail to reach the high incidence of common-source outbreaks; and they follow a protracted course of a year or two—occasionally even three or four years when the population is scattered and sparse, as in Greenland settlements in the Arctic (Gordon & Babbott, 1959). Under endemic conditions, a seasonal peak in late spring and summer is usual (Huncal, 1961; Malherbe et al., 1963).

The incubation period is among the more regular epidemiologic characteristics. Clinical manifestations typically appear two or three days after exposure. For example, the usual incubation period in shigellosis is less than four days. This period is also usual for the group of undifferentiated infections and for most others specifically identified.

The duration of communicability is not well known. Most of the evidence relates to shigellosis, in which infectiousness continues for the duration of symptoms and briefly thereafter (Philbrook & Gordon, 1958). Chronic convalescent carriers are stated to be few. Existing observations, however, relate mainly to adults and to patients in good nutritional state. The longer clinical course of diarrhea among malnourished children of less developed regions, and the tendency of the disease to relapse, suggest that communicability may be appreciably longer under such conditions—a possibility supported by the high carrier rates for *Shigella* in many communities (Gordon et al., 1962c), of the order of 8%.

In a closed institution for young children in Guatemala, heavily seeded with *Shigella*, carrier states persisted as long as five months (Mata et al., 1966) in chronic, recurrent shigellosis. The convalescent carrier state after acute attacks was longer than usually estimated. In a school outbreak in Great Britain, convalescent carrier states of a month or more were observed, frequently with interposed negative findings (Beer et al., 1966). The subject needs further investigation by serial studies of convalescent and healthy carriers in open communities of these regions.

Limited studies suggest that carrier rates for *Esch. coli* may be greater than the numbers usually identified. *Salmonella* carriers in acute diarrheal disease of early childhood have had minor attention, and appear to be few (Hardy & Watt, 1945).

The known facts about resistance and susceptibility to infection are also limited. In the developing countries breast feeding is the rule and the number of cases during the first six months of life is relatively few (Yekutieli et al., 1958) compared with those in later years. During the second six months, few infants escape diarrheal disease. Thereafter, incidence decreases with age, so that attack rates in schoolchildren are much lower and the incidence in the adult population is far less.

Repeated attacks of acute diarrheal disease in the course of the first and second years are the rule in the developing countries. In the authors' Guatemalan experience, about one-half of the children had more than one

attack during their second year. It is evident that a single attack gives no general immunity, and yet it is equally certain that resistance increases with age. The suggestion is that a pattern of resistance develops comparable to that occurring in influenza, in which specific and enduring immunity to most of the locally prevailing agents is gradually acquired with age. A particular pattern holds for a particular area. Transfer to another region and contact with a new set of infectious agents results in a fresh need to accommodate, as evidenced by the well-known diarrhea of travelers (Hanelvold, 1960; Kullander & Heinlaid, 1963; Banta et al., 1964).

The spread of acute diarrheal disease of early childhood in families and other groups of persons, and the decline in incidence with increasing age, clearly suggest that most cases have an infectious origin despite the common failure to isolate microbial agents. The broad behavior of the disease suggests that cases originate mainly from factors related to the sanitary state of the environment (Hunt, 1963), household hygiene (Robertson, 1957), and nutrition (Sabin, 1963). The relative significance of these several determinants is to be sought in the results of field investigation. The two studies now to be discussed are from opposite sides of the world, and yet the findings are in such agreement as to suggest the existence of a common principle.

### Weanling Diarrhea in the Punjab, India

#### Collection of data

These observations in northern India were part of a broader field study of population dynamics lasting from 1954 to 1960 (Gordon & Wyon, 1960). A continuing count of births and deaths was made by household visits to all families of eleven villages in Ludhiana District (Gordon et al., 1961). The area is rural and wholly agricultural. The people live in villages, which in the study area had populations that ranged from roughly 280 to 1900.

Over a period of four years, among about half the population of 12 000 additional data were collected on illnesses and injuries in children (Gordon et al., 1963). Observations were on a cohort basis, starting with newborn infants and continuing for the duration of the study. Thus, four annual cohorts were accumulated, the first observed for four years and the last for a single year. Feeding practices and weaning were correlated with frequency of attack of acute diarrheal disease and with deaths from that cause. The number of children observed during the first year of life was 775, since all four cohorts were represented; those of the second year, drawn from three cohorts, numbered 462; there were 221 children between two and three years of age; and children in their fourth year numbered 46. The numbers decreased for each year of age, primarily because one fewer cohort was

represented, but also as a result of natural attrition incidental to deaths and migration.

Case finding of acute diarrheal disease and information on feeding practices was obtained through monthly visits by non-medical field investigators working under the supervision of a physician. For an estimated 10% of visits, the interval was up to three months, but occasionally it was as long as six months; these longer intervals were due, in most instances, to absence of mother and child from the village. The information in these cases was obtained retrospectively, through history taking. Deaths were confirmed promptly through field investigation by a physician of the study group. Changes in feeding practices incident to the start and completion of weaning were analysed by three-month periods.

Diarrheal disease was related to a particular feeding program by its presence or absence in the quarterly period, not by the number of attacks that may have occurred during that time. Case incidence as used in this study is calculated on that basis. This rate approximates closely to an incidence derived from actual numbers of attacks, because, when monthly visits to a subsample of the population were made by a physician, two separate attacks of diarrhea within a three-month period were found to be rare.

### Feeding of infants

The fate of newborn infants in many pre-industrial areas seems to depend largely on whether they are breast fed or not—either they are nursed or they die (Hartemann, 1961). This is supported by the data on the 775 babies presented in Table 24. Sixteen infants received no food, death occurring shortly after birth—13 infants died within minutes or hours, while three survived for one to five days. These deaths were from obstetrical difficulties

TABLE 24. DEATHS AND DEATH RATES BY FEEDING REGIMEN IN SEVEN PUNJAB VILLAGES 1955-1959

Feeding regimen	Newborn infants		Neonatal deaths, 0-28 days inclusive		Postneonatal deaths, 29 days to 11 months inclusive		Infant mortality, 0-11 months inclusive	
	No.	% of total	No.	Deaths per 1000	No.	Deaths per 1000	No.	Deaths per 1000
No food given	16	2.1	16	1000.0	—	—	16	1000.0
Artificial feeding from birth	20	2.6	15	750.0	4	200.0	19	950.0
Breast-fed at birth	739	95.3	34	46.0	55	74.4	89	120.4
Total	775	100.0	65	83.9	59	76.1	124	160.0

and congenital anomalies, and also from prematurity, which rendered breast or other feeding impossible under the existing conditions. Twelve infants were males, and four were females.

Twenty other infants were fed artificially from birth, and 19 died: 11 within the first week, 4 others before the end of the first month, 3 within the remaining months of the first half-year, and one in the third quarter. The fact that one infant was living at the end of two years was remarkable in that she had survived no fewer than four attacks of acute diarrheal disease, a respiratory infection with pneumonia, a local and a general sepsis, and whooping cough.

The need for artificial feeding arose in 5 instances from causes associated with the mother: two mothers died in childbirth, two had no milk, and one was critically ill with pneumonia. In 10 other cases, breast feeding could not be instituted because of weakness of the child; and 5 would not take the breast. Of the 20 infants in this group, 15 were full term, and 5 were premature or born weak and small. In contrast to the group who died shortly after birth, 5 of this second group were males, and 15 were females. The usual food was milk—goat milk most commonly, but also milk from cows and the water buffalo. Five had only honey and water, or sugar and water. As a group, these infants were clearly no average risk; but the death rate in the absence of breast feeding was appalling.

Fortunately, 95.3% of the 775 infants in the series were breast fed. Their infant mortality was 120 deaths per 1000 live births, in contrast to a rate of 950 for the artificially fed. By almost universal custom in the Punjab, nursing starts on the third day of life. For the first two days the child is given water, sweetened with honey in the winter months and sugar in the summer. Highly diluted milk from a cow or other animal is also offered, which the baby sucks from a cloth or from cotton wool dipped into a brass bowl containing the mixture. The procedure lacks sanitary protection. Although the milk is boiled, the water is not, and the bowl containing the mixture usually sits under the bed until its contents are exhausted. The amount taken is relatively small.

Breast feeding followed no regular program, being essentially on demand and at the usual meal times of the family. It continued for long periods, as seen in Table 25. At least two children were still partially breast fed at the end of four years.

### **Weaning procedures**

Weaning was a gradual process, usually lasting a year or more, with breast feeding commonly continuing until the next pregnancy was recognized, or even longer. Weaning is interpreted here as beginning when food supplements are regularly added to breast milk. It ends when breast feeding ceases and the child is wholly on a general diet. An infant in the course of

being weaned, or during the three months immediately after breast feeding ends, is termed a "weanling".

The usual practice was to supplement breast feeding with other milk at about the sixth or seventh month. Goat's milk was preferred; that of the cow ranked next; and milk of the water buffalo was also much used. It was administered by cup, after having been diluted with an equal amount of water. If milk was given at an earlier age, a small teapot-like vessel, from which the child sucks or drinks, was usually used, or, occasionally, a medicine dropper or any bottle equipped with a rubber nipple. The milk was invariably boiled, but not the diluting water. Powdered or other processed milk was almost unknown.

