# CONTROL OF INFANT DIARRHEAS IN THE LIGHT OF RECENT SCIENTIFIC PROGRESS*

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## Part I

### MORTALITY

### Introduction

Acute diarrheal diseases either have been or are now the major disease problem of infants and children in all countries. Present wide variations in total mortality in these age groups in different geographical areas are related chiefly to differences in the rapidity with which these preventable diseases have been controlled. In some cities and countries, present mortality from these causes is less than one per cent of that of earlier years. In others, for various reasons, there is little evidence that the downward trend has been initiated.

As an example of a country which had a sharp decline, the mortality experience of the United States is considered first, demonstrating the nature of the problem and a record of progress in its control. Illustrative statistical data are given next to indicate the current mortality from diarrheal diseases in other countries of the Americas. The findings appear to be identical to those observed in the United States of America in earlier years. Limited observations from other countries indicate that, on a world-wide basis, the acute diarrheal diseases are still the greatest single cause of death in infants and children. History establishes that these deaths are preventable. The major task in the prevention of diarrheal diseases is for the present and the future, but past accomplishments are assurance that success is attainable.

### Mortality from Diarrheal Diseases in the United States of America

While acknowledging inadequacies and inaccuracies in records of mortality, these are still the best index available of past and present incidence of diarrheal diseases. Data for the City of New York are available from 1868 and Table 1 presents mortality from diarrheal diseases by year. Earliest records reveal in excess of 400 and reaching as high as 572 deaths per 100,000 population per annum. In the 25 years following 1875, the mortality declined from the 400 to the 200 level. In the first decade of the present century, there was a further fall from 200 to 100. A rapid and progressive reduction brought the mortality from 100 to 10 in the next 20 years. Since 1930, there has been a slow downward drop

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TABLE 1.—*Deaths per 100,000 population from acute diarrhea in New York City by years*

| Year | Rate | Year | Rate | Year | Rate | Year | Rate |
|---|---|---|---|---|---|---|---|
| 1868 | 488 | 1890 | 267 | 1912 | 92 | 1934 | 10 |
| 1869 | 387 | 1891 | 279 | 1913 | 81 | 1935 | 9 |
| 1870 | 475 | 1892 | 282 | 1914 | 76 | 1936 | 9 |
| 1871 | 405 | 1893 | 255 | 1915 | 81 | 1937 | 8 |
| 1872 | 572 | 1894 | 236 | 1916 | 63 | 1938 | 7 |
| 1873 | 456 | 1895 | 247 | 1917 | 68 | 1939 | 6 |
| 1874 | 379 | 1896 | 225 | 1918 | 52 | 1940 | 5 |
| 1875 | 388 | 1897 | 204 | 1919 | 49 | 1941 | 4 |
| 1876 | 379 | 1898 | 230 | 1920 | 52 | 1942 | 4 |
| 1877 | 353 | 1899 | 187 | 1921 | 39 | 1943 | 5 |
| 1878 | 282 | 1900 | 201 | 1922 | 31 | 1944 | 5 |
| 1879 | 279 | 1901 | 200 | 1923 | 27 | 1945 | 4 |
| 1880 | 364 | 1902 | 164 | 1924 | 21 | 1946 | 4 |
| 1881 | 387 | 1903 | 140 | 1925 | 21 | 1947 | 3 |
| 1882 | 363 | 1904 | 172 | 1926 | 18 | 1948 | 2 |
| 1883 | 296 | 1905 | 168 | 1927 | 14 | 1949 | 3 |
| 1884 | 321 | 1906 | 160 | 1928 | 18 | 1950 | 2 |
| 1885 | 297 | 1907 | 167 | 1929 | 15 | 1951 | 2 |
| 1886 | 297 | 1908 | 150 | 1930 | 14 | 1952 | 2 |
| 1887 | 312 | 1909 | 127 | 1931 | 10 | 1953 | 3 |
| 1888 | 287 | 1910 | 136 | 1932 | 8 | | |
| 1889 | 287 | 1911 | 106 | 1933 | 10 | | |

towards the present level of 2 deaths per 100,000 population from all diarrheal diseases.

Statistical data from a few other cities in the United States of America are available prior to 1900. Table 2 records observations for the 30 years beginning in 1900 for cities selected as representative of those with low, medium, and high mortality. Everywhere there was a problem of similar nature to that in New York City, but in all, during the three decades, there was a rapid decline from excessively high to moderately low mortality from these diseases. In general, rates for states as a whole were appreciably lower than in cities, since at that time the mortality from diarrheal diseases was generally less in rural than in urban populations.

At the turn of the century, mortality from diarrheal diseases was high everywhere in the United States. In some states there was early and rapid progress in control while, in others, control measures employed were less effective. Thus, in later years, variation in mortality has been great, from high in a few to very low in others. This wide distribution is illustrated by data for 1936. In Puerto Rico, recorded mortality from diarrheal diseases was 480 per 100,000 population; in Arizona and New Mexico, the rates were approximately 100. In the remaining states, they varied from just under 50 to a low of 4.

TABLE 2.—*Deaths per 100,00 from diarrhea and enteritis for selected cities, 1900–1929*

| Year | Rates by cities | | | | | |
|---|---|---|---|---|---|---|
| | Minneapolis | St. Louis | Philadelphia | Providence | Pittsburgh | Fall River |
| 1900 | 67 | 95 | 115 | 165 | 215 | 345 |
| 1901 | 70 | 93 | 104 | 190 | 210 | 307 |
| 1902 | 42 | 86 | 96 | 165 | 221 | 315 |
| 1903 | 49 | 99 | 113 | 182 | 193 | 334 |
| 1904 | 45 | 88 | 133 | 153 | 198 | 301 |
| 1905 | 56 | 82 | 144 | 119 | 191 | 353 |
| 1906 | 69 | 90 | 172 | 155 | 230 | 334 |
| 1907 | 57 | 92 | 147 | 154 | 209 | 438 |
| 1908 | 60 | 84 | 138 | 129 | 183 | 353 |
| 1909 | 52 | 88 | 130 | 110 | 157 | 394 |
| 1910 | 93 | 105 | 168 | 140 | 201 | 401 |
| 1911 | 51 | 106 | 133 | 90 | 146 | 352 |
| 1912 | 41 | 83 | 107 | 87 | 130 | 267 |
| 1913 | 48 | 87 | 113 | 89 | 156 | 256 |
| 1914 | 52 | 74 | 120 | 89 | 120 | 325 |
| 1915 | 36 | 56 | 100 | 77 | 112 | 256 |
| 1916 | 42 | 62 | 101 | 72 | 131 | 251 |
| 1917 | 32 | 58 | 107 | 68 | 151 | 245 |
| 1918 | 25 | 51 | 104 | 74 | 139 | 269 |
| 1919 | 20 | 36 | 72 | 33 | 99 | 137 |
| 1920 | 21 | 36 | 71 | 50 | 88 | 164 |
| 1921 | 15 | 26 | 50 | 56 | 80 | 140 |
| 1922 | 13 | 20 | 50 | 28 | 56 | 133 |
| 1923 | 11 | 23 | 38 | 40 | 70 | 82 |
| 1924 | 10 | 28 | 36 | 24 | 59 | 81 |
| 1925 | 16 | 32 | 35 | 16 | 60 | 61 |
| 1926 | 11 | 28 | 27 | 17 | 42 | 66 |
| 1927 | 5 | 19 | 21 | 14 | 25 | 45 |
| 1928 | 8 | 18 | 23 | 23 | 25 | 28 |
| 1929 | 3 | 15 | 18 | 10 | 19 | 24 |

Furthermore, in individual states there has been a wide variation in different areas and in different population groups. Within the same geographical area, some segments of the population may have little or no enteric disease, while in others the mortality may equal that which generally prevailed more than 50 years ago. In Hidalgo County, Texas, in 1942–45 the mortality rate for diarrheal diseases in permanent residents in comfortable economic circumstances was 12 per 100,000 population while in the families of recent laborer immigrants it was 400. Similar wide variations have been evident in California on comparing the general population with the families of transient migrating laborers. In the United States, the major remaining problem is to provide effective control measures in such scattered foci of high incidence.

Illustrative age specific death rates are given in Table 3. These pro-

TABLE 3.—*Age specific death rates (per 100,000 population for diarrheal diseases in New York City, by years*

| Age | 1901 | 1910 | 1920 | 1930 | 1935 |
|---|---|---|---|---|---|
| Total | 200 | 136 | 52 | 14 | 8 |
| -1 | 4496 | 3806 | 1796 | 665 | 508 |
| 1-4 | 470 | 295 | 120 | 22 | 10 |
| 5-9 | 23 | 8 | 5 | 2 | 1 |
| 10-14 | 12 | 4 | 1 | .3 | 1 |
| 15-19 | 6 | 1 | 1 | 1 | 1 |
| 20-24 | 7 | 2 | 1 | 1 | 2 |
| 25-34 | 14 | 5 | 2 | 1 | 1 |
| 35-44 | 16 | 5 | 3 | 2 | 2 |
| 45-54 | 30 | 16 | 5 | 2 | 1 |
| 55-64 | 100 | 44 | 11 | 4 | 2 |
| 65-74 | 249 | 125 | 29 | 10 | 7 |
| 75+ | 529 | 329 | 124 | 15 | 8 |

vide full justification for emphasis on the control of diarrheal disease in infants. When there were 200 deaths per 100,000 total population in New York City, there were 4,496 infant deaths per 100,000 population under 1 year of age. It is observed, in contrast, that the death rate in older children and young adults was low, but in individuals of more than 75 years, there was again a substantial rise to a maximum of about $\frac{1}{10}$ the rate for infants. An examination of age specific rates further shows that, in the decline of mortality, there was an earlier and more rapid fall in the mortality in older children and adults as compared with a slow and delayed decline in infants. Thus, the need for control in infants was more urgent and attaining prevention was more difficult.

Control of the related enteric infection, typhoid fever, received early and concentrated attention by public health workers. Programs designed specifically to prevent this infection were actively applied. The control of diarrheal diseases has never received similar intensive attention. This is remarkable in view of the striking contrast in the magnitude of the problem. In New York City, the mortality from typhoid fever throughout the years was approximately $\frac{1}{10}$ that from the acute diarrheal diseases. While this ratio varies in different cities, in all, the deaths from diarrheal diseases have consistently far exceeded those from typhoid fever. In the light of recent knowledge, it may now be emphasized that the specific enteric infections which give rise to the diarrheal diseases are a much more important cause of mortality than typhoid fever. Future planning demands that the relative importance of problems be accurately weighed. If this is done, it may be anticipated that specific programs for the control of diarrheal diseases will receive even greater emphasis than programs designed to prevent typhoid fever.

When infant mortality is high, many infants ordinarily die without receiving medical attention. The occurrence of these deaths may be reported, but the cause of death will be listed either as undetermined or a symptomatic diagnosis of uncertain reliability, as "diarrhea", may be recorded. This was a problem of earlier decades in the U.S.A. when in some states as many as ¼ to ⅓ of reported infant deaths had no secure diagnosis as to cause. Under such conditions, the computed mortality rates from diarrheal diseases in infants can not present a true picture. The problem could be even greater than the rates would indicate. On the other hand, in cases in which the symptomatic diagnosis of "diarrhea" is recorded, there is no evidence whether this is a primary enteric infection or a terminal manifestation of some other major disease. Thus, there have been and still are problems in the interpretation of recorded mortality data, particularly with reference to diarrheal disease in infants. Mortality rates can not be more accurate than the diagnoses recorded. Despite these limitations, the accumulated observations in the United States clearly indicate the past magnitude of the problem and the progress in its control.

