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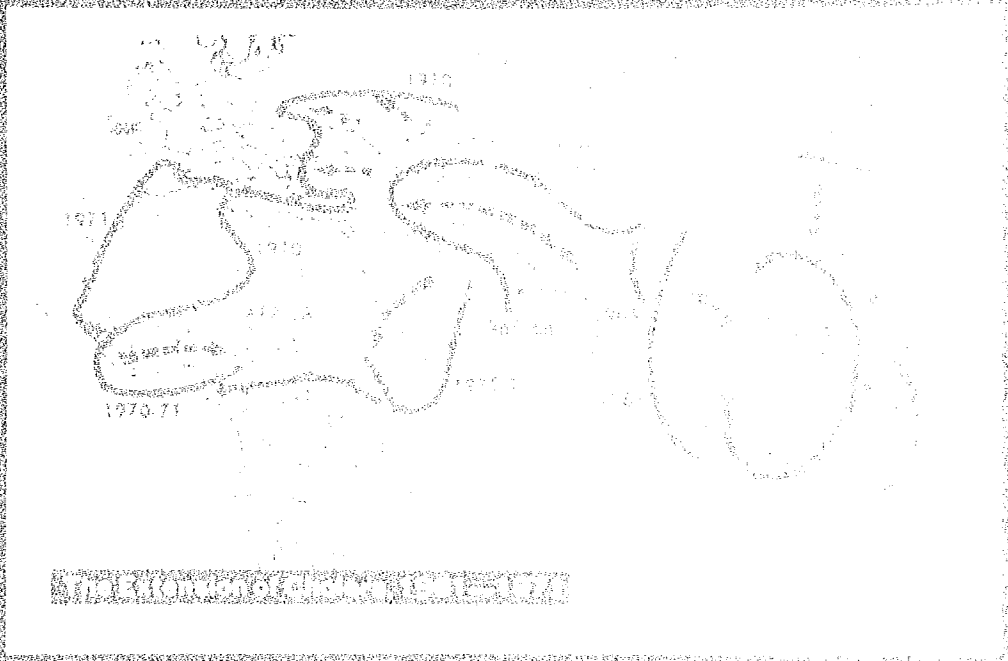

AGENCY FOR INTERNATIONAL DEVELOPMENT

Washington, D. C.

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INTERIM REPORT

of

THE TASK FORCE ON CHOLERA

Coordinator: Richard C. Parsons

Members: Jean F. Rogier, M.D.

Robert W. Babione, M.D.

June 17, 1971

An intent of the Interim Report is to stimulate discussion, forward planning and the frank exchange of information on cholera among public health authorities and institutions throughout the world

Inquiries or comments relative to the Report would be appreciated and are encouraged by the A.I.D. Task Force on Cholera. Correspondence may be directed to: Cholera Coordinator, Agency for International Development, Department of State, Washington, D. C. 20523.

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ADDENDUM

Several members of the cholera scientific community who had participated as expert consultants to the A.I.D. Advisory Group on Cholera and the Expert Panels, recently have revised their thinking and recommendations on the subject of utilization of cholera vaccine. This revision of expert opinion reflects a growing conviction that evaluations of the currently available vaccines, which indicate their limited value as an effective means to control cholera, should be taken into account when planning cholera control programs; and that their use in mass immunization programs does not compare favorably with other known control measures from the cost-benefit standpoint.

This divergent opinion raised the basic issue of whether or not the Agency for International Development should continue to encourage the use of vaccine by participating in its supply in response to epidemic or potentially epidemic situations.

The Cholera Task Force, noting that such opinion would alter the priority assigned to vaccine as recommended in Section VII of the Interim Report, convened an ad hoc Panel on Vaccine Utilization in Washington on March 16, 1972 to discuss the issue and to solicit the guidance of experts in this field.

The following consensus was reached by the Panel:

-- A.I.D. may continue to supply currently available vaccines, but only in response to urgent expressions of need. In lieu thereof highest priority should be given to assistance in the development of treatment capability, including the prepackaging of dry chemicals for preparation of solutions for oral rehydration of cholera patients.

-- A.I.D. may assist in upgrading of vaccine production laboratories and in the promotion of practical immunization programs in recognition that cholera vaccine will continue to be manufactured and used by other countries. It was recognized that numerous corollary benefits to other disease control programs will result from these efforts.

-- A deliberate retrogression of emphasis on the use of currently available killed organism vaccines should not reduce support of research directed toward the production of an immunizing agent which would confer effective and long-term protection against cholera.

-- The United States Government, while recognizing that improvement of environmental sanitation is the ultimate means for the elimination of cholera, should stimulate Member States of the World Health Assembly to reduce their reliance upon currently available vaccines, stressing instead the need to place greater emphasis on cholera treatment, including oral rehydration.

-- This Addendum hereby modifies the Cholera Program Priorities appearing in Section VII of the Report.

Members of the Ad Hoc Panel on Vaccine Utilization were:

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Richard C. Parsons	Coordinator, Cholera Task Force
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Robert W. Babione, M.D.	Member, Cholera Task Force
Jean F. Rogier, M.D.	Member, Cholera Task Force

March 1972

ADDENDUM

Since the completion of the Interim Report of the Task Force on Cholera in June 1971 two actions taken by the Agency and information relative to the current status of the Seventh Pandemic are noteworthy.

1. On August 30, 1971 following Agency review of the Interim Report, the Administrator authorized a two-year extension of the A.I.D. Task Force on Cholera. The Task Force is directed to serve as the focal point within the Agency for all matters pertaining to cholera, to assist multilateral and regional organizations in the implementation of actions needed to reduce the immediate threat, and to stimulate the formulation of a long-range plan for the prevention of future cholera pandemics.

2. In response to an urgent appeal from the World Health Organization (WHO) for an additional pledge of cholera vaccine, a cash contribution of $200,000 from the A.I.D. Contingency Fund was made on June 30, 1971 to the WHO Voluntary Fund for Health Promotion, Special Account for Cholera Programme. These funds were used for the purchase of ten million milliliters of vaccine.

3. The cholera pandemic continues to invade new areas. During the third quarter of calendar year 1971 the Weekly Epidemiological Records of WHO listed 34 countries infected with cholera. The list includes Spain and Portugal and 23 countries in the African continent. France and Sweden have reported imported cases and there is a report of non-confirmed cases in Cuba. A total of 66 countries now have been infected during the course of the Seventh Pandemic.

October 1971.

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SUMMARY

Starting from the Celebes in Indonesia in 1961 the seventh recorded pandemic of cholera swept across two-thirds of the world, invading in rapid succession all of the countries of the Far East, the Middle and Near East, several countries of Southern Europe and widely separated areas on the African Continent. By early 1971 cholera was firmly established in sixteen countries in sub-Sahara Africa with its heaviest concentration in West Africa. It is predicted that cholera will advance from there to the Caribbean Islands and South America in the early future. To date more than half the total world population lives in cholera infected areas.

The causative agent is a particularly hardy strain of Vibrio cholerae called El Tor, and its principal danger lies in its unusually high ratio (as much as 100:1) of subclinical, or inapparent infections, to recognizable clinical cases. For this reason movement of the vibrio is impossible to monitor by known practical methods.

It can be fairly stated that beginning in 1961 cholera was exported successively by East Asia to the Near East, to Europe and to the African continent. An over-all strategy must be aimed at eliminating newly established areas of endemicity that can serve as sources of infection in future years.

In September 1970, as a result of widespread epidemics, first in the Near East, then in Europe and Africa, many of which produced frantic calls for disaster relief assistance from the United States, the Administrator of the Agency for International Development directed the establishment of a Task Force on Cholera to serve as the focal point for Agency response to the emergency. The Task Force is located in the A.I.D.'s Bureau for Technical Assistance, Office of Health and is headed by a Coordinator provided by the Bureau for Near East and South Asia. Staff support and administrative servicing are provided by the Bureau for Technical Assistance. The functions assigned to the Task Force were

twofold:- (1) mobilizing resources, including disaster relief, and coordinating with the World Health Organization (WHO) and other donor organizations on emergency measures to combat cholera, and (2) to develop and propose to the Administrator a long-range strategy for the eventual control of the current pandemic and to prevent future cholera pandemics.

The funding of emergency actions recommended by the Task Force has been provided either under Disaster Relief authority, exercised by A.I.D. country missions or by the allocation of A.I.D. Contingency Funds to Disaster Relief accounts for use by the Task Force.

Largely as a result of guidelines transmitted to U. S. Missions abroad that were designed to strengthen the position of WHO's role of leadership in the anticholera effort, the U. S. direct assistance emergency phase diminished by the end of 1970 and the Task Force was able to concentrate its efforts on its strategic and long-term planning function. A decision was made to submit the following Interim Report and to seek approval in principle of the general scope and thrust of a comprehensive, long-range cholera plan before undertaking the extensive studies and negotiations that would be essential to the development of such a plan in its full, substantive detail.

The conclusions reached by the Task Force and the features of the plan described in the Interim Report are based on the recommendations of a Working Group and four Expert Panels convened by the Task Force and composed of a wide spectrum of the foremost cholera expertise available in the United States. The recommendations of the experts indicate that:

-- Successful control and prevention of the epidemic spread of cholera lies in rendering the threatened areas unreceptive to introduction of the vibrio.

-- It is essential to monitor all acute diarrheas in order to detect the early presence of the cholera vibrio and to establish effective control measures.

-- Cholera vibrios are transmitted from person to person principally by fecal contamination of drinking water and food; therefore, the major preventive effort must be directed toward improvement of water supplies and excreta disposal facilities, supported by health education which emphasizes personal hygiene.

-- Mass vaccination of populations at risk using vaccines now available is expensive and ineffective in the prevention or control of transmission of cholera.

-- A realistic national or international program for cholera control should be based on a rational use of available control measures and resources so that best possible results are obtained for the least expenditure.

The expert consultants recommended that a comprehensive plan should focus on four problem areas: Vaccine Production, Control of Transmission, Surveillance and Therapy. The long-range plan thus developed is divided into two phases:

Phase I - Immediate Activities, or those actions which should be initiated without delay to mitigate the consequences of the current pandemic over the next several years; and

Phase II - Continuing Activities whose initiation may be at a later date and continue into the long-term with the goal of preventing future pandemics.

The Phase I activities, in order of priority, are recommended by the Expert Panels, as follows:

1. Vaccine

-- Use of excess local currencies to purchase vaccine manufactured abroad.

-- Contributions of U. S. vaccine to WHO under extreme emergency situations.

-- Assistance in the improvement of several strategically located vaccine production laboratories.

2. Surveillance

-- Development of "early warning" capabilities in threatened areas through the improvement of country and regional reference laboratories, and the development of surveillance systems for acute diarrheal diseases.

-- Establishment of pilot surveillance projects in selected countries for demonstration and training purposes.

3. Therapy

-- Development of in-country treatment resources such as intravenous solution production, prepackaging of chemicals for the preparation of oral replacement solutions, etc.

-- Preparation of training manuals for the treatment of acute diarrheal diseases.

-- Contributions to WHO of antibiotics and other essential supplies needed in cholera therapy.

4. Control of Transmission

-- Improvement of community sanitary utilities, including design, construction, operation and management of water supplies and excreta disposal systems.

-- Demonstration, study and training projects for the reduction of diarrheal diseases in rural populations through simple techniques for the protection of small water supplies and excreta disposal.

-- Demonstration projects to introduce low cost water treatment facilities for small towns, as developed by A.I.D. sanitary engineers in Viet-Nam.

5. Health Education

-- Assistance in the sponsorship and promotion of health education campaigns aimed at promoting better sanitary practices and personal hygiene in cholera infected areas.

Although an estimate of cost of the Phase I Activities is in the neighborhood of $4,138,200 (see Illustrative Proposals, Appendix B), it

is not anticipated that this total expenditure will be at the account of A.I.D. More exact cost estimates and the share to be borne by A.I.D. will be contingent upon (a) field surveys, some of which will be done in cooperation with WHO; (b) negotiation of cost sharing of the various activities with WHO and other international donor organizations; and (c) selection of activities which can be funded appropriately by use of local currencies, where such are available. The plan is designed with a built in flexibility that takes into account the variable resources of A.I.D. This permits a selective schedule of implementation which is consistent with the desirability or availability of A.I.D. support during a given period.

Finally, the strategy of the comprehensive plan will help to create indigenous capabilities in the lesser developed countries (LDCs) which will reduce their vulnerability to frequently recurring disasters by a variety of communicable diseases in addition to cholera. These disease disasters will result in an inevitable continuing outflow of dollar cost assistance from the U.S. - all highly inefficient as a result of their emergency nature. Direct costs to the U.S. of cholera emergency assistance alone has amounted to at least $500,000 annually since 1961. The U.S. dollar contribution to the Southeast Asia Treaty Organization's (SEATO) Cholera Research Program increases this figure to over $1,000,000 annually. On the other hand, surveillance systems, laboratories, sanitary facilities, and health education are commonly essential to the control of all communicable diseases and their development in the LDCs will have a telling effect in reducing the potential for disease disasters.

The intent of the plan is to deemphasize A.I.D. bilateral assistance, and implementation will be achieved by working with and through the World Health Organization and various other international and regional organizations.

INTERIM REPORT OF THE A.I.D. TASK FORCE ON CHOLERA

A STUDY OF A MULTINATION DISEASE PROBLEM RESULTING FROM ENVIRONMENTAL POLLUTION BY HUMAN WASTES

The magnitude of the cholera problem is such that the ultimate scope and success of a program for its control requires the collective action of the nations and multilateral organizations who are concerned with the disease. The complications and diversity of approaches inherent in the development of such a program has led the Task Force on Cholera to the conclusion that an Interim Report should be submitted to the Agency and reviewed and approved in principle before comprehensive project development for major elements of the program is undertaken.

In his weekly Focus Report for March 15-19, 1971 Dr. John A. Hannah, Administrator of the Agency for International Development, advised the Secretary of State of the world cholera situation and of the actions taken by the Cholera Task Force. By this means the Secretary was apprised of the functions of the Task Force and of its concommitant responsibility to develop a long-range plan for an A.I.D. supported effort to control the present cholera pandemic and to prevent its recurrence in the LDCs.

I. INTRODUCTION

Long-range planning activities of the Cholera Task Force have been on a continuing basis since its establishment in October 1970. On October 6 an A.I.D. Working Group on Cholera, consisting of experts on cholera drawn from U. S. universities and U. S. Government agencies was convened for the purpose of providing guidance to the Task Force on specific problem areas on which an A.I.D. cholera plan might focus attention. The categories identified were: Vaccine Production, Surveillance, Control of Transmission and Therapy. In ensuing months a series of four Expert Panels were assembled by the Task Force to subject each of the above categories to in-depth examination by a wide range of cholera expertise, and to promulgate specific recommendations upon which an action program might be based.

A total of 38 recommendations were developed by the Expert Panels (Appendix C). Of these, 30 are judged to be specifically qualified under current or projected guidelines for U. S. Government sponsored stimulation or for direct A.I.D. assistance.

These exercises utilized 36 man-days of consultant time; they included 30 experts in their respective professional specialties drawn from universities, the World Health Organization (WHO), U. S. Government agencies and private industry (Appendix E). Coordination with WHO was established at the Director General level and with its various working units. The WHO has submitted an outline of its concept of long-range planning for the control of cholera and has indicated the specific problem areas in which U. S. Government assistance is desired (Appendix A-7). The thinking of WHO in this respect coincides closely with conclusions reached independently by the A.I.D. Expert Panels.

Limitations of staff resources and time did not permit the Task Force to translate recommendations of the Expert Panels into specific proposals for implementation, although there are a few cases where urgent action is clearly indicated and rational solutions appear to be available. Preliminary actions, such as site visits by consultant teams, extensive negotiations with other agencies, and development of technical details which would extend beyond present limitations of the Task Force are necessary before adequately quantified proposals for action can be derived. Definitive project proposals will be contingent upon authorization to undertake these preliminary actions.

II. SCOPE AND NATURE OF THE PROBLEM - THE SEVENTH PANDEMIC

Development of a comprehensive plan for a long-range attack on cholera requires first an understanding of the nature and scope of the problem. This is best achieved by review of a brief history of epidemic cholera through the current Pandemic VII, and comments relative to its behavior.

Background

It was a mistake to think that, because of the great advances in medicine and public health in recent years, there was little risk of cholera spreading far beyond the delta of the Ganges and Brahmaputra Rivers in eastern India and East Pakistan where it has been domiciliated since the beginning of recorded history. There are no records of cholera epidemics involving other parts of the world prior to 1817. However, between 1817 and 1923 cholera broke out of its traditional home in six pandemics, spreading over most of the globe along the established trade routes.

The sixth pandemic lasted from 1889 to 1923 and thereafter cholera retreated to its endemic homeland in Asia. For almost 40 years until 1961 there were only sporadic outbreaks, except for the disastrous epidemic in Egypt in 1947. Its power of dispersion, which made it the most terrifying disease of the nineteenth century, seemed to have vanished.

In London in 1854 John Snow showed that epidemic cholera could be brought under control by inactivating the community well, thus demonstrating the significant role of contaminated water in the spread of the disease. However, it was not until after 1884, when Robert Koch isolated the causative organism V.Cholerae, that Great Britain and the United States initiated better public sanitation which prevented further epidemics in those countries.

Classical (Asiatic) Cholera and El Tor Cholera

The cholera of the principal endemic focus in Asia, and that of the great pandemics of the nineteenth century, is caused by the classical Ogawa and Inaba serotypes of Vibrio cholerae. However, a more remote focus of cholera was discovered in 1937 when a cholera-like disease appeared in Sulavesi (Celebes) in Indonesia. This illness was caused by a little known biotype of the cholera vibrio called El Tor, after its original identification at the El Tor Quarantine Camp in Egypt in 1905. The disease did not show any great tendency to spread and medical

scientists were lulled into the belief that it was not an epidemic strain. However, in 1961 the Sulavesi El Tor defied all theorems promulgated about its non-epidemic nature, and for reasons still unknown started on its present pandemic rampage.

Generally speaking, El Tor vibrios are more resistant to environmental factors and to antibiotics than are the classical cholera strains. The ratio of infected persons to clinical cases is higher with El Tor cholera and even a few chronic carriers of this biotype have been recorded. The clinical disease caused by the El Tor biotype is indistinguishable from that caused by the classical variant; this prompted the Fifteenth World Health Assembly in 1962 to determine that it should be considered to be the same disease as that caused by classical V.cholerae.

The current pandemic, the seventh, spread rapidly through Southeast Asia extending as far north as Korea by 1963. In 1964 the disease moved across South Asia, penetrating the Middle East to the borders of Turkey in 1965-1966. In 1969, after a brief lull, cholera was more widespread geographically than in the preceding three years (Appendix A-1). By the end of 1970, the worst year to date, the disease was dispersed widely around the Mediterranean. Its most significant excursions were to countries of Southern and Central Europe and to broad areas of Africa where it appeared for the first time in nearly a century. During the past decade cholera has been reported from more than 50 countries, while other countries have deliberately suppressed information of its occurrence (Appendix A-2,3&4). Some newly infected areas have become truly endemic.

General Epidemic Features

Like other infectious diseases cholera has a seasonal pattern, although the season varies from place to place. Thus in Dacca it follows the monsoon rains, but in Calcutta it generally precedes the monsoon. In some areas of the Philippines it reaches its peak during

the rainy season, while in the Near East it occurs during the dry summer months. A seasonal pattern for sub-Sahara Africa has not been demonstrated yet.

Cholera usually affects individuals of the lower socioeconomic groups living under unsanitary conditions. There are no reported nutritional deficiencies or gastrointestinal factors that predispose to cholera. Sex is usually not a decisive factor, but when an epidemic strikes a new area the earliest cases are often predominantly adult males - boatmen, offshore fishermen, farmers and unskilled laborers. Once the disease is established in a community the case rate is equal in both sexes. The age distribution follows relatively simple rules: in newly invaded areas persons of all age groups become ill, while in endemic areas children are the more susceptible.

Transmission of Cholera

The transmission of cholera, either from a severe case or from a carrier, to a susceptible individual depends upon the ingestion of water or food contaminated with cholera vibrios. Although a cholera patient excretes vibrios for a few days the carrier, particularly in the case of El Tor cholera, poses the greatest problem in the transmission of the disease in or between neighboring countries.

The ratio of severe cases to mild or inapparent infections (carriers) is 1:5 to 1:10 for classical cholera, and can be as high as 1:100 for El Tor cholera. The presence of relatively large numbers of unidentified carriers makes wide dissemination of the vibrios possible within a brief period. There is no practical method for identifying carriers among a transient population.

The present El Tor outbreak was at first restricted to people living in slum areas, to offshore fishermen living under bad sanitary conditions, and to other populations with subminimal sanitary facilities. Nearly all the invaded areas lack adequately protected or treated drinking water supplies or excreta disposal. The second phase of the

pandemic in Africa is characterized by the propagation of the disease in desert and semidesert areas with scattered large cities having municipal water supplies, but surrounded by suburbs where people live under unfavorable hygienic conditions. The nomadic and migrant populations in many of these areas move across borders without restraint and generally inhabit localities having the poorest sanitary conditions.

Cholera can occur in any part of the world where overcrowding and poor sanitation exists, and the threat of infection is magnified by the current availability of rapid transportation. In 1970 occurrence of the disease showed an alarming tendency to escalate into higher socioeconomic levels as a result of seasonal migrations to beach areas that are polluted by the discharge of untreated sewage. For example, this circumstance renders vulnerable much of the Mediterranean littoral. The standards of environmental health in many of the countries through which cholera is spreading have changed little since the nineteenth century. In some cities as a result of the population explosion and the influx of people from rural areas, overcrowding has resulted in a lowering of standards. Even the best sanitary installations and the most enlightened public health measures remain ineffective when they are not accepted by everyone, are improperly managed, or are unaccompanied by suitable personal hygiene practices acquired by adequate public health education.

Future of Pandemic VII

The present pandemic may diminish in intensity but because of widespread substandard sanitary conditions its potential for recrudescence will remain great. Epidemiologists who are expert in cholera, including officials of the United States Public Health Service, the World Health Organization, and others predict that Pandemic VII will continue to spread in the countries already infected and others will be invaded. The invasion of Central and South Africa is expected momentarily, if it has not already begun. Even though no serious cholera outbreaks have occurred in the Western Hemisphere since 1873 it is predicted that the Americas may be invaded in the near future.

There may be sporadic importations into the United States, but the general level of sanitation and health services render unlikely the occurrence of epidemic outbreaks.

Excessive and discriminatory quarantine measures and cessation of traffic in goods has strangled the commerce and movements of people of some of the infected countries. Cholera has become not only a public health problem, but also an economic and political one because of its high emotional impact.

III. THE COSTS OF CHOLERA

1. Economic Losses due to Cholera

The indirect costs of cholera include (1) the economic losses in wages or productivity due to illness and death of members of the labor force, and (2) losses to the economy due to disruption of trade and tourism. Although there is no reliable source data on the impact of cholera on the productive segment of the population in countries newly invaded during the Seventh Pandemic, the cost to the economy will be greater in those countries than, for example, in India and for the following reasons:

-- The attack rate is higher in newly epidemic situations.

-- The attack rate will be higher among adults than in children in a newly infected area.

-- The low level of medical care and inexperience with the disease will result in greater severity and longer illness in newly infected areas.

In India the expectancy of productive life of the labor force has been determined for both males and females, in both urban and rural groups. The total economic losses due to cholera deaths, which for India are about 3,000 per annum, has been calculated at about $3,000,000. It is impossible to extrapolate these losses per death to other countries. Nevertheless the 3,000 cholera deaths reported from Nigeria during the first two and one-half months of 1971 undoubtedly resulted in losses at least equivalent to those in India and probably were greater for reasons given above.

During 1970 about 50,000 cases of cholera were reported from 35 countries. Actual figures were undoubtedly much higher. In spite of deficiencies of data there is no question that the resulting economic losses ran into many millions of dollars.

Losses in International Trade

Cholera affects international trade when cholera-free countries impose an embargo on commodities normally imported from the cholera-infected countries. Cholera-free countries also may prohibit their ships from visiting cholera-infected countries, thus reducing both imports and exports. These restrictions are often in excess of the International Sanitary Regulations and are beyond reason or necessity. For example, during the 1965 epidemic in Iran, Switzerland refused to accept airmail originating in Iran and Russia stopped chromate ore importations from Iran. These extreme measures injure the economy of the countries affected, particularly if the embargoed material is perishable. It is extremely difficult to calculate this type of loss and its magnitude is deliberately minimized by infected countries. It depends on the type goods, the value of the trading that is interrupted, the duration of the embargo, etc. Taiwan recorded a loss of $6,000,000 as a result of neighboring countries closing their seaports during the 1962 epidemic. In 1970 Ethiopia prematurely declared the country cholera-free because of damage being suffered by her economy. The ban on trade is most often due to panic, but this can cause just as great economic losses as if the fears were well-founded. Losses are worse for those countries which have been free of the disease for a long time and are suddenly hit by a ban on trade. Hong Kong had such an experience in 1961 with its small epidemic of 130 cases and 15 deaths. Severe controls were applied both by Hong Kong and by its neighbors at a direct cost of $US 440,000 to control the epidemic, and an estimated loss of exports and imports of about 40 million dollars each.

In the Philippines cholera broke out in 1961 and the export of fruit and fish dropped four per cent below the previous year. All of the drop was in perishables. Canned fruit and prepared fish exportation was not affected.