TABLE 25. CASES AND DEATHS FROM ACUTE DIARRHEAL DISEASE AMONG WHOLLY BREAST-FED CHILDREN, BY QUARTER YEARS, IN SEVEN PUNJAB VILLAGES, 1955-1959

Age in months inclusive	No. of children breast-fed throughout period	Received breast milk only		Cases of acute diarrheal disease among breast-fed only	Incidence: cases per 100 wholly breast-fed children per year	Deaths from diarrheal disease among wholly breast-fed children
		No.	%			
0- 2	736	524	71.2	178	135.9	4
3- 5	685	380	55.5	118	124.2	0
6- 8	669	196	29.3	90	183.7	3
9-11	638	91	14.3	29	127.5	0
12-14	421	31	7.4	7	90.3	0
15-17	378	17	4.5	5	117.6	2
18-20	296	3	1.0	1	133.3	0
21-23	252	1	0.4	0	---	0
24-26	100	1	1.0	0	---	0
27-29	77	0	---	—	---	0

Solid foods were not generally given before the sixth month, because of the popular belief that early administration resulted in liver disease likely to persist through life. They were introduced from the sixth to the twelfth month—somewhat earlier if milk was not available. By the twelfth month, 50% of children received some solid food. Preparation of special foods for the baby, in semi-solid or other form, such as gruels or mashed vegetables, was rare. The child partook of the family diet, preferably an unleavened bread from maize; bread made from wheat, *chapatti*, was avoided when possible because of the belief that it tended to lodge in the throat. Eggs, some fruits, fish, and meat were forbidden because they are "hot" foods.

A number of herbal infusions, commonly made from rose petals or a plum-like fruit, *jamon*, were used regularly to counteract constipation.

#### Acute diarrheal disease among wholly breast-fed children

The children recorded in Table 25 as breast-fed throughout a particular quarter-year include those nursed to the end of the indicated three-month

period or, in case of death, as long as they survived. Children wholly weaned from breast milk during a particular period or those lost to the study by emigration were not counted.

The same conditions apply to children recorded as receiving only breast milk. They had no other food, except that they were sometimes given small morsels from the family table, even within the early months. These were administered more as a tranquilizer than as nourishment and are so regarded in this analysis. The differences in numbers in the second and third columns of the table represent children still breast fed but receiving some other food. They are accounted for in succeeding tables.

During the first three months of life, 71% of breast-fed children received only breast milk, and more than a half still received only breast milk during the second quarter-year. Thereafter the proportion declined sharply as other foods were added to the diet. An inconsequential number were stated to have had only breast milk well into the second year and, in one instance, until the beginning of the third year. In view of the fallibility of information on minor events (Gordon et al., 1962a) and the expected failure of breast milk to meet nutritional requirements after six months, the validity of statements regarding breast feeding exclusively for more than one year is doubtful.

From birth until six months of age, case rates of acute diarrheal disease among infants fed wholly on breast milk were about 130 per 100 children per year. During the third trimester, the rates rose significantly, and then returned toward the end of the year to a level essentially the same as that previously prevailing. If anything, the values thereafter were somewhat less; the numbers of children were, however, too small to judge reliably. The increase in rates in the third quarter coincided with the usual beginning of weaning and the introduction of other foods.

Why there was a rise in acute diarrheal disease in wholly breast-fed children is undetermined. There is the possibility that some other foods were given, despite a history to the contrary. The third quarter is also the time when children are more exposed to infection, as they begin to creep about and put things in the mouth; teething starts at about that time.

At all ages at which numbers were sufficient to permit reasonable comparison, not only was acute diarrheal disease less frequent among the wholly breast-fed than among those with subsequent dietary regimens, but it was often less fatal. The case fatality rate was 2.1%.

#### **Diarrheal disease during weaning**

Since the Punjab is a good agricultural region and the people live mainly in small villages, milk of the cow, water buffalo, or goat was commonly available and was usually the first food introduced, either with the intent of weaning or by necessity, because of failing breast milk. The usual progres-

sion thereafter was to solid foods and eventual weaning from the breast. For 42 children, solid foods were the first addition; no extra milk was given.

It is to be emphasized that, in the tabulations, the amounts of milk and other foods and their precise nature are unknown; dietary histories were not taken. The information is based on the statement of the mother that a particular program was followed at the time indicated. Variations in amount and kind of supplementary foods are known to have been material, according to social and economic status as judged by caste; and the foods children received were often palpably insufficient to meet the needs for protein and other essential nutrients. Milk, when given as the main supplement, was sometimes in such small amounts or so heavily diluted as to result promptly in malnutrition.

#### *Breast-fed children with added milk*

In this experience, as shown in Table 26, 29% of breast-fed infants were receiving the single supplement of other milk by the end of the first three months, and close to a half by the time they were nine months old. At 12 months, the proportion subsisting on a wholly milk diet—breast or other—decreased rapidly as solid foods were added; and the child came within the next category—“breast milk, other milk, and solid foods”. A comparison with the data in Table 25 shows that the incidence of acute diarrheal disease was greater among children having milk supplements than among those on breast milk alone, whatever ages are compared. Deaths from diarrheal diseases also were more numerous, the case fatality rate being 3.0% for the group as a whole, compared with 2.1% for strictly breast-fed infants.

#### *Breast-fed children with solid foods the initial and only addition*

Relatively few breast-fed children started the weaning process with solid foods (Table 26). Those who did had usually continued to be wholly breast fed for longer than normally, the change being made late in the first year of life. The case rate for diarrhea among this group was slightly in excess of that for children who started weaning with milk, although the numbers are too small for any certainty, especially at the older ages.

Children on this regimen tended to be completely weaned from breast milk to a general diet earlier than were children who had both a milk and a solid food supplement. Only two infants persisted through the twenty-sixth month on breast feeding with a supplement of solid food. At that time, the 77 children still on the breast were receiving other milk plus solid foods.

There were no deaths among the 38 cases of acute diarrheal disease in children on breast milk and solid food only.

TABLE 26. ACUTE DIARRHEAL DISEASE AMONG BREAST-FED CHILDREN IN THE COURSE OF WEANING, BY DIETARY SUPPLEMENT, IN SEVEN PUNJAB VILLAGES, 1955-1959

Age in months inclusive	No. of children observed	Breast-fed throughout period	Breast milk with other milk			Other milk plus solid foods			Solid foods, no milk		
			No.	Cases of acute diarrheal disease	Incidence: cases per 100 per year	No.	Cases of acute diarrheal disease	Incidence: cases per 100 per year	No.	Cases of acute diarrheal disease	Incidence: cases per 100 per year
0-2	775	736	210	91	173.3	0	—	—	2	0	—
3-5	696	685	294	129	175.5	5	1	80.0	6	2	133.3
6-8	682	689	328	170	207.3	127	75	236.2	18	8	177.8
9-11	667	638	258	97	172.4	256	164	220.1	24	9	150.0
12-14	482	421	98	30	122.5	277	144	207.9	16	8	213.3
15-17	449	378	43	9	83.7	300	119	168.7	18	5	111.1
18-20	438	298	13	5	163.9	270	128	189.6	10	2	80.0
21-23	429	262	4	1	100.0	240	76	126.7	7	3	171.4
24-26	221	100	0	0	0	97	39	160.8	2	0	200.0
27-29	218	77	0	0	0	77	20	103.9	0	0	0
30-32	217	57	0	0	0	67	18	126.3	0	0	0
33-36	215	49	0	0	0	49	15	122.6	0	0	0
36-38	46	5	0	0	0	5	3	240.0	0	0	0
38-41	46	3	0	0	0	3	1	133.3	0	0	0
42-44	45	2	0	0	0	2	0	—	0	0	0
45-47	45	2	0	0	0	2	0	—	0	0	0

*Breast-fed children with added milk and solid foods*

There is some evidence that the addition of solid foods in general was longer delayed when other milk was the first supplement than when weaning began with solid foods. At the end of the first year, 47% of breast-fed children were receiving all three foods; after the second year, 95%; and, by the end of the third year, the practice was universal among children still breast fed (Table 26).

At all ages, children given solid foods had more acute diarrheal disease than children on a milk diet. The progression was: lowest rates for the wholly breast fed, intermediate for those given additional milk, and highest for children on the more complex diet.

**Acute diarrheal disease after weaning**

The maximum impact of the weaning process on diarrheal disease occurred at the end of breast feeding, and the rates continued high for several months thereafter. An increase in diarrheal disease began with the first supplementation of breast milk; it ended with adjustment to the new diet. The after-effects of that experience continued to influence the general health and the growth and development of the child for a long time.

Table 27 presents the observed frequency of diarrheal disease by quarterly periods according to the age at which the change to a general diet was completed. The right-hand section of the table shows the experience of children of the same ages who had been weaned in the immediately preceding three months.