**Mortality from Diarrheal Diseases in Other Countries of the Americas**

Limited statistical data are at hand for the other countries of the Americas, chiefly from the 4 year reports submitted to the XIV Pan American Sanitary Conference. The five major causes of death in 1952 have been reported by 16 countries. In 9, diarrhea and enteritis, gastroenteritis or diseases of the digestive system were the major cause of all deaths and, in 3 others, these diseases were second in order of importance as a cause of death. In 4 countries only, these diseases did not appear as one of the first five causes of death. On the basis of this evidence, the prevention of diarrheal diseases must be acknowledged as the major public health problem in most of the countries of the Americas.

The magnitude of the present problem is indicated by the mortality data in Table 4. These are taken from a summary of the principal causes of death in 1952 for 16 countries other than the U.S.A. In four (Argentina, Paraguay, Peru and Uruguay), the diarrheal diseases were not among the 5 major causes of death and the reported mortality was apparently under 50 deaths per 100,000 population. In two others, as shown in the table, the rates were under 100; in 6 they were between 100 and 200; in 2 between 200 and 300, and in 2 over 300. Considering that these are rates for countries as a whole, the current problem in most of the countries of the Americas apparently exceeds that which prevailed in the United States of America at the turn of the century.

An evaluation of mortality statistics requires consideration of the additional data given in Table 5. Except where laboratory facilities are available and used, the major clinical difference in cases dying of "dys-

TABLE 4.—*Deaths from diarrheal disease in 12 countries of the Americas, 1952*

| Country | Disease classification | Deaths per 100,000 population |
|---|---|---|
| El Salvador | Gastro-enteritis | 347 |
| Guatemala | Diarrhea and enteritis | 298 |
| Mexico | Gastro-enteritis | 247 |
| Venezuela | Gastro-enteritis | 183 |
| Costa Rica | Gastro-enteritis | 170 |
| Honduras | Intestinal infection (94) and diarrhea (53) | 147 |
| Colombia | Diarrhea and enteritis | 130 |
| Dominican Republic | Gastro-enteritis | 123 |
| Bolivia | Diarrhea and enteritis (58) and dysentery (20) | 78 |
| Panama | Diarrhea and enteritis (under 2 years) | 69 |
| Brazil | Diseases of digestive system | 306 |
| Chile | Diseases of digestive system | 172 |

entery," as compared with those attributed to "diarrhea and enteritis," is that the former have grossly bloody stools at some time in the illness. In assessing the problem, all diarrheal diseases must be considered together. Furthermore, the proportion of deaths when the cause is ill-defined or unknown must be weighed. For example, reported mortality due to dysentery and diarrhea and enteritis combined was lower in Venezuela than in Colombia (Table 5). However, in the former, the cause of death was classified as ill-defined or unknown in about one half of all reported deaths, while in the latter, the proportion with cause

TABLE 5.—*Deaths reported as due to diarrheal disease and proportion of all deaths with cause ill-defined or unknown*

| Year | Deaths per 100,000 population | | | Per cent of all deaths with cause ill-defined or unknown |
|---|---|---|---|---|
| | Dysentery | Diarrhea and enteritis | Diarrheal diseases, total | |
| **Venezuela** | | | | |
| 1933 | 26 | 120 | 146 | 41 |
| 1938 | 11 | 101 | 112 | 62 |
| 1942 | 10 | 101 | 111 | 59 |
| 1948 | 8 | 98 | 106 | 49 |
| **Colombia** | | | | |
| 1935 | 24 | 155 | 179 | 16 |
| 1938 | 23 | 161 | 184 | 13 |
| 1941 | 17 | 141 | 158 | 19 |
| 1948 | 11 | 143 | 154 | 24 |

TABLE 6.—*Deaths from gastro-enteritis per 100,000 population by age*

| Age group | Venezuela 1951 | Dominican Republic 1949 | Colombia 1948 | Costa Rica 1953 |
|---|---|---|---|---|
| Total | 85 | 118 | 144 | 155 |
| -1 | 1517 | 2116 | 2302 | 2642 |
| 1–4 | 193 | 220 | 363 | 326 |
| 5–9 | 14 | 19 | 28 | 24 |
| 10–14 | 3 | 6 | 10 | 2 |
| 15–24 | 2 | 4 | 12 | 4 |
| 25–34 | 3 | 5 | 15 | 3 |
| 35–44 | 4 | 9 | 26 | 4 |
| 45–54 | 11 | 10 | 23 | 14 |
| 55–64 | 17 | 28 | 55 | 47 |
| 65–74 | 37 | 46 | 141 | 165 |
| 75+ | 71 | 96 | 379 | 313 |

unknown was much less. Considering these percentages of deaths with cause unknown, it may be estimated that true mortality from diarrheal diseases was at least as high in Venezuela as in Colombia.

The age distribution of deaths from diarrheal diseases for selected countries is given in Table 6. As in the United States, the excessive mortality is in infants and children, and to a much less extent, in the aged. Furthermore, reporting of causes of death, in general, is less complete in the young and aged. As mentioned earlier, to evaluate reports adequately one should know for each age group the per cent of deaths at that age with cause ill-defined or unknown, but these data were unavailable.

### Diarrheal Diseases Elsewhere

Highly favorable mortality reports have been presented consistently by New Zealand, Australia, the Scandinavian countries, Canada and, to a lesser extent, by the northern European countries. The population of these countries combined is small as compared with that of Asia and Africa where, insofar as is known, the mortality from infant diarrhea continues to be excessive. On a world-wide basis, the acute diarrheal diseases almost certainly still remain as the greatest single cause of infant mortality and possibly as the greatest single cause of death.

### Discussion

The public health history of numerous cities and several countries establishes beyond doubt that the mortality and morbidity from diarrheal disease of infants and children are almost entirely preventable. However, in the past, preventive measures were initiated when there was meager knowledge of the etiology or epidemiology of the disorders. Progress in control was laborious and slow. The battle was virtually

won in some areas before any highly effective specific therapeutic agents became available. Now there is at hand a body of highly useful new scientific knowledge and it is therefore reasonable to believe that the gratifying progress of some areas in preceding decades may now be attained elsewhere in a very much shorter time.

In general, where diarrheal diseases are most prevalent, the medical and public health facilities are underdeveloped and vital statistics are least dependable. Thus, an evaluation of the magnitude of the problem cannot rest on computed mortality rates alone. These are likely to understate rather than over-emphasize the task. Certainly, available evidence indicates that the control of diarrheal diseases is the foremost public health problem in most of the American countries. Is this conclusion being given adequate attention in developing public health programs?

Subsequent evidence will support the opinion that severe diarrheal diseases are predominantly specific primary intestinal infections most commonly due to *Shigella* or *Salmonella*. Hence the task before us is to evolve specific programs designed to prevent these specific infectious diseases. Advances in medical science have provided new tools. Are there practicable public health programs which will assure an effective application of this new knowledge?

A measure of our success in the years ahead will be the rapidity of decline in mortality from the acute diarrheal diseases of infants and children.

## Part II

### ETIOLOGICAL CONSIDERATIONS

#### An Etiological Classification of Acute Diarrheal Diseases

The acute diarrheal diseases etiologically fall into three groups as shown in Table 7. Primary infectious diarrhea is caused by different pathogens which establish themselves and grow in the lumen or wall of the enteric tract. These include *Shigella*, *Salmonella*, the *Vibrio Comma*, and, possibly also, strains of coliform organisms and the slow lactose fermenting paracolon organisms. Amebic dysentery is a primary infectious diarrhea and other parasitic agents are known to give rise to a diarrheal disease occasionally. Knowledge of the etiological role of filterable agents is meager. In the laboratories of the New York State Health Department, specific diseases with major enteric manifestation have been proven to be due to filterable agents, presumably viral. With newer tissue culture technics in virological study, it may be anticipated that there will be a rapid accumulation of scientific data on the role of viruses as independent or associated agents in the production of primary infectious diarrheal disease.

TABLE 7.— *A Clinical and Etiologic Classification of Diarrheal Diseases*

| Group | Clinical entities | Usual course | Usual severity | Etiologic agent |
|---|---|---|---|---|
| Primary infectious diarrhea | Bacillary dysentery (acute shigellosis) | Acute | Mild to very severe | *Shigella dysenteriae* and *paradysenteriae*, chiefly varieties Shiga, Flexner, Sonne, Newcastle (Boyd 88) and Schmitz (ambigua) |
| | Salmonellosis | Acute | Mild to very severe | *Salmonella*—chiefly varieties in groups B and C |
| | Cholera | Very acute | Very severe | Cholera vibrio |
| | "Diarrhea of the Newborn" | Acute | Severe | Variety of ill-defined agents, including possibly virus, "Pathogenic" coliform organisms |
| | Other bacterial infections | Variable | Mild | Slow lactose fermenting paracoli and pseudomonas are under suspicion |
| | Amebic dysentery | Acute to chronic | Severe | *Endameba histolytica* |
| | Parasitic diseases | Variable | Variable | Various helminths and flagellates |
| | Virus diseases | Variable | Variable | Unidentified viruses |
| Secondary and parenteral diarrhea | Tuberculous enteritis | Chronic | Severe | Tubercle bacilli |
| | Parenteral diarrhea | Acute | Moderate to severe | Various acute generalized and localized non-enteric infectious due to staphylococci, streptococci, pneumococci and others |
| | Generalized infections | Variable | Variable | Variable |
| Non-infectious diarrhea | "Food poisoning" | Acute | Moderate to severe | Toxin producing staphylococci and possibly other organisms |
| | Nutritional diarrhea | Sub-acute | Mild | Dietary deficiency and "insults" |
| | Allergic diseases | Acute to chronic | Variable | Variable |
| | Neuropsychiatric disorders | Chronic | Variable | Variable |
| | Other | Chronic | Severe | Local ulcerative or obstructive lesions as those due to neoplasm and lymphogranuloma venereum |

In secondary and parenteral diarrhea, the gastroenteric disturbance is one part of a symptom complex. There may be a true secondary invasion of the enteric tract as tuberculous enteritis. The pathogenesis of the diarrhea which frequently occurs in acute infectious disease, in paranasal sinusitis, in otitis media and in other localized or general infections is not clearly understood.

Acute non-infectious diarrhea may be caused by the ingestion of toxic or irritating substances. The classical example is epidemic staphylococcal food poisoning; the symptoms, which appear early and may be very severe, are due to the ingestion of pre-formed toxin. Characteristically, this disease involves adults rather than infants or children. Gross nutritional defects are undoubtedly of substantial importance in the cause of diarrheal diseases in infants, particularly in the economi-

cally poor populations. Diarrhea may be a manifestation of a specific nutritional deficiency, as for example in pellagra, although more commonly a nutritional diarrhea in infants will be due to the ingestion of food of inappropriate quality. Such disorders tend to be mild but prolonged. The other non-infectious diarrheal diseases all tend to be chronic and ordinarily involve adults. They are of little quantitative importance in the study and control of infant diarrhea as a public health problem.

Having in mind these causes of diarrhea, the first problem is to determine the relative importance of each. It is now evident that the etiology of diarrheal diseases varies by area, by season, and by the age of the individuals concerned. There can be no statement generally applicable as to the relative importance of etiological entities. Data from the United States, therefore, are presented only as illustrative.

