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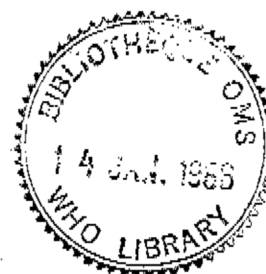

DEVELOPMENT OF A PROGRAMME FOR DIARRHOEAL DISEASES CONTROL

Report of an Advisory Group

(Geneva, 2–5 May, 1978)

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1. INTRODUCTION

An Advisory Group on Development of a WHO Programme for Acute Diarrhoeal Diseases Control met in Geneva from 2 to 5 May 1978. Dr H. Mahler, Director-General, opened the meeting and said that the Organization was committed to giving the highest priority to the Diarrhoeal Diseases Control Programme in view of the extent, importance and complexity of the problem of diarrhoeal diseases in developing countries. Member States had urged WHO to help develop the activity as a technical cooperation programme at the national and international level. He counted on the continued partnership of UNICEF and on further bilateral and multilateral collaboration. He asked the Group to be very realistic in assessing the value of different control strategies and looked forward to studying its recommendations for development of the Diarrhoeal Diseases Control Programme.

2. JUSTIFICATION OF THE PROGRAMME

2.1 Diarrhoeal diseases as a major health problem

The acute diarrhoeal diseases constitute one of the greatest social evils - not only do they kill people living in hunger and poverty but they retard the growth of young children and impair the quality of life of those who survive. The problem is overwhelming and complex as it involves deep-rooted cultural and behavioural factors in addition to the more obvious socioeconomic inequalities.

Although there is a lack of reliable information on incidence and associated mortality from diarrhoeal diseases, particularly from countries where the problem is serious, some data are available which allow a fair assessment of the magnitude of the problem:

On a global scale it has been estimated that in 1975 there were about 500 million episodes of diarrhoea in children below five years of age in Asia, Africa and Latin America, resulting in 5 to 18 million deaths[1] which is comparable to the situation seen in the industrialized countries at the end of the last century.

In the South-East Asia Region, the incidence of diarrhoeal diseases in different countries has been shown to vary from 1.5 to 12 per 1 000 population of all ages.[2]

In one report published by PAHO in 1973 describing patterns of childhood mortality in Latin America, diarrhoeal diseases accounted for 28.6% of 35 095 deaths due to all causes in children below five years of age and were by far the major single cause of death in the study areas.[3]

In a study conducted by a WHO Diarrhoeal Diseases team working in 7 developing countries in 1960-65, diarrhoeal disease monthly incidence rates in young children were in some instances as high as 40%.[4]

In addition to the high incidence of diarrhoeal diseases many studies have convincingly demonstrated a close association between diarrhoea and malnutrition. These conditions thrive in the same socioeconomic and cultural surroundings, and by perpetuating each other, contribute to high rates of childhood morbidity and mortality and hinder efforts to regulate fertility. While malnourished children have a higher incidence of diarrhoeas which are often more severe causing a higher rate of diarrhoea-related mortality, diarrhoeal diseases are probably the most important contributors to malnutrition because of food withdrawal, anorexia and malabsorption.

In the developing countries more than one third of the beds in children's hospitals or wards are occupied by cases of diarrhoea receiving expensive antibiotics and intravenous fluid, putting a heavy load on the limited budget for health care in these countries.

Since 1961, cholera has been reported by 80 countries in Asia, Africa and Europe and has caused major outbreaks and become endemic in those areas where the incidence of acute diarrhoeal diseases is high and water supplies and sanitation facilities are inadequate. In cholera-endemic areas, however, cholera accounts for less than 5-10% of all acute diarrhoea cases in non-epidemic seasons; even when it occurs, in more than 90% of instances cholera is clinically indistinguishable and is treated in the same way as other acute diarrhoeas. Although most cases are mild, cholera can spread fast and be fatal even in adults; the economic losses of countries can be great and the sufferings of the people considerable. After a quiescent period in 1975-76, cholera has recrudesced in several countries and has extended most recently to the Gilbert Islands in the South Pacific and the Maldives, illustrating the need for preparedness for epidemic control as the prevailing pandemic shows no sign of ending.

2.2 Recent research developments

Intensive research activities stimulated by the current cholera pandemic have made available abundant new knowledge about diarrhoeal diseases. This includes:

- The discovery that a single modality - oral rehydration fluid - can be used to treat most cases of dehydration from watery diarrhoea, including cholera, in all age-groups;

- The recognition of the role of new viral and bacterial agents which makes it possible to identify etiological agents in more than 80% of diarrhoeas; this is a reversal of the situation prevailing a few years ago when 80% of cases remained undiagnosed and were called "acute undifferentiated diarrhoeas";

- The understanding of the pathogenesis of most of the acute diarrhoeas, opening up other possibilities for improving treatment and prevention, including development of vaccines;

- The demonstration that the provision of safe drinking water supplies alone is not sufficient to prevent acute diarrhoeal diseases;

- The finding that travellers' diarrhoea though caused by a variety of diarrhoeal pathogens is commonly due to enterotoxigenic *Escherichia coli*, in which case judicious use of antibiotics like doxycycline may have a preventive role;

- The demonstration that aluminium adjuvanted whole-cell cholera vaccines may provide better protection in children and longer protection in adults than the generally available vaccine, justifying their further study.

Among these and many other advances of fundamental and applied importance, the discovery of oral rehydration therapy is considered to be of special significance as it has made it possible to undertake immediately a common programme for reducing deaths from *all* acute diarrhoeal diseases while efforts continue to attain the long-term objective of their prevention and control.

2.3 Need for a WHO-supported programme

There is a widespread awareness of the problem of diarrhoeal diseases but there has been a lack of definite commitment to deal with it. This is partly due to inadequate dissemination of information to those in the medical profession and other health-related fields about the available technology that can be used. Member States have expressed concern and have pressed the Organization for technical cooperation in this field. It is therefore necessary to make information available to all health workers and those involved in socioeconomic development in order to enlist their participation in and commitment to a concerted, unified, multi-disciplinary, medium-term programme for diarrhoeal diseases control. Such a programme will also lay the foundation for early detection of epidemics, particularly of cholera, and consequently their rapid control. There is also an important need for the transfer of managerial skills to assist in reorienting national activities for the control of acute diarrhoeal diseases including the re-allocation of funds so that the most beneficial use is made of available resources, both financial and human.