TABLE 27. ACUTE DIARRHEAL DISEASE AMONG ORIGINALLY BREAST-FED CHILDREN AT AGE WEANED FROM BREAST AND AT SUBSEQUENT AGES, BY QUARTER YEARS, IN SEVEN PUNJAB VILLAGES, 1955-1959

Age in months, inclusive	Breast-fed throughout	Weaned from breast				Previously weaned			
		No.	Cases of acute diarrheal disease	Cases per 100 per year	Deaths from diarrheal disease	No.	Cases of acute diarrheal disease	Cases per 100 per year	Deaths from diarrheal disease
0- 2	736	3	2	266.7	0	-	-	-	-
3- 5	685	4	1	100.0	0	3	2	266.7	2
6- 8	669	8	7	350.0	0	4	1	100.0	1
9-11	638	11	8	290.9	0	7	3	171.4	1
12-14	421	30	18	240.0	0	11	6	218.2	0
15-17	379	31	13	167.7	0	40	15	150.0	2
18-20	296	79	42	212.7	0	61	35	229.5	0
21-23	252	39	15	153.8	0	138	54	156.5	1
24-26	100	34	14	164.7	0	87	30	137.9	0
27-29	77	21	7	133.3	0	120	26	86.7	1
30-32	57	20	9	180.0	0	140	53	151.4	0
33-35	49	8	3	150.0	0	158	45	113.9	0
36-38	5	2	1	200.0	0	39	7	71.8	0
39-41	3	2	1	200.0	0	41	9	87.8	1
42-44	2	1	0	---	-	42	6	57.1	0
45-47	2	0	-	---	-	43	5	46.5	0

The three-month period after breast-feeding ceased carried the greatest risk of diarrheal disease. In general, incidence was numerically greater than for equivalent ages of the wholly breast fed (Table 25) or for those in the process of weaning but still breast fed (Table 26). Few children were weaned completely during the first year of life; most of them were weaned during the second year; a fair number, in the third year; and an occasional child, not until the fourth year. The mode in this study was 19.4 months.

The appreciable increase in diarrheal disorders associated with the introduction of solid foods while the child was still breast fed is a feature of the data presented in Table 26. When breast feeding stopped and the infants continued on solid foods and milk, as most of them did, another increase in diarrhea occurred. Presumably, the solid foods then given were in greater amount and of more diverse kinds; and, in some cases, malnutrition worsened because of the inadequate nutritive value of these foods. Again, the relatively few children who were weaned directly to a milk diet, particularly those of an early age, had more diarrhea than those given milk as a supplement to continued breast feeding.

The occurrence of diarrhea among children weaned in the preceding three months was of about the same order of magnitude as among children of the same age who were still in the course of weaning. The essential difference was in case fatality. In this study (Table 27), no deaths occurred in the actual weaning period; fatalities were relatively frequent in the three-month period immediately succeeding weaning. In both circumstances, cases were concentrated among children weaned at an early age, and deaths in the subsequent post-weaning period were more numerous than expected.

### Seasonal factors

The annual peak of acute diarrheal disease in the Punjab is in May and June, death rates then being 396 per 100 000 of the population per year (all ages), in contrast to 77 in winter. The common time to begin weaning is from the sixth to the eighth month of life.

Further evidence of the synergistic action between nutrition and infection was obtained by distributing the 1451 births in 11 villages of the larger study area by month of birth and determining the number of deaths from diarrheal disease during the first and second years of life. The observations in Table 28 are arranged by the accepted five seasons that characterize the Punjab, namely, the spring months of March and April, the hot dry season of May and June, the hot wet season of July, August, and September, and the succeeding autumn and winter. The small numbers of deaths preclude statistical significance.

Children born in spring and during the hot dry season, shortly before and at the height of diarrheal prevalence, had the lowest death rates for diarrheal

disease during the first year of life. They were predominantly breast fed at the time of major risk. Children born in autumn, with weaning beginning in the hot dry season, at the time of greatest risk, had the highest death rates of any cohort, as determined by month of birth. This is seemingly due to more than the administration of contaminated food; it stems from a combination of seasonal risk of attack, the greater dehydration when diarrhea occurs at that time, and an enhanced susceptibility incident to weaning.

TABLE 28. DEATHS FROM ACUTE DIARRHEAL DISEASE AMONG INFANTS AND YOUNG CHILDREN OF ELEVEN VILLAGES IN THE PUNJAB, DURING THE FIRST AND SECOND YEARS OF LIFE, BY MONTHS OF BIRTH, 1955-1959

Season born	First year of life			Second year of life		
	No. of children	Deaths from diarrheal disease	Deaths from diarrheal disease per 1000 per year	No. of children	Deaths from diarrheal disease	Deaths from diarrheal disease per 1000 per year
Spring:	219	5	23	117	2	17
March-April						
Hot dry:	209	6	29	136	2	15
May-June						
Hot wet:	380	14	37	200	4	20
July-Aug.-Sept.						
Autumn:	273	12	44	176	3	17
Oct.-Nov.						
Winter:	370	13	35	230	7	30
Dec.-Jan.-Feb.						
Total	1451	50	34	859	18	21

It would be expected that fewer children born in winter would start weaning at the time of peak incidence of diarrheal disease; and the observed rates for deaths from diarrhea were less (35 per 1000 infants per year) than they were for children who had started weaning before the seasonal peak, i.e., the July-August-September cohort. During the second year of life, rates were not only lower by more than a third, but, with allowance for the small numbers, were also much more consistent.

The season at which weaning took place was an unimportant factor in the diarrheas of the second year of life.

#### Deaths from acute diarrheal disease

During three of the four years of the study, deaths and their causes were determined for infants born in the entire study area of eleven villages. The data on deaths from all causes and deaths from acute diarrheal disease during the first four years of life are analysed in Table 29. They show a progressive decline in deaths from all causes during the pre-school years. The significance of diarrheal disease is evident, since this single cause was responsible for 22% of deaths in the first year, 27% in the second year, and 9% in the

TABLE 29. DEATHS AND DEATH RATES PER 1000 INFANTS AND PRE-SCHOOL CHILDREN PER YEAR IN ELEVEN PUNJAB VILLAGES, FROM ALL CAUSES AND FROM ACUTE DIARRHEAL DISEASE, 1965-1969

Cohort	First year of life			Second year of life			Third year of life			Fourth year of life		
	No. of children	Deaths	Deaths per 1000 per year	No. of children	Deaths	Deaths per 1000 per year	No. of children	Deaths	Deaths per 1000 per year	No. of children	Deaths	Deaths per 1000 per year
1965	121	17	140	103	7	68	93	1	11	92	1	11
1966	446	64	143	371	30	81	338	9	27	—	—	—
1967	463	72	156	385	29	75	—	—	—	—	—	—
1968	421	73	173	—	—	—	—	—	—	—	—	—
Total	1461	226	155	859	66	77	431	10	23	92	1	11
							Deaths from all causes					
1965	121	3	25	103	2	19	93	0	—	92	1	11
1966	446	13	29	371	12	32	328	1	3	—	—	—
1967	463	17	37	386	4	10	—	—	—	—	—	—
1968	421	17	40	—	—	—	—	—	—	—	—	—
Total	1461	50	34	859	18	21	431	1	2	92	1	11
							Deaths from acute diarrheal disease					

third year. The age-specific diarrheal death rate for the combined four years was 23% of the death rate from all causes.

The seasonal rise in the general death rate in April, May, and June coincided with the rise in death rates for diarrheal diseases. Death rates for acute diarrheal disease were the same in males and females.

The significance of diarrheal disease in the Punjab and other similar areas becomes apparent when disease-specific death rates there are compared with those in the USA. The death rate from acute diarrheal disease in the Punjab in the first year of life was 56 times greater, and, in the one- to four-year age group, 133 times greater than in the USA. Yet the present Punjab rate of 3446 per 100 000 infants is better than the rate for the year 1900 in the USA, when it was 4523.

The relation of the weaning process to diarrheal disease is better appreciated if one divides the first- and second-year deaths into six-month periods, as in Table 30. The diarrheal death rate in the first six months was relatively low, 20.6 per 1000 infants of that age per year, whereas, in the second six months, it was 53.6. In the second year, the rates were 34.8 in the initial half and 7.4 in the second. The correlation with weaning is outstanding. The rate for diarrheal deaths in the second year was about two-thirds that of the first year. With weaning largely completed, deaths were far fewer in the third year (Table 29) about 2 per 1000 per year among children of that age

TABLE 30. DEATHS AND DEATH RATES FROM ACUTE DIARRHEAL DISEASE DURING THE FIRST TWO YEARS OF LIFE, BY SIX-MONTH PERIOD, IN ELEVEN PUNJAB VILLAGES, 1955-1959

Age (months)	No. of children	Deaths from acute diarrheal disease	Deaths per 1000 per year
0- 5	1451	15	20.6
6-11	1305	35	53.6
12-17	860	15	34.8
18-23	813	3	7.4

### Weanling Diarrhea in Guatemala

#### Clinical and epidemiologic features

The field observations of acute diarrheal disease among rural Mayan Indian populations of the Guatemalan highlands reported below were made between the years 1958 and 1964. The climate borders on temperate because of the altitude, and the general area is representative of the less developed regions of Latin America. In most instances the data were collected by resident, non-medical workers visiting homes twice monthly. Professional and laboratory services were supplied by a staff based at the Institute of Nutrition of Central America and Panama (INCAP), in Guatemala City.