During recent years, the National Institutes of Health of the U.S. Public Health Service have maintained field laboratories for the investigation of diarrheal diseases in representative areas. Studies have been conducted in New Mexico, Louisiana, Georgia, New York City and Puerto Rico. Institutional inmates, among whom clinical disease and sub-clinical infections were relatively common, were studied also. These investigations have provided evidence as to the relative importance of the various etiological groups of diarrheal diseases in the populations examined.

The proportion of endemic diarrheal diseases found culturally positive for *Shigella*, using newer techniques to be described, is shown in Table 8. The findings in New Mexico and Georgia were similar and

TABLE 8.—*The cultural findings for Shigella paradysenteriae in endemic diarrheal disorders by age, severity of disease and area*

| | New Mexico and Georgia cases[a] | | | | | | New York City cases[b] | | |
|---|---|---|---|---|---|---|---|---|---|
| | Severe | | | Milder | | | | | |
| | Exam. | Positive | | Exam. | Positive | | Exam. | Positive | |
| | | No. | % | | No. | % | | No. | % |
| Under 6 mo. | 41 | 26 | 63 | 27 | 9 | 33 | 57 | 4 | 7 |
| 6–12 mo. | 45 | 31 | 69 | 44 | 23 | 52 | 21 | 4 | 19 |
| 1 yr. | 55 | 43 | 78 | 56 | 37 | 66 | 27 | 9 | 33 |
| 2–4 | 30 | 28 | 93 | 61 | 42 | 69 | 38 | 26 | 68 |
| 5–14 | 9 | 9 | 100 | 22 | 15 | 68 | 37 | 28 | 76 |
| 15–44 | 49 | 37 | 76 | 43 | 25 | 58 | 7 | 5 | 71 |
| 45 and over | 18 | 12 | 66 | 11 | 2 | 18 | 3 | 2 | 67 |
| Unknown | 2 | 2 | 100 | 4 | 2 | 50 | 1 | 0 | 0 |
| | 249 | 188 | 76 | 268 | 155 | 58 | 191 | 78 | 41 |

[a] Cases first examined during acute phase of illness.

[b] All cases—chiefly first examined during acute phase of illness.

these data are shown together. These cases were examined culturally at least once during the acute phase of the disease. It is noted that 76 per cent of the severe and 58 per cent of the milder cases were culturally positive for some variety of *Shigella*. Furthermore, there was an increase in the proportion of positive cases as the number of examinations during illness increased, from 62 per cent in severe cases with one examination to 90 per cent in those with more than three examinations. In New York City, where the total incidence is low, in contrast, *Shigella* infections were relatively rare, particularly in infants and children. Throughout these studies, the percentage of positive findings was lower in infants under six months and particularly so in those with mild disorders.

The study of endemic acute diarrheal diseases in Louisiana emphasized the variability in etiology of acute diarrhea. Of 174 cases admitted to the Charity Hospital in the northern section of the state, 133 (76%) were positive for some variety of pathogenic *Shigella*. Cases due to *Salmonella* were not found. In the New Orleans Charity Hospital some 300 miles distant, by identical methods of study during the same months, of 428 cases, 107 (25%) were positive for *Salmonella* and 202 (47%) were positive for *Shigella*. The total proportion of culturally positive cases in the two hospitals was similar, but in one region there was little or no *Salmonella* infection and in the other it was of substantial importance.

There is no secure evidence concerning the true etiology of the minority of cases which were not positive for either *Shigella* or *Salmonella*. Undoubtedly, some were additional cases of shigellosis or salmonellosis, even though careful laboratory examinations had been negative. Some cases may have been due to less well defined pathogens, such as strains of coliform organisms now considered by many to be pathogenic. In these investigations the cases ordinarily were not examined for *E. histolytica*. From recent findings in the study of diarrheal diseases of infants in Puerto Rico it is clear that this etiological agent must be considered. There was little clinical evidence that these cases of diarrheal disease were secondary either to other infections or to nutritional disorders. As a whole, however, despite the admitted inadequacies of knowledge as to the true etiology of some of the cases under observation, it was still evident that the major problem was specific enteric infections, due primarily to *Shigella* and, to a less extent, to *Salmonella*.

The early American medical literature concerning the diarrheal diseases is notable for the variability in findings and conclusions. The investigation by Flexner and Holt in northeastern United States cities in 1903 is, however, of high significance. In their bacteriological study of 421 cases of acute diarrheal diseases, 273 (66%) were positive for the Shiga or Flexner bacillus or for both. These results were obtained with early culture procedures at the cost of painstaking and tedious labor. It must be assumed that use of selective cultural media, as now available,

would have very substantially increased the proportion of positive findings. These data provide strong historical evidence that the usual cause of the severe acute diarrheal diseases of infants in that period was *Shigella* infection.

There is, therefore, a substantial body of evidence from studies in the United States which clearly establishes that the serious diarrheal diseases of infants and children and predominantly specific primary enteric infections usually due to *Shigella*, occasionally to *Salmonella*. The problem of control is, therefore, that of the prevention of specific infectious diseases.

The nature of the problem in one country or locality does not necessarily indicate the observations to be anticipated in another. It is not unreasonable, however, to assume, by analogy with the early experience in the United States of America, that when diarrheal disease is very prevalent in infants, it is almost always a primary infection and the major etiologic agent is *Shigella*. Specific data, nevertheless, are notably inadequate for countries with very high mortality. A limited investigation in Puerto Rico, at a time when the reported mortality was between 300 and 400 deaths per 100,000 population from diarrheal disease, clearly established that problems of study mount with increasing mortality. The population involved tends to be relatively inaccessible, and effective medical and public health services not readily available. The limited laboratory studies in Puerto Rico indicated that primary infectious diarrhea was common, but secure data as to the various etiological factors involved were not obtained. There is still need for further studies in populations with high mortality from these diseases.

It is beyond the scope of this introductory paper to review and report on the important work which has been done on the diarrheal diseases in many Latin American countries, but it is hoped that those with first-hand knowledge of this work will report on it at the Conference.

## Laboratory Studies of Etiology

There are no differential manifestations in acute diarrheal diseases which permit reasonably dependable etiological diagnoses based on clinical findings alone. Laboratory studies are essential. Only the general nature of required procedures, which should be understood by the administrator and clinician, are described here.

Shipped specimens are not satisfactory for the laboratory examination of acute diarrheal diseases. Bacteriological tests on other than very fresh specimens are misleading rather than helpful, since Shigellae do not survive for long in passed feces. Thus, the diagnostic facilities must be readily available to the patient. Furthermore, to be of clinical value, techniques must provide dependable findings at the earliest possible time. The initial work, if it is to be handled effectively, must be done in local laboratories.

The fecal specimens required may be obtained in two ways. In hospital practice, passed specimens may be taken promptly to the laboratory. These should be cultured within minutes of passage. With delay, the possibility of obtaining positive cultures becomes progressively less. The alternative procedure is the collection of specimens by rectal swabs. This procedure is very simple. The usual cotton tipped applicator is employed. In infants, particularly those with diarrheal diseases, the anal sphincter is relaxed. With the child lying on its stomach, and with the buttocks held widely apart, the swab is easily inserted beyond the anal sphincter. Material for culture is collected by rotating the swab as it is swept in a circular motion. Mucopurulent exudate is collected directly from the rectal mucous membrane. This swab is used directly and immediately for the inoculation of culture media as described below.

In older children, and particularly in adults, it may be practicable to collect material for culture during sigmoidoscopic examination. That obtained by swabbing areas of maximum pathology has superior value for bacteriological purposes. In comparative studies, approximately six positive cultures were obtained from these specimens, as compared with five when the same cases were cultured by rectal swab. The latter gave a few more positive cultures than inoculations from freshly passed fecal specimens. On the basis of convenience and reliability, the rectal swab technique may be used with confidence in the culture examination of cases of acute diarrheal diseases.

Highly selective culture media are now available for enteric bacteriology. The most valuable and reliable single plating medium is the S.S. (Shigella-Salmonella) agar. This grows readily all common species of *Shigella* and *Salmonella* and, in general, inhibits coliform organisms and other non-pathogenic species. This medium should be used in all examinations of acute diarrheal diseases. It alone is adequate in testing for shigellosis. A less selective medium, as MacConkey's or desoxycholate agar, is needed for special studies of possibly pathogenic coliform organisms. Two specialized media which greatly increase the reliability of examinations for *Salmonella* are also available. The initial inoculation is into an enrichment broth, either tetrathionate or selenite F. *Salmonellae* multiply readily in this, whereas most other enteric organisms grow poorly if at all. After incubation, inoculation to an additional solid selective medium is required. S.S. agar may be used but in our hands, brilliant green agar has been of superior value for this. Thus, a dependable examination for *Shigella* is provided by the use of one culture medium, but in studying for Salmonella and other organisms additional media are needed.

It is a convenient practice in hospitals to take a plate of S.S. agar, and, where possible, also a tube of enrichment broth, to the bedside and immediately on taking specimens to inoculate the media. The swab employed for the collection of the specimen is used directly to streak the

plate and it is then placed in the enrichment broth. The inoculation must be carefully regulated to provide the maximum amount of inoculum which will still give the desired distribution of isolated colonies on the plate being used. The laboratory worker must be fully familiar with approved procedures and be expert in the application of these. This bedside inoculation of culture media is the procedure of choice.

Representative suspicious colonies on the plates inoculated from the initial specimen, or from the enrichment broth, are picked to a differential solid medium. The best now available, in our opinion, is Kligler's iron agar with 1 per cent sucrose added. The most important and the most difficult step in the isolation of enteric pathogens is the picking of plates. This must be done by a carefully trained and very dependable worker. Reliable enteric bacteriology demands that appropriate culture media be properly inoculated and that the suspicious colonies on these be carefully picked by a competent worker.

The reactions after over night incubation of Kligler's iron agar permit an identification of the possible *Shigella* and possible *Salmonella*. The prevalent proteus organisms may provide a reaction on Kligler's which is identical to that given by *Salmonella*. A simple rapid urease test which may be read after one hour provides a ready method of eliminating most of these. The remaining cultures require further examination for *Salmonella*. In general, most cases from the same geographic region tend to be caused by a very few varieties of organisms. Thus appropriate antisera can be made available, and using a slide agglutination technique the laboratory can readily provide a presumptive diagnosis which has a high reliability.

After this preliminary screening, and the presumptive serology tests, a small number of organisms of uncertain significance usually remain. Preferably the identification of these should be left to a Central Public Health Laboratory.

It is economical to perform the definitive diagnostic studies of enteric pathogens in a larger central laboratory. Organisms known or presumed to be pathogens may be sent from the small local to the larger central laboratory on the Kligler's slants used for initial isolations. The appropriate biochemical and serological studies may be performed to provide the specific typing of *Shigella*, *Salmonella* and coliform organisms. To perform this requires the availability of approximately 100 different antisera as well as specialized media used for biochemical studies. The exact information so obtained is valuable for epidemiological purposes, whereas the early presumptive report has high importance for the direction of clinical therapy.

The *in vitro* testing of sensitivity is becoming of increasing importance. If practicable, this should be a part of the work of the local laboratory, but it is often necessary to leave these tests to the larger central laboratory.

### The Organization of Laboratory Services

The diagnosis of enteric infections calls for a cooperative organization of laboratory services. Diagnostic responsibility should be shared by a local and a central laboratory. A "reference laboratory" is needed also. In the United States, laboratories at these levels are represented, first, by the hospital, local public health, and private laboratories; second, by the central state public health laboratories and; thirdly, by the laboratories of the Communicable Disease Center of the U.S. Public Health Service.

