Surveillance for Epidemic Cholera in the Americas: An Assessment

Duc J. Vugia, M.D., M.P.H. Jane E. Koehler, D.V.M., M.P.H. Allen A. Ries, M.D., M.P.H. Enteric Diseases Branch Division of Bacterial and Mycotic Diseases National Center for Infectious Diseases Centers for Disease Control

Summary

In January 1991, epidemic cholera appeared in Peru and quickly spread to many other Latin American countries. Because reporting of cholera cases was often delayed in some areas, the scope of the epidemic was unclear. An assessment of the conduct of surveillance for cholera in several countries identified some recurrent problems involving surveillance case definitions, laboratory surveillance, surveillance methods, national coordination, and data management. A key conclusion is that a simple, well-communicated cholera surveillance system in place during an epidemic will facilitate prevention and treatment efforts. We recommend the following measures: a) simplify case definitions for cholera; b) focus on laboratory surveillance of patients with diarrhea primarily in the initial stage of the epidemic; c) use predominantly the "suspect" case definition when the number of "confirmed" cases rises: d) transmit weekly the numbers of cases, hospitalized patients, and deaths to regional and central levels; e) analyze data frequently and distribute a weekly or biweekly summary; and f) report the number of cholera cases promptly to the World Health Organization.

INTRODUCTION

Background

Cholera is a highly preventable and treatable disease. Chlorinating water supplies and implementing other emergency measures can prevent transmission, and providing ready access to oral and intravenous rehydration therapy can dramatically lower death rates. Prevention and treatment efforts can function optimally when there is cooperation between regional and central public health offices, as well as at national and international levels. The movement of the cholera epidemic, the need for supplies, and the effectiveness of control measures are better assessed with a clear and representative picture of the epidemic. A simple, widely accepted, well-described surveillance system is the best means of obtaining that epidemic picture.

After January 1991, when epidemic cholera first appeared in Peru, the disease quickly spread to many other Latin American countries (1,2). Because this epidemic was unexpected, some countries had little time to prepare for it. However, many countries had already drafted and implemented preparedness plans for the control of cholera.

An ideal plan for cholera control has several essential components, including health education, environmental sanitation, clinical management, laboratory diagnosis, epidemiologic investigation, and surveillance (3). During a cholera epidemic, surveillance is essential to estimate the incidence and the fatality rate, to assess the movement of the epidemic, to plan the distribution of supplies for treatment and prevention, to plan timely epidemiologic investigations, and to determine the effectiveness of control measures.

During investigations of the cholera epidemic in many countries, epidemiologists from CDC have identified several recurrent problems with cholera surveillance, including difficulties with collection, transmission, and analysis of data. These problems often have caused delays and obscured the scope of the epidemic regionally, nationally, and internationally. In addition, some national surveillance systems for cholera use elaborate, complex case definitions that hinder smooth, rapid reporting of cases. This report outlines selected problems that characterize cholera surveillance systems in some Latin American countries and includes recommendations to facilitate cholera surveillance both nationally and internationally.

SURVEILLANCE ISSUES AND RECOMMENDATIONS

Case Definitions

One common problem with cholera surveillance is the case definition. A case definition is a set of objective criteria (symptoms, signs, and laboratory data) that lead to a reliable, reproducible report of the disease. In defining cases, many countries use two main categories of cases of cholera—"suspect" and "confirmed." Often, within each main category, multiple case definitions are used. One country, for example, uses three definitions for a "suspect" case of cholera: a) profuse diarrhea, with severe dehydration, affecting a person \geq 5 years of age; b) acute diarrhea in an area with confirmed cholera; and c) acute diarrhea affecting a person who traveled through an infected area within 5 days before onset of illness. In another country, only one definition is used for a "suspect" cholera case: acute diarrhea affecting a person \geq 5 years of age; however, this country also uses the additional category of "probable" cholera case, defined as dehydrating diarrhea, vomiting, cramps, and malaise affecting a person epidemiologically associated with other cholera cases. Multiple definitions such as these increase the difficulty of reporting and are likely to confuse the analysis of surveillance data.

Most countries use 5 years as the lower age limit for cholera surveillance. Although the World Health Organization (WHO) has previously recommended 10 years as the lower age limit for initial identification of cholera (3), changes to lower this age are in progress (Dr. J. Tulloch, Director, Division of Diarrhoeal and Acute Respiratory Disease Control, WHO, personal communication). Five years is a useful lower age limit since it corresponds with the transition from preschool to school age; schoolchildren may be more likely to be exposed to some communicable diseases, including cholera, than are younger children. For most countries, much of the morbidity from all causes of diarrhea occurs in the <5-year age group (4). Using 5 years as the lower age limit in a cholera case definition excludes more of the cases of diarrhea that are not cholera and, in effect, renders the definition more specific.

