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ENTERIC INFECTIONS

Report of a WHO Expert Committee

		Page
1.	Introduction	4
2.	Terminology and classification	5
3.	Data on morbidity and mortality attributed to enteric infections	7
4.	Pathology and pathophysiology of enteric infections and diarrhoeal diseases	8
5.	Pathophysiological basis for management of diarrhoeal disease	13
6.	Factors contributing to the occurrence of enteric infections	15
7.	Preventive measures	21
8.	Research needs	24
9.	Application of control measures in public health practice	28
Annex 1:	Mortality from cause group B36 in comparison with level of health	31
Annex 2:	An autopsy study of 63 children in Guatemala City, 1958 and 1960	31
Annex 3:	Classification of the acute diarrhoeal diseases on the basis of histological and cytological patterns and microbiological correlation	33
Annex 4:	Effect of sanitary facilities on prevalence of enteric infections: data reported from California, Georgia and Kentucky, USA, and from Guatemala	34

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WHO EXPERT COMMITTEE ON ENTERIC INFECTIONS

Geneva, 12-16 November 1963

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ENTERIC INFECTIONS

Report of a WHO Expert Committee

The WHO Expert Committee on Enteric Infections met in Geneva from 12 to 16 November 1963. The meeting was opened by Dr P. Dorolle, Deputy Director-General of the World Health Organization, on behalf of the Director-General. Dr G. J. Dammin was elected Chairman, Dr S. D. Nosov Vice-Chairman and Dr J. Olarte Rapporteur.

In his introductory statement Dr Dorolle outlined the past work of WHO in the field of enteric infections and indicated to the Committee its terms of reference.

The Organization has for some years paid special attention to the control of enteric infections, since, in many developing countries, they represent the most important cause of sickness and death among children. They not only undermine health but also impede economic progress.

WHO has in the past called experts to discuss these diseases and their control (the Study Group on Diarrhoeal Diseases, which met in 1958), and has established a special team (the Diarrhoeal Diseases Team, set up in 1959), in order to promote the control of enteric infections on an international basis. Courses have been held (in 1962 and 1963) for epidemiologists and microbiologists to facilitate the organization of national studies and control programmes.

In order to promote laboratory work in this field WHO has assisted and encouraged the establishment of international reference centres for Enterobacteriaceae. In 1949, the Organization undertook to provide support for the International Salmonella Centre in Copenhagen, and promoted the establishment of International Shigella Centres in the USA and the United Kingdom and the International Enteric Phage Typing Centre in the latter country. Many national reference centres all over the world co-operate with these international reference laboratories.

Some regional offices of WHO and especially the Pan American Health Organization have developed projects for the control of diarrhoeal diseases.

Dr Dorolle expressed the hope that the Committee would provide in its report a review of our present knowledge and recommendations for procedures that could be followed in order to get under way a programme for the control of enteric infections; also that the Committee would suggest schedules for improving or developing facilities as the con-

trol programmes are advanced; and finally, that it would indicate specifically the research needed to improve control measures.

It was emphasized that the deliberations of this Committee should give guidance to public health administrators in their efforts to control enteric infections.

1. INTRODUCTION

The significance of the enteric infections as a leading cause of deaths among infants in a majority of the countries of the world is evident from available vital statistics and from results of epidemiological and laboratory studies. The Committee recognized that many of these deaths could be prevented by the application of knowledge already available, and that properly delineated research could extend and accelerate efforts to control enteric infections.

The Committee further recognized that priorities had not been established for the control and investigation of enteric infections according to the nature and magnitude of the problem as it might present itself in different geographic areas. Since it was considered highly desirable to develop and have available sets of priorities, attention was directed to the formulation of recommendations that would outline control programmes and their implementation, according to the stage of development of the area or community concerned. Recommendations would therefore pertain to the solution of problems as they might be encountered under specific circumstances. For example:

(1) In areas where infectious enteric diseases are highly endemic—that is, where the rates of infant mortality exceed 100 per 1000 live births—what factors provide a rationale for the application of control measures in the absence of resources for detailed laboratory and epidemiological work, and what control measures should be applied?

(2) In areas where progress has been made in the control of enteric diseases, what measures are needed to permit a more precise delineation of problems and a more direct attack on the foci of infection?

(3) In local areas where control is well advanced—that is, where infant death rates are of the order of 30 per 1000 live births—what research should be undertaken to improve methods of control, to provide a better understanding of the pathogenesis of enteric infections, to improve clinical management, and to raise the level of control on a regional as well as a local community basis?

In considering the problem of control of enteric infections in areas of high endemicity, it was agreed that attention should be directed to

the use of the most readily available control measures without further epidemiological or other studies. In the course of applying such control measures, decisions could be developed on the priority of other measures that would further advance control. In this connexion, consideration was centred on the observed association of low rates of enteric infection with high levels of sanitation, nutrition and medical care.

In considering improvement of control programmes in more advanced communities, it was agreed that attention should be paid to the identification of specific types of infection—for example, typhoid and other salmonelloses—and to more specific types of control—for example, food sanitation. In such communities, various types of surveys, including detailed laboratory and epidemiological studies for more precise information on the prevalence of specific pathogens and their role, are indicated, along with studies of environment, hygienic practices, nutrition, and other factors involved in the occurrence of enteric diseases. Furthermore, such communities could become demonstration and training centres for health personnel engaged in control work in other areas.

Finally, due attention was given to the need for further clinical, laboratory and field studies of particular importance to the development of better procedures for epidemiological appraisal, control and treatment of enteric infections.

2. TERMINOLOGY AND CLASSIFICATION

2.1 Terminology

The term " enteric infections " refers to a variety of clinical syndromes of heterogeneous etiology which are endemic in areas with poor sanitation and a low level of economic development and which may occur epidemically in other types of environment. Where enteric infections are endemic, there are high rates of infant mortality due to acute diarrhoeal disease that may be aggravated by malnutrition and other factors. Enteric infections in epidemic form usually result from failures of personal hygiene and/or community situation, and afflict the older as well as the younger age-groups.

Diarrhoea [1] is a cardinal sign of most infectious enteric diseases; it is most frequent in children under five years of age, among whom occur

[1] " Diarrhoea is ... a disturbance of intestinal motility and absorption which, once and by whatever means initiated, may become self-perpetuating as a disease through the production of dehydration and profound cellular disturbances, which in turn favour the continuing passage of liquid stools " (Ordway, N. K. (1960) Diarrhoeal disease and its control. *Bull. Wld Hlth Org.*, **23**, 73).

most of the deaths attributed to these infections. Some infections—for example, cholera and typhoid—are separable from this complex because they are characterized by particular epidemiological and clinical features. "Acute diarrhoeal disease" is recognized as a clinical syndrome and as an epidemiological entity. The high rates of infant mortality in areas where infectious enteric diseases are endemic are largely attributable to "acute diarrhoeal disease".

2.2 Classification

A classification system for the infectious enteric diseases should permit the separate tabulation of specific entities when a differential diagnosis has been made, and should provide a single category for the undifferentiated enteric disease in which diarrhoea is the predominant clinical sign. The Committee has suggested to the WHO Expert Committee on Health Statistics that the following non-specific categories of the International Classification of Diseases, in which the undifferentiated enteric diseases are now included, should be eliminated and that a single category should be adopted.

048 Unspecified forms of dysentery

571 Gastro-enteritis and colitis, except ulcerative, age 4 weeks and over

572 Chronic enteritis and ulcerative colitis

578 Other diseases of intestines and peritoneum

764 Diarrhoea of newborn

773 Ill-defined diseases peculiar to early infancy

785.6 Diarrhoea, age 2 years and over

795.0 Other ill-defined conditions.

It has been further suggested that provision should be made for specific coding of all recognized or suspected pathogens, such as bacteria, viruses, protozoa, helminths, toxic substances, and other etiological agents for those cases in which an etiological agent is established. A suggested classification has been found acceptable to the WHO Expert Committee on Health Statistics Sub-Committee on Classification of Disease, the category proposed for the undifferentiated diarrhoeal disease being:

031 Diarrhoeal diseases

031.0 With mention of malnutrition

031.1 Without mention of malnutrition.

3. DATA ON MORBIDITY AND MORTALITY ATTRIBUTED TO ENTERIC INFECTIONS

The deficiencies of available vital statistics with respect to both completeness and accuracy are well known and the desirability of improvement in reporting systems is generally accepted. In this regard the attention of Committee was principally devoted to a consideration of how existing data—despite their inadequacies—could be used in planning control operations and how additional information essential for effective planning could most readily be obtained.

