Cholera in Mexico: The paradoxical benefits of the last pandemic

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Summary

Objectives: To describe the impact of preventive and control measures in Mexico prior to, and during, the cholera epidemic of 1991–2001.

Methods: When cholera appeared in Latin America in January 1991, the Mexican government considered that it represented a national security problem. Therefore, actions were implemented within the health sector (e.g. epidemiological surveillance, laboratory network and patient care) and other sectors (public education and basic sanitation).

Results: The first case occurred in Mexico in June 1991. The incidence rate remained below 17.9 per 100 000 inhabitants and affected mainly rural areas. The last cholera report occurred in 2001. The disease never became endemic. The population benefited not only from acquisition of knowledge about preventive measures, but also from modification of risky practices and from reinforcement of city and municipal drinking water supplies.

Conclusion: Control strategies had an overall impact in decreasing diarrheal mortality among children under five years of age. Additionally the country did not suffer from a decrease in tourism or economic consequences. This experience can be considered as the operationalization of a new public health system spanning multi-sectorial activities, involving community participation, political will and with impact on public health and economic issues.

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Cholera history

Cholera is an acute infectious disease that was first described by Hippocrates in the 5th century BC. Although several epidemics occurred in Asia during the 15th and 18th centuries, it was not until the 19th century that John Snow first described preventive measures for the disease during an epidemic in London, UK. In 1883, Robert Koch described the causal agent, Vibrio cholerae, as a curved bacillus with great mobility. More recently, one of the most important advances in the treatment of the disease has been the documentation of the efficacy of oral rehydration therapy. During the 19th and 20th centuries seven cholera pandemics occurred of which the second, third, fourth and seventh spread into the American continent. The seventh pandemic has been underway since 1961. Cholera is one of the most important causes of morbidity and mortality in Asia and Africa and, since 1991, it has also become a major public health problem in Latin America.

This disease is a consequence of an intestinal infection that is caused by toxigenic Vibrio cholerae O1. Clinical manifestations of cholera may be severe and characterized by loss of large volumes of watery stool, vomiting, rapid dehydration, metabolic acidosis, and hypovolemic shock. While 50% of untreated severe cases are fatal, adequate treatment reduces mortality to less than 1%. Until 1992, only toxigenic V. cholerae O1 caused epidemic cholera. However, in 1992, large outbreaks of cholera began in India and Bangladesh which were caused by a previously unrecognized serogroup of V. cholerae, designated as O139. Isolation of this vibrio has now been reported from 11 countries in South-East Asia.

Global cholera situation in 1991

During the re-emergence of cholera in 1991 as part of the seventh pandemic, there were 594 694 cases reported in 59 countries that stretched across four different continents and had a global rate of infection of 100 cases per one million inhabitants. During that year, there were 19 295 cholera-associated deaths with a case fatality rate of 3.2%.

Of the total number of patients with cholera in 1991, 25.7% of them occurred in 21 countries in Africa. The rate in the African continent was 527 cases per million inhabitants. The fatality rate was 9.1%, the highest of the pandemic. Meanwhile Asia accounted for 8.4% of the total cholera cases reported that same year, resulting in 49 791 patients across 16 countries in the continent and 1286 deaths. The rate of infection was four cases per million inhabitants and the fatality rate was 2.6%. Europe, on the other hand, reported less than 1% of the total number of globally reported cases, with only 316 patients, 9 deaths, and an overall fatality rate of 2.8%.

The cholera epidemic in the Americas

Although cholera epidemics occurred in the Americas during the 19th century, transmission was interrupted for more than a hundred years, with the exception of a few sporadic cases. During the 20th century, in 1973, cholera was reported for the first time in the USA in the Gulf of Mexico, followed by eight cases in Louisiana in 1978. Then in 1981, 16 cases were reported in Texas and, in 1983, a tourist from the USA developed cholera in Cancun, Mexico. Between 1973 and 1990, there were 57 cases of autochthonous cholera in the USA. Prior to 1991, there were only two reports of isolation of toxigenic V. cholerae O1 from the sewage waters of Rio de Janeiro, Brazil, although the bacteria were not isolated from human samples. In 1988, non-toxigenic V. cholerae O1 was cultured from two tourists from the USA in Peru.