Losses in Tourism

Losses in tourism due to cholera can be severe where this industry is an important factor in the economy. Hong Kong, normally increasing its tourist visits by 40,000 a year, suffered a setback as a result of cholera and had a growth of only 30,000 in 1962. Tourist traffic resumed its growth but at a rate of 50,000 visits per year following control of the epidemic. The Philippines experienced a similar loss when cholera was reintroduced in 1961 after an absence of 25 years.

2. Direct Costs

The Costs of Treatment

The present day regimen of treatment for patients severely ill with cholera can reduce the mortality to less than one percent in all ages. The populations affected by outbreaks of the disease are usually of the lower socioeconomic groups living under unsanitary conditions, and the costs of treatment in relation to the meager financial resources of the individual and the community are such that treatment places a heavy burden on the economy of the LDCs.

The average cost of treating patients severely ill with cholera differs widely from country to country and calculations of the costs are subject to many variables.

Estimates for treating a case of cholera made by the World Health Organization varied from a minimum of US $10 in some parts of India to a maximum of US $180 for Singapore. In India itself the cost varied between US $10 and US $45. The average costs for Taiwan were US $28 vs US $52 for the Philippines and US $128 for Hong Kong.

The principal variables to be considered in estimating the cost of treating a case of cholera are related to the regimen of treatment employed. Intravenous replacement solutions are more costly than oral

replacement solutions. However, the initial use of intravenous solutions will usually be required until the vital signs are stabilized, acidosis is corrected, and the patient is able to drink. The use of antibiotics reduces the duration of treatment and the amount of replacement solutions required by approximately 50 per cent, with resultant savings in the cost of fluids and hospitalization.

Cost of Hospitalization

The cost of maintenance of a patient in a hospital differs according to the type of hospital. The cost per patient per day will vary considerably for hospitalization in a general hospital or an infectious disease hospital, and the average cost of a bed per day in such hospitals may not give a true indication of the cost of hospitalizing a cholera case. Calculation of food costs should include the cost of feeding an attendant, particularly in the case of children.

Professional and Paramedical Services

The cost of services of physicians, nurses and paramedical personnel will depend upon the pay scales and standards of medical care of the country involved.

With data collected from several communities in Southeast Asia, WHO has projected the costs of hospital treatment in endemic areas and for newly invaded areas (see tables 1 and 2, page 17). The clinical course of a hospitalized case of cholera is essentially the same everywhere, but due to familiarity with treatment methods the existence of indigenous facilities for producing rehydration fluids and having essential supplies on hand, treatment in endemic areas will be considerably cheaper than in the newly invaded areas. Use of Tables 1 and 2 permits an estimation of hospital beds, manpower, rehydration fluids and antibiotics needed according to the expected number of cases. From the above estimates the cost of treating 10,000 patients in newly invaded areas will range between 400 and 700 thousands of dollars. Although the cost of oral fluid is negligible, it must be emphasized that the care of the cholera patient is not simpler

TABLE 1

COST OF HOSPITAL FACILITIES, DRUGS AND MANPOWER REQUIRED FOR TREATMENT OF A CHOLERA CASE IN WELL-ESTABLISHED TREATMENT CENTRES IN AN ENDEMIC AREA[1]

Cost of	Treatment with rehydration fluid (parenteral) only			Treatment with rehydration fluid (parenteral) and antibiotics		
	Quantity	Cost: Rupees	US $	Quantity	Cost: Rupees	US $
Total hospital stay (days)	9	135.00	17.00	4	60.00	8.00
Fluid needed (litres)	18	92.00	12.00	8	40.00	5.00
Drugs needed (dose)	0	0		Tc. 16 capsules	16.00	2.00
Physician's time (hours)	12	48.00	6.00	5	20.00	2.50
Nurse & auxiliary time (hours)	20	40.00	5.00	10	20.00	2.50
TOTAL COST (approximate)		315.00	$40.00		156.00	$20.00

[1] These data have been collected from the Infectious Diseases Hospital Cholera Ward, Calcutta.

TABLE 2

COST OF HOSPITAL FACILITIES, DRUGS AND MANPOWER REQUIRED FOR TREATMENT OF A CHOLERA CASE IN A NON-ENDEMIC AREA

Cost of	Treatment with rehydration fluid (parenteral) only		Treatment with rehydration fluid (parenteral) and antibiotics	
	Quantity	US $	Quantity	US $
Total hospital stay (days)	9	18	5	10
Fluid needed (litres)	20	32	10	16
Drugs needed (dose)	0	0	Tc. capsules	3
Physician's time (hours)	10	10	6	6
Nurse & auxiliary time (hours)	20	10	12	6
TOTAL COST	US $70		US $41	

with the introduction of oral therapy. The same degree of care in measuring fluid input and output must be taken with oral, as it is with intravenous therapy. In the face of very limited supplies of suitable intravenous fluids, the use of oral fluids should be considered as a practical method for maintenance therapy, after the initial rehydration and stabilization of the vital signs have been achieved by the administration of fluids intravenously.

IV. A.I.D. POLICY ON CHOLERA

In spite of large amounts of palliative assistance contributed by A.I.D. in past years (see Section VIII), the Agency has no policy on cholera per se. Nevertheless the basic position has been established that the social, emotional, health and economic problems created by cholera constitute valid reasons on humanitarian grounds alone for the U.S. Government to respond positively to requests for assistance in cholera emergencies. Agency experience in coping piecemeal with Pandemic VII has led the Task Force to the conclusion that the effective management of anticholera measures can only be achieved through coordination of resources on a worldwide scale by a multilateral agency having recognized international health responsibilities. Therefore the Task Force recommends that:

-- A.I.D. reaction to epidemic threat be exercised with and through the multilateral and regional organizations to the maximum feasible extent.

-- Every effort be made by A.I.D. to strengthen the leadership role of the World Health Organization in the worldwide anticholera effort.

-- A strong attempt be made to reduce dependency by the LDCs on U.S. and other donor nations' contributions of critical supplies wherever it is feasible to develop indigenous capability to produce such supplies in the cholera-prone areas of the world.

-- A maximum effort be made to develop indigenous institutions and services in the LDCs to improve their capability to cope with the cholera threat and to diminish their reliance on outside assistance.

V. STRATEGY CONSIDERATIONS

An A.I.D. General Notice dated October 23, 1970 announced the decision of the Administrator to establish a Task Force on Cholera and assigned it two principal functions:

(1) Mobilizing resources and coordinating with the World Health Organization and similar donor organizations on emergency measures to combat cholera in threatened areas.

(2) Developing and recommending a long-range A.I.D. strategy for prevention, control and surveillance of cholera in LDCs.

An over-all strategy for a long-range, worldwide attack on cholera assumes that Pandemic VII will continue to spread to new areas over the next several years (Appendix A-2), and that new foci of endemicity of the disease are being established in areas which recently have been infected. This expectation is based on the advice of cholera experts in the U.S. and abroad who have studied the disease for many years. It is consistent with past experience and it leaves the Agency with the choice of either initiating immediate action to mitigate the serious consequences of continued spread of the disease and preventing its recurrence, or of reacting on a Disaster Relief basis to a continuing series of epidemic emergencies far into the future. This latter alternative is expensive, and it includes the certain concommitant of heavy loss of life, emotional and social disruption, and high economic cost.

Over-all strategy must also accept the premise that there are some elements of a long-range plan which must be implemented without delay in particularly vulnerable areas; other elements which must be initiated as quickly as programmed funds can be made available in order to carry them to completion within the next several years (during the projected duration of the present pandemic); and still other elements which either may be initiated at once or in the more distant future, and which will require a sustained effort over a number of years in order to diminish the threat of major future outbreaks. For planning purposes these are grouped as Phase I, Immediate Activities and Phase II,

Continuing or Long-Range Activities (Section VII). Illustrative proposals for the types of activities which may be considered under the two Phases are shown in Appendix B.

Due to difficulties experienced by A.I.D. in the management of stockpiles over the long-term, the Task Force does not advocate the establishment of stocks of A.I.D. owned strategic supplies as an element of a comprehensive Cholera Plan.

The A.I.D. Working Group on Cholera in October 1970 indicated the basic strategy for the development of a long-term program (Appendix C) by focusing attention on the need for practical approaches to (a) prevent the spread of cholera, (b) improve early warning of the invasion of an area by cholera, and (c) reduce the severity of impact of the disease by adequate treatment and by immunization. This led to the formation of the Expert Panels, whose conclusions (Appendix C) emphasized that a sound strategy must take into consideration the following:

-- Cholera will continue to spread and the threat of this infection to parts of the world where it has been absent for many years is magnified by the current availability of rapid transportation.

-- Cholera has become not only a public health problem, but also an economic, social and political one.

-- Cholera spreads primarily via contaminated water and food.

-- Cholera usually affects individuals of the lower socioeconomic groups living under unsanitary conditions.

-- Cholera caused by the El Tor biotype of Vibrio Cholerae exhibits the "iceberg phenomenon", with the ratio of severe cases to mild or asymptomatic infections in a community being 1:25 to 1:100.

-- Currently available cholera vaccines confer only partial and temporary protection and in varying degrees. Its use may be justified to reduce morbidity and mortality in areas where environmental sanitation is underdeveloped and facilities for treatment are inadequate.

-- Surveillance is the heart of a cholera control program. It is essential to case detection, monitoring spread of the disease, guiding the attack, and measuring progress toward elimination of the reservoir of infection.

-- Cholera therapy can reduce the mortality to less than one per cent in all ages, thereby allaying the panic created by invasion of the disease.

-- Improvement of environmental sanitation, thereby making the country nonreceptive to the cholera vibrio, is the only effective approach to preventing the spread of cholera.

-- Positive health education programs directed toward motivating the individual and the community to improve personal hygiene, and to accept the use of sanitary installations are prime requirements.

Relation of cholera to other acute intestinal diseases

When epidemic cholera appears to have burned itself out and the emotional impact created by widespread clinical cases subsides, official interest wanes and attention and resources are diverted elsewhere. It is paradoxical that the more dangerous period of the pandemic is when discrete transmission is no longer evident. Its control at this time requires a sustained monitoring of all acute diarrheal diseases, and a strategy for cholera must focus specifically on all such diseases. It has been observed that there is a significant increase in the level of severe diarrheas in the period immediately preceding an epidemic outbreak of cholera. Therefore any unusual increase of severe diarrheas must be considered suspect and investigated for the presence of cholera vibrios in order to achieve the "early warning" that is essential to the prevention of epidemic conditions.

While cholera creates psychological havoc because of its rapid and high mortality in adults as well as in children, the human phenomenon of cholera is only one of many varieties of acute diarrhea. Many of these are more persistent than cholera, more widespread, and often with greater mortality effect on specific population groups such as

children and debilitated adults. Shigella (acute dysentery), typhoid, salmonella, and many other infections are highly prevalent. These adverse environmental effects of poor sanitation, all of which are spread by fecal contamination, not only produce illness, but precipitate malnutrition among the vulnerable age groups, i.e., the very young and the old.

It follows that the beneficial outcome of a program to control cholera, by its very nature, also controls an entire group of intestinal diseases caused by environmental pollution.

VI. AVENUES OF ASSISTANCE

Strategic planning recognizes the need to exploit any or all of the several avenues open to A.I.D. through which positive action might be taken in combating cholera on an international level. These are:

Contributions in Funds and in Kind to United Nations Organizations

Such actions would strengthen the leadership role of WHO and the Pan American Health Organization (PAHO) in anticholera activities, and enable them to respond rapidly and effectively to requests for assistance in mitigating the effects of the present pandemic, and to accelerate and expand the Organizations' long-term programs for improvements in environmental sanitation.

Implementation through Regional Organizations

The United States is assisting in the implementation of cholera research programs through its membership in the Southeast Asia Treaty Organization (SEATO); the United States - Japan Cooperative Medical Research Program; and the development of a plan for the surveillance of enteric diseases, including cholera, under Central Treaty Organization (CENTO) sponsorship. Other regional organizations, such as in the Organization for Cooperation and Coordination of the Fight Against Grand Epidemics (OCCGE) in West Africa; the Organization for the Control of Endemic Diseases in Central Africa (OCEAC); and the Committee of the Ministers of Health of the Caribbean should be encouraged to stimulate the development of national cholera control programs among their member states.

Bilateral Agreements

A.I.D. has utilized this instrument for many years in providing technical and development assistance in various endeavors to many countries. The device is still valid for use in selected cases to implement elements of the recommendations of the Expert Panels (Appendix C).

Stimulation of International Banking Institutions

International banking institutions have assisted in the financing of environmental sanitation programs which have the support of resolutions of international meetings. The financing of water supplies programmed in the Resolutions of the Punta del Este Meeting of the Organization of American States (OAS) is an example. The inclusion of environmental sanitation programs as a "Condition Precedent" to the approval of development loans would lend substantial support to efforts aimed at rendering a country nonreceptive to cholera.

Utilization of Local Currency

PL 480 currency might be used to purchase the products of existing indigenous laboratories and pharmaceutical houses to meet the immediate needs of multilateral and regional organizations in mitigating the effects of the current pandemic. Local currency has been used to enable U. S. pharmaceutical manufacturers to assist local entrepreneurs in the development of pharmaceutical industries through the utilization of the Cooley Loan Legislation. It might also be used to support sanitary surveys, and the construction of safe water supplies and excreta disposal systems in small cities and rural areas.

A.I.D./Washington Programmed Funds

Financing is available to A.I.D./Washington for the production and printing of manuals and other publications for the guidance and use of health and sanitation personnel. A simple, well-illustrated manual for the management and treatment of cholera cases for medical and paramedical personnel, with appropriate translations, is an example of the materials needed. Research funds programmed through the Research

Advisory Committee and interregional funds programmed in AID/W may be made available.

VII. CHOLERA PROGRAM PRIORITIES

The recommendations as to what the Agency might do singly or in collaboration with other U. S. agencies and organizations, in assisting multilateral and regional organizations in long-range anticholera planning fall into two classifications: Immediate and Continuing activities. Also it is imperative that priorities be established for their implementation, although it must be recognized that economic, social, emotional and other considerations might preclude strict adherence.

Whereas the only certain safeguard against invasion by the disease is the improvement of environmental sanitation, this is an ultra long-range objective that leaves vulnerable the interim period until such a goal can be achieved. There is an urgent need for assistance during this interim period, and in conformance with the following priorities:

1. Development of systems for surveillance of all diarrheal diseases to provide "early warning" capability to detect the presence of cholera at its earliest stages of invasion.

2. Establishment of treatment capability - both centers and mobile teams - to reduce mortality and continued transmission.

3. Development of indigenous capacity for vaccine production on a regional basis, and promotion of a practical immunization policy.

Nevertheless, a realistic view dictates that in the absence of nominal health delivery systems, such as disease surveillance programs, and adequate medical treatment resources, it is not practical for health authorities to refuse to administer vaccine to populations at risk of epidemic threat; therefore, the development of vaccine resources becomes the highest priority activity in a comprehensive cholera plan.

PHASE I - IMMEDIATE ACTIVITIES

It is proposed that these be implemented in the following order:

Vaccine

Even though present day cholera vaccine confers only partial and short-lived protection, health authorities of the LDCs will continue to request vaccine for use in mass immunization in epidemic situations, or in the face of the threat of invasion. To provide emergency partial protection, to relieve pressure of public opinion and allay fear, it is proposed that:

-- Excess local currency be used to purchase cholera vaccine manufactured by indigenous laboratories abroad for distribution by WHO.

-- Contributions of U.S. manufactured vaccine be made to WHO to meet emergency situations.

-- Assistance to augment, or to include cholera vaccine production, be provided to not less than four strategically located vaccine production laboratories.

Surveillance

Recognizing that surveillance is the heart of a cholera control program it is proposed that:

-- Assistance be provided in the strengthening of not less than 20 indigenous laboratories, including the training of personnel in bacteriological methods and the identification of the causative organisms of enteric diseases, including cholera; and the development of epidemiological services capable of evaluating the results obtained from the bacteriological examination of stool specimens and directing appropriate actions for control measures.

-- Assistance be provided in establishing four pilot surveillance projects. However, prior to the initiation of the projects the existing health and laboratory facilities and personnel capabilities should be surveyed, and a determination made concerning the interest of the authorities of the country in mounting such pilot projects. The countries suggested for such projects are Nigeria, the Cameroons or Liberia, Turkey and Jamaica or Brazil.

-- Assistance be provided to regional organizations such as OCCGE, OCEAC, CENTO and SEATO, in the establishment of programs for the surveillance of enteric diseases. Such programs would include case detection, reporting, analysis of data, epidemiological investigation, and the preparation of a monthly newsletter for distribution to all who have a need to know.

Therapy

The effective treatment of patients severely ill with cholera can reduce the mortality to less than one percent in all ages, thereby allaying the fear created by the invasion of the disease. Therefore, it is proposed that:

-- Assistance be provided in not less than 35 countries in developing in-country treatment resources such as the production of intravenous replacement fluids and the prepackaging of electrolyte-glucose-glycine dry powder mixtures for the preparation of oral replacement fluids.

-- Assistance be provided in the preparation and distribution of a simple, well-illustrated manual on the management and treatment of acute diarrheal diseases for the use of medical, paramedical and nursing personnel, with translations into the languages of the countries where cholera is present or threatened by the invasion of the disease.

Control of Transmission

Recognizing that improvements in environmental sanitation, particularly the provision of safe water supplies and the safe disposal of human wastes, are the only effective methods for the control and prevention of the spread of cholera, it is proposed that:

-- Assistance be provided in carrying out sanitary surveys of existing piped water supply systems, including plant operation, quality and quantity of water delivered and condition of the distribution systems, in not less than 35 countries where cholera is epidemic or threatened with invasion.

-- Consultant teams be provided to not less than 35 countries for the development and implementation of training courses for personnel charged with management and operation of water supply systems.

-- Research programs be developed for the design of efficient, low cost, simple water supply systems for small cities and villages. Pilot projects for the demonstration and introduction of such systems should be developed in not less than 12 countries.

-- Rural sanitation study and demonstration projects, using simple techniques, be set up in six LDCs to demonstrate that a reduction in acute diarrheal diseases can be accomplished through the protection of small water sources and the installation of excreta disposal facilities for hamlets and family dwellings.

Health Education

Recognizing that health education programs are of paramount importance in obtaining acceptance and participation of the individual, as well as the legislative and financial support of the political and administrative echelons of government for improvement of environmental sanitation facilities in both urban and rural areas, it is proposed that:-

-- Appropriate health education programs be developed and implemented which emphasize personal hygiene and the acceptance and use of sanitary installations in the LDCs where cholera is now epidemic or threatened by invasion.

-- Educational programs be developed for government and health personnel at all levels which emphasize the necessity and benefits of programs of environmental sanitation in the control of acute diarrheal diseases, including cholera.

PHASE II - CONTINUING ACTIVITIES

The ultimate goal of anticholera programs is to render countries nonreceptive to the establishment of the cholera vibrio, and to eliminate endemic foci of the disease.

Recognizing that the only effective methods for reaching this goal are the stimulation of, and assistance to the development of programs for the provision of safe water supplies and the safe disposal of human wastes in both urban and rural areas; in programs of health education which emphasize sanitary practices; and continuing

research and evaluation of methods for the control and prevention of cholera, it is proposed that:

1. The illustrative proposals concerned with therapy, surveillance, improvements in environmental sanitation, training of personnel and health education presented in Appendix B be expanded to include all of the LDCs where cholera is epidemic or threatened by the invasion of the disease.

2. Assistance be provided to institutions or agencies for:

-- Research programs for the design of efficient and low cost water treatment and distribution systems for small towns and hamlets.

-- Research programs for the provision of safe water supplies in rural areas.

-- Research programs for the design and development of an efficient and economic method for the disposal of human excreta in urban and rural areas.

--Research directed toward increased understanding of the epidemiology, pathophysiology and immunology of cholera.

-- Research directed toward the production of an immunizing agent which confers complete and long-lasting protection against cholera.

-- Research directed toward the simplification of treatment techniques.

-- Evaluation of the effectiveness of sanitary measures as related to cholera control.

-- Improvements of transport media and bacteriological methods for the identification of the causative agents of enteric diseases.

-- Development of operational epidemiological techniques for the control or mitigation of cholera outbreaks.

-- Evaluation of health education methods and procedures for motivation of individuals and communities toward improved personal hygiene, and their acceptance and use of sanitary measures.

VIII. DIRECT CHOLERA ASSISTANCE BY U.S. AND OTHERS

1. U.S. Government Assistance

The cost to the U.S. Government of direct assistance in cholera emergencies over the past decade probably is in excess of $5,000,000 more than half of which has been borne by A.I.D. appropriations. This average expenditure of approximately $500,000 per year may continue indefinitely unless an investment is made to remove the causal factors that produce the contingencies.

The following table is illustrative of the magnitude and recipients of A.I.D. contributions since 1963. The data does not include contributions made prior to 1963; personnel costs for A.I.D. financed consultants; miscellaneous donations to various countries of supplies and equipment; losses incurred in stockpiling of essential cholera supplies; AID/W support staff costs; assistance provided through use of A.I.D. financed measles-smallpox teams from the Center for Disease Control including vehicles and equipment, in West African countries during the 1970-1971 cholera epidemics; and contributions by other U.S. Government agencies such as Department of Defense, who have provided technician teams, equipment, air transport, etc., as their contribution.

BURMA	1963	$ 20,000
VIET NAM	1964	1,813,326
IRAN	1965	46,229
SUDAN	1966	21,875
IRAQ	1966	34,977
SYRIA	1966	39,074
WHO (CAMBODIA)	1967	2,488
TURKEY	1967	121,607
EAST PAKISTAN	1967	1,521
CENTO	1967	2,335
WHO (MALAYSIA)	1968	9,196
WEST PAKISTAN	1968	116,183
KOREA	1969	155,222
CYPRUS	1970	1,100
ETHIOPIA	1970	25,000
IVORY COAST	1970	9,040
WHO (Special Requests)	1970-1971	236,000
CARRIED FORWARD	Sub-total	$2,655,173

BROUGHT FORWARD	Sub-total	$2,655,173
Estimated value of other U. S. Contributions		2,500,000
	Total	$5,155,173

2. Assistance by Other Donors

For a variety of reasons, usually political, the full magnitude of assistance by donor countries is not always publicized. Appendix A, Item 6, indicates by country the quantities of vaccine, rehydration fluid and other supplies provided by WHO, and the WHO source of funding for these items during 1970. The WHO Voluntary Fund for Health Promotion, Special Account for Cholera Programme includes voluntary contributions from member states, but whose identities are not indicated.

In recognition of the importance of the anticholera activities of WHO and A.I.D.'s own desire that WHO assume a greater role of leadership in the effort, United States Missions have been instructed to refer requests for assistance to WHO for action. In addition to the United States, Canada, China, Denmark, Federal Republic of Germany, France, Hungary, India, Iran, Malaysia, Pakistan, Philippines, Sweden, Switzerland, Thailand, United Arab Republic (Egypt) and the Swiss Serum Institute donated cholera vaccine to WHO during 1970-1971. Appendix A, Item 5, indicates quantities of vaccine donated between 1 August 1970 - 16 April 1971.

In addition, a wide variety of other donors such as foreign voluntary agencies, missionary groups, CARE, League of International Red Cross Societies, foreign commercial interests, etc., regularly contribute supplies and services which undoubtedly have totalled many millions of dollars during the course of Pandemic VII.

