

Geographical patterns of cholera in Mexico, 1991–1996

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| Background | The seventh cholera pandemic has been ongoing in Mexico since 1991 and threatens to become endemic. This paper aims to determine the geographical pattern of cholera in Mexico to define areas at high risk of endemic cholera. |
| Methods | Ecologic research was conducted based upon the cartography of disease incidence. The 32 Mexican states were grouped into five strata according to the value of the 1991–1996 cumulative incidence rate of cholera. Rate ratios were computed for strata of states classified by geographical situation, urbanization, and poverty level. |
| Results | Cholera incidence was 2.47 times higher in coastal states than in the interior (95% CI : 2.42–2.52). The disease was negatively associated with urbanization. Incidence in the least urbanized stratum was four times as high as in the most urban stratum (95% CI : 3.9–4.12). The poorest stratum showed the most remarkable incidence, i.e. 5.9 times higher than the rate in the least poor stratum (95% CI : 5.73–6.04). |
| Conclusions | This ecologic research suggests that high poverty level, low urbanization, and southern location are the most important predictors of endemic cholera in Mexican states. It is hypothesized that the natural environment of the coastal plains in southern states may also play a significant role in cholera incidence. Poor communities residing in the southern, predominantly rural, coastal states should be prioritized when it comes to investing in safe water supply facilities, adequate excreta disposal systems and cholera surveillance. |
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The seventh cholera pandemic reached Mexico in June 1991. The first cases were reported from a community located on the banks of the San Miguel river. Control measures were implemented rapidly but the disease spread across the basin of the Sultepec river and the Tula valley.¹ A total of 43 536 cholera cases were notified from 1991 to 1996. Toxigenic *Vibrio cholerae* serogroup O1 El Tor biotype has been held responsible for the disease. Incidence rose from 1991 through 1993, and after a remarkable decline in 1994 the number of cases peaked in 1995, dropping again in 1996.² Two features suggest that cholera may become endemic in Mexico. First, cholera outbreaks have recurred seasonally for six consecutive years, with most cases reported during the summer months.² Second, the proportion of children under 15 who have contracted the disease has shown a rising trend.²

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Endemic cholera has displayed a particular geographical pattern in many nations of the world. It has predominated in poor populations living in coastal areas, particularly in low-lying coastal plains.³ Endemic cholera has been reported in the delta of the Ganges and Meghna rivers in Bangladesh,⁴ the delta of the Irrawaddy and Salween rivers in Burma (Myanmar),⁵ and in coastal areas of Indonesia⁶ and Africa.⁷ Endemic foci have also arisen on the Gulf coast of the US⁸ and on the island of Sardinia, Italy.⁹ Incidence rates have also been higher in coastal administrative territories in The Philippines,^{10–12} Indonesia (Aceh province),¹³ Malaysia,¹⁴ Taiwan,¹⁵ Italy,¹⁶ Portugal,¹⁷ Peru,¹⁸ Ecuador,^{18,19} and Colombia.²⁰ This geographical pattern of cholera largely depends on ecologic factors which are thought to play a major role in the long-term survival of toxigenic *V. cholerae* O1 in aquatic environments of estuaries and low-lying coastal plains.^{3,6} However, cholera has not spared inland countries such as Chad,²¹ Mali,²² and Bolivia.²³

Studying the geographical patterns of cholera in Mexico can prove useful in defining the territories where the disease is most likely to remain endemic. In fact, determination of risk areas

is a most important objective of the National Program for Cholera Prevention and Control.² This paper presents an ecologic research design based upon the cartography of cholera incidence.²⁴ The purpose is to identify territories at high risk of endemic cholera. These territories would be appropriate targets to set up priorities for investing scarce financial and material resources on safe water supply facilities, adequate excreta disposal systems, and cholera surveillance.

