REVIEW OF REPORTED CHOLERA OUTBREAKS WORLDWIDE, 1995–2005

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Abstract. The global temporal and spatial distribution of cholera is underappreciated, given the lack of surveillance in endemic areas and economic disincentives to report outbreaks. To judge the use of specific novel interventions such as vaccines or anti-secretory agents, we compiled a database and analyzed cholera reports from the Program for Monitoring Emerging Diseases from 1995 to 2005. Of the 632 reports meeting the search criteria, 66% originated in Sub-Saharan Africa, followed by 16.8% from Southeast Asia. Reported outbreaks in Africa tended to be larger in size. The most common risk factors were water source contamination, heavy rainfall and flooding, and population dislocation. While cholera reporting is sub-optimal, this review provides a detailed sub-national quantification of cholera, identifies foci of endemicity in Africa, and describes risk factors by region. We highlight the need for more extensive outbreak reporting to justify investments in new interventions.

INTRODUCTION

In 1961, the seventh cholera pandemic began in Indonesia and spread throughout the world, reaching Africa in 1970 and South America in 1991 after an absence of > 100 years. Cholera has long been endemic in large parts of South Asia, but in the current pandemic, it has established endemicity throughout the African continent.1 The lack of infrastructure and economic development has made many parts of Africa susceptible to cholera, a disease associated with a lack of clean water and poor sanitation.

The mechanisms of transmission for cholera include water, unwashed contaminated food, and seafood that comes from Vibri cholerae endemic estuaries.2 Known risk factors for cholera outbreaks include poverty, lack of development, high population density, low education, and lack of previous exposure.3–6 Studies in Bangladesh have also shown environmental associations with V. cholerae, including water temperature and depth, rainfall, and copepod counts.7 These factors may contribute to the seasonality and secular trends seen in cholera outbreaks.

An additional risk for cholera outbreaks is a sudden change in the balance between functional hygiene/sanitation services (potable water, latrines, etc.) and the population density. Natural disasters, such as flooding, can disrupt sanitary conditions and concentrate the population to the extent that there are inadequate hygiene services.8 The sudden flux of displaced persons or refugees can overwhelm water and sanitation resources as occurred during the refugee crisis in Goma, the Democratic Republic of Congo (formerly Zaire) in 19949 and numerous other sudden population displacements.

The World Health Organization (WHO) maintains a public database of cholera outbreaks and provides outbreak updates and an annual cholera summary of national aggregate data in the Weekly Epidemiologic Record. Official notification of cholera outbreaks by WHO member states is mandatory under the International Health Regulations (IHR). Despite this, reporting of cholera is considered incomplete by the WHO because of surveillance difficulties and its potential social, political, and economic costs.10 Governments that report cholera indirectly admit to having their water supply contaminated by feces and therefore run the risk of severe economic repercussions, such as restrictions to food export and tourism losses.11 These strong disincentives preclude complete reports.

An alternative monitoring system provides a complementary perspective of the epidemiology of diarrhea and cholera. The Program for Monitoring Emerging Diseases (ProMED), initiated in 1994, operates as an on-line forum for infectious disease specialists, microbiologists, and public health officials and has been administered through the International Society for Infectious Diseases since 1999. ProMED disseminates information about outbreaks of infectious diseases. Its sources include official government and multinational agency reports, print and online media reports, and information from local observers. A team of expert moderators study the validity of reports and edit them for content. Because ProMED is an on-line forum, it is less constrained by political and economic interests, is open to all with internet access, and has > 30,000 subscribers in > 180 countries.12 While it is a passive reporting system, it complements the WHO cholera reports by not only referring to WHO reports and annual summaries but by also providing supplemental detailed data with subjective and objective discussion of outbreaks, ~5-fold of those reported by the WHO.

The WHO’s annual cholera summary does not provide information on sub-national, spatial, or monthly temporal distribution of cases, nor does the WHO website provide a detailed cholera report for each reporting country. Therefore, publicly available cholera data preclude the ability to assess sub-national epidemiologic data and an accurate burden of disease beyond annual incidence data from reporting countries. ProMED is more inclusive in that it not only posts the WHO outbreak reports but also posts from its other sources.

One study of the global burden of cholera estimates that it accounts for 0.6% of all diarrhea cases, or 11 million cases per year, excluding outbreaks and cases in adults.13 The lack of complete reporting and the spatial and temporal variability complicate the estimation of the true global burden. This review of past outbreak reports specific to time, place, and risk factor could provide further insight of its likely future distribution and guide the use of cholera-specific interventions.

