

Technical

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Washington, D.C. October 1974

Agenda Item 19

CSP19/DT/10 EN

7 October 1974 ORIGINAL: ENGLISH

STUDIES AND STRATEGIES TO REDUCE MORBIDITY AND MORTALITY FROM ENTERIC INFECTIONS

REPORT OF THE TECHNICAL DISCUSSIONS

The Technical Discussions held during the XIX Pan American Sanitary Conference (Washington, D.C.) took place on 4 October 1974, on the following theme: "Studies and Strategies to Reduce Morbidity and Mortality from Enteric Infections."

Dr. Oswaldo Lopes da Costa acted as Moderator, Dr. Pedro Guedez Lima as Rapporteur and Dr. Ruperto Huerta (PASB) as Technical Secretary.

The subject was introduced at the beginning of the discussions by the authors of the six working papers presented, which were: "The Present State of Enteric Infections" by Dr. Nelson Moraes; "Clinical Diagnosis and Treatment, Including Oral and Intravenous Rehydration" by Dr. Pablo Mendoza; "The Laboratory in Enteric Disease Control Programs" by Dr. Oscar Grados; "Nursing Care and Assistance Required in Health Services and in the Community in the Control of Enteric Infections" by Maria Valderez Borges, Nursing Consultant (PAHO/WHO); "The Significance of Feeding and Nutrition in the Pathogeny and Prevention of Diarrheic Processes" by Dr. Moisés Béhar; and "Importance of Environmental Sanitation in the Urban and Rural Environment in the Control of Enteric Infections" by Dr. A. Wolman. In the absence of Dr. A. Wolman, his paper was presented by Eng. Harry Hanson, Sanitary Engineer (PASB).

After a summary of the papers by their respective authors, two experts, Dr. Eugene Gangarosa (Communicable Disease Center, Public Health Service, United States of America) and Dr. Herbert Dupont (University of Texas, United States of America) commented on the papers presented and discussed the main subject with other members of the panel.

Questions and comments followed and led to a wide-ranging discussion in which the two specialists and those present at the meeting took part.

There was general agreement with the ideas and proposals put forward in the working papers. Effective means of reducing morbidity and mortality resulting from acute enteric infections, particularly those affecting young children, are already in existence, but are not currently being applied as intensively or extensively as they should be.

It was pointed out that research constitutes an integral part of any full-scale control program and that there was an urgent need for better information on important aspects of the problem, such as etiology, nutrition, local problems and epidemiological field studies, in which simple methods could be used which would be effective in directing control measures along the right lines and intensifying them.

Lastly there was discussion of the strategy to be followed if the goal of reducing the present death rate from enteric infections by 50 per cent as put forward by the Ministers of Health of the Americas was to be achieved.

Bearing in mind these main points which apply to nearly all areas, and with a view to summarizing the discussions more effectively the topics dealt with will be grouped in the following categories:

I. Nature and magnitude of the problem

Enteric infections represent an important public health problem in most of the Latin American and the Caribbean countries, particularly among the lower age groups and in communities with difficult socioeconomic conditions, on account of the high morbidity rate (about 25 per cent of the cases seen in outpatient centers) and the high case fatality rate, particularly during the first year of life and when malnutrition is also present.

At the end of the last decade enteric infections were one of the three greatest causes of death in children under one year of age in 22 countries of the Region of the Americas. Furthermore in 11 countries with a population equivalent to 69 per cent of the total of 20 countries, these diseases were responsible for over 15 per cent of the total deaths occurring before the fifth month of life.

The Inter-American Investigation of Mortality in Childhood carried out under the auspices of PAHO in ten countries of the Americas has confirmed the above data by revealing that enteric infections constitute the main cause of death among the group of infectious and parasitic diseases, the corresponding death rates ranging in the various areas where projects were carried out from 203 to 980 per 100,000 and being much higher in the first year of life.

This group of diseases constitutes a heavy social and economic burden with its toll of human lives, the cost of medical and hospital care, and absences from work.

Although there has been no cholera in the Hemisphere since the nineties of the last century, the present pandemic represents a serious standing threat to the countries of the Region in view of the rapidity and ease of modern communications with infected areas.

The magnitude of the problem of enteric diseases was made perfectly clear in the Ten-Year Health Plan for the Americas for the period 1971-1980 which included among its recommendations the reduction by at least 50 per cent of the present death rates from those diseases, particularly in infancy and childhood.