It has been emphasized that bacteriological studies of the diarrheal diseases must be performed on assuredly fresh specimens. Thus, to provide available services many laboratories must be prepared to handle the initial diagnostic service. Of particular importance are the laboratories in the hospitals with pediatric services. Likewise, health departments with clinics to which ill children are admitted should have suitable laboratory service available. The provision of such local laboratories comprises a part of the problem of bringing adequate medical services to all communities. With appropriate cooperation, such local laboratories can provide needed service with modest facilities and with personnel of limited training. In the central public health laboratory, in contrast there must be professional personnel and facilities which will permit the application of all diagnostic tests needed for the detailed identification and for the typing of enteric pathogens. It is their responsibility, likewise, to aid the smaller laboratories by providing both guidance and diagnostic materials not easily available as for example, antisera. A true spirit of partnership and cooperation is essential.

A reference laboratory to serve a wide area is also of high importance. The scientific qualities of the laboratory's performance and the scientific enthusiasm of their workers may be greatly elevated by a reference laboratory. Its function should be both educational and consultive. Its staff should be prepared to provide short courses of intensive instruction both at the reference laboratory and in conveniently located central or local laboratories. The reference laboratory also receives problem cultures for study. These provide a continuing contact with workers in other laboratories in the area served. Thus, there should grow up a closely related group of laboratory workers drawing their scientific leadership from highly competent scientists and teachers within the reference laboratories.

The specific nature and location of the local, central and reference laboratories may vary widely. The latter, for example, might be organized independently, might function within a school of public health or by cooperative agreement could be affiliated with some selected central public health laboratory. It is to be emphasized, however, that the provision of laboratory services calls for a balanced development of local and central laboratories with at least one accessible reference laboratory.

A field laboratory also may serve special purposes. It may be designed to meet emergency needs when other facilities are inadequate or it may be primarily a research activity. It has served well in making practicable the detailed epidemiological, clinical, and laboratory studies upon which more effective programs of control are based. It could be the initial laboratory in an area which would give guidance to the control program for the region.

Effective application of newer knowledge needs the participation of a laboratory. There is, however, general realization that in some countries of the Americas, often in those with high death rates from diarrheal diseases, laboratory services are seriously inadequate. Improvement in laboratory service is an essential part of the program of the Pan American Sanitary Bureau for strengthening national and local health services and it is to be hoped that in the not too distant future all countries will have the network of laboratories described above.

Nevertheless it is not to be inferred that nothing can be done if laboratory services are not available to examine all cases. What is needed is knowledge of the nature of the problem to permit effective application of therapeutic and control measures. Guiding knowledge may be obtained by a dependable examination of a sample of representative cases. Even though only a small percentage of all cases may have a definitive diagnosis established by laboratory tests, this knowledge will help handle more effectively those which are not tested.

**Comment and Questions Warranting Consideration**

In developing a program for the control of diarrheal diseases the first step is an assessment of the adequacy of knowledge as to etiology in the particular country and area. On the basis of findings in the United States it can be assumed that severe diarrheal diseases are predominantly specific enteric infections. Is there any conclusive evidence that this is not true elsewhere? What proportion of cases have been found due to *Shigella* or *Salmonella* in other countries? To what extent are the remaining cases apparently due to other infections? How important are nutritional factors as the primary cause of illness in fatal cases of diarrheal diseases?

Since laboratory studies are essential for an etiological diagnosis of diarrheal diseases, the development of laboratory services in countries with high mortality demands critical consideration. This is a part of the problem of planning for adequate medical and public health services. In the United States local diagnostic, central public health, and an area reference laboratory have all been found to be essential. These have been supplemented by laboratories for special studies. Is this or some other plan of development desirable and practicable for other American countries? What are the immediate and pressing laboratory needs? Are trained workers available if physical facilities could be provided?

The needs are great. In other public health crusades, as against yellow fever or malaria, special facilities for special programs were provided. The activities were notably successful. Should there not be a comparable emphasis on the current major problem of the control of diarrheal diseases? The newer scientific knowledge gives strong assurance that such a special program also would be highly effective.

## Part III

### EPIDEMIOLOGY

The Epidemiology of the acute diarrheal diseases is the separate and distinct epidemiology of the different etiological entities. Attention will be limited here to shigellosis and salmonellosis for the reasons stated in the two preceding sections.

### Shigellosis

An outstanding feature of *Shigella* infections is the variability in manifestations in infected individuals. Previously generally held belief that bacillary dysentery is always severe is not correct. Shigellosis may result in severe to mild clinical disease, or in disturbance so trivial that the individual suffers little inconvenience. Furthermore, infection without any clinical manifestations whatsoever is common, particularly in adults. Thus an understanding of the natural history of *Shigella* infections must involve extensive studies of the healthy as well as those who are or have been ill.

*Shigella* are encountered frequently in monkeys in captivity and at rare intervals have been isolated from domestic pets. Shigellosis as it ordinarily occurs, however, is an infection which involves humans exclusively and spreads only from man to man.

### Incidence

In the course of studies in the United States culture surveys of normal population groups were conducted. Those examined were selected without prior knowledge of the presence or absence of diarrheal disease. Clinical histories were obtained, however, at the time of the examinations. In New Mexico the mortality from diarrheal diseases was approximately 100 per 100,000 population in 1937 and 1938. During these years, 2,198 "normal" individuals were examined bacteriologically for *Shigella* and 239 (11%) were positive. In different communities and groups the percentage varied from 3 to 20. Comparable examinations in Georgia when mortality from diarrheal diseases was about 20 per 100,000 established a 3 per cent prevalence rate. In Puerto Rico, with a high mortality rate, very limited studies revealed a 4 per cent prevalence rate for shigellosis in the general population. In New York City, by contrast, positive findings were very rare. Knowing that the average duration of

untreated *Shigella* infection is about 6 weeks, it is evident that, where diarrheal diseases were moderately or highly prevalent, the annual incidence of infection must be very high. In institutional populations, where cultures could be taken at frequent intervals, virtually all persons acquired *Shigella* infection at least once in a year's observation.

The ratio of clinical and sub-clinical infection varied markedly with age. Infants if infected usually but not always were ill. As age increased, the proportion of passive carriers increased. At 3 years of age and over, there were always more passive carriers than current or recent (within 3 months) cases. In general, for each current clinical case, a total of 9 convalescent or passive carriers were found concurrently.

Of the 380 culturally positive persons encountered in these surveys only 2 were under the care of a physician. One, acutely ill when found on the survey, was admitted to the hospital the following day and died 2 days later. In the absence of a special study, these 2 might have been tested culturally and thus there would have been 2 demonstrated and 378 undetected infections with *Shigellae*. Thus, for every known infection (manifest source) there are numerous unrecognized infections (hidden source). In the light of these findings it is not surprising that endemic diarrheal diseases commonly appear to be scattered sporadic cases. These seemingly unrelated infections may arise from a single source or be joined by a series of undetected infections. This knowledge is essential for the interpretation of the epidemiology of the acute diarrheal diseases.

The true incidence of clinical disease due to *Shigella* is not indicated by morbidity or mortality data even with superior reporting procedures. For each death there are several severe clinical cases. For each severe clinical case there are many mild clinical infections; for each clinical case of any degree of severity there are about two passive carriers. Thus, one death from shigellosis suggests the occurrence of scores of infections of other degrees of severity including the subclinical infections.

### Household Attack Rates

The attack rates for shigellosis in affected households were studied in New Mexico, Georgia, and New York. Based largely on single culture tests, about one half of the members of affected households were found positive. It seems certain that the majority of the household contacts of shigellosis would have been found infected if these tests had been repeated and continued through a period adequate to measure incidence rates. There was similar evidence in the study of small communities and institutional groups with known clinical cases.

### Age

Infection with *Shigella* organisms shows a relatively characteristic age distribution in the general population of areas with a moderate to high

endemic occurrence. Prevalence rates are low in the first six months of life, rising during the next six months to a level which remains fairly constant during the next few years. About the fourth year, the prevalence rate gradually declines reaching a second level at about age 15 after which it remains at a fairly constant level.

Clinical disease produced by *Shigellae* has a different age distribution pattern. It is relatively infrequent in the first few months of life, has its greatest frequency between 6 to 18 months and thereafter falls rapidly to a much lower level. Thus, when infants acquire *Shigella* infection, most of them become ill, many with severe disorders or even fatal illnesses. At three years of age, severe illnesses are uncommon, mild illnesses are frequent but more than one half of the infections are subclinical. An even higher proportion of the infections in adults are subclinical.

### Season

Shigellosis is largely a "summer diarrhea". In general, the colder the winter months, the later in the summer do high rates appear. In those sections of the southern United States where the winters are mild, a rise in *Shigella* prevalence usually begins in March, April, or May. This is frequently followed by a sharp drop in prevalence in the very hot months (when there are few flies) followed by a secondary rise in the fall. In areas which have colder winters, there is usually a single peak occurring in the latter half of summer. The explanation of this high prevalence in the warm seasons is not fully understood. In part, but not entirely, it appears related to the variations in fly prevalence.

### Modes of Spread

Shigellosis is almost limited to humans. The organisms are discharged in the feces, often in profuse numbers. Consequently, the maintenance of a high level of *Shigella* infection in a group depends upon the more or less direct transfer of human feces containing *Shigellae* from one person to another. The major question concerns the relative importance of the various modes of spread.

Direct person-to-person transmission is regarded as the mode of spread of first importance. Cases were found with notable frequency in homes defective in personal and environmental cleanliness. The infection among institutional inmates commonly became prevalent and troublesome in buildings for the low-grade mental defectives and the deteriorated and disturbed inmates of mental hospitals. Also, in military groups, high prevalence coincided with a lack of personal cleanliness. Finger contamination with feces would be assumed under these conditions and was demonstrated culturally. *E. coli* was recovered in 82 per cent of 235 finger cultures obtained from clean inmates of mental hospitals. Furthermore, *Shigellae* were isolated from the fingers of 4

(10%) of 39 persons with positive fecal cultures and from 2 (1%) of 229 with negative fecal cultures. Having reached the fingers the organisms could be transferred from person to person directly or by articles handled in common. In several institutional outbreaks there was strong evidence against other possible channels of spread.

The role of the mild and unrecognized cases and the subclinical cases in the spread of shigellosis calls for emphasis. These far outnumber the identified and suspected cases combined. Clinical shigellosis usually appears in individuals with no history of exposure to preceding cases. The unsuspected human source, however, may be close at hand and the organisms may be passed relatively directly from this person to the one who develops manifest disease.

Other modes of transmission occasionally occur and assist the person-to-person spread. Water-borne outbreaks of shigellosis are rarely reported. Historically, the change from an unsatisfactory to a safe water supply was repeatedly marked by an immediate and deep decline in typhoid mortality, but without a comparable sharp drop in deaths from the diarrheal diseases.

Milk *per se* as a means of introducing *Shigellae* into homes is notably free from suspicion. In the United States of America the poor, who suffer most from diarrheal diseases, commonly use the highly sanitary canned and dehydrated products which in the United States of America are less expensive than the bottled fresh milk. On the other hand, although milk may not have significance as a mass means of spread, it, like any other food or substance which enters the mouth, may be the vehicle for transmitting infection from one member of the household to another.