The other main category, the confirmed case, is usually defined as *Vibrio cholerae* O1 infection verified by laboratory methods. The most commonly used method is stool culture, with confirmation that the isolate is O1 *V. cholerae.* Where infection is extremely rare, it can be helpful to demonstrate that the isolate produces cholera toxin, because some nontoxigenic O1 strains of *V. cholerae* have been documented (5). Serologic diagnosis, based on measurement of acute- and convalescent-phase titers of vibriocidal or antitoxin antibodies, is available, although rarely used. Simply counting laboratory isolates as cases may obscure the true picture of the epidemic. In one country, for instance, routine culturing of specimens from family members and close contacts of patients with previously confirmed cholera identified some persons with asymptomatic infections. These asymptomatic persons were then reported as having confirmed cholera cases. In fact, asymptomatic cholera infections are numerous in epidemics, but cannot be identified as cases by clinical signs and symptoms alone. Reporting persons without diarrhea as confirmed cholera case-patients can distort surveillance data.

The major difficulty with simple case definitions for cholera lies in the broad spectrum of illness associated with this infection. Over 70% of infected persons are asymptomatic, and an additional 15%–23% of infected persons have mild or moderate nonbloody diarrhea similar to diarrhea from other causes. Some persons who meet a "suspect" case definition may not have cholera, although they are likely to represent only a small proportion of the reported cases in the epidemic setting. A case definition based solely on an adult cholera patient's having dehydrating diarrhea (approximately 2%–5% of those infected) will be more specific than a case definition based on patients with any type of diarrhea, but will also miss many infected persons. In the context of public health action, an accurate report of the number of symptomatic infections is a more useful measure. No single case definition is perfect; a balance is needed between sensitivity and specificity to provide a representative picture of the epidemic in any given area.

Recommendations

For surveillance in a cholera epidemic, a case definition should be brief and simple to facilitate uniform and rapid reporting of cases. To simplify case reporting, cholera case definitions should be limited to two categories, the "confirmed" case and the "suspect" case. A confirmed cholera case is laboratory-confirmed *V. cholerae* O1 infection of any person who has diarrhea. In the epidemic setting, we suggest that a suspect case of cholera be defined as acute, watery diarrhea affecting a person ≥ 5 years of age.

Laboratory Confirmation and Environmental Surveillance

The laboratory is a central component of cholera surveillance. It is essential for confirming that *V. cholerae* O1 has arrived in an area and is infecting humans, for monitoring its continued presence or documenting its disappearance, for determining its antimicrobial susceptibilities, and for identifying its presence in the environment. Preliminary isolation and confirmation of *V. cholerae* O1 require trained personnel using thiosulfate-citrate-bile salts-sucrose (TCBS) agar and polyvalent antisera (6). In the current cholera epidemic in Latin America, most countries were able to staff some laboratories with trained personnel and minimal supplies shortly after the first few cholera cases had been confirmed. However, as epidemic cholera advanced, many laboratories were quickly overwhelmed with demands for confirmation of numerous suspect cholera patients. Reporting of laboratory results slowed because of this increased amount of work.

Recommendations

In regional laboratories, trained personnel are needed to confirm *V. cholerae* O1 infection using TCBS agar and polyvalent antisera. At the central laboratory, trained personnel are also needed to confirm field isolates.

Initially, for an area threatened with cholera, a sample of persons with suspect cases should have specimens taken for culture. After a sufficient number of suspect cases have been confirmed to indicate that cholera is epidemic in that area (e.g., 10–20), the local or regional laboratory may then reduce the frequency of performing cholera stool cultures from that area (e.g., 10 specimens/month) to confirm the continuing presence of *V. cholerae* O1 and to monitor its antibiotic susceptibility. Every laboratory that identifies *V. cholerae* O1 should provide weekly reports of the total number of patient isolates to designated regional and central offices.

In locations where cholera has not been confirmed, especially those bordering areas with cholera, Moore swabs (7) can be placed in the sewage effluents of a limited number of sentinel towns and cities every 1–3 weeks. If *V. cholerae* O1 is isolated from sewage or from a person in a given area, the presence of the organism in the area has been established, and the surveillance with Moore swabs can be discontinued. Thereafter, laboratory-based surveillance in that area should focus on patients with diarrhea.

When *V. cholerae* O1 is identified in a country for the first time, the isolate should be referred to an international reference laboratory for confirmation and further characterization (e.g., using molecular biological techniques), which may be helpful in determining its origin.