The year of 1991 will be remembered as the one during which cholera re-entered the New World. The American continent suffered the greatest number of cases during 1991, with 65.7% of all cases notified globally. In America, during 1991 there were 391 220 cases in 16 countries, with 4002 deaths. The overall continental rate was 521 cases per million inhabitants with a case fatality rate of 1.0%. The majority of cases occurred in Peru (82.4%) followed by Ecuador (11.8%), Colombia (3.0%) and the remaining 2.8% were derived from 13 countries. Correspondingly, the highest rate per one million inhabitants was in Peru (14173) followed by Ecuador, Colombia, Guatemala, and Panama. According to the proportion of deaths, the most affected country was Bolivia because 5.8% of its patients died, followed by Chile with 4.8%, El Salvador with 3.5% and Panama with 2.4%.

The case of Peru

The consequences of cholera have been enormous. In Peru, for example, during the first month of the epidemic 13 provinces had more than 45 000 cases, 10 000 hospital admissions, and 190 deaths. During
the second month, the epidemic had spread to 21 provinces and the number of reported cases had increased to more than 120,000. Hospital admission also increased to 15,000 as did the number of deaths to 850.

A study conducted in Trujillo, Peru, determined an association between blood group O and severe cholera. Blood group O was strongly associated with severe cholera: infected persons had more diarrheal stools per day than persons of other blood groups, were more likely to report vomiting and muscle cramps, and were almost eight times more likely to require hospital treatment.

In addition to human suffering, cholera outbreaks have a tendency to cause widespread fear, alter the social and economic structure of a country, and represent an obstacle to the development of the affected communities. Unjustified panic-induced reactions by other countries included curtailing or restricting travel from countries where a cholera outbreak was occurring and/or the imposition of import restrictions on certain foods. Furthermore, within the cholera-affected countries, resources intended for exports and productivity were diverted to the care of cholera patients. The 1991 cholera outbreak in Peru, for instance, had a direct impact on the country since it lost US$770 million simply from food trade embargoes and adverse effects on tourism.

**Mexico 1991 in context**

In 1991, Mexico as a country was economically stable, large social programs were being developed, negotiations towards the signature of the North American Free Trade Agreement treaty were progressing, and it was about to enter the Organization for Economic Co-operation and Development. However, with the outbreaks of cholera in neighboring countries came an air of political uncertainty and fear because of the obvious and not so obvious public health consequences associated with the disease. The less obvious outcomes included a decrease in tourism, cancellations of Mexican exports by other countries and an overall halt in negotiations. Mexico’s immediate identification of cholera as a national security issue lead to an aggressive implementation of preventive and control measures that helped to ameliorate some of the political and economic costs associated with cholera. An essential part of the rapid response was the high-level political will to mobilize key resources several months before the first case of cholera was reported in Mexico.

**Prevention and control measures implemented in Mexico before the first outbreak**

The timely reporting and diagnosis of the first cholera case was achieved thanks to the implementation of concrete preventive and control measures a few months before. These included: (1) establishing a system of epidemiologic surveillance; (2) ensuring the delivery of timely and adequate patient care; (3) reinforcing laboratories and creating a national laboratory network; (4) studying and controlling outbreaks; (5) promoting health education to the public; (6) training and building the capacity of health personnel; (7) providing necessary supplies; (8) establishing a basic environmental sanitation system; and (9) following international sanitation guidelines. Two of the authors of this review were directly involved in the control strategies. One of the authors (JS) was at that time (1990—1994) Undersecretary of Health and Coordinator of the National Program for Cholera Prevention and Control.