3. CURRENT WHO ACTIVITIES

During the last few years the Organization has been working towards the development of a multi-disciplinary programme for acute diarrhoeal diseases control and has established interdisciplinary groups in Headquarters and the Regional Offices. These groups, working in close collaboration with the complementary programmes of the Organization on environmental health, maternal and child care, nutrition, food hygiene, health education and appropriate technology, have taken up the promotion of oral rehydration as one of their main activities. For this purpose they have organized field studies on the feasibility, acceptability and effectiveness of oral rehydration when delivered through the existing health services facilities in countries with different cultures and health service infrastructure. These studies convince local health administrators of the practicability and benefits of the procedure and serve as entry points to a broader control programme. Such studies are in progress or have been completed in Costa Rica, Egypt, El Salvador, Guatemala, India, Iran, Laos, Liberia, Nigeria, Philippines and Turkey. In addition to these field evaluations being carried out at the community level, at least 15 more countries are known to have introduced oral fluid for routine treatment of acute diarrhoeas and also for treatment of cholera during epidemics.

Interregional, regional and national courses to train different levels of health workers have been held in Bangladesh, Brazil, Congo, Dominican Republic, Guatemala, India, Indonesia, Liberia, Panama, Papua New Guinea, Philippines, Singapore, Thailand and Yemen.

Several manuals and guidelines[5-13] for workers at different levels have been published and distributed widely.

Regional Advisory Committees on Medical Research of five of the six WHO regions have given priority to diarrhoeal diseases research, determing priority research areas, and identifying institutions and individuals to undertake the work. Some Regional Offices have already made a special budget allocation for this purpose.

Close collaboration exists with UNICEF for the promotion of oral rehydration and the improvement of water supply. The Government of the United Kingdom has made a contribution to the WHO Voluntary Fund for Health Promotion for diarrhoeal diseases control.

These activities represent the beginning of the expanded multi-disciplinary programme for acute diarrhoeal diseases control which is planned to be complementary to and supportive of other WHO activities in primary health care and overall health development.

4. OBJECTIVES OF THE PROGRAMME

After reviewing the nature and extent of the problem and recent scientific advances, the Advisory Group strongly endorses the current WHO policy, as outlined by the Director-General, and urges WHO to establish a global Programme for Diarrhoeal Diseases Control with the following objectives:

(i) The immediate and medium-term objective of the Programme is to increase technical cooperation with Member States (a) in reducing mortality and preventing other ill effects of the acute diarrhoeal diseases, particularly deterioration of nutritional status, through the implementation of oral rehydration programmes and (b) in decreasing morbidity through the improvement of water supply and sanitation. The objective will also include research on various aspects of the problem to develop and improve other possible means of prevention and control.

(ii) The long-term objective is to prevent and control acute diarrhoeal diseases by ensuring adequate water supply and sanitation and other appropriate control measures so that they cease to be a major public health problem.

5. POSSIBLE CONTROL STRATEGIES

This section of the report is a brief factual review of the main strategies that can be and have been used to treat, prevent and control the acute diarrhoeal diseases.

5.1 Management of acute diarrhoeal diseases

There are three aspects of management of acute diarrhoeal disease:

5.1.1 Treatment and prevention of dehydration

The primary cause of mortality from diarrhoeal disease is dehydration. In cholera, the most severe of the diarrhoeal illnesses, fluid losses can reduce body weight by 10% in 4-6 hours. Rapid administration of appropriate intravenous fluid has brought mortality rates from cholera and other diarrhoeal illnesses in hospitalized patients to well under 1%. The disadvantages of this type of therapy are that these fluids are only available in hospitals and treatment centres, they are costly and they need aseptic precautions in their preparation and administration.

The recent development of oral rehydration solution has vastly simplified the procedures of rehydration. The solution contains glucose and essential electrolytes which when administered orally are absorbed in the small intestine even in the presence of copious diarrhoea. Many studies have shown that this solution can be used successfully, both orally and by nasogastric infusion, to treat most cases of dehydration both in the hospital and at home. In the absence of glucose, sucrose can be substituted without compromising the usefulness of the fluid. Delivery of the fluid in most areas at the moment is primarily through a pre-packaged mixture of glucose and salts which is added to an appropriate volume of water. Home-made solutions containing locally available sugar and salt prepared by "pinch and scoop" methods or by spoon measures are under evaluation.

The challenge today is to provide replacement of diarrhoeal losses with oral rehydration fluid as early as possible during illness. At present this cannot be done on the massive scale necessary by depending on the existing health care delivery systems with their limited coverage and outreach. This problem can be overcome only by a more universal dissemination of rehydration services which in the case of diarrhoea in children must include participation of mothers in this health care process.

5.1.2 Dietetic management

Of all the common childhood diseases diarrhoea has the greatest impact on nutrition mainly as a result of:

- withholding of food by mothers because they believe that fasting is important for curing diarrhoea;

- decrease in food intake due to anorexia which is associated with dehydration;

- nutrient losses through malabsorption and protein leakage, particularly during dysentery which is associated with destruction of the intestinal epithelium.

WHO-supported studies in the Philippines and Turkey have shown that oral rehydration coupled with education on proper feeding practices during and after diarrhoea results in better weight gain than when no oral rehydration is used, and thus may reduce the ill effects of diarrhoea on nutritional status and constitute an important step in interrupting the diarrhoea-malnutrition cycle.

Adequate feeding of a child during and after diarrhoea is of definite nutritional importance. In a borderline or malnourished child fasting for any period of time is inappropriate and potentially dangerous. Breast feeding should continue uninterrupted unless severe vomiting makes it difficult; children receiving artificial milk should be given it temporarily in more diluted form. Any foods the child consumes regularly can continue to be offered during diarrhoea. During convalescence all foods should be given in greater than normal quantities by feeding the child more frequently.

5.1.3 Drugs

Antimicrobial agents are beneficial in the treatment of diarrhoeal disease only in a few specific circumstances. These include treatment of *Shigella* dysentery, severe cholera and typhoid fever. These agents should not play a primary role in diarrhoeal disease control programmes because most diarrhoeas are not due to these diseases; moreover, their use diverts the attention of health workers from the more important tasks of rehydration and dietary management. Spasmolytics are also inappropriate because they do not alter the duration or severity of the disease, may prolong the carriage of organisms in the gut, and are associated with many toxic side effects, particularly in children.

Other time-honoured remedies such as iodo-hydroxy-quinoline, kaolin and charcoal have not been shown in careful studies to offer any reduction in frequency or change in composition of diarrhoeal stools.