3.1 Indications from mortality data

Cognizance was taken of the direct relationship between high rates of mortality among infants from all causes and high rates of mortality attributed to acute diarrhoeal diseases (see Annex 1). Since this relationship is consistent for countries from which data are available, the Committee believed that a tenable estimate could be made of the magnitude of problems related to acute diarrhoeal diseases in areas where mortality data are available but specific data on diarrhoeal diseases are lacking. In areas of high endemicity such an estimate of rates is considered an adequate basis for undertaking the planning and launching of control programmes.

3.2 Desirability of local assessment of problem

In areas where resources permit, local appraisal should be made of the nature and magnitude of the diarrhoeal diseases problem. The reports of the WHO Diarrhoeal Diseases Team serve as one of many examples of how such studies could be made, and the Committee urged that these reports should be published as soon as possible. Although exact procedures will vary from area to area, the protocol and methods of analysis will provide useful guides. It was noted that in certain circumstances local surveys need not necessarily include laboratory examination to determine the prevalence and distribution of pathogens. This information is desirable if local facilities and logistics permit its collection, but it is not a prerequisite to the planning of an effective control programme. Usually, data on the relative frequency of pathogens in the groups afflicted with acute diarrhoeal disease are more useful than such data obtained from measurements made among the population as a whole.

Surveys not only serve to characterize local problems but also provide an effective means of training personnel. Further, they provide data

that are useful in obtaining financial and administrative support. One of the several purposes of surveys is to provide bases for control operations. This should be kept firmly in mind so that efforts will remain focused on the collection of data relevant to the problem of diarrhoeal disease control, and not be dissipated on activities unrelated to the primary mission of the survey.

3.3 Standardization of procedures

Rigid standardization of procedures and record forms for the purpose of comparing data from various countries does not appear to be practicable at present. However, efforts should be made to employ uniform terminology and to ensure that procedures be as consistent as conditions permit. In this connexion, it is suggested that such procedures as those used by the WHO Diarrhoeal Diseases Team and recommended in this report should be used as guides in an attempt to arrive at more comparable data.

3.4 Need for data on the cost of enteric infections

Note was taken of the impetus given to efforts aimed at the control of hookworm disease in southern states of the USA after the sociological and economic aspects of this disease had been elucidated by comprehensive studies conducted for this purpose. The Committee was of the opinion that a similar stimulus would be given to the control of enteric infections if precise information were available concerning expenditures for medical care and the extent of economic impairment through loss of productive effort resulting from these infections. The Committee accordingly recommended that WHO should assemble available information and obtain additional data by special studies that would provide tenable indications of the cost of enteric infections at various levels of intensity.

4. PATHOLOGY AND PATHOPHYSIOLOGY OF ENTERIC INFECTIONS AND DIARRHOEAL DISEASES

The major form of enteric infection is that which manifests itself clinically as " acute diarrhoeal disease ". It is this syndrome that accounts for most of the morbidity and mortality attributable to the enteric infections, and for this reason attention should be focused on it.

Acute diarrhoeal disease is believed to have its basis in bacterial infection, despite the observation that specific enteric pathogens may

be isolated from only a relatively small percentage of individuals afflicted with diarrhoea. *Shigella* is accepted as the most common cause of this clinical disease entity; *Salmonella*, enteropathogenic *Escherichia coli*, and *Vibrio cholerae* may also cause acute diarrhoeal disease. This is not to deny (*a*) the etiological importance of other agents in occasional individuals or groups of individuals, or (*b*) the importance of subacute, chronic or recurrent forms of enteric infection. Other agents that may be the cause of acute diarrhoeal disease include the enteroviruses and, occasionally, the protozoa *Entamoeba*, *Giardia* and *Balantidium*.

Acute diarrhoeal disease must be regarded as a clinical rather than a pathological entity, and its immediate management must consist in the correction of fluid and electrolyte imbalance, irrespective of (*a*) the enteropathogenic organism identified or suspected, and (*b*) the intestinal lesion related to it. Of secondary importance to the patient is the eradication of the enteropathogens.

4.1 Microbiological and immunological diagnostic procedures

The most important procedure of the many that may be considered under this heading is the identification of causal agent. Although studies of copro-antibody and serum antibody may reflect the presence of a bacterial enteropathogen, these tests will not identify the pathogen with the promptness and precision possible through use of the bacteriological procedure that involves (*a*) rectal swabbing, (*b*) direct plating on selective agar, (*c*) sub-culture of suspected pathogens, (*d*) biochemical characterization and (*e*) serological identification by employment of pooled, then type-specific, antisera. This approach to the identification of *Shigella* and *Salmonella* is well recognized. Bacteriological methods for the identification of the enteropathogenic *E. coli* vary. The fluorescent antibody technique recently developed is applicable in the identification of enteropathogenic *E. coli* and deserves wider use.

Isolation of enteroviruses as a cause of acute diarrhoeal disease has practically only an epidemiological significance. In younger age-groups ECHO and Coxsackie types have been suspected of having such a relationship, but several studies have revealed the presence in faecal specimens of a large variety of enteroviruses that could not be related to clinical illness; nor has it been possible to establish the role of viruses as accessories in the pathogenesis of bacterial enteric infections.

The patient's immune response may be misleading as an attempt to identify the agent that may be the cause of acute diarrhoeal disease.

It should be stressed that although identification of the causal agent is an important procedure, this step is exceeded in importance by the need for a prompt assessment of the patient's deficit of fluid and electrolytes and a prompt initiation of measures to correct this deficit. Iso-

lation of an enteropathogen and recognition of its relationship to diarrhoeal disease can be the basis for specific antibacterial chemotherapy, but such information also has important epidemiological significance and can give direction to control measures.

4.2 Morphological changes

The clinical entity of acute diarrhoeal disease may be associated with any one of several possible bacterial agents, including all of the common enteropathogens—namely, the cholera vibrio, *Shigella*, enteropathogenic *E. coli* and *Salmonella*—and also other intestinal inhabitants, which, when present in abnormal numbers in the proximal portion of the small intestine, may be the cause of diarrhoeal disease under certain circumstances. The last may be accepted as a pathogenic mechanism on the basis of a detailed autopsy study in Guatemala, [1] where malnutrition among children is common. Malnutrition was present in the absence of diarrhoeal disease, and by itself could not be identified as a cause of diarrhoea (see Table 1 of Annex 2). However, diarrhoea occurred in the malnourished infant and child in the absence of recognized enteropathogens but in the presence in the jejunum of abnormally large numbers of bacteria not classifiable as pathogens. In the Guatemalan children studied no causal agent (bacterial or viral) was identified in about half of those with diarrhoea (see Table 2 of Annex 2). Although four-fifths of the cases had diarrhoea, in less than half of them was a bacterial pathogen isolated (see Table 3 of Annex 2). Neither protozoa nor helminths could be identified as causal agents in these children with diarrhoea.

In *Shigella*, enteropathogenic *E. coli* and *Salmonella* infections, the gross appearance of the mucosal surface of the intestine is distinctive primarily because of the presence of extreme hyperaemia ulceration and necrosis, which are absent in cholera. In cholera the vibrios may be cultivated from the intestinal contents, but not from the intestine itself, which remains intact. In *Shigella* infections the bacteria may be cultivated from the intestinal contents and also the intestinal wall. In *Salmonella* and enteropathogenic *E. coli* infections, there may be deeper penetration of the host, and the organisms may be cultivated not only from the intestinal contents and the intestinal wall but also from the mesenteric lymph-nodes, and occasionally from the peripheral blood. It is important to recognize that differentiation of the above infections can be made on the basis of morphological alterations of the intestine and interrelationships between the agent and the tissues of the host (see Annex 3).

