Cholera in the United States, 1995 2000: Trends at the End of the Twentieth Century

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To evaluate recent trends in cholera in the United States, surveillance data from all cases of laboratory-confirmed toxigenic Vibrio cholerae O1 and O139 infection reported to the Centers for Disease Control and Prevention between 1995 and 2000 were reviewed. Sixty-one cases of cholera, all caused by V. cholerae O1, were reported. There was 1 death, and 35 (57%) of the patients were hospitalized. Thirty-seven (61%) infections were acquired outside the United States; 14 (23%) were acquired through undercooked seafood consumed in the United States, 2 (3%) were acquired through sliced cantaloupe contaminated by an asymptomatically infected food handler, and no source was identified for 8 (13%) infections. The proportion of travel-associated infections resistant to trimethoprim-sulfamethoxazole, sulfisoxazole, streptomycin, and furazolidone increased from 7 (8%) of 88 in 1990 1994 to 11 (31%) of 35 in 1995 2000. Foreign travel and undercooked seafood continue to account for most US cholera cases. Antimicrobial resistance has increased among V. cholerae O1 strains isolated from ill travelers.

Cholera remains one of the most feared epidemic diseases throughout much of the world. Persons living in the United States most often acquire cholera through travel to cholera-endemic areas or through consumption of undercooked seafood from the Gulf Coast or foreign waters. The following case reports illustrate these 2 mechanisms.

CASE DESCRIPTIONS

Returning traveler. In June 1998, the Alaska Department of Health and Social Services was notified about a case of cholera in a 53-year-old New York State man. On 13 June, after a 3-week visit to the Philippines, he became ill on board a flight from Taiwan to New York. He had a history of peptic ulcer disease and gastrectomy, and his medications included antacids. Because of his symptoms of severe watery diarrhea, vomiting, and abdominal cramps, the plane made an emergency landing in Anchorage. He was discharged from an Anchorage emergency room after receiving intravenous fluids and having a stool culture done. The patient stayed at a local hotel until continuing his flight to New York on 15 June. One day after arrival in New York, he was hospitalized with persistent watery diarrhea and acute renal failure. Toxigenic *Vibrio cholerae* O1, biotype El Tor, serotype Ogawa, was isolated from his stool.

Seafood fancier. In September 1998, the Colorado Department of Public Health and Environment was notified of a case of cholera in a 73-year-old woman. On 19 September, the patient and 11 family members ate blue crabs that had been harvested along the Gulf Coast, precooked, and commercially distributed by a Louisiana company. She had not traveled out of state. On 21 September, about 2 days after the meal, she developed profuse watery diarrhea, nausea, dehydration, and lethargy requiring hospitalization. Toxigenic *V. cholerae* O1, biotype El Tor, serotype Inaba, was isolated from a stool culture.

BACKGROUND

In the early 1990s, coincident with the spread of the seventh cholera pandemic through South and Central America and the emergence and spread of the new *V. cholerae* O139 serogroup in Asia, reports of cholera in the United States increased substantially [1]. Between 1990 and 1994, 195 cases were reported, 134 (69%) of which were associated with travel to Latin America [2, 3]. An outbreak among passengers on a commercial airline flight originating in Lima, Peru, accounted for 75 of these cases [4]. Cholera due to V. cholerae O139 infection was diagnosed in 6 travelers returning from Asia during this same 5-year period [5, 6], while only 4 cases (2%) were associated with consumption of Gulf Coast seafood [2, 3]. In addition, emerging antimicrobial resistance in *V. cholerae* O1 and O139 was a growing concern [3]. To determine whether these trends had continued during the second half of the decade and to make recommendations, we reviewed national cholera surveillance data from 1990 through 2000.

METHODS

State and local health departments submit all clinical isolates of suspected V. cholerae O1 and O139 to the Foodborne and Diarrheal Diseases Laboratory at the Centers for Disease Control and Prevention (CDC) for testing for the presence of the cholera toxin gene and for antimicrobial resistance. State and local health departments and CDC epidemiologists collect clinical and epidemiological information on all CDC-confirmed cases of cholera. We reviewed available information on all confirmed cholera cases occurring in the United States and its territories from 1 January 1995 through 31 December 2000. Previously published summaries for 1990 1994 were reviewed [2, 3], and selected isolates from those years were further characterized in the laboratory.

A case of cholera was defined as a diarrheal illness (>= 3 loose stools in 24 h) with either isolation of toxigenic *V. cholerae* O1 or O139 or with serologic evidence of infection. Serologic evidence of infection was defined as a vibriocidal antibody titer >= 1 : 640 or a cholera antitoxin titer >= 1 : 400 in a person who was part of an outbreak of diarrheal illness who had >= 1 culture-confirmed toxigenic *V. cholerae* O1 infection [7].