Methods

Definition of a cholera case

In Mexico, laboratory confirmation is required for a suspected case to be defined and recorded as a cholera case.²⁵

The definition of a suspected cholera case depends on whether or not the presence of cholera has been demonstrated in the area (area, whether urban or rural, has been defined previously²⁵). In areas where the presence of cholera has not been demonstrated, the definition is: a patient >5 years old with at least five episodes of acute watery diarrhoea within 24 hours, with or without vomiting or dehydration. In areas where the presence of cholera has been demonstrated, the definition is: a patient of any age with acute diarrhoea, or patient of any age with diarrhoea who is a contact of a confirmed cholera case.

A confirmed cholera case is defined as a suspected cholera case with laboratory confirmation of the presence of toxigenic *V. cholerae* O1 through stool culture or demonstration of a significant rise in antibody titres against vibrios or cholera toxin.²⁵

Geographical and statistical analyses

Cumulative incidence rates of cholera were calculated for the 32 Mexican states by including all cholera cases reported over the period 1991–1996. The source of the cholera incidence was the National Directorate of Epidemiology at the Health Secretariat of Mexico (*Dirección Nacional de Epidemiología/Secretaría de Salud*) database.² The population database was obtained from the 1990 Population Census of Mexico conducted by the National Institute of Statistics, Geography, and Information (*Instituto Nacional de Estadísticas, Geografía e Informática*).²⁶ This is the most reliable source of demographic information in Mexico.

The 32 Mexican states were classified into five strata according to the value of the 1991–1996 cumulative incidence rate of cholera. The cutoff points for each interval were determined by the method of natural break using the Geographical Information System (GIS) MapInfo Professional for Windows, version 4.0 (MapInfo Corporation®). The cumulative incidence rates of cholera were also mapped using GIS. Different shadings were used to distinguish each interval.

A spatial auto-correlation statistic, Moran's I ,²⁷ was computed to determine patterns of spatial clustering of states with similar cumulative incidence rates. In calculating Moran's I , the spatial weighting function was scaled according to the length of the common boundaries, under the assumption that states sharing longer boundaries are more inter-connected than states sharing shorter boundaries or no boundary at all.²⁷ Clustat Software, version 1.0 was designed and integrated to the platform of MapInfo GIS by one of the authors (RMP). This software was used to calculate Moran's I and its significance level.

Cholera incidence rates were computed for strata of states grouped by each of the following variables:

Geographical location of the states (coastal or interior)

The coastal state stratum was divided into two regions: Gulf of Mexico and Pacific Ocean (Appendix 1). The population-based rate ratio was calculated for the strata of coastal states by taking the stratum of interior states as reference.

Urbanization level

Four urbanization strata were determined, each representing a quartile of states. Since Mexico is made up of 32 states, each quartile was composed of eight states (Appendix 1). The indicator of urbanization used was the proportion of the state population residing in settlements of $\geq 15\,000$ inhabitants in 1990. This data was obtained from the National Statistical Institute.²⁸ Population-based incidence rate ratios were calculated for each stratum by taking that of higher urbanization as reference.

Poverty status

A composite poverty index (CPI) was defined for each state based upon three variables: (1) Dwellings without connection to sewerage or septic tank (per cent of total state dwellings); (2) overcrowding (average number of people per bedroom); and (3) illiteracy rate in people aged ≥ 15 years (%). This information refers to year 1990 and was also obtained from the National Statistical Institute.²⁸ Each variable was standardized to have mean zero and a standard deviation of one. The CPI for each state was obtained by calculating the mean of the algebraic sum of the standardized values of the three variables. The CPI values were plotted on a frequency histogram to classify the states into three poverty levels: I high; II medium; and III low (Appendix 2). Population-based incidence rate ratios were calculated for strata I and II by taking stratum III (the low poverty stratum) as reference.

Finally, ecologic double-stratification analyses were conducted, i.e. population-based incidence rate ratios were determined for coastal versus interior states within each urbanization and poverty stratum. The objective was to explore whether cholera incidence rate was associated with geographical situation taking into account urbanization stratum and poverty level.

The 95% CI for rate ratios and χ^2 of linear trends were computed using EpiInfo, version 6.03.

Results

There is a positive and statistically significant spatial auto-correlation (Moran's I statistic = 0.295, z -value = 2.99, $P = 0.0001$). It reflects a north-south gradient, with spatial clustering of southern states with higher incidence rates. States with lower incidence rates are clustered in the north (Figure 1).