[1] Data supplied by G. J. Dammin.

4.2.1 Shigella *infections*

In *Shigella* infections ulceration of the mucosa is the rule, and this is generally more striking in the large intestine than in the small intestine. The entire surface of the mucosa is hyperaemic owing to the diffuse inflammatory reaction and, where ulceration has not produced defects in the mucosa, the surface of the mucosa is dull because of the presence of fibrinopurulent exudate. The thickness of the bowel wall is increased, and this may be due to a swelling of all the layers. The submucosa is thickened and spongy. The muscularis also is swollen because of cellular infiltration and oedema, which may extend into the serosa. In severe cases, with deep ulceration, the inflammatory reaction may extend to the peritoneal surface, which may be covered by exudate. Microscopically, numerous defects in the mucosa may be found, and where exudate is adherent to the surface it is apparent that it has incorporated into it necrotic mucosa and portions of the submucosa. The remarkably thickened submucosa manifests considerable oedema and cellular infiltration, which consists primarily of polymorphonuclear leucocytes. Where ulceration is superficial or lacking, large numbers of polymorphonuclear leucocytes are found in the gland crypts and also in the lamina propria and submucosa. The character of the faecal specimen can be anticipated from the above, in that it may be scanty and consist almost entirely of mucus and fibrinopurulent exudate.

4.2.2 E. coli *and* Salmonella *infections*

In enteropathogenic *E. coli* and *Salmonella* infections the findings may be quite comparable one to another. In both, the lesions consist of focal ulcerations in both the small and large intestines. Hyperaemia is pronounced in both portions of the intestines. Although the ulcerative lesions are usually focal, the gross lesion may also resemble that seen in *Shigella* infections. The abnormal mucosal surface has a dull granular appearance because of the presence of fibrinopurulent exudate. In the mucosa and the surface exudate polymorphonuclear leucocytes are abundant, and these extend into the muscularis and serosa. In most instances the intestinal contents may still have a normal brown colour, but there will be an admixture of exudate, excessive mucus and blood.

Certain exceptions should be mentioned. Although in acute diarrhoeal disease related to *Shigella*, *Salmonella* or enteropathogenic *E. coli* infection there is often an associated ulcerative intestinal lesion, disabling diarrhoea can be caused by those agents in the absence of ulceration. However, the presence of an inflammatory process in the mucosa can

be detected by examination of a stained film of the faecal specimen, which will reveal the presence of polymorphonuclear leucocytes. These observations are summarized in Annex 3.

4.3 Intestinal flora, nutritional and other factors

In some malnourished Guatemalan children with diarrhoea and non-specific intestinal infections, an anatomical similarity to cholera has been observed.[1] It has been suspected that the presence of an abnormal number of non-pathogens in the jejunum may be the cause of fatal diarrhoeal disease. It is not known whether intestinal motility is reduced in this type of malnutrition, but it is known from animal experiments that any delay in the passage of the intestinal contents through the small intestine increases the susceptibility of the host to infection, presumably because of the multiplication of organisms in the small intestine. Thus, diarrhoeal disease in the malnourished child may occur in the absence of enteric pathogens because of the proliferation of non-pathogens in abnormal numbers in the proximal part of small intestine.

Additional information about the pathogenesis of *Shigella* infections has come from study of the germ-free guinea-pig. This host is essentially defenceless against *Shigella*. A small inoculum introduced orally results in an infection ending in death in 24-48 hours. This contrasts with the conventional guinea-pig, which must have intestinal motility reduced and be starved or given carbon tetrachloride in order to induce susceptibility to *Shigella*. It was found that oral introduction of *E. coli* into germ-free guinea-pigs causes no illness but gives protection against a subsequent challenge of *Shigella*, although *Shigella* and *E. coli* differ antigenically.

The Committee took note of interesting studies in the NCS mouse, which manifested resistance to a number of enteric and other pathogens when the number of lactobacilli in the intestinal tract was relatively high. With the addition of casein to the diet, this rodent host became susceptible to the pathogens that it was able to resist when the lactobacilli predominated in the intestinal tract. The presence of lactobacilli may constitute an expression of the nutritional and physiological well-being of the animal, and may also determine the survival of other bacteria in the intestinal flora and thereby the response of the animal to infection and toxins.

These and other studies indicate the need for further study of the basic physiology of the intestine, intestinal flora, and nutritional and other factors in the pathogenesis of diarrhoeal disease.

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[1] Data supplied by G. J. Dammin.

4.4 Pathophysiological changes

The morphological and physiological alterations in the host are of the utmost importance, and do not vary qualitatively with respect to a particular enteropathogen, but only in degree. The most profound alterations, and those occurring most rapidly, are related to infection with the cholera vibrio. From this extreme, there are gradations through the serious forms of fluid and electrolyte depletion that occur in infants and children with both specific and non-specific intestinal infections, to the adult who may present only a mild and transitory form of the alterations noted in the more grave circumstances. The immediate problem is the restoration of fluid and electrolyte balance during the diarrhoeal phase, and the maintenance of this balance during the early phases of recovery.

Recent publications have described the major pathophysiological alterations in the patient afflicted with acute diarrhoeal disease. Faecal specimens will be voluminous, and, in cholera, will consist of fluid and electrolytes without protein and without significant cellular content. The same type of faecal specimen characterizes the non-specific infection that occurs in the malnourished child. In *Shigella*, *Salmonella* and enteropathogenic *E. coli* infections, the faecal specimen is less voluminous and contains an abundance of inflammatory cells and protein. The massive loss of fluid and electrolytes leads promptly to renal insufficiency and acidosis. The acidosis is accompanied by a loss of potassium from the cells, which leads ultimately to general potassium depletion of the host. The resulting dehydration is followed by haemoconcentration, hypovolaemia, and ultimately hypotension and shock. Accompanying this is oliguria or anuria. If the patient is managed properly through the shock phase, there may still be a prolonged oliguric phase with pronounced nitrogen retention. Successful management of this leads to another phase, characterized by a period of invalidism.

5. PATHOPHYSIOLOGICAL BASIS FOR MANAGEMENT OF DIARRHOEAL DISEASES

In addition to the major symptom of diarrhoea, nausea and vomiting may supervene as dehydration progresses. This may occur in both cholera and the other bacterial enteric infections. However, with the other infections the presenting picture may be one of systemic infection with high fever, rapid pulse and respiratory rate, and abdominal pain, but without diarrhoea. In the major forms of acute diarrhoeal disease

there is a self-perpetuating sequence that results from dehydration and leads to profound cellular disturbances from electrolyte loss, these in turn favouring the continued passage of liquid stools. This sequence is manifested particularly in infants and young children who suffer from diarrhoea and malnutrition. The nausea and vomiting and accompanying fever accentuate the loss of body fluids and electrolytes. In hot climates, where the most serious forms of acute diarrhoeal disease are encountered, the fluid losses are aggravated by sweating.

The clinical course may be divided into three principal stages. The first stage usually lasts no more than three days and is the one characterized by shock because of the sequence of fluid loss, dehydration, hypovolaemia, haemoconcentration and, ultimately, hypotension. The second stage is characterized primarily by renal insufficiency, the degree of which is determined by the character of the management during the first stage. The clinical management of the second stage differs, of course, because of the presence of oliguria or anuria, and therefore administration of fluids must be limited to the amount of fluid estimated to be lost or removed from the body through the skin, lungs and urinary and intestinal tracts. Acidosis and potassium depletion, with nitrogen retention, characterize this second stage, which may least for two or three weeks beyond the first stage. Proper management of this second stage usually leads to recovery and entry into the third stage, which represents a period of convalescence that may last several months. If renal insufficiency during the second stage has been extreme, then the ability of the kidney to concentrate normally may not return for several months. Principles of therapy with particular reference to fluid and electrolyte replacement are to be found in the literature. [1]

As emphasized above, the treatment of acute diarrhoeal disease has two distinct phases, the initial one being concerned with the correction of fluid and electrolyte imbalance, and the second with the control of the infection with specific drugs. Resistance of enteropathogens to antibiotics continues to progress, along with the increasing abuse of antibiotic treatment in enteric infections. Knowledge of the susceptibility of the enteropathogen to antibiotics is necessary for successful control of the infection in the individual patient, particularly for curtailing the duration of the convalescent carrier stage, and hence for the control of infection within a group or community.