Food-borne outbreaks have been reported. Although explosive outbreaks of shigellosis are rare, when they occur they are most frequently food-borne outbreaks. Feig, in a study of 476 outbreaks of bacterial gastrointestinal disease which occurred in the U.S.A. during the period 1945–1947, found only that 14 (2.9%) were due to *Shigella* organisms and of these 14 outbreaks, 9 were food-borne. In a few of the institutional outbreaks studied, carriers among the food handlers and kitchen helpers evidently contributed to the spread of infection, but there was no indication of heavy contamination of a particular article of food.

Shigellosis and flies appear at the same seasons and in the same general environment. The Public Health Service studies in Hidalgo County, Texas, established that in that area fly control on a community-wide basis resulted in about a 50 per cent reduction of *Shigella* infections. However, an appreciable amount of shigellosis did remain in this area in spite of the intensive efforts at fly control. In a community in which flies do not have ready access to human excrement or in which houses are well screened, flies can play only a minor role in the spread of *Shigella* organisms. Furthermore, among institutional inmates, a ready spread

of this infection, for which neither water nor food was responsible, has been observed frequently in the absence of flies. Considering all the evidence, it may be concluded that flies do spread shigellosis, that in some communities its incidence may be reduced by 50 per cent by effective fly control, but shigellosis can and does spread in the absence of flies.

**Salmonellosis**

The natural habitat of *Salmonella*, other than *S. typhosa* and related paratyphoid organisms, is lower animals or birds. The infection in man is an accidental and an unusual occurrence. Of major significance in the epidemiology of salmonellosis is the determination of modes of spread from lower animals or birds to man.

Early studies of salmonellosis gave exaggerated emphasis to the role of rodents. Contamination by the excreta of mice or rats was thought to be of high epidemiological importance. It is now appreciated that this is of minor significance.

Explosive food-borne outbreaks gradually called attention to the role of fowl. It is now known that domestic fowl are often infected with varieties of *Salmonella* in addition to *S. pullorum*. Furthermore, eggs from infected birds often carry the infecting organism. Thus, dissemination to humans was frequently attained in foods containing uncooked or under cooked egg as, for example, in salad dressing. The problem was accentuated through the commercial dehydration of pooled eggs. The heat required for processing did not kill the *Salmonella* and, in the pooling, the infection in a few eggs, contaminated the large volumes processed at one time. Thus, it was found that relatively high percentages of the dehydrated eggs were culturally positive for *Salmonella*. Numerous epidemics attributable to this food product were studied. Here, the source of the infection was fowl but the major feature of the problem was in the wide dissemination of this infection in the commercial processing of the food.

Recent studies in Florida have demonstrated essentially the same problem in the processing of meats. Prior to slaughter a comparatively small proportion of birds were infected with *Salmonella*. However, these few provided contamination to the tables, utensils and instruments used in the processing plants. It was clearly shown that this contamination spread to the edible meat. Though few of the living birds were infected, a substantial portion of the fowl prepared for the markets were contaminated with *Salmonella*.

To an even more marked degree, salmonellosis was spread among swine in the day or two before slaughter, during the course of marketing, transportation, and in the "holding pens" at the abattoirs. Furthermore, within the abattoirs a wide distribution of contamination with *Sal-*

*monella* was readily demonstrated. Thus, edible meats and especially the pooled and mixed meat used in sausage were frequently found positive for *Salmonella*. In and on such food products the viable organisms reach the kitchens. Some survive the cooking process and may account for epidemics attributed to the consumption of pork or fowl. Through other channels the contaminant may reach other foods, thus causing sporadic cases or family outbreaks.

Commercially prepared dog meals which contain meat were frequently positive for *Salmonella* also. This may partially explain the wide dissemination of this infection in domestic pets in the U.S.A. Of 1,626 normal household dogs cultured in Florida, 15 per cent were positive for *Salmonella*. Limited examinations indicated that the infection was prevalent in cats also.

Through these various channels, therefore, it is evident that there is frequent exposure to salmonellosis. The rarity of the clinical disease, rather than its occurrence, needs explanation. McCullough and Eisele clearly demonstrated, through feeding varying doses of *Salmonella* to human volunteers, that the frequency of clinical disease increased with the increasing dosage of organisms. Very low dosages could be given without the organisms being demonstrable later in the feces. With increasing numbers, subclinical infection with repeatedly positive stools tended to occur while with higher doses there was clinical disease in some or all of the volunteers. All *Salmonella* tested were found to be pathogenic for humans but there was clinical disease in *S. pullorum* infection only with massive doses. Under natural conditions, clinical disease is most likely to be acquired when *Salmonella* multiply in human food, thus providing massive doses of the infecting agent. However, bacteriological examination of food handlers has demonstrated that subclinical infection is both widespread and common. Presumably the numbers of organisms commonly acquired at one time is less than that required to initiate disease.

In clinical and public health practice, salmonellosis comes to attention chiefly as food-borne epidemics or as sporadic infection in infants. The latter are probably explained by spread from infected adults, from contaminated kitchens or from domestic pets. Evidently, as in shigellosis, the infant is more highly susceptible than the adult.

The dissimilarity in the epidemiology of these two enteric infections was illustrated by the studies of Watt and Lindsay in Texas. Fly control reduced the prevalence of shigellosis by approximately 50 per cent, but had no effect on the prevalence of salmonellosis.

### Comment and Questions Warranting Consideration

Etiological diagnosis is the beginning of epidemiological study. There can be no adequate understanding of the occurrence of acute diarrheal diseases without a knowledge of etiology and of the natural history of

the etiological agent. This has been attained in the United States by special studies. The conclusions for one area cannot be applied entirely to another. Thus, there is the problem in each country to examine critically, in the light of findings elsewhere, the epidemiology of diarrheal disease occurring within its area.

Administrative control of specific infections is based on their epidemiology. Methods must differ, since the epidemiology of different enteric infections differ. However, in shigellosis and salmonellosis, the recognized clinical case is but one of many sources for the spread of infection. Safe disposal of known infectious excreta is essential, but there is no evidence to suggest that a rigid isolation of cases occurring in a community would provide effective control. Is there justification for using public health time to control the isolation of these infections which spread from so many sources?

The improvement of water supply has been given credit for reducing the incidence of diarrheal diseases. The effect however appears to be due to improved cleanliness from more readily available water. Is there evidence that viable *Shigella* or *Salmonella* (other than typhoid and paratyphoid) are often acquired through drinking water?

Poverty and a high prevalence of acute diarrheal diseases are commonly associated. Can this be explained on the basis of the effect of crowding, flies, and lack of personal and environmental cleanliness?

The epidemiology of typhoid fever has been studied in detail in many countries. Should we not give at least comparable attention to the enteric infections which give rise to diarrheal diseases and which commonly produce about ten times as many deaths as typhoid fever?

## Part IV

### CLINICAL

The clinical descriptions of diarrheal diseases usually found in medical texts are those of hospitalized cases. During the course of field studies of these disorders carried out during the past fifteen years in the United States, clinical cases of all degrees of severity have been studied. Detailed histories were recorded and all cases were examined bacteriologically. Subsequently, they were separated into their etiological groups on the basis of the bacteriologic findings. The description following is based on the study of more than 1,000 culturally positive clinical cases.

### Shigellosis

An outstanding observation in these studies was the wide variation of clinical severity. There was a full range from fulminating rapidly fatal illnesses due to *Shigella* to, at the other extreme, "just a few loose stools". Asymptomatic carriers with no history of preceding disease were identified frequently also.

Three clinical types of shigellosis have been described and were seen.

(a) In *fulminating infections*, a previously healthy infant or child rapidly becomes gravely ill and the total course of the illness may be less than 24 hours until death. Fortunately, these cases are very unusual and stand apart from the less severe clinical illnesses. (b) The *dysenteric* type is bacillary dysentery as ordinarily described. The bloody, mucopurulent evacuations, tenesmus, abdominal pain and severe general manifestations point clearly to bacillary dysentery. A relatively high proportion of hospitalized cases fall in this group due to the apprehension caused by bloody stools. (c) The *diarrheic* type of shigellosis, a simple diarrhea, is the most common manifestation of these infections in the United States. Grossly, the stools are free from blood and exudate but often contain mucus. General symptoms, as fever, nausea, and anorexia, tend to be mild if present at all. Of the varying causes of this common complaint, *Shigella* infections are of high importance.

After an incubation period of from one day to one week, the clinical illness in shigellosis has a relatively abrupt onset. The initiating symptoms ordinarily are diarrhea, vomiting, and abdominal pain. In infants, convulsions are not infrequent as one of the symptoms of onset. The prominent manifestation is the diarrhea. The number and character of stools vary in accordance with the degree of severity. In very severe infections, there is almost continuous straining. Associated complaints include fever, particularly at the onset. A protracted fever is not unusual in infants who received no specific therapy. Anorexia, nausea and vomiting are troublesome and contribute substantially to the marked dehydration. Abnormal physical findings are notably few, other than abdominal tenderness and the signs of dehydration. Prolapse of the rectum and meningismus are occasionally observed.

### Other Diarrheal Diseases

In our studies there were no distinctive clinical findings which permitted a dependable differentiation of *Shigella* and *Salmonella* infections in the individual case. In groups of cases, the general manifestations, notably the fever, were more pronounced in salmonellosis than in shigellosis. Dysenteric stools were observed occasionally in salmonellosis but much less frequently than in shigellosis. Grave complications as meningitis occasionally were associated with salmonellosis but not with shigellosis. Apart from laboratory observations, therefore, there was no secure method of differentiating between shigellosis and salmonellosis.

Epidemics of diarrhea in nurseries for the newborn have been reported, in some countries, with distinctive epidemiological characteristics. In the individual case, however, there were no differential clinical features of importance. The illnesses were an acute diarrhea with an early dehydration frequently proceeding to a fatal termination. It is

to be hoped that by maintaining existing practices of keeping babies with mothers and not constructing large nurseries, Latin American countries will avoid such epidemics.

*E. histolytica* infection of young children has not been studied adequately. A distinctive feature of these cases is the mildness of clinical manifestations as contrasted with the gross abnormality in the stool. Though these signs are clinically suggestive, dependable diagnosis requires laboratory examination.

Acute infectious diarrhea commonly involves infants or children in preceding good health. A child in vigorous health one day will be acutely ill the next. This is in contrast to the diarrheal disorders occurring in association with malnutrition. The initial condition of the patient is much less satisfactory and the diarrhea, itself, tends to be milder. It is known, however, that there is increased susceptibility to specific infections in children of poor general health. It is necessary, therefore, to rule out by negative laboratory findings the occurrence of specific enteric infections before accepting a diagnosis of a non-infectious diarrheal disorder.

### Laboratory Observations other than Bacteriological

Microscopic examination of fresh feces in a portion of the cases reveals many leucocytes, red blood cells and some macrophages. This finding suggests shigellosis, but a similar exudate may be observed in salmonellosis or other primary enteric infections. Furthermore, the absence of this exudate has little weight in excluding a diagnosis of shigellosis. Microscopic findings are of high importance in identifying promptly cases of acute amebic disease.

The total white count and the differential remains within normal limits as a rule. Secondary anemia becomes apparent if the illness is protracted. There are the chemical changes in the blood which are associated with dehydration.

The important laboratory procedure is the bacteriologic examination for enteric pathogens. Simplified techniques have been described. This test is essential in the diagnosis of diarrheal diseases.