Cholera incidence was 2.5 times higher in the coastal stratum than in the interior. The incidence rate was remarkable in states on the Gulf of Mexico coast such as Campeche, Yucatan, and Tabasco (Figure 1 and Table 1). However, the disease also struck some interior states, particularly Morelos, Tlaxcala, and Puebla.

Cholera incidence displayed an inverse association with urbanization (Table 2) and a direct relationship with poverty level (Table 3). The least urban stratum showed a fourfold rate ratio over the most urban one. The incidence rate of the poorest stratum was about six times as high as that of the least poor stratum.

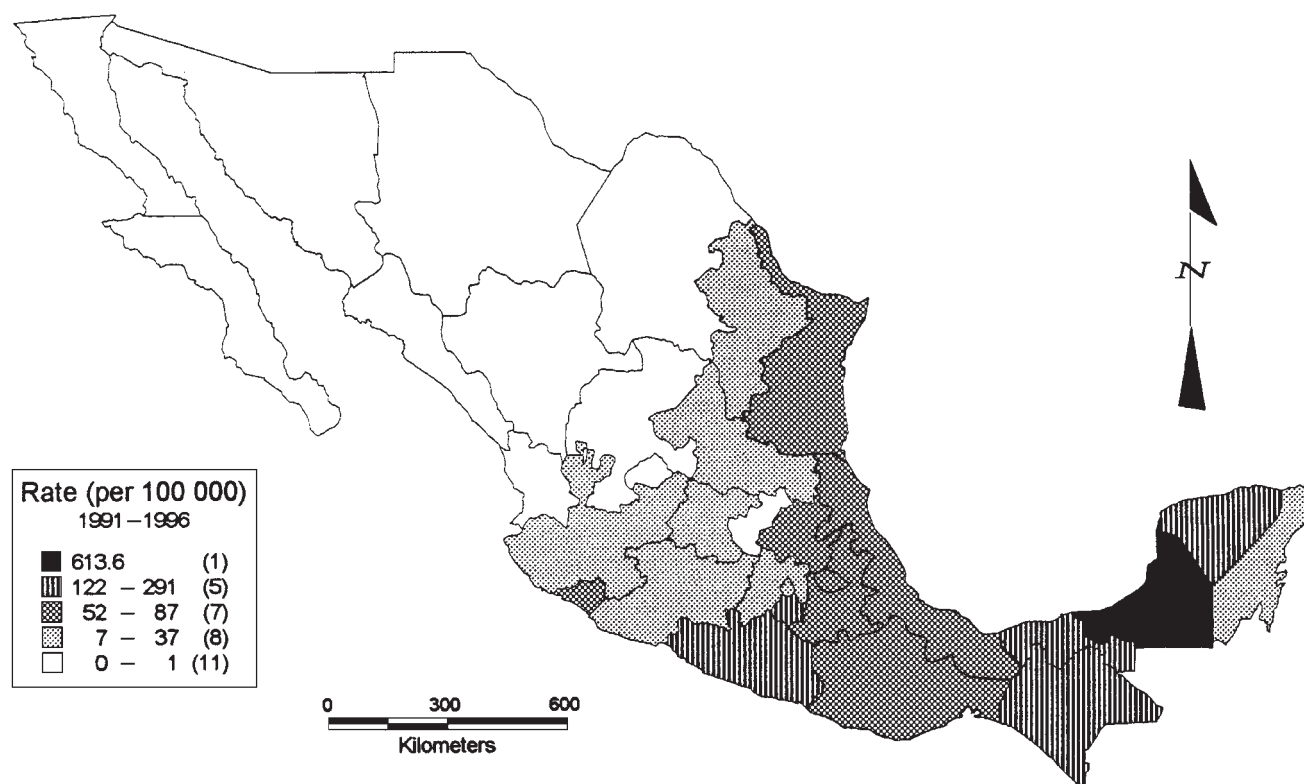


Figure 1 Cholera incidence in States of Mexico

Table 1 Cholera incidence rate and population-based rate ratio by strata of states classified according to geographical situation, 1991-1996

