

Environmental Determinants of Cholera Outbreaks in Inland Africa: A Systematic Review of Main Transmission Foci and Propagation Routes

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Cholera is generally regarded as the prototypical waterborne and environmental disease. In Africa, available studies are scarce, and the relevance of this disease paradigm is questionable. Cholera outbreaks have been repeatedly reported far from the coasts: from 2009 through 2011, three-quarters of all cholera cases in Africa occurred in inland regions. Such outbreaks are either influenced by rainfall and subsequent floods or by drought- and water-induced stress. Their concurrence with global climatic events has also been observed. In lakes and rivers, aquatic reservoirs of *Vibrio cholerae* have been evocated. However, the role of these reservoirs in cholera epidemiology has not been established. Starting from inland cholera-endemic areas, epidemics burst and spread to various environments, including crowded slums and refugee camps. Human displacements constitute a major determinant of this spread. Further studies are urgently needed to better understand these complex dynamics, improve water and sanitation efforts, and eliminate cholera from Africa.

Keywords. cholera; *Vibrio cholerae*; Africa; epidemiology; environment; lakes; cities; seasons; reservoirs.

During the past decade, except for the current Haitian outbreak, which is linked to the importation of a cholera strain from Asia [1, 2], most cholera epidemics, cases, and deaths have been reported in sub-Saharan Africa [3–5]. In 2009, for instance, 98% of the 221 226 notified cases worldwide were from Africa [6]. Yet, most studies assessing the determinants of cholera outbreaks have been conducted in the Bay of Bengal estuaries, its traditional home, or in other coastal areas all over the world. They have revealed strong links between this prototypical waterborne disease, aquatic environments, and climate. Designated as the cholera paradigm by Colwell [7], these links have been assumed to be relevant worldwide.

Nevertheless in recent years, remarkable epidemics struck various African regions located far from the coast. For instance, in 2008–2009, Zimbabwe experienced the

largest cholera outbreak ever recorded in Africa, with >100 000 cases and 4000 deaths [8]. In 2010–2011, the Lake Chad Basin, a Sahelian region between Nigeria, Niger, Chad, and Cameroon, was also severely affected [9]. These examples stress the need to better characterize cholera outbreaks in noncoastal regions of Africa and their links with coastal cholera outbreaks. They also question the coastal origin of the recent cholera epidemics in Africa. Although many inland outbreaks have been described by specific reports, no thorough review has compiled these data and specifically addressed this problem. The present article aims more particularly at exploring the main environmental determinants of cholera epidemics in inland Africa.

MATERIALS AND METHODS

A systematic PubMed query was conducted using the terms [“cholera OR *Vibrio cholerae*”] AND [“Africa” OR the current or past names of all sub-Saharan African countries] between 1970 and September 2012. Given the extent of the issue, citations were selected for articles published in English or French, whose title or abstract addressed cholera or *Vibrio cholerae* infection outbreaks or epidemiology in Africa. Complementary