APPENDIX "A"

RELEVANT INFORMATION

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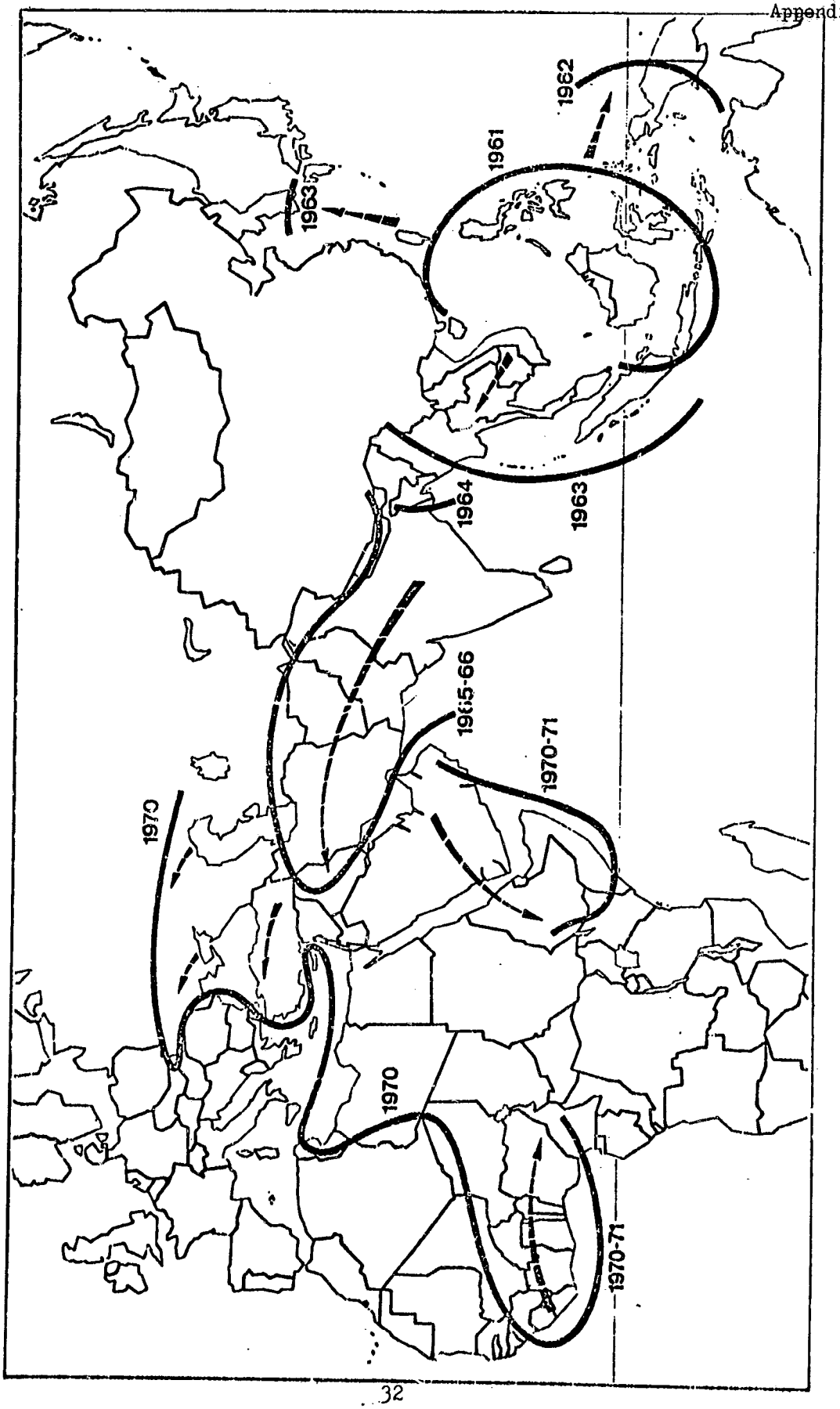
EXTENSION OF CHOLERA 1961-1971



WORLD CHOLERA SITUATION

CATEGORY I/1		CATEGORY II /2		CATEGORY III /3	CATEGORY IV
Infected Countries-August 1970 to May 31, 1971		Additional Countries under Immediate Threat in 1971		Possible New Areas of Infection 1971-1975	Areas of Pos .ble Importation with low Risk of Epidemics
		A F R I C		A	
Cameroons	Niger	Angola	Portuguese Eq.Africa	South Africa	
Dahomey	Nigeria	Botswana			
Chad	Sierra Leone	Burundi	Senegal		
Ethiopia	Somali Rep.	Central Africa Republic	Mozambique		
Ghana	Sudan		Rhodesia		
Guinea	Togo	Congo (Brazzaville)			
Ivory Coast	Tunisia	Congo (Kinshasa)	Rwanda		
Kenya	UAR (Egypt)	Gabon	Southwest Africa		
Liberia	Upper Volta	Gambia			
Mali		Libya	Spanish Morocco		
		Lesotho			
		Malagasy Rep.	Tanzania		
		Malawi	Uganda		
		Mauritania	Zambia		
		Morocco			

/1 Countries infected between August 1, 1970 and May 31, 1971. Includes countries listed by WHO, as well as those unofficially reported by reliable sources. Countries infected and declared cholera free are assumed to be still harboring the disease.

/2 Countries under suspicion of having cases, but without official confirmation.

/3 Countries and areas which are non-contiguous to infected countries or areas of immediate risk, but which harbor conditions which render them susceptible to infection.

/4 Countries or areas where importation of cholera is possible, but whose health and medical resources and level of environmental sanitation render them unsusceptible to transmission.

WORLD CHOLERA SITUATION

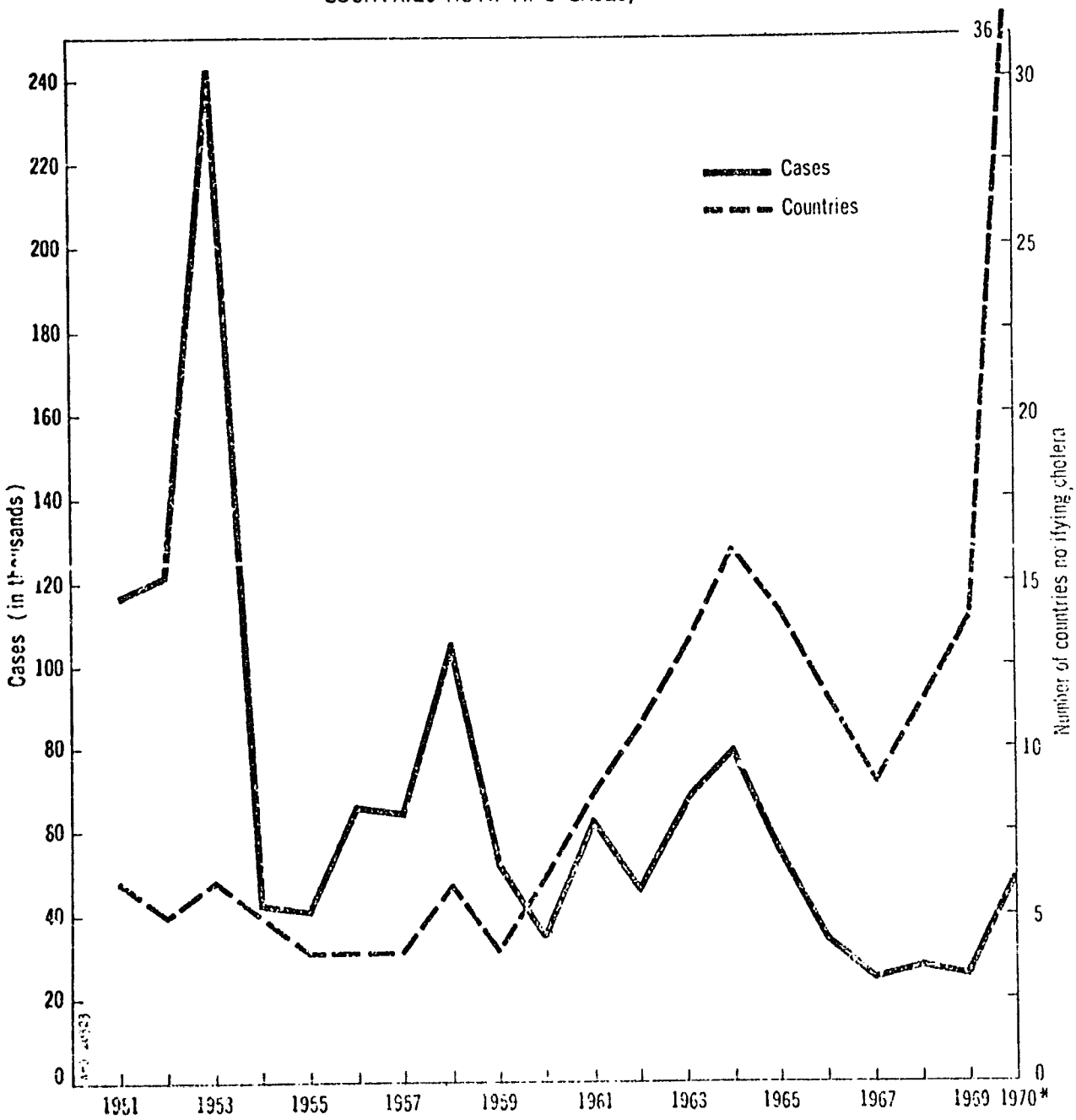
CATEGORY I /1	CATEGORY II /2	CATEGORY III /3	CATEGORY IV /4
Infected Countries August 1970 to May 31, 1971	Additional Countries under Immediate Threat in 1971	Possible New Area of Infection 1971-1975	Areas of Possible Importation with low Risk of Epidemics
	NEAR EAST AND SOUTH ASIA		
Afghanistan Cyprus India Iran Israel Jordan Lebanon Muscat & Oman Nepal Pakistan (East) Pakistan (West) Kuwait Qatar Saudi Arabia Syria Turkey	Iraq Yemen		
	EAST ASIA AND FAR EAST		
Indonesia Malaysia Philippines Viet Nam Rep. Burma Brunei Korea	Singapore Thailand Cambodia Laos	Pacific Islands Taiwan	Australia Japan New Zealand

NOTE: No information from Mainland China available.

WORLD CHOLERA SITUATION

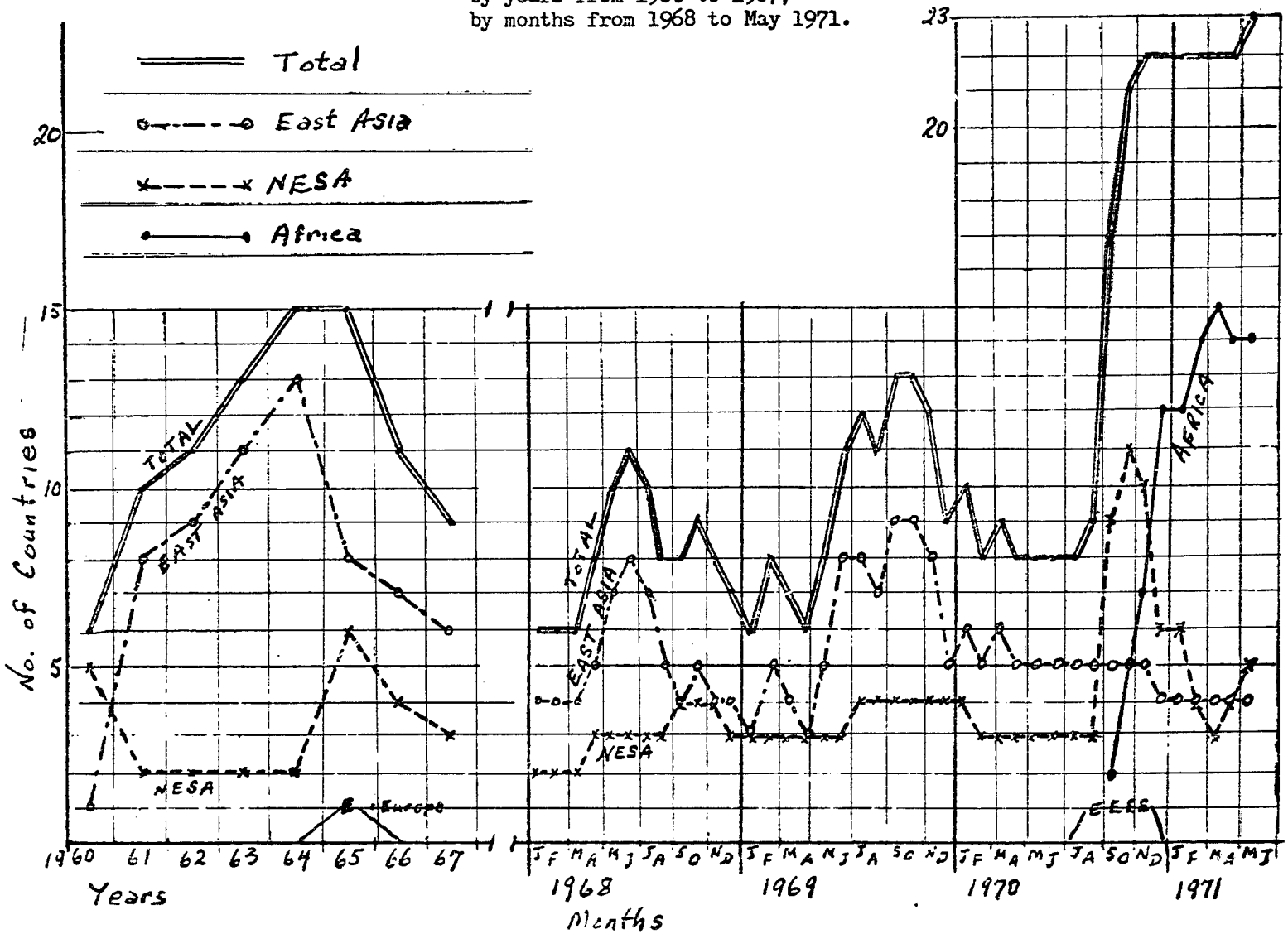
CATEGORY I /1	CATEGORY II /2	CATEGORY III /3	CATEGORY IV /4
Infected Countries August 1970 to May 31, 1971	Additional Countries under Immediate Threat in 1971	Possible New Area of Infection 1971-1975	Areas of Possible Importation with low Risk of Epidemics
	EUROPE		
Bulgaria Yugoslavia Czechoslovakia Hungary Russia	Albania Greece Romania Portugal Italy Spain	Azores Canary Islands Cape Verde Islands	United Kingdom France
	THE AMERICAS		
	Brazil Jamaica	Caribbean Islands Central America South America	Canada United States

INCIDENCE OF CHOLERA AND NUMBER OF COUNTRIES NOTIFYING CASES, 1951-1970



Figures according to World Health Statistics Reports.
* Provisional figures

NUMBER OF COUNTRIES OFFICIALLY REPORTING CHOLERA, BY REGIONS
by years from 1960 to 1967;
by months from 1968 to May 1971.



CHOLERA VACCINE AND OTHER SUPPLIES DONATED TO WHO SPECIAL ACCOUNT
FOR THE CHOLERA PROGRAMME DURING EMERGENCY SITUATION
AUGUST 1970 - APRIL 1971

Country	Quantity (doses)	Value (US$)
1 August - 31 December 1970		
Canada	255 350	49 067
China	300 000	1 800
Denmark	50 000	15 000
Federal Republic of Germany	200 000	16 394
France	1 000 000	75 676
Malaysia	200 000	4 000
Hungary	200 000	2 667
Pakistan	250 000	5 000
India	1 000 000	15 000
Iran	2 000 000	131 148
Philippines	50 000	750
Sweden	325 000	32 000
Switzerland	1 000 000	46 296
Thailand	300 000	4 500
United States of America	10 000 000	180 000
United States of America (tetracycline capsules, syringes, needles)	-	12 270
United Arab Republic	28 440 000	568 000
Swiss Serum Institute	925 000	42 823
Total period August - December 1970	46 495 350	1 202 391
1 January - 16 April 1971		
France	500 000	38 043
Japan (tetracycline capsules, TCBS Agar Eiken)	-	7 140
Switzerland	1 000 000	46 296
Total period January - April 1971	1 500 000	91 479
Total 1 August 1970 - 16 April 1971	47 995 350	1 293 870

CHOLERA VACCINE, REHYDRATION FLUID AND OTHER SUPPLIES
PROVIDED TO COUNTRIES DURING EMERGENCY SITUATION, 1970

Legend

EB SpFd = Executive Board Special Fund for Emergencies

Reg = Regular budget

VFHP = Voluntary Fund for Health Promotion Special Account for Cholera Programme

Country or territory	Vaccine (thousand doses)			Rehydration fluid (litres)		Tetra-cycline (000's)	TCBS media (lb)	Diag-nostic sera (sets)
	EB SpFd	Reg	VFHP	EB SpFd	Reg	Reg	Reg	Reg
Abu Dhabi		30						
Afghanistan	25		500					
Algeria	50							15
Botswana		0.5						
Burundi	1		3.5					3
Cameroon	10			250		0.3	5	5
Central African Republic	30			250		0.3	5	
Chad	30			250		0.3	5	
Comoro Archipelago	2							
Congo, Democratic Republic of	30			300		0.4	10	5
Cyprus			850	250		5.0	2	
Dahomey	20		50	250	1 008	3.3	5	
Dubai			125					
Equatorial Guinea	5		500	100		0.2	3	
Ethiopia			8 900	4 000	1 516		2	
Gabon	10			100		0.2	3	
Gambia		10		250		0.3	5	5
Ghana	55		300	500		1.0	5	3
Guinea		400			4 800	100	7	3
Israel	700							
Ivory Coast	58	452	675.26	1 500		1.3	12	2
Kenya	25				250	0.3	5	2

Country or territory	Vaccine (thousand doses)			Rehydration fluid (litres)		Tetra-cycline (000's)	TCBS media (lb)	Diag-nostic sera (sets)
	EB SpFd	Reg	VFHP	EB SpFd	Reg	Reg	Reg	Reg
Lebanon			3 650		2 000			
Lesotho	2	0.2						
Liberia	30	20	50	3 000		4.9	10	2
Libyan Arab Republic			500					
Madagascar			30		304	0.4	1	1
Malawi	2							
Mali			700	1 000	1 000	4.8	10	2
Mauritania	30			500		0.7	5	
Mauritius		10			100	0.2	3	3
Morocco					250			
Niger	30			250		0.3	5	
geria	100		725	1 000		1.3	10	2
People's Democratic Republic of Yemen			700		1 000	200		
People's Republic of the Congo		65		500		1.7	5	5
Qatar			15					
Republic of Korea			200					
Saudi Arabia			3 000					
Senegal	10		200	2 000		2.9	10	2
Sierra Leone	150			1 500		5.0	10	3
Somalia			2 100		2 050	5.0		1
St Helena		0.1						
Sudan			7 000	1 000				
Swaziland	6	0.2						
Syria			1 000					
Togo	20		150	250	350	3.3	5	1
Tunisia	35	0.2	3 714.84		100			3
Turkey		775	1 375					
nda	50			250	250	0.7	5	1

Country or territory	Vaccine (thousand doses)			Rehydration fluid (litres)		Tetra-cycline (000's)	TCBS media (lb)	Diag-nostic sera (sets)
	EB SpFd	Reg	VFHP	EB SpFd	Reg	Reg	Reg	Reg
United Republic of Tanzania			50	500		0.7	5	1
Upper Volta	30			250		0.3	5	1
Yemen			250					
Zambia	25				100	0.2	3	
Other		1.1						
UNRWA		50	400					
Total	1 571	1 814.3	37 713.15	20 000	15 078	345.3	166	71

PROPOSAL FOR POSSIBLE USAID COOPERATION WITH WHO IN THE FIELD OF CHOLERA CONTROL

(As suggested informally by WHO)

At the present moment at the midst of the Seventh Pandemic of cholera the need for close cooperation of all agencies dealing with the combat of cholera on international level is needed. The following principles are suggested as guidelines for promotion of cooperation between USAID and WHO in the field of cholera in order to achieve the best results with available resources through joint efforts.

1. General principles of control of cholera

1.1 Aims

1.1.1 The immediate aim is to mitigate the present pandemic.

1.1.2 Further goal is to improve sanitary and health conditions in newly invaded areas so that cholera could be eradicated there and these areas rendered, if possible, non-receptive for cholera.

1.1.3 Ultimate goal would be to improve sanitary and health conditions in the endemic foci of cholera and thus make impossible further spread of cholera from them and possibly also eradicate the disease in these foci as well.

2. Programme of Action

The programme of cholera control has been stated in World Health Assembly and Executive Board resolutions[1] and by a number of scientific consultative bodies[2] (Expert Committees and Scientific Groups on cholera, etc.). Relevant documents are listed in the references. According to the principles and views expressed in the above documents WHO programme of action was formulated. The programme consists of the following main types of activities in the field of (a) cholera control and (b) cholera research.

2.1 Cholera control programmes

This consists of emergency assistance and long-term programmes based on national cholera control programmes.[4]

2.1.1 Emergency Assistance

In case of invasion of cholera into a country WHO

2.1.1.1 provides technical advice (consultants, clinicians, bacteriologists, epidemiologists, sanitary engineers, vaccine and/or rehydration fluid production experts, etc.)

2.1.1.2 supply of rehydration fluid and antibiotics

2.1.1.3 diagnostic reagents, sera and media

2.1.1.4 disinfectants (if required)

2.1.1.5 training of local professional and ancilliary staff

2.1.1.6 diverts other WHO staff and facilities (e.g. malaria eradication and/or smallpox eradication teams) to assist in dealing with cholera.

2.1.2 Short-term programmes

These comprise, besides above,

2.1.2.1 strengthening of rehydration and treatment centres

2.1.2.2 strengthening of diagnostic laboratory facilities

2.1.2.3 strengthening of epidemiological unit

2.1.2.4 strengthening of health services in general

2.1.2.5 improvement of sanitary conditions

2.1.2.6 training of health personnel

2.1.2.7 health education of the public

2.1.3 Long-term programmes

These comprise, besides above,

2.1.3.1 establishment of rehydration fluid production

2.1.2.2 establishment of vaccine production laboratories

2.1.2.3 establishment of rehydration and treatment centres

2.1.2.4 programme for sanitation (water supply and excreta disposal) for affected areas.

2.2 Cholera Research Programme

This programme consists of assistance to research institutions in pursuing studies of direct importance for cholera control.[2, 3] Main activities are as follows:

2.2.1 Study of the cholera vaccines aiming at production of more effective and less reactogenic vaccines[2] (e.g. toxoids and live vaccines).

2.2.2 Study aimed at improvement of treatment techniques especially for children (e.g. oral rehydration maintenance, therapy, etc.[3])

2.2.3 Study of the effectiveness of various environmental sanitation measures in control of cholera (e.g. studies of effect of water supplies and privies in Philippines)[4].

2.2.4 Study of bacteriological and serological procedures to improve diagnostic techniques[2,3].

2.2.5 Study of basic importance for understanding of pathophysiology, immunology, etc., of cholera[2,3].

The improvement of control measures is impossible without continuous research and evaluation of various existing and new control measures.

3. Priorities

At present priorities in mitigating the 7th pandemic are as follows:

3.1 Areas and population of the world.

3.1.1 Control and prevention of cholera in newly invaded countries in East and West Africa and in the Middle East.

3.1.2 Preparation of vulnerable areas to which cholera could spread (Caribbean, Latin America) to prevent and possibly combat cholera by improvement of sanitation and health services (surveillance of diarrheal diseases in particular).

3.2 Activities and Methods

3.2.1 Sanitation is a most important and essential measure in the control of cholera. Even with limited resources considerable improvements and impact on cholera can be made.

3.2.2 Vaccination is considered a necessity only when sanitation cannot be applied. Mass immunization in the moment of invasion of cholera in new areas is inevitable because of the pressure of public opinion and governments, but soon after efforts should be directed towards sanitation.

3.2.3 Health Education of the public as well as information of authorities is essential for success of control measures; sanitation in particular.

3.2.4 Training of medical staff and auxiliaries in countries with no or little experience in cholera is essential for saving human lives and avoiding panic.

3.2.5 Surveillance of all diarrheal diseases is of paramount importance for any cholera control programme. Details of the methods are to be found in WHO publications.[3,4].

3.3 Strategies of cholera control have been clearly stated in WHO documents[4] and could be found there.

4. Proposed joint action for which USAID assistance is needed.

4.1 Production of rehydration fluid

Assistance to national rehydration fluid-producing laboratories in:

a) West Africa (Ghana, Nigeria, Senegal).

b) East Africa (Kenya, Ethiopia).

c) Middle East (Turkey, Iran, Iraq).

d) Latin America.

4.2 Production of Vaccine

Assistance to national vaccine production laboratories:

a) Senegal (Dakar: Institute Pasteur).

b) Turkey (Ankara: Reyfik Seydam Institute).

c) India (Kasauli: C.R.I.).

d) possibly other countries.

4.3 Surveillance

Strengthening of laboratories in order to provide services for surveillance:

a) West Africa - all countries

b) East Africa - all countries

c) Latin America - all countries (with emphasis on Caribbean)

d) Middle East

4.4 Research

Assistance to the research programmes.

4.4.1 Sanitary measures (water, excreta disposal similar to study done in the Philippines). The study and evaluation of sanitary measures in:

Indonesia, Malaysia, Nigeria, Ghana, Kenya (one or more of the Caribbean countries or Latin American countries).

4.4.2 Study of effectiveness of new types of vaccines (when they become available) and of various immunization schedules (intradermal versus subcutaneous in view of saving vaccine).

4.4.3 Study of effectiveness of various control programmes: Operational study of delivery of the services and their effectiveness.

When and if an agreement on principle is made and certain activities selected, we will be ready to make detailed proposals.

5. References

1. WHO (1969) Handbook of Resolutions and Decisions of the World Health Assembly and the Executive Board (June 1948 - February 1969), 10th ed., Geneva.
2. WHO Scientific Group on Cholera Immunology (1969) Report (World Health Org. techn. Rep. Ser., No. 414).
3. WHO Expert Committee on Cholera (1967) Second Report (World Health Org. techn. Rep. Ser., No. 352).
4. Strategy of Cholera Control (1971) WHO unpublished document BD/CHOLERA/71.1.
5. Principles and practice of cholera control (1970) World Health Org. Public Health Papers, No. 40).

APPENDIX "B"

ILLUSTRATIVE PROPOSALS

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Illustrative Proposals

This appendix to the Interim Report comprises a number of [illegible] that have been developed for the purpose of highlighting the recommendations made by the four expert panels. They are illustrative of the types of activities which are essential to a comprehensive attack on cholera, whether sponsored by donor countries, multilateral or regional organizations, or by individual local governments.

The development of these or other proposals into positive action programs is contingent upon careful scrutiny by experts in the several disciplines involved.

TRAINING COURSES IN THE MANAGEMENT AND OPERATION OF WATER SUPPLY SYSTEMS

1. Purpose:

To provide assistance to multilateral and regional organizations for the development of training courses for management and operations personnel of water supply systems in the cities and towns of lesser developed countries where acute diarrheal diseases, including cholera, are endemic.

2. Problem:

Although many cities and towns of the lesser developed countries have piped water supply systems of some magnitude, they are usually deficient in operation and maintenance.

3. Plan of Action:

It is proposed that assistance be provided to multilateral and regional organizations in the development and implementation of training courses for personnel charged with the management and operation of water supply systems in about 35 countries. Assistance would include the provision of consultants for preparation of courses of instruction, training facilities and a Water Supply Management and Operations Manual for the guidance of personnel charged with management and operation of individual water systems. Additional consultants would be provided for implementation of the courses.

4. Estimated Costs:

a.	Preparation and publication of 10,000 manuals	$ 25,000
b.	Consultant team for preparation of a programmed course of instruction	10,000
c.	Implementation of training courses - 35 countries @ $10,000 per country	350,000
	Total.	$385,000

WATER MANAGEMENT CONSULTANT TEAMS

1. Purpose:

   To survey the management of water supply and excreta disposal utilities and recommend improvements in major cities of 35 countries which are infected, or threatened with infection by cholera.