| Geographical location | Cholera cases ^a | Population ^b | Rate (per 100 000) | Rate ratio (95% CI) |
|----------------------------------|----------------------------|-------------------------|--------------------|---------------------|
| Coastal | 29 491 | 3 733 1979 | 79 | 2.47 (2.42-2.52) |
| Gulf of Mexico and the Caribbean | 17 471 | 12 370 966 | 141.23 | 4.42 (4.33-4.52) |
| Pacific Ocean | 12 020 | 24 961 013 | 48.16 | 1.51 (1.47-1.55) |
| Interior | 14 035 | 43 917 666 | 31.96 | Reference |

^a Source of cholera cases: Ref. 2.

^b Source of state population: Ref. 26.

Table 2 Cholera incidence rate and population-based rate ratio by strata of states classified according to urbanization stratum, 1991-1996

| Stratum (urbanization %) | Cholera cases ^a | Population ^b | Rate (per 100 000) | Rate ratio (95% CI) |
|--------------------------|----------------------------|-------------------------|--------------------|---------------------|
| I Very low | | | | |
| (19.9-38) | 14 816 | 15 103 046 | 98.1 | 4.01 (3.9-4.12) |
| II Low | | | | |
| (40-51) | 13 867 | 21 045 578 | 65.89 | 2.69 (2.62-2.77) |
| III Medium | | | | |
| (53.7-67.4) | 7455 | 14 906 438 | 50.01 | 2.04 (1.98-2.11) |
| IV High | | | | |
| (68.4-98.3) | 7388 | 30 194 583 | 24.47 | Reference |

χ^2 for linear trend = 10 843.6 ($P = 0.000001$)

^a Source of cholera cases: Ref. 2.

^b Source of state population: Ref. 26.

Table 3 Cholera incidence rate and population-based rate ratio by strata of states classified according to poverty level, 1991–1996

| Stratum (Poverty range) | Cholera cases ^a | Population ^b | Rate (per 100 000) | Rate ratio (95% CI) |
|------------------------------------|-------------------------------|-------------------------|-----------------------|------------------------|
| I High | | | | |
| (−2.17 < CPI ^c < −0.68) | 26 733 | 23 458 068 | 113.83 | 5.88 (5.73–6.04) |
| II Medium | | | | |
| (−0.48 < CPI < 0.33) | 9857 | 21 937 416 | 44.91 | 2.32 (2.25–2.39) |
| III Low | | | | |
| (0.58 < CPI < 1.63) | 6936 | 35 810 635 | 19.36 | Reference |

χ^2 for linear trend = 22 700.5 ($P = 0.000001$)

^a Source of cholera cases: Ref. 2.

^b Source of state population: Ref. 26.

^c Composite poverty index.

Table 4 Cholera incidence rate and population-based rate ratio by strata of states classified by urbanization strata and geographical situation, 1991–1996

| Stratum (urbanization %) | Geographic location | Cholera cases ^a | Population ^b | Rate (per 100 000) | Rate ratio (95% CI) |
|-----------------------------|------------------------|-------------------------------|-------------------------|-----------------------|------------------------|
| I Very low | | | | | |
| (19.9–38) | Coastal | 12 829 | 11 177 080 | 114.78 | 2.27 (2.16–2.4) |
| | Interior | 1987 | 3 925 966 | 50.61 | Reference |
| II Low | | | | | |
| (40–51) | Coastal | 9979 | 12 515 677 | 79.73 | 1.75 (1.7–1.82) |
| | Interior | 3888 | 8 529 901 | 45.58 | Reference |
| III Medium | | | | | |
| (53.7–67.4) | Coastal | 5111 | 9 728 786 | 52.53 | 1.16 (1.1–1.22) |
| | Interior | 2344 | 5 177 652 | 45.27 | Reference |
| IV High | | | | | |
| (68.4–98.3) | Coastal | 1572 | 3 910 436 | 40.2 | 1.82 (1.7–1.92) |
| | Interior | 5816 | 26 284 147 | 22.13 | Reference |

^a Source of cholera cases: Ref. 2.