5.2 Nutrition of the child and mother

The composition of human milk is uniquely sufficient and ideal for the nourishment of infants. No other product can equal it for this purpose. In addition, breast feeding contributes directly to immunological adaptation to extra-uterine life. In all societies it is free of such potential hazards associated with artificial feeding as allergic disorders and metabolic derangements including tetany, hyper-osmolar dehydration and obesity. In developing countries, however, it is even more important in that it avoids the risks of over-dilution leading to malnutrition and contamination of bottles, rubber teats and milk which so often results in acute diarrhoeal diseases. In one study area milk in feeding bottles has often been found to contain a large number of faecal and non-faecal bacteria. It is not therefore surprising that early weaning in developing countries is associated with a high incidence and greater severity of diarrhoeal diseases and malnutrition in young infants.

To be maximally effective breast-feeding should begin as soon as possible after the moment of birth and, except in unusual circumstances such as illness in the mother, should continue unsupplemented as the child's sole source of fluids and nutrients for a period of between 4 and 6 months. Attempted supplementation by the bottle is often a sad delusion, since in general this causes a decline in breast milk production in the same proportion as the volume of milk given by bottle.

The lactation performance of the mother is affected not only by socio-psychological factors like confidence and satisfactory mother-child relationship, but also by her own health and nutritional status. The nutritional requirements of women increase during pregnancy and lactation and they must be met to prevent delivery of low birth weight infants and to facilitate production of breast milk in sufficient quantity to permit breast feeding to continue for an adequate period of time.

Full lactation by the mother also diminishes fertility, thereby helping to maintain better birth spacing which has significant health benefits for her and her babies. On the other hand, if pregnancy occurs the volume of breast milk greatly diminishes.

5.3 Water supply, sanitation and food hygiene

For the eventual elimination of diarrhoeal diseases as a major health problem interventions in water supply, sanitation and food hygiene, combined with improved personal hygiene, are the most effective. Despite the progress made by Member States in the provision of water supply and sanitation during the period 1970-1975[14], the actual situation expressed in real terms as a percentage of population served was as follows:

	% Population Served	
	Urban	Rural
Water supply	77%	22%
Excreta disposal	75%	15%

Until recently, water supply and sewage disposal facilities have mainly been provided to the privileged urban communities rather than to the deprived and under-served populations of rural and fringe urban areas.

The role of water supply and sanitation as an essential health measure, particularly with respect to rural and urban-fringe populations, was emphasized by the recommendations of HABITAT - the United Nations Conference on Human Settlements, 1976, and the United Nations Water Conference, 1977, which were echoed in Resolution WHA30.33 adopted by the World Health Assembly in May, 1977. Concurrently the Organization has been reinforcing its cooperation with Member States in preparing for the International Drinking Water Supply and Sanitation Decade which aims at providing safe drinking water and sanitation for all by 1990.

Given the limited resources available in developing countries, the best strategy for approaching the problem of diarrhoeal diseases associated with unsanitary conditions from a cost-effective perspective is through primary health care. To this end, and following a decision of the twenty-first session of the UNICEF/WHO Joint Committee on Health Policy on this subject, a study is presently being undertaken on water supply and sanitation as integral parts of primary health care. A key factor in this approach is the enlisting of community participation to reduce the cost of installation and ensure the proper maintenance and utilization of these facilities. In keeping with this approach, over recent years there has been a growing awareness of the need to develop appropriate technologies to facilitate the provision of water supply and sanitation in different situations. Nevertheless, there still remains scope for adaptation of existing technologies that are appropriate to various needs and conditions. There is also a need for coordinated multi-sectoral (health, agriculture, public works) approaches for water supply and sanitation in order to meet the needs of the populations in the urban-fringe and rural areas.

Recent studies, however, have demonstrated that provision of safe drinking water supplies alone is not sufficient to control the acute diarrhoeal diseases. This is because (1) the use of contaminated water for non-drinking purposes (e.g., bathing and cooking) also contributes to transmission of diarrhoeal diseases, and (2) diarrhoeal diseases such as shigellosis and rotavirus infection may be transmitted through non-waterborne routes. Thus, control efforts comprising the supply of safe water must be complemented by a combination of efforts to provide proper means of waste disposal and to educate the public on proper personal and food hygiene practices such as handwashing, avoidance of the use of polluted water for irrigation, and use of only safe water for washing fruits, vegetables and utensils.

5.4 Health education

In the control of acute diarrhoeal diseases health education should not be regarded as a separate strategy in itself but as an integral part of all strategies. As a general principle, to be effective health education activities must take into consideration the beliefs and health practices of people and their communities. Since health education is behaviour-oriented, activities should be based as far as possible on an individual approach. Collaboration with persons who are well respected in the community as opinion leaders is beneficial. The mass media, particularly the radio, are very useful as a tool for reinforcing health education activities. Health education programmes for diarrhoeal disease control must be directed towards those concerned at every level, namely:

- top decision makers, to ensure priority in the allocation of resources;
- health workers, to assure technical guidance;
- mothers, to encourage them to provide care promptly and correctly;
- community members, to obtain their active participation in the use of oral rehydration and in improving water supply, waste disposal, and personal and food hygiene.

5.5 Epidemiological surveillance

In the present context surveillance can be defined as the continuous appraisal of the occurrence of diarrhoeal diseases in a community based on information supplied by persons involved in some way in the delivery of health care. Its primary objective is to provide information on the prevalence or incidence of diarrhoea and to define population groups who are at greatest risk of infection. Other types of surveillance programmes looking at specific indicators of disease (e.g., water and sewage sampling) are also useful, particularly in surveillance of cholera.

Although laboratories are not essential for conducting surveillance, they are very beneficial in that they provide information on the most prevalent pathogens and thus facilitate specific control measures.

In the absence of regular surveillance, studies or ad hoc surveys can provide information on the prevalence of different etiological agents in a particular locality, including their antibiotic-susceptibility pattern. Besides the more traditional enteric bacterial pathogens (Salmonellae, Shigellae, Vibrios, enteropathogenic E. coli) and foodborne pathogens (enterotoxin producing Staphylococcus aureus, Vibrio parahaemolyticus, Bacillus cereus and Clostridium perfringens), a large number of additional pathogens have now been recognized as causing diarrhoea. These include:

- Enterotoxigenic E.coli which cause an illness similar to cholera and are a common cause of diarrhoea in young children and also in adults and travellers to endemic areas;

- Newly recognized bacterial pathogens - Yersinia enterocolitica and Campylobacter jejuni - which have unusual isolation requirements and have not been adequately investigated in many countries;

- Rotaviruses, which in most studies are the most commonly recognized causes of infantile diarrhoea, accounting for 50-60% of diarrhoea cases in children aged 6-24 months;

- Other small viruses, such as parvoviruses, which cause diarrhoea in adults and whose importance is not yet defined.