The outstanding feature of attack rates in the communities, as presented in Table 31, is the extent to which diarrheal disease was concentrated in children aged six months to two years, the period of weaning. The peak incidence of diarrheal disease and the mode for completed weaning coincided, and both were about six months later than in the studies in India.

TABLE 31. ATTACK RATES OF ACUTE DIARRHEAL DISEASE IN FOUR GUATEMALAN VILLAGES,\* 1956-1959

Age group	Number of persons	Cases of diarrhea	Attack rate: cases per year per 100 persons
0-5 months	92	43	46.7
6-11 months	79	87	110.1
1 year	135	162	120.0
2 years	122	129	105.7
3 years	119	66	55.5
4-6 years	406	86	21.2
7-14 years	839	69	8.2
15+ years	2390	109	4.6
Total	4182	751	18.0

\* Santa Tomas Milpas Altas, Santa Lucia Milpas Altas, San Antonio Aguas Calientes, and Santa Catarina Barahona.

Acute diarrheal disease was relatively infrequent during the first six months, when the children were almost wholly breast fed. After weaning was completed, usually early in the third year, incidence declined sharply, so that at age six years, the year of entering school, the attack rate was only 21.2 per 100 children of that age per year. The rates for schoolchildren of 7 to 14 years were only a fraction of those characteristic of early childhood, and for adolescents and adults over 15 years incidence was approximately half that for schoolchildren. This progressive decline with age is well authenticated for many parts of the world.

What is not so well recognized is the concentration of cases during the period of weaning. This lack of understanding comes about because of the common statistical practice of considering data for the second to fifth years of life as a single group. The dangerous second year of life is thus obscured.

### Death rates

Disease-specific mortality rates from acute diarrheal disease follow the same general age trend as case incidence. The data in this instance are from three other villages—not those providing the information on diarrheal morbidity. They are derived from the local village registers of deaths and consequently lack the reliability of information collected by survey. They cover a ten-year period and a cumulative population of 106 456, during the years 1950 to 1959 inclusive.

Death rates for diarrheal disease were greatest in the second year of life (Table 32). Indeed, they were more than twice those of the first year; and

they were still at the high level of 9.6 deaths per 1000 population during the fifth year. For schoolchildren and adults, the rates were far less than for those in the earlier years of life.

TABLE 32. DEATHS RATES FROM ACUTE DIARRHEAL DISEASE, BY AGE, IN THREE GUATEMALAN VILLAGES,\* 1950-1959 INCLUSIVE

Age (years)	Deaths from acute diarrheal disease	Diarrheal deaths per 1000 population per year	Diarrheal deaths as % of all deaths	Ratio of diarrheal death rates, Guatemalan villages to those in USA, 1960
Under 1	87	17.0	14	25
1	123	35.6	41	
2	102	28.0	53	
3	44	12.2	43	
4	34	9.6	55	519
1-4	303	21.3	46	
5-14	70	2.6	41	
15 +	117	2.0	16	115
Total	577	5.4	27	

\* Santa Cruz Balanya, Santa Maria Cauqué, and Santa Catarina Barahona (cumulative population 106 456).

The significance of deaths from acute diarrheal disease is brought out in a different fashion by determining the proportion of deaths from this cause in relation to deaths from all causes (Moore et al., 1966a). For the general population of the Guatemalan villages, 27% of deaths were due to diarrheal disease—a finding in agreement with the frequently cited national rate, for in Guatemala diarrheal disorders are the first cause of death and the highest for any Latin American country. Despite a high attack rate in infancy, fatalities from this cause accounted for only 14% of total deaths at that age, appreciably less than the 27% average for the general population. For the critical ages of one to four years, the proportion was 46%, and, in two of the years, the third and fifth, it was more than a half. These data are especially meaningful. Although death rates from acute diarrheal disease were greatest in the second year of life, in the subsequent pre-school years the proportion of deaths from that cause in relation to all deaths remained the same, 41%.

The true significance of the situation is often difficult to appreciate from a mere comparison of death rates from different causes. The importance of acute infections of the intestinal tract in countries like Guatemala is perhaps better understood by comparing relative death rates from this cause (Table 32) with those prevailing in more favored societies. For infants under one year, the death rate attributed to gastro-intestinal infections in the Guatemalan villages was 25 times that for infants in the USA. For the pre-school group, it was 519 times greater; and, for the general population, the excess in Guatemala was 115 times.

To stress further the magnitude of this health problem in terms of death and disability in Guatemala and in comparable countries (Moore et al., 1965a) seems purposeless. Its concentration in the early pre-school years is

evident, and should be the guide in developing effective programs for control. To this end, other characteristics of the behavior of the diarrheas of early childhood as a community disease are now examined.

### **Index case in family outbreaks**

Knowledge of the manner in which an infectious disease progresses through a community is one of the decisive factors in formulating a program for control. The usual sequence of events in family outbreaks of the common communicable diseases of childhood is an initial illness contracted by a schoolchild, less commonly by an adult. Secondary cases within families then follow, the attack rate being high among pre-school children and proportionately less among older family members, depending on their immunity status.

Acute diarrheal disease in the villages showed a striking departure from this formula. The usual index or primary case was not an older child or adult. In 71% of 390 family outbreaks during 12 months (Bruch et al., 1963), the disease first appeared in a pre-school child, aged five years or less. Schoolchildren provided the index case less frequently than did adults, but the differences were inconsequential—12% for schoolchildren and 17% for adults. These frequencies were out of all proportion to the numbers of persons in the different age groups within families. Adults and schoolchildren together made up 80% of members of households; they provided the index case in only 29% of family outbreaks.

No less than a third of all index cases were infants under one year old. More than a half were children in the first three years of life. Because a household in Guatemalan villages usually comprises several closely related family units, there were few households with only pre-school children. In 27 such families, there were 22 family epidemics of diarrheal disease during the period of observation; and a pre-school child was the index case in 19 of them. Twelve of 28 families with only adult members suffered outbreaks during the year.

Multiple index cases (the appearance of the disease in more than one member of a family within a period of 24 hours) occurred in only 5 of 390 family outbreaks. Multiple index cases are characteristic of common-source epidemics, as from water or milk. Their low frequency in this study supports the conclusion that the major means of transmission was by some other mechanism.

Several possibilities can be advanced in explanation of the preponderance of index cases among infants and toddlers. The reservoir of infection may be a healthy adult or older child who acts as a carrier, though he himself may be immune through previous attack. A host factor may be at fault—for example, poor nutritional state, which permits clinical disease through activity of an infectious agent not ordinarily pathogenic. The explanation

may rest in an unusually large infecting dose of an otherwise benign agent, a circumstance favored by deficiencies in environmental sanitation.

In amount and kind, supplementary feeding is usually grossly inadequate for good nutrition, and the food is almost invariably contaminated. Goodwin et al., (1966) observed a similar situation in Arizona. A detailed, long-term study of successive attacks experienced by a small group of children from birth to school age, together with the concomitant reaction of other family members, is a promising approach now under way to determine the relative significance of these factors.

### **Familial secondary attack rates**

Secondary cases of an infectious disease are those occurring in susceptible members of a family within an accepted incubation period following a primary or index case. In the case of acute diarrheal disease, secondary attack rates are necessarily computed from total family members, excluding the index case, because of inability to identify susceptible persons.

In the present study, the incubation period was taken as one to seven days. On this basis, the over-all secondary attack rate for the 390 family outbreaks was only 1.4%, suggesting either that most family members were immune or that communicability of the agent was low.

A more reliable datum is obtained by considering only children of pre-school age, who may be judged as more regularly susceptible. The secondary attack rate for that age group was 4.1%. Similar age-specific secondary attack rates were 1.3% for schoolchildren and 0.3% for adults aged 15 years or older. Of a total of 450 cases in these families, 86.7% were primary cases, only 7.5% were secondary infections, and 5.8% were tertiary or subsequent cases. A case was recognized as a new or primary case when the interval between cases was more than seven days, the established maximum incubation period.

The subsequent spread of infection within the family was no different when a pre-school child was the index case than when an older person introduced the disease. The family secondary attack rate with the primary case a child under six years was 1.2%; with a schoolchild, 1.6%; and, with an adult index case, 1.8%. These observations support the conclusion that most older family members were immune to the prevailing agents of diarrheal disease; at least in these communities, diarrheal disease did not spread with any frequency to adults within families, regardless of age of the index case. Significantly greater familial secondary attack rates were observed with measles in these same localities when the index case was a schoolchild than when the first case was in a child of pre-school age (Gordon et al., 1965a).