Before the occurrence of the first case, during the month of May, the rural physician of the community where the first case occurred was trained on cholera diagnosis and management. Supplies for diagnosis (rectal swab with Cary—Blair medium) and treatment (oral rehydration therapy (ORT), intravenous fluids, and antibiotics) were available at the local clinic. The state laboratory had recently been standardized to be able to culture *V. cholerae*. Timely reporting of the case at both local and national levels by the epidemiological surveillance system occurred. The strain was submitted to the national referral laboratory (National Institute of Diagnosis and Epidemiological Reference) where it was typed.

**Public health surveillance**

Epidemiological surveillance took place at two levels: the first was focused on the detection of arriving cholera patients and the second was focused on the timely detection of autochthonous cases. In the former category, controls were placed at international entry points, including airports, seaports, and borders, and all travelers and crew members were informed that if they developed clinical symptoms compatible with cholera they should immediately seek medical care and inform appropriate health authorities. Individuals who became symptomatic were sampled for *V. cholerae*. In addition, any food, waste, and/or water from ships arriving into the ports from other
countries were disposed of in a safe and adequate manner.

At the national level, environmental surveillance activities were also implemented, such as the monitoring of diarrheal diseases and the studying of new outbreaks in a timely manner. Periodic monitoring of waste, sewage waters, and certain foods such as seafood, fruits, and vegetables, were also endorsed by the Ministry of Health, as well as the chlorination of potable water in urban areas.

Once the prevention and control strategies were standardized, they were published in the official gazette of Mexico to promote dissemination and wide-spread compliance. Several key messages were included in the publication. First, it recommended that all suspicious cases of diarrhea should undergo epidemiological and microbiological study. All states were required to have at least five laboratories with sufficient infrastructure to isolate and identify V. cholerae O1. In addition to confirming cases of choler a, health professionals were advised to practice the following control activities: study and control of suspected cases; monitor and regulate potential sources and infectious vehicles; provide timely medical care to patients; improve basic sanitation systems; and promote awareness campaigns to educate the general public.

Cholera laboratory network

Within a few months of the arrival of cholera in Peru in January 1991, a network of 239 laboratories were established across the 32 states of Mexico with the capacity to identify V. cholerae. Cascade training of laboratory personnel took place; initially personnel in the state public health laboratories received training, these individuals trained other personnel both in public and private laboratories. Equipment, reagents, and supplies were purchased to reinforce laboratories and a central reference laboratory was established to conduct confirmatory and antimicrobial susceptibility tests, produce antiserum for co-agglutination tests, and supervise laboratory-screening procedures.

Basic sanitation

Among the many activities that were reinforced in preparation for a cholera outbreak, the most important was provision of potable water (defined by non-detectable Escherichia coli in any 100 ml sample). Provision of potable water was the responsibility of the National Commission of Water at the federal level, of the State Water Commissions at the state level and of municipalities at the local level. These levels coordinated with other public and private sectors to promote the appropriate quality of water both outside the household through chlorination of water supplies and within the household through boiling and household chlorination. Packages containing chloride tablets (sulfacloramine, 9 mg) and instructions on usage were distributed among the population.

Another important procedure was for the adequate disposal of waste and monitoring of the maintenance of drainage systems. Legal amendments were also issued to prohibit the use of residual waters to irrigate crops designed for human consumption. In addition, local communities placed a special emphasis on construction of latrines while food vendors were monitored to ensure compliance with basic sanitation laws.

Medical care

A special commission was established to develop treatment guidelines for cholera victims. This commission was responsible for developing training materials for health workers and identifying the supplies that should be made available to clinics and hospitals.

