CHOLERA—ITS NATURE, MANAGEMENT AND PREVENTION*

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The seventh and current pandemic of cholera has been in progress for almost 10 years. Starting in the Celebes in 1961 it affected all neighbouring countries, invaded the Indian subcontinent and the Middle East and it has now appeared in Africa south of the Sahara for the first time this century. That this is a continuing and expanding invasive process has been demonstrated by the recovery of the eltor biotype of *Vibrio cholerae* from all infected areas, including those zones of cholera endemicity outside the Indonesian archipelago where classical cholera asiatica has been entrenched in the past. In fact, the eltor biotype has acted as a marker of the progress and extent of the current invasion and has again demonstrated that despite rigorous quarantine measures cholera continues to move as insidiously, erratically and as unpredictably as in the past. It has also demonstrated that, if allowed to go unchecked, cholera eltor causes chaos, morbidity and mortality every bit as disruptive to community life as cholera asiatica.

The recent appearance of cholera in Guinea where there have been at least 2 000 cases and more than 60 deaths[1] is a sharp reminder that the seventh pandemic is still on the move and that further spread in Africa is by no means a remote possibility. Many health administrations in Africa have already recognized this and instituted varying degrees of surveillance and quarantine measures.

The last cholera invasion of East and Central Africa took place in the course of the fourth pandemic of 1863 - 1875. Appearing in Ethiopia in 1865 via Jidda, Suakin and Massawa, cholera infection was carried along the trade routes into East Africa, affecting the Kilimanjaro region in 1869. From there it spread both south and east. Infiltrating south along Lakes Tanganyika and Nyasa it eventually reached Mozambique and the headwaters of the Congo basin; from Mozambique it was carried to Madagascar in 1870 and 1871. From Kilimanjaro it also spread east to Zanzibar, causing the death of some 70 000 persons in 1869 - 1870.[2]

During the same period, caravans from Morocco are reputed to have been the means of transmission of cholera to West Africa where it appeared first in 1868 in Podor on the Senegal River and subsequently in Gambia and Portuguese Guinea. French West Africa was again infected in 1893.[3] Since that time there has not been any outbreak of cholera in Africa south of latitude 10° N until the recent episode in Guinea.

Reports of cholera in South Africa are scanty but Clemow records that Durban was infected in 1890. In his review of the geographical distribution of cholera at that time he comments: 'The infection has been several times imported to the shores of South Africa (one of the most recent instances occurred in Durban in 1890) but has never gained a footing there'.[4]

In the global context of the ability of cholera infection to spread widely from the zones of endemicity, it is relevant to note that, during the fourth pandemic, points in the Americas as far apart as New York and Buenos Aires, the Caribbean Islands, Chile and Bolivia were all infected. The Americas were again infected during 1892 - 1895. However, cholera has not maintained itself in Africa, America or Europe in between the 7 pandemics that have been documented. It is only in the Indian subcontinent and the Indonesian archipelago that foci of endemicity have continued to persist.

The current pandemic has not been noticeably contained by the application of international quarantine measures nor is there any evidence that community-wide immunization against cholera has been effective in limiting its spread. Further, despite the higher standards of environmental hygiene at sea and on land that have been applied extensively in recent years to both the means of transport and the passengers being carried, the rapidity of communication by air has tended to offset the advantages gained. For example, an individual may be in a cholera endemic zone or exposed to an epidemic focus of infection on one day and yet be thousands of miles away and in a susceptible and unprepared community the next. Under these circumstances, if the dislocation and often the hysteria induced by the appearance of cholera is to be avoided, it is essential to have a clear understanding of the nature of the disease, its management and prevention. The cardinal points to be observed in planning measures to deal with cholera are an increased surveillance of diarrhoeal disease, the earliest possible definitive diagnosis in cases suspected of cholera, the proper management of the clinical case and of those in immediate contact with the patient, and the application of measures of environmental sanitation based on a knowledge of the epidemiology of cholera. If these measures can be implemented, cholera can be controlled and severe community involvement can be prevented.