^b Source of state population: Ref. 26.

Table 5 Cholera incidence rate and population-based rate ratio by strata of states classified according to poverty level and geographical situation, 1991–1996

| Stratum (Poverty range) | Geographic location | Cholera cases ^a | Population ^b | Rate (per 100 000) | Rate ratio (95% CI) |
|------------------------------------|------------------------|-------------------------------|-------------------------|-----------------------|------------------------|
| I High | | | | | |
| (−2.17 < CPI ^c < −0.68) | Coastal | 22 218 | 17 448 116 | 127.18 | 1.69 (1.64–1.75) |
| | Interior | 4515 | 6 009 952 | 75.07 | Reference |
| II Medium | | | | | |
| (−0.48 < CPI < 0.33) | Coastal | 6153 | 10 322 068 | 59.57 | 1.87 (1.79–1.95) |
| | Interior | 3704 | 11 615 348 | 31.88 | Reference |
| III Low | | | | | |
| (0.58 < CPI < 1.63) | Coastal | 1120 | 9 532 304 | 11.75 | 0.53 (0.5–0.57) |
| | Interior | 5816 | 26 278 331 | 22.13 | Reference |

^a Source of cholera cases: Ref. 2.

^b Source of state population: Ref. 26.

^c Composite Poverty Index.

The incidence rate was higher in the coastal state stratum than in the interior one of each urbanization stratum (Table 4) as well as in the high and medium poverty strata. The opposite pattern was observed in the least poor stratum (Table 5).

Discussion

The results of this study suggest that high poverty level, low urbanization, and southern location are the most important ecologic (i.e. group-level) predictors of cholera incidence in Mexican states. Cholera seems to have become endemic in the poorest and most rural coastal states of southern Mexico, notably in Campeche, Yucatan, Tabasco, Chiapas, Guerrero, and

Oaxaca. However, it may also remain endemic in some interior states such as Puebla and Hidalgo. This disease is known to attack individuals with insufficient knowledge of and inappropriate attitudes towards hygienic practices, and who live in dwellings that lack access to a safe drinking water supply and to adequate facilities for sewage disposal and treatment.^{6,29} These are common problems for many communities in the poorest states of Mexico, whether coastal or interior.^{28,30} In fact, drinking faecally-polluted waters has been reported as the most important cholera transmission route in Mexico.²

Lower cholera incidence rates in northern Mexico may have been influenced by both, social and climatic variables. Firstly, northern states such as Sonora, Chihuahua, Coahuila, Nuevo

Leon, and both, Baja California, and Baja California Sur are among the least poor and more urbanized in Mexico. Secondly, the widest daily and annual temperature oscillations in Mexico are recorded in the north.³¹ Mean daily temperature in winter is normally below 10°C (most markedly in January). In summer, daily temperatures can reach values above 40°C, particularly in Sonora and Chihuahua states. These temperature extremes may prevent mesophilic *V. cholerae* from surviving and multiplying in the environment. Moreover the north is remarkably dry, with <200 mm of annual rainfall in arid areas.³¹ A scarcity of surface water bodies may also be a factor limiting survival of the microbe, though this observation should be noted with caution, as cholera has struck populations in extremely dry areas like the Sahelian region of Chad in Africa.²¹

The ecologic population-based double-stratification analyses suggest that poverty and urbanization alone cannot fully explain the higher incidence of cholera in coastal states, particularly in southern Mexico. We hypothesize that the natural environment has played a significant role in cholera incidence. Endemic cholera has been associated with the natural environment of coastal areas, whether in developed or developing nations. The environment of the coastal states of southern Mexico is more favourable for both *V. cholerae* survival and cholera transmission than that of states in the interior. In Mexico, an important difference is that populations of coastal states reside, on average, at lower altitudes than the population in the interior.^{31,32} It is argued below that endemic cholera in southern Mexico is probably associated with altitude, as poor communities living in coastal states (i.e. at lower altitudes) are more likely to be exposed to an environment that is more favourable for both *V. cholerae* survival in aquatic environments and cholera transmission. This hypothesis consists of six arguments.