### Prognosis

The case fatality rates prior to modern methods of combatting dehydration and before the availability of specific therapeutic agents varied widely. In our study, there were 38 (9.4%) deaths in 406 cases of proven *Shigella* infection in New Mexico, one (1.5%) in 67 in Georgia and none in the 82 positive cases in New York City. In these cases the fatality rate in infants under one year was 30.7% and in the second year of life, 10.2%. There were no deaths in older children or adults.

With the recent advances in the treatment of dehydration, and with

the advent of sulfonamides and antibiotics, the prognosis of shigellosis has greatly improved. In fact treatment is usually so effective that occurrence of a death from this infection suggests delay in seeking medical attention or some defect in the medical care provided.

There is a wide range in the duration of the illness. In general, older children and adults usually recover after two to four days even in the absence of treatment. In infants without treatment the symptoms frequently persist for two to six weeks. Specific therapy of shigellosis is ordinarily followed by prompt recovery.

**Differential Diagnosis**

Acknowledged enteric disorders are, on the whole, inadequately diagnosed rather than erroneously diagnosed. A mere description of the illness as "diarrhea and enteritis", "dysentery" or "simple diarrhea" cannot be accepted as satisfactory when etiologic diagnoses are possible. In clinical medicine, the latter is a basic requirement as a guide to specific therapy, and in preventive medicine and public health, it is essential for effective control.

A positive diagnosis of the etiology of acute diarrheal diseases can be made only in the laboratory by the isolation of the causative agent. This involves delay. Moreover, laboratory facilities are not always available. Therefore, as a guide to the prompt initiation of specific therapy, satisfactory working impressions are needed.

An accurate knowledge of the nature of a disease and of the entities from which it must be differentiated is a prerequisite for clinical diagnoses. A marked adjustment of the prevailing concept of the findings which warrant a consideration of shigellosis is needed. It must be appreciated that the varieties of *Shigella* which prevail rarely give rise to the bacillary dysentery ordinarily described in medical texts. A simple diarrhea with watery fecal movements is the common manifestation of shigellosis and when this occurs this specific enteric infection is to be considered.

Of first importance in differential diagnosis is a secure knowledge of the prevailing types of diarrheal diseases in the particular area and group concerned. In the United States of America, for example, prior to special studies of diarrheal diseases in New Mexico and Georgia, bacillary dysentery was regarded as a rare tropical disease and *Shigella* infections were diagnosed infrequently. After demonstration that a high percentage of the usual endemic cases of diarrhea, particularly those which came to the attention of physicians were shigellosis, this diagnosis was made more often. Since the nature of diarrheal diseases occurring in various countries and areas may differ widely, this type of information needs to be accumulated in representative localities. This may be obtained through the cooperation of practitioners and health depart-

ments with an effective bacteriological laboratory. Without such studies, the diarrheal disorders will continue to be inadequately diagnosed.

## Treatment

1. *Fluids and elecirolytes*

Effective therapy of diarrheal disease in infants requires recognition that the major difficulty is the metabolic disturbance, disorder in body fluids and electrolytes, which is produced. Thus, immediate emergency attention needs to be given to correction of this disturbance and prevention of further losses. Detailed description of therapy of dehydration is beyond the scope of this paper, but excellent references are available and a typical plan followed at one university is reproduced as an appendix.

The essential principles of treatment of severe cases are:

(a) Immediate treatment of "shock", restoration of normal circulation. This is accomplished through the use of whole blood transfusions or intravenous plasma, in combination with glucose solution.

(b) Replacement of previous losses and correction of metabolic imbalance. This is accomplished through administration of balanced solutions of electrolytes, including potassium and glucose in water. The parenteral route is usually necessary, at least at the beginning, but the oral route has been used successfully far more extensively in recent years. Therapy can begin according to general rules, but control through measurement of serum $CO_2$ and Chloride is highly desirable.

(c) Gradual resumption of feeding, utilizing a standard milk mixture or breast feeding.

2. *Sulfonamides and antibiotics*

While "chemical therapy is more important in infant diarrhea than chemo therapy", proper administration of the latter in cases of shigellosis will materially shorten the duration of the infection and usually of the diarrhea itself. Sulfadiazine is the sulfonamide of choice, being more effective than the so-called slowly absorbed drugs such as sulfasuxidine or sulfaguanidine. An important consideration is that an early and dangerous accompaniment of dehydration in infants is depressed circulation, which in turn is conducive to crystallization of the sulfadiazine in the kidneys, leading to renal blockage. Thus, sulfadiazine should not be administered until the child is urinating

Appearance of sulfonamide-resistant *Shigella* occurred in a United Nations prisoner-of-war camp in Korea, necessitating use of various antibiotics. Under the direction of a "Joint Dysentery Unit", sponsored by the Commission on Enteric Infections of the Armed Forces Epidemiological Board of the United States of America, it was established

that chlortetracycline (Aureomycin), chloramphenicol (Chloromycetin) and oxytetracycline (Terramycin) were all effective against *Shigella.*

Dividing the daily dose into 3 portions at 8-hour intervals was the most effective schedule. Since the problem of renal blockage does not arise with the antibiotics it is probably desirable to use one of them first, although usual effectiveness and low cost of sulfadiazine still makes it a very useful drug for shigellosis.

*In vitro* sensitivity tests are highly important as a guide to therapy. Laboratory tests rather than clinical trial can indicate the therapeutic preparation of choice in the prevailing infections.

The problem of the specific treatment of *Salmonella* infections is markedly different. These infections remain relatively or highly resistant to virtually all available antibacterial therapeutic agents. Chloramphenicol has been used widely due to its demonstrated effect in typhoid, but clearcut evidence of efficacy in other *Salmonella* infections is lacking. In salmonellosis, therefore, reliance must be placed on therapy of the dehydration.

3. *"Symptomatic" therapy*

Drugs for the purpose of controlling the symptoms of diarrhea do not appear to be useful in children. Metals such as bismuth are not effective in the severe case and unnecessary in the mild one. Absorbents and materials like pectin may decrease the frequency of stool excretion but do not affect the crucial loss of fluid into the bowel.

### Comment

Control of infant diarrheas calls primarily for prevention, but it is important also to prevent deaths through proper early treatment. In general, infantile diarrhea requires, primarily, treatment of the fluid and electrolyte disturbance, for which highly effective routines have been developed. When the diarrhea is due to *Shigella,* most common etiological agent, specific therapy with certain antibiotics and sulfadiazine is very useful. Recent emergence of resistant strains makes desirable *in vitro* testing to discover the most useful agent. Unfortunately, except for typhoid fever, no effective antibiotic or chemotherapeutic agent has been found for salmonellosis.

## Part V

### PREVENTING MORTALITY AND REDUCING MORBIDITY

### Control Measures in the Past

The methods used in the control of many communicable diseases can be stated simply. For example, in smallpox, there is vaccination and, in many insect-borne infections, eradication of the vector is the method of choice. However, considering the reasons for decline of diarrheal

diseases in the countries which now have low rates it is evident that multiple factors were involved. There is no quantitative measure of the relative importance of these various influences which contributed to the progressive reduction of mortality and morbidity. Conclusions must be based on a critical evaluation of all available evidence.

It is assumed widely that where diarrheal diseases have been controlled this was predominantly a by-product of the programs of community sanitation which have almost eliminated typhoid fever. Major credit is given to the installation of safe public water systems. Historically, the importance of public water supplies in the spread of cholera and typhoid fever is beyond question. In numerous cities in the United States of America, there was an immediate and marked decline in typhoid mortality and morbidity with the availability of safe water supplies. It may be predicted with confidence that under similar conditions there would be the same decline elsewhere. However, with the change in water supply, there was no comparable evidence of any prompt decline in the mortality from diarrheal diseases. This is well illustrated by the experience of Pittsburgh and Philadelphia, as shown in Table 9. There is substantial evidence that the infections which produce the acute diarrheal diseases of childhood are rarely water-borne. *Shigella*, the pre-

TABLE 9.—*Mortality per 100,000 population from typhoid fever, diarrhea and enteritis in Philadelphia and Pittsburgh, 1900–1919*

| Year | Deaths per 100,000 population | | | |
|---|---|---|---|---|
| | Pittsburgh | | Philadelphia | |
| | Typhoid | Diarrheal diesases | Typhoid | Diarrheal diseases |
| 1900 | 144 | 215 | 37 | 115 |
| 1901 | 120 | 210 | 35 | 104 |
| 1902 | 136 | 221 | 47 | 96 |
| 1903 | 133 | 193 | 72 | 113 |
| 1904 | 136 | 198 | 55 | 133 |
| 1905 | 107 | 191 | 51 | 144 |
| 1906 | 141 | 230 | 74 | 172 |
| 1907 | 131 | 209 | 60 | 147 |
| 1908 | 49 | 183 | 35 | 138 |
| 1909 | 25 | 157 | 22 | 130 |
| 1910 | 28 | 201 | 18 | 168 |
| 1911 | 26 | 146 | 15 | 133 |
| 1912 | 13 | 130 | 13 | 107 |
| 1913 | 20 | 156 | 16 | 113 |
| 1914 | 15 | 120 | 8 | 120 |
| 1915 | 11 | 112 | 7 | 100 |
| 1916 | 9 | 131 | 8 | 101 |
| 1917 | 12 | 151 | 6 | 107 |
| 1918 | 11 | 139 | 5 | 104 |
| 1919 | 7 | 99 | 4 | 72 |

dominating causative agent dies rapidly outside of the human body and authentic reports of water-borne outbreaks of shigellosis are rare indeed. *Salmonella* is spread predominantly in foods. Important as was the purification of water supplies, this cannot be credited with any major contribution to the prevention of the diarrheal diseases of infants in the United States.

There is some evidence that the availability of water for personal cleanliness does correlate with the incidence of diarrheal diseases. Limited studies in labor camps in California indicated that *Shigella* infections were 8 times as prevalent in families who had to carry water for domestic use as compared with those who had water immediately available from faucets by or in the house.

A community water supply may contribute to the control of diarrheal diseases in two ways. Flush toilets for the disposal of human feces are usually installed soon after the water is available. Then enteric pathogens from human carriers, mild and unrecognized cases, as well as from the acknowledged case, are disposed of safely. Concurrently, a basin with running water is installed conveniently. Epidemiological evidence indicates that a relatively direct person-to-person spread of contamination by soiled hands is of substantial importance in the spread of shigellosis. Undoubtedly, improved hand washing habits resulting from convenient facilities contributes effectively to the control of diarrheal diseases. Thus, community water supplies apparently aided in the control of diarrheal diseases, not by preventing the ingestion of *Shigella* and related pathogens in impure water, but by providing means for a safe disposal of human feces and conveniences which resulted in an improvement of personal cleanliness.

The installation of sanitary privies for rural homes had general importance also, but the downward decline in diarrheal diseases was well advanced before there was any public health emphasis on the importance of these sanitary devices.

It has long been recognized that a high incidence of diarrheal disease and a high prevalence of flies are usually associated. The characteristic high incidence in summer has suggested that flies must have an important role in the spread of infection. The studies in Hidalgo County, Texas, have established what was suspected previously. There the control of flies resulted in approximately a 50 per cent reduction in the prevalence of shigellosis. Historically, fly control in urban areas was brought about slowly by industrial and community development, quite as much as by public health activity. The horse gave way to the motor car. With the disappearance of stables, the most prolific source of fly breeding was removed. Programs for garbage disposal and general community cleanliness further reduced fly breeding. An increase in screening and a widespread concern with the protection of human food from

flies were important. Public education, as for example, through the popularization of the slogan "Swat the fly", gave a general appreciation of the fly hazard. Their control undoubtedly did have an important part in reducing the prevalence of diarrheal diseases. In the light of findings in Hidalgo County, Texas, it is reasonable to believe that in many areas the control of flies accounted for about one-half of the reduction of shigellosis, and of the severe acute diarrheal diseases.