THE NATURE OF THE DISEASE

Cholera has an incubation period ranging from a few hours to 7 days; most commonly it lies in the range of 2 - 5 days. In the florid case, copious vomiting and diarrhoea, muscular cramps and severe prostration appear early, going on to advanced dehydration. The algid, dry-tongued, emaciated, hollow-eyed patient with poor skin turgor, 'washerwoman's hands' and copious, uncontrollable rice-water stools presents a dramatic picture. Equally remarkable is the rapidity of resuscitation and recovery of apparently moribund patients if adequate treatment is given by the replacement of fluids and electrolytes within 3 - 6 hours of the onset of symptoms. The mortality from untreated cholera is high and rates of 60% or more may be expected where adequate treatment facilities are not available; this is particularly so in severe common-source outbreaks in recently invaded susceptible groups. Modern methods of rehydration and of replacement and maintenance of electrolytes, however, have reduced case fatality rates to less than 1%, even when such treatment is given under relatively primitive conditions in rural areas; in fact, under such circumstances, unless there is some pre-existing underlying pathology, cholera should no longer be a fatal disease.

*Date received: 4 November 1970.

The Biotypes

The two main biotypes of *Vibrio cholerae* are cholera asiatica and cholera eltor; the most frequently encountered serotypes common to both are Ogawa and Inaba. Although the two biotypes can be readily differentiated bacteriologically and there are increasingly well-defined differences in epidemiological characteristics, as far as the management of outbreaks of cholera is concerned, these differences are of little import clinically or epidemiologically. Whatever the biotype, *Vibrio cholerae* or the 'comma bacillus of Koch' represents a highly communicable infection, which, once introduced into a community, spreads rapidly, widely and unpredictably, preponderantly by the faecal-oral route. Unless a common source vehicle is heavily contaminated by a case or carriers, such as an unprotected water supply or a widely used article of food or drink, the disease appears sporadically and has a low attack rate. On the other hand heavy inocula acquired from a common source will give high attack rates of severe cholera among the exposed group.[5] Although transmission from one individual to another generally appears to be directly through close physical proximity, the contamination of water or articles of diet in the immediate environment and which are consumed within short periods of time after contamination has taken place, must also play an important part in the dissemination of infection. In the general community only about 1% of those infected will have clinically manifest cholera with rice-water stools.

Where a clinically evident case of cholera occurs it can be expected that between 7 and 25% of living space contacts—that is family, work, hostel or play contacts where there is close physical proximity—will become infected and excrete cholera vibrios without any evident illness. These contact or 'healthy' carriers are most often undetected, move freely in the community and are excreting cholera vibrios apparently just as choleragenic as those from an overt case of the disease. The immediate environment of the clinical case also becomes heavily contaminated and *Vibrio cholerae* can be recovered from moist surfaces, from kitchen equipment, in particular chopping blocks and food preparation areas, from drains and especially from latrine buckets if such are used.[6]

Source of Infection

Outside the human body the vibrio is a fragile organism and a poor competitor. It may survive for some days in water or on moist surfaces in kitchen or living-room areas but will not multiply as in a favoured medium. If water supplies are heavily and continuously found to be infected, as proved by serial examinations, then it is certain that continuous reinfection is taking place. Fruits, fish, drinks and other articles of diet are very exceptionally responsible for persistence of cholera infection over short periods of time; certainly they are not responsible for transport over long distances.[7] The only source from which *Vibrio cholerae* have been consistently and universally recovered is the bowel of man and the only proved vehicle of transport of cholera infection over long distances is either the case incubating the disease or the symptomless carrier. Infected man is undoubtedly the source of contamination of water supplies found to be infected and of articles of food or drink incriminated during an outbreak.[8]