These observations departed so much from anticipated results, as judged by behavior of common communicable diseases of childhood in advanced countries, that the study was repeated over a period of 17 months in still

another community, Santa María Cauqué. Attention was focused primarily on diarrheal disease in children under five years of age. Among 504 affected families, a pre-school child was found to be the first or primary patient in 94.5% of instances. Even allowing for the evident bias due to selection of cases, this finding is clearly in accord with the preceding series. The concentration of index cases, again, was high among children in the first three years of life; no multiple index case was noted; and the secondary attack rate was highest, 8.4%, among pre-school children.

### **Endemicity and epidemicity**

Interest in manner of transmission extends naturally from behavior in the family unit to spread within the community. Acute diarrheal disease in Guatemala is commonly described as endemic or, more exactly, as hyper-endemic. Actually, it is neither. Communicable diseases of this general class are recognized as fluctuating endemic processes, continuously present with occasional and irregularly interspersed epidemics; however, acute diarrheal disease is not exactly that either.

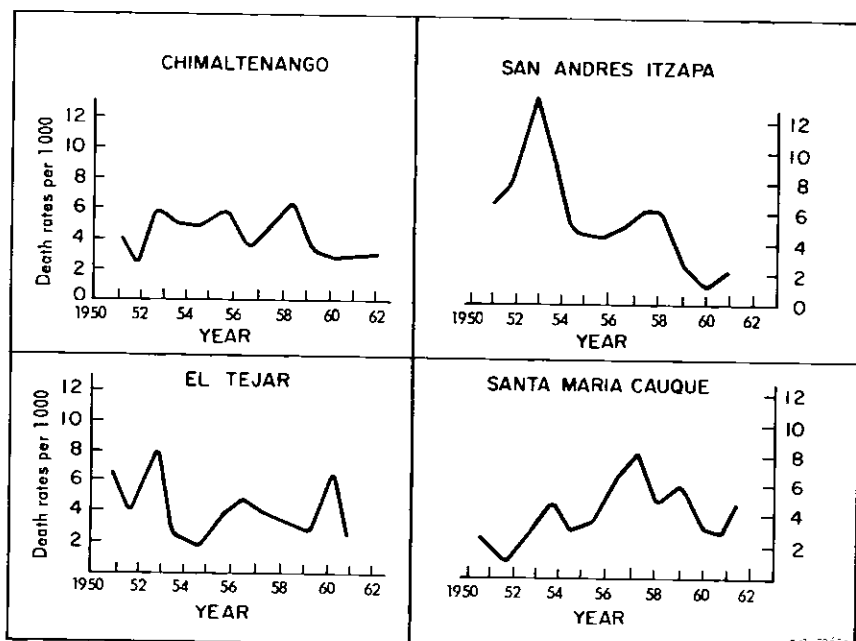
Deaths from acute diarrheal diseases were examined over a ten-year period for some twenty village communities, the data being obtained directly from the local village registers in consultation with the official recording the information. Analysis showed that what happened was a succession of epidemics of fairly regular periodicity, commonly three outbreaks every ten years, each of relatively long duration, with an excess of deaths through a year or more and, occasionally, over a two- or even three-year period. In no epidemic examined did the outbreak develop sharply, last a brief time, and end with much the same abruptness as it began, as is characteristic of common-source outbreaks related to water or another vehicle of spread. Rather, the epidemic evolved slowly and continued active through many consecutive months. The experience of four villages, including both small and larger communities, is illustrated in Fig. 5. The broad behavior is better characterized as fluctuating epidemicity rather than fluctuating endemicity.

The periodicity of acute diarrheal disease was found to be comparable to that of measles, which in the same region has about three outbreaks in a village population in ten years. The behavior of measles is usually attributed to development of a new crop of susceptible persons by birth. The predominance of toddlers in the second and third years of life in outbreaks of both diarrheal disease and measles suggests a similar mechanism in the two diseases.

The experience of the village of San Andrés Itzapa is indicative. This community, in 1952, had a measles outbreak of exceptional size and severity incident to a longer than usual interval between epidemics—about five years. Some two months later, indeed as the measles epidemic was subsiding, the outbreak of acute diarrheal disease shown in Fig. 5 made its appearance. It was an epidemic of greater magnitude than any other in

this study, although the associated events suggested that some of the cases of diarrhea may have been incident to kwashiorkor. A minor outbreak of measles occurred in 1955, and one of moderate size in 1957-58, an experience also closely paralleled by the frequency of acute diarrheal disease in those years.

FIG. 5. DEATH RATES FROM ACUTE DIARRHEAL DISEASE, AS COMPILED FROM LOCAL REGISTERS OF FOUR GUATEMALAN COMMUNITIES, 1950-1962



Populations: Chimaltenango, 14 838; San Andrés Itzapa, 5277; El Tejar, 1923; Santa María Cauqué, 923

### Modes of transmission

The INCAP studies on acute diarrheal disease have had as a principal aim an improved definition of causality, viewed in its broad sense. With good reason, modes of transmission have had a prominent place in that effort; their direct relation to practical control measures was an added incentive. For present purposes, a summary of family and community observations must suffice.

Numerous epidemiologic facts point to direct contact as the chief method of spread. The general course and behavior of observed epidemics is best explained by contact dissemination. The extreme prevalence of index cases among young children suggests an origin of infection within the family, rather than from outside sources, because infants of this age have relatively

fewer general contacts. Carriers of known pathogens are numerous among older children and adults. The paucity of multiple index cases is decidedly against a common-source origin. Perhaps, most important of all, the hygienic habits of siblings as well as family adults are compatible with spread by personal contact, a feature abetted by the limited amounts of water usually available.

Common-source epidemics apparently do not contribute materially to the bulk of acute diarrheal disease in these communities. Milk as a vehicle is largely eliminated because little is available; and, when it is, the source is usually the family cow. Common eating establishments scarcely exist in the villages. Such food-borne infection as occurs is restricted in large part to the family group, although religious and other festivals, which often are attended by large numbers of people, introduce special hazards.

Water is the most likely vehicle of a common-source epidemic. Common water sources are usual in the villages. They supply appreciable parts of the population and are known to be frequently contaminated. However, the most frequently observed age of attack of diarrheal disease is within the first three years of life, in contrast to the broad age distribution characteristic of water-borne infection. Children of this age are not the heavy water-drinkers of the population.

In one village, Santa María Cauqué (Fig. 5), with a water supply proven to be contaminated, forceful and successful effort was made in 1960-61 to provide a safe water supply. This did not, however, prevent the development of an epidemic in 1961 (Gordon et al., 1965a) in which *Shigella dysenteriae* type 1, the original Shiga bacillus, was involved, as well as five serotypes of *Sh. flexneri*. The majority of cases were undifferentiated.

These observations are not intended to imply that water, food, and milk have no part in the genesis of diarrheal disease among young children in these village communities. What does appear certain is that the consistently high rates cannot be attributed to appreciable epidemics of common-source origin.

The part of flies in mechanical transmission of acute diarrheal disease under conditions of the usual Guatemalan village is as yet ill defined. It would appear to be a secondary consideration, ranking below contact spread and the agency of food and water. The seasonal peak of diarrheal disease occurs in May and June (Table 33), before flies are prevalent. Flies appear in late June and attain their greatest numbers in September, a time when the monthly incidence of diarrhea begins to decline. Furthermore, the rates are high throughout the year, with the exception of December.

Obviously, the significance of all modes of transmission relates to care and efficiency in the disposal of human feces. Many features of environmental hygiene and sanitation have an influence on the frequency of acute diarrheal disease, among them disposal of wastes other than feces, food storage and preparation, and housing and rodent control—in addition to

water and flies, already mentioned (Bruch et al., 1963; Moore et al., 1965b). Feces disposal is singled out for consideration because, in the final analysis, it is basic to all.

TABLE 33. NEW CASES OF DIARRHEA BY MONTH IN THREE GUATEMALAN HIGHLAND VILLAGES\* AS DETERMINED BY HOME VISITS, MAY 1959-APRIL 1963

Month	Cases of acute diarrheal disease	Percentage of annual total
January	256	7.0
February	342	9.4
March	349	9.5
April	264	7.2
May	408	11.2
June	329	9.0
July	304	8.3
August	357	9.8
September	309	8.5
October	256	7.0
November	301	8.2
December	180	4.9
Total	3655	100.0

\* Santa María Cauqué, Santa Catarina Barahona, and Santa Cruz Balanya.

Attack rates of acute diarrheal disease in village families having privies were compared with those in families that lacked such facilities. This was not an experiment in introducing privies and seeing what happened. A health department program for the construction of outdoor toilets had been undertaken several years previously, and privies were no innovation.