Educational activities

The educational campaign that was launched to inform public health professionals as well as the general public had several components: (1) radio and television were used to disseminate announcements on basic hygiene, adequate disposal of waste and water chlorination; (2) videos and other audiovisual materials were developed and used to emphasize the importance of basic sanitation, including the construction of latrines and water chlorination; and (3) educational materials were produced for use by teachers, health professionals, laboratory workers and decision makers. To further increase awareness of the disease, a biweekly periodical called the Cholera and Diarrheal Diseases Bulletin was first published in May 1991, one month before the first cholera case. Furthermore, official guidelines and operational procedures were established to standardize all control activities.
Re-emergence of cholera in Mexico

The re-emergence of cholera in Mexico occurred on 17 June 1991, when a 68-year-old man living in San Miguel Totolmaloya, a small community located in the mountainous region of Sultepec Municipality, was reported as a probable cholera case. The patient was hospitalized in the state capital. The next day, the state laboratory was able to culture and type the isolate of toxigenic *V. cholerae* O1, biotype El Tor, serotype Inaba. In the months that followed, up until December of that year, 2381 additional cases were reported at an infection rate of 36.1 cases per million inhabitants.

During the first few days of the outbreak, 27 additional cases in the same municipality were reported. As a result, the following control measures were quickly implemented in this community: 2500 households were visited to find any new cases; cholera patients received treatment while nearby relatives or contacts received chemoprophylaxis; environmental sanitation of possible sources of infection was reinforced; sanitary education was disseminated to the public; latrines were constructed and water was chlorinated; and a local laboratory was established.

Even at this early stage, health authorities were able to draw some conclusions about how cholera got to Mexico. First, the initial hypotheses suggesting that airports, seaports, borders and tourist areas would be the main entry points of the disease proved to be wrong because it appeared in an isolated mountainous area in the center of the country. Instead, it appeared that an infected person from South America arrived in Mexico on a flight that used one of several illegal airstrips in the area for drug trafficking purposes. Most probably, epidemic cholera was introduced on multiple and unexpected occasions, as a result of the direct movement of people. A similar situation occurred in North Africa where the epidemic strain was introduced via smugglers’ boats. Secondly, the hypothesis that the initial outbreaks could be controlled by aggressive containment measures was also proved wrong because transmission surpassed sanitary quarantine, chemoprophylaxis, and the chlorination of adjacent water sources. Further outbreaks in neighboring communities also disproved this theory, particularly because three months after the first cholera case there were four more outbreaks bringing the total number of cases to 402 with 83 hospitals admissions and three deaths. The average duration of each of the outbreaks was 20.4 days. In total, during 1991, there were 2690 cholera cases and 34 deaths in 16 states (Figure 1).

**Prevention and control measures implemented during the epidemic**

Health authorities implemented measures at four levels. First, public health surveillance and control ensured that every new case was considered as a cholera outbreak and therefore initiated surveillance and control activities. All suspected and confirmed cases were surrounded by a *cordon sanitaire* (a barrier designed to prevent the disease from spreading, at least 8 blocks (urban areas) or 5 km (rural areas) around the affected household). Limits were established around each case and authorities conducted measures within the established boundaries that included treatment to symptomatic individuals, chemoprophylaxis to contacts, chlorination of water, appropriate waste disposal, construction of latrines and educational measures.

Secondly, emphasis was given to ensure appropriate medical care to those affected by the disease. Guidelines that reinforced the appropriate usage of oral rehydration therapy were disseminated and their compliance was ensured. More than 400 sentinel units were established in hospitals to promote early detection of suspected cases, outbreaks, or deaths related to diarrheal diseases.

Thirdly, the laboratory infrastructure was reinforced to ensure that all cases were bacteriologically confirmed. The laboratory network had an annual processing capacity of 638 000 samples, including cultures and rapid diagnostic tests. An external proficiency evaluation of the entire network was conducted in collaboration with the Cen-
ters for Disease Control of the USA throughout the period 1991—1995. Between 1991 and 1993, the network of laboratories processed 52,180 human samples and 26,646 environmental samples of cholera. Toxigenic V. cholerae O1 was cultured from 47.7% of the human samples and 12.8% of the environmental samples. Although drug resistance was not widespread, there were a few isolated cases with this problem. Drug testing of 14,928 strains revealed that 2.0% were resistant to ampicillin, 1.0% to doxycycline, 0.8% to tetracycline, 0.7% to trimethoprim—sulfamethoxazole, 0.5% to chloramphenicol, and 0.09% to erythromycin. A second epidemic strain, easily differentiated by its antimicrobial resistance profile (resistant to furazolidone, sulfisoxazole, and streptomycin), which became dominant in at least some parts of Central America, was also present in Mexico.