Increasing environmental stress on the pathogen at higher altitudes

Vibrio cholerae is subject to several sources of environmental stress in faecally-polluted surface freshwater. These stressing factors are more intensive at increasing altitudes due to the following:

Lower temperature

The optimal temperature for *V. cholerae* O1 multiplication is 30–37°C.^{33,34} Growth is inhibited below 15°C. Due to the decrease in temperature with increasing altitude, the waters of rivers, lakes, and dams in mountainous regions of inland Mexico are colder than in the warmer low-lying coastal plains that are closer to the sea level.

Lower content of organic matter and nutrients

The metabolism of toxigenic *V. cholerae* O1 El Tor biotype requires carbohydrates, nitrogen, sulphur, phosphorous, and sodium.³⁴ Nutrients and organic matter that enter rivers are transported downstream, where their concentrations are usually higher. The flow of water in rivers and streams is more rapid in mountainous areas, since slopes are steeper than in the plains of lower altitudes. The faster the flows the better the oxygenation of waters. These reasons explain why river water is usually cleaner at higher altitudes. In ecosystems with lentic (stagnant) surface freshwater, such as lakes, ponds, and dams, the magnitude of eutrophication (i.e. the over-enrichment of waters

with nutrients) is less significant in mountainous regions than in low-lying plains.³⁵

Higher intensity of ultraviolet radiation (UVR)

Vibrio cholerae is highly susceptible to UVR. Less atmospheric turbidity at higher altitudes allows more penetration of UVR in mountainous regions than in low-lying plains. In fact, it has been proposed that sunlight could be useful to disinfect drinking waters at high altitudes.³⁶

More turbulence of water flows

Since the flow of surface waters is often faster at higher altitudes they are also more turbulent. The uptake of nutrients by the cholera pathogen is enhanced in the turbulence-free environment of stagnant waters on low-lying plains.

There is at least one study conducted in Peru supporting this argument. In search of aquatic reservoirs of *V. cholerae* O1, Tamplin and Carrillo sampled waters from four sites: Lake Titicaca in the Andes (>3000 m above sea level); the Amazon river in the region of the tropical rainforest; the Rimac river (near Lima city), a few metres above sea level; and the Pacific coast.³⁷ *Vibrio cholerae* O1 was isolated more frequently and in higher numbers from the warm waters of the Amazon and Rimac rivers than from Lake Titicaca's cold waters (12°C).

In summary, less environmental stress at lower altitudes means better possibilities for the multiplication and long-term survival of *V. cholerae* in faecally-polluted surface freshwater. Hence, it could enable the pathogen to maintain high enough infecting doses, thus posing threats for individuals who depend on these contaminated bodies of water for drinking and other purposes (e.g. bathing and utensil washing).

Less plankton at higher altitudes

Toxigenic *V. cholerae* O1 can survive and multiply in association with species of phytoplankton (mainly blue-green algae³⁸) and zooplanktonic copepods³⁹ present in surface freshwaters, whether or not faecally-polluted. The multiplication of these planktonic species is more difficult at increasing altitudes because: (1) there is less availability of nutrients that are essential for planktonic growth (such as nitrates and phosphates) in bodies of surface freshwater located in mountainous regions. (2) The water is colder, thus preventing green and blue-green algae from multiplying, as they require temperatures from 25 to 35°C.⁴⁰ (3) Cloudy days are more frequent at higher altitudes. Moreover, in a mountainous landscape the sun rises later and sets earlier than on plains, since mountains are physical barriers. Hence, less sunlight arrives in mountainous areas, thus inhibiting photosynthesis which is required for phytoplankton multiplication. The more intense biological activity of UVR at higher altitudes also checks planktonic growth. (4) Phytoplankton tends to multiply less in the rapidly-flowing waters typical of mountainous regions and if any plankton grew, it would be transported downstream.