Stages of Surveillance

When epidemic cholera appears in a region, two stages of surveillance are observed: an early stage, when cultures are obtained from many patients with diarrhea to diagnose cholera, and a later stage, when cholera is firmly established in the region and larger numbers of people are ill. In the early stage, the number of persons with confirmed cases may be small and may represent a minor proportion of the persons with suspect cases. Most countries report only culture-confirmed cases at this stage. However, as the cholera epidemic grows, more cases are confirmed, and the number of patients with suspect cases more accurately reflects the cholera situation in that area. Many countries, nonetheless, continue to report only cultureconfirmed cases in this later stage of cholera surveillance, because of concerns about public response and adverse economic consequences if the larger number of suspect cases is reported.

Recommendations

In a cholera-threatened area, available diarrhea surveillance data can be reviewed to detect trends suggesting early cholera outbreaks. Any report of acute dehydrating diarrhea affecting a person ≥5 years of age should immediately alert local public health workers to investigate for possible cholera. Early in a cholera epidemic when small numbers of cases are being confirmed, a region may report only culture-confirmed cases. However, when the number of confirmed cases becomes sufficiently high, surveillance should shift to using the "suspect" case definition because it allows simpler, more timely, and more accurate reporting, and because it avoids overburdening laboratory resources. For a region in this later stage of cholera surveillance, it may be appropriate to limit culturing to a sample of the suspect cases

that should continue to be reported. The decision as to when the number of confirmed cases becomes sufficiently high to change from reporting only confirmed cases to reporting cases in both "suspect" and "confirmed" categories should be made promptly on an individual basis after all implications have been assessed. Since most cholera outbreaks are large and often well established when confirmed, early shifting to reporting suspect cases may be more appropriate.

When the cholera epidemic wanes and the number of infections decreases to the level of the early stage of the epidemic, some countries may revert to reporting only confirmed cases. However, in many areas, cholera appears seasonally, with numbers of cases increasing in warm months and decreasing in cold months. Therefore, it may be useful to report suspect cases for at least a year after the epidemic wanes, until it is clearly shown that cholera is controlled in an area. At that time, it is reasonable to return to reporting only confirmed cases for that area.

Information from Patients with Cholera

Some countries have administered lengthy, detailed questionnaires to every patient with cholera. In one country, the information about the patient on the questionnaire included demographic data, clinical signs and symptoms, laboratory results, characteristics of the feces and vomitus, travel history, food history, contact history, and additional comments by the person filling out the questionnaire. Although detailed information may be helpful in describing a sample of cholera cases clinically, it is of epidemiologic interest only in the earliest phase of an epidemic. Thereafter, as the number of cholera cases increases, the forms may be incomplete or ignored, and much of the data will be unmanageable and unanalyzed unless data-handling resources are diverted from other worthwhile programs. Exposure information collected from patients alone will not determine the modes of transmission, because cholera may be transmitted by common foods or beverages or by multiple sources that vary from place to place. Well-designed and well-administered case-control investigations in affected areas are a more effective approach to identify vehicles of transmission. In summary, lengthy surveillance questionnaires waste scarce human resources and impede handling of surveillance data.

Recommendations

For cholera, exposure histories are best reserved for investigations. Surveillance should be streamlined, using simple case definitions and concentrating on timely and accurate reporting of data. At the local level, including all treatment centers, information gathered about patients who meet the cholera surveillance case definition should be basic, including age, gender, date treated, and home address. The information transmitted to regional and central levels may include age, gender, and location, but it should primarily focus on the numbers of cases, hospitalized patients, and deaths.

Communication, Analysis, and Timely Reporting of Surveillance Data

Surveillance and laboratory information is of little value unless it is communicated clearly and promptly. Timely reporting of laboratory results to a regional epidemiology office will allow early identification of cholera-affected areas and permit immediate investigations; timely reporting to the central laboratory will allow early confirmation of the isolates; and, to complete the information loop, timely feedback to the original submitter of the isolates will help validate diagnoses and improve patient care. Similarly, timely reporting of the total number of cases and basic analysis results from a central epidemiology office back to the laboratories and regional epidemiology offices is essential to allow the epidemic to be characterized and to ensure continued cooperation at all levels. In some locations, information dissemination among these major components in the surveillance process sometimes has not been timely and complete. Early in the cholera epidemic in Latin America, for example, some countries instituted emergency daily reporting of the number of cases to a central office, yet did not communicate the total and cumulative number of cases by region to their constituents until months later. The suitable form of information flow among local and central levels must be worked out country by country.

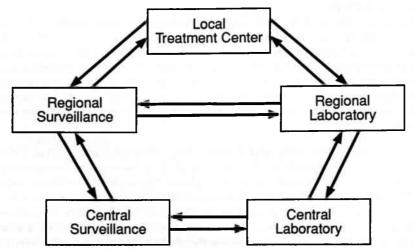
Recommendations

A proposed communication system includes both reporting to a central office and feedback to regional offices (Figure 1).