A travel-associated case was defined as cholera in a person who traveled outside the United States or its territories during the 7 days before illness onset. Persons who were diagnosed with cholera while traveling or residing outside the United States were not included. A case was considered to be associated with the US Gulf Coast if the patient had eaten seafood harvested from Gulf Coast waters during the 7 days before symptom onset and if the Gulf Coast strain of *V. cholerae* O1 was isolated from the patient's stool specimen [8]. Persons who met the clinical and serologic definition for cholera were also considered to be associated with the Gulf Coast if they were epidemiologically linked to a coincident culture-confirmed Gulf Coast associated case.

Isolates of suspected *V. cholerae* O1 and O139 were referred to the CDC for confirmation of serogroup and for testing for the presence of cholera toxin gene sequences by polymerase chain reaction [9]. Isolates identified as *V. cholerae* serogroup O1 were serotyped and biotyped by standard methods. The disk diffusion technique was used to determine susceptibilities to a standard panel of 10 antimicrobial agents (ampicillin, chloramphenicol, ciprofloxacin, furazolidone, kanamycin, nalidixic acid, streptomycin, sulfisoxazole, tetracycline, and

trimethoprim-sulfamethoxazole [TMP-SMZ]). Interpretive criteria for *V. cholerae* have been established only for ampicillin, chloramphenicol, sulfonamides, tetracycline, and TMP-SMZ [10]. Tentative zone-size criteria have been proposed for furazolidone and nalidixic acid [11]; criteria standardized for the Enterobacteriaceae were used to interpret results for ciprofloxacin, kanamycin, and streptomycin. Selected isolates were further characterized by pulsed-field gel electrophoresis (PFGE), as described elsewhere [12]. Gulf Coast strains of toxigenic V. cholerae O1 were distinguished by the following characteristics: serotype Inaba, hemolytic on sheep blood agar, and a typical banding pattern by PFGE [8, 12].

RESULTS

All cases. From 1 January 1995 through 31 December 2000, 18 states and 2 US territories reported 61 cases of cholera to the CDC, for a rate of 10.2 cases/year. Thirty-seven (61%) cases were travel associated; the other 24 (39%) were acquired in the United States (figure 1). The median age of patients was 40 years (range, 6 months 89 years), and 57% were male. Among 58 patients whose race or ethnicity was specified, 20 (34%) were Hispanic, 20 (34%) were white, 17 (29%) were Asian/Pacific Islander, and 1 (2%) was African. Of the 53 persons for whom resident status was specified, 47 (89%) were US residents.

Figure 1. Cases of Vibrio cholerae O1 infection, by year and source, 1995 2000 (n = 61).

By definition, 100% of cases had diarrhea. The median maximum number of stools in 24 h was 10 (range, 3 35 stools). Other reported symptoms included vomiting (67%), nausea (64%), abdominal cramps (58%), muscle cramps (42%), headache (22%), fever (22%), and shock (9%). Only 1 patient reported bloody stools. For 45 patients for whom information was available, the median duration of illness was 7 days (range, 1 19 days). Thirty-five (57%) of 61 patients were hospitalized (median stay, 4 days; range, 1 31 days). One patient, an 89-year-old man, died as a result of his illness. Other reported complications included electrolyte disturbances, renal failure, and cyanosis. For the 60 patients for whom information was available, 21 (35%) reported significant medical history. Eleven (22%) patients had underlying gastrointestinal conditions and were taking antacids; 5 (10%) others reported taking corticosteroids. Antimicrobial treatment was prescribed after illness onset to 52 (88%) of 59 patients; 33 (56%) received a fluoroquinolone.

Travel-associated cases. Cholera was acquired during travel to 14 countries by 37 persons: 18 (48.6%) to Latin America, 18 (48.6%) to Asia, and 1 (3%) to Africa. Among 27 patients who specified a reason for travel, 16 (59%) were visiting relatives or friends, 4 (15%) were immigrating to the United States, 4 (15%) were traveling for business, and 3 (11%) were tourists.

Domestic cases. Fourteen (58%) of 24 domestic cases were associated with eating seafood: crab (4 cases), imported fish (3 cases), mixed seafood (3 cases), sushi (2 cases), and shrimp (2 cases). For 6 cases, the seafood was from the Gulf Coast (figure 1); 2 cases were in persons who purchased and ate precooked commercial Gulf Coast crab. Two (8%) cases, acquired through contaminated sliced cantaloupe, represent the first well-documented instance in the United States of cholera transmission from an asymptomatic food handler [13]. The source for 8 (33%) domestically acquired infections was not identified; 2 of these 8 persons lived in US territories (1 in Guam and 1 in Saipan), 2 persons had traveled, but >7 days before illness onset (1 to Mexico and 1 to Japan), 1 person lived in Louisiana and had an isolate that was consistent with the Gulf Coast strain, 1 person lived in California and ate imported dried fish. No potential etiology was proposed for the other 2 cases of infection.