2. Problem:

   Community water and sewer utilities in the lesser developed countries usually operate at a financial loss with no fair share return on initial investment to be plowed back into operational expenses and improvements to the systems. As a result, the growing populations of towns and cities are being provided with increasingly less adequate sanitary utilities and are being exposed to higher risk of infection by all waterborne diseases, including cholera. This problem can be largely overcome by applying modern utilities management techniques, including rate structures, installation costs, improved operational practices, etc.

3. Plan of Action:

   It is proposed that two/three-man consultant teams be sent to 35 countries to survey the quality of management of sanitary utilities in the principal cities of each and to recommend improvements and training programs where appropriate. This activity may be developed jointly with WHO and may include grant assistance to the WHO Special Fund for Community Water Supplies.

4. Estimated Costs:

   Consultant teams - 35 countries at an estimated cost of $18,000 per country.

   Total. $630,000

SANITARY ENGINEERING CONSULTANTS

1. Purpose:

To provide consultant teams to carry out sanitary surveys of existing water supply and excreta disposal systems, including design, operation, quality and quantity of water delivered and the condition of the distribution systems and treatment facilities, in the major cities of 35 countries where acute diarrheal diseases, including cholera, are epidemic to determine what assistance may be required to upgrade them.

2. Problem:

Cholera can occur in any part of the world where overcrowding and poor sanitation exists. As a result of the population explosion and the influx of people from rural areas, the systems and facilities for delivery of safe water and disposal of human wastes in many cities of the countries where cholera is endemic or threatened with invasion are overtaxed or outmoded.

3. Plan of Action:

It is proposed that consultant teams survey existing water supply systems in the principal cities of 35 countries where cholera is endemic or threatened with the invasion of the disease; to recommend changes and assistance required to upgrade existing water systems, or to provide systems which will supply sufficient safe water to meet daily requirements.

4. Estimated Costs:

Consultant teams - 35 countries @ an average of $15,000 per country.

Total. $525,000

RURAL SANITATION DEMONSTRATION AND STUDY PROJECTS

1. Purpose:

To demonstrate that the incidence of diarrheal diseases, including cholera, can be reduced significantly among scattered rural populations by low-cost, simple methods of water source protection and sanitary excreta disposal; to study cost factors and benefits of such demonstrations.

2. Problem:

A principal factor in the transmission of cholera and other diarrheal diseases is fecal contamination of drinking water. The majority of countries now infected or threatened by the pandemic have predominantly rural populations, usually scattered in small villages. Study projects have been done by WHO in the Philippines and elsewhere which indicate that simple, primitive techniques of sanitary protection of water supplies for single families and small villages can be done at small per capita cost. The same applies to simple, water-seal pit privies. A study of the results of installations in barrios of approximately 100 families indicated significant reductions in incidence of diarrheal diseases when either protected water sources or pit privies were installed and much greater when both were constructed. WHO has suggested repeating the demonstrations in other areas in order to derive more exact cost figures and to make a definitive analysis of the results in terms of prevention of transmission of cholera and other diarrheal diseases.

3. Plan of Action:

It is proposed that a demonstration area be set up in six countries, each area to consist of 8-12 small villages having a total population of 5,000 - 6,000. The countries are to be selected for epidemiological importance relative to cholera, as well as representing a variety of cultural and climatic features. In each demonstration area some villages will be provided with protected water sources, some with water-seal type pit privies and some with both. Installations will use only local materials and local effort requiring minimal training. Training, supervision and studies of results will be performed by WHO or by appropriate regional organizations, possibly with grant assistance.

4. Estimated Costs:

It is estimated that such installations would cost about $2 per capita. Six countries x 6,000 people x $2 per person.

Total. $72,000

PILOT PROJECTS FOR THE INTRODUCTION OF LOW COST WATER SUPPLIES IN SMALL TOWNS

1. Purpose:

To provide assistance in the establishment of pilot projects for the demonstration and introduction of efficient, low cost, simple to operate water supply systems for small cities and villages in not less than 12 African or Middle East countries.

2. Problem:

Improvements in environmental sanitation, including the provision of safe water, is the only effective method for control and prevention of acute diarrheal diseases, including cholera. However the installation and operation of many of the conventional methods for supplying safe water are beyond the financial and operational capabilities of many of the towns and villages of the lesser developed countries.

3. Course of Action:

It is proposed that assistance be provided to multilateral and regional organizations for the introduction of low cost, simple to operate water supply systems, such as those developed by A.I.D. sanitary engineers in South Vietnam. Assistance will consist of the cost of installation of water supply systems in not less than four small towns of two to three thousand people, in each of 12 African and Middle East countries. It is anticipated that sanitary engineering personnel of the multilateral and regional organizations will provide necessary supervision for construction and operation of the systems.

4. Estimated Costs:

Four water supply systems in each of 12 countries @ $5,000 per system.

Total $240,000

CHOLERA VACCINE PRODUCTION

1. Purpose:

To provide assistance to strategically located vaccine (human) producing laboratories for the production of cholera vaccine.

2. Problem:

Ample supplies of cholera vaccine are essential to immunization programs in epidemic situations, or in the face of invasion of the disease. Production capability of cholera vaccine is limited or non-existent in many countries recently infected or threatened by the disease.

3. Plan of Action:

It is proposed that consultant teams survey the vaccine production capabilities of not less than four laboratories in selected countries for the purpose of assisting each laboratory to produce about ten million milliliters of cholera vaccine per year. The consultants will assess current availability of personnel and equipment, and additional equipment required to produce the above quantities of vaccine.

4. Estimated Cost:

a.	Consultants - 4 countries @ $3,000 each	= $12,000.
b.	Equipment - 4 laboratories @ $50,000 each	= $200,000.
	Total	$212,000.

DEVELOPMENT OF CHOLERA TREATMENT RESOURCES

1. Purpose:

   To provide assistance to selected countries in developing in-country production of intravenous replacement solutions, and the prepacking of an electrolyte-glucose-glycine dry powder mixtures for the preparation of oral replacement solutions.

2. Problem:

   The administration of replacement fluids designed to replace the water and electrolytes lost in stool of patients severely ill with cholera can reduce the mortality to less than one per cent in all ages. Nevertheless, supplies of intravenous replacement fluids in the majority of countries infected are inadequate to treat patients with cholera in an epidemic of any magnitude, and the use of oral replacement fluids is virtually unknown.

3. Plan of Action:

   It is proposed that consultant teams survey the production capabilities for intravenous replacement solutions and for prepackaged, dry powder mixtures for the preparation of oral replacement solutions in not less than 35 countries where diarrheal diseases, including cholera, are epidemic. Goals should be to provide assistance required to produce 700,000 liters of intravenous replacement solution (175,000 patients receiving an average of four liters each) and prepackaging of sufficient chemicals (one package per liter) to make up 1.75 million liters of oral replacement solutions (175,000 patients receiving an average of 10 liters each) annually.

4. Estimated Costs:

   a. Consultants - 35 countries @ $1,500 each . . . . . .$ 52,500

   b. Equipment and supplies, including bottles to produce 700,000 liters of intravenous replacement solutions annually @ $15,000 per country. 525,000

   c. Equipment and supplies to package 1.75 million packages of oral replacement solution mixture annually @ $5,000 per country. 175,000

   Total $752,500

PREPARATION OF A MANUAL FOR THE MANAGEMENT AND TREATMENT OF ACUTE DIARRHEAL DISEASES

1. Purpose:

To provide assistance in the preparation and publication of a simple, well-illustrated manual on the management and treatment of acute diarrheal diseases for the use of medical, paramedical and nursing personnel; translation into the languages of the countries where cholera is now present or threatened by the invasion of the disease.

2. Problem:

Cholera is generally of little concern to a country until it is actually present, or at its frontiers. By this time an emergency situation exists and there are frantic requests for assistance to allay the emotional and economic consequences resulting from the presence of the disease, and the high mortality in untreated cases. Recognizing that the effective treatment of patients severely ill with cholera can reduce the mortality in all ages to less than one per cent, the availability of teaching materials for the instruction of health personnel on how to deal with and treat the disease is important.

3. Plan of Action:

It is proposed that assistance be provided for the preparation and publication of a simple, well-illustrated manual for the management and treatment of acute diarrheal diseases for medical, paramedical and nursing personnel. In addition to the administration of single formula intravenous and oral replacement fluids and antibiotics, the manual should emphasize the importance of round-the-clock care of the cholera patient by a trained staff, the use of the cholera cot in collecting and measuring the diarrheal discharges, and the use of charts for recording the input and output of fluids.

4. Estimated Cost:

Preparation, translation into ten languages, and publication of 25,000 manuals - $50,000.

STRENGTHENING OF PUBLIC HEALTH LABORATORY AND EPIDEMIOLOGICAL SERVICES

1. Purpose:

To provide assistance in strengthening indigenous public health laboratories, including training personnel in bacteriological methods and identification of the causative organisms of acute diarrheal diseases including cholera; development of epidemiological services capable of evaluating results obtained from laboratory examinations, making epidemiological investigations of outbreaks, and issuing instructions required for control measures.

2. Problem:

In many of the lesser developed countries where cholera is epidemic facilities and trained personnel essential to identification of the causative organism of acute diarrheal diseases, epidemiological investigations of outbreaks, guiding the attack, and measuring progress toward control of acute diarrheal diseases, including cholera, are minimal. Upgrading of laboratory and epidemiological services is essential in order to develop an early warning system for alerting health authorities to the presence, distribution and incidence of cholera within a country.

3. Plan of Action:

It is proposed that consultant teams survey the availability of health and laboratory facilities, personnel resources, and the level of interest and support from local governments in strengthening the public health laboratory and epidemiological services of the health departments of 20 countries where cholera is epidemic or threatened with infection.

4. Estimated Costs:

a.	Consultants - surveys of 20 countries @ $3,000 per country	$ 60,000
b.	Equipment and supplies for upgrading 20 laboratories @ $10,000 per laboratory	200,000
c.	Training of 40 laboratory technicians in bacteriological methods @ $2,000 per technician	80,000
d.	Training of 20 epidemiologists @ $3,000 per epidemiologist	60,000
	Total.	$400,000

PILOT PROJECTS FOR THE INTRODUCTION OF DIARRHEAL DISEASE SURVEILLANCE PROGRAMS

1. Purpose:

To provide assistance in the establishment of pilot projects for demonstration of country-wide surveillance of acute diarrheal diseases including cholera in selected countries where cholera is epidemic, or threatened with the invasion of the disease.

2. Problem:

Surveillance is the heart of programs for the control of acute diarrheal diseases including cholera. Nevertheless in many countries where cholera is epidemic or at risk, facilities and trained personnel essential to laboratory identification, case detection, epidemiological investigations of outbreaks, guiding the attack, and measuring progress toward control and elimination of acute diarrheal diseases are minimal.

3. Plan of Action:

It is proposed that consultant teams survey the health and laboratory facilities, personnel capabilities, and the level of interest and support of the governments of Nigeria, the Cameroons or Liberia, Turkey, and Jamaica or Brazil with the view toward establishing country-wide surveillance programs for acute diarrheal diseases. These would serve both to identify the presence distribution and evidence of diarrheal diseases in general, and as an early warning system against invasion of cholera and for monitoring movements of cholera in those countries now infected.

4. Estimated Cost:

a.	Consultants - surveys of 4 countries @ $5,000 per country	$20,000
b.	Laboratory equipment and supplies for upgrading laboratories @ $15,000 per country	$60,000
c.	Training of 10 laboratory technicians @ $2,000 per person	20,000
d.	Training of 4 epidemiologists @ $3,000 per person	12,000
	Total.	$112,000

ASSISTANCE TO REGIONAL ORGANIZATIONS IN ESTABLISHING DIARRHEAL DISEASE SURVEILLANCE PROGRAMS

1. Purpose:

To provide assistance to regional organizations such as the Organization for Cooperation and Coordination of the Fight Against Grand Epidemics (OCCGE) in West Africa, the Organization for the Control of Endemic Diseases in Central Africa (OCEAC), the Central Treaty Organization (CENTO), the South East Asia Treaty Organization (SEATO) and the Pan American Health Organization (PAHO) to stimulate establishment of surveillance programs for acute diarrheal diseases.

2. Problem:

Surveillance is essential to the control of acute diarrheal diseases, including cholera. In the majority of the member states of the regional organizations mentioned above, facilities and trained personnel necessary for laboratory identification and case detection, epidemiological investigations, collection of morbidity and mortality data, analysis and reporting of data and planning for control measures based on sound epidemiology are inadequate.

3. Plan of Action:

It is proposed that the regional organizations be approached for the purpose of stimulating them to encourage and assist member states to establish surveillance programs for acute diarrheal diseases. Such programs would include laboratory identification, case detection, epidemiological investigations of outbreaks and analysis and reporting of data. The establishment of Preventive Medicine Mobile Teams such as those now operating in Iran should be considered. Such teams should be responsible for conducting initial investigations of outbreaks of acute diarrheal diseases and should have capability to establish treatment facilities. Seminars, training courses and observation visits to centers where cholera research is in progress should be arranged for senior laboratory personnel, clinicians and epidemiologists who have responsibility for treatment and surveillance of acute diarrheal diseases.

4. Estimated Costs:

The implementation of the above Plan of Action could be accomplished by means of grants or bilateral arrangements with the respective regional organization. Total. . . . $50,000.

HEALTH EDUCATION

1. Purpose:

To provide assistance for development of health educational programs which emphasize personal hygiene, acceptance and proper use of sanitary installations for the general population; and orientation of the political and administrative echelons of governments to the need for programs of environmental sanitation for control and prevention of acute diarrheal diseases, including cholera.

2. Problem:

Cholera usually affects individuals of the lower socio-economic groups living under unsanitary conditions. Even the best sanitary installations and the most enlightened public health measures remain ineffective when they are not accepted by everybody, or properly employed, or accompanied by personal hygiene practices that are acquired by effective health education and training. Legislative and financial support of governments is essential to the development and operation of adequate programs of environmental sanitation.

3. Plan of Action:

It is proposed that a plan be developed jointly with the World Health Organization for the purpose of assisting in the development of (1) health education programs which emphasize personal hygiene and the acceptance and use of sanitary installations for the population in general; and (2) educational programs for all levels of government and health personnel to emphasize the necessity and benefits of programs of environmental sanitation to the control and prevention of acute diarrheal diseases in countries where cholera is epidemic or at risk.

4. Estimated Costs:

Implementation of the above Plan of Action might be financed by the Voluntary Fund for Health Promotion Special Account for the Cholera Programme of the World Health Organization.

Total. . . . $20,000.

SUMMARY BUDGET

TRAINING COURSES IN THE MANAGEMENT AND OPERATION OF WATER SUPPLY SYSTEMS	$385,000
WATER MANAGEMENT CONSULTANT TEAMS	630,000
SANITARY ENGINEERING CONSULTANTS	525,000
RURAL SANITATION DEMONSTRATION AND STUDY PROJECTS	72,000
PILOT PROJECTS FOR THE INTRODUCTION OF LOW COST WATER SUPPLIES IN SMALL TOWNS	240,000
CHOLERA VACCINE PRODUCTION	212,000
DEVELOPMENT OF CHOLERA TREATMENT RESOURCES	752,500
PREPARATION OF A MANUAL FOR THE MANAGEMENT AND TREATMENT OF ACUTE DIARRHEAL DISEASES	50,000
STRENGTHENING OF PUBLIC HEALTH LABORATORIES AND EPIDEMIOLOGY SERVICES	400,000
PILOT PROJECTS FOR THE INTRODUCTION OF DIARRHEAL DISEASE SURVEILLANCE PROGRAMS	112,000
ASSISTANCE TO REGIONAL ORGANIZATIONS IN ESTABLISHING DIARRHEAL DISEASE SURVEILLANCE PROGRAMS	50,000
HEALTH EDUCATION	20,000
TOTAL.	$3.448,500
CONTINGENCIES, 20% . .	689,700
GRAND TOTAL	$4,138,200

APPENDIX "C"

REPORT OF A.I.D. WORKING GROUP ON CHOLERA and PROCEEDINGS OF EXPERT PANELS

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Report of a Meeting of the A.I.D. Working Group on Cholera

The A.I.D. Working Group on Cholera met in Washington, D. C. on October 6, 1970, with the following persons present:

Chairman	
Richard C. Parsons	Coordinator, Cholera Task Force
Consultants	
Abram S. Benenson, M.D.	University of Kentucky
Oscar Felsenfeld, M.D.	Tulane University
Eugene Gangarosa, M.D.	Center for Disease Control, USPHS
J. L. Gregg, Major, S.C., U.S.A.	Office of the Surgeon General, U. S. Army
Andre Lebrun, M.D.	Medical College of Wisconsin
Jack Millar, M.D.	George Washington University
Margaret Pittman, Ph.D.	Division of Biologics Standards, NIH
John Redmond, Jr.	National Academy of Sciences
Morris Shiffman, D.V.M.	University of North Carolina
Harry Smith, Ph.D.	Jefferson Medical College
A.I.D. Staff	
Lee M. Howard, M.D.	Director, Office of Health Bureau for Technical Assistance
Robert W. Babione, M.D.	Member, Cholera Task Force
Jacob Landes, M.D.	Member, Cholera Task Force

The meeting was opened at 1:00 p.m., and following the distribution of background information on the current cholera situation, Dr. Howard described its purpose and the objectives as follows: There have been seven recorded pandemics of cholera and there is nothing in present technological developments to negate the probability of another one in the future. The Agency desires the counsel of this group of experts as to the actions, if any, that A.I.D. might take to (1) prepare itself to meet the demands of the present emergency, and (2) reduce the risk of disastrous consequences resulting from further spread of the disease into new areas. What steps might A.I.D. take to forestall a recurring series of emergency situations over an indefinite period in the future?

Facts on the present situation

1. For the first time in 100 years cholera has reached sub-Sahara Africa. Of particular significance is its appearance on the West Coast, along the traditional route of transmission to South America and the Caribbean Islands. According to a recent statement by the Director General of the World Health Organization there is a strong possibility that it will again follow this path.

2. More countries are reporting cholera in 1970 than during the peak years of 1965-1967. In the period from July 1 to October 1, 1970, cholera had been reported officially by WHO in 22 countries and is suspected to exist in at least six more.

3. As of October 6, 1970 A.I.D. has received requests from WHO for about 8,500,000 doses of vaccine, as well as syringes, needles, drugs, typing sera, etc. A pledge of ten million doses of vaccine has been made to WHO. A special Task Force on Cholera has been established in the Agency to handle such requests and to advise the Administrator as to the future actions which A.I.D. might take.

4. Past experience of A.I.D. with handling cholera emergencies and the difficulties encountered in attempting to maintain a stockpile of essential supplies was described.

5. A.I.D. Disaster Relief is a special category of aid, available only in case of a formally declared disaster.

6. All requests for assistance made to A.I.D. in the cholera emergency are being referred to WHO to strengthen the organization's leadership role in dealing with the emergency.

Summary of Deliberations

Against this background the group began its deliberations of what could profitably be done to:

1. Prevent the spread of cholera - Immunization with currently available vaccines is incapable of accomplishing this; providing sanitary water supplies are essential but distant except for emergency

procedures; sanitary human waste disposal is desirable but also very remote.

2. Improve early warning of actual or impending invasion of an area or country by cholera so that appropriate steps can be taken to reduce its impact. This was considered to be very important. Several things can be done - upgrade diagnostic laboratory services; educate physicians to use them in all cases of severe diarrhea; and delete cholera from the list of internationally quarantinable diseases.

3. Reduce the severity of impact of invasion of the disease by (a) adequate treatment of severe cases and (b) immunization.

There was recurring discussion of the importance of upgrading diagnostic and vaccine production laboratory services, and of the need to educate and motivate medical personnel and the population in general, to comply with known measures for the control and treatment of the disease.

I. <u>On Interrupting Transmission</u>

Transmission appears to be due primarily to contamination of drinking water by the fecal discharge of carriers of the disease or of actual cases. Foods in which cholera vibrios can multiply may be equally important. An overt clinical attack may not result from ingestion of a million vibrios. Usually it requires a hundred million or billion. In debilitated persons or those with lowered general immunity, a smaller amount of contagium can produce the same result.

Safe waste disposal is an impossibility, at least for many years to come, in many areas. It is not practiced even in many of the more advanced localities such as Beirut. Even primitive measures are probably medium or long-term. Merely providing safe water to everyone is an impossible task for the foreseeable future, although it is gradually improving. Simple emergency chlorination of water supplies is important and can be done if hypochlorite (chlorinated lime) is provided. Health education is most important. Even where running water and sanitary toilets have been provided, the people frequently

are not educated as to their proper use. It is often forgotten that the vomitus of a cholera patient is as infectious as his feces. Person to person transfer appears to be common in this pandemic. Raising the level of personal hygiene and improved standards of food handling merit attention.

Results of health education are slow and often not immediately apparent. Nevertheless, this should be an unrelenting effort. Simple, practical, substantive material must be put out by those with practical knowledge of the problem. Customs and beliefs must be considered. The advice of cultural anthropologists should be sought. Moslems will defecate near water used in purification rites, rather than use latrines located away from such water; these rites are frequently performed in common pools, or in water also used for drinking.

Immunization with currently available vaccines will not stop transmission. It does not prevent the carrier state, which may last for a long time. Its place is to reduce the risk of the individual from severe illness. It should have no place in international quarantine, and should be removed as an international travel requirement. It gives a false sense of security. One member reported observing a traveler, who had an obvious fecal discharge on his clothing, cleared through immigration because his cholera immunization certificate was in order. The United States Delegation to the next World Health Assembly should take a strong stand in favor of deleting cholera from the list of internationally quarantinable diseases as well as the vaccination requirement for travel. This would encourage uniformity in reporting.

It was considered infeasible at the present time to try to eradicate cholera from an endemic, established foci, such as the Ganges Delta, but it may be feasible to clear it from those countries where it has recently been introduced. New foci are established by each outbreak. After the cholera outbreak in Uzbekistan in 1965 some areas were still showing vibrios in water supplies two years ago. It may be possible in the future to contain cholera within its permanent endemic foci.

For the long-range control or elimination of cholera from any country, improved sanitation is the primary answer. This will require many more health educators and trained and sensitized people than now exist in the developing countries. For example, when there was a shigella and salmonella outbreak in Honduras characterized by a severe, cholera-like diarrhea, a U. S. team of epidemiologists found that the water supply of a large town had been without chlorine for two years. They hyperchlorinated the water because of the many leaks in the system and heavy contamination. However, the people then went to the river for drinking water, and the day the team left Honduras, the local people turned off the chlorinator again. They would not drink the "poisoned" water.

Dissemination of cholera in the West Pakistan outbreak in 1967 appeared to be along the route of the railroad. Although water supply, sewage disposal and food handling in railway stations and in many airports are unsanitary and provide a ready mechanism for the transmission of disease, it is recognized that timely and practical measures are extremely difficult to administer. Some primitive sanitary methods should be worked out in advance to suit local conditions, and health educators trained to promulgate their use.

Introduction of cholera into the Western Hemisphere was not considered nearly as likely as its spread from Asia to the Near East to Africa, because the poorer and less sophisticated people who are most subject to cholera rarely travel across the major oceans and even more rarely travel by air. If cholera is brought to Latin America, it would most likely be brought by ships, by members of the crews. Once introduced, it could spread freely in much of Latin America. Port cities should remain alert to this risk.

II. Surveillance and Laboratory Services

Surveillance is the heart of a cholera control program. It was defined as the orderly collection, analysis and reporting of data to the responsible authorities to be translated into positive action.

This requires a two-way flow of information from the field to regional and national health centers, with alerts or instruction to the field for actions to be taken once cholera is confirmed.

The group was not unanimous as to what population groups should receive surveillance. The majority favored routine stool culture of severe diarrheas in adults in threatened areas, especially those who seek medical attention. A few members thought more cholera cases would be found by culturing mild cases too, and perhaps a somewhat earlier warning might result. Most thought the additional cases found would be small in relation to the effort expanded. All agreed that a concentrated effort should be made to upgrade diagnostic laboratory services through training of personnel and the provision of requisite equipment and supplies.

There was unanimous agreement that logic and good health practice dictates an effort to identify the causative agent in all severe diarrhea cases, not just in those in which cholera alone is suspected. For instance, a research laboratory in Cairo found the cholera vibrio in stool specimens two years before the first case was reported in Egypt.

It is suggested that all countries threatened with cholera should have an adequate surveillance system, as described, with the capability and skill to identify the cholera vibrio. Identification can be done in the laboratory within a few hours using selective culture media and identification sera. It was pointed out that special media facilitate the task, but ordinary bacterial culture media can be used if special media are not available.

Paramedical personnel such as midwives, sanitarians and malaria personnel can provide invaluable services in detecting and reporting cholera-like illnesses in remote areas or along borders if asked to do so.

According to experience in Hong Kong, surveillance also can be done on routinely collected sewage samples, especially those collected from

buckets or neighborhood collection pits. A highly sophisticated system or team is not necessary, but special training and upgrading of laboratories is needed. At least one qualified laboratory should be available in each district of a country, but modern transportation facilities make it possible to collect and ship specimens and obtain a good recovery of vibrios 30 days later. The only supplies needed are screw-capped glass vials containing a simple transport medium. (See WHO publication "Cholera Review for WHO Seminar WHO/ED/Cholera 70-19", for a description of methods).

It was noted that the principle of surveillance is being increasingly accepted by governments. It was felt that if cholera were removed from the list of internationally quarantinable diseases there would be a much freer reporting of the disease by the infected countries, although some stigma of backwardness in sanitation might still be attached to it.