In 1993, the capacity of the laboratory network was strengthened to include the identification of other common enteropathogens in addition to V. cholerae, such as Salmonella, Shigella, Yersinia, Escherichia, and Campylobacter.

Fourthly, among the main objectives of the cholera control efforts coordinated by the Minister of Health at the national and state levels, was the increase in coverage of health services and basic sanitation to all of the population. Between 1990 and 1991, access to potable water improved considerably following the creation of the Clean Water Program by the federal government, which aimed to increase the quality of water for human consumption (Figure 2). In 1993, the second stage of this Program began to promote safe, drinkable water in the 320 municipalities which were most affected by the cholera epidemic by chlorinating water supplies, disinfecting high risk sites, adding lime to sources of infection, and distributing colloidal silver. By 2002, 88.8 million inhabitants or 95% of the total population living in Mexico had benefited from the chlorination efforts. Two strategies that were particularly effective in the fight against disease outbreaks caused by consumption of contaminated water were: (1) the Project of Integral Sanitation in Rural Communities and (2) the Program of Clean Water at Home. These two programs were implemented in rural communities with a high epidemiologic risk due to a high incidence of diarrheal diseases and a high degree of marginalization.

**Epidemiological characteristics of the cholera epidemic in Mexico**

Although there have been cholera epidemic peaks during the ensuing years, the fatality rate has been low, particularly after 1996. Between the years 1991 and 2002 the number of cases totaled 45,977 with a fatality rate of 1.2% (Figure 3, panel A). Distribution of cases by gender was similar. The greatest proportion of cases occurred in individuals aged 25 to 44 years, although the highest rates occurred in individuals aged over 65 years (Figure 3, panel B). This distribution differs from that observed in endemic regions.
where the majority of cases occur among children younger than five years old and women of reproductive age.

During the first months of the cholera epidemic, the number of cases increased by almost 50% every two weeks. The epidemic was characterized by successive outbreaks that were controlled rapidly. Up until December 1991, the majority of the cases had occurred in the highlands in the center of the country.27

Clinical analyses of 469 patients revealed that 96% of them had watery diarrhea, 82% had diarrhea, 46% had muscular cramps, 31% had rice stools, and 10% went into shock. Clinical symptoms were most frequent among older individuals, probably associated with a greater likelihood of exposure due to occupational and eating habits.

Transmission occurred mainly in rural and suburban areas where basic sanitation infrastructure was lacking while outbreaks in urban areas were more rare and easier to control. Although intrafamilial transmission was high, fortunately, there were few severe cases and deaths. Overall, the fatality rate was almost 1%, which is lower than that reported in endemic areas.28 Although cholera transmission was high, fortunately, there were few severe cases and deaths. Overall, the fatality rate was below 1%. The highest incidence rates occurred in the southern and northern regions. The proportion of rural areas, households with earthen floors, and lack of sanitation are greatest in the southern and central regions. Although these indicators are better in the northern region, higher incidence rates may have been due to a better surveillance system.

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Benefits of the cholera epidemic

There were several benefits that were obtained from the re-emergence of cholera in Mexico. The infrastructure for diarrhea control was reinforced substantially. The coverage of potable water was increased nationwide. The Secretariat of Health implemented monitoring of water quality through usage of Moore swabs and surveillance of microbiologic contamination of food, particularly seafood, fruits and vegetables. The Secretariat of Health and the National Commission of Water maintained drinking water systems. Appropriate methods such as boiling and chlorination were promoted. Other sanitation measures promoted included adequate waste disposal, maintenance of sewage systems, banning of the use of residual waters for irrigation of vegetable crops and promotion of adequate technology for sanitary disposal of feces such as self-built latrines. Finally, compliance of food vendors to sanitary regulations was promoted. Public education was improved and the general population modified practices that frequently put them at risk of infection by enteropathogens. The surveillance of diarrheal diseases also improved considerably. This was supported by improvement of the infrastructure and coverage of the laboratory network. Finally, there was considerable improvement in the way that diarrheal diseases were treated both at the outpatient level as well as for patients requiring hospitalization.