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[1] See, for example: Phillips, R. A. (1963) The patho-physiology of cholera. *Bull. Wld Hlth Org.*, **28**, 297.

6. FACTORS CONTRIBUTING TO THE OCCURRENCE OF ENTERIC INFECTIONS

Infectious enteric diseases, including acute diarrhoeal disease, are public health problems of varying degrees of severity in all areas of the world where one or a combination of the following conditions occurs:

(1) Knowledge of personal hygiene is inadequate to prevent transmission of enteric organisms by personal contact.

(2) Sanitation facilities are inadequate to prevent contamination of the environment with human excrement.

(3) Economic resources are insufficient to provide adequate nutrition.

(4) Care of children is inadequate to protect them from infection.

(5) Medical resources are inadequate or are not properly utilized.

Because of the complex interrelation of biological, social, and economic factors that enable diarrhoeal diseases to persist, it is as well to mention some of these factors with a view to developing bases for selecting or developing control techniques.

6.1 Infection

Recognition of acute diarrhoeal disease as a clinical syndrome and an epidemiological entity includes recognition ot the role played by specific enteric pathogens in precipitating some of these cases. The pathogenicity of *Shigella*, *Salmonella*, enteropathogenic *E. coli*, and certain parasites in producing this and other syndromes of enteric infection has been established by clinical, epidemiological and laboratory studies. Evidence is also accumulating on the association of certain viruses with acute diarrhoeal disease. However, the various etiological entities cannot be differentiated by clinical criteria and in a large proportion of cases no recognized etiological agent can be demonstrated in acute diarrhoeal disease. Thus, while the importance of micro-organisms associated with diarrhoea cannot be minimized, it is apparent that synergistic or potentiating factors may profoundly affect the response to infection. The possibility of a non-infectious etiology of acute diarrhoeal disease should not be overlooked. In common with most other infections, clinical manifestations vary from minimal response to severe illness and death.

Various studies have suggested that response to enteric infections is determined by host resistance and immunity. The fact that acute infections are observed more frequently among young children, together

with the characteristic age distribution of certain bacterial pathogens, supports this impression. Recent studies have shown that the majority of secondary cases following a case of diarrhoea in a family occur among the children of pre-school age.[1] This observation implies greater resistance among older persons and also suggests that communicable agents are responsible for the diarrhoea.

6.2 Nutrition and nutritional habits

It has long been recognized that acute diarrhoeal disease occurs more frequently and with greater severity among malnourished children than among children who are well nourished. Information that corroborates this impression is at present becoming available from studies in Guatemala.[1] The work of the WHO Diarrhoeal Diseases Team in Mauritius indicated, however, that malnutrition and diarrhoea exist independently. The occurrence of malnutrition was uniform throughout the year but diarrhoea tended to follow a seasonal pattern, with most cases occurring during the warm months. Studies of the seasonal association of malnutrition and diarrhoea in some countries of the Americas suggest that diarrohea may enhance the seriousness of existing malnutrition.[2] However, it has been pointed out that factors connected with the seasonal availability of food must be well understood in order to make a tenable correlation.

The precise relation between malnutrition and diarrhoea is not clear but it seems apparent that overt malnutrition may be precipitated by diarrhoea when nutritional adequacy is tenuous. Likewise, the malnourished child appears to be more susceptible and to have more frequent and severer episodes of diarrhoea than the well-nourished child.

The WHO Diarrhoeal Diseases Team in Mauritius called attention to the " forgotten toddlers ", who after reaching the age of one year no longer receive free or cheap milk from the maternal and child health centre. Malnutrition is most common between this age and the age of five years, when children enter school and receive nutritional supplements. It has also been pointed out that diarrhoea during the period of weaning is due to a combination of malnutrition and infection, and that death during the second year of life should be considered an indication of poor nutritional status.[3]

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[1] Gordon, J. E., Guzmán, M. R., Ascoli, W. & Scrimshaw, N. S. (1964) La enfermedad diarreica aguda en los países en vías de desarrollo. II. Sus características epidemiológicas en la población rural de Guatemala. *Bol. Ofic. sanit. panamer.*, **56**, 424.

[2] Verhoestraete, L. J. & Puffer, R. R. (1958) Diarrhoeal disease with special reference to the Americas. *Bull. Wld Hlth Org.*, **19**, 23.

[3] Gordon, J. E., Chitkara, I. D. & Wyon, J. B. (1963) Weanling diarrhea. *Amer. J. med. Sci.*, **245**, 345.

6.3 Environmental factors

The consistent decline in morbidity and mortality from diarrhoeal disease in some areas of the world during the past century has been attributed largely to improvements in environmental sanitation. While public health workers do not question the propriety or desirability of control through environmental sanitation, there is disagreement as to whether priority should be assigned to preventive or to curative programmes in areas with acute problems resulting from enteric infections.

Environmental control may be defined broadly as the control of those factors in man's physical environment that influence the spread of disease or result in man's discomfort. Properly used control measures that suppress or preclude direct or indirect anal-oral transmission of faecal material and contamination of food, water and soil include: (*a*) a safe, adequate water supply under pressure within each home; (*b*) sanitary methods for excreta disposal within each dwelling, and prevention of faecal pollution of ground- and surface-water supplies; (*c*) sanitary collection and disposal of human, animal and industrial wastes; (*d*) prevention of access of vectors—namely, insects and intermediate hosts of schistosomes—to human or animal faeces; (*e*) housing which is spacious enough to avoid excessive crowding and which is free from rodents, vermin and domestic animals; and (*f*) sanitary controls governing the production, processing, storage and consumption of milk and food.

In general, the highest morbidity and mortality rates are experienced in those populations with a level of environmental sanitation lower than the national or community average. Although it is difficult to isolate and demonstrate the effect of a single environmental factor, several studies have been conducted to provide quantitative data on the relative significance of specific sanitation deficiencies as factors contributing to high rates of enteric disease, with a view to determining the priority of sanitation improvements.

6.3.1 *Water supply*

The evidence of the importance of safe municipal water supplies in controlling and preventing water-borne outbreaks of typhoid fever and cholera is highly persuasive. Similar evidence, however, of the effect of such developments on the reduction of morbidity and mortality due to diarrhoeal disease is largely presumptive. For example, the results of studies in California, Georgia, Kentucky, and Guatemala on prevalence rates of *Shigella* show an inverse relationship of these rates with the presence of sanitary facilities, as summarized in Table 1 of Annex 4. High rates of prevalence in Guatemala, as in the USA, were associated with the lack of sanitary facilities, poor housing, limited water supply, and

poor personal hygiene.[1] Data from California [2] show that the infection rate of *Shigella* in children of ten years of age or under living in dwellings with no inside water supply was approximately twice that observed in children whose homes had an inside water supply under pressure. In Georgia [3] *Shigella* infections were approximately one and a half times more frequent among families living in dwellings with water sources off the premises than among families with water sources outside their dwellings but on the premises. The studies also reported no significant differences in infection rates between families using municipal water supplies and those who obtained their water from open, dug wells, although the dug wells were subject to pollution. The results of investigations in coal-mining camps in eastern Kentucky [4] showed a significant inverse relation between the availability of water and the prevalence of *Shigella*, the incidence of *Ascaris* infections, and morbidity from diarrhoeal disease (see Table 2 of Annex 4). In these studies the rate of infection with *Shigella* in pre-school children living in dwellings with an outside water supply was more than twice the rate in children residing in dwellings with water inside. Similarly, the rates of morbidity from diarrhoeal disease and the incidence of *Ascaris* among people living in dwellings with water outside the premises were approximately one and a half times greater than the rates among people residing in dwellings with an inside water supply. Where the source of water was outside the dwelling unit, the rates of infection with *Shigella* and *Ascaris* were comparable, regardless of the location of the source of water in relation to the premises. As in the Georgia studies, transmission of enteric pathogens by polluted water could easily have occurred, but no indications were found to indicate that such water-borne transmission took place.