In summary, planktonic populations are more abundant in the surface freshwater of low-lying coastal plains. Therefore, *V. cholerae* can maintain higher infecting doses in these aquatic environments by attaching to planktonic species. For instance, in a laboratory microcosm experiment, Huq *et al.* observed that toxigenic *V. cholerae* O1 can reach infecting doses in association with species of planktonic copepods.³⁹ They argued that filtration of surface freshwater through locally-available filters can

significantly reduce the number of cholera vibrios attached to the plankton present in the waters commonly drunk by people settled in the low-lying coastal plains of Bangladesh, where the disease is endemic. It would be interesting to study whether consumption of untreated, though non-faecally polluted, surface freshwater containing high enough infecting doses of toxigenic *V. cholerae* O1 attached to plankton has been a significant transmission route causing cholera in poor individuals residing in low-lying plains of southern Mexico.

Frequent consumption of seafood by people living in coastal settlements

Toxigenic *V. cholerae* O1 require sodium ion (Na^+) for metabolic purposes. The optimal salinity level for survival and growth of this microbe is 20 parts per 1000,³⁴ a typical value in estuarine environments. This pathogen is thought to be an autochthonous member of the microbial flora of estuaries and coastal wetlands.³

Species of fish, oysters, clams, crabs, shrimps, and lobsters are abundant in the estuarine environments of the Gulf of Mexico.^{31,41} These species may be contaminated in estuaries and coastal wetlands where the vibrios can thrive. Fisheries are important sources of income for many communities residing near this coast. Furthermore, seafood is a significant component of the daily diet of these populations. It has been reported that consumption of raw fish and oysters have been important infection sources and transmission routes in this nation.² We hypothesize that people living in coastal communities are more frequently infected by this transmission route since they consume more seafood than people who reside in interior mountainous territories, thus contributing to the higher incidence rate of cholera observed in coastal states.

Unfavourable natural conditions for appropriate sanitation at lower altitudes

In low-lying coastal plains, unfavourable topographic, soil, and hydro-geological conditions make it difficult to achieve and maintain high sanitation standards among populations living in these territories. Hydromorphic soils are common in low-lying plains and uncommon at higher altitudes. This soil type predominates in coastal areas of Campeche, Tabasco, and Veracruz,³¹ and presents two features that hinder the construction of appropriate sewage-disposal systems. Firstly, low infiltration rates favour overflow of soakaway pits of septic tanks. This is a most acute problem in communities where the emptying and cleaning of soakaway pits is not performed with the necessary frequency. Secondly, the underground water table is close to the surface (usually less than one metre). Even though it makes drawing groundwater easier, it also increases the probability of groundwater contamination with faecal material, as the distance between the bottom of a pit latrine and the water table are usually short.⁴²

Higher frequency of floods at lower altitudes

Floods are more frequent in low-lying coastal plains of Mexico (most notably in the states of Veracruz, Tamaulipas, and Tabasco) than in interior mountainous regions.³¹ Floods usually disrupt safe water supply facilities and sanitation services.⁴³ Water wells used for drinking purposes are frequently polluted by floodwaters that harbour the pathogen agent. Floods spread

V. cholerae in the environment, thus contributing to endemic cholera in coastal states.

Downstream movement of sewage

In Mexico, untreated, pathogen-containing sewage is usually discharged into rivers that transport pollutants to low-lying territories. Hence, downstream residents who depend on untreated river water for drinking and other purposes (and who do not usually boil water prior to drinking) are likely exposed to higher doses of vibrios than upstream residents who use less polluted river waters.

Limitations of this research

In Mexico, cholera surveillance has relied upon both active and passive procedures.⁴⁴ Passive surveillance may have caused underreporting of cholera cases, particularly in remote areas of southern states where access to health care is difficult.

The results of the spatial auto-correlation analyses should be interpreted with caution. Firstly, differences in sizes and shapes among Mexican states limit the scale of the spatial patterns that can be detected. Secondly, there are only 32 states, a relatively small number for spatial auto-correlation analysis.²⁷

The indicator used to incorporate the sanitation dimension into the CPI, i.e. dwellings without connection to sewerage or septic tank, is rather crude. In Mexico, conventional sewerage systems serve mainly high and middle income urban populations but these systems are affected by obstructions and overflows, particularly in decaying inner-city areas of large urban centres. Conversely, low cost sanitation systems (such as pit latrines) predominate in isolated, backward rural areas and in peri-urban shanty towns and slums. However, some low cost sanitation systems, if properly maintained, do not pose threats to health (e.g. ventilated-improved pit latrines).