Considered from the clinical point of view, acute diarrheal diseases constitute an ubiquitous syndrome with varying degree of severity (ranging from a clinically imperceptible and inapparent infection to serious manifestations with a high death rate) and in which there are characteristic differences peculiar to certain zones and types of environmental conditions. It is impossible to distinguish clinical entities in any particular situation, although etiologically distinct diseases do exist.

To term acute diarrheal diseases a clinical syndrome does not mean that there are not clearly distinct nosological entities within the group. Epidemiological evidence indicates that this syndrome is of a bacterial nature and connected with a great variety of disease agents, although it is only in a relatively small percentage of patients that specific enteropathogenic agents can be isolated. It is only a relatively small proportion of the acute diarrheas that occur throughout the world that can be distinguished as pathological entities.

Specific and identified infectious diseases such as shigellosis, salmonellosis and <u>E. coli</u> diarrhea normally represent only a small part of the total. In underdeveloped regions in which high morbidity rates are found, the three bacterial agents mentioned, with their multiple serotypes, are generally found in fewer than 20 per cent of cases. In general the frequency is slightly above this level, but only in a few cases does it reach 40 per cent and it is exceptional to find 60 per cent of diarrheas associated with any of the specific bacterial pathological agents.

Little is known about the relative importance of other microorganisms or conditions, such as viruses, protozoa (Entamoeba, Giardia and Balantidium), helminths and malnutrition among others.

Although not much is yet known of any of the physiopathological mechanisms, it is obvious that malnutrition favors the onset and development of diarrheal processes and that they in their turn precipate and aggravate malnutrition. This inter-relationship, which may be termed synergistic, and the very size of the problem explain why in the Inter-American Investigation of Mortality in Childhood mentioned above diarrheal illness was the most important principal cause of death in every sample investigated. It was found, moreover, that in 60.8 per cent of the deaths from diarrhea, malnutrition was an associated cause. In brief, the etiology of most diarrheal diseases is not yet known.

The isolation of a pathological agent from a patient's faeces naturally does not establish a causal relationship. Moreover, in no fewer than 12 per cent of the cases of diarrhea in a survey carried out in Guatemala by the INCAP group in which the presence of an identified pathogenic agent was demonstrated, two or more bacterial agents were found and this raises the question of which of them, if any, was responsible for the disease.

Recently great progress has been made in elucidating the causes of diarrhea. Microorganisms which had hitherto been designated as "normal intestinal flora" have been shown to be capable of producing potent toxins which are active in the small intestine, while others invade the intestinal mucosa and produce severe inflammatory lesions. Recently it has been demonstrated by direct examination under the electron-microscope that viruses which had not hitherto been cultivated occur commonly in cases of diarrhea and gastro-enteritis in children in Australia, Canada, the United States of America and Guatemala.

New laboratory techniques (electron-microscopy, animal models and tissue culture systems), now make it possible to establish the etiology of most cases of diarrheal disease.

These methods, which are highly complex, are at present unsuitable for general use because of their high cost and the need for highly qualified personnel. There is however a probability that in the not too distant future it will be possible to use simpler methods, mainly of a serological nature.

Infections in other systems, particularly in the respiratory tract and its adnexa, may possibly cause intestinal disorders.

Foods in themselves may cause acute diarrhea without infection necessarily been present. Various food deficiencies exert the same effect: pellagra, beri-beri and the multiple deficiency syndrome of childhood. Some foods cause diarrhea by depositing food residues in the colon, while others, such as certain varieties of fungus and fish, are toxic in themselves.

The toxins which form in foods as a result of the proliferation of staphylococci and other bacteria constitute a common source of epidemic diarrheas, and to a certain extent also of endemic ones.

II. Epidemiological features and their relation to control measures

By virtue of their epidemiological features enteric diseases may be considered as a group. These features differ from one locality to another according to factors relating to the host (such as age and type of nutrition), the level of organization of the community and patterns of behavior.

As already stated, not all acute enteric diseases are of infectious origin, though most of them are. If they are considered as a group, although they can be caused by undefined and varied agents, the reservoir of infection is made up almost entirely by man, although in some cases, such as salmonellosis, the infections may also be of animal origin.

In all the diarrheal diseases specifically identified, carriers occupy an important place together with the cases that arise in the reservoir of infection in the community.