6.3.2 *Disposal of excreta*

It is generally acknowledged that reductions in typhoid fever as well as in helminthic and protozoal infections follow the installation of facilities for sanitary disposal of excreta. Furthermore, a 50 % reduction

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[1] Beck, M. D., Muñoz, J. A. & Scrimshaw, N. S. (1957) Studies on diarrheal diseases in Central America. I. Preliminary findings on cultural surveys of normal population groups in Guatemala. *Amer. J. trop. Med. Hyg.*, **6**, 62.

[2] Hollister, A. C., Jr, Beck, M. D., Gittlesohn, A. M. & Hemphill, E. C. (1955) Influence of water availability on *Shigella* prevalence in children of farm labor families. *Amer. J. publ. Hlth*, **45**, 354.

[3] Stewart, W. H., McCabe, L. J., Jr, Hemphill, E. C. & DeCapito, T. (1955) Diarrheal disease control studies. The relationship of certain environmental factors to the prevalence of *Shigella* infection. *Amer. J. trop. Med. Hyg.*, **4**, 718.

[4] Schliessmann, D. J., Atchley, F. O., Milcomb, M. J. & Welch, S. (1958) *Relation of environmental factors to the occurrence of enteric disease in areas of eastern Kentucky*, Washington, D.C., US Government Printing Office (*Public Health Service Monograph*, No. 54).

in the diarrhoea and enteritis death rate in Costa Rica over an eight-year period has been attributed to the installation of more than 10 000 privies.[1]

Referring again to the studies in a migratory labour camp in California (see Table 1 of Annex 4), rates of *Shigella* infection in children of families having privies were approximately twice as high as the rates observed in families having an inside toilet. Similar comparisons of data reported for families in Georgia and for pre-school children in Kentucky indicated rates of five times and twice as high, respectively. The Guatemalan studies [2] disclosed that the prevalence of *Shigella* was approximately three times greater among families living in areas where inside toilets were available in less than 50 % of dwellings than among those where more than 50 % of dwellings had such facilities. Subsequent studies in Guatemala [3] showed a general reduction in morbidity in the total population following the installation of privies but failed to show any effects on rates of diarrhoea in infants.

In addition to recording the association of prevalence of the *Shigella* with various conditions of excreta disposal, the Kentucky studies [4] reported that persons living in dwellings having privies experienced approximately twice as many cases of diarrhoeal disease as persons residing in houses with inside toilets. *Ascaris* infection rates were approximately four times higher among persons using privies than among those using inside toilets.

Flies have been traditionally incriminated as vectors of diarrhoeal disease. Classic studies in Texas [5] and subsequent studies in Georgia [6] demonstrated that significant reductions in diarrhoeal disease morbidity and *Shigella* infections could be accomplished by fly control. Likewise, in Egyptian villages [7] comparison of rates of mortality between 1949 and 1950 showed that the reduction in rate could be attributed largely

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[1] International Co-operation Administration (1956) *Technical co-operation in health*, Washington, D.C., US Government Printing Office.

[2] Beck, M. D., Muñoz, J. A. & Scrimshaw, N. S. (1957) Diarrheal disease control studies. The relationship of certain environmental factors to the prevalence of *Shigella* infection. *Amer. J. trop. Med. Hyg.*, **4**, 718.

[3] Beck, M. D., Muñoz, J. A. & Scrimshaw, N. S. (1957) Studies on diarrheal diseases in Central America. I. Preliminary findings on cultural surveys of normal population groups in Guatemala. *Amer. J. trop. Med. Hyg.*, **6**, 62.

[4] Schliessmann, D. J., Atchley, F. O., Milcomb, M. J. & Welch, S. (1958) *Relation of environmental factors to the occurrence of enteric disease in areas of eastern Kentucky*, Washington, D.C., US Government Printing Office (*Public Health Service Monograph*, No. 54).

[5] Watt, J. & Lindsay, D. R. (1948) Diarrheal disease control studies. I. Effect of fly control in a high morbidity area. *Publ. Hlth Rep. (Wash.)*, **63**, 1319.

[6] Lindsay, D. R., Stewart, J. H. & Watt, J. (1953) Effect of fly control on diarrhea disease in an area of moderate morbidity. *Publ. Hlth Rep. (Wash.)*, **68**, 361.

[7] Weir, J. M., Wasif, I. M., Hassan, F. R., Attia, S. M. & Kadar, M. A. (1952) An evaluation of health and sanitation in Egyptian villages. *J. Egypt. publ. Hlth Ass.*, **27**, 56.

to control of fly-borne diseases. Installation of bored-hole privies in a Georgia community [1] curtailed breeding of houseflies in privies but did not significantly reduce populations of houseflies in the community. The exclusion of flies from faecal material, however, resulted in significant reductions in *Shigella* infections in children under ten years of age and in rates of morbidity from diarrhoeal disease. In addition to the above, the work of the WHO Diarrhoeal Diseases Team in surveys in countries of Asia and Africa has tended to confirm the above results. Further, while no detailed data are available, housing and the provision of sanitary controls for the safe production, processing and storage of milk and food products are essential elements of environmental sanitation.

In summary, environmental sanitation is accepted as a basic factor in the improvement of conditions favourable to healthy existence. It is difficult to conceive of circumstances in which improvements in sanitation would be contra-indicated if resources were available for their accomplishment. The Committee supports the view of Gordon, Béhar and Scrimshaw [2] that: "The traditional acceptance of environmental sanitation as the fundamental feature in long-term control of acute diarrhoeal disease in total populations is wholly justified".

6.4 Socio-economic and educational factors

The association of severe problems of enteric infection with poor economic circumstances is axiomatic. The elaboration of this point is not likely to disclose a relationship that can be considered specifically for the control of enteric diseases. However, economic limitations must be taken into account in developing plans for control so that the measures projected will be practicable for the countries in which they are to be applied.

Lack of knowledge or lack of initiative, or both, are probably the most significant factors in the persistence of enteric infections. The full benefit of sanitary improvements has often not been realized because the facilities thus provided are not properly used. Further, it is recognized that the persistence of acute diarrhoeal disease in areas with satisfactory sanitary facilities can be attributed to the poor hygienic practices of individuals. Appropriate instruction of the population is an essential accompaniment of environmental improvement. On the other hand, in the absence of satisfactory sanitary facilities instruction in hygienic practices is likely to be ineffective.

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[1] McCabe, L. J. & Haines, T. W. (1957) Diarrheal disease control by improved human excreta disposal. *Publ. Hlth Rep. (Wash.)*, **72**, 921.

[2] Gordon, J. E., Béhar, M. & Scrimshaw, N. S. (1964) La enfermedad diarreica aguda en los países en vías de desarrollo. III. Métodos de prevención y control. *Bol. Ofic. sanit. panamer.*, **56**, 436.

The practices and circumstances favouring the spread of enteric diseases are often linked with time-honoured beliefs and customs that may have deep roots and purposes in the society concerned, such as the social gathering round the village well, the communal feeding in the kibbutzim, or the low social status accorded to food handlers. Sometimes risks arise from ignorance, as in the case of the mother who is unaware of the principles of hygiene in infant-feeding; sometimes they emerge in situations motivated by expediency, as when workers suffering from mild diarrhoea are transferred from their normal tasks and given lighter work to do in the canteen; sometimes, in countries where cleanliness is held in high esteem, the risks are underrated or there is a reluctance to diagnose enteric diseases, and euphemisms such as " gastric flu " are used, implying that no one has been guilty of lack of hygiene.

In some areas the basic problem is not one of gross deficiency of resources, but rather of failure to use them. Often this can be traced to lack of proper instruction or failure to consider the cultural mores of the population. It has been noted that readily available foods that would provide adequate nutrition for young children are not used because of custom or cultural prejudice.