Lessons learned

After more than a decade since the arrival of cholera in Latin America, there are several lessons that can be drawn from this experience. First is the fact that cholera control in the medium-term requires political commitment and involvement in order to implement a comprehensive and timely, multidisciplinary approach. In the case of Mexico, several strategies were crucial to the successful management of the cholera epidemic. At the environmental level, measures were taken to ensure that rural as well as semi-urban communities and households had access to clean water. Meanwhile, on the educational front, special measures were taken to make sure that everyone was properly trained on the prevention and control of cholera, including health personnel, political authorities, teachers and parents. Furthermore, information was disseminated through mass media campaigns on the radio and television, as well as in print with the distribution of brochures, manuals, and booklets. At the epidemiological level, immediate action to control the outbreak once the first cholera cases began to appear was instrumental as was the careful monitoring and surveillance of all suspected cases, sources of infection, potential contacts, etc. Also of great importance was the foresight that officials had in making sure that all state and local laboratories were fully equipped and had the capacity to conduct timely diagnoses of cases, and study human and environmental samples well before the first case of cholera occurred. Finally, training and supplies were made available to provide adequate and timely treatment of all cholera cases. Environmental sanitation has also led to important collateral benefits. Among those observed in Mexico is the decrease of mortality due to all causes of diarrheal episodes among children younger than five years of age.

Questions that remain to be answered

There are several questions that remain unanswered regarding the prevention and control of this disease. We are still unable to predict the time and place of a new cholera outbreak. It has been postulated that in the future, it may be possible to predict a cholera epidemic by monitoring the movement of plankton by satellite. However, more data are needed to support this method. Currently, we do not know if it is possible to prevent the re-emergence of cholera or how well protected the population in Latin America is against cholera. Although we know that *V. cholerae* is often found in aquatic environments as a component of the normal flora and plankton of brackish water and estuaries, researchers are unable to detect the appearance of new strains in the environment that may cause epidemics. Since it is still unclear whether *V. cholerae* O139 will spread to Latin America, careful epidemiological monitoring of the situation is being maintained. Finally, we are still waiting for a vaccine, available for public health use, which is capable of producing, with a single oral dose, long-lasting protective immunity regardless of blood group or age.

Conclusions

When cholera appeared in Latin America in January 1991, the Mexican government considered that it represented a national security problem. Therefore, actions were implemented within the health sector (e.g. epidemiological surveillance, laboratory network and patient care) and other sectors
(public education and basic sanitation). Five months after the arrival of cholera in Peru, the first case occurred in Mexico in June 1991. Timely diagnosis of the patient occurred and strategies were implemented including: (1) the establishment of a public health surveillance system; (2) the delivery of timely and adequate patient care; (3) reinforcement of laboratories and the creation of a national laboratory network; (4) the study and control of outbreaks; (5) promotion of health education to the public; (6) training and capacity building of health personnel; (7) provision of the necessary supplies; (8) establishment of a basic environmental sanitation system; and (9) the following of international sanitation guidelines. The consequences included maintenance of incidence rates below 17.9 per 100,000 inhabitants and mainly rural areas being affected; there have been no cholera reports since 2001 and the disease never became endemic. The population benefited not only from acquisition of knowledge about preventive measures but also from modification of risky practices and from reinforcement of city and municipal systems of water potabilization. These measures have had an overall impact in decreasing diarrheal mortality among children younger than five years of age. Additionally the country did not suffer from a decrease in tourism or economic consequences. This experience can be considered as the operationalization of a new public health policy spanning multisectorial activities, involving community participation, political will and with impact on public health and economic issues.

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