The duration of the excretion of cholera vibrios by an infected human is generally short, although recent work has indicated that long periods of infectivity are more common than previously believed. In the 'convalescent carrier', or the patient recovered from clinically manifest cholera, the carrier state lasts on the average for a week to 10 days in the majority of individuals who have not received antibiotics during therapy.[3] Recent work by Pierce *et al.*[9] has recorded periods of 50 - 331 days in 3 carriers persisting among 81 convalescent cholera patients, of whom the majority had had antibacterial treatment, a prevalence of 3·7%. In the Philippines one individual who had cholera in 1961 has been excreting cholera vibrios intermittently over a period of 7 years during which antibacterial treatment has not been given.[10] However, if patients have had tetracycline in adequate dosage during treatment, the excretion of vibrios does not usually last for more than 36 hours.[11] In the contact carrier infected by exposure to an overt case, the duration of excretion is generally short, lasting for 5 - 10 days, but durations of excretion of up to 42 days have been described by Pollitzer.

Control

For effective control it is essential to know the longest period of days between exposure to a source of infection and the excretion of vibrios by a contact. In the past, the internationally accepted quarantine period has been 5 days. Many authorities have considered this period to be too short and Forbes *et al.* have documented periods of up to 7 days between exposure and the appearance of vibrios in the stools of some contacts.[12] Bearing in mind that the International Sanitary Regulations stipulate 5 days as the quarantine period for international travel, for purposes of internal or domestic control, the period of surveillance of untreated contacts should be not less than 7 days.

Certain antibiotics, notably tetracycline, given in supervised regimens of treatment of both cases and carriers will terminate the excretion of vibrios in a matter of hours.[11-13] Unfortunately this has led in some instances in the past to an indiscriminate exhibition of antibacterial drugs during an outbreak which has not only proved to be ineffective as a control measure but can be dangerous in inducing drug resistance in circulating strains of vibrios.

Mass immunization of communities with cholera vaccine has not noticeably influenced the transmission of the disease either within infected groups or across national boundaries. Carefully controlled trials of cholera vaccine in endemic areas have shown clearly that, depending on the vaccine used, there will be anything from 45 to 80% fewer overt cases of the disease among well-immunized populations.[14] However, there is no convincing evidence that cholera vaccination will lessen in any degree the number of apparent or inapparent infections in an exposed community or will mitigate the virulence of the cholera vibrios excreted by vaccinated persons. Accordingly, while the reduction in the number of clinical cases of cholera in a well-immunized population make a cholera immunization campaign one of the important instruments of protection of individuals, it is not the ultimate answer to the control of the transmission of infection in the exposed community.

THE MANAGEMENT OF A CHOLERA OUTBREAK

Diagnosis

As the first indication of the arrival of cholera can be expected to be a clinically evident case, the surveillance of diarrhoeal diseases should be intensified in communities exposed to the risk of cholera during a pandemic episode. Because of the rapidity of dissemination of the infection once it is introduced it is better to act initially on a clinical diagnosis of suspected cholera and be wrong, than to wait on laboratory confirmation of cholera which may take several days and so critically delay the institution of control measures. This is particularly so in rural areas without readily available laboratory facilities.

There is a simple technique for the direct examination of stool specimens which can be used at the bedside, in the field or at a quarantine station after a minimum of training and which will give a presumptive bacteriological confirmation in better than 80% of cases. Using dark-field microscopy and Ogawa/Inaba specific antisera a presumptive diagnosis can be made within a matter of minutes. This is based on the immobilization by specific antisera of the highly motile cholera vibrios described by Koch as a 'host of gnats' when viewed against the dark ground.[15] In the absence of such facilities, confirmation of a clinical diagnosis will take from 16 to 18 hours for a presumptive, and 36 to 48 hours for a definitive, bacteriological diagnosis after the arrival of a specimen of stool or a rectal swab at the laboratory. Further, unless a specially prepared medium is used for transport there may be considerable difficulty in isolating cholera vibrios from a stool specimen or rectal swab. For the transport of specimens, the medium developed by Monsur has proved highly effective under field conditions.[16]