Many earlier inquiries, as well as the recent studies of the WHO Diarrhoeal Diseases Team, indicate that professional as well as lay persons failed to use available facilities. Moreover, physicians are sometimes ill-advised in their choice of procedure for diagnosis and treatment. Widespread, indiscriminate use of drugs is reported from some treatment centres, where many of the bacteria isolated are resistant to the drugs used.

It has also been widely noted that many fatal cases of diarrhoea occur because mothers fail to recognize or appreciate the signs of dehydration. The inadequacy of child care not only is an important factor in the occurrence of enteric infections but also tends to aggravate their consequences.

7. PREVENTIVE MEASURES

7.1 Education

Understanding of the health and social significance of water supply and excreta disposal and of methods of food handling and of baby care is a foundation of health education in the prevention of enteric infections. Health education has contributed to the prevention of enteric diseases by developing the health consciousness of mothers, by teaching good practices to food handlers and those in charge of sanitary installations, by encouraging public demand for sanitation through health authorities, and by interpreting the principles of food and water hygiene. The accep-

tance of health education leads to the prevention of enteric infections and also forms an essential background for the public acceptance of legislation. Health education with emphasis on the importance of controlling the enteric infections should begin in primary school and continue in secondary school. It should be given special attention in schools for the training of nursing aides, nurses, sanitarians and others, and in schools of medicine and public health.

The customs, beliefs and cultural practices of a people must be heeded and woven into the fabric of any preventive medicine programme. The Committee noted that much information already exists on a regional and local basis through the work of social anthropologists. Reports of such work should be utilized by health workers in order that knowledge of the basic facts of family and community living may be incorporated into the planning of public health activities and practices.

7.2 Sanitation

The Committee examined data that clearly show a correlation of lower rates of diarrhoea and certain enteric infections with higher levels of environmental sanitation. It was acknowledged that, despite the multiplicity of etiological agents and differences in mode of spread, prevention of enteric infections is dependent upon the availability and use of those environmental sanitation facilities that reduce direct and indirect transmission of infectious agents and preclude faecal contamination of the environment. In order of priority, factors essential to the suppression of enteric infections seem to involve water supply, excreta disposal, municipal and industrial waste disposal, vector control, housing, and sanitation of food and milk products.

It was recognized that remediable deficiencies could seldom be corrected all at the same time, that requirements would vary from place to place and that procedures must be adapted to local conditions. While all the factors listed above have an impact of varying degree in reducing the prevalence of enteric infections, no single factor approaches the significance of a safe, adequate water supply. The Committee recognized that the optimum type of water supply can be provided only in a minority of cases. However, experience has shown that in few, if any, situations is improvement in water supplies not possible within the resources available to the local area. Thus, major emphasis should be placed on the provision to each dwelling of, first, a safe supply of water and, second, facilities for the sanitary disposal of excreta. Concentration of effort on other environmental controls should be deferred until these objectives are attained. It is also recognized that environmental improvements are enhanced through well-planned programmes of health education.

7.3 Management of the sick and convalescent patient for the prevention of spread of infection

Although diverse procedures have been employed for the treatment of carriers of typhoid and other enteric bacteria, the Committee felt that proper personal and community hygiene practices offer the best hope of preventing familial and community spread and that no specific recommendations concerning therapy seem justified at the present time.

In reducing the hazard that the patient and the convalescent carrier of enteropathogenic bacteria may represent to their immediate environment the emphasis should be on good personal hygiene (e.g., proper disposal of excreta and washing of hands after attending to the patient). The administration of antibiotics cannot replace such practices, and, at best, can be expected to accomplish only a reduction in the duration of the convalescent carrier state.

7.4 Child-rearing practices

Note was taken of the lower rates of acute diarrhoeal disease among breast-fed infants in comparison with infants fed artificially or given supplemental food in addition to breast milk. It was felt that in this regard contamination of food was a factor as well as nutrition.

Note was taken of the success of the Institute of Nutrition of Central America and Panama in developing an inexpensive, acceptable dietary supplement that has been effective in reducing certain nutritional diseases among populations in Guatelama. The results in terms of reduction of acute diarrhoeal disease are awaited with interest.

It was apparent from discussions that particular attention should be given to the nutritional adequacy of diets for children after weaning in view of the increase in the number of deaths from acute diarrhoeal disease during this period.

The importance of personal hygiene in infant care was stressed. Regardless of other factors, reduction of direct faecal transfer to the infant by those who care for it will reduce the possibility of infection.

7.5 Immunization

After reviewing results of recent studies, the Committee concluded that the effectiveness of enteric vaccines had been proved only for typhoid vaccine.[1] A recommendation for wide public health vaccination pro-

[1] See, for example: Yugoslav Typhoid Commission (1962) A controlled field trial of the effectiveness of phenol and alcohol typhoid vaccines. *Bull. Wld Hlth Org.*, **26,** 357; and Yugoslav Typhoid Commission (1964) A controlled field trial of the effectiveness of acetone-dried and inactivated and heat-phenol-inactivated typhoid vaccines in Yugoslavia : report. *Bull. Wld Hlth Org.*, **30,** 623.

grammes against other enteric infections cannot be made on the basis of the evidence now available.

Typhoid vaccine may be administered to children as young as two years of age, and is advised in areas where typhoid fever is an important problem. Other vaccines, both inactivated and live attenuated in type, for other enteric infections are being studied but are not yet available.

7.6 Socio-economic measures

Alleviation of economic distress would undoubtedly effect reductions in rates of enteric infections. However, social and economic improvement is a gradual evolutionary process and is not amenable to specific campaigns or " crash " programmes. The Committee felt no that specific recommendations for the control of enteric infections could be made in this area.

8. RESEARCH NEEDS

The Committee recognized that a listing of lacunae in knowledge of infectious enteric diseases would indeed be a long one. It noted that the delineation of specific objectives would be helpful in obtaining additional information to accelerate a reduction of enteric infections, provided attention were focused on clearly defined needs for improvement of prophylaxis and clinical management and environmental sanitation.

The Committee emphasized that the initiation of control programmes against enteric infections in areas of high endemicity does not depend on the results of further research, and that effective programmes can be launched through the application of current knowledge. Research proposals from every area should be evaluated critically to determine whether or not such activities are the most appropriate ones for the improvement of control measures in the area concerned.

8.1 Causative and contributory factors of illness and death

In areas of high endemicity—i.e., where rates of infant mortality are of the order of 100 per 1000 live births—it may be expected that the rates will be lowered as a result of improvements in community sanitation and personal hygiene. Further research in such areas is not a prerequisite for the introduction and execution of control programmes.

Attention was directed to the following problems, which are pertinent primarily to the control of enteric infections in areas of moderate endemicity after sanitary improvements have been undertaken.

(1) Further studies should be made to determine precisely the etiological significance of *E. coli* in sporadic cases of diarrhoea, as well as in outbreaks.

(2) The etiological significance of enteric viruses in diarrhoeal disease should be determined.

(3) The relation of specific nutritional and dietary deficiencies to infectious agents and diarrhoea should be investigated in several geographic areas where this combination of circumstances exists.

8.2 Effectiveness of measures for prevention and treatment of enteric infections

8.2.1 *Environmental studies*

The Committee acknowledged the vital importance of environmental sanitation but noted that most of the evidence on the relation between good sanitary facilities and low rates of diarrhoea has been obtained through study of associations in established rather than experimental situations. Few efforts have been made to measure rates of diarrhoeal diseases concurrently with attempts at control. Although available evidence is highly persuasive, more definitive data should be gathered through the following studies:

(1) Investigations should be conducted to evaluate the effect on the prevalence of enteric infections and diarrhoeal disease of various environmental modifications, such as improvement of water supplies and of waste disposal, fly control and soil sanitation.

(2) Studies should be made to develop techniques for motivating communities and citizens to take action in obtaining improvements in sanitation.

(3) In each local area attempts should be made to develop techniques for using locally available materials to permit practical and economical construction of sanitary facilities.