MATERIALS AND METHODS

We reviewed ProMED reports of cholera outbreaks from 1995 to 2005 to identify risk factors to help develop predictive

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models for disease burden and geo-spatial and temporal distributions of disease. Using the web site’s (www.promedmail.org) search archives function, we extracted all messages with the search term “cholera” from 1995 to 2005. A total of 1111 postings, including 142 that were aggregate reports referring to an additional 829 unique or follow-up reports were identified, yielding 1,798 reports for review. Inclusion criteria to identify distinct reported outbreaks required 1) reported, clinically diagnosed, or culture confirmed cholera; 2) identification of a sub-national location; 3) either the number of cases or the number of deaths; and 4) a specific month of onset. Reports of isolated cases that were identified as imported were excluded. Of the 1,798 reports, 632 unique outbreaks were identified. Outbreaks were categorized by risk factor based on the primary cause cited by the report’s author. Countries were classified into specific regions and sub-regions based on their geographic location. Information about cholera sub-type was not included in this analysis because of the paucity of data reported.

RESULTS

The distribution by region and sub-region of the 632 reported outbreaks and tabulated cases from those outbreaks are shown (Table 1). Of the reported outbreaks, 66% occurred in Sub-Saharan Africa followed by Southeast Asia (16.8%). Sub-Saharan Africa accounted for 88% of the total number of cases of all outbreaks included in the review. There was considerable variability of reported cholera over time for each region (Figure 1). Africa consistently reported the most outbreaks, followed by Southeast Asia. Reports of cholera declined greatly in the Americas after 1999. Each region experienced a peak in 1998–1999, and all regions but the Americas and Europe experienced another peak in 2005.

The sub-national distribution of cholera outbreak reports is shown for Africa (Figure 2A). The highest concentration of multiple outbreak reports was in the Eastern Democratic Republic of Congo and Western Uganda, which share a border. Eastern and Southeastern Africa also showed high concentrations, along with parts of West Africa. There were almost no outbreak reports from the Saharan region in North Africa or Southwestern Africa. In South Africa, the outbreak reports were limited to its western provinces near the border with Mozambique, which reported outbreaks throughout each province. The sub-national distribution of cumulative cholera cases is also shown for Africa (Figure 2B). The highest number of cases was reported in the eastern part of Democratic Republic of Congo, Mozambique, and eastern South Africa.

The 12 most commonly cited risk factors identified from 306 of the reports are listed with abstracted descriptions of how they contributed to outbreaks (Table 2). Sub-regions showed variability of the reported risk factors for cholera outbreaks (Table 3). In West and Southern Africa, the most commonly cited risk factor was heavy rainfall and flooding, which accounted for 33% and 39% of all the risk factor reports, respectively. In contrast, rainfall and flooding only accounted for 10% of reports in East Africa; a further 36% of reports identify a refugee or internally displaced persons setting as the primary risk factor. In Western Africa, a refugee setting accounted for only 5% of the total, and in Southern Africa, there were no outbreaks attributed to refugee settings. In West, Southern, and East Africa, water source contamina-
tion was the second most common risk factor reported, representing 32%, 30%, and 24% of the total, respectively. In Central Africa, water source contamination was the most common, accounting for 30% of the total, respectively. In South America and East Asia, the most commonly noted risk factor for cholera outbreaks was transmission associated with food, accounting for 32% in South America and 71% in East Asia. In 52% of the outbreak reports, no statement about risk factor was included by the author of the report.

Globally, the three most common risk factors were water source contamination (29%), rainfall and flooding (25%), and refugee settings (13%). In South America and East Asia, the most commonly noted risk factor for cholera outbreaks was transmission associated with food, accounting for 32% in South America and 71% in East Asia. In 52% of the outbreak reports, no statement about risk factor was included by the author of the report.

Of the 632 outbreak reports, 521 (82%) indicated the number of cases and 433 (69%) indicated the number of deaths. A total of 484,246 cases (median, 38,363; range, 19,180–114,444) and 19,631 deaths (median, 1,555; range, 483–3,700) were reported from 1995 to 2005. Africa accounted for 88% of the cumulative cases and deaths. The largest reported outbreak occurred in South Africa in 2000 with 103,320 cases.

The number of cases and distribution of reported outbreaks varied by sub-region (Figure 4). In general, the size of the reported outbreaks correlated with the number of reported outbreaks. Areas with greater frequency of outbreaks tended to be larger and uncontrolled. Countries that reported fewer outbreaks tended to have smaller outbreaks. All of the sub-Saharan African regions reported a high number of large outbreaks.