As pointed out in the section on epidemiology, shigellosis is often a serious endemic disease in the absence of flies. Yet when flies are numerous, reduction of their prevalence will very likely have a favorable effect on the spread of the disease. Fly control is not easy. It involves general sanitation, disposal of garbage and industrial and agricultural wastes, and, for the individual home, adequate screening. Insecticides, such as DDT and dieldrin, are of only limited usefulness because of the relatively rapid emergence of resistant strains of flies. Constant attention is necessary; in the Hidalgo County studies, even after two years, when the special program was stopped, both fly prevalence and *Shigella* infections returned promptly to their previous high levels.

Developing interest in the special problems of children resulted in the simultaneous development of pediatrics as a division of clinical medicine and of child hygiene as a community interest. Thus, pediatricians from the beginning were as much interested in preventive as in curative medicine. In the preventive field, the early French leadership, in seeking to provide health supervision for all children, was paralleled by similar developments in other countries. Networks of child health clinics were gradually established, watching over the health of infants and instructing mothers in safe methods of care in the importance of cleanliness in preparing and giving the child food. General practitioners, as well as pediatricians, have gradually adopted supervision of the well child as an integral part of their practice. Public health nurses visited homes giving the same message and providing individual instruction and demonstration. Obviously, like other essential components of the public health program, there has been considerable variation in the degree to which child health services have been developed in different countries. It is of importance to note that in the long-range program adopted by the First World Health Assembly, maternal and child health was included in the list of first priorities. This type of program is an essential part of the broad preventive attack on infant diarrhea.

Concurrently with the decline in mortality from diarrheal diseases in the United States of America, there were broad changes in socio-economic conditions which affected a high percentage of the population to a variable degree. There were improvements in housing and less overcrowding, refrigeration became generally available with consequent marked changes in food supply, and mothers with more available time

had fewer children to care for. The public health significance of such changes can be acknowledged but their relative importance is not measurable.

Thus, in the control of diarrheal diseases in the United States, many influences were active. The factors of major importance appear to be the safer disposal of human feces, better personal cleanliness (both facilitated by installation of public water supplies), the control of flies, and marked improvement in infant hygiene in the home. The accomplishment was remarkable in view of uncertainty as to etiology, lack of knowledge of epidemiology, without specific medication, and with limited help from organized public health.

**Presently Available Control Measures**

The advances in scientific knowledge which contribute most to the control of the diarrheal diseases are: (a) Etiology. Using new highly sensitive bacteriological technics it is now known that the acute diarrheal diseases are predominantly specific enteric infections due chiefly to *Shigella*, to a much lesser extent to *Salmonella* and in a small percentage of cases to other ill-defined pathogens probably including pathogenic strains of coliform organisms and viruses. (b) Epidemiology. The most common source for *Shigella* is the mild unrecognized human case and the asymptomatic carrier. Spread is from person-to-person usually through relatively direct contact, and rarely by common vehicles as water, milk or food. Flies play an important role, though of varying significance in different areas. Fecal contamination spreads much more readily than previously believed, even in modern hospital nurseries. *Salmonella* is disseminated from lower animals and birds, particularly through edible fowl, eggs, and meat products and, to a degree, through contact with domestic pets. (c) Therapy. There have been equally important advances in two lines. (1) It is now known that deaths from diarrheal diseases are due chiefly to disturbances in fluid and electrolyte balance. Proper replacement therapy can prevent deaths. (2) The most common cause of severe acute diarrheal disease, *Shigella*, responds readily to sulfonamide or antibiotic therapy or to both. *Salmonella* is however quite resistant.

In addition to this accumulation of new scientific knowledge, the practice of public health has matured markedly in recent years. New competency in the application of knowledge obviously has high practical significance.

In the light of the advances in scientific knowledge and public health practice, and with a consideration of available resources, control measures may be selected to satisfy varying situations. There will be two objectives: to prevent deaths of those already ill, and to prevent the occurrence of cases. The former will call for a prompt use of effective

therapeutic procedures, the latter primarily will demand the use of appropriate public health measures to prevent the spread of specific enteric infections. In the former, attention will be concentrated on the sick individual and his care, and in the latter, the concern will be with broad population groups where improvements in community and home sanitation, in personal cleanliness, and infant hygiene, will need to be attained.

The activities designed to attain these objectives will flow through three different but interconnected channels, namely, organized public health, medical service and socio-economic development.

### Organized Public Health

The responsibility for the control of diarrheal diseases cannot be delegated to any one division. There are essential activities which should and must involve virtually all components of organized public health. A broad team approach is required.

Measures of proven value may be applied immediately. Human feces must be disposed of safely and facilities which favor personal cleanliness are to be improved. Both of these are facilitated by the installation of public water supplies. Control of flies and particularly the protection of infants from flies is of major importance. All measures which will promote better infant hygiene are indicated. To these may now be added the adoption of every device to assure that infants and children with acute diarrheal disease receive appropriate therapy promptly. This program may be initiated with limited staff and without added knowledge. These are only the beginning and immediate activities, which should be followed by a more adequate program as soon as it can be developed. For descriptive purposes, these later activities may be grouped as follows:

1. Epidemiology, laboratory and vital statistics. These essentially comprise the fact finding activities. The etiology and epidemiology of diarrheal diseases vary from area to area. Preventive programs to meet particular needs can be devised only on the basis of adequate information on the local problem. Representative situations will need to be examined in the light of accumulated knowledge. The endemically occurring diarrheal diseases deserve the same epidemiological study which they would receive if they occurred in explosive outbreaks. Intensive field studies are particularly important. The diarrheal diseases, as compared with the other enteric infections—cholera and typhoid fever—have received little epidemiological attention, and evidence to guide in control is correspondingly limited. It is particularly urgent that dependable data be collected in areas of very high mortality. Often this can be best accomplished by the technique of mass survey of representative samples of the population.

Laboratory studies are essential to epidemiology, but they are required also for diagnosis and the guidance of therapy. This public health laboratory service must be made readily accessible both to clinicians and to public health clinics. The laboratory played a key role in the control of diphtheria; it has a different but no less important place in the control of acute diarrheal diseases.

Vital statistics provide a relative measure of the extent of the problem and equally important a continuing record of progress in control. Greater reliability of findings can be obtained only through fostering a more complete reporting with more liable diagnoses.

2. Sanitation. The availability of water, the means of disposal of feces, garbage collection and community fly control all require attention. For the latter, reliance should be on sanitary measures to prevent fly breeding since experience has established that insecticides will have temporary value only.

3. Maternal and child health activities, public health nursing and health education. The public health physician trained in infant and child hygiene will have a key role in the control of diarrheal diseases. He and the public health nurse establish contact with parents at clinics and at home. Initially, problems in therapy as well as in infant and child hygiene will need to be handled. Certainly every necessary means will be required to assure that the ill child receives appropriate treatment promptly.

Education will be as important as the provision of individual health service. Parents must be taught how best to care for infants under existing conditions. Instruction is required on the essentials of infant and child feeding and care, the hazard of flies and the means of their control, and the importance of personal cleanliness and environmental sanitation. These must be so taught that people will act in accordance with teaching. This can be done, in part, by physicians and nurses in clinic and home. In larger and well organized health departments, the participation of a qualified health educator will be a valuable asset.

4. Public health administration. This administration has the responsibility for organization, direction and providing the means for accomplishing work. The form of organization may vary, but efficiency of operation must be assured. A comprehensive and stable official public health agency, national and local, is essential to accomplish the broad program required for the control of diarrheal diseases, including all of the above activities.

### Medical Service

Knowledge is now adequate for the prevention of death in almost all cases of acute diarrheal disease. This represents a most important ad-

vance. Personnel and facilities to permit the application of this knowledge are as yet inadequate in many areas. Programs to provide these essential services will need to be developed on a national or local basis. This may call for a consideration of the better training of more physicians and their distribution and support in areas inadequately served. More readily available clinics and pediatric hospital beds presumably will be required. It requires time, even under ideal conditions, to obtain basic developments of this type.

The acute diarrheal diseases are predominantly specific enteric infections. Effective treatment to prevent deaths and to rapidly control sources of infection, is an acknowledged concern of public health. Thus, there should be cooperative participation of practitioners and health departments in making available the needed medical service required for the diarrheal diseases. The effective programs will be those designed to fit local conditions and to meet particular needs.

**Socio-Economic Development**

In multiple ways, infant health is beneficially influenced by socio economic improvement. This is an effective method for the control o diarrheal diseases, but these changes also come slowly and the imme diate problem is to control diarrheal diseases under existing conditions

**Supporting Aid**

The control of diarrheal diseases, involving as it does problems in home hygiene, personal cleanliness and infant care, calls predominantly for local action, but certain needed aid may properly be a part of the supporting national or international public health organization.

There is sound guidance for planning in other programs of established value. In venereal disease control in the United States, the V. D. Research Laboratory has provided leadership. The nature and present high quality of laboratory service is related to the investigation, teaching and evaluation programs of this public health organization. The first demonstration of the value of penicillin in syphilis came from this laboratory. Regional laboratories of comparable nature have been developed to serve other countries of the Americas. There is need for a similar reference, research and training center to give leadership in the control of infant diarrhea.

The functions of such an "Infant Hygiene Training Center and Laboratory" should include: (a) Research. Again, it must be emphasized that the nature of the problem varies and there are marked inadequacies in present knowledge, particularly in areas with very high mortality. (b) Development and operation of a demonstration program. This is essential both to test and to teach effective methods as part of the

general public health program. (c) A reference laboratory for enteric infections. (d) The training of clinicians and laboratory workers both at the center and elsewhere.

A favorable location for such a center would be in connection with a school of public health and children's hospital. But of great importance is accessibility to problems in the field. The staff would need to combine the interests and abilities of the investigator, teacher, and practical public health worker.

Further aid could be provided through the fellowship program. To help to meet the problem of the control of diarrheal diseases, more pediatricians will need to obtain their basic training in public health and to have additional training in this specialty. It is to be stressed, however, that there should be provision for supplementary field training in some area where the control of diarrheal diseases is a continuing major problem.

Thus, the supporting aid for the control of the diarrheal diseases would be primarily educational. More physicians with better training will be a basic need. Able leadership in pediatrics and the maternal and child health activities in public health will be required. A wide distribution in laboratory service will call for additional qualified workers in this field. In the competition for public health funds, these activities directed toward the prevention of diarrheal diseases should be given a very high priority.

## Comment

A major need in the control of diarrheal diseases is a general appreciation of the importance of the problem. There should be high concern with disease producing excessive mortality in adults, particularly if this occurred in epidemics. The loss of infant life from diarrheal disease has never aroused the same concern, partly because it occurs regularly without startling epidemic waves. Possibly the importance of this work should be measured in "person-years" of productive life conserved. The high importance of protecting the lives of the young must be stressed. Here, there is a conservation of individuals for the complete productive life ahead, not as in the aged merely adding years to a life already spent.