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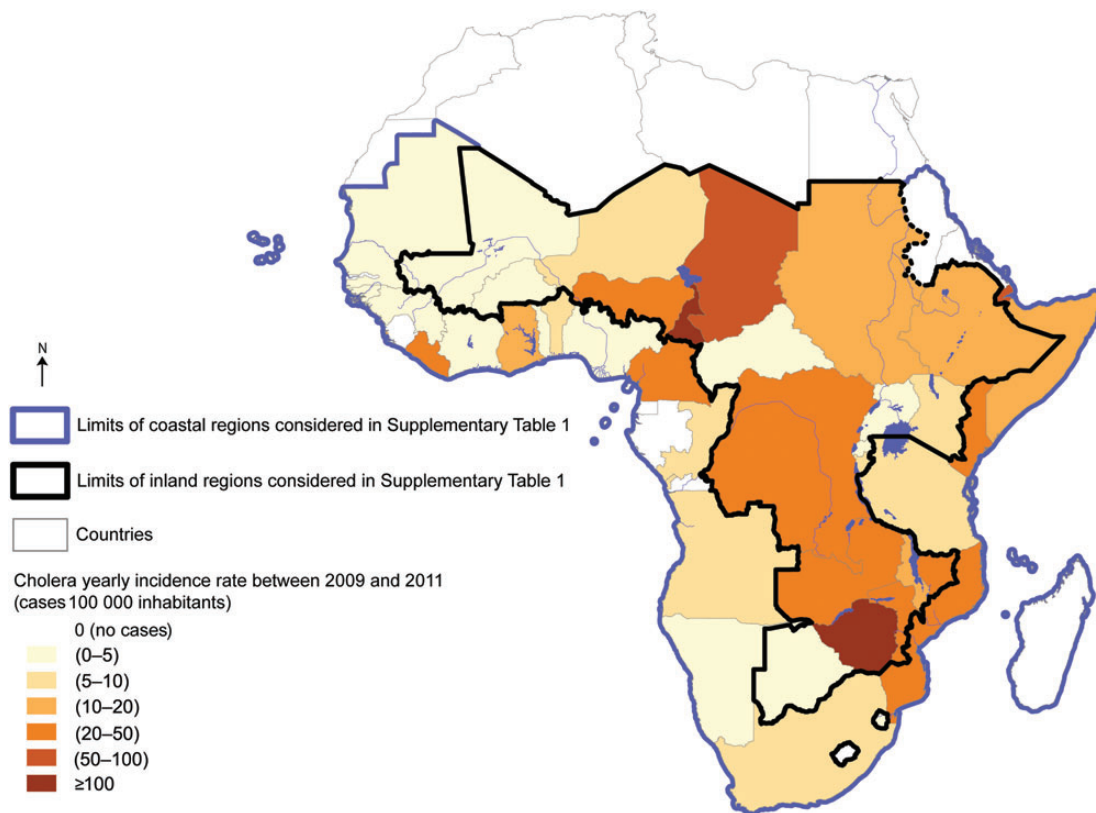


Figure 1. Cholera yearly incidence rates in inland and coastal Africa. Incidence rates were computed using data in [Supplementary Table 1](#). The bold line denotes the borderline between inland and coastal regions, according to available subnational cholera and population data. The dotted black line is used for Sudan because no precise cholera data at the state scale could be obtained. Nevertheless, various reports indicate that cases were almost exclusively located in southern Sudan, around Khartoum, and in Kordofan and Darfur states.

articles from nonindexed journals and reports from various agencies were additionally searched using Google, Google Scholar, and reference lists from key textbooks and other articles. ProMED-mail alerts were also investigated by searching the archives (available at: <http://www.promedmail.org>) for the term “cholera” and relevant country names. This screening process was performed independently by 2 of the authors (S. R. and B. S.). Selected full texts were assessed as eligible for inclusion if they gave information on cholera morbidity or outbreak processes. Data describing cholera outbreaks were extracted, including exact location and local environmental characteristics; year and season of beginning, peak, and ending; population affected; epidemic dynamics; suspected origin and underlying factors; local environmental isolation of *V. cholerae*; and genotyping of epidemic strains. In the present review, only reports relevant for countries having no access to the sea (defined as “inland countries”) and, if available, for regions of seaside countries located >100 km from the coast or from an estuary (defined as “inland regions”), were included ([Supplementary Figure 1](#)). Links between cholera and the environment in coastal African regions have been addressed in a distinct review [10].

To assess the relative importance of both coastal and inland regions in the overall cholera burden in Africa, cases reported to the World Health Organization (WHO) between 2009 and 2011 were analyzed ([Supplementary Table 1](#)). When morbidity and population data were available at subnational levels, countries with access to the sea were divided into 2 coastal and inland regions. Their respective cholera cases numbers and incidence rates were then calculated and mapped using Quantum GIS software (QGIS), version 1.7.3 (available at: <http://www.qgis.org/>), and ESRI shape files from the Map Library (available at: <http://www.maplibrary.org>; [Figure 2](#)). After aggregation of these regions and exclusion of North African countries (which have barely notified cholera cases for the past 2 decades), case numbers and yearly incidence rates were computed for both coastal and inland Africa.