The results in Table 34 show that, for children under one year of age, the presence of a privy in the household compound was associated with numerically more diarrheas than in households without that facility, although the difference was not statistically significant. Children one to five years old had more diarrhea when they lived in a home without a privy, but only at a

TABLE 34. ANNUAL CASE RATES OF ACUTE DIARRHEAL DISEASE, BY AGE, IN HOUSEHOLDS WITH AND WITHOUT PRIVIES, IN FOUR VILLAGES OF RURAL GUATEMALA, \* 1956-1959

Age (years)	With privies			Without privies		
	Persons at risk	No. of cases	Rate per 100 persons	Persons at risk	No. of cases	Rate per 100 persons
Under 1	136	123	80.7	35	21	52.8
1- 5	524	365	60.3	122	107	80.3
6-14	795	81	8.3	180	24	11.7
15 +	2109	113	4.6	410	35	7.3
Total	3564	682	16.8	747	187	22.4

\* Santa Tomas Milpas Altas, Santa Lucia Milpas Altas, San Antonio Aguas Calientes, and Santa Catarina Barahona. The rates are based on a pool of information from the four villages, two of which were under observation for 12 months and two for 16 months. Proper adjustment has been made for the difference in observation period.

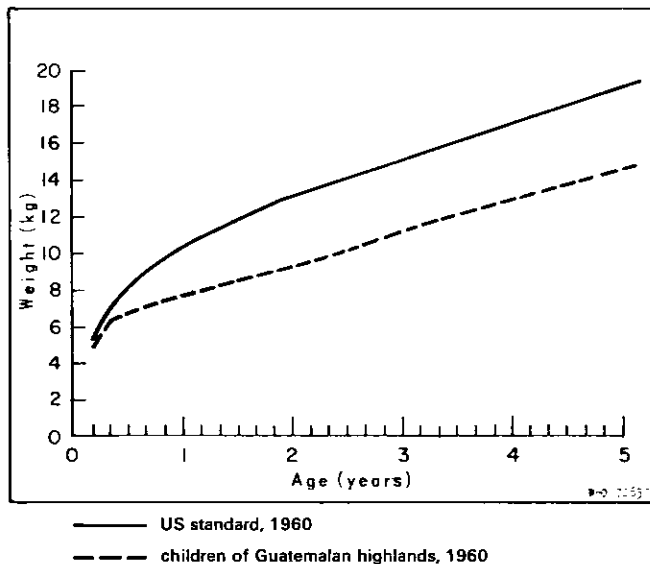
5% level of significance. This significance disappeared when children in the second year of life were omitted from consideration. The data thus gave no indication that privies as used in the villages had any influence on the diarrheas of children in the first two years of life, when most cases occurred. For adults and for the population as a whole, the presence of privies did contribute to a lower incidence of acute diarrheal disease.

Food has been considered briefly as a mechanism in common-source epidemics of acute diarrheal disease and, as such, has been judged unimportant in these village populations. Two other relations are significant: first, the role of contaminated food in the spread of the ordinary sporadic disease, especially among infants and young children; and, second, the place of inadequate nutrition in favoring clinical disease after infection.

#### Nutritional state and diarrheal disease

Perhaps no clinical impression is more firmly fixed among physicians in pre-industrial populations than the belief that acute diarrheal disease is a more frequent and a more serious disease among the malnourished than among persons of normal nutritional state. Although few quantitative data have been advanced in support of this hypothesis, clinical observations are many (Graham et al., 1966; Hansen et al., 1962; Robertson et al., 1960; Truswell et al., 1964; Woodruff, 1965; Shaker et al., 1966); and there is some laboratory support (Truswell, 1963; Wittman et al., 1967).

FIG. 6. INCREASE IN WEIGHT OF MALE INFANTS WITH AGE



Using a standard classification based on weight, that of Gomez and associates (1958), the frequency of acute diarrheal disease in Guatemalan children was determined on the basis of three degrees of malnutrition: weight deficiency more than 10% and less than 25% by the accepted standard; weight deficiency between 25% and 40%; and weight deficiency in excess of 40%.

By the standards used, most of the children in this population suffered an appreciable degree of malnutrition (Fig. 6). This is in accord with numerous other and extensive investigations of nutritional state in this area (Scrimshaw et al., 1957a) and in others (Marsden & Marsden, 1965; Wittmann & Hansen, 1965), in which it becomes evident that infants do well nutritionally during the first six months of life, but that thereafter, especially during the weaning period, they depart broadly and consistently from the accepted standards. Table 35 shows that diarrheal disease occurred with significantly greater frequency in the malnourished, that attack rates

TABLE 35. ATTACK RATES OF ACUTE DIARRHEAL DISEASE, BY AGE AND BY DEGREE OF MALNUTRITION, SANTA MARIA CAUQUÉ, 1961

Age (years)	No. of persons	Cases of diarrhea	Attack rate: cases per year per 100 persons
Normal			
Under 1	22	27	86.6
1	1	5	—
2	0	0	—
3	1	2	—
4	1	1	—
Total	25	35	98.8
1st-degree malnutrition			
Under 1	16	55	242.6
1	14	40	201.7
2	20	29	102.4
3	12	31	182.3
4	12	17	100.0
Total	74	172	164.1
2nd-degree malnutrition			
Under 1	2	31	—
1	20	93	328.2
2	16	57	251.5
3	16	56	247.0
4	17	17	70.6
Total	71	254	252.5
3rd-degree malnutrition			
Under 1	1	1	—
1	3	20	—
2	3	11	—
3	2	3	—
4	0	0	—
Total	9	35	274.5

increased progressively the greater the degree of malnutrition, and that these relationships held at all pre-school ages.

The related question of greater severity of disease among the malnourished is illustrated by the data in Table 36. Diarrheas were recognized as mild or moderate according to a duration of less or more than four days and the absence of mucus and blood in the stools. Patients with either mucus or blood in the stools were classed as severe, irrespective of the duration of the diarrhea. A difference was established between the frequency of a severe form of diarrhea in the malnourished as compared with normal children; it increased regularly with advancing age, nutritional deficiency presumably being longer continued. However, the significance is discounted by the small numbers of persons in the normal group and a heavy loading with those in the first year of life.

TABLE 36. TOTAL CASES AND SEVERE CASES OF ACUTE DIARRHEAL DISEASE AMONG CHILDREN AGED 0-4 YEARS, BY NUTRITIONAL STATE, GUATEMALA, FEBRUARY 1961 THROUGH JUNE 1962

Nutritional state	Number of children	Person-years	No. of cases	Cases/100 person-years	No. of severe cases	Severe cases/100 person-years
Normal	25	35.4	35	98.8	8	22.2
First-degree malnutrition	74	104.8	172	164.1	65	61.9
Second-degree malnutrition	71	100.6	254	252.2	74	73.3
Third-degree malnutrition	9	12.8	35	274.5	14	107.7

### Concentration of diarrheal disease in the weaning period

Most Guatemalan highland children are breast fed from birth—in this study, 98.7% of 301 infants for whom data were available. Infants and young children fed wholly on breast milk had relatively low attack rates of acute diarrheal disease, as shown in Table 37, including those continuing to nurse at an older age, due allowance being made for the small numbers and the probability, despite a history to the contrary, that they received some other foods. The frequency with which supplementary feeding is instituted at about the sixth month is indicated by the decided decline during the six- to nine-month period in the numbers stated to be wholly breast fed. No child in this series was wholly breast fed past the fourteenth month.

The weaning process begins ordinarily at about six months of age, with the addition of foods other than breast milk. It ends shortly after the close of the second year, breast feeding ceasing at a mode of 25.5 months. For some children in this study the weaning process continued past the thirty-sixth month (Table 38). The stress induced by weaning is of two orders. An initial exposure to contaminated food after safe breast milk is one

source of difficulty. The second is through substitution of food of poorer quality and commonly of insufficient amount to meet current and progressively greater requirements.

TABLE 37. CASES OF ACUTE DIARRHEAL DISEASE AMONG WHOLLY BREAST-FED CHILDREN, BY QUARTER YEARS, IN THREE GUATEMALAN HIGHLAND VILLAGES,\* 1959-1962

Ages (months, inclusive)	Total No. of breast-fed children	Breast milk only		Cases of acute diarrheal disease among wholly breast-fed children in three-month period	Incidence: cases per 100 wholly breast-fed children per year
		No.	%		
0- 2	294	284	97	51	72
3- 5	290	239	82	100	167
6- 8	288	95	33	45	190
9-11	280	13	5	7	215
12-14	261	3	1	3	400
15-17	221	0			
Total		634		206	130

\* Santa Cruz Balanya, Santa Maria Cauqué, and Santa Catarina Barahona.

TABLE 38. INCIDENCE OF ACUTE DIARRHEAL DISEASE AMONG BREAST-FED CHILDREN IN COURSE OF WEANING, IN THREE GUATEMALAN HIGHLAND VILLAGES,\* 1959-1962

Age (months, inclusive)	Total No. of breast-fed children	Breast milk supplemented with other foods		
		No. of children	Cases of acute diarrheal disease in three-month period	Incidence: cases per 100 per year
0- 2	294	9	1	44
3- 5	290	48	17	142
6- 8	288	190	103	217
9-11	280	264	187	283
12-14	261	254	178	280
15-17	221	220	164	298
18-20	169	168	124	295
21-23	124	123	79	257
24-26	72	72	36	200
27-29	44	44	31	282
30-32	23	23	15	261
33-35	9	9	10	444
36-38	5	5	3	240
39-41	2	2	0	0
42-44	0	0	—	—
45-47	0	0	—	—
48-50	0	0	—	—
Total	2082	1431	948	265

\* Santa Cruz Balanya, Santa Maria Cauqué, Santa Catarina Barahona.