It was reported that the Pan American Health Organization (PAHO) has arranged for a special course for laboratory personnel on the laboratory diagnosis of cholera to be given at the Center for Disease Control (CDC), Atlanta, November 2-7, 1970. Trainees from 12 Latin American countries are invited. Both bacteriological and serological techniques will be taught.

Serological techniques are useful in the final identification of suspected cholera colonies on culture media and also in community screening for a rise in antibodies. Surveys every six months of the percentage of positives in 100 persons may show a rise in antibody titre between one survey and the next, suggesting the passage of cholera through the community during the interval. These tests are not always specific. The Panel suggested that a regional reference laboratory for serological testing would be desirable for cholera surveillance.

It was noted that good surveillance alone cannot keep cholera out of an area or a country; it can only give early warning of the presence

of the disease and alert health authorities to take action to control its spread and reduce its impact.

III. Therapy

Modern cholera therapy depends on the rapid replacement of lost fluid and electrolytes; and the use of antibiotics to shorten the course of infection and terminate the carrier state. The earliest possible change from the intravenous to the oral route for fluid replacement in the treatment of clinical cases, even in the presence of vomiting, has reduced by 80% the need for intravenous fluids.

The usual adult formula for intravenous fluid-electrolyte replacement preparations can be used in small children safely, thus allowing a single intravenous preparation to be stocked and distributed. The Dacca (5:4:1) formula is simple and inexpensive: 5 grams of common salt, 4 grams of bicarbonate of soda, and 1 gram of potassium chloride per liter. Several similar combinations are in use, all more or less equal in effectiveness. All depend on the rapid restoration of fluid and electrolyte losses and the correction of acidosis. With proper treatment mortality from cholera can be reduced to less than one per cent.

The Panel agreed that intravenous fluids should not be stockpiled, particularly not in the United States, due to high cost of manufacture and shipping. However, if stockpiled as solution, or as powders to be autoclaved, sodium bicarbonate cannot be used. Sodium lactate, acetate or gluconate will serve as well and will remain stable in storage. In the present state of knowledge long storage in plastic bottles is not considered advisable for intravenous solutions.

A resource for intravenous fluid manufacture on short notice should be available in each country or a regional source should exist. A.I.D. might help by providing large stills for the necessary distilled water. Glassware could be provided. Needles and tubing and connectors compatible with the type of bottle to be used must be available.

To be effective intravenous fluids must be in the hands of the ultimate user, ready for use on a moment's notice, for treatment of any

type of severe diarrhea, including cholera. There should be no expiration date on sterile pyrogen-free water in sealed glass containers. Rubber stoppers do deteriorate in long storage. Stockpiling of electrolyte mixtures in plastic bags, ready for making solutions with the addition of sterile, pyrogen-free water, is now feasible.

For oral therapy, glucose (or sucrose if glucose is not available) must be added to the electrolyte mixture and the formula could be designated 20:4:4:1; namely 20 grams of glucose, 4 grams of common salt, 4 grams of bicarbonate of soda, and 1 gram of potassium chloride per liter of water. Twenty grams of glycine is considered a useful, but not a necessary addition to the above. These ingredients could be put up in larger plastic bags ready for making a solution by the addition of drinking water, or in small plastic bags to be dissolved in a pitcher or other container of specified volume. Such packaged materials could be stockpiled.

Several antibiotics, including tetracycline, are effective in reducing the volume and duration of the diarrhea and terminating the carrier state. They should be used in every clinical case. The adult dosage of tetracycline is 500 mg. every six hours for two days. They are also worth using in all family contacts of whom 20% may be infected at the same time as the patient. One gram per day for five days is the optimum dosage of tetracycline for an adult for prophylaxis of disease and clearing the carrier state.

Tetracycline, stored in a warm place, deteriorates forming toxic end products. There are ample stocks of this antibiotic on the commercial shelves at all times, always fresh, and no need exists for stockpiling. WHO has supplied the needs of some countries for this drug, but not from U. S. suppliers, due to its higher cost in the United States.

One important aspect of rehydration therapy which is often neglected is the measurement of fluid lost by the acutely ill patient. Especially needed is a canvas cot with a hole under the buttock, a

plastic sheet with a similar hole and sleeve, and a calibrated bucket to collect and measure the fluid discharged. Plastic sheets with a hole and the attached sleeve, and plastic buckets can be produced in many places at small cost. All treatment centers for acute diarrheas giving intravenous or oral fluids should have this equipment. Fluid losses by vomiting must be measured also.

For small children, use of the same intravenous fluid formula as required by adults can overload them with sodium. For this reason, water by mouth should be given early. This is feasible in many places only if the mothers are allowed on the ward. Unnecessarily strict isolation rules for cholera patients sometimes prevent this to the detriment of the child patient's welfare.

IV. Immunization and Vaccine Production

Immunization can be amply justified in the presence of a spreading outbreak, despite the incomplete protection afforded by presently available vaccines. It will reduce the number and the severity of cases of cholera (morbidity and mortality) more than enough to justify its use, if it is used in persons not already infected and not too far in advance of their exposure to the disease.

Immunization with the present type of vaccine is not advisable in a country before cholera has arrived. The protection is of too short a duration, three to six months. Cholera vaccine may at best be 70% to 80% effective in preventing clinical disease, but unless the threat of cholera is imminent it is not realistic to believe that more than a small fraction of the people will accept immunization. When cholera does strike, the people demand the vaccine, even violently, and the health officials cannot refuse to give it, even if they wished.

Vaccinated people may excrete organisms for several weeks without ever showing clinical symptoms of the disease.

Vaccination, as carried out, in some areas may entail greater risk than the disease. An incident was described where a vaccinator

got on a bus and injected all the passengers with the same syringe and needle. Many cases of hepatitis followed.

Since it is evident that vaccine is necessary under certain circumstances, and will continue to be widely used, steps should be taken to improve its production. It should be a standardized product meeting international standards.

The situation calls for upgrading regional or country vaccine production laboratories. When asked if it were politically feasible for A.I.D. to select laboratories as regional laboratories in the cholera areas and undertake to upgrade the quality of their production by providing technical assistance and equipment, it was pointed out that the Agency did this in the case of the vaccine laboratory at the Refik Saydaam Institute in Turkey in 1967 with the result that its output has greatly improved. It is now providing some regional service. This was done under the umbrella of the Subcommittee on Health of the Central Treaty Organization (CENTO).

The reluctance of one country to accept another country's vaccine product may be changing. WHO has a standardized specification about to be released for cholera vaccine. This will assist the present situation. If a laboratory certifies that its vaccine meets WHO standards, other countries may more readily accept it. It was suggested that regional laboratories could be developed under the auspices of WHO.

Some vaccine production facilities other than health laboratories might be used. For example, Nepal has no facility for making human vaccine, but the Food and Agriculture Organization (FAO) has a huge operation for making animal vaccines that could produce cholera vaccine easily.

It is believed that there are many laboratories in existence in cholera areas which could be upgraded with modest help (equipment, supplies and training of personnel) to produce satisfactory vaccine. It was suggested that better efficiency would result if only a few

regional laboratories went into cholera vaccine production while the rest should concentrate on cholera surveillance. Lack of proper containers for both vaccines and fluids were cited as a frequent production problem.

Stockpiling of bulk vaccine might be feasible over long periods (10 years in some cases). Vaccines grown on agar are more stable than those grown in broth. The concentrates stand up better than the diluted vaccine. Dried vaccine is very stable, but the rubber stoppers for the vials needed for reconstituting in the field will deteriorate in time unless the vial is packaged in nitrogen in an airtight can.

In many cases, expiration dates are arbitrary and illogical. Vaccines often have been used beyond the expiration date with good results. Nevertheless this cannot be depended upon and therefore is not good practice.

Jet injector apparatus is preferred to needles and syringes for efficiency and to avoid the risk of hepatitis in vaccination campaigns. They can be used in most situations. However, in some situations needles and syringes will still have to be used. In these cases, disposable needles and syringes should be used whenever possible.

A list of actual and possible vaccine producers in the United States and developing countries was distributed, and the help of the Working Group was requested in selecting those most appropriate for upgrading assistance in the areas threatened by cholera.

Not only is it feasible to upgrade cholera surveillance and vaccine producing laboratories, but the cholera pandemic offers the possibility of building up laboratories which later could be used against other diseases.

There was some discussion of whether or not too much emphasis and money was being spent on vaccination as compared with sanitation. It was apparent that the vaccination demand in the face of an epidemic is usually almost irresistable, and that if the money was withheld from the vaccine program it would probably not go to a better water supply, or other health measures needed for controlling cholera. The

United States Delegation to the next World Health Assembly might be advised to attempt to put cholera vaccination in a truer perspective, and to draw attention to the greater need for sanitation, surveillance and treatment facilities when speaking on cholera.

There was also discussion of the argument advanced by some non-medical policy makers, both national and U.S., that cholera is a natural means of population control and money should not be spent that would result in an increase in the population. The Panel was of the opinion that family planning programs will not be accepted by the people until they feel sure that their children will survive after they have voluntarily limited the number of births.

CONCLUSIONS AND RECOMMENDATIONS

The Working Group on Cholera assembled by the A.I.D. Task Force on Cholera, in the course of its broad discussions on control, surveillance, treatment and prevention of cholera arrived at the following conclusions and recommendations.

Control of Transmission

1. Improved water sanitation and human waste disposal is the only effective approach for the control and prevention of the spread of cholera. Permanent measures of this type are in the distant future. Simple and primitive emergency measures for safer drinking water and excreta disposal could and should be taught. Some transmission of cholera may be related to those foods in which vibrios are able to multiply.
2. Health education on a large scale and well-directed is essential both for immediate and long-term anticholera measures. It must be accurate, practical, and stimulating of motivation.
3. Immunization alone is inadequate to prevent the spread of cholera and should be dropped as a requirement on international travel immunization certificates.

4. Cholera should be dropped from the list of internationally quarantinable diseases, and the United States Delegation to the next World Health Assembly should be advised to advocate this action.

5. It is impractical to consider the clearing out of the old endemic foci of cholera in the Indian subcontinent at the present time. Newly established foci might be cleared up. A carrier state may persist for years and cholera vibrios may be found in localities long after the epidemic has passed, transmitted between asymptomatic carriers. This leaves the potential for a subsequent outbreak.

Surveillance and Laboratory Services

6. Surveillance is the heart of a control program. Information must pass both ways, from the field to central offices, and vice versa. A system should be established and working in every threatened country that will result in prompt confirmation and notification of cases, and taking appropriate actions for control and treatment.

7. Basically every threatened country should have a system of stool sample submission and the laboratory capacity to identify cholera through appropriate culture of stools. This capacity should be built up by improving equipment and training personnel in existing facilities. Once established, it will be beneficial in controlling other diarrheal diseases.

8. Screening should be directed first at the culture of stools from all diarrhea cases in adults who seek medical attention. These are the groups most likely to be positive. Cultures of severe diarrheas in children and mild diarrheas in adults may then be done, but the percentage showing cholera will be much lower. Human wastes from disposal systems should be cultured where feasible.

9. The use of a suitable transport medium permits efficient operation of regional laboratories. Many laboratories exist which could be easily upgraded to identify cholera vibrios.

10. Education of all medical services, including paramedical personnel, and motivating them to be on the alert for cholera and to submit stool specimens, is crucial to successful surveillance.

11. Testing of blood sera for cholera antibodies can show where cholera has been present. Regional laboratories or reference centers can be helpful for this purpose.

Therapy

12. Modern therapy, based on restoring fluid and electrolyte losses and correcting acidosis as rapidly as possible, either intravenously or by mouth, can cut the death rate to one percent or less. A sterile solution of salt, soda and potassium chloride suffices for intravenous use. For oral therapy glucose (or sucrose) must be added.

13. Replacement solutions can be given by mouth as soon as the patient can swallow. This route of therapy will save about 80 percent of the intravenous solution requirement, resulting in great economy of money, and avoiding stockpiling. It does require stricter supervision in order to assure adequate fluid intake, except when administered through naso-gastric tubes. These tubes should be included in supplies to treatment centers.

14. It is not practical to stockpile large quantities of intravenous solutions. However, an appropriate dry, sterile electrolyte mixture, for addition to one liter of sterile pyrogen-free water, could be pre-weighed and packaged, together with a fluid administration set (needles and plastic tubing) and stockpiled. For oral therapy a dry, prepackaged, electrolyte-glucose-glycine mixture to make up ten liters of oral solution, together with a fifteen liter plastic bag might be stockpiled. Final preparation of the solution would require the addition of ordinary drinking water and thorough mixing. Prepackaged chemicals for addition to a liter of water and mixed in an ordinary pitcher is practical.

15. Instead of stockpiling intravenous solutions, countries or regions might be assisted in obtaining the distillation equipment and glassware needed to make large amounts of pyrogen-free water on short notice. Plastic is suitable for short-term storage but not for long-term storage of fluids.

16. Tetracycline, at an adult dosage of 500 mg. every six hours for two days, can shorten the course of illness, and prevent some deaths after the initial shock is corrected. At one gram daily for five days it will prevent infection in contacts, or cure the carrier state.

17. Tetracycline need not and should not be stockpiled. There is always an adequate supply in the market place, and it deteriorates on storage at warm temperatures, forming toxic end products.

Immunization and Vaccine Production

18. Although not completely effective, immunization is useful for protecting the individual against a clinical attack or at least reducing the severity of illness and the risk of death. It reduces the burden of high morbidity and mortality on the community. It does not prevent the carrier state, and by itself will not halt transmission. It should be used only in the face of an expanding epidemic. Given too far in advance, the protection is wasted, as it lasts only three to six months with presently available vaccines.

19. A.I.D. probably cannot refuse to support requests for help in immunization programs, but can insist on the need for correct criteria in its application, and on adequate attention to surveillance and sanitary measures. The U.S. Delegation at the next World Health Assembly should take a stand on these points.

20. Vaccines should be standardized and the new WHO specification will be a great help. The vaccine should be refined enough so as not to clog a jet injector.

21. Jet injectors should be used as much as possible, but there always will be a need for syringes and needles. A.I.D. might help in the supply and maintenance of jet injectors.

22. A.I.D. should not enter into vaccine supply and stockpiling in the United States for long-range assistance, but rather the Agency should give assistance in upgrading existing laboratories in developing countries or regions for vaccine production. It is considered technically preferable to have a few good laboratories producing on a regional

basis than a large number of small ones, although sometimes this might not be politically acceptable. The Working Group would be prepared to advise on laboratories most suitable for upgrading.

23. Stockpiling in the regions is feasible. Vaccine, preferably as a concentrate, can be stored up to 10 years or more under proper conditions. From the concentrate it can be made ready for use in four to six weeks.

Health Education

24. Health Education and proper motivation are essential at all stages in cholera control and prevention. The results are often slow, and much effort is often wasted due to misdirection. Reduction of death from diseases such as cholera is necessary before poor people will accept family planning.

Proceedings of the Panel on Cholera Vaccine Production and Storage of the A.I.D. Working Group on Cholera

The Panel on Cholera Vaccine Production and Storage met in Washington, D. C., on December 14, 1970, with the following persons present:

Chairman

Lee M. Howard, M.D.	Director, Office of Health, Bureau for Technical Assistance

Consultants

John H. Brown, Ph.D.	Wyeth Laboratories, Inc.
John Feeley, Ph.D.	Division of Biologics Standards, NIH
Joseph Lowenthal, Sc.D.	Walter Reed Army Institute for Research
Yoshikazu Watanabe, M.D.	University of Texas

A.I.D. Staff

Robert W. Babione, M.D.	Member, Task Force on Cholera
Jacob Landes, M.D.	Member, Task Force on Cholera

The objectives of the Panel were described by Dr. Howard and the present state of the cholera emergency was summarized by Dr. Landes.

The World Health Organization (WHO) has been supplying vaccine to countries on request but in accordance with its own estimate of their needs, and within the available supply in the world market. All the vaccine requested has not been supplied in every case by WHO, but only the quantity that the emergency seemed to warrant. U.S. assistance (in vaccine) has been channeled through WHO and this method of screening requests has worked very satisfactorily. Bilateral assistance is not ruled out for the provision of other items that WHO cannot supply.

The United States has supplied WHO with four million doses of vaccine to date. A number of vaccine requests have been filled from other than U.S. sources by WHO. However we are not informed about all of these. In recent months WHO has sent vaccine to:

Ethiopia	8,000,000 doses	Mali	500,000 doses
Ghana	600,000 doses	Togo	250,000 doses
Ivory Coast	600,000 doses		

Various countries have started giving 0.2 ml. of vaccine intradermally in order to conserve vaccine. The Panel noted that this route of administration lacks scientific confirmation of its efficacy.

Other countries apparently have made or obtained elsewhere their own vaccine requirements. Countries which have used vaccine without making a request to WHO include Turkey, Iran and Egypt. Many Asian countries, including the endemic areas and European countries, produce enough vaccine for their own needs.

The current availability of vaccine in the United States was examined. The Defense Supply Agency (DSA) of the Department of Defense (DOD) has agreed to keep its cholera vaccine stockpiles at maximum levels. This provides a ready reserve from which A.I.D. can purchase vaccine in cases of emergency need. New contracts have recently been let by the DSA with Lederle Laboratories and Wyeth Laboratories, Inc. for cholera vaccine.

The Wyeth contract calls for delivery in April 1971 but they can start delivery in mid-January if the potency and safety tests are completed on schedule, because the company began work on production before the contracts were signed.

The contracts are in two parts: an initial contract for the production of vaccine to the stage of concentrated or bulk storage, and a storage fee that can be extended from year to year. The stored vaccine is rechecked yearly to assure potency that would permit 18 months of useful life after dilution and packaging. A separate contract for the dilution and/or packaging comes into play when finished vaccine is desired.

The questions presented to the Panel on the production and utilization of cholera vaccine have many interlocking facets; some basic ones are answerable only in relation to the whole picture.

I. The question of areas to be helped is relatively easy. The cholera endemic countries such as India, Thailand, and Pakistan, apparently do not need help. They make their own vaccine and are satisfied with it. Outside this area Iran, Turkey, Israel and other

Near East countries may be self-sufficient. Egypt and Lebanon may be in this category.

Only Africa and Latin America seemed to be areas which should be considered for the establishment of regional cholera vaccine production laboratories.

II. The proposition of setting up regional laboratories was considered to be subject to numerous practical difficulties, although promising enough in theory.

The laboratory at the Refik Saydaam Institute in Ankara, Turkey was discussed. It seems to have achieved a good capacity, but its regional use was considered to be limited. There are two sides to the problem:- (1) Turkey would probably not release vaccine to another country if they needed it themselves; and (2) most countries are prone to question the validity of certification by another country of its own products. Even cholera vaccine produced in the United States has been questioned. When the vaccine has not been certified by an independent agency like the Division of Biologics Standards of the National Institutes of Health (NIH), there is much more questioning. WHO cannot provide personnel for assessing the capabilities of a laboratory, or for evaluating the process of production or the product itself in order to certify that international standards have been met, without extra funds.

The Panel was strongly against attempting to build up a large number of small laboratories to make cholera vaccine. The expense could not be justified if it were directed to cholera vaccine alone. For the long-range there might be a justification for cholera vaccine production if other vaccines such as Diptheria and Tetanus toxoids, and a combined Diptheria, Tetanus, Pertussis Vaccine (DTP) are also produced. A further reason for avoiding the indescriminate build-up of cholera vaccine producing units is that as soon as the cholera emergency is over, the unit would fall into disuse and all its skills would be lost.

Wyeth Laboratories have tried to upgrade two overseas laboratories to make smallpox vaccine, with very disappointing results. The workers resist suggestions and would not follow instructions. They prefer their own ways and resist change. However where the basic capacity to make other vaccines exists, and there are personnel and physical resources in place, it might be feasible and economical to introduce cholera vaccine production. A good laboratory can produce large amounts of cholera vaccine if an intensive effort is made.

The question of how much it would cost to upgrade another laboratory to the level of producing good cholera vaccine, and the selection of the laboratories which should be upgraded was felt to be completely beyond the capability of this Panel without site visits by a team of experts. Such team should have not only a scientist, but also a production expert who knows the requirements for large-scale vaccine production. It also should have a managerial representative to talk with the Minister of Health and other officials to determine if there exists on the part of government a bona fide intention to build up, support and maintain a general vaccine production laboratory meeting high standards.

A compromise solution was suggested for the next few years, at least for those countries where basic equipment and skills to produce quality vaccine would be needed. For the same costs large amounts of vaccine could be made and stored in concentrated form in the United States, and tested and certified as to potency after dilution of a sample. The using countries or a regional laboratory would then dilute, bottle and label the concentrate. The capability of making sterile dilutions and bottling injectable drugs exists in many countries. Little savings could result if rubber-stopper vials had to be flown out along with concentrate. With the safety, potency and constant storage conditions which are required in the United States, certification might be more acceptable to the using countries. Better control of the distribution of stockpiled material, greater speed in delivery

and less restrictions in its use in countries where it is needed would result. The cost might be less than upgrading a number of small, poorly equipped laboratories whose staff would need training.

The Panel believed that cholera vaccine production could best be grafted onto existing vaccine producing laboratories. When a decision is reached as to what laboratories would be helped, and a determination made as to what assistance would be needed to produce an adequate quantity of vaccine, the comparative costs of United States manufacture and storage against partial or complete production overseas can be easily calculated.

Wyeth Laboratories has 29 plants around the world, all of them capable of making and bottling injectable solutions. Only one (in Portugal) makes a few biologicals.

There are many laboratories in South America which make biologicals and have facilities that could easily be shifted to make cholera vaccine. Dr. Canessa of PAHO is assisting Colombia to improve her vaccine production facilities of all types at this time. He would be available to help other Latin American countries change to cholera vaccine production if the need arises. Various countries probably have the skill already, merely lacking experience in working with cholera.

The Food and Agriculture Organization has a number of very good laboratories producing large quantities of animal vaccines. These are sometimes better than laboratories producing biologicals for human use. Many laboratories with famous names and reputations actually have little capability at present.

Since it may be a long time between cholera epidemics it would be a great waste to develop the plant and equipment needed for producing cholera vaccine for that purpose alone. The long-term solution would be to build up laboratories which have the capacity to produce other biologics between cholera epidemics. The goal of the assisting agencies should be

to build up well-balanced products production competence in the developing countries. Surveillance laboratory skills may be the first order of business. In anticipation of this need PAHO recently gave a one-week course for diagnostic laboratory directors from 12 Latin American countries.

III. Technical Aspects of Production and Storage.

a) Vaccine should be stored in the wet form. It keeps in either concentrated or dilute form for five years or more. Five years is the longest experience our production laboratories have had with bulk storage of the concentrate; it is the most economical method of storing vaccine.

Only the agar method of culture of the vibrio permits preparation of the concentrate. The tank (broth) method of culture produces dilute vaccine.

There seems to be no reason to consider a dried vaccine at this time. The storage life of the wet form is already so long that there is little need for lengthening it by lyophilization. The cost of drying and reconstituting would probably be more than the cost of making a new batch if the old one lost potency. It was considered to be simpler to have a finished vaccine than to supply a dry vaccine and reconstituting fluid in the field. There would be no economy in sending two vials instead of one.

Also, in five years there may be a new product that will supersede the presently available vaccine.

b) Storage conditions. For wet vaccine, either concentrated or diluted, 2-8° C, average 5° C. However, nonrefrigerated shipping and field use conditions do not pose a problem. Temperatures of 80° F. to 90° F. for one to two weeks or more in the field outside of refrigeration, have not harmed potency.

Potency standards are set high enough that there should be 18 months of shelf life after the potency tests. The potency tests are repeated each year thus extending further the expiration date.

It seems illogical to store bulk vaccine prepared in the United States in other countries. The endemic regions already are covered by their own resources. In nonendemic regions stockpiling is not indicated unless there is good reason to expect an outbreak to occur within the region that the country of storage can serve. A United States stockpile is considered to be economical due to good standardization and acceptability, and ready access of air routes to all parts of the world.

c) Stockpiling levels: How much vaccine ought to be stockpiled and in what locations can only be determined by epidemiologists forecasting regional needs.

d) Timetable: To prepare a large order to the stage of concentrated vaccine 50 days are required.

To dilute, perform potency and safety tests, fill vials and label, about 60 days from start of dilution to shipment. Part of a stockpile could be kept in the bulk dilute form, instead of concentrate. From this condition it could start flowing into shipment channels within 14 to 16 days (the time needed for sterility and safety tests).

All of the present DSA stockpile (12.5 million doses) is kept in bulk dilute form. Wyeth dilutes their product later, while Lederle makes the dilute form direct in the process of manufacture (tank method). Storage space needed for the dilute form is tenfold greater than for the concentrated form.

e) A list of equipment (see pages 93-96) has been prepared by Dr. Brown, showing each item needed in each step of vaccine production. The space required also was shown for an operation producing batches of 300,000 doses each. Two workers and one supervisor could handle this production.

The requirements for dilution, testing, filling, labeling, and packaging are shown in separate steps, for convenience, if a partial operation were to be carried out overseas.

IV. Utilization: The Panel offered some suggestions on the technique of vaccination. The excessive viscosity of cholera vaccine produced in Iran prevented its use in jet guns in Iran in 1965. This problem does not seem to have occurred in vaccines produced in the United States.

It was suggested that since vaccination alone will not control transmission, the vaccinator should carry with him some simple information on basic sanitation, either cartoons and pamphlets, or an oral presentation. The vaccine is useful only for a short time; the health education message might have more lasting value.

V. Courses of Action:

a) Site visits will have to be made by a team before upgrading of a vaccine production laboratory can be attempted. The team should comprise a cholera expert, a vaccine production man, an A.I.D. administrator and a WHO representative to assist in coordination.