## DISCUSSION

Although ProMED data are limited in that it is a passive reporting system, it is subject to scrutiny by the academic, infectious disease, and public health communities and is often accompanied by notes on verification by the service’s moderator. Our data set is not a record of all cholera outbreaks and cases over the selected time period, but rather a compilation of outbreaks that were recognized by a government, the media, or an independent source and reported to
ProMED. While the sources for ProMED may not have the same access to sensitive data that national governments may report to the WHO, they do provide timely in-depth information about the specific location, size, and time period of outbreaks to the general public. Compilation of this data can aid in understanding the nature of reported cholera and the development of models to estimate regional disease burden and targeted modalities for control. Of the 131 outbreak reports posted by the WHO between 1996 and 2005, 92% were also posted on ProMED in either their exact form (101 of 131) or by another source (21 of 131).

A disproportionate number of cholera outbreaks were reported in Africa. In addition, these outbreaks tended to be much larger than those in other areas, suggesting that they are poorly controlled. While cholera is known to be endemic on the Asian sub-continent, there was a paucity of reports from that region. It is difficult to ascertain if the incidence of outbreaks in Africa truly exceeds that of other regions or if it reflects under-reporting in South Asia where cholera is known to be endemic. Outbreaks in Africa may be more likely reported in areas where there is international interest and less commercial consequences.

In Africa, the highest concentration of multiple outbreaks was found along the Democratic Republic of Congo and Uganda border. This may relate to the continued humanitarian and media interest in this region after the massive refugee crisis and cholera outbreak in Goma in 1994 from the Rwandan civil unrest. The concentration of outbreaks may also relate to the vigilance of health personnel and observations by non-governmental organizations. Alternatively, it may represent an area of endemicity or persistence, which is exacerbated by poor living conditions and may be directly related to the scale and magnitude of the continued refugee crises in many parts of the region.

Overall, the largest identified risk factor for cholera outbreaks is a contaminated water source. However, the dominant risk factor varies among sub-regions. In a more developed region, the risk factor is more likely to relate to seafood or vegetables that have not been properly washed or cooked rather than a lack of water and proper sanitation. Risk factors were grouped based on broad categories according to what was stated in the report. We recognize that this is a limitation and acknowledge that there is a need for a clearer definition of risk factor parameters.

Climate factors can potentially explain seasonal and annual variability in outbreak reports. While we observed some seasonality for certain regions (data not shown), there have been

![Figure 3](image-url)  
**Figure 3.** Total number of cases and deaths by year (1995–2005).

![Figure 4](image-url)  
**Figure 4.** Distribution of outbreak size per sub-region as indicated by number of cases per outbreak. Number of outbreaks (n) per region is indicated with the median, 25th and 75th percentiles (box), 5th and 95th percentiles (whiskers), and outliers (circles).

<table>
<thead>
<tr>
<th>Sub-region</th>
<th>Central America</th>
<th>South America</th>
<th>Eastern Europe</th>
<th>North Africa</th>
<th>West Africa</th>
<th>Central Africa</th>
<th>East Africa</th>
<th>South Africa</th>
<th>West Asia</th>
<th>South Asia</th>
<th>East Asia</th>
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<th>Oceania</th>
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<td>3</td>
<td>9</td>
<td>3</td>
<td>67</td>
<td>27</td>
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<td>32</td>
<td>11</td>
<td>26</td>
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<tr>
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<td>3</td>
<td>1</td>
<td>19</td>
<td>8</td>
<td>6</td>
<td>17</td>
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<td>8</td>
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<td>Water source contam.</td>
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<td>18</td>
<td>12</td>
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<td>13</td>
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The extreme weather conditions of higher temperature, increased rainfall, and consequent flooding may explain the global increase in the number of reported outbreaks from 1997 through 1999.

We have alluded to several limitations on the use of reported data through ProMED. Besides the inherent limitations of passive reporting systems, access to media services and internet is likely to be limited in areas prone to cholera. This, along with the exclusion of reports that did not meet our inclusion criteria, underestimates the burden of cholera. While not all reported outbreaks of clinically diagnosed cases may be cholera, we suspect that misdiagnosis is rare given the severity and distinct symptoms of this disease, especially among experienced health professionals.

The assessment of cholera burden is an iterative process that can be improved with better outbreak reporting that includes standardized case definitions, microbiologic sub-type information, better descriptions of populations and their risk factors, and discreet identification of time and place. We recommend that reporting systems such as ProMED begin to use a standard format for initial reports that include these and additional criteria to allow for future systematic analyses.

This review provides a better understanding of the sub-national distribution of reported cholera over the last 10 years representing a level of refinement of the geo-temporal distribution of a disease where refined epidemiologic data has traditionally been elusive. Subsequent analyses of risk factors can provide increased understanding of cholera disease burden and its distribution to help appreciate the use of novel public health interventions.

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