Initially, treatment centers and regional offices may wish to report to the central office daily by a rapid method (e.g., radio, telephone, telegram) the number of suspect cases, the number of confirmed cases, the number of patients who were hospitalized, and the number who died. A rapid switch to weekly reporting will often reduce the burden of work created by daily reporting without compromising the main goals of surveillance. The administrative level to which each treatment center's report should be sent must be clearly identified.

Surveillance data should be analyzed promptly and frequently. Basic tabulation and comparison of data should be performed at the local and regional level if trained personnel are available. At the central level, epidemiologists should analyze reports of suspect and confirmed cholera cases by region and by week to track the spread of the epidemic, to determine whether unexpectedly large numbers of cases are occurring in any region, and to evaluate the impact of interventions. The results should be disseminated to all levels and used to estimate resources needed at local levels and to decide whether epidemiologic investigations are needed. When surveil-

FIGURE 1.



lance data suggest an increase in the number of cases in an area, an epidemiologic investigation should be conducted to determine the modes of transmission and identify further prevention measures. The results of these investigations should be reported to all categories of participants in the surveillance system.

International Reporting

Cholera is one of three internationally notifiable diseases, and countries are requested to report cases to WHO promptly. Some governments may be concerned that reporting a large number of cases could have a detrimental impact on economic factors such as tourism and food exportation. Prompt and accurate reporting, however, will improve national and international efforts to allocate resources to control cholera morbidity and mortality.

Recommendations

The number of cholera cases should be reported to WHO in a timely manner.

Summary of Recommendations

Case definitions for cholera

- In a cholera epidemic, use only two categories, "suspect" and "confirmed."
- Define a suspect case as acute, watery diarrhea affecting a person ≥5 years of age.
- Define a confirmed case as laboratory-confirmed *Vibrio cholerae* O1 infection of any person who has diarrhea.

Laboratory confirmation and environmental surveillance

- Use trained personnel in regional and central laboratories to isolate and confirm *V. cholerae* O1.
- Confirm the diagnosis bacteriologically of several suspect cases in newly threatened areas.
- After cholera has become established in an area, use stool cultures only to confirm the continuing presence of *V. cholerae* O1 and to monitor its antibiotic susceptibility.
- Consider using Moore swabs to identify *V. cholerae* O1 in sewage in cholera-threatened areas where cholera has not been confirmed.

Stages of surveillance

- In a cholera-threatened area, investigate cases of acute dehydrating diarrhea affecting persons ≥5 years of age.
- When the number of "confirmed" cases rises, shift to using primarily the "suspect" case definition.
- Continue to report suspect cases for at least 1 year after the epidemic wanes.

Information from patients with cholera

- Refrain from using lengthy surveillance questionnaires.
- Collect basic information on patients at the local level.
- Transmit summary data (primarily the number of cases, hospitalizations, and deaths) to the central level.

Communication, analysis, and timely reporting of surveillance data

- Report surveillance results to a central office weekly by a rapid method.
- Analyze surveillance data and disseminate surveillance reports to all components of the surveillance system quickly and frequently.
- Conduct epidemiologic investigations in areas with increasing numbers of cases.

International reporting

Accurately report the country's cholera situation to WHO in a timely manner.

References

- CDC. Update: cholera western hemisphere, and recommendations for treatment of cholera. MMWR 1991;40:562–5.
- 2. CDC. Update: cholera-western hemisphere, 1991. MMWR 1991;40:860.
- WHO. Programme for Control of Diarrhoeal Disease. Guidelines for cholera control. 1986;WHO/CDD/SER/80.4 REV.1.
- 4. Snyder JD, Merson MH. The magnitude of the global problem of acute diarrhoeal disease: a review of active surveillance data. Bull WHO 1982;60:605–13.
- 5. Morris JG, Picardi JL, Lieb S, et al. Isolation of nontoxigenic *Vibrio cholerae* O group 1 from a patient with severe gastrointestinal disease. J Clin Microbiol 1984;19:296–7.
- Gangarosa EJ, Dewitt WE, Huq I, Zarifi A. Laboratory methods in cholera: isolation of Vibrio cholerae (El Tor and classical) on TCBS medium in minimally equipped laboratories. Trans R Soc Trop Med Hyg 1968;62:693–9.
- 7. Barrett TJ, Blake PA, Morris GK, Puhr ND, Bradford HB, Wells JG. Use of Moore swabs for isolating *Vibrio cholerae* from sewage. J Clin Microbiol 1980;11:385–8.