If the problem is viewed as sufficiently important, it will receive special attention. Up to the present, this has not been true of the diarrheal diseases. It is contended that the control of diarrheal diseases, due to its magnitude and to the need for evolving new programs to use new knowledge, should receive the special attention of a selected group of clinicians and laboratory workers. The training of these must receive careful consideration. With such leadership in a broad program of public health and pediatric care, there is the possibility of attaining in one

decade the degree of effective control of these diseases which was reached elsewhere only during the first half of this century.

## APPENDIX

### MANAGEMENT OF METABOLIC DISTURBANCE IN DIARRHEAL DISEASE IN INFANTS*

**I. Principles:**

1. Treat or prevent disturbance in blood circulation and renal function.
2. Repair losses in water and electrolytes.
3. Maintain in equilibrium as feeding is gradually restored.

**II. Moderately ill case:**

1. Discontinue food and milk.
2. Offer by mouth, every 3 to 4 hours, 25 ml/kilo body weight, *diluted* glucose-electrolyte solution:

Concentrated Solution:

| | |
|---|---|
| NaCl | 1.5 grams |
| KCl | 2.0 grams |
| $H_2O$ | 15.0 ml. |
| Syrup q. s.ad. | 75.0 ml. |

(Dissolve salts in water, then add syrup.)

Before use, *dilute* 1 teaspoonful to 60 ml. or the whole amount to 1 liter.

In home situations, where no pharmacist is available, some benefit will result from a solution of:

| | |
|---|---|
| Salt | 1 level teaspoonful |
| Corn syrup or sugar | 2 level tablespoonfuls |
| Water | 1 liter |

The mixture should be boiled.

3. After 12 to 24 hours, if child is urinating, taking solution eagerly, and looks well, replace ¼ of solution at each feeding with a standard milk mixture; or if baby is breast-fed, resume nursing for one to two minutes.
4. Gradually, over 3 to 4 days, replace solution completely with milk mixture or breast feeding.

**III. Severely ill case:**

1. Discontinue all oral intake.
2. Immediate intravenous infusion, in 30 to 60 minutes, 40 ml/kilo body weight, of either:
   a. Equal parts 0.9% NaCl and 5% Glucose in $H_2O$, or
   b. 1 part M/6 Sodium Lactate, 2 parts 0.9% NaCl, 3 parts 5% Glucose in water.
3. In extremely ill children follow with plasma or blood, 20 ml/kilo body weight.
4. Repeat step 2, giving 60 ml/kilo body weight, over next 4 to 8 hours.
5. Offer by mouth, every 3 to 4 hours, the diluted glucose-electrolyte solution described in II, 2, above.

*Adapted from *Department of Pediatrics, School of Medicine, Louisiana State University, U. S. A.*

If oral fluids are not tolerated, but the child is urinating, a sterile solution of

| | |
|---|---|
| NaCl | 1.5 |
| KCl | 2.0 |
| Glucose | 100.0 |
| $H_2O$ to make | 1000.0 |

may be given by intravenous drip, 150 ml/kilo body weight each 24 hours. This solution cannot be given subcutaneously, but a similar one, containing only 33 grams of glucose, can be given subcutaneously.

**NOTE:** Potassium solutions, important to recovery, may be toxic if the kidneys are not functioning well. They should not be given until urination is established.

6. During first 24 hours, total intake should be about 200 ml/kilo body weight.

7. Feeding should be resumed as under II, 3, above.

## REPORT OF COMMITTEE I (Technical Matters)*

Committee I examined and approved, with some changes, the report of Working Party B relative to the control of infant diarrheas in the light of recent scientific progress.

The discussion centered on acute infant diarrheal disorders of which the morbidity and mortality principally affect children under 2 years of age. The excellent paper on this topic (Document CSP14/27) presented by Dr. Albert V. Hardy, Director, Bureau of Laboratories, Florida State Board of Health, United States of America, was used as a basis for the discussion. The author had subdivided his survey into five sections: mortality, etiology, epidemiology, clinical considerations, and control.

The following account summarizes the various opinions of the delegates present on each of the above aspects, and the recommendations appearing at the end of the report are based on the opinions expressed.

**Mortality.**—It was unanimously agreed that the acute forms of infant diarrhea are one of the principal causes of mortality in many countries of America, which justifies any effort that may be made to gain a fuller knowledge of the problem so as to establish efficacious measures applicable to both prophylaxis and treatment. In most American countries, the mortality figures are not quite accurate, and there are reasons to suppose that the actual condition is more serious than these figures indicate. This is due to the fact that the causes of death registered are based on a very low percentage of medical certificates, and therefore do not always reflect the true clinical picture. Thus it is that many deaths caused by acute diarrhea appear in the records as due to simple meningitis, bronchial pneumonia, nutritional disorders, etc. If any evident improvement is to be made in the evaluation of mortality from infant diarrheas, surveys should be confined to statistical data on representa-

* Doc. CSP14/79, Rev. 1, *Pan Amer. San. Org.* (Part II).

tive groups of population that are subject to medical and public health supervision. It should not be surprising if the mortality and morbidity rates for such groups increase as a result of more precise knowledge and registration of diseases, even though health, nutritional, or cultural conditions may improve. In countries where inadequate records are kept, the causes of death under this heading should be studied and evaluated by means of a comparative critical analysis of infant mortality, both general and specific, by age group, and seasonal incidence.

**Etiology.**—Severe infant diarrhea is almost always an enteric infection. It was unanimously agreed that *Shigellae* are the most frequent etiological agents; *Salmonellae* are less often responsible and other biological agents, known and unknown, are even more rarely. One of the representatives, however, pointed out that in his country the most common etiological agent of enteric infections in the rural areas is *Salmonella*. In some countries, infection by *E. histolytica* is observed in from 2 to 5 per cent of infant diarrheas.

Identification of etiological agents can be made considerably more accurate by use of selective cultural media and adequate technique when selecting suspicious colonies for study. A search for the causative organism at the outset of illness will yield a substantially higher proportion of positive results than in the later stages.

Despite the progress achieved in bacteriological techniques, there are a certain number of cases in which the agent responsible for the disease cannot be isolated. As in the case of statistical records, it is likewise advisable to undertake bacteriological research with representative population groups, when the resources available do not permit mass investigations.

**Epidemiology.**—The fact that enteric infections are observed in every region of a country is indicative of the spread of the infection.

There are seasonal fluctuations in endemic cases, and the highest incidence rates are recorded during the spring and summer months.

In shigellosis, contagion is generally spread directly by the hands of patients or carriers, and indirectly through flies. Transmission through water, milk, and other foods is exceptional.

Breast-fed babies are less liable to infection, this explains, to a large extent, the difference in the recorded number of cases of shigellosis among breast-fed babies and those fed artificially.

Unlike *Shigellae*, which affect only human beings, the sources of infection with *Salmonellae*, other than *S. typhosa*, are animals. Transmission to human beings takes place through infected or contaminated foodstuffs, particularly eggs, poultry, meat; or by direct contact with animals, which explains the higher rate of incidence of this infection in certain rural areas. In both types of infection, the risks of contagion are greater in the poorer segments of population.

**Clinical.**—Infection with *Shigellae* and *Salmonellae* can give rise to diverse clinical types, ranging from the fulminating toxic variety to the very mild forms. Observation of the patient cannot determine the etiology of the different diarrheal manifestations; etiological diagnosis depends upon the laboratory.

Diarrheal disease easily upsets the fluid and electrolyte balance and it is most frequently as a result of this disturbance that death of the child ensues. In undernourished patients, the severity of the infection and of its complications is greater.

In recent years great advances in treatment have been made, especially with respect to:

(a) prompt correction of fluid and electrolyte disturbance by the systematic administration of fluids, electrolytes, glucose, plasma, and blood; and

(b) the proper use of antibiotics and sulfonamides.

Attention was drawn to the advisability of providing facilities for the application of these treatments in outpatient clinics as a means of relieving the shortage of hospital beds.

**Control.**—The Working Party unanimously acknowledged that economic and social progress, which results in improved environmental hygiene, is a decisive element on behalf of the campaign against diarrheal diseases. The promotion of economic development does not fall primarily within the province of public health administrations; they may, however, adopt a methodical series of control measures, which are summed up in the following recommendations:

(1) That accurate record of causes of death be established through the adoption of a simple classification of digestive disorders in accordance with the International List of Causes of Disease and Death adopted by the WHO.

That until a satisfactory record of this type is established, it is suggested that death certificates of children who were attended by a physician should be classified separately, and the specific death rates be compared with those of infant mortality in general and by age groups, as well as with those by seasonal incidence and geographic distribution.

(2) That indispensable laboratory services should be established or improved at the regional, national, and local levels.

That an endeavor be made for these laboratories to adopt uniform methods in the various countries, so as to obtain reliable and comparable data.

That the laboratories, thus organized, make careful surveys of representative samples of the population.

(3) That the training of general and public health physicians, as well as laboratory workers and other paramedical personnel, with respect

to diagnosis, treatment, and control of infant diarrheas, should be intensified.

Stress is laid on the desirability of organizing short intensive courses specially adapted to the needs of personnel working far away from large urban centers.

(4) That it is essential to organize a broad system of medical and public health services not only in urban but also in rural areas in order to provide prompt treatment to the sick child, and medical supervision to the healthy child.

(5) That personal hygiene should be improved by the provision of a water supply system to homes, supplementing this by educational measures to encourage the adoption of good habits in personal care and the use of soap and water.

(6) That environmental sanitation measures should be put into effect for the safe disposal of human excreta and for fly control.

(7) That infant feeding should be improved by means of widespread instruction in child care, and, whenever possible, by the distribution of basic foods, especially powdered and evaporated milk, to children living in the poorest sectors. Breast feeding should be encouraged, taking into account the nutritional state of the mother.

(8) That a request should be made to the Director of the Pan American Sanitary Bureau for Bureau assistance in:

(a) training the personnel required in the control of infant diarrheas, including the sending of technical experts on request;

(b) facilitating the international exchange of scientific knowledge on this subject; and

(c) facilitating the supply of standardized diagnostic reagents to national laboratories.

(9) That UNICEF should be asked to consider, in agreement with the Pan American Sanitary Bureau, the adoption of programs furthering, as far as applicable, the implementation of the foregoing recommendations.

(10) That the Director of the Bureau should be requested to distribute as widely as possible the paper prepared by Dr. Albert V. Hardy and the recommendations contained in the present document, and that at the next meeting of the Directing Council he submit a report on the steps taken by the Bureau in the control of infant diarrheas.

## CONTROL OF INFANT DIARRHEAS*

THE XIV PAN AMERICAN SANITARY CONFERENCE,

Considering the importance of infant diarrheas as a predominant cause of sickness and death in many countries of the Americas; and

* CSP14, Res. XXVII, Final Act, *Pan Amer. San. Org.*

Bearing in mind the discussions held in the Working Party appointed to study this topic, and the report and recommendations proposed by that Working Party,

RESOLVES:

1. To approve the technical recommendations on control of infant diarrheas set forth in the report of the *ad hoc* Working Party, as modified by Committee I (Document CSP14/79, Rev. 1).

2. To recommend that the Director of the Bureau encourage, insofar as possible, the implementation of the technical recommendations contained in the above-mentioned report, and inform the Directing Council, in his annual reports, of the steps taken with respect to this matter.

3. To instruct the Director of the Bureau to give wide distribution to the paper prepared by Dr. Albert V. Hardy (Document CSP14/27 Addenda I and II) and to the report of the *ad hoc* Working Party (Document CSP14/79, Rev. 1).