Laboratory results. Toxigenic V. cholerae O1 was isolated from the stool samples of 57 (93%) patients. No toxigenic V. cholerae serogroup O139 was identified. Of the 57 isolates, 53 (93%) were biotype El Tor, and 4 were atypical. Forty-four (83%) of the El Tor isolates and the 4 (8%) atypical isolates were serotype Ogawa; the rest were serotype Inaba. Infection was diagnosed serologically in 4 patients, including 1 Gulf Coast associated case. All 5 Gulf Coast isolates were sensitive to all antibiotics tested, whereas 13 (59%) of the remaining 17 isolates from domestically acquired infections were resistant to sulfisoxazole, streptomycin, and furazolidone. Among travel-associated cases, the proportion of strains susceptible to all antimicrobials tested fell from 55% to 9%. This decrease in susceptibility occurred among isolates from both Latin America and Asia. Resistance to TMP-SMZ, sulfisoxazole, streptomycin, and furazolidone increased from 7 (8%) of 88 in 1990 1994 to 11 (31%) of 35 in 1995 2000; resistance to tetracycline increased from 4 (5%) of 88 to 3 (9%) of 35; and resistance to nalidixic acid increased from 2 (2%) of 88 to 5 (14%) of 35. No isolates tested were resistant to ciprofloxacin (table 1). All 3 tetracycline-resistant isolates and all 5 nalidixic acid-resistant isolates were acquired by travelers to Asia.

Table 1. Toxigenic Vibrio cholerae O1 isolates resistant to specific antimicrobial agents, United States, 1990 1994 and 1995 2000.				
Isolate susceptibility or resistance, agent	**Travel associated (no. of isolates tested)**		**Domestically acquired (no. of isolates tested**	
	19901994 (n = 88)	**19952000 (n = 35)**	**19901994 (n = 19)**	**19952000 (n = 22)**
Susceptible	55	9	84	41
Resistance				
SSZ	36	57	16	59
SSZ + TMP-SMZ	2	11	0	0
SSZ + TMP-SMZ + tetracycline	3 [1]	6	0	0

SSZ + TMP-SMZ + nalidixic acid	2	14	0	0
SSZ + tetracycline	0	3	0	0
Any SSZ	43	91	16	59
Any tetracycline	5	9	0	0
Ciprofloxacin	0	0	0	0
Other	1 [2]	0	0	0

NOTE. Data are percentage of isolates resistant to the specified agents. SSZ, sulfisoxazole, streptomycin, and furazolidone; TMP-SMZ, trimethoprim-sulfamethoxazole.

[1] One isolate was also resistant to chloramphenicol.
[2] One isolate was resistant to sulfisoxazole, streptomycin, TMP-SMZ, tetracycline, chloramphenicol, and kanamycin.

DISCUSSION

The average annual incidence of cholera for the 5-year period 1990 1994 was 39.0 cases/year, compared with an average annual incidence of 10.2 cases/year for the 6-year period of 1995 2000. Much of this decline was due to fewer cases associated with travel to Latin America, which paralleled the global decrease in cases attributed to the Latin American epidemic [14]. Nonetheless, on average, >10 confirmed cases of cholera were diagnosed in the United States each year, highlighting the need for physicians, microbiologists, and public health authorities to consider cholera in the differential diagnosis of patients with severe watery diarrhea and to react accordingly.

The cases described in Case Descriptions highlight the issues to be addressed by clinicians and microbiologists when patients present with severe watery diarrhea. Health care providers need to consider cholera in the differential diagnosis and to obtain a travel and food history. If cholera is suspected, a stool culture on thiosulfate-citrate-bile salts sucrose agar should be requested, and the patient should be treated with appropriate rapid fluid and electrolyte replacement, to avoid complications. Multiple antimicrobial resistance is increasingly common among V. cholerae strains isolated from ill travelers. Thus, although rehydration therapy remains the mainstay of cholera treatment, when antimicrobial therapy is indicated, care should be given to choose an agent to which the isolate is susceptible. Appropriate choices for empiric antimicrobial therapy for suspected cholera would still include doxycycline or tetracycline, or a fluoroquinolone [15]. Laboratories are required to report all cases of cholera to local or state health departments so that effective national surveillance can be maintained.

No toxigenic *V. cholerae* serogroup O139 cases were reported in the past 5 years. The Gulf Coast strain continues to cause domestic cases of cholera, accounting for 4 (2%) cases in 1990 1994 and 6 (10%) cases in 1995 2000. The case that was associated with eating commercially distributed cooked seafood underscores the need for regulatory agencies in state and national governments to continue working with the seafood industry to ensure the safety of commercial seafood products.

Overall, foreign travel still accounts for the majority of cholera cases diagnosed in the United States. As illustrated by the case reports, it behooves airlines to prepare for cases of cholera among passengers by stocking oral rehydration salts on board all flights longer than a few hours duration. Consistent with previous reviews, half the travel-associated cases occurred in persons visiting friends and relatives, a group that has been difficult to reach through travel clinics. Effective means to reach this population are needed if full advantage is to be taken of the development and licensure of newer more effective cholera vaccines. Information for clinicians and travelers on how to prevent cholera and other illnesses by avoiding unsafe beverages and foods is available on the CDC web page at http://www.cdc.gov/travel/index.htm or through the CDC fax information service at 888-CDC-FAXX (232-3299).

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