Enteric infections, whether they have a well-defined etiology or are merely undifferentiated forms of enteritis, have similar mechanisms of transmission (depending on the ingestion of excreta), except for food poisoning which spreads in a special way.

There are, nevertheless, differences according to types of distribution. Endemic and sporadic enteric infections are transmitted mainly by direct contact, from hands to mouth. Indirect transmission through objects recently contaminated with faeces is of less importance. The fingers which do not play a part in direct contact spread the infection by contaminating the food that they touch and occasionally the water stores in the home.

Epidemic enteric infections generally arise from a common source and spread through water, milk or solid foods and outbreaks occur and disappear suddenly.

Not much is known regarding the length of time for which acute enteric infections can be transmitted. Most of the existing data in this respect relate to shigellosis, whose infectious period essentially corresponds to the duration of the symptoms plus a short time thereafter. It has been asserted that chronic convalescent carriers are few and that the carrier state in general comes to an end after a few days or weeks. Nevertheless, the observations made relate mainly to adults and well-nourished persons. The slower clinical evolution in malnourished children and the tendency to relapse indicate that the transmission period may be much more protracted, a possibility which is confirmed by the high percentage of carriers in many communities (sometimes as high as 8 per cent).

Not much is known either regarding resistance and susceptibility to acute enteric infections. In underdeveloped areas cases in the first month of life are rare, but in the following six months there are few children who escape infection. Subsequently the incidence decreases with increasing age so that the infection rate in the last years of childhood is much lower and the incidence in the adult population is lower still. This suggests that a type of immunity develops which is strengthened and consolidated with increasing age, whose elements can be considered to a certain extent to be specific and permanent, and which is effective through its antagonism to most of the pathogenic agents.

The studies carried out by Gordon and his colleages in rural communities in Guatemala demonstrated that diarrheas predominate between six months and two years of age, i.e. during the weaning period. It was found that during the first six months of life, when babies are fed almost entirely at the breast, cases of acute diarrhea are rare. Once weaning has begun with the introduction of other foods to supplement the child's nutrition, and finally when breastfeeding has ceased altogether, there is a considerable increase in the incidence of diarrheal diseases. This occurs independently of the age at which babies are weaned and explains why in some communities diarrheal diseases are more prevalent during the first months of life while in others an increased incidence is found only at the end of the first year or during the second year of life. This is due to the established custom of taking together all the cases in the first year of life, and then grouping the results for the period 2-5 years. In any case the risks of the weaning period and particularly of the second year of life are obvious.

This situation was lucidly discussed by Gordon, who characterized it epidemiologically as an entity and named it "weaning diarrhea". It appears to be associated not with a specific agent but with the high degree of contamination with common bacteria caused by the feeding of the child in an unhygienic environment.

Control measures must be based on maternal and child hygiene and particularly on nutrition, education of the community and medical care for the patients. Environmental sanitation measures are less effective for this age group although they are considered essential for long-term control of acute enteric disease in the community.

The death rate from acute diarrheal diseases follows the same trend as the morbidity rate. The highest death rate is found in the second year of life more than double the rate for the first year) and remains high during the third year. There is then a sharp reduction from the fifth year onwards. The rate among school children and adults is only a fraction of the corresponding rate for the first years of life.

According to Gordon's study, the death rate in children under one year of age was 25 times as high as the rate for children the same age in the United States of America. In the preschool group it was 519 times as high and in the general population 115 times as high as in the United States of America.

It is obvious that acute diarrheal enteric diseases are concentrated among preschool children and that this must be borne in mind in any effective control program.

There is a large body of epidemiological evidence to show that the main method of spread is by direct contact. The best explanation of the general course and development of the epidemics observed is that they spread through contact.

The exceptionally high frequency of index cases among young children (0-5 years - 71 per cent) suggests that the infection originates in the family rather than from external sources. Carriage of known pathogenic agents is common and there are many carriers among older children and adults.

The rarity of multiple index cases in family epidemics is solid evidence against a common source. Perhaps, the most important source of all is that the habits of hygiene among sibling children, as among the adults in the family, favor spread by direct contact between babies and this in turn is made worse by the scarcity of water for personal hygiene.

III. Control methods

Control methods are of two types: reduction of morbidity and hence of mortality and reduction of mortality by medical care of the sick.