RESULTS

Predominance of Cholera in Inland Africa

According to the yearly cholera global surveillance summaries of the WHO [11], one third of the 1.5 million cases reported in Africa between 2001–2010 were located in inland countries.

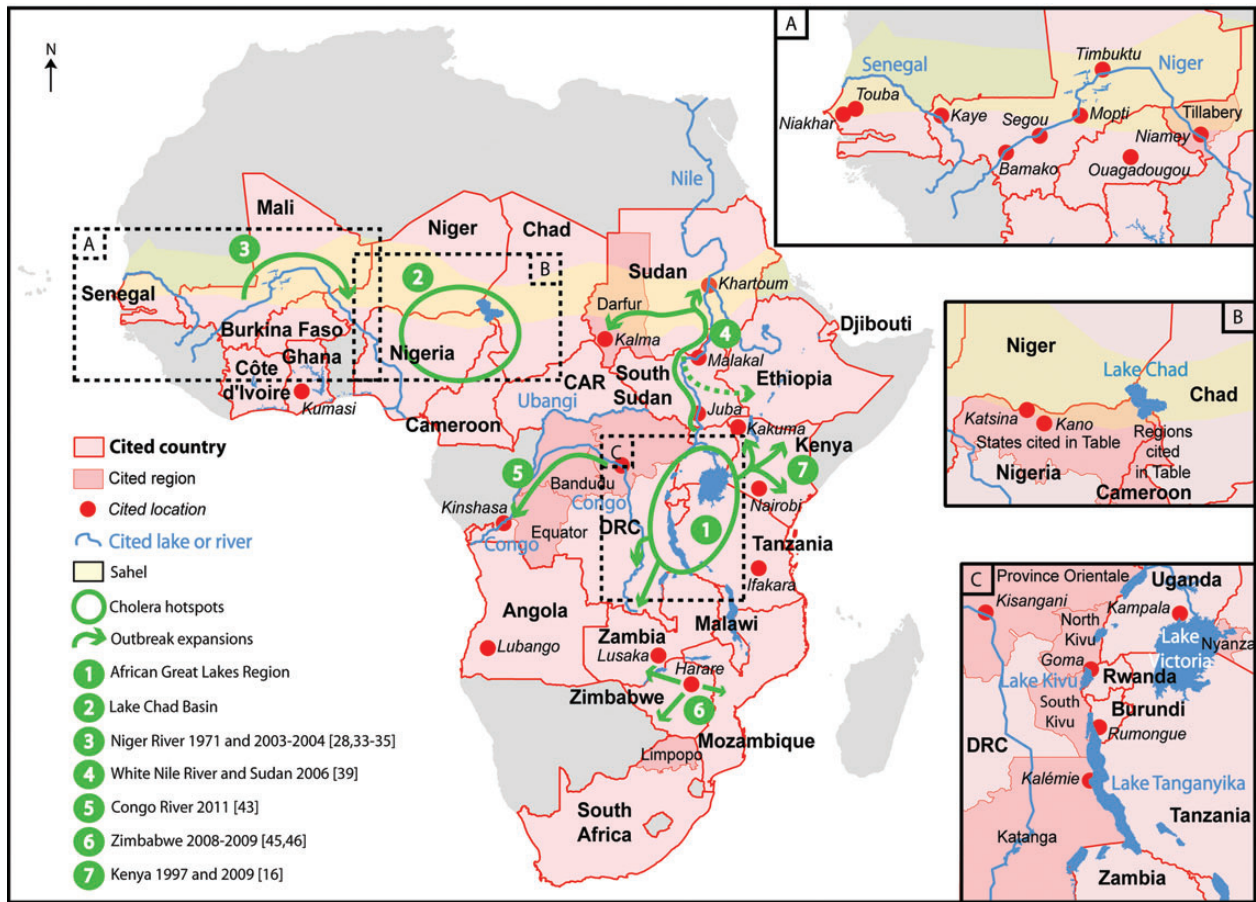


Figure 2. Places cited in the text, main cholera hotspots and outbreak expansions. Abbreviations: DRC, Democratic Republic of the Congo; CAR, Central African Republic