Care of the Patient

The immediate and urgent need to rehydrate a desperately ill victim of diarrhoea will be apparent to the clinician concerned. The initial replacement of fluid lost through vomiting and diarrhoea can be taken to be the equivalent of 10% of the body-weight if more precise means of measuring this requirement are not available. For a patient of 50 kg this 10% represents 3 000 ml of intravenous fluid made up of sodium chloride 5 g, sodium bicarbonate 4 g and potassium chloride 1 g in a litre of distilled water. Given at the rate of 100 ml/minute this will accomplish the necessary initial rehydration and replacement of electrolytes. Thereafter fluid losses in the stools should be measured so that the subsequent replacement of fluids and electrolytes can be in balance. These measurements can be made most conveniently and readily by nursing the patient on a cholera 'cot'.[17] Under tropical conditions an additional allowance should be made for an insensible water loss of 1 ml/kg/hour. Urine losses in the dehydrated state will be small but should be measured to check on the re-establishment of urinary function.[17,18]

For a precise measurement of the state of dehydration, the copper sulphate method of estimating the specific gravity of the plasma provides a simple means of calculating the precise amount of fluid replacements required.[18]

Although the replacement of losses of fluids and electrolytes by mouth has recently been shown to be effective in some instances, in all cases of severe cholera the early initial replacement by the intravenous route is essential.[19] A practical guide to the point at which fluids by mouth can effectively replace intravenous fluids is said to be the stage at which the patient is able to sit up and hold a container of the oral electrolyte solution in his hand.[20]

Oral tetracycline in doses of 500 mg every 6 hours for 8 doses as an adjunct to treatment with intravenous fluids will shorten the duration of diarrhoea from 4½ to 2 days. It also renders the stool negative for vibrios within 36 hours.[21] The recent studies of Pierce and his colleagues have shown that long-term convalescent carriers may exist among patients treated with antibiotics who can be identified by purging with magnesium sulphate.[9] However, this is a feature which has been uncovered in endemic zones and it is unlikely to have epidemiological significance in a recently infected area unless a community is heavily infected and an endemic focus has already been established and is persisting under conditions of poor environmental sanitation.

Convalescent patients may be discharged from treatment centres as soon as the diarrhoea has stopped, they are eating normally and have an adequate urinary output. From the point of view of community protection, however, they should be kept in hospital or under close surveillance until 3 successive bacteriologically negative stools have been obtained. In the event of persistence of the vibrios in the convalescent carrier after the exhibition of tetracycline in the acute phase, regimens of up to 14 g of oral tetracycline spread over 7 days have been found effective.[9]

The Management of the Contacts

This is believed to be the crucial activity in the control and prevention of outbreaks. Close physical proximity to an index case of cholera, particularly of those individuals living in the same unit of the premises in which the case occurs, will give rise to a symptomless carrier state in some 7 - 25% of contacts. It is important to identify the contacts of a patient early and determine the carriers among them by daily stool examinations or rectal swabbing, if possible under quarantine conditions but certainly under strict surveillance in the home for a period of 7 days from the last exposure to the index case. The contacts found to be infected should then be given antibiotic therapy which is adequate to render them non-infectious. Various regimens have been used for this purpose but oral tetracycline or oral streptomycin have been shown to be epidemiologically effective.[5,12,13] The former can be given in 500-mg doses every 6 hours for 8 doses; oral streptomycin has been given in 1-g doses hourly for 8 hours to adults and has proved effective in 90% of cases. Control of effectiveness by examination of the stool for vibrios is important to both regimens; if clearance does not take place within 24 - 36 hours then heavier dosage of tetracycline or the use of another known effective antibiotic must be considered. So far no major problem of resistance to adequate dosages of tetracycline and streptomycin given under supervision has been encountered but, in this connection, it is desirable and helpful to have available, early in an outbreak, an antibiotic sensitivity profile for the strains of vibrios isolated.

In some instances, all contacts of an index case have been given prophylactic antibiotics under supervision as soon as the total group has been identified.[12,13] This is

simpler, less expensive in resources and time and does not unduly interfere with the movements of apparently healthy individuals. Again, however, it cannot be too strongly stressed that bacteriological surveillance is essential and that the indiscriminate issue of antibiotics or antibacterial drugs of unknown efficacy to the community at large or groups of unsupervised contacts is not only ineffective but can be prejudicial.