Laboratories should be surveyed to determine their present equipment and skills. Some might be assisted for the purpose of increasing their production capacity; others might only dilute, test, fill and package from bulk concentrate. Dr. Brown will estimate the cost of the materials and work needed, as reported by each team, and calculate alternative methods to achieve the same result.

The site visits must be made before definite plans are made, including cost projections.

The current level of skill of existing laboratories will be difficult to check. Some of them will not allow their vaccines to be taken out of the country for fear they will be tested and found to be below standard.

Even if one does equip a laboratory its future maintenance is often a problem. A piece of equipment breaks and it takes many months to repair it. Trained personnel must be available. To start training from the ground up for cholera vaccine production alone is unwise. The interest of the country is essential; the authorities may be interested while cholera threatens, but when the emergency is over, their interest quickly fades.

b) Someone has to decide what is a reasonable stockpile. The projected cost of various alternatives can be made when the size of the stockpile has been determined.

SUMMARY

The United States has been assisting WHO in meeting requests for cholera vaccine from member governments by supplying vaccine drawn from the Defense Supply Agency (DSA) of the Department of Defense (DOD) stockpiles. Arrangements have been made which enable A.I.D. to purchase vaccine from the DSA on an emergency basis.

The technical aspects of the production and storage of cholera vaccine in the United States, the vaccine production capabilities of countries where cholera is endemic, and countries outside the endemic areas were discussed at length. It was the consensus of the Panel that there is no reason to consider dry vaccine in view of the storage life of the wet form, and that Africa and Latin America are the only areas worth considering at present for the establishment of regional vaccine production laboratories.

In spite of anticipated future requests and the continuing needs of WHO for cholera vaccine, the Panel agreed that A.I.D. should not attempt to stockpile vaccine, but rather it should assist WHO in the selection and upgrading of a few strategically located vaccine laboratories for the production of cholera vaccine which meets international standards. The ultimate selection of an existing laboratory for upgrading would be dependent upon a site visit by a team of experts to determine administrative and technical feasibility, and the attitude of the host government toward using such a laboratory to produce vaccine for export.

RECOMMENDATIONS

1. A.I.D. should assist WHO in the selection and upgrading of a few existing human vaccine production laboratories for the production of cholera vaccine. The laboratories selected should be strategically located in relation to countries where cholera exists or are threatened by the invasion of the disease.
2. Cholera vaccine should be a standardized product meeting international (WHO) standards.
3. Cholera vaccine should be used only in the face of an expanding epidemic or actual invasion of a country by the disease. Given too far in advance, the three to six month period of protection afforded by presently available vaccines is wasted.
4. A.I.D. should not enter into U.S. vaccine production and stockpiling. The present agreement with the Defense Supply Agency (DSA) enables A.I.D. to meet requests for U.S. assistance in the supply of cholera vaccine.
5. Jet injectors (PED-O-JETS) should be used whenever possible for immunization programs. However, needles and syringes (preferably disposable) will be needed in some situations.
6. Cholera vaccine production in facilities other than health laboratories might be feasible.
7. Programs of health education and proper motivation must be developed as an integral part of cholera immunization programs.

CHOLERA VACCINE PRODUCTION

provided by

John H. Brown, Ph.D.

Wyeth Laboratories, Inc.

1. Production Laboratory

A. Personnel

1. 2 individuals - knowledgeable in basic bacteriological procedures - supervised by an experienced bacteriologist.

2. Production cycle for 2 individuals:

300 povitsky bottles per cholera strain (total of 600 bottles) will provide sufficient concentrate to formulate a 300 liter lot of market product.

Day 1 - Preparation of media

Day 2 - Inoculation of Inaba strain

Day 3 - Harvest of Inaba strain and start inactivation

Day 4 - Decontaminate and wash bottles

Day 5 - Preparation of media

Day 6 - Inoculation of Ogawa strain

Day 7 - Harvest of Ogawa strain and start inactivation

Schedule can be modified depending on availability of personnel, space and production bottles

B. Production Facilities and Equipment

1. General work room - 21' x 15' (minimum) 315 sq. ft.

a. Preparation of media

b. Storage of empty bottles and bottles containing media

c. Microscopic examination and agglutination tests

d. Records

e. Equipment:

(1) Microscope

(2) Flasks, graduates, pipettes, bottles, test tubes, etc.

(3) Laboratory rotary shaker, table top for slide agglutination test

(4) Balance - weighing out ingredients for media

(5) Reagents and media

(6) 400 Povitsky bottles - overall size - 18"x6"x4½"- 0.3 cu. ft.

Total space required = 120 cu. ft.

Growing area of bottle = 14" x 5"

(7) Kettle and stove to prepare 90 liters of media; 300 ml. media per bottle; 300 bottles = 90 liters

2. Glassware Preparation and Sterilization of Media

a. Space requirements depend upon method as to prepare glassware, i.e., machine washing vs hand washing.

b. Dry heat oven for sterilization and drying - optional since autoclave can be used in most situations.

c. Autoclave:

(1) Size - depending on production schedules and capacity

Sterilization cycle = 250°F for 50 minutes

Autoclave Size	No. of Bottles Per Cycle
84"x42"x48"	102
84"x36"x42"	80
48"x24"x36"	40

d. 300 or 100 liter tank for formulation of diluent

3. Incubator

a. Size 12' x 12' with 2 chromolox electric heaters Model #UB20, Model B, 2 electric fans and 1 temperature regulator and recorder - will hold 8 racks described below

b. Racks for povitsky bottles

1 rack, with wheels 52"L x 19"W x 68"H will hold 80 bottles, 4 racks required for 300 bottles

c. Incubation time - 24 hours per lot.

4. Inoculation and Harvesting:

   a. Sterile room 9' x 12' will hold 1 rack 52x19x68 + 2 individuals

   b. 1 Filamatic machine Model DAM

   c. 1 vacuum pump

   d. 20 liter carboys with syphons and stainless steel 200 mesh screen. 300 bottles harvested with 100 ml. saline per bottle will yield 32 liters of concentrate after addition of phenol which is stored in 2 carboys; 16 liters per carboy. Each carboy occupies 3.75 cu ft (1'X1'X 1 3/4') a total of 7.5 cu ft., to be maintained at 20-28°C for 6-9 days.

   e. Concentrates to be stored at 2-8°C 7.5 cu ft

5. Formulation of Market Lot - 300 liters

   a. 300 liter stainless steel tank with stirring mechanism, inlet and outlet ports and installed on a movable carriage. (Note: tank is to be sterilized by autoclaving; will require an adequate size autoclave.)

   b. To be stored at 2-8°C. Occupies 34 cu ft (5.5 X 2.5' X 2.5')
      Note: A 100 liter tank requires 12 cu ft (3'X2'X2')

6. Control Testing

   a. Sterility - If a separate area is not available, the production sterile room can be used.

   b. Potency and Toxicity Test

      (1) Potency Test - Ogawa and Inaba Strain

         (a) 200 mice per strain - 400 mice total, including titration and uninoculated controls

         (b) Mouse boxes per 16 mice - L 14" X W 9" X H 16"
             Rack for 15 boxes - L 55" X W 15" X H 66"
             Require 2 racks for complete test.

      (2) Toxicity Test - 10 to 20 mice per test - 1 box

      (3) Space - If animal holding space is not currently available, a room 11' X 12' with proper vertilation and heat would be required.

      Note: Suitable strain of mice required that are susceptible to cholera organism when combined with a suitable preparation of mucin

7. Filling

   a. 300 liter market lot will provide for 14,000 - 20 cc vials, or 5,000 - 50 cc vials.

   b. Filling schedule per 1 filling machine (Filamatic DAB) using 2 individuals; 1 filling, 1 stoppering
      20 cc vials - 5,000 - 7,000 vials per day (100-140 l.)
      50 cc vials - 3,000 - 5,000 vials per day (150-250 l.)

   c. Equipment

      1 Filamatic DAB
      1 Laminar flow hood, vertical flow 5' X 3' per team of 2 girls

   d. Capacity - Can be increased by adding 2 girls per each additional filling machine.
      Required work area for each team is 5'X 3' with laminar flow hood.

   e. Storage of Filled Containers at 2-8°C

      15,000 - 20 cc bottles - 22 boxes L30" X W 13.5" X H 4" (1 cu ft)
      22 boxes = 22 cu ft
      5,000 - 50 cc bottles = 13 boxes = 13 cu ft

8. Packaging - Hand Operation

   a. Stamping control number and expiration date on prepared labels
      100 labels/hour/girl

   b. Attaching labels onto vials
      100 bottles/hour/girl

   c. Packaging into a nested multiple container
      400 bottles/hour/girl

Proceedings of the Panel on the Surveillance of Cholera of the A.I.D. Working Group on Cholera

The Panel on the Surveillance of Cholera met in Washington, D. C. on January 25, 1971, with the following persons present:

Chairman	
Richard C. Parsons	Coordinator, Cholera Task Force
Consultants	
Oscar Felsenfeld, M.D.	Tulane University
Eugene J. Gangarosa, M.D.	Center for Disease Control, USPHS
William F. McCormack, M.D.	Harvard Medical School
Robert Oseasohn, M.D.	University of New Mexico
Harry Smith, Ph.D.	Jefferson Medical College
Liaison with WHO	
Dhiman Barua, M.D.	Division of Communicable Diseases, WHO, Geneva
A.I.D. Staff	
Lee M. Howard, M.D.	Director, Office of Health Bureau for Technical Assistance
Robert W. Babione, M.D.	Member, Cholera Task Force
Jean F. Rogier, M.D.	Member, Cholera Task Force

The objective of the meeting was briefly outlined. The current pandemic of cholera is expected to continue in an epidemic or endemic form for years to come, especially in Africa. On October 6, 1970 the A.I.D. Cholera Working Group produced general guidelines for specific areas of attention in developing a long-range plan for the prevention, control and treatment of cholera. A series of expert panels are being convened by the Cholera Task Force to enable it to provide the Administrator of A.I.D. with detailed, practical guidance which he might consider for Agency assistance in controlling the present pandemic in the immediate, as well as in the more distant future.

The Panel agreed that surveillance should be based primarily on bacteriological methods. They are comparatively simple, rapid and economical. They are more specific than serological methods and clinical

diagnosis. Bacteriological methods have become practical because of the availability of good transport media which are able to keep specimens from patients or suspected sources of infection in good condition for weeks without refrigeration.

The serological methods are cumbersome and may be falsely positive; also, they may remain positive long after the infection occurs.

Reporting by village chiefs of suspected occurrences of cholera was fairly good in East Pakistan and provided an alerting mechanism after the people become aware of the characteristics of cholera. However, all such alerts required bacteriological examination to confirm the diagnosis.

Almost all African countries now have bacteriological laboratories of varying degrees of competence. The problem is how to improve and maintain their interest in cholera diagnosis once the epidemic state is over. Theoretically, a central cholera diagnostic laboratory need not be in every country. Local laboratories can take fecal material brought to them in preserving media, streak it out, pick out suspicious colonies, and send the isolate to a central laboratory for definitive diagnosis. Personnel with relatively little skill, training and equipment can do this.

It is not considered advisable to train too many people in highly specialized techniques which they will rarely use and soon forget. Training should take place in the environment where the people will work.

Besides collecting samples (stool or rectal swab) from suspected cholera patients, a good surveillance system might also collect samples of water, sewage and washings of food from suspected sources. However, one must be careful not to overload the system with specimens of little or no probability of showing some bacterial pathogen. This is especially important if every specimen comes directly into one central diagnostic laboratory. For example, at the Pakistan SEATO Cholera Research Laboratory in Dacca 65,000 stool swabs were cultured and only 120 showed

V. cholerae. As the result of this experience the Laboratory finally settled on taking specimens only from people sick enough with diarrhea to come to medical attention. They stopped active search for diarrheal cases in the community and thus avoided a vast quantity of negative cultures.

Organization of a Surveillance Service

The key activity is the central laboratory. Most countries will want one or more of their own, as they sometimes are not willing to entrust to a laboratory in another country the responsibility of determining if cholera is present in their own country. The location, number and size of central laboratories will have to be determined by epidemiologists after on-the-ground study of the existing facilities and medical needs of a country. If a laboratory is to serve more than one country, the political realities of the situation should be considered.

There already exists in South and Central America laboratories which could easily serve as regional (reference and training) laboratories.

The objective of the surveillance service will depend upon whether or not cholera is expected, or is actually present. In Latin America the objective would be to watch for the first indication of the introduction of cholera into the Western Hemisphere. It was stated that Jamaica is already concerned about this and with good reason. Other Caribbean Islands which trade with Africa, and the north and central coast of Brazil, are the most likely areas where cholera may enter from Africa. This is a result of maritime trade. In Africa cholera is established and it will continue to spread. West Africa, south of the bulge, is particularly under risk. The objective here is to assist these countries in monitoring the spread of cholera within the country.

It will be a difficult problem to establish a corps of skilled people, if there is no health service already in existence to support a cholera surveillance service. Even with laboratories already in existence in many countries, the goal of a capability for complete diagnosis of all diarrheal diseases in every country is a long way off.

What can be done now is to identify and improve established regional laboratories. A cholera expert should be assigned to work with them and to stay with the problem. One of his functions would be to maintain interest in cholera on the part of the countries over an extended period. This is necessary in order that adequate surveillance can be achieved. Latin America should rate high in this effort.

Although the eventual target is at least a minimal early warning system in each country, the first step would be to create a system of regional laboratories for definitive laboratory work and to provide assistance to country laboratories. Some countries may not be willing to exchange or accept each other's laboratory reports because of the stigma attached to cholera. In such cases each country should have its own laboratory. Some Panel members thought that an international regional advisor would be needed to visit, stimulate and review the work done in the country facilities. Training programs should include international, as well as in-country training. A general diarrheal disease surveillance system alone will not suffice; the diagnosis must be specific for cholera.

There can be a flood of specimens if everything is done in one central laboratory in a country. Isolation should be done in provincial laboratories; definitive diagnosis in a central facility. Provincial laboratories were established rapidly in Iran during the epidemic of 1965. Technicians were trained in two weeks to make preliminary isolations. Africa may be a different story. For example, Kenya is an advanced country, but they decided that they could not put provincial laboratories into the field; therefore they decided that one central laboratory would be satisfactory.

A cholera service may begin by taking rectal swabs from the high risk group only. By this is meant only those who have severe diarrheal disease. The cholera personnel should work within an existing health system which will indicate who to swab, where and when. Any existing laboratory can be adapted to culture the specimens. Cholera

bacteriology is a simple thing to do and learn, and effective training programs can be devised and conducted locally.

The simplest way would be to set up the early warning system in existing hospitals and health centers. It was suggested that the respective directors could be offered a monetary incentive to submit stool specimens from each diarrheal case. Thereafter, the most difficult part of the system would be to induce the hospital staff to cooperate and maintain cooperation over a long period. It was recognized that any change in an established routine is hard to accept. It takes a sophisticated person to improvise, and a well-motivated one to accept and to keep on doing something he is not used to doing routinely. It was noted that malaria eradication programs have developed passive surveillance systems in hospitals and clinics, but a strong central authority is required to keep the systems functioning.

The stimulus to a country's medical and public health services to mount an adequate effort may well be based on the impact of the disease on the economy of the country. WHO has made two studies on the cost/benefit of cholera control and the economic impact of the disease. These and similar studies should be the basis for justification of a long range-effort.

The Main Action: Demonstration Pilot Projects

A series of demonstration projects is needed to show that surveillance will work and produce good results at low cost. Each demonstration requires the supervision of indigenous personnel who are interested in cholera and who can be relied upon to push the project to completion and to maintain an interest in it. A model (pilot) project should be set up and its costs determined. This information is needed in order to make realistic future plans.

The system must cover more than just cholera, or any other single diarrheal disease in order to maintain continuing interest and support. If the focus were on cholera alone, and none was present, interest in cholera surveillance would rapidly disappear and the effort would

collapse. Typhoid is not common enough, and dysentery is rarely serious enough to create a stimulus and to maintain the interest and financial support needed for such a service. However cholera is a disease having a strong, concentrated impact which would produce the necessary impetus to initiate and give momentum to the surveillance of all acute diarrheal diseases.

The Panel suggested that existing regional organizations might be instrumental in stimulating action and assisting the establishment of such services. Of these, two organizations in Africa were mentioned, the Organization for Cooperation and Coordination of the Fight Against Grand Epidemics (OCCGE) in West Africa and the Organization for the Control of Endemic Diseases in Central Africa (OCEAC).

The value of utilizing regional organizations was illustrated by a description of actions being undertaken by Turkey, Iran and Pakistan in attempting to establish a regional surveillance system for "cholera-like" diseases under sponsorship of the Subcommittee on Health of the Central Treaty Organization (CENTO). CENTO recommended that the three countries establish a Regional Coordinating Board for Communicable Diseases in which each country would be represented by a high enough echelon of its Ministry of Health to enable the Board to make policy decisions. The Board's first meeting, scheduled for March 1971 hopefully will recommend joint participation in the establishment of a regional surveillance system.

Some countries would not be able to halt the spread of cholera if its presence was confirmed. However the finding of cholera should serve as the notice to prepare for vaccination and the treatment of cases.

The Panel considered it was impossible to predict where in Africa surveillance systems should be established to be in front of movement of the disease. A certain periodicity could be observed in Thailand inasmuch as every five years another epidemic outbreak of cholera occurred. It appeared reasonable to suppose that cholera would spread further southward in Africa by contiguity. The Cameroons and the Congos might

be next. If it is possible to put a surveillance pilot project in the line of epidemic travel, its usefulness would be greatly improved.

Selection of Countries for Pilot Projects

The Panel considered a number of countries in which surveillance pilot projects would be useful and could be set up economically. Of the various countries discussed the following seemed to be logical locations for the establishment of demonstration surveillance projects:

-- Turkey would be a logical country. Turkey has relatively good laboratories with knowledgeable and well-trained technicians. They should be permitted to continue to use their own bacteriological techniques with which they are familiar, inasmuch as a particular technique is not important. The functioning of the collection and notification system must be developed. Turkey is a key country in the spread of cholera from the East to the West, and should be stimulated to maintain an active interest in cholera surveillance.

-- In Africa it was considered logical to try to set up pilot surveillance systems in a large country, a small country, and one extremely backward and undeveloped, in order to obtain representative types of experience. Probably one could not start in all countries at one time, but it was agreed that a start should be made, and the sooner the better. A surveillance program should be put into effect before all the countries are infected. Otherwise, it would become impossible to compare the value of a surveillance effort before and after infection becomes established in a country.

-- The Cameroons was considered the next country likely to be involved in Africa. It has a center, the Institute of Health Sciences at Yaounde, which could be used.

-- Liberia was suggested as representative of a small African country.

-- Nigeria was considered to be a promising example of a large African country with the capacity to become a training and demonstration center for other African countries.

-- Ethiopia would be a good place to start from two considerations: They have a great need, having been infected recently by cholera; and they have a capable man who would be interested in developing a surveillance program.

-- In the Western Hemisphere Jamaica would be a good country for a cholera surveillance pilot project. They have a well-equipped and staffed reference laboratory, and strong government interest and support for an enteric disease surveillance system. Jamaicans are aware of the menace stemming from the extensive traffic between West Africa and Jamaica. The Communicable Disease Center in Atlanta would be enthusiastic about helping Jamaica in such a program.

-- Brazil's coastline, at least the portion of its eastern bulge facing Africa, is also subject to the risk of cholera arising from maritime traffic with West Africa.

When asked to indicate priorities in the foregoing list, the Panel rated four as a tentative working list: (1) Cameroons (not yet infected) and Liberia (a small country); (2) Nigeria (a large country); (3) Turkey; (4) Jamaica or Brazil (its Atlantic ports only).

In all these countries a preliminary survey covering the health services and facilities as well as the laboratory services is needed. The survey team should determine the quality and quantity of equipment and capabilities of personnel, and the interest and determination of higher authorities to carry on such a project.

Even the demonstration projects will have to depend on a high degree of motivation in the indigenous Public Health Services. While a regional backup by a multilateral organization is needed, and most logically by a man in the WHO Regional Office, the outcome will depend on the country itself. To make a pilot project work, there must be responsible personnel in the country. A WHO cholera team can set up a project, but someone will have to revisit each one periodically to stimulate continued interest. World Health Organization presently has no regional laboratory for the cholera man to work out of, but the need for a permanent external stimulator was strongly underscored by the Panel.

There is lack of both a long-range plan for surveillance such as a 10, 20 or 30 year plan, and a facility that will provide long term support for the projects, like a WHO laboratory and the necessary senior advisory personnel to provide continuing guidance.

The WHO liaison suggested that WHO would not be able to provide laboratories but could assist the individual country laboratories with technical and other assistance. Reference laboratories can give technical support for diagnostic procedures. The WHO Regional Office Headquarters and the Cholera Teams are providing backstopping which seems to be sufficient to meet current needs.

The WHO permanent cholera team is available to review problems and train personnel in any country requesting such help. Also, WHO can provide national laboratories with an expert or a team to assist in training indigenous laboratory technicians.

The following requirements are needed to mount a successful pilot surveillance scheme:

Personnel: This will be the most variable item and outside experts might be needed as staff members and to train nationals in laboratory procedures (about two months) and in epidemiology (duration variable, depending upon available resources). World Health Organization should be able to provide this type of assistance providing budgeted funds are available.

Equipment: Many countries are eager to improve their laboratory equipment. The Panel cautions that some countries might justify requests on the basis of the threat of cholera; however, once the equipment is provided, and technicians trained in its use, it may never be used again. This is where planning and follow-up becomes important.

Surveys: Each country will have to be surveyed carefully before a pilot project is approved. In Manila a small pilot project for active surveillance was approved covering 15 000 people. It is staffed by one supervisor, three specimen collectors and two technicians. However, such an active (paid employee) collection system was considered too

costly for the area covered. An alternative is a passive notification system (a term used in malaria eradication) where one man visits hospitals, clinics, other health stations, and private practitioners to stimulate their cooperation in providing surveillance over a much larger area. A less intensive but broader geographical coverage results.

The usable functionaries who already exist to collect specimens must be determined in each situation. In some countries midwives, sanitarians, malaria and smallpox eradication program personnel might be used to gather information and perhaps specimens.

A surveillance program should be set up to cover acute diarrheal diseases in general, not cholera alone. The transport media available will readily cover most of the diarrheal diseases. The surveillance of such diseases could be valuable to Central America, Jamaica and Brazil because of recent epidemics of serious (fatal) types of dysentery in those areas. On the other hand, the laboratories in those countries would lose interest quickly if only cholera were looked for and none found.

The pilot projects described above should use the severe diarrhea cases coming to hospitals and clinics as the preferred subjects to be sampled. Cost-benefit studies have been done by WHO on cholera in India, Thailand, Malaysia, Hong Kong, the Philippines, and Korea. These studies are not highly refined and the Panel agreed that more such studies are needed.

Whatever is done in assisting countries in establishing cholera surveillance programs should be preceded by a survey team, consisting of a laboratory man and an epidemiologist. Personnel from WHO and CDC working jointly might comprise excellent survey teams. The time needed for a survey also would vary: Jamaica, Liberia, 1 week; Turkey, others, 2-3 weeks.

Such team operations should not be limited to the countries named by the Panel. Conditions may change or other countries may offer better

possibilities. The Panel agreed that WHO should continue its program for training surveillance laboratory personnel.

Summary of Conclusions and Recommendations

1. Surveillance is the first step in managing the cholera problem.

2. Surveillance should be based on bacteriological methods of diagnosis.

3. Every country should have a central laboratory of its own, capable of definitive bacteriological identification of cholera and other acute diarrheas, or access to an acceptable regional central laboratory.

4. The upgrading of existing laboratories is not difficult. Bacteriological methods are simple.

5. Available transport media facilitate the collection of stool and rectal swab specimens, and their shipment and holding for several weeks before primary isolation is made.

6. In larger countries the first bacteriological step, primary isolation of suspected bacterial colonies, can best be made in a number of small provincial or district laboratories, with final identification of the isolates to be made in a central laboratory. In small countries one laboratory can serve the entire country.

7. The establishment of a continuing system of collection and submission of stool or rectal swab specimens from suspected cases is more difficult. This requires capable and dedicated personnel, plus interest and support of the local government.

8. While cholera gives the strongest impulse for establishing a system of diarrheal disease surveillance, interest will soon fade if cholera alone is monitored, and it fails to appear or it disappears after it is found. The system should be set up to cover "Acute Diarrheal Diseases", including at least bacillary dysentery and typhoid fever, as well as cholera.

9. Pilot projects for establishing surveillance systems for cholera (and other acute diarrheal diseases) were recommended for representative large and small countries in Africa, some already invaded and others not yet invaded by cholera, as well as for Turkey and Jamaica or Brazil.

10. World Health Organization has a cholera team available for assistance in any cholera emergency, including the upgrading of laboratories and training personnel at all levels, and is prepared to set up additional teams, but lacks the required funding.

11. A surveillance system requires more than a bacteriological laboratory. It also requires a capable epidemiological service to evaluate information received and to direct appropriate action.

12. Either bilateral or multilateral assistance could be used in building up a surveillance system.

13. Whatever assistance may be contemplated, it should be preceded by a visit of a survey team to determine the needs in terms of personnel and equipment, and the level of interest and support of the government for a long-term, ongoing acute diarrheal disease surveillance system.