Communities where such studies are developed should be used as training centres for personnel in adjacent areas.

8.2.2 *Immunization*

(1) Studies should be made to improve techniques for the control of enteric infections through immunization by further investigating the the most effective and simplest schedules of immunization with typhoid vaccines of known potency.

(2) Studies are recommended for developing new vaccines and testing them in field trials. These studies should include laboratory and field trials of oral *Shigella* and possibly *E. coli* and other vaccines.

(3) The Committee recommends detailed studies of the role of various foods in the etiology of enteric infections as well as the effect of breast-feeding and artificial feeding.

(4) The Committee recommends further study of the basic physiology and pathophysiology of the intestine, including the study of intestinal flora and quantitative and qualitative changes of this flora due to the use of antibiotics and to various nutritional and other factors, and their relationships to acute diarrhoeal disease.

8.2.3 *Treatment*

(1) Further studies should be made on the development of simple methods and techniques for the conducting of mass programmes to prevent deaths due to dehydration from diarrhoeal disease.

(2) Further attention should be given to the development of new drugs and additional antibiotics for the treatment of enteric infections.

(3) Attention should be given to the development of more effective methods for treating carriers of enteric infections.

(4) The use of phage in the treatment of diarrhoea should be evaluated.

(5) Studies should be made on the possibility of biological control of enteric infections by using non-pathogenic organisms that may be competitors of pathogens.

8.2.4 *Diagnostic procedures*

(1) Efforts should be made to develop simple techniques for determining the degree of dehydration and fluid and electrolyte requirements.

(2) Further studies are needed for the development of quicker and simplified diagnostic procedures, such as fluorescent antibody techniques, that might be used both for epidemiological studies and for the initiation of specific treatment.

(3) Continous study of the resistance of enteric pathogens to antibiotics, and their genetic changes in this connexion, should be pursued.

(4) Development of reliable serological and skin tests should be encouraged.

8.3 Studies at local and national levels

(1) The Committee re-emphasized that where high rates of infant mortality occur the rates of deaths from diarrhoeal diseases are correspondingly high, and stated its belief that extensive surveys and measurements to elaborate this point are not justified. However, proper assessment of local problems is desirable by short-term, cross-sectional studies, such as those made by the WHO Diarrhoeal Diseases Team, in general accordance with the programmes developed. It was noted that for such studies extensive laboratory and epidemiological facilities are not required.

(2) The Committee recommended that public authorities at all levels should undertake the development of adequate systems of disease reporting according to the accepted international system.

(3) The Committee strongly urged that demonstration control projects be undertaken in hyperendemic areas to emphasize the fact that facilities do not have to be pretentious or expenditures beyond the resources of the local community to accomplish some reduction in diarrhoeal diseases.

(4) Information on the cost of illness due to enteric infections should be obtained at local, national and international levels, in order to serve as a guide in the selection and planning of control measures.

(5) The Committee recommended that national and international Enterobacteriaceae reference centres should assist in preparing regular periodic reports, not only on the type of strains isolated but also on the endemic and epidemic occurrence of enteric infections.

(6) It was strongly urged that national reference centres should assist in control programmes by collaborating with local epidemiologists and directors of control programmes.

8.4 Co-operative international studies

(1) The Committee urged that all countries should co-operate in the development of adequate systems of reporting to permit realistic comparison of problems resulting from diarrhoeal diseases in various parts of the world.

(2) It was recommended that laboratory methodology should be standardized at the national level but evaluation of diagnostic accuracy should be available from international reference centres.

(3) The Committee considered that national and international Enterobacteriaceae reference centres should also co-operate closely in collecting data on the global epidemiology of salmonelloses and other enteric infections.

9. APPLICATION OF CONTROL MEASURES IN PUBLIC HEALTH PRACTICE

The major objective in the control of acute diarrhoeal disease is to prevent the transfer of infectious agents from person to person—i.e., to prevent the faecal contamination of the environment. The Committee recognized that progressive steps must be taken to initiate and develop control programmes, that these must usually be undertaken with the limited means available to the local community, and that a logical sequence of steps should be planned to take advantage of resources as they develop. The following recommended outline of procedures lists, in order of priority, the control methods suggested for areas at various levels of intensity of enteric infection. It was recognized that the sequence of the various steps taken, or the necessity of omitting certain of them, will depend on local conditions.

Obviously, national recognition of the problem of enteric infections is a prerequisite to taking the first step in developing a programme for their control. Persuasive, indicative data are available in all but a few areas. In those rare instances where they are lacking, WHO should take the initiative in directing attention to the problem and in stimulating the development of programmes.

9.1 Initial methods for areas of high endemicity

Areas of high endemicity are arbitrarily defined as those in which rates of infant mortality approach or exceed 100 deaths per 1000 live births and which are characterized by low personal income, lack of essential sanitary facilities, inadequate diet, insanitary housing and limited medical services. In such areas the primary consideration in control should be the prevention of enteric infections, rather than the management of clinical cases. This can be accomplished by the development of programmes for motivating and sustaining the participation of citizens in:

(1) construction of (basic) sanitary water supply and excreta disposal systems with services to each dwelling;

(2) education of mothers in proper care of children, including personal and familial hygiene, and the recognition and oral treatment of dehydration; and

(3) provision and promotion of use of the most adequate medical facility within the scope of available resources.

The success of the programme will depend on enlisting the full support and co-operation of national and local governments and the active participation of citizens; where total resources may not be available to permit the development of highly specialized facilities, initiative and imagination must be exercised by programme personnel to make full use of local materials and resources.

The following initial steps are recommended for areas, communities or villages where resources are lacking:

(1) The best-qualified public health workers available should survey the area, and examine the circumstances in sufficient detail to determine what assets and behavioural habits of the population have a positive value for the prevention of disease and how these may be used as a basis for control measures. They should also determine how, in what sequence, and on what schedule the following can be accomplished.

(2) The establishment of a basic level school should be promoted, if one does not already exist, the germ theory of disease should be taught and instruction given in personal, familial and community hygiene. In the absence of such a facility, the best-qualified person available—for example, the local medical aide, midwife, nursing aide, or sanitary inspector—should begin health education according to a systematic plan.

(3) Such improvements as are possible should be made in the water supply according to the procedure outlined in a monograph published by WHO.[1] When the recommended procedures cannot be performed, any possible techniques for improvement should be adopted.

(4) Similarly, efforts should be made to develop techniques for the sanitary disposal of excrement.

(5) A health centre or its equivalent should be established. This might well be directed by a person trained only in the rudiments of personal hygiene and the use of simple drugs. This person should provide instruction in child care and personal hygiene, and should be informed of the proper procedures for instructing mothers in the recognition and oral treatment of dehydration. He may make his headquarters anywhere—e.g., in a vacant building or in a room in the home of the village headman—but he should be in that place on a definite schedule, preferably every day. More adequately trained personnel should, of course, be used if and when they become available.

(6) As soon as positive results are achieved in a community or region, this should be used for the demonstration of methods.

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[1] Wagner, E. G. & Lanoix, J. N. (1959) *Water supply for rural areas and small communities*, Geneva (*Wld Hlth Org. Monogr. Ser.*, No. 42).

9.2 Methods for areas where initial steps have been accomplished

When progress has been made in the initial programmes, the following steps should be taken:

(1) Concerted efforts should be made to provide recommended water supplies and systems for excreta disposal.

(2) Programmes for vector control and milk and food protection should be initiated.

(3) The health centre should be expanded to include facilities for parenteral rehydration when necessary, and oral electrolyte solutions should be widely distributed according to a plan that has been developed and proved successful in a comparable community or region.

(4) Health education should be expanded.

(5) Diagnostic competence in the identification of the common enteric pathogens should be developed at regional level, and at a national level if not already established.

9.3 Methods for consolidation of control programme

(1) Efforts to provide recommended water supplies and systems for excreta disposal should be maintained.

(2) The characterization of local problems should be pursued through the maintenance of appropriate records and the collection of specimens from acute cases of diarrhoea for laboratory examination to determine the relative prevalence of pathogens and their antibiotic sensitivity.