Mere treatment of all patients, however effective it may be, is insufficient for controlling a disease. On the other hand preventive measures do not always suffice to eradicate a disease and in general constitute a long-term solution. In the case of acute diarrheas the question of priority is not a matter of concern, since any well-conceived program must include both activities.

Control activities may be divided into two types: those of a social nature, which are the responsibility of the health services, and those in respect of individuals.

As has already been said, in the countries most affected by acute diarrheas the disease is most common in the first year of life and during the remaining period before starting school, and is more prevalent in the second year of life than in the fifth. These data demonstrate the advisability of following an age-adjusted order of priority. Control measures among small children are different and consist of educational and other work in regard to maternal and child health, whereas measures for the general public concentrate on environmental sanitation. The present methods of controlling enteric diseases fall into three categories: diagnosis and treatment of cases, environmental sanitation and the promotion of personal hygiene. these aspects are interdependent. Environmental sanitation will not be successful if it is not supported by effective educatin of the public on the importance, the use and the adequate maintenance of installations and services. On the other hand, treatment, in addition to its main purpose of preventing deaths, helps to reduce the number of sources of infection in a community. Education of the community is of prime importance because many of the preventive measures are directly related to hygiene and to individual habits connected with health. Such measures can only be applied if the initiative of the individual is taken into account and their application can only be effective if the individual knows how to make proper use of them or is convinced of their value. The three methods constitute an essential part of any adequate and well-planned control program.

Thus, the problem of priorities, which is often a source of anxiety for administrators, consists in estimating the relative value of the various methods within a category and then, in accordance with the local situation, judging the special attention which should be given to them, although they must all be applied to some degree or another. It is also necessary to decide whether the basic objective is to combat the serious diarrheas that are rife in the first years of life or to combat all enteric diseases in the population as a whole. Another point to be established is whether the program's objective is to achieve a short-term or a long-term effect.

There is no doubt that environmental sanitation is an essential condition for long-term control of acute diarrheal diseases among the population in general, even disregarding the numerous social and economic benefits that result from it.

To achieve this goal is a difficult and complex task but less expensive than many suppose. It is always being said that as a goal it is realistic, expensive and practically impossible. In the Americas the facts have shown that this argument is largely fallacious.

Twelve years ago bank loans granted for water supply schemes in urban areas in the Americas totalled some US\$100,000. In 1973 they amounted to over 1,000 million U.S. dollars. To this figure must be added US\$2,600,000,000 of capital investment by local communities. In other words the total has increased in 12 years from 100,000 to some 3,700 million U.S. dollars. This hardly suggests a task impossible to carry out. Water supplies have been provided for more than 75 per cent of the population, a percentage that would have been unthinkable a decade ago.

The situation in the rural areas is not comparable. Roughly only 12 per cent of the total funds have been invested in the rural areas. It is much more difficult to improve conditions in the rural environment but it is essential to do so. This problem is being tackled by the Governments, the World Bank and the Pan American Health Organization.

In the urban areas excreta disposal lags even further behind that of the rural areas. This task is a problem that must be tackled forthwith.

While therefore, improved sanitation and a higher standard of life for the population are measures that will have appreciable long-term effects, the effectiveness of measures of medical care to avoid deaths from acute diarrheal disease is of great and immediate importance for the planning and development of the program.

The principal causes of death from diarrhea are acute dehydration and the metabolic disorders caused by the loss of liquids and electrolytes, and it has been convincingly demonstrated that if simple and economical measures are applied to avoid these, an important reduction can be achieved in the incidence of dehydration and in death rates from diarrhea. Attention must be drawn to the important progress made in recent years, especially as a result of studies on cholera, in the treatment of diarrheal diseases by means of oral therapy for the replacement of liquids and electrolytes. According to well-documented evidence, diarrheal diseases not accompanied by cardiovascular failure can be successfully treated if oral therapy is used on its own. It is possible to bring about an immediate reduction in mortality from diarrheal diseases in the Americas by means of a program aimed at providing this type of treatment in all clinics and departments by using

ready-prepared mixtures of liquids and electrolytes. The cost is very small and the necessary ingredients can be obtained everywhere. WHO recommends the following formula for oral treatment of diarrheal diseases:

Potable water (gm/l)

Glucose	20.0
Sodium chloride	3.5
Sodium bicarbonate	2.5
Potasium chloride	1.5

This mixture can be prepared and packed in advance in all countries and distributed on a large scale for the treatment of patients with diarrheal diseases. Treatment can easily be given by mothers following the instructions and training given by paramedical personnel.