SUMMARY

Surveillance is the heart of a cholera control program. It will be possible to maintain a watchfulness over the distribution and trends of incidence of the disease through the orderly collection of the stool specimens and their bacteriological examination, a conclusive epidemiological investigation of each outbreak, and the systematic collection of morbidity and mortality data. The distribution of this basic information on a regular basis to those who need to know is essential to monitoring extension of the disease, to making decisions on control measures, and to measure progress toward prevention of transmission.

International organizations have the capabilities to assist member states in upgrading indigenous laboratories, including the training of personnel in identification of the causative organisms of all severe diarrheas, and in the development of epidemiological services. This can be done through the use of cholera teams and formalized training programs abroad.

The Panel pointed out that, while cholera gives a strong impulse for establishing surveillance systems, interest will soon die out if

cholera alone is monitored. It suggested that the system should be organized so as to cover acute diarrheal disease in general. Pilot projects for the establishment of surveillance systems were recommended for selected large and small African countries which were recently infected with cholera, for example Nigeria and the Cameroons or Liberia; a country which has had cholera and has developed bacteriological laboratories, but needs to be stimulated to maintain surveillance activities such as Turkey; and Western Hemisphere countries, Jamaica and Brazil, which are threatened with the invasion of cholera. The Panel cautioned that prior to providing assistance for the establishment of a surveillance program the countries selected should be visited by a survey team to determine the availability of health and laboratory facilities, personnel resources, and the level of interest and support of government for a long-term, acute diarrheal disease surveillance program.

RECOMMENDATIONS

1. Surveillance activities should be established in those countries where cholera is now present in order to monitor the extension of the disease, guide the attack, and measure progress made toward the elimination of the disease within the country.
2. Surveillance activities should be established in countries threatened by the introduction of cholera for all acute diarrheal diseases, not for cholera alone.
3. Surveillance activities should be based on bacteriological methods.
4. Assistance should be provided in upgrading indigenous laboratories, including the training of personnel in the culture and identification of the causative organism of all severe diarrheas, including cholera.
5. An orderly system in the collection of stool specimens from persons with severe diarrheas, their culture and analysis, and the reporting of results to appropriate health authorities should be established.
6. An epidemiological service, capable of evaluating the results obtained from the bacteriological examination of stool specimens and issuing

appropriate instructions for control of the spread and impact of a cholera outbreak, must be established as an integral part of the surveillance program.

7. Assistance should be provided in setting up pilot surveillance projects in, for example:

a. Nigeria - a large African country recently infected with cholera, with fairly sophisticated health services.

b. The Cameroons or Liberia - both small African countries recently infected with cholera, with only moderately developed health services.

c. Turkey - a Near East country which has had cholera recently and has developed bacteriological laboratories for the identification of the vibrio, but should be stimulated to maintain an active surveillance program.

d. Jamaica or Brazil - Western Hemisphere countries which are threatened with the introduction of cholera, and which have an interest in and laboratory facilities for carrying out surveillance activities.

e. Prior to the initiation of pilot surveillance programs in the above countries, or others of similar status, the health and laboratory facilities and personnel capabilities should be surveyed to determine the requirements for equipment and personnel training, and the interest of the authorities of the countries concerned in mounting surveillance programs. The survey team should be composed of not less than an epidemiologist and a laboratory man. The use of both WHO and CDC, USPHS personnel in the conduct of the surveys is recommended.

8. Regional organizations such as the Organization for Cooperation and Coordination of the Fight Against Grand Epidemic Diseases (OCCGE) in West Africa, the Organization for the Control of Endemic Diseases in Central Africa (OCEAC), the Central Treaty Organization (CENTO) and the Southeast Asia Treaty Organization (SEATO), should be used to stimulate action and assist in establishing surveillance programs for acute diarrheal diseases within member countries.

9. An educational program for all levels of health personnel which treats with the necessity of, and benefits to be derived from, a surveillance program is desirable.

Proceedings of the Panel on the Control of Transmission of Cholera of the A.I.D. Working Group on Cholera

The Panel on the Control of Transmission of Cholera met in Washington, D. C., on February 11, 1971, with the following persons present:

Chairman

Richard C. Parsons	Coordinator, Task Force on Cholera

Consultants

Janet Anderson	U. S. Public Health Service
Weyburn D. Davies	Sanitary Engineering Advisor, USAID, Saigon, Vietnam
Alexander D. Langmuir, M.D.	Harvard University Medical School
Andre Lebrun, M.D.	Medical College of Wisconsin
Hildrus Poindexter, M.D.	Howard University Medical School
Morris Shiffman, D.V.M.	University of North Carolina School of Public Health

A.I.D. Staff

Lee M. Howard, M.D.	Director, Office of Health Bureau for Technical Assistance
Elizabeth Hilborn	Public Health Advisor (Acting) Office of Technical Assistance Coordination, Bureau for Africa
Jean M. Pinder	Public Health and Population Office of North African Affairs Bureau for Africa
Joe L. Stockard, M.D.	Research Advisor, Office of Health, Bureau for Technical Assistance
A. Dale Swisher	Sanitary Engineer, Office of Health, Bureau for Technical Assistance
Robert W. Babione, M.D.	Member, Cholera Task Force
Jacob Landes, M.D.	Member, Cholera Task Force
Jean F. Rogier, M.D.	Member, Cholera Task Force

The Chairman briefly outlined the purpose of the meeting, and asked the Panel to suggest a practical plan of action that can be recommended to the Administrator of A.I.D. for his consideration and guidance in responding to countries who seek assistance in protecting themselves against the transmission of cholera. Such plans should be specific enough to permit cost estimates to be made.

The current status of the Seventh Pandemic was described. Cholera has spread from the Middle East to North Africa and by August 1970 it was in West Africa. It is likely to spread southward into the rest of Africa. In previous pandemics in West Africa it crossed from there to the Western Hemisphere.

The Panel considered that is is impossible to prevent the future spread of the present pandemic, and stated that current efforts must be directed to control its spread once it enters a country. In the long range, countries must be rendered nonreceptive to cholera becoming established. No country can stop the entry of all carriers of the cholera vibrio.

Panel discussion is summarized under the following headings:

I. Probable Routes of Infection
II. Courses of Action to Halt Transmission
III. Control Through Improved Water Supply
IV. Control Through Sanitation of Food Supply
V. Control Through Disposal of Human Wastes
VI. Control Through Surveillance and Therapy
VII. Control Through Vaccination
VIII. Control Through Travel Restrictions
IX. Control Through Health Education
X. Recommendations

I. Probable Routes of Infection

There are many ecological unknowns which complicate giving firm advice for controlling transmission of the disease. Cholera organisms are believed to survive in the human gut only, but this is

not certain. For practical control considerations it is probable that cholera is passed through the environment from the anus of a cholera patient, or carrier, to the mouth of a susceptible person. Carriers are very important in the cycle of transmission, especially with El Tor which can have a ratio of carriers to clinical cases as high as 100:1.

The minimum infectious dose is usually very large (up to a billion vibrios), but may be much less depending on the condition of the host, and particularly the level of his stomach acidity.

The usual mode of transmission involves the ingestion of polluted water and/or contaminated food. Gardens irrigated with fecally contaminated water or fertilized with human feces can be a source of infected raw vegetables. It was pointed out that Jerusalem had a very atypical experience in 1970, best explained by transmission of the cholera vibrio on green vegetables washed in sewage polluted streams.

The Panel agreed that the first point of attack should be on the usual modes of transmission.

The recent route of the geographical spread of cholera was considered. It is believed to have been carried from Egypt to West Africa by students returning home by airplane. It then spread along the West coast and up its rivers carried by fishermen and smugglers. Another route of direct extension is by nomads, herdsmen and tradesmen, who cross borders indiscriminately well inland from the coastal areas. Fairs also have been identified in the spread of cholera in West Africa. People come from miles around, become infected and carry the infection back to their villages. Tradesmen travel even greater distances, thus spreading the infection. Other movements exist, such as young men coming to cities to work. Laborers move from one country to another in large numbers, traveling by trucks and river boats for considerable distances.

II. Courses of Action to Halt Transmission

Problems of transmission can be categorized as being urban or rural:

-- The urban transmission is easier to control inasmuch as large numbers of people live in limited areas.

-- Rural transmission occurs in small units, is more diffuse and variable and it is difficult to focus an attack on it.

The alternate courses of action interrupting transmission are:

a) Work on the causative agent. Since no promising changes in the cholera vibrio are in sight, the control of transmission will depend on either concentrating on the environment or improving the condition of the host, or both.

b) Alter the environment.

c) Alter the physical condition or the behavior of the host (man). Depending on the circumstances, any one of the latter alternatives will bring about an interruption in the transmission of the disease.

Education of people to boil water or to purify it has been successful. Boiling water is feasible but only where fuel is readily available. Chlorination or other purification of water complicates its use, but people can be educated to do this.

Cholera has been present in Vietnam for years. The incidence is higher in the dry season when wells dry up and people go to the rivers for drinking water. To combat this natural phenomen in Vietnam, a Sanitary Hamlet Program has been highly successful both against cholera and plague. Examples were cited where cholera infections were traced to the discharge of waste from hospitals.

Health education aimed at safer disposal of feces has been effective in a number of places. It was recounted that the provision of water-seal latrines and health education reduced the fly population by about 99% in a Congo project.

There may be different types of transmission in a country, and various methods available for halting it in each type of situation. Inasmuch as it is impractical to provide for all possible situations, it is necessary to know what are the major routes and geographical foci of transmission, and what points in the transmission sequence are most vulnerable to attack by preventive measures. This calls for a depth of epidemiological analysis which has not yet been applied in most outbreaks.

The Panel agreed that very little more than general recommendations are possible without thorough study of where and how transmission is occurring in each country. It was recommended that an epidemiological team should be sent to each infected country to advise what to do in that particular situation. After an appraisal the country could then decide what could be done on its own initiative and what outside assistance would be needed.

The Panel felt that comprehensive Health Education programs and improvement of the environment are always long-term goals, but some aspects of such programs also can be short-term. Wherever community water supplies now exist a practical, immediate course of action is to see that they are well-operated and maintained. A visiting consulting team would be useful for this purpose. Since some African countries are small, they could be assisted by a regional effort through the use of a regional epidemiological unit and a sanitation team.

III. Control Through Improved Water Supply

Precise information is lacking as to the occurrence of cholera in relation to the presence or absence of piped water supplies, but experience indicates a considerably reduced attack rate when piped water is available.

An example was given of the value of a good piped water supply. Saigon has had an enormous growth in population and has an immense increase in population density. However it also has had an excellent

water supply throughout this period of growth. Although cholera is endemic in South Vietnam, it has not invaded Saigon.

In the urban setting cholera is often limited to slum housing areas having little or no sanitary facilities. The panel stated that water piped from a safe central supply could be beneficially extended to these areas and that it would pay to double or triple the number of public hydrants available.

Although capital cities gererally have piped water supplies of some magnitude, they frequently are deficient in operation and maintenance. The Panel recommended that consideration be given to the establishment of training courses for water plant operators and that a system for their supervision be initiated.

In Africa it was estimated that 80% of the people live in rural settings, i.e., villages of less than 500 population and without piped water supplies. In fact, piped water frequently is lacking in cities as large as 25,000 population.

Rural areas seldom have deep wells or other protected sources for water, and likewise no latrines. As a result, health education in individual sanitary practices and personal hygiene must be relied upon to assist in the control of transmission.

For small towns A.I.D. advisers in South Vietnam have developed a simple, slow sand filtration plant, using locally available materials. These plants are able to produce water free of coliform bacteria from any polluted source. Local people can be taught to operate it in a very short time. A plant with enough capacity for 2,000 persons at 30 liters per person per day covers an area 30 feet square and can be installed at a cost of approximately two dollars per capita. Only pumps, plastic pipe and fittings need to be bought.

IV. Control Through Sanitation of the Food Supply

There is need for high caliber epidemiological investigation before blaming foodstuffs in any cholera outbreak. Shrimp caught in polluted waters have been implicated, as well as vegetables grown

in the fields fertilized with human wastes. The most common food contamination is the practice of washing green vegetables with water from polluted sources. This is often done while in transit to market. Safe water should be supplied at supervised washing points for fresh vegetables enroute to markets. This was considered a most important measure in connection with food supply.

Adequate sanitation measures in food handling are also important. Control mechanisms applied to retail food outlets are not practical; therefore as much as possible should be done in the wholesale markets.

V. Control Through Disposal of Human Wastes

Adequate systems for human waste disposal is a long-range problem. In rural South Vietnam water-seal latrines are being used effectively. They are economically feasible and widely acceptable. The two bags of cement needed for construction are paid for by the villagers. Heavy surface pollution in the new slum areas of big cities could be greatly reduced by a sanitary privy program.

Effective programs for the disposal of human wastes will make a country much less receptive to the importation and the spread of cholera. A.I.D. has no policy at present for long-range promotion of such measures. Its efforts in the past in this line have dwindled and should be strengthened.

Considerable money is needed both for programs of better water supply, as well as human waste disposal. These must be "sold" on the basis of their benefits to controlling acute diarrheal diseases as a whole, and not on the basis of their benefits in the control of cholera alone.

The Panel was in agreement that efforts to strengthen or improve existing sanitary installations cannot progress without the sincere interest of the country itself to see the job done.

When cholera strikes, improvements in waste disposal, like water supply will depend primarily on health education if there are no sanitary facilities already available.

VI. Control Through Surveillance and Therapy

Adequate surveillance is necessary in order to achieve early identification of cholera, to determine its attack rate and direction of spread. This should be followed by therapy of the identified cases and prophylactic treatment of their contacts with tetracycline or other effective drugs.

In many Middle East and African countries there is great reluctance to admit that cholera is present. This suppression of information prevents factual reporting of the extent and the severity of the disease, and the early warning of contiguous areas. The Panel observed that the provision of good treatment removes fear of the disease and reduces reluctance to acknowledge its presence. It recommended that resources should be made available to infected countries which would provide them with the technical competence and materials needed to treat cholera cases correctly. The treatment is simple, and well-trained and supervised nonmedical people can do it easily while reducing mortality appreciably. Treatment centers can be set up any place with a minimum of equipment and personnel.

VII. Control Through Vaccination

The Panel gave the use of cholera vaccine a low priority on its list of measures to control transmission. However the Panel recognized that vaccination does have value in reducing morbidity and mortality in those areas where health facilities for treatment are inadequate or lacking, and in allaying the emotional response of a population threatened with cholera. Also, it may provide useful leverage for health authorities in obtaining financial support for treatment facilities and sanitary measures.

VIII. Control Through Travel Restrictions

The culturing of the stools of prospective travelers and their detention in isolation camps prior to departure are impractical measures and are of doubtful value.

Although many countries require that travelers from areas where cholera is present possess a valid international cholera

vaccination certificate for entry, the Panel was of the opinion that there is no evidence that the spread of cholera has been prevented by this travel requirement. The Panel stated that in the absence of adequate sanitary measures and safe water supplies, surveillance is of paramount importance in the control of transmission through travelers.

IX. Control Through Health Education

Health education is an integral feature of all approaches to the control of the transmission of cholera.

The Panel recognized that in the organization and implementation of a health education program, the methods to be employed will depend upon the stage of development of the health facilities and sanitary measures of the countries already infected, or at risk to the introduction of cholera.

In areas which depend upon open wells and streams and lakes for their water supply, the approach would be one of education of the public in personal hygiene. Instruction in sanitary practices and implementation of measures to assure a safe water supply, such as boiling or chemical purification of water used for drinking, cooking and washing dishes and food containers, should be emphasized.

In those areas served by piped water supplies, emphasis would be on the development of a surveillance system and the improvement and extension of existing sanitary measures.

In both the urban and rural areas there must be an educational program directed toward the effective disposal of human wastes in order to prevent contamination of the environment through the diarrheal discharges and vomitus of the cholera patient, and even more important, through fecal contamination by the carrier.

Educational programs must be tailored to the individual or the community to be reached. The participation of each in a program in which the benefits to be derived are positively identified is essential. Success of the program depends upon unrelenting effort directed toward motivating the political-administrative decision maker, the professionals

who will design and implement the program, and the consumer to take positive action in control of the transmission of cholera.

The threat of cholera to a country requires that vigorous action be taken toward convincing the political-administrative echelon of government to give legislative and financial support to programs of environmental sanitation.

Following discussion of the various avenues to be utilized in controlling the transmission of cholera, the Panel considered the methods by which countries might be stimulated to organize and carry out programs for the control of transmission of cholera:-

a) The World Health Assembly, by means of a resolution on cholera surveillance and reporting, health education and programs of environmental sanitation, might stimulate greater activity of its members.

b) The World Health Organization has cholera teams available for assistance in surveillance activities. These teams should cover environmental sanitation and health education, in addition to the epidemiology and surveillance of cholera. In addition the Regional Offices and Country Representatives of WHO, including its Regional Office for the Americas (PAHO), should be used to influence countries to request assistance in the improvement of their sanitation measures and health education programs.

c) The Organization for Cooperation and Coordination in the Fight Against Major Endemic Diseases (OCCGE) in West Africa and the Organization for Control of Endemic Diseases in Central Africa (OCEAC) should be encouraged to sponsor cholera teams and to stimulate and assist member states to establish surveillance and reporting activities.

d) The Central Treaty Organization (CENTO) member states should be encouraged to cooperate in the surveillance and reporting of enteric diseases.

e) An approach should be made to the international banking institutions to insist on the inclusion of environmental sanitation programs as prerequisites to development loans.

In summary the Panel stated that there is no immediate, easy, or cheap solution to control the transmission of cholera. Surveillance is of paramount importance, and making the environment nonreceptive to the cholera vibrio requires the provision of safe water and systems for the disposal of human wastes. Development of such programs requires interest at the national level, well trained dedicated personnel, and adequate financing.

The Sanitary Hamlet Program in Vietnam appears highly beneficial at a low cost. The government is putting the equivalent of about $1,000 into each hamlet. Wells are made safe and water-seal latrines are built. In Peru and Guatemala simple, practical solutions are being tested by the University of North Carolina. Regional or subregional organizations could be used advantageously in Africa.

X. Recommendations

All or part of the following may be found suitable for A.I.D. sponsorship in assisting lesser developed countries to reduce cholera transmission in and between countries; and existing multilateral and regional organizations should be used to a maximum extent for this purpose:

1. Provide consultant teams to survey water supplies and to inspect plant operations.
2. Assist in the development of training courses for water plant operators and managers.
3. Support the design and field trials of small, inexpensive water treatment systems for small cities and towns.
4. Support pilot projects for the control of cholera transmission based on epidemiological studies in selected countries having continuing transmission.
5. The Philippine studies on cholera control should be repeated in other areas.

6. Assist countries with courses for health educators.
7. Study better ways to bring presently active health educators into short-range, as well as long-range cholera control efforts.
8. Assist in sending a cholera control team to each threatened country, utilizing regional organizations such as OCCGE and OCEAC, as well as WHO, to a maximum extent.
9. Explore a working arrangement with the Conference of Ministers of Health of the Caribbean and with PAHO to strengthen protective measures in the Caribbean and Latin America against the incursion of cholera into the Western Hemisphere.

SUMMARY

The Panel pointed out that the reservoir for the cholera vibrio is man, and that the disease is maintained by a cycle of transmission of the vibrio from man to man through the environment in which he lives, chiefly by water and to a lesser extent food. It concluded that the only effective method of preventing the spread of the disease is to improve the sanitation and water supply, much of which is long-range, although some actions are possible in the very short-range.

Programs of health education are extremely important in obtaining acceptance and participation of the individual and of the community, and in promoting the legislative and financial support of the political administrative echelons of government in gaining improvement of environmental sanitation. The importance of good public health education programs cannot be overemphasized. Cholera, a disease of the poor and ignorant, can be controlled by properly applied public health measures if the people are informed how they will benefit from them. The training of food handlers in sanitary practices in retail outlets was not considered to be practical.

International organizations and agencies should assist and stimulate member states to establish surveillance programs and report acute diarrheal diseases; provide consultant teams to conduct sanitary surveys; develop training courses for water plant managers and operators; support the design and field trials of efficient, low cost, simple water supply systems for small cities and villages; and promote programs for the safe disposal of human wastes.

The Panel members were unanimous in their belief that an adequate safe water supply, conclusive epidemiological investigation of each outbreak, and appropriate health education activities are prime requirements to the control of the transmission of cholera.

RECOMMENDATIONS

1. Sanitary surveys should be made of existing piped water supplies, including plant operation, conditions of the distribution system, and the quality and quantity of the water delivered, to determine what action is needed to assist in their upgrading.
2. Assistance should be provided in the form of consultant teams for the development of training courses for personnel charged with management and operation of water supply systems.
3. Research and development programs should be directed toward the design of efficient, low cost, simple water supply systems for small cities and villages. Pilot projects to introduce such systems into the lesser developed countries should be sponsored by the international agencies.
4. Assistance should be provided to multilateral and regional organizations in the promotion of programs for the safe disposal of human wastes in both urban and rural areas.
5. Safe water should be provided for the washing of fresh vegetables enroute to market.
6. Health education programs should be developed for motivating the individual and the community to take positive actions as related to personal hygiene, and to measures to assure a safe water supply and an effective disposal of human wastes.

7. The Organization for Cooperation and Coordination in the Fight Against Major Epidemics (OCCGE) in West Africa, the Organization for Control of Endemic Disease in Central Africa (OCEAC), the Central Treaty Organization (CENTO), and the South East Asia Treaty Organization (SEATO) should be encouraged to sponsor cholera teams, and to stimulate and assist member states in the establishment of surveillance programs, the reporting of acute diarrheal diseases and coordination of preventive measures between countries.

8. The Committee of the Ministers of Health of the Caribbean should be encouraged to stimulate and assist member countries in establishing surveillance programs for acute diarrheal diseases, and to strengthen protective measures against the invasion of cholera through the provision of better environmental sanitation facilities.

9. Assistance should be provided by the Regional Offices and Country Representatives of WHO and PAHO in the training of health educators, the development of audiovisual materials for improvement of environmental sanitation, and in promoting vigorous action aimed at convincing the political and administrative echelons of governments to give legislative and financial support to programs of environmental sanitation.

10. An approach should be made by A.I.D. to the international banking institutions to require the inclusion of environmental sanitation programs as a condition precedent to the approval of development loans.

Proceedings of the Panel on the Therapy of Cholera of the A.I.D. Task Force on Cholera

The Panel on the Therapy of Cholera met in Washington, D. C., on February 22, 1971, with the following persons present:

Chairman	
Jean F. Rogier, M.D.	Member, Cholera Task Force
Consultants	
Abram S. Benenson, M.D.	College of Medicine University of Kentucky
Richard A. Cash, M.D.	School of Medicine University of Maryland
Thomas L. Cooper	Abbott Laboratories
Craig K. Wallace, M.D.	School of Medicine The Johns Hopkins University
Raymond H. Watten CAPT, M.C., U. S. Navy	Commanding Officer NAMRU II, Taipei, Taiwan
Liaison with WHO	
Dhiman Barua, M.D.	Division of Communicable Diseases WHO, Geneva
A.I.D. Staff	
Lee M. Howard, M.D.	Director, Office of Health Bureau for Technical Assistance
Richard C. Parsons	Coordinator, Cholera Task Force
Robert W. Babione, M.D.	Member, Cholera Task Force

The Coordinator of the Cholera Task Force described the events leading up to the formation of the Task Force and its responsibilities, which are to respond to the demands for emergency assistance from countries newly infected with cholera, and to develop a plan of action which the Agency might take to reduce the emotional, social and economic consequences of the current pandemic, and to prevent further spread of the disease. To aid the Task Force in developing a plan of action for the A.I.D. Administrator, a Working Group on cholera met in Washington in October 1970 and suggested that a series of Panel discussions be held

to develop specific recommendations relating to Cholera Vaccine, Surveillance, Control of Transmission and Therapy of Cholera.

For orientation of the Panel Members there was a brief review of the proceedings of the earlier panels.

The principal discussions of the Panel on Therapy of Cholera are reported under the following headings:

I. General Considerations.

II. Intravenous vs Oral Therapy.

III. Formulas for Rehydration Solutions

a. Intravenous
b. Oral

IV. Production, Packaging and Logistics Problems of Fluids.

V. Antibiotics.

VI. Other Supply and Equipment Requirements; Personnel.

VII. Stockpiling, Calculations of amounts.

VIII. Education in Treatment Methods.

a. Medical
b. Public

IX. Conclusions and Recommendations.

I. General Considerations.

Cholera generally is of little concern to a country until it is actually present, or at its frontiers. By this time an emergency situation exists and there are frantic requests for assistance to allay the emotional and economic consequences resulting from the presence of the disease and the high mortality in untreated cases.

Preparatory instruction of health personnel on how to deal with and treat the disease when it strikes is paramount. An example of the value of such preparation was cited in which, as the result of the instructions and experience gained by the visit of the Public Health Officer of the Liberian American-Swedish Minerals Company to the Pakistan SEATO Cholera Research Laboratory in Dacca, East Pakistan, the appearance of cases of cholera in areas covered by the Company's activities was met with efficient treatment and no panic occurred.

The second essential is one of logistics - how to deliver treatment services where the cases are. The delivery system is often lacking. However, the elements for treatment are simple and can be set up almost anywhere.

II. Intravenous vs Oral Therapy

The key to cholera therapy is rapid replacement of the water and electrolytes lost in the copious diarrhea, and the correction of acidosis and shock. The quantities of fluid lost and requiring replacement are often enormous and can be as high as 60-75 liters in an extremely severe infection.

Rapid rehydration with sterile intravenous solutions to restore fluid balance and to correct acidosis, followed by the slower administration of measured amounts to match the continuing loss of fluid and electrolytes, has reduced the mortality of cholera to near zero.