Initiation of the weaning process, with the addition of other foods to breast milk, was associated with a greatly increased frequency of diarrheal disease, whether weaning began at an early age or relatively late. Table 38 shows that, in general, the rates more than doubled. Few children in this study received milk as a supplementary food. Other liquids in the form of

gruels or semi-solid pastes were common, but various solid foods were the main addition.

The highest rates for acute diarrheal disease prevailed during the time that weaning was being completed, namely, the three-month period during which breast feeding ended and the child transferred to a completely independent diet. The rates shown in Table 39 are measurably greater than those for corresponding ages when children were in the course of weaning. The quarter-year immediately following that in which weaning was completed was also associated with high rates.

The results just presented on the relation of breast feeding and the weaning process to incidence of acute diarrheal disease agree in principle with those of the previously described field study in the rural Punjab area of India. Attack rates were greater in Guatemala, but death rates were less. In relation to total deaths, diarrheal deaths were in much the same proportion in the two areas. If anything, the proportion for the second and third years was greater in Guatemala, where weaning was completed later (as previously noted, the mode for completed weaning in India was 19.4 months).

Although the introduction of contaminated foods explains the increase in diarrheal episodes in the weaning and post-weaning periods, it does not in itself account for the high mortality. Even given the factor of a higher dosage of infectious agents, experience elsewhere indicates that such high death rates from diarrheal disease are not seen in populations of well-nourished children. The answer seemingly is in an existing synergism between nutrition and infection. As malnutrition develops because of the poor weaning diet, acute diarrheal disease becomes increasingly likely to lead to death. At the same time, diarrheal disease reduces appetite, increases metabolic loss of nitrogen, and leads to further dietary restriction, all of which hastens the lowering of resistance to infection (Burgess, 1961) and sometimes leads to the full-blown syndrome of kwashiorkor.

What is definite is that the diarrheas occurring at the time of weaning are by far the most important aspect, numerically and as a cause of death and disability, of the general problem of diarrheal disease in less developed regions. They possess characteristics sufficiently individual to justify recognition as an epidemiologic unit: weanling diarrhea. Specific measures directed to their management are an essential feature of general programs for the control of acute diarrheal disease in those areas.

### **Prevention and Control of Weanling Diarrhea**

#### **Preventive measures**

We depart from tradition in placing health education of the public first in rank among preventive measures against weanling diarrhea. The reason is

TABLE 39. INCIDENCE OF ACUTE DIARRHEAL DISEASE AMONG ORIGINALLY BREAST-FED CHILDREN AT AGE WEANED FROM BREAST AND DURING SUBSEQUENT QUARTER YEAR, IN THREE GUATEMALAN HIGHLAND VILLAGES,\* 1959-1962

Age (months, inclusive)	Total No. of breast-fed children	Weaned from breast this period			Weaned from breast three months previously		
		No.	Cases of acute diarrheal disease in three-month period	Incidence: cases per 100 per year	No.	Cases of acute diarrheal disease in three-month period	Incidence: cases per 100 per year
0-2	294	0	—	—	0	—	—
3-5	290	0	—	—	0	—	—
6-8	288	0	—	—	0	—	—
9-11	280	1	1	400	0	—	—
12-14	261	3	4	633	1	400	400
15-17	221	8	5	250	4	800	800
18-20	189	13	14	431	2	100	100
21-23	124	20	13	280	4	338	338
24-26	72	24	19	317	13	180	180
27-29	44	18	7	156	15	320	320
30-32	23	13	6	186	20	176	176
33-35	8	6	6	400	12	187	187
36-38	6	2	1	200	6	—	—
39-41	2	2	1	200	2	—	—
42-44	0	0	—	—	2	—	—
45-47	0	0	—	—	2	—	—
All ages		110	77	275	95	51	214

\* Santa Cruz Balanyé, Santa María Cauqué, and Santa Catarina Barahona.

twofold. In the first place, many of the important preventive measures relate directly to personal or household hygiene, diet, and other health practices applicable only through individual initiative (Ortiz & Ceballos, 1961). The second reason is that control measures originating as a community effort and instituted through official agencies frequently fail in their potential usefulness because the individual person lacks knowledge of their proper application or does not practice them because he remains unconvinced of their value (Gordon et al., 1964c).

Educational methods are directed toward both mother and child. Mothers benefit from instruction on how to prepare foods properly; on the appropriate supplements to breast feeding and the diet after weaning; on protecting food from flies, rodents, and other sources of contamination; and on storage and preservation of food, and the management of left-overs. In many cultures, food prejudices and superstitions are such that certain foods are unwarrantedly considered dangerous. Their prohibition leads to nutritional difficulties. In other circumstances, food itself is viewed as the cause of the acute diarrhea, which it may well be, although more because of its bacterial content than its composition. As a result, food is withheld from the sick child for long periods, malnutrition is exaggerated, and the infectious process is aggravated even to the point of death.

Children require training in hygienic habits at an early age, from washing the hands before eating to such elementary matters as not eating food dropped on the floor. Adults, too, must be taught the hazard of contaminating food with dirty hands.

The observed principal age of attack in the first years of life, the high fatality at that time, and the association with the weaning process make maternal and child health services a main feature of control programs. Spread of infection by contact predominates, which indicates a clear relationship to the hygienic practices of the mothers and other attendants (Jelliffe, 1965).

Breast feeding is close to universal in most of the developing countries; but cultural changes in many areas lead increasingly to substitution of artificial feeding, with disastrous results if improved personal hygiene and sanitary practices have not kept pace with the change. Breast feeding for at least twelve months is desirable but, without supplementation, must not be relied upon to provide adequate nutrition beyond six months. Cleanliness in preparation of food supplements has special importance in this first contact of the infant with enteric pathogens.

The traditional acceptance of environmental sanitation as a fundamental feature of long-term community control of diarrheal disease is fully justified. Because of the factors involved in the origin of the disease in early childhood, sanitary measures have less direct effect in control of weanling diarrhea than of diarrheas at older ages. The fact is inescapable, however, that, for satisfactory control of the diarrheas of early childhood, the sources of

infection of the disease must be eliminated; and these are in the diarrheas of older members of the population. Control in this group is primarily through environmental sanitation.

The water-borne epidemics so prominent a feature in urban communities of technically underdeveloped countries are apparently of lesser consequence in the diarrheal disease of those rural populations that have been well studied. Emphasis is too frequently on purity of water to the neglect of quantity and availability. Personal hygiene has been stressed as a prominent control measure. This requires adequate amounts of water. When supplies have to be transported several kilometers in earthen jars carried on the head, quantity is necessarily limited, which discourages ordinary cleanliness.

Disposal of human feces is a critical concern, and yet so often in developing countries the privy is looked upon as no more than a monument to Hygea, and is not something that the people understand, use, or appreciate. The value of improved facilities has repeatedly been dissipated by lack of health education to assure their proper use. Evidence has already been presented of the minimal direct effect of privies in restricting the frequency of diarrhea among infants and young children, the ages at which the disease exerts its major influence.

Disposal of wastes other than feces enters into sanitary control as a means of preventing fly breeding. More direct means of fly control have significance in many localities. Improved housing can be expected to have a favorable influence on the incidence of infantile diarrhea; dirt floors and creeping children are a bad combination.

Neither chemoprophylaxis nor prophylactic administration of antibiotics has a place in the control of the acute diarrheal disease of developing countries; such methods are equally unsuitable for protection of family contacts and for general community control, epidemic or otherwise (Gordon, 1965b). Whatever application they may have is in more highly developed countries with confirmed shigellosis, and even that use is questionable (Great Britain, Public Health Laboratory Service, 1955; Moorhead & Parry, 1965).

Food and nutrition necessarily attain greater prominence among control measures as the place of weaning diarrhea within the total problem becomes better appreciated. The greater incidence and severity of acute diarrheal disease among malnourished children than among well-nourished infants and toddlers emphasize the importance of an adequate diet in any planned program for less developed regions. Too early addition to the infant diet of foods other than breast milk, or premature abandonment of breast feeding, also increases the risk of infection.

Supplementary feeding during the weaning stage needs to depart from the haphazard process so common in underprivileged populations (Mead, 1964). An orderly regimen accomplished through health education and the guidance of workers in maternal and child health needs to be instituted. The most

critical period is when the child is transferred completely to a general diet. In less developed regions, a child's nutritional state has often deteriorated measurably by this time, as indicated by the deviation from normal growth curves. Under present conditions in many of these areas, the increased risk of diarrheal disease because of the malnourished state of the child continues for many months, and may still be a factor in later pre-school years.