Laboratories involved in diarrhoeal diseases surveillance need not be elaborate, and with innovation in their design, can function with a minimum of funds and equipment. Developments in recent years which have greatly facilitated laboratory diagnosis include:

- The use of transport media which can sustain bacterial life for long periods for transporting rectal swabs to the laboratory. On an even simpler scale, blotting paper moistened with stool has been shown to be an excellent transport material on which vibrios can survive for weeks;

- For the isolation of vibrios, the development of TCBS medium which does not require autoclaving;

- Most recently, the employment of simplified ELISA[a] assays which, for example, can detect rotavirus antigen in stool within four hours of collection.

A simple surveillance system functioning properly should be able to provide an early warning system for the detection of epidemics, especially of cholera, by reporting changes in the pattern of age and seasonal incidence and severity of cases. When these are observed, prompt laboratory and epidemiological investigations can be set up to take samples for determining the etiology and mode of spread. While these investigations are being conducted, treatment and sanitation facilities can be reinforced with the necessary staff and supplies.

Another benefit of surveillance is that it provides an opportunity to undertake operational and basic research.

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[a] Enzyme-linked immunoadsorbent assay

5.6 Epidemic control

Of the epidemic diarrhoeal diseases, cholera deserves special attention as it can kill very rapidly and spread very fast in receptive areas. The speed and volume of travel and trade is such today that no country is able to prevent the introduction of cholera, but its spread within a country can be controlled by good surveillance and a high standard of sanitation.

WHO has developed an effective mechanism for responding to requests for epidemic assistance from Member States. The need to maintain and strengthen the capability of the Organization to respond promptly to such requests has been underlined by World Health Assembly resolution WHA24.26 (May, 1971) and Executive Board resolution EB47.R31 (January, 1971). Several documents and guidelines have been prepared describing strategies for epidemic control in different situations[7-10,12,13]. (See also Sections 5.7 and 5.8 concerning immunization and mass chemotherapy.)

Countries that have already adopted a medium-term programme for diarrhoeal disease control will be in a better position to detect and control epidemics of enteric infections. Countries confronted with epidemics may find it opportune to develop such a programme using the experience gained and resources mobilized during the epidemic period.

5.7 Role of immunization

In general, the development of enteric bacterial vaccines has been unable to take into account the optimum mechanism for enhancing local immune response in the host because the nature of gut-associated immunity against enteric infections is still very poorly understood. The following is a review of vaccines that may be used in control of some of the diarrhoeal diseases.

Cholera

A number of controlled field trials of bivalent whole-cell cholera vaccines in endemic areas during the last two decades have demonstrated up to 50%-60% protection for 3-6 months in adults receiving one dose.

Efforts to improve the cholera vaccines have continued and in recent years two aluminium adjuvant bivalent whole-cell vaccines have been found to protect children in endemic areas in India and Indonesia to a much greater extent than the generally available vaccines; they also provided about 50% protection for approximately 14 months in adults. However, since the number of cases was small in both areas, these observations need to be confirmed.

During the last decade there has also been considerable interest in a toxoid vaccine prepared from cholera enterotoxin. In a single large field trial one such preparation was found to convey little protection, but another field trial is planned to assess the efficacy of a purified toxoid and a combined toxoid-bacterial vaccine. Because of shared antigenicity between cholera enterotoxin and the heat-labile toxin of enterotoxigenic E. coli there is a prospect that a cholera toxoid may protect against both diseases. Since enterotoxigenic E. coli are the leading cause of travellers' diarrhoea there is an additional impetus for the development of this vaccine.

Naturally occurring and laboratory mutants of Vibrio cholerae have been tested as oral vaccines and have been found ineffective or unstable. A streptomycin-dependent mutant has been tested with some encouraging results in primates, but the need for multiple oral doses and its potential for reversion preclude its usefulness. Multiple oral doses of toxoid afforded no protection to animals or volunteers. Prolonged protection was achieved in animals by combined subcutaneous and oral administration of cholera toxoid but this has not been tested in volunteers.

Typhoid

Since 1954, controlled field studies have been conducted in areas where typhoid fever was endemic to test the effectiveness of acetone-killed and dried, formalin-killed, heat-killed phenol-preserved, and alcohol-inactivated vaccines. While the acetone-killed and dried vaccine is generally considered to be superior, properly prepared heat-killed phenol-preserved vaccine was only slightly less effective; alcohol-inactivated vaccine (preserving Vi antigen) was less effective than either.

A field trial with a vaccine prepared from a non-motile strain of S. typhi showed lack of effectiveness. A recently developed "unaltered" Vi antigen has attracted interest and may be field tested. Interest in a live streptomycin-dependent typhoid oral vaccine has waned because of the danger of reversion, but an epimerase-less strain has shown some promise in volunteer studies and is presently being field-tested. Killed oral preparations are marketed in several countries, but no protective effect has been observed in three field studies.

Practical application of cholera and typhoid vaccines

Mass immunization programmes for the control of cholera with existing vaccines cannot be justified because (1) although high levels of protection have been observed in some field trials of cholera vaccines, their effectiveness has not been demonstrated in epidemic control; claims that have been made about their usefulness cannot stand scientific scrutiny; (2) even when potency can be ensured, they provide only about 60% protection to adults in endemic areas for about 2-3 months; (3) they do not materially interrupt transmission; (4) they do not affect the carrier state; (5) they do not prevent the introduction of cholera into a country; (6) they give a false sense of security to those who receive them; (7) they give a false sense of accomplishment to those who administer them; (8) there are more effective control measures such as treatment and simple sanitation supported by health education which are also less expensive; and (9) very often mass vaccination is performed using the same needle for several persons which allows transmission of viral hepatitis - a much more serious disease. However, selective vaccination of high-risk population groups using appropriate techniques and potent vaccine may be advisable in circumstances where there is little or no possibility of providing treatment facilities or instituting simple sanitation measures supported by health education.

Carefully selected typhoid vaccine of known potency would probably be useful in known endemic areas if a high-risk group has been determined by surveillance and in selected outbreaks where there is evidence to suggest a continuing common source.

Shigella

Streptomycin-dependent strains of Shigella flexneri and S. sonnei have been developed, extensively studied and field-tested. High levels of type-specific efficacy have been demonstrated in children and members of the armed forces but protection lasted for less than one year. Laboratory reversion of these strains and in one instance reversion in man of a vaccine strain have been reported. These facts and the need for multiple doses seriously limit the possibilities of public health application of these vaccines.

Live oral vaccines prepared from recombinant Shigella and E. coli have been tested but have not been shown to protect.