Oral therapy was originally set up as a partial substitute for intravenous (IV) therapy where IV fluids were not available in sufficient quantity to meet the treatment needs. Sterile intravenous solutions are essential in those cases admitted in shock or coma, or vomiting, but with the addition of oral therapy a limited supply of IV fluids can be stretched to cover 4 or 5 times as many patients. The use of oral therapy has been given field trials in East Pakistan by personnel from the Pakistan-SEATO Cholera Research Laboratory in Dacca, to determine its practicability under field conditions. Laboratory personnel have demonstrated that an oral solution can be given by mouth, but administration by the use of nasogastric tubes requires less patient supervision. This method permits the patient to sleep while receiving fluids and the intake is easier to control. Oral therapy has also been tried in the Philippines, Indonesia and Ethiopia with various formulae and with generally satisfactory results. In the Philippines it was thought to require more nursing attention. However with either the intravenous or the oral therapy regimen, administration must be continued on a 24 hour basis with an accurate measurement of output

(stools) and input (fluids). The decision as to which regimen to use depends upon the age and condition of the patient. If he is vomiting, pulseless and in coma, there is no option other than to start treatment with intravenous solutions. Children under two years of age cannot be managed by the oral route. They do not stand dehydration well and are more prone to complications. Hence rehydration with intravenous solutions is the method of choice.

Although time motion studies have not been done, the number of personnel required to administer and supervise the rehydration of the patient is essentially the same for either regimen. Insofar as children are concerned, the Panel was in agreement that constant attention is essential and a family member is suitable for this purpose.

The Panel agreed that both intravenous and oral solutions have their place and each has its advantages and disadvantages. The important thing is to get the patient rehydrated as quickly as possible.

ADVANTAGES

ORAL SOLUTIONS	INTRAVENOUS SOLUTIONS
Ingredients are usually readily available on local market.	Essential for treating young children and patients in shock, unconscious or vomiting excessively.
Reagent grade chemicals not required.	Rapid and certain in the correction of fluid loss and acidosis.
Prepackaging of chemicals relatively simple.	Less constant supervision needed.
Easily made available to patients.	

DISADVANTAGES

Useless in patients in shock or unconscious, or with excessive vomiting.	Prepared solution is expensive, and bulky to ship and store.
Requires more attention unless given by nasogastric tube.	Glass bottles, preferred to plastic, are heavy, hard to obtain and fragile.
Not suitable for children under two years of age.	Requires fluid giving sets and skill in technique of venepuncture.

III. The Formulas for Rehydration Solutions

The Panel agreed that for practical purposes a single formula for both adults and children is feasible and desirable. The oral formula must be modified somewhat from the intravenous formula, at least by the addition of glucose. The further addition of glycine to the oral formula makes it more effective per unit. The addition of flavorings makes the oral solution more palatable.

Solutions for Intravenous Use

Several formulas have been used successfully in the past in the preparation of intravenous solutions. World Health Organization has found Ringer's lactate to be a most convenient and satisfactory solution even though it is low in potassium and in bicarbonate equivalent. The additional administration of potassium, particularly in children, is most important. In addition to being a standard solution, Ringer's lactate is used in many other conditions requiring rehydration and is widely stocked in various parts of the world. Nevertheless, it was the consensus of the Panel that better formulas are known, and that only a single complete formula for sterile intravenous solutions should be recommended. Such a formula should withstand autoclaving, contain all the chemicals needed, and in sufficient amounts for restoring the electrolyte losses and correcting the acidosis.

There was agreement that for correcting acidosis, acetate was the preferred ion for use in stored intravenous solutions. Although less rapid than sodium bicarbonate in restoring the acid-base balance, it is more convenient to use because it can be autoclaved. The lactate ion is also effective, but subject to growing mold while in storage. Other alkalinizing salts have been used effectively, but acetate is the one of choice.

There was general agreement that the Dacca 5:4:1 formula is satisfactory and is easy to prepare.

Dacca 5:4:1 Solution

Na	133 milliequivalents	5 gms.	sodium chloride
HCO_3	48 milliequivalents	4 gms.	sodium bicarbonate (or equivalent as acetate)
K	13 milliequivalents	1 gm.	potassium chloride
	per liter of water		per liter of water

There was some question among the Panel members whether 133 milliequivalents of sodium might be too high for children. Once the deficit is restored they probably should be changed to the oral route for maintenance, and receive more water as soon as they are able to drink.

Dr. Watten stated that in 1958 he had successfully used a formula of sodium 120 milliequivalents, potassium 10 milliequivalents and acetate 30 milliequivalents. He now considers the latter two could advantageously be increased. He considered that 120 milliequivalents was the best all-purpose level for sodium, but acetate should be raised to 40, and potassium could be either 10 or 15 milliequivalents.

Glucose adds to the stability of intravenous solutions, but the Panel did not consider the benefits sufficient to justify its addition to the essential ingredients. An occasional undernourished child may be hypoglycemic and need some glucose, but this is so rare that the addition of glucose to the usual routine formula is not justified.

The Panel did not agree on any ideal intravenous formula for either adults or children. They agreed that several would work, and in the final analysis the dedication of the attendant and careful measurement of output and intake was more important than the minor differences in the electrolyte content of the solution.

Two not widely varying formulas were suggested:

	Dacca 5:4:1 Formula	Watten Formula (revised)
Na	133 milliequivalents	120 milliequivalents
K	13 milliequivalents	10 or 15 milliequivalents
Acetate	48 milliequivalents	40 milliequivalents
	per liter of water	per liter of water

Formulas for Oral Replacement Solutions

The Dacca oral solution formula has had large-scale trial and has proved its effectiveness. It has the virtues of low cost, ready availability of ingredients, and the simplicity and safety in use.

It has been found that glucose was a necessary addition, while sodium chloride could be reduced somewhat over that of the intravenous formula to preserve the osmolarity of the solution. However, sea salt should not be used because of its laxative salts content. The basic formula developed in Dacca follows:

Na	120 milliequivalents	4 gms. Sodium Chloride
K	15 milliequivalents	1 gm. Potassium Chloride
HCO_3	48 milliequivalents	4 gms. Sodium Bicarbonate
Glucose	110 millimoles	20 gms. Glucose
	per liter of water	per liter of water

When 8.25 gms. (110 millimoles) of glycine was added to the above formula the results improved. Diarrhea lasted an average of 46 hours. when cases were treated with a formula containing glucose alone, and 27 hours when the formula contained both glucose and glycine. The quantity of stool output, and thus the amount of fluid needed, was also substantially reduced from 15.5 liters to 9.5 liters. The cost of ingredients, including glycine, per liter was increased but the quantity needed was less. The addition of glycine raised the cost of chemicals as much as 80 per cent, but this will vary with the source of glycine, a common and plentiful amino acid.

People differ greatly in their acceptance of oral therapy measures and procedures. In India people would not drink enough fluid unless someone stood over them and insisted on it. The use of nasogastric tubes requires much less supervision of patient care on the part of the nurses.

It was observed that in Manila drinking was preferred over taking fluid by nasogastric tube. The oral route was well-accepted in Ethiopia when administered by a missionary nurse. Glycine makes the oral solution taste like green coconut water, and this is agreeable to most people.

Substituting potassium citrate for potassium chloride also improved the flavor, as did the addition of lime juice. Artificial flavors such as Kool Aid also improved acceptance. In the Philippines grape flavor was most popular. An expert consultant in the field of preferences for flavors would be Mr. Henry Walters, Chairman of the Board, International Flavors and Fragrances, New York, New York.

IV. Production, Packaging and Logistics Problems of Intravenous and Oral Solutions.

A. Intravenous Solutions

Sterile intravenous solutions are costly to prepare and ship and they require lead time in their preparation. In Manila about two weeks are required for delivery of sterile pyrogen-free water.

Local manufacture of pyrogen-free water and the preparation of intravenous solutions can be undertaken in some places in Africa. Dakar and Abidjan now have this capacity, but they lack glassware and filters. The distillation capacity is very small in many countries.

The Panel agreed that in emergencies water that is not pyrogen-free can be used in order to save life, although this will result in febrile episodes.

Glass bottles, which usually must be imported with high import duty, are a problem in many countries. Bottles can be re-used but this is not considered good practice for stockpiling and is prohibited by law in some countries. Used bottles may have invisible chips or cracks that permit leakage or harbor contamination. Ordinary glass bottles are acceptable if the product is to be used promptly, but special pharmaceutical glass is needed for storage for more than one year.

Plastic bottles have been used successfully for the packaging of prepared solutions. Plastic technology exists, but manufacturers do not want to guarantee the quality of solutions stored for extended periods in soft plastic bags. Some manufacturers now are working on the production of semirigid plastic bottles. Use of such bottles would reduce breakage and save some weight over glass containers. Soft

plastic bags are easy to ship, store and use, but preparation is more difficult and stability of the solution is not guaranteed.

The transport of large quantities of intravenous solutions into remote areas presents difficulties which severely limit their use, even though an ample supply may be centrally available.

B. Oral Solutions

For the preparation of oral solutions the preweighing and packaging of dry chemicals in plastic bags is practical. The proper quantity of chemicals for adding to 1, 15 or 20 liters of ordinary drinking water has been packaged and used. After long storage (1 year) the glucose may turn brown and the admixture becomes hard. Nevertheless, it is still effective; it merely takes longer to dissolve when mixed in the water.

A double plastic bag, with printed instructions placed between the inner and outer bags, is the recommended method for packaging. A problem arising from the use of powders is that people will not take time to see that they are completely dissolved and thoroughly mixed with the water. To overcome this the chemicals for preparation of the oral solution could be packaged as a concentrated solution.

V. Antibiotics

The use of antibiotics is indicated in the treatment of cholera. They will shorten the duration of diarrhea and reduce hospitalization by several days, and should be given as soon as the patient can swallow. Their use also prevents the carrier state. Tetracycline and furazolidone are equally good, but the latter is somewhat cheaper. Tetracycline has a wide availability, but it was felt that furazolidone could be manufactured in any quantity if there was sufficient demand. The minimum treatment is three days with a total of three grams of tetracycline, or 1.2 grams of furazolidone.

Chloramphenicol is highly effective, but it has somewhat greater hazards, and the other two are preferred. Other drugs have been reported

to be effective, but not sufficiently so to justify their use over tetracycline or furazolidone.

The Panel was unanimous in stating that the inexperienced practitioner tends to think first of antibiotics for treatment, whereas the only lifesaving measure is the rapid restoration of fluid and electrolyte losses and correction of acidosis.

VI. Other Supply, Equipment and Personnel Requirements:

In addition to the intravenous and oral solution preparations and means for administering them, cholera cots, plastic sheets and plastic buckets for collecting and measuring diarrheal discharges and vomitus are essential, together with charts for recording the input and output of fluids. A scale for weighing the patient and experience in estimating when he is sufficiently rehydrated will suffice for the management of initial rapid rehydration. Thereafter, measurement of input and output is essential, and this requires cholera cots and buckets.

Continuous, twenty-four hours a day patient care is essential. Hence, means for illumination of the treatment area and an ample well-trained staff are required. It was emphasized that the techniques are quite simple and that nurses and ward boys can learn them in a few days of supervised on-the-job training.

It is highly desirable that mothers be permitted on the ward with babies and children to assist in their feeding and care. The children do better with their mothers present, whether on intravenous or oral therapy. The risk of infection to the attendant is negligible. Positive cultures were not found in family attendants upon their leaving the hospital.

VII. Stockpiling, Calculations of Amounts.

The Panel considered that it would be desirable to stockpile the following items:

a. Limited amounts of formulated intravenous solutions.

b. Prepackaged, electrolyte powders for making up oral solutions.

c. Reagent grade chemicals, in bulk, for making up intravenous solutions.

d. Glass bottles and/or plastic bottles with stoppers or screw caps for intravenous solutions.

e. Fluid administration sets.

f. Needles, including pediatric scalp vein sets.

These items could be stored in a central depot in each country or geographical subdivision of a country. The Panel suggested that WHO might store such items regionally for groups of small countries.

Cholera cots, with plastic sheet and sleeve, and calibrated buckets should be prepared in advance, but need not be stored centrally. Two or three cots with sheets and buckets should be available in each hospital or major dispensary, and used regularly for severe diarrhea cases. They could serve as models for local manufacture of more of the same, if the needs of the hospital suddenly increased due to an influx of severe diarrheas, including cholera cases.

The Panel suggested that the quantity of intravenous solutions to be stockpiled should be calculated on the basis of a minimum treatment kit for 100 patients that could be transported readily anywhere and be in use immediately upon arrival. If oral treatment is also used, the average case will need three to four liters of intravenous solution, plus nine or more liters of oral solution. For example, about 400 liters of intravenous solution and a sufficient number of packets of chemicals for the oral mixture to make up 1,000 liters of oral solution should be stockpiled centrally or peripherally, for each treatment center planned. It is self-evident that no one can predict how many or where cholera cases will occur in any given outbreak.

The kit should also include needles and fluid administration sets for 100 cases; enough plastic tubing (Levine tubes) for use as naso-gastric tubes, bottles to hold the oral solutions and tubing clamps; cotton, alcohol, adhesive tape, etc. Antibiotics should be added to the kit just before it is issued for use. The contents of the kits should be rotated periodically to insure against deterioration while in storage.

The Panel did not advise large stocks of kits, but they should be immediately available without having to look for the materials when an emergency strikes.

The shelf-life of plastic tubing is longer than that of rubber, but neither one is indefinite.

Commercial firms allow five years maximum shelf-life for stable intravenous solutions, with three years for the less stable ones.

Intravenous solutions stored in Fenwall plastic bags are cheaper but contamination with fungi occurs; also, their shelf-life is shorter than for those in glass bottles.

Stockpiling of dry chemicals for intravenous solutions could be useful, but this requires a local capacity to make sterile pyrogen-free water and facilities for autoclaving the formulated solution.

Insofar as possible, it is better to stimulate countries to develop their own facilities and to build up reserves of their own in order to avoid the experience of the A.I.D. stockpile at Izmir, Turkey (1967-70) where a limited demand for the supplies resulted in substantial waste.

Educational materials, both for medical and for lay people, could very well be included in the kits.

The Panel suggested that consideration should be given to stimulating the development of local facilities, either government or commercial, for the production of formulated intravenous solutions and for packaging materials readily dissoluble for the preparation of oral solutions. It was suggested that A.I.D. might assist in the procurement of the finished product or raw materials, or in the upgrading of production facilities, while WHO could take responsibility for stockpiling materials in strategic locations.

VIII. Education in Treatment Methods

Education of medical, nursing and paramedical people is basic to a successful therapy program. Instructions should be made available to doctors, nurses and other paramedical personnel. There should be simple, standard, step-by-step nursing instructions. Illustrated instruction

material prepared by experts in teaching brochures should be extremely valuable. The WHO booklet, "Principles and Practice of Cholera Control", Public Health Papers No. 40, contains excellent advice on the therapy of cholera. Reprints of the chapters on therapy could be translated and distributed. The Panel recommended improving the formula for Ringer's lactate solution, but did not reach a consensus on a new formula.

Treatment demonstrations with cholera cots, using patients dehydrated with other diarrheal diseases, is very important. Defects in the equipment and kits should be discovered before cholera strikes. The cholera cot should be used regularly in all cases of acute diarrhea.

A professional expert may be needed to influence authorities at high levels of government, but the major work of teaching cholera therapy should be done by practical instructors working in hospital wards and giving demonstrations of care and management using real patients. A doctor, a nurse and a ward boy with experience in the therapy of cholera could be sent as a team to each hospital within each country where the above type of demonstration and practice is needed. The Panel suggested that WHO is the logical agency to provide a master team to train the local instructor teams.

If packages of rehydration salt mixtures for making oral solutions are available locally, the public should be taught how and when to use them. The instructions that go on or in such packages are important. They should be labeled "For Treatment of Diarrheal Diseases". Cholera should not be prominently mentioned, although it should be listed among the diseases for which contents of the packet are being made available.

Health education of the public should go along with all other measures to improve therapy. The people must be informed about where to seek therapy and they must be motivated to seek it at the earliest onset and without waiting until the patient is critically ill.

Conclusions and Recommendations

1. Adequate treatment will bring the mortality from cholera to almost zero; it will remove the fear of the disease.

2. Treatment is simple and inexpensive, but advance preparation of materials and training of the patient care staff are essential.

3. Rapid restoration of fluids and electrolytes is essential, and both the intravenous and oral routes of administration have their place in the treatment regimen. The intravenous route is necessary if the patient is unconscious or in shock. The oral route is simpler for less skilled hands; it is cheaper and needs no special equipment.

4. A single formula should be selected; one that will serve for both adults and children. For an intravenous solution, Ringer's lactate is not ideal, but it is the closest standard commercially available single solution. If large stocks of fluid are to be procured, they would be in the chemical range of the Dacca or Watten formulas (see page 130).

5. For oral therapy, glucose must be added, and glycine will produce further advantages if added to the formula. The increased cost due to the addition of glycine will be offset by the smaller amounts of the oral solution needed.

6. Oral solutions can be made up with locally available ingredients.

7. Commercial prepackaging and distribution of the powder mixture for making up oral solutions should be encouraged.

8. Stockpiling of large amounts of intravenous solutions is not recommended. They are expensive to make and to ship. Nevertheless a minimum stock in units suitable for treating 100 patients should be available in each country at risk in order to meet the first impact of cholera. WHO, with A.I.D. assistance, could build up the capacity to produce intravenous solutions on a regional basis, end even develop a regional stockpile. Assistance could be given to larger countries in building up a stockpile.

9. Plastic containers are easier to ship and to use but glass is better for long storage.

10. Reagent grade chemicals not readily available could be stockpiled centrally and in bulk.

11. Antibiotics have value in the treatment of cholera. Tetracycline or furazolidone are the drugs of choice, and the latter is the cheaper of the two. They should be included in the patient treatment kits mentioned in item 8 above, but should not be added until the kits are issued for use in treatment centers.

12. A.I.D. could work through WHO to develop regional depots of supplies that are difficult to obtain.

13. Cholera cots, plastic sheets, buckets and as many other supplies as possible should be obtained locally. Every hospital should have a few cholera cots and should use them regularly in all cases of severe diarrhea.

14. Medical and nursing personnel should receive practical, on-the-job training in the therapy of cholera. Demonstration teams made up of a doctor, a nurse and a ward boy should be sent to each hospital in the country to make demonstrations.

15. Education of lay people in handling of severe diarrheas is important, and could be improved with application of skills in printing pamphlets, comic books, and other educational materials.

SUMMARY

Effective treatment of cholera can reduce the mortality to less than one per cent in all ages. The treatment consists of the administration of replacement fluids designed to replace the water and electrolytes lost in the cholera stool. The fluid-electrolyte replacement is divided into two phases: (1) Rehydration, carried out as rapidly as possible with sterile intravenous solutions with a goal of correcting the cardiovascular collapse and restoring normal hydration and the acid-base balance; and (2) Maintenance which is accomplished by replacing the measured stool output with intravenous solutions, or with an oral electrolyte-glucose solution.

Intravenous solutions are essential for use in the treatment of severely ill patients and children under two years of age. The addition of antibiotics, tetracycline or furazolidone, will reduce the replacement fluid requirements, the duration of the diarrhea and the period of hospitalization, but the replacement of the water and electrolytes lost in the cholera stool is the lifesaving measure.

The Panel was in agreement that a single formula for both adults and children is feasible and desirable. The addition of flavors to the oral solution improves acceptance, while the use of a nasogastric tube facilitates administration. Constant care and supervision of the cholera patient is essential and use of the cholera cot with its plastic sheet and sleeve and buckets facilitates the collection and measuring of the cholera stool.

Preparatory instruction of health personnel in the treatment of cholera presents no particular problems, but it is extremely difficult to predict how many cases will occur, or where, in any given outbreak. In order to take care of the initial outbreaks, the Panel suggested that WHO might stockpile minimum treatment kits for 100 patients consisting of intravenous solutions, fluid administration sets and needles, and prepackaged electrolyte powders for making up oral solutions. However, insofar as possible countries threatened with cholera should be encouraged to accumulate reagent grade chemicals, bottles and equipment for producing their own intravenous replacement solutions and fluid administration sets.

Cholera cots, plastic sheets with sleeves and calibrated plastic buckets should be standard equipment for use in the treatment of severe diarrheal diseases in every hospital.

Programs of health education are essential to inform the public of the effect of proper treatment in the mortality resulting from acute diarrheal diseases and obtaining their participation in handling severe outbreaks.

RECOMMENDATIONS

1. Facilities for the prompt treatment and constant care of patients stricken with cholera should be established in all countries affected or threatened by cholera.
2. Assistance should be provided for the training of indigenous medical and paramedical personnel in the treatment of acute diarrheal diseases, including cholera.
3. A single formula for a sterile intravenous replacement solution for the treatment of both adults and children is feasible and desirable.
4. A single formula for an oral electrolyte-glucose-glycine solution for the treatment of both adults and children is feasible and desirable.
5. In-country production of standard intravenous replacement solutions should be stimulated, and technical assistance, equipment, and supplies provided if necessary.
6. Consideration should be given to the stockpiling of reagent grade chemicals required in the production of intravenous replacement solutions.
7. In-country prepackaging of electrolyte-glucose-glycine dry powder mixtures for the preparation of oral solutions should be encouraged.
8. Fluid administration sets, needles, including pediatric scalp vein sets, and nasogastric (Levine) tubes should be stockpiled.
9. Antibiotics (tetracycline or furazolidone) should be provided if not readily available on local markets.
10. Treatment kits for 100 patients containing intravenous replacement solutions (400 liters), fluid administration sets and needles, sufficient prepackaged dry mixture to make up 1,000 liters of oral solutions and antibiotics might be stockpiled by WHO and PAHO in strategic locations in countries affected or threatened by cholera.
11. Cholera cots, plastic sheets with sleeves and calibrated plastic buckets should be produced, or obtained locally, and become standard equipment for use in the management and treatment of acute diarrheal diseases.

12. A simple, well-illustrated manual for the management and treatment of cholera for medical and paramedical personnel should be prepared by WHO. Translation into the language of the countries affected or threatened is desirable.

13. Health education programs should be developed for motivating the individual and the community to seek treatment promptly for any acute diarrhea, including instructions on how to use oral replacements if these are made available.

APPENDIX "D"

REFERENCES

Snow, J., SNOW ON CHOLERA, Richardson, B. W. (ed), New York: The Commonwealth Fund, 1936

Felsenfeld, O., THE CHOLERA PROBLEM, St. Louis: Warren H. Green, Inc., 1967

CONTROL OF COMMUNICABLE DISEASES IN MAN, Eleventh Edition, 1970, New York; Published by The American Public Health Association

PRINCIPALS AND PRACTICE OF CHOLERA CONTROL, Public Health Paper - 40, Geneva: World Health Organization, 1970

Gangarosa, E. J. and Mosley, W. H., ASIATIC CHOLERA, TICE'S PRACTICE OF MEDICINE, W. F. Prior Company, New York

CHOLERA - TB MSD 138; NAVMED P-5052 - 23; AFP 161-8, 31 July 1969

Cash, R. A., et al: A CLINICAL TRIAL OF ORAL THERAPY IN A RURAL CHOLERA TREATMENT CENTER, The American Journal of Tropical Medicine and Hygiene, Vol. 19, No. 4, July 1970, pp. 653-656

Hare, W. H., et al: CHOLERA - METHOD OF THE PAKISTAN-SEATO CHOLERA RESEARCH LABORATORY, CURRENT THERAPY 1970 by W. B. Saunders Company

MEETING THE THREAT OF CHOLERA: WHO Chronicle: Vol. 20, No. 7, July 1966

WHO Expert Committee on Cholera, Second Report: WHO TECHNICAL REPORT SERIES, No. 352, Geneva 1967

Mathen, K. K., COST-BENEFIT AND COST-EFFECTIVENESS CONSIDERATIONS IN CHOLERA CONTROL (unpublished document WHO/BD/Cholera/70.3)

CHOLERA - A REVIEW FOR WHO SEMINARS (unpublished document WHO/BD/Cholera/70.19, Rev. 1)

Wood, W. E., CHOLERA CONTROL THROUGH ENVIRONMENTAL SANITATION, BASIC CONSIDERATIONS: (unpublished document WHO/EH/70.1)

Cvjetanovic, B., SANITATION VERSUS VACCINATION IN CHOLERA CONTROL - COST-EFFECT and COST-BENEFIT ASPECTS (unpublished document WHO/BD/Cholera/71.1)

COMMUNITY WATER SUPPLY PROGRAMME, Progress Report by the Director General: WHO/A23/P & B/5, 10 April 1970

CHOLERA, PRESENT TRENDS AND PROBLEMS, WHO/EB 47/WP/8, 15 Jan 1971

Mathen, K. K., Barua, D., Cvjetanovic, B., and Uemura, K., COSTS OF TREATMENT AND PREVENTION AND ECONOMIC LOSSES DUE TO CHOLERA (unpublished document WHO/BD/Cholera/71.1)

Mosley, W. H., ROLE OF IMMUNIZATION IN THE CHOLERA CONTROL PROGRAM: (unpublished document WHO/BD/Cholera/71.1)

SUMMARY OF THE PRELIMINARY REPORT ON EFFECTIVENESS OF ENVIRONMENTAL SANITATION IN CHOLERA CONTROL - PHILIPPINES: Cholera Committee (unpublished document WHO/BD/Cholera/71.1)

BULLETIN, WHO 1970, 43:360-363

THE SURVEILLANCE OF CHOLERA: WHO Chronicle, Vol. 24, No. 2, February 1970

THE SEVENTH CHOLERA PANDEMIC: WHO Chronicle, Vol. 25, No. 4, April 1971

APPENDIX "E"

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