### Care of the patient

In caring for patients, there is no substitute for good medical care, which should include hospitalization of severely ill children. The facilities available in less developed countries are often such that other provision must be made. If health centres exist, a rehydration clinic for management of the acute diarrheas is essential. Lacking that, much can be accomplished among village populations by health educators or public health nurses through home visits to instruct in simple procedures of home management (Ortiz & Ceballos, 1961; Ortiz, 1965). A program followed to advantage in several countries emphasizes the measures hereafter described.

The first duty is to inform mothers of young children of the dangers of dehydration, how to recognize it, how to prevent it, and how to correct it, at least in its early stages. In the Punjab, the local name for the diarrheal syndrome is *Sukho*, which means dried up and is generally recognized as of particular moment when ambient temperatures are high.

In infants and young children, feeding should be discontinued for no more than 6 to 12 hours (Sood, 1963). Fluids should be given by mouth, in the form of water with sugar and small amounts of salt, or locally available fruit juices. The important consideration is that the fluids be administered in small amounts, repeated frequently day and night until the child can take larger amounts and food tolerance returns. Most deaths from acute diarrheal disease are from dehydration. Rehydration is the basis of all good treatment (Ordway, 1960), and thus of any plan of home management.

After 6 to 12 hours, diluted, boiled milk is begun, the concentration being progressively increased during the succeeding 48 to 72 hours until whole milk is given. Concurrently, cereals, vegetables, fruits, and meats are offered in increasing amounts until, by the third day, the child is receiving an adequate diet for his age in accordance with local availability of food and the food habits of the population. This regimen is to be followed even in the continued presence of loose stools (Sood, 1963). The severity of the diarrheal process and its complications are frequently due to an over-restricted diet, and children sometimes die as much from lack of food as from the diarrhea itself.

It is recommended that the use of drugs be avoided in home management of diarrhea. Antibiotics, sulfonamides, and numerous other drugs are now

available through shop-keepers and chemists, even in isolated villages with no organized medical services. None are of startling benefit (Ordway, 1960; Ordway & Yankauer, 1964; Ascoli & Mata, 1965; Severs et al., 1966), although opinion is more varied on this matter than on most other features of acute diarrheal disease (Ducas, 1963; Kahn et al., 1963).

A survey of the customary practices of the area in the care of children with diarrheal disease is included to advantage in the investigation of epidemics, next described. Some of the common measures are distinctly harmful. In the Guatemalan highlands, as in many cultures, administration of purgatives is usual; and, still worse, strong vermifuges may be given, in the mistaken belief that the ascarids so frequently expelled by children early in diarrheal attacks are the real cause of the disease. In the Punjab, dietary restrictions relate particularly to the complicated beliefs about "hot" and "cold" foods and there is great reliance on vaguely understood herbal infusions. Such practices, along with the failure to recognize dehydration, are the main reasons for the high fatality from diarrheal disease in young children.

### **Epidemic control**

So far as epidemics are concerned, the problem is not that of the large and small outbreaks of common-source origin, so frequent in towns and cities, characterized by a sharp rise and a rapid decline, and sometimes involving hundreds, or even thousands, of people. The common epidemic of diarrheal disease among young children is different. It occurs with regularity in small communities the world over, most of them rural and in the less developed countries. Usually the outbreak remains unrecognized locally until it has reached its height; for these epidemics are of slow evolution and long duration, and the spread is by direct personal contact. Commonly they run a natural course, for the popular tendency is to view them as an unavoidable feature of life in these localities. Recognition of such events requires a system of reporting that does not exist in most places where they occur. A special means has been suggested, the use of death registers, in which deaths rather than cases are the index of epidemicity.

To attempt investigation and control of all outbreaks in the numbers that occur is wholly impractical. This would overwhelm the resources of most health departments in affected regions. What is suggested is designation of one physician of a health agency to operate under a policy of continuing investigation of some of the outbreaks, sufficient to give an understanding of representative geographic distribution and seriousness. The immediate accomplishment in limiting deaths and disability would be inconsequential. The main objectives would be educational—to engender among village residents an appreciation of the basic problems of environmental sanitation and nutrition and to show that control is feasible and that therapeutic

measures are possible, thereby encouraging preventive action against the otherwise certain outbreaks of the future. The direct gain to health agencies rests in improved understanding of the extent of weanling diarrhea regionally, an assessment of deaths not to be had from the usual vital statistics, and better information on the practicability of control with locally available resources.

### Research

In recent years investigation of the acute diarrheal diseases has put primary emphasis on modern laboratory and clinical methods. This is admirable, has been productive, and has contributed appreciably to control. Research has followed this trend because it is the kind of investigation best fitted to advanced countries, where most research is done and where acute diarrheal disease is neither prevalent nor clinically serious.

Regions with much diarrhea need knowledge of the ordinary behavior of the disease in nature (Cvjetanovič, 1963). This can be derived through operational epidemiology, and bears directly on the practical problem of control. Research of this type is in four possible directions:

(1) Periodic surveys, in selected hyperendemic areas, of a few representative rural and urban populations to determine how much diarrheal disease exists, the dominant mode of transmission, the influence of maternal and child health practices, and the relation of nutritional state to incidence and fatality.

(2) Concentrated and continuing prospective epidemiologic investigations of a small, selected group of recognized family outbreaks, each observed until infection disappears from the household. An epidemiologic case study includes three elements: patient, close contacts, and the immediate environment. The community prevalence survey, short-term and cross-sectional, is believed to have been much overdone; such fundamental information as may be had by this means is already at hand. The more promising approach to causality is by intensive study of family outbreaks from index case through last carrier. Although such studies combine to advantage field and laboratory procedures, they are profitable as wholly ecologic investigations.

(3) Long-term prospective studies of a fixed population over a period of years. From a world standpoint, investigations comparable with those described in this chapter would be useful in the less developed areas of Africa, South America, and Asia (Benavides et al., 1964).

(4) The study of selected epidemics. Epidemics have traditionally been a favored feature of field research. Although the primary objective is control, a policy of intensive study of occasional outbreaks in areas of high

incidence contributes to the information necessary if control methods are to be improved. Again, field methods alone will yield important information even when microbiological studies cannot be included.

Field research has been emphasized in these suggestions because it is within the capability of official and other health agencies in developing countries, and because the main need there is for better information on local conditions. Also, it relates directly to practical control. There is, however, no suggestion that field research is an exclusive substitute for the carefully ordered investigations of laboratory and clinic. Ideally, the approach is through a combination of the three.

### **Priorities**

Administratively, programs for disease control always raise questions of priority. The usual concern is with technical matters, a choice of one method over another, or the emphasis to be accorded a particular activity in relation to other parts of the health program. The first question can usually be settled by the epidemiologic evidence; the second involves important considerations of human and material resources, as well as professional judgment.

Within recent times the question of priorities has extended to higher levels, to the place to be accorded public health itself in the general effort toward the social and economic betterment of mankind. More than anything else, the population crisis, the growth of populations beyond material resources, has precipitated an occasionally negative attitude toward health activities, particularly among some development economists and others responsible for improved living in less developed regions. This reflects a serious misunderstanding of the influence of health programs on population growth.

The greatest restraint on the increasing numbers of people in less developed parts of the world today is clearly the high death rate of children up to the age of five years (Johnson, 1964). Malaria and weanling diarrhea are the two diseases mainly responsible for this wastage of young lives. The gains in malaria control within recent years are such that more serious attention can now be given to the diarrheas of young children, by the methods outlined here. This endeavor lacks the grounds on which development economists justify malaria control: that prevention of illness among working adults promotes productivity.

Humanitarian considerations in the care of sick children are sufficient to justify public health action against childhood diarrhea, and political pressure from parents will support such activities. There are, however, adequate economic reasons for controlling weanling diarrhea. The prolonged bouts of diarrhea that have been described combine with malnutrition to produce an impact on human growth and development that is strongly apparent in developing countries (Senecal et al., 1962). The limited physical and mental

stature of adults in poor economies and their low productivity can often be traced to the permanent damage in childhood that comes so largely from the synergism of malnutrition with infectious disease.

Directly relevant to the population problem is a realization that family planning cannot be promoted with much success until parents have some assurance that the children they have will survive. It is fatuous, if not immoral, to suggest that health programs should be withheld until birth rates come down. All experience with population control shows the advantage of bringing down death rates and birth rates together. Parents require no clearer demonstration of the need to have only three children in order to raise three than a decrease in deaths in early childhood.

Weanling diarrhea must be interpreted in terms of both nutrition and infection in order to achieve proper allocation of effort toward prevention and control. If generalization of present-day approaches is permitted, emphasis has been too much on the obligations and duties of public health agencies, with too little appreciation of the fact that much of control rests in what people must do for themselves, as good epidemiologic evidence shows. Health education thus has a prominent place among priorities.

This judgment in no way disparages wholly constructive measures such as the building of privies, the improvement of water supplies, provision of laboratory facilities, and the pasteurization of milk. What is implied is that correction of faulty practices in personal hygiene, an understanding of food requirements, an improvement of dietary habits, and more effective maternal and child health procedures have direct and special application to the control of acute diarrheal disease at the ages at which it is most prevalent and its impact is greatest—among infants and young children.

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