Rotavirus vaccine

Increasing titres of antibodies against rotavirus with increasing age associated with decreased susceptibility to the disease suggest the possible usefulness of a rotavirus vaccine. Although rotavirus strains appear to be morphologically similar, there may be subtle antigenic differences and this question is being studied as a step towards the development of a vaccine.

5.8 Role of chemoprophylaxis

The term chemoprophylaxis usually implies administration of antimicrobial drugs to a person to prevent disease in that particular individual, but such drugs are now being increasingly used for mass treatment for the prevention and control of epidemics when it may be more appropriate to use the term mass chemotherapy.

Travellers' diarrhoea

This syndrome, which may affect as many as 60% of travellers to the developing countries within a few weeks of arrival is considerably hindering the development of the tourist industry. One tablet of 100 mg of doxycycline daily has recently been found to significantly reduce the incidence of travellers' diarrhoea due to enterotoxigenic E. coli in a field trial among Peace Corps Volunteers in Kenya. It must, however, be recognized that travellers' diarrhoea can be caused by a variety of organisms, some of which are resistant to tetracyclines. Thus, while doxycycline may offer some degree of individual protection to travellers in certain circumstances, hygienic measures remain the best method of prevention.

Cholera

Tetracycline has been shown in clinical field trials in Dacca, Calcutta, and the Philippines to reduce the transmission of V. cholerae among close contacts of cases, although in one endemic area the effect was repeatedly shown to last only a day or two longer than the period of treatment. Tetracycline was administered in most of these trials in multiple doses for 3 to 5 days; one large daily dose given for 5 days was less effective. Recently, however, doxycycline in only one 300-mg dose was found to be almost as effective as multiple doses of tetracycline given over 3 days.

A long-acting sulfa drug - sulfadoxine (Fanasil) - was also found in a field trial in a newly affected area in Africa to shorten the period of vibrio excretion by close contacts but the appearance of new carriers among them - i.e., transmission - was not looked for. In another trial in Calcutta, sulfadoxine was found as effective as tetracycline in reducing transmission but was slower in action, being less effective during the more important first 48 hours.

These findings have led countries to use antimicrobials like tetracycline, chloramphenicol, sulfadoxine, and streptomycin in the control of cholera epidemics but their effectiveness has never been properly evaluated. All these drugs have potentially serious side effects, particularly when administered in an unsupervised manner. Tetracycline may cause liver damage and is contraindicated in pregnant women, young children and persons with renal disease; sulfadoxine may cause blood dyscrasias and hypersensitivity reactions including Stevens-Johnson syndrome; chloramphenicol can cause aplastic anaemia; and all of these drugs can promote the development of multiple drug resistance and alter intestinal flora.

A WHO working group[15] discussing this problem concluded that the evidence for the effectiveness and safety of drugs used for preventive medication against cholera is not such that they could recommend any of them for mass application. It has also been pointed out that, as in a community usually not more than 5% of persons will be infected with V. cholerae at any one time and of them less than 5% may go on to develop cholera, it may be necessary to treat about 400 persons to prevent one case. Thus, the risk-benefit ratio does not justify mass treatment. Multiple symptomatic cases of cholera in a family are very rare. With the system of surveillance available in most areas, by the time an epidemic is recognized the infection is generally too widespread to be controlled by mass chemotherapy or even by treatment of close contacts.

This kind of therapy with the appropriate drug may, however, be effective in controlling outbreaks in small, rather isolated and stable communities, e.g., refugee camps, on board ships, etc. Doxycycline or other tetracyclines given in appropriate dosage may be suitable for that purpose. Clinical experience with other antimicrobials is limited and does not allow a critical assessment though chloramphenicol and trimethoprim-sulfamethoxazole may be considered as alternative drugs.

Other diarrhoeas

Mass chemotherapy may also be effective in controlling outbreaks of shigellosis and other severe bacterial intestinal infections in small, stable communities as described above if the pathogen and sensitivity pattern can be determined and the effective antimicrobial drug obtained quickly.

It is difficult to find a technical justification for the use of chemoprophylaxis or mass chemotherapy in the control of diarrhoeal diseases in circumstances other than those special situations mentioned above.

6. RECOMMENDATIONS

The Group's recommendations are presented in 5 areas: appropriate strategies; implementation; evaluation; training, education and dissemination of information; and research.

6.1 Appropriate strategies

After reviewing the various possible strategies and considering their applicability under the circumstances prevailing in the areas where the programme is needed most, the Group recommends five appropriate strategies for inclusion in the WHO Diarrhoeal Diseases Control Programme: management of acute diarrhoeas; nutrition of the child and mother; water supply, sanitation and food hygiene; epidemiological surveillance; and health education. For reasons discussed in Sections 5.7 and 5.8, the Group does not feel that the strategies of vaccination and chemoprophylaxis should be included in the Programme, except in special epidemiological circumstances, and therefore they are not discussed in this section. The role of WHO in technical cooperation with Member States in the control of epidemics due to cholera and other enteric infections is closely linked with this Programme as described in Section 5.6.

While the Group recognizes the value of an interdisciplinary approach for ultimate control of diarrhoeal diseases and believes that the Programme will need to be flexible so that priorities accorded to different strategies can be adjusted as required in different situations, it wishes to emphasize its strong feeling that the strategy that can be applied now with available means and which will have the greatest immediate impact on a global basis is wide implementation of oral rehydration therapy. The Group also believes that the Diarrhoeal Diseases Control Programme should be complemented by other related WHO programmes in environmental health, maternal and child care, nutrition, food hygiene, health education, bacterial and viral diseases, primary health care, and appropriate technology.

6.1.1 Management of acute diarrhoeas with particular reference to oral rehydration

Because oral rehydration therapy based on administration of oral rehydration fluid along with proper dietary instructions

- provides a balanced fluid and electrolyte replacement at low cost;

- is easily administrable not only in hospitals and treatment centres but also by community-based workers and family members; and

- improves appetite and allows better feeding and thus prevents malnutrition

the Group recommends that programmes be instituted immediately to apply this therapy with the principle objective of reducing mortality and other ill effects from diarrhoea, especially in children. The Group believes that the provision of such services to persons with diarrhoea will also contribute to the promotion and success of other control strategies. While making this recommendation the Group emphasizes that there is a great need for more operational research to determine alternative ways that are suited to the situations prevailing in given

regions and countries for delivering oral fluid therapy along with dietetic education.