Management of the Environment

Concurrently with the management of the contacts it is essential to thoroughly disinfect the immediate environment in the premises from which the index case has come. The commonly infected sites are the toilet or latrine areas, the kitchen, particularly food preparation and kitchen utensils, and drain outlets.[6] The application of common-sense measures of cleansing and disinfection suitable to the areas likely to be involved is all that is required. Outside the living space, it is important to investigate also the water supply, and eating places frequented by the case and by infected contacts. Where children are found to be carriers, the play and immediate school associates should also be investigated.[12]

Where domestic water supplies come from unprotected wells or where there is a supply additional to a piped, purified source, particular care is needed to identify the site from which the unprotected supply is drawn. In areas or times of water shortage it is common practice to use well supplies to eke out purified supplies and it is not unknown for such wells to be so sited as to be contaminated by leakage from sewage pipes, septic tanks and other sources of faecal contamination. Where bucket latrine systems are in use, especially in depressed socio-economic circumstances, particular vigilance is necessary; in this connection it is important to note that night-soil can be an indicator of the extent of spread in a community which is served by bucket latrine sanitation.[6]

The sanitation of markets is also important although the persistence of cholera vibrios in or on articles of diet, both food and drink, is exceptional. A particular danger may be the selling of cooked foods or cut fruits under insanitary conditions by itinerant hawkers who should be brought under general supervision of the relevant sanitary authority during a cholera emergency.

Immunization Against Cholera

The use of whole-cell cholera vaccine prepared according to the internationally accepted standards will give protection against overt disease ranging between 45 and 80% and will give a significant immunity for 3 - 6 months. Generally speaking, an injection of 1 ml of standard vaccine, containing 8 000 million organisms, will suffice for an adult and will meet the international requirements for immunization. Some administrations may require two doses of vaccine at an interval of 7 - 10 days for the first vaccination against cholera. Once an adult has had a primary course of vaccine, 'booster' doses of 1 ml of standard vaccine will suffice even if more than 6 months have passed since the last dose was given. For children over 1 year of age and under 10 half the adult dosage is usually recommended to be adequate. There are very few adverse systemic reactions to cholera vaccine and local reactions at the injection site are rare.

If used as a community measure of control, cholera vaccine must be given as comprehensively as possible to the total group exposed and repeated after 6 months on the same comprehensive scale for as long as the risk of cholera exists. If this can be achieved the reduction in the numbers of overt cases will be worth while epidemiologically and economically.[5] On the other hand the reality of the situation is that mass immunization will not prevent overt disease in all persons vaccinated and will not reduce the incidence of symptomless excretors of cholera vibrios in an infected community. Night-soil studies in Hong Kong showed that the dispersion of cholera vibrios was still rapid and widespread in a comprehensively vaccinated community.[6] Japanese quarantine authorities during the period 1961 - 1967 identified 51 bacteriologically confirmed symptomless carriers of *Vibrio cholerae* coming from cholera-infected local areas but who had satisfactory evidence of vaccination against cholera within the 6 months before their identification.[22]

Accordingly, while vaccination against cholera must be freely available for the protection of individuals against overt disease, it should not be regarded as other than one of the major measures to be applied to a community or to specific groups exposed to the risk of cholera.

International Quarantine Procedures

The International Sanitary Regulations dealing with cholera are designed to facilitate travel while affording the maximum of protection against the transmission of the disease. The possession of a valid international certificate of vaccination against cholera by persons coming from a declared cholera-infected area is required generally by all health administrations. In addition such persons may be placed under surveillance; if they are also suffering from symptoms indicative of cholera and have left a cholera-infected area within 5 days of the symptoms occurring, then other quarantine measures may be applied at the point of arrival. Stool specimens may be required from such persons but routine rectal swabbing is specifically prohibited by the Regulations. Under Article 68 of the Regulations, action for the control of foodstuffs, beverages and other articles capable of transmitting cholera vibrios may also be taken.