Some parts of the coastal states have landscapes more in common with the mountainous regions of interior states than with coastal plains. Poverty and urbanization variables are not homogeneous within states either. Hence, the observed ecologic associations between poverty levels, urbanization, geographical situation of states, and cholera incidence rates may be affected by flaws typical of ecologic designs,^{45,46} particularly the ecologic fallacy. Effect modification may have biased these ecologic associations, since urbanization, poverty, and north-south location are highly correlated, i.e. the more urbanized, less poor states tend to be in the north, whereas less urbanized, poorer states tend to be in the south.

The areas at high risk of endemic cholera identified in this study are large territories defined by political boundaries, i.e. the states. In future studies the spatial resolution should be augmented by including variables of the natural environment that would allow stratification of the states according to geographical landscape, each representing a different level of risk (e.g. mountainous highlands, hilly uplands, low-lying plains). Geographic Information System technology can prove useful in the input, storage, analysis, and display of these geographically-referenced databases.⁴⁷

In conclusion, this research suggests that the influence of environmental risk factors on the occurrence of cholera in Mexico is multifactorial and that high poverty level, low urbanization, and southern location are the most important ecological predictors of endemic cholera in Mexican states. We

hypothesize that the natural environment of coastal plains in the southern states may also play a significant role in cholera incidence. Poor communities residing in the southern, predominantly rural, coastal states should receive priority when it comes to investing in safe water supply facilities, adequate excreta-disposal systems, and cholera surveillance. The determination of risk-areas of cholera should be replicated in other Latin American nations where this disease also threatens to become endemic.

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Appendix 1 Classification of States of Mexico according to poverty strata, urbanization level, and geographical situation^a

| Poverty stratum | States | | |
|-----------------|--|--------------------------------|----------------------------|
| | Coastal | | Interior |
| | Gulf of Mexico and Caribbean Sea | Pacific Ocean | |
| High | Campeche II ^a (613.62) ^b | Chiapas I (146.05) | Hidalgo I (70.54) |
| | Veracruz II (86.25) | Guerrero I (126.23) | Puebla II (77.14) |
| | Yucatan III (290.11) | Oaxaca I (52.13) | |
| | Quintana Roo III (7.5) | | |
| Medium | Tabasco I (216.55) | Durango II (0.15) | Guanajuato III (22.05) |
| | Tamaulipas IV (69.88) | Michoacan II (36.98) | Zacatecas I (0.24) |
| | | Nayarit I (0.73) | Querétaro II (27.49) |
| | | Sinaloa II (0.5) | Tlaxcala I (85.65) |
| | | | Morelos III (122.67) |
| Low | | | San Luis Potosi II (20.67) |
| | | Baja California IV (0) | Aguascalientes IV (0.69) |
| | | Baja California Sur III (0.94) | Chihuahua IV (0.74) |
| | | Colima III (69.08) | Coahuila IV (1.47) |
| | | Jalisco III (15.31) | México IV (27.85) |
| | | Sonora III (0.49) | Distrito Federal IV (33.3) |
| | | | Nuevo León IV (9.26) |

^a Roman numbers refer to urbanization stratum: I Very low, II Low, III Medium, IV High.

^b The 1991–1996 cumulative cholera incidence rates of each state are shown in parentheses (cases per 100 000).

Appendix 2 Composite Poverty Index (CPI) by states of Mexico, 1990!!!^a Dwellings without connection to sewerage or septic tank (% of total state dwellings).^b Illiteracy rate among people ≥15 years (%).^c Overcrowding (average number of people per bedroom).^d CPI = (Z₁+Z₂+Z₃)/3.^e Z₁, Z₂, and Z₃ are variables 1, 2, and 3 expressed in standard deviation units.