The Group believes that oral rehydration programmes will be incomplete without the inclusion of appropriate dietary management of children during and after diarrhoea. The practice of withholding food from children with diarrhoea must be strongly discouraged. Children who are receiving cow or goat milk should be given it in diluted form. Some restrictions, particularly of solid and semi-solid foods, may be needed in cases with severe vomiting but adequate feeding with usual foods must be resumed as soon as possible. Under no circumstances should breast feeding be discontinued; in fact, positive efforts should be made to maintain it. Immediately after the acute stage, efforts should be made to compensate for nutrient losses which are inevitable during diarrhoea by advising mothers to feed the children more than the usual amounts of food during the convalescent period; this may require a change in the intra-family distribution of foods and in the frequency of feeding the child and the mother needs to be convinced of its importance.

It is recognized that primary care or basic health service workers, especially those involved in the delivery of maternal and child health care, will be primarily responsible for providing this basic therapeutic health care service. Most of the cost of provision of oral rehydration at the community level can be met by the savings in reduction of hospitalization and need for expensive intravenous fluids and drugs.

Antimicrobials so often used in the treatment of diarrhoeas should be discouraged except for the management of dysentery, severe cholera or typhoid fever. Antimicrobials should not be used as prophylaxis for diarrhoea except in persons from non-endemic areas travelling in highly endemic areas, when doxycycline or other tetracyclines may be beneficial in certain circumstances. The use of spasmolytics should be discouraged but non-specific diarrhoeal drugs (e.g., kaolin), while not recommended for therapy, may be considered as harmless practice and have been used by some workers as entry points for the introduction of oral fluid therapy.

6.1.2 Nutrition of the child and mother

Because of the protective value of breast feeding and the risk associated with too early introduction of other foods, the Group recommends that efforts be made to ensure that infants are fed exclusively from the breast for their first 4 to 6 months of life. This is particularly important in developing countries and for families living in an insanitary environment without sufficient resources and facilities to ensure safe artificial feeding, although there is now evidence that under any circumstances (including those in the industrialized countries) breast feeding has many advantages over artificial feeding.

Health workers should promote breast feeding by

- educating mothers about the importance of lactation and improving their nutrition;

- facilitating during postnatal care such practices as early mother-child contact and rooming-in, and discouraging bottle-feeding of babies during the first days of life;

- refuting propaganda that advocates artificial feeding.

Breast feeding should be continued even when a child become sick; if he has to be hospitalized he should be admitted together with his mother. To facilitate breast feeding governments should be encouraged to enact legislation and promote social measures to restrict the importation and control the advertising of infant formulas and sale of bottles for artificial feeding, to promote the creation of creches and to grant adequate maternity leave.

The health of the mother is very important for ensuring the provision of adequate amounts of breast milk with sufficient nutrients. Thus, health workers must identify pregnant and lactating mothers who are nutritionally deficient and ensure their rehabilitation by providing food supplements, if necessary.

Special efforts should be made to inform obstetricians, paediatricians, general practitioners, public health personnel, nurses, midwives and all cadres of paramedical personnel of the importance of breast feeding. Particular attention must be directed to medical and other related curricula; these should include lectures on the scientific attributes of breast milk with special emphasis on the possibility of disease transmission by artificial feeding. Every effort must be made to promote breast feeding in the community. Through every medium available - the press, radio, television, word of mouth, etc. - the public must be made aware of the advantages of breast feeding and attention must be given to the enlightenment of men as well as women. The nutritional value of human milk and the advantages of breast feeding should be taught in primary and secondary schools as part of health and nutrition education and of preparation for family life and responsible parenthood. To achieve this there is an urgent need to educate teachers and to provide them with material for inclusion in their syllabus.

Starting from the 4th - 6th month of life infants need other foods in addition to breast milk to satisfy their nutritional requirements. In families living in an insanitary environment and with an inadequate concept of personal hygiene this is a period of great danger (weanling diarrhoea). To help control diarrhoeal diseases in this period the Group believes that health and nutrition education programmes emphasizing proper methods of preparing solid and semi-solid foods from those normally eaten by adults should be carried out. The use of bottles should always be discouraged.

6.1.3 Water supply, sanitation and food hygiene

The Group recognizes the need for an all-out effort in improvement of water supply, sanitation and food hygiene for reducing morbidity from diarrhoeal diseases. The best prospects for success lie in mobilizing entire communities to prevent diarrhoeal diseases through measures that are culturally acceptable and feasible. There must, however, be support for the development and transfer of appropriate water supply and sanitation technologies that can be applied at the primary health care level, especially in the underserved rural and fringe urban areas. These technologies should be simple in their design and, especially, in their maintenance. Further innovations in materials, equipment and practice are needed. Improvements in only one of these areas (e.g., water supply) are not sufficient; an attempt must be made to effect these innovations in the 3 areas of water supply, sanitation and food hygiene.

WHO manuals [12,13] can be of general guidance in the planning and implementation of these programmes though it is emphasized that intervention measures will vary greatly between countries and areas with different geography, climate, and sociocultural characteristics.

To be effective in the control of diarrhoeal diseases, water and sanitation programmes must consider the behavioural and sociocultural characteristics of the community and its ability to participate and use alternative technologies so that those concerned become agents for improving their own quality of life.

The approach to the provision of water supply and sanitation should be simple, innovative and acceptable to the community at a cost that they can afford now. There should be encouragement for the utilization of well-known simple techniques for the supply of safe, adequate and accessible water and the control of excreta disposal such as the protection of existing water sources from pollution, the utilization of slow sand filtration, sanitary latrines, low cost sewage collection and treatment methods, etc. These approaches should be reinforced and simplified to reduce cost through the transfer of technologies developed by operational research, particularly at the national level.

Prior to and during the application of these technologies, intensive efforts in health education are needed in order to enhance their impact. This should be carried out by workers at all levels of the health and other social services. For example, programmes on environmental sanitation and personal and food hygiene should be part of school syllabuses; the message in these programmes should inform children of the dangers of insanitary conditions and habits and of the simple measures that must be taken by each individual, which can in turn influence both family and community attitudes and practices. The implication of this is that sanitary habits can be instilled at a very early age and that each individual has a responsibility for his or her own health and the health of the community. Water supply and sanitation facilities should be provided in schools as an important health measure, and at the same time serve as part of the educational programme.

The Group recognizes also the important role that women play in educational programmes both as educators for hygiene and sanitation within the community and the family and as the primary procurers and users of water and preparers of food.

The Group emphasizes that there should be no conflict between activities to promote oral rehydration and activities to improve water supply, sanitation and food hygiene. The former have as their main objective the reduction of mortality and improvement of nutrition and they can be implemented immediately at a relatively small cost. The latter, however, represent the ultimate means of reducing morbidity and controlling diarrhoeal diseases and will require more time, efforts and resources for their realization.