(3) Medical assistance should be obtained, at least on a part-time basis, or provision made for the transport of severely ill patients to a treatment centre.

(4) The number of man-hours devoted to the health centre's operation should be expanded as the growth of the programme demands.

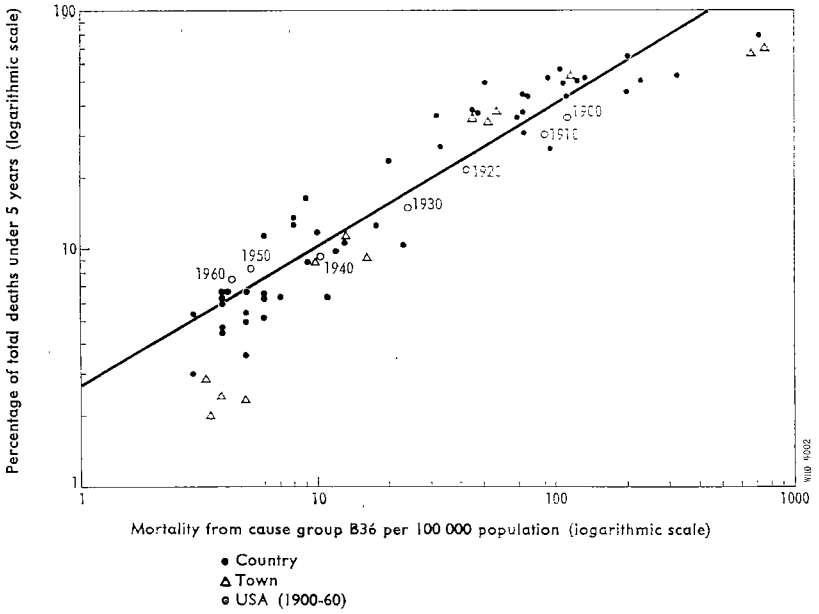
(5) Rural health centres should be set up in areas with developing programmes to provide specific training for medical and paramedical personnel to enable them to perform specific tasks in the control of enteric infections.

ACKNOWLEDGEMENT

The Committee acknowledges the special contribution made during the deliberations of the Committee by Dr W. J. van Zijl, Leader, WHO Diarrhoeal Diseases Team.

Annex 1

MORTALITY FROM CAUSE GROUP B36 * IN COMPARISON WITH LEVEL OF HEALTH



* Gastritis, duodenitis, enteritis, and colitis, except diarrhoea of the newborn.
The regression line refers to the statistics of 51 countries.

Annex 2

AN AUTOPSY STUDY OF 63 CHILDREN IN GUATEMALA CITY, 1958 AND 1960 *

TABLE 1. RELATIONSHIP BETWEEN DIARRHOEA AND MALNUTRITION IN THE 63 AUTOPSIED CASES IN GUATEMALA CITY

	Malnutrition		Total
	Present	Absent	
Diarrhoea present	35	15	50
" absent	5	8	13
Total	40	23	63

TABLE 2. ISOLATION OF BACTERIA AND VIRUSES FROM INTESTINE IN THE 63 AUTOPSIED CASES IN GUATEMALA CITY AND IN 51 FATAL CASES OF DIARRHOEA IN CHILDREN IN MEXICO CITY

Agents recovered	Guatemala City rates (%)		Mexico City rates [a] (%)
	Diarrhoea (50 cases)	Non-diarrhoea (13 cases)	Diarrhoea (51 cases)
Shigella , *Salmonella* and *E. coli* alone or in association with one another or viruses	46	23	54
Viruses alone or in association with bacteria	18	15	33
Viruses alone	6	7.7	13
Shigella alone	12	0	8
Salmonella alone	2	0	6
E. coli alone	18	0	17
Shigella + viruses	2	0	6
Salmonella + viruses	4	0	4
E. coli + viruses	6	7.7	4
No agents isolated	48	69	33

[a] Data supplied by J. Olarte.

TABLE 3. ISOLATION OF BACTERIAL PATHOGENS FROM INTESTINE IN THE 63 AUTOPSIED CASES IN GUATEMALA CITY

	Bacterial pathogens		Total
	Present	absent	
Diarrhoea present	23	27	50
" absent	3	10	13
Total	26	37	63

* Data for Guatemala supplied by G. J. Dammin.

Annex 3

CLASSIFICATION OF THE ACUTE DIARRHOEAL DISEASES ON THE BASIS OF HISTOLOGICAL AND CYTOLOGICAL PATTERNS AND MICROBIOLOGICAL CORRELATION *

	Cholera	*Shigella*	*E. coli*	*Salmonella*	Non-specific
Mucosa:					
intact	+	−	−	−	−
bacteria	−	−	+	+	?
Lymph-node:					
bacteria	−	−	+	+	?
Bacteraemia	−	−	+	+	?
Stool cytology (leucocytes)	−	+	+	+	−

+ = positive or present. − = negative or absent. ? = not known.

* Data supplied by G. J. Dammin.

Annex 4

EFFECT OF SANITARY FACILITIES ON PREVALENCE OF ENTERIC INFECTIONS: DATA REPORTED FROM CALIFORNIA, GEORGIA AND KENTUCKY, USA, AND FROM GUATEMALA *

TABLE 1. PREVALENCE RATES FOR *SHIGELLA*, IN RELATION TO SELECTED SANITARY FACILITIES IN CALIFORNIA, GEORGIA AND KENTUCKY, AND IN GUATEMALA

Sanitary facilities	California [a] 1952-53		Georgia [b] 1949-53		Kentucky [c] 1954-56		Guatemala [a] 1955-56	
	No. of cultures	% positive	No. of cultures	% positive	No. of cultures	% positive	No. of cultures	% positive
Water and flush toilet inside dwelling	985	1.6	2 988	0.4	5 017	1.1	—	—
Water inside dwelling, privy outside	688	3.0	5 392	2.2	2 195	2.4	1 451 [d]	6.3
Water and privy outside	4 438	5.8	5 586	5.0	3 994	5.9	891 [e]	9.4
(Water on premises)	—	—	2 791	4.1	1 988	5.8	—	—
(Water off premises)	—	—	2 975	5.8	2 006	6.0	—	—

[a] Cultures from children ten years of age and under.

[b] Data from Stewart, W. H., McCabe, L. J., Jr, Hemphill, E. C. & DeCapito, T. (1955) Diarrheal disease control studies. The relationship of certain environmental factors to the prevalence of *Shigella* infection. *Amer. J. trop. Med. Hyg.*, **4**, 718.

[c] Cultures from pre-school children.

[d] Facilities (including toilet) in more than 50% of dwellings.

[e] Facilities in less than 50% of dwellings.

* After Schliessman, D. J. (1959) Diarrhoeal disease and the environment. *Bull.Wld Hlth Org.*, **21**, 381.

Annex 4 (*continued*)

TABLE 2. DIARRHOEAL DISEASE, RATES OF INFECTION WITH *SHIGELLA* IN PRE-SCHOOL CHILDREN, AND PERCENTAGE OF POPULATION INFECTED WITH *ASCARIS*, IN RELATION TO SELECTED SANITARY FACILITIES, IN KENTUCKY, 1954-56

Sanitary facilities	Morbidity rates				*Shigella* prevalence		*Ascaris* incidence	
	0-4 years		All ages		No. of cultures	% positive	All ages	
	PME [a]	Rate [b]	PME [a]	Rate [b]			No. specific	% positive
Water and flush toilet inside dwelling	5 040	428	33 961	139	5 017	1.1	960	7
Water inside dwelling, privy outside	2 200	829	14 821	238	2 195	2.4	665	25
Water and privy outside dwelling	3 881	1 140	21 602	360	3 994	5.9	1 038	42
(Water on premises)	1 900	953	10 883	307	1 988	5.8	533	41
(Water off premises)	1 981	1 320	10 719	413	2 006	6.0	505	43

[a] Person-months experience.

[b] Rate per 1000 per annum.

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