The more serious cases need care in hospitals, health centers or rehydration centers but even in such circumstances there are simple methods of treatment which if properly carried out will save many lives.

In view of the fact that the regions with a high incidence of diarrheal diseases are mainly rural and do not have available hospitals, organized dispensaries or the medical services generally found in the urban centers, it is essential to draw up and try out a simple program of treatment adapted to local conditions and which can be used in the absence of doctors by employing trained and supervised auxiliary personnel and knowledge of which is spread by means of health education among mothers of small babies.

With the advent of the antibiotics, particulary of the broadspectrum type, that have decisive effects on the normal bacterial flora
of the intestine, a new diarrheal process has appeared. Destroying the
existing balance between the microorganisms of the faecal mass, such
antibiotics lead to an increase in the number of Proteus, staphylococci,
Pseudomonas and certain fungi, which begin to dominate the internal milieu,
thus leading to serious diarrheal disorders. In some countries where antibiotics are notoriously misused, even by the medical profession, this
problem is becoming extremely important in the big cities. In addition,
the appearance of pluriresistan strains of intestinal pathogens is the
result of prolonged and illogical utilization of medicaments, thus creating
a serious public health problem.

Antimicrobial agents generally do more harm than good. They cannot replace the patient's lost liquids and electrolytes. Moreover, many if not most enteric infections fail to respond to such treatment and in some of them, such as the salmonelloses, the infective process may actually be worsened or prolonged by it. The unsupervised use of antimicrobials may lead to dangerous intoxications. Indiscriminate use of these medicaments should be forbidden.

Control activities to reduce morbidity and mortality from enteric infections are carried out through the local health services at the various levels of outpatient and hospital care. At the same time programs of environmental sanitation and health education in which use is made of schools and the various community bodies concerned with social problems must be drawn up and developed.

In respect of the local health services, emphasis must be laid on the importance of the laboratory playing its part in the control of enteric infections, since it is certain that intestinal infection cannot be definitely established without the isolation and identification of the causal agent. In this regard the laboratory should be so organized as to take into account the possible etiological agents, the geographical environment, the social, economic and cultural conditions and the age groups on which the work is to be done.

The organization of the laboratory service so that it can contribute to the diagnosis and treatment of enteric infections requires, in addition to the establishment of new departments, an effective strengthening of the existing laboratories by determining and setting standards for levels of care in order to facilitate the correct taking of specimens in urban or rural public or private consulting centers with a view to processing the material in the health center laboratory or the laboratory of the nearest district hospital.

The establishment of regional or national reference laboratories is essential to provide support and facilitate supervision and quality control in the process of diagnosis, treatment and follow-up of enteric infection. The establishment of a reference laboratory for the whole Continent is to be highly recommended.

In addition to the activities of the doctor, the engineer and the educator, who are the basic elements in the program for the control of enteric infections, importance also attaches to nursing staff at the professional and auxiliary level and also to groups of community workers who with basic but simplified training would make it possible to extent the coverage of the control activities to a larger number of persons at risk in the peripheral urban areas and/or the rural areas with a scattered population. The nursing staff should be given responsibility for carrying out a certain range of activities which combine the promotion of health education, direct medical care and participation in epidemiological research, thus facilitating the planning of the program and determination of the strategy to be followed.

The activities should be: (a) to promote early detection of cases of intestinal infections, thus preventing them developing to a serious stage; (b) to take steps to ensure that proper treatment is given; (c) to take measures to avoid cross-infection in hospital establishments, and (d) to participate in epidemiological research.

IV. Strategy for reducing morbidity and mortality from enteric infections

As already mentioned, the Ten-Year Health Plan for the Americas recommended the reduction of present mortality from enteric infections by least 50 per cent, with particular emphasis on infants and young children.