6.1.4 Health education

Factors responsible for diarrhoeal diseases are basically behaviour-related. Therefore, the Group strongly believes individuals and communities should be educated to be more active in practicing healthy behaviour. Moreover, since communities differ in their dynamics of decision-making, efforts must be made to plan educational activities to conform with these patterns and practices as opposed to following stereotyped patterns which may not necessarily meet the needs of the particular situation. Community participation resulting from effective health education can ensure proper utilization of the various services as well as active involvement of the people in preventive and promotive measures.

Health education should be considered as an essential function of every health worker at every stage of health activity, and health education specialists should assist these workers by providing them with guidelines and in-service training. Particular attention should be given to the importance of educating government decision makers on the need for multisectorial commitment to the control of diarrhoeal diseases. Emphasis should be given not only to the health benefits, but also to the value of such a programme in ensuring the success of education, family planning, urban development and other national investments. A broad appreciation of the problem and its importance for the health and economy of the society will ensure that sufficient manpower and fiscal resources are allocated to attain the programme objectives.

6.1.5 Epidemiological surveillance

The Group believes that epidemiological surveillance should play an important role in the Diarrhoeal Diseases Control Programme by providing information on the incidence and etiology of diarrhoea in different population groups and by forming the basis of an early warning system for the detection of epidemics. Surveillance programmes, whenever possible, should be integrated into other national communicable disease surveillance programmes. They should use simple definitions and forms for collecting data on vital events and diarrhoea cases, or at least deaths due to diarrhoeas, and should have a strong feedback component to provide an interpretation of the data for those collecting it. Although it is not absolutely essential, diagnostic laboratories should be involved in surveillance where possible, and analyse specimens on a sampling basis, especially when an epidemic is suspected.

In its simplest form, a surveillance system based on reporting of changes in the pattern of age and seasonal incidence or in the severity of diarrhoeas in a locality as observed by the persons delivering health care (e.g., oral rehydration) can provide an early warning system for prompt detection of an epidemic or recrudescence which would then be confirmed by laboratory and epidemiological investigation. Ancillary personnel who are also involved in some way in health care delivery, like traditional medical practitioners, pharmacists, village leaders, teachers or religious leaders, can also provide useful information about excess deaths due to diarrhoea and draw attention to an epidemic.

6.2 Programme implementation

The Group recognizes that the Diarrhoeal Diseases Control Programme constitutes a part of the overall WHO programme of technical cooperation with Member States. The basic interpretation of "technical cooperation" endorsed by the WHO Executive Board[16] is that:

"Technical cooperation means activities which have a high degree of social relevance for Member States in the sense that they are directed towards defined national health goals and that they will contribute directly and significantly to the improvement of the health status of their populations through methods that they can apply now and at a cost they can afford now, and which conform to the principle and aim of developing national self-reliance in matters of health".

There can be no doubt that the WHO Diarrhoeal Diseases Control Programme satisfies all these criteria and will bring benefit to a very substantial number of people, particularly children, in the developing countries.

The mechanism envisaged for implementation of the Programme is for WHO to work with national authorities as partners in all stages of their programme development. It is anticipated that the basic approach to be adopted by national authorities for implementing the programme will be through their existing infrastructures, particularly primary health care and programmes of maternal and child health care, environmental health, or the basic health services as they are available at the community level, with a focus on the rural and peri-urban areas. A national programme in general usually evolves from pre-existing activities aimed at coping with identified specific problems. The Group believes that the identification of national personnel with the necessary competence, motivation and influence to ensure the implementation of the programme is probably the single most important factor for its success. Unless active national commitment and participation is secured, including that of the communities involved, no long-term impact can be expected.

In applying oral fluid therapy, which is a strategy given high priority, efforts should be made to use and strengthen existing systems. It is most important that the development of systems for oral fluid delivery should be used as an occasion for strengthening community capacity to handle other health problems as the development of diarrhoeal disease control activities should be linked with other health care activities within the community.

National and/or local conditions must be the principal determinant of the nature, scope and elements of the programme. Whatever changes may be found necessary or desirable, they should be the outcome of constructive exchanges of experience gained within or outside the country; in other words, the programme must be adapted to local conditions and gradually integrated into the existing health and social services activities both at the local and national level.

Countries may find it desirable to implement a diarrhoeal diseases control programme on a limited basis in a state, region or a subdivision before embarking on a countrywide programme. With this experience planning for a national programme will be facilitated as regards estimating costs and having an experienced cadre of health workers available.

In its role of promoter of and partner in technical cooperation concerning this Programme, WHO in collaboration with UNICEF can provide critical inputs, depending on circumstances and local needs. Examples of such inputs are:

- technical cooperation in assessment of the nature and extent of the diarrhoeal disease problem and in the formulation, implementation and evaluation of national programmes;

- collection, evaluation and distribution of relevant scientific information (see Section 6.4);

- organization and management of training activities such as seminars, meetings, training courses, including the preparation and provision of educational and teaching aids (see Section 6.4);

- procurement and/or development of local facilities for production of essential supplies (e.g., ingredients for oral rehydration) and equipment through the establishment of national or regional centres as required;

- production, standardization and distribution of essential laboratory reagents;

- support to countries which have identified water supply and sanitation as priority areas for underserved rural and fringe urban areas;

- provision of technical services by staff members or consultants.

The Group, having considered the global magnitude and severity of diarrhoeal diseases and their health and socioeconomic implications, and realizing the urgent need to improve the present unsatisfactory situation on a technical cooperation basis, recommends to the Director-General that:

(a) a suitable mechanism for consultation with representatives from interested organizations within the United Nations system and other national, international and non-governmental organizations be established by WHO Headquarters to ensure coordination and support to this Programme, and

(b) technical advisory groups be set up both at Headquarters and Regional Offices to review periodically the strategies and the overall Programme progress.

Although consideration must be given to the fact that there is a need for improving the currently available methods for the treatment, prevention and control of diarrhoeal diseases, it is clear that many lives can be saved and the quality of life improved by wide application of oral fluid therapy, the effectiveness of which has been proved. It would not be justified to postpone action while waiting for better methods to become available; by pursuing a pragmatic approach, the Programme will be able to incorporate new knowledge as it is generated by basic research and by operational activities in the field.

6.3 Programme evaluation

Evaluation of national diarrhoeal disease control programmes will have to be encouraged and supported by WHO to ensure the progress and effectiveness of the activities that have been selected and undertaken. Two aspects need to be considered: (1) operational evaluation and (2) impact evaluation.