The appearance of cholera in a previously non-infected community tends to produce a quite unwarranted state of 'cholera hysteria'.[23] The result has been an entirely unrealistic insistence on control measures in excess of those laid down in the International Sanitary Regulations and quite unrelated to the epidemiology of cholera. There has been a consequent dislocation of travel and, in some instances, serious economic loss through the banning or confiscation of articles and commodities entirely unrelated to either the requirements of the Regulations or facts of the transmission of cholera vibrios.

Health Education and Public Relations

Modern communications media have vastly facilitated the dissemination of information and advice on preventive measures. The advent of the transistor radio enables advice, information and reassurance to be widely broadcast particularly to nomadic, mobile and isolated rural groups. The nature of the disease and its curability, the simple hygienic precautions necessary, the importance of

seeking medical help early, the location of treatment centres and outlines of plans being put into effect, such as vaccination campaigns, are all subjects which can be presented in acceptable programme forms in appropriate languages and dialects.

Public relations are based on timely information and full knowledge of the facts. The co-operation of all sections of the public is essential to the effective control and elimination of an infection which can spread so widely and rapidly and cause grave dislocation of everyday life if not recognized early. There is no need for undue anxiety but there is need for planning ahead and for vigilance at critical points of entry to centres of population. Bearing in mind that cholera is a family or living-space disease and man the vehicle of transmission, increased observance of measures of family hygiene, optimum standards of cleanliness in food preparation and eating places, and the intensified surveillance of diarrhoeal diseases are all key activities in the face of a threat of its introduction.

SUMMARY

The current pandemic of cholera has been in progress for almost 10 years and despite rigorous quarantine measures has continued to invade communities which have not experienced the disease for 80 - 100 years. West Africa is now infected and East and Southern Africa, last infected during the period 1868 - 1890, must be considered to be at risk.

Given early treatment by the rapid replacement of the fluids and electrolytes lost through the massive diarrhoea, the case fatality rate of cholera should be less than 1%.

Infected man is the source of persistence of cholera and is predominantly responsible for the transport of the infection across national and geographical boundaries. The first appearance of cholera in a previously non-infected community will almost certainly be a clinical case of the disease. For each index case appearing, between 7 and 25% of the contacts living in close physical proximity will excrete cholera vibrios within 7 days of the last exposure, without symptoms or with only minor illness which does not incapacitate. The duration of excretion will be in the range of between 7 and 42 days for 'healthy' carriers and from 7 to 10 days in patients convalescing from cholera. Tetracycline in adequate dosage during treatment will render some 96% of the patients free of cholera vibrios within 36 hours. Tetracycline or oral streptomycin in adequate dosage will render healthy carriers free of infection in the great majority of instances.

Immunization with cholera vaccine is an international requirement for persons travelling from cholera-infected local areas. Certain national health administrations may stipulate their own requirements in this regard which are in excess of those laid down in the International Sanitary Regulations. While cholera immunization gives a substantial degree of protection against clinically evident cholera in between 45 and 80% of persons, it will not prevent symptomless infection of individuals or reduce their infectivity to others.

For the control and prevention of cholera early diagnosis is the key to success. Accordingly, in those countries at risk intensive surveillance of diarrhoeal diseases with adequate bacteriological facilities for early definition of causal agents is a major measure of protection. Centres with facilities for the rapid rehydration and replacement of electrolytes in cases of severe diarrhoea will ensure low case fatality rates and establish public confidence. Thereafter the management of contacts of index cases is a prime measure of control. This, in conjunction with the disinfection of premises infected and intensive supervision of water supplies and environmental hygiene, will control cholera and prevent it spreading and so causing a dislocation of community life and often the disruption of the local economy.

Good public relations and information are essential to proper management of a cholera outbreak and to the preservation of community morale and confidence.

Southern Africa has experienced cholera before and although cholera is unlikely to establish itself in an endemic form in this geographical region, nevertheless the region must be considered to be at risk of the infection during the current pandemic.

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