There was a consensus that for this purpose it would be necessary to:

- (1) Establish, in the context of the health services and with appropriate cooperation by other bodies, adequate coordination making for the smooth development of programs for the prevention and early and effective treatment of enteric infections.
- (2) Improve the system of statistical information with a view to obtaining reliable figures, in good time, reflecting as closely as possible morbidity and mortality rates due to enteric infections, with a view to developing and evaluating programs based on a reasonably sound scientific methodology.
- (3) Promote adequate education policies providing motivation to enlist community cooperation on a permanent basis in the control of enteric infections.
- (4) Establish and consolidate, within the context of the existing health services and of an expeditious health care reorganization, activities implying a timely and effective response to the demand generated by enteric infections at the level of both ambulatory care (health care centers) and hospitalization (rehydration centers and hospital services in general). These activities should form an integral part of infant health programs, and hence follow-up should be borne in mind, the patients being provided with special facilities for the strict supervision of their growth and development processes and improvement of their nutritional status.
- (5) Ensure the supply of adequately trained and rationally distributed professional and auxiliary personnel.
- (6) Assure the availability of facilities for laboratory diagnosis and for adequate supplies of drugs and other therapeutic apparatus (hydration equipment).
- (7) Support efforts to achieve wider coverage of the following programs: water supply (80 per cent in urban and 50 per cent in rural areas); adequate excreta disposal (70 per cent in urban and 50 per cent in rural areas); vector control and improvement in the preparation, handling and preservation of food stuffs.

- (8) Conduct studies directed toward discovering new methods for the treatment and control of enteric infections, with special attention to the problem of strains resistant to antibiotics.
- (9) Establish an epidemiological surveillance system for enteric infections, particularly cholera, as part of the national surveillance system. However, it is not sufficient to compile, copy, tabulate and record the information obtained; it must be analyzed and used as a basis for planning and action, and the information interpreted must be transmitted in good time to all those who need to be informed. Mention was made of the tragic delay of a full year before the dysentery epidemic in Central America, which caused thousands of deaths, was recognized.
- (10) Train personnel for the laboratory diagnosis and treatment of cholera, and take the necessary steps to assure availability of the antibiotics and rehydration agents necessary for the early treatment of cases of the disease.

V. Studies needed to improve knowledge and reduce morbidity and mortality from enteric diseases

In order to reduce morbidity and mortality from enteric infections, urgent information is required concerning a series of basic problems.

As was pointed out previously, over the last few years considerable progress has been made in elucidating the causes of enteric diseases. The application of modern laboratory techniques makes it possible to determine the etiology of the majority of cases of acute diarrhea. However, such methods are costly and require specialized personnel. Hence it is necessary to try to simplify the procedures and make them less costly so that they will be accessible to the majority of laboratories.

Once the etiology has been established, it will be possible to carry out a series of related researches, all of them important for an understanding of the ways and means of combating enteric infections. It is possible to determine the clinical differences between the various types of enteric diseases— which would help medical practitioners in selecting the laboratory examinations appropriate for their patients.

In regions affected by enteric diseases there is an extremely urgent need for current data on the natural history of the diseases in conditions prevailing locally. These data have to be obtained through epidemiological research. Field research is important because it maintains a direct relationship with the practical problems of control; also, it is within the means of official and other bodies in the less developed countries. This type of research should be combined with laboratory studies, essentially using the new methods.

Although it is a known fact that there is a close relationship between malnutrition and enteric diseases, there is a need to investigate the most effective and least costly means of supplementary feeding acceptable to the population in general and garanteeing a nutritionally satisfactory diet.

The improvement of environmental sanitation is undoubtedly the most important means of controlling enteric infections, since preventive medicine procedures require certain previous or simultaneous conditions which are achieved through sanitation. On the other hand, curative medicine procedures, while representing an important factor in the reduction of mortality rates, leave the morbidity aspect untouched.

Although considerable progress has been achieved in regard to environmental sanitation in many urban centers, there is a need for greater attention to be paid to it in rural zones. Before large scale, costly programs are introduced, it is important to evaluate the resources available in each locality for water supply and effective excreta disposal services.

It is essential to carry out cost-benefit analyses, taking into account the population, the incidence of enteric diseases and the cost of effective water supply and excreta disposal systems.

Studies designed to identify the factors and conditions which have stood in the way of large scale application of the knowledge and resources available to combat enteric infections will no doubt help to improve the effectiveness of control programs.

Adoption of the new technology is a slow process in the developing countries. Studies carried out with a view to applying new resources—vaccines, courses of treatment, and simple sanitation measures—will help to activate this process for the good of the people.

Effective, harmless vaccines, low in cost and easy to apply, represent an extremely useful resource in the control of enteric infections. It is therefore necessary to stimulate research designed to discover new immunizing agents.