Operational evaluation can be used to assess and measure the progress of programme inputs against pre-established targets; for example, there may be a need to evaluate the programme of procurement or manufacture of oral rehydration supplies and of their distribution, delivery and use. Similar targets will be needed for the development of water and sanitary facilities if not already established. A time schedule for each programme operation will serve as a guide to progress. At periodic intervals (i.e., weekly, monthly), the national programme coordinator can review each of these parameters and determine and rectify the causes of shortcomings. Evaluation can be based on such operational indicators as the following:

- number of packages of ingredients for oral rehydration manufactured, distributed or consumed;

- personnel trained in their administration;

- sanitary facilities provided or improved;

- production of supplies and equipment (e.g., for sanitation).

Impact evaluation is important to assess the benefits of the programme in reducing the ill effects of the diarrhoeal diseases problem. The ultimate objective is to reduce mortality and morbidity. This may be difficult to measure because of unavailability and unreliability of vital statistics, the need for a large population base to reliably measure impact on mortality and the tendency for aberrant increases in incidence to appear as surveillance is improved. Impact indicators may include:

- number of deaths from diarrhoea, with age-specific data, if possible;

- number of diarrhoea cases in hospitals, health centres or outpatient departments;

- awareness of mothers;

- sales of supplies for bottle feeding;

- acceptance of treatment by the population;

- nutritional status surveys;

- nursery school attendance; and

other parameters which remain to be defined.

It may be possible to select several representative areas of a country or region to measure impact by serial collection of data before and after intervention, but it should be stressed that other variables which cannot be easily controlled or recognized often operate and influence findings. It may not be essential to demonstrate impact as certain information derived from other countries can also be accepted and applied.

These evaluation techniques complemented by surveillance information can facilitate early recognition of problems, permitting rapid corrective actions. They may also indicate a need to modify goals and objectives, to obtain additional resources, or to request technical guidance from within the country or from WHO.

6.4 Training and education; dissemination of information

The Group believes that, for the success of this Programme, WHO should give high priority to technical cooperation in the training and education of national health workers. The following specific training needs are recognized:

- intercountry/interregional seminars for the motivation of policy-making senior public health administrators and paediatricians;

- national/intercountry training courses for professional and auxiliary health personnel and community workers on technical aspects of oral rehydration therapy including dietetic management, surveillance, and water supply, sanitation and personal and food hygiene;

- development of educational and training material, communicational technology and manuals for education and training of the public and health personnel on these control strategies; preparation of a handbook of simple measures for community hygiene and sanitation which emphasizes their relationship to diarrhoeal disease control, for use at the community level and in schools;

- organization of training courses to teach laboratory workers well established and newly devised laboratory techniques (e.g., ELISA assays) in enteric bacteriology and virology;

- supporting countries in the training of personnel in the operation, maintenance and surveillance of sanitation facilities. Water supply and sanitation facilities require that personnel (particularly at the local level) be trained in the operation and maintenance of these facilities as frequent breakdowns reduce considerably the health benefits derived from these installations.

The Group also feels that WHO should retrieve all available information and experience and disseminate widely material on:

- the effectiveness of different strategies for delivery of oral fluid;

- the unique advantages of breast feeding and means of promoting it.

Regarding breast feeding, the Group urges WHO to continue to cooperate with countries in their activities to discourage the inappropriate use of milk formulas and unethical advertising practices. In order to encourage countries that have declining trends in breast feeding WHO should disseminate information on countries where such trends have been reversed; the results of the WHO cooperative study on breast feeding in seven developing and two developed countries should be used for this purpose.

6.5 Research needs

The Group recognizes the great importance of continuing research and presents below, under the different strategies, what it considers to be the priority needs that should receive further WHO support.

6.5.1 Management of acute diarrhoeas including feeding practices

- Development of technology for cheaper packaging of oral rehydration salts using the presently recommended formula;

- Research to develop appropriate methodology for implementation of oral rehydration therapy using either packages, the "scoop and pinch" method, or spoon measures by peripheral health workers, community leaders or family members;

- Research to explore the linkage of oral therapy with other health activities (e.g., fertility regulation, nutrition, expanded programme on immunization, etc.);

- Research to determine the most suitable diet for use during and after diarrhoeal episodes, taking into consideration the availability of foods and local practices;

- Search for effective anti-diarrhoeal drugs, particularly antisecretory agents to block the action of enterotoxins at different levels, to be used as an adjunct to rehydration;

- Research to improve or modify for simplification the composition of oral fluid (e.g., need for bicarbonate and potassium, possibility of using sucrose instead of glucose);

- Studies of traditional remedies used in treatment of diarrhoea.

6.5.2 Water supply and sanitation

- Search for and review of existing information on operational studies that further quantify the beneficial effect against diarrhoeal diseases of individual and collective control measures concerning water, food, liquid and solid wastes - i.e., to identify the relative importance of each of these sanitary/hygienic interventions;

- Promotion of the acceptance and utilization of appropriate technologies through strengthening the capabilities of the existing network of collaborating centres for water supply and wastes in the adaptation and testing of appropriate water supply and sanitation technologies for the prevention and control of diarrhoeal diseases - e.g., use of faecal wastes for composting, biogas, etc., slow sand filtration for the treatment of water supplies, etc.

- Research to ascertain the effect of travellers' diarrhoea on the tourist industry with a view to encouraging the intensification of measures for the provision of water and sanitation and improving food safety in touristic areas.

6.5.3 Epidemiology

- Studies to define the etiology and epidemiology of diarrhoeas in different age-groups and populations of varying socioeconomic status and environment (e.g., rural vs urban and dry vs wet areas). Particular emphasis should be placed on rotavirus and enterotoxigenic E. coli which are known important causes of diarrhoea in children. These studies should also look into the relationship between specific agents and malabsorption;

- Studies to define the importance of small viruses as a cause of diarrhoea;

- Development of simplified and rapid techniques for laboratory diagnosis of diarrhoeal diseases;

- Field studies to demonstrate the effectiveness of surveillance based on reporting by community-based health workers;

- Studies on economic aspects of diarrhoeal diseases and their control.

6.5.4 Health education

- Research to determine cultural and societal traits influencing behaviour as it relates to diarrhoeal diseases and to explore methods for effective intervention.

6.5.5 Vaccine development

- Studies on the nature of gut-associated immunity and on optimal ways of enhancing the intestinal immune response;

- Studies of the immunological relationships of enterotoxins produced by different enteric pathogens;

- Development and field testing of oral (live or killed) and improved parenteral vaccines, especially against cholera and typhoid fever;

- Studies on methods of cultivation and antigenic characteristics of rotaviruses and development of rotavirus vaccine;

- Studies on the role of antitoxic immunity in E. coli diarrhoea and on the development of a toxoid for its prevention;

- Studies on the mechanisms of colonization of small intestinal pathogens.

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