Furthermore, according to ProMED-mail [3, 12], a few national reports from the WHO [13–16], and a transborder epidemiological assessment in the Lake Chad Basin [9], many major outbreaks affecting countries having access to the sea actually occurred in their inland areas (Figure 2).

Thus, taking into account subnational morbidity and population data available for Nigeria, Cameroon, Democratic Republic of the Congo, Mozambique, Kenya, and Sudan, as well as national data for the other countries (Table 1, Figure 1, and Supplementary Table 1), it can be estimated that a minimum of 76% of all reported cholera cases in sub-Saharan Africa actually affected noncoastal regions in 2009–2011. During this period, the yearly incidence rates in inland and coastal Africa were 72.86 and 26.75 cases/100 000 inhabitants, respectively.

Geographical Determinants: The Role of Lakes and Rivers

For the past 2 decades, most cases reported in Africa have indeed clustered in 2 lakeside locations: the African Great Lakes Region

[17] and the Lake Chad Basin [9]. The African Great Lakes Region spreads along the Albertine Rift and comprises parts or totality of the Democratic Republic of the Congo (formerly Zaire), Uganda, Kenya, Rwanda, Burundi, and Tanzania. Sprinkled with lakes, this overpopulated and repeatedly war-torn area has hosted many refugee camps and concentrated many cholera cases. Since its likely importation from Tanzania in 1978, cholera has annually been encountered in eastern Democratic Republic of the Congo, especially along the shores of Lake Kivu and Lake Tanganyika. Exhibiting a meta-stable pattern, in which cholera stability on a regional scale originates from interactions between asynchronous local foci prone to extinction [17], this area has accounted for most of the 370 000 cases reported by the country during this period [11, 17]. Further south and north along the Rift, cholera has also repeatedly affected other lakeside regions, in Zambia [18, 19] and Ethiopia [20, 21]. Proximity to the lakes was a significant risk factor for cholera in several ecological studies conducted at various geographical scales in Kenya [22], Democratic Republic of the Congo [23, 24], and Rumonge, a

Table 1. Estimates of the Burden of Cholera in Inland and Coastal Regions of Sub-Saharan Africa During 2009–2011

Variable	Total Sub-Saharan Africa ^a	Inland Africa ^b	Coastal Africa ^b
Population in 2010 ^b	850 274 779	451 945 491	398 329 288
2009			
Reported cholera cases ^b	219 601	176 181 (80)	43 420 (20)
Estimated incidence rate ^c	25.83	38.98	10.90
2010			
Reported cholera cases ^b	110 480	87 403 (79)	23 077 (21)
Estimated incidence rate ^c	12.99	19.34	5.79
2011			
Reported cholera cases ^b	105 786	65 714 (62)	40 072 (38)
Estimated incidence rate ^c	12.44	14.54	10.06
2009–2011			
Reported cholera cases ^b	435 867	329 298 (76)	106 569 (24)
Estimated yearly incidence rate ^c	51.26	72.86	26.75

Data are no. or no. (%) of cases, unless otherwise indicated.

^a Morocco, Algeria, Tunisia, Libya, and Egypt were excluded from analysis.

^b For definitions and references, see [Supplementary Table 1](#).

^c Data are cases/100 000 inhabitants.

Burundian town on the shore of Lake Tanganyika [25]. On these lakesides, cities like Goma and Kampala have experienced particularly severe outbreaks. In 1994, during the weeks following the genocide in Rwanda, almost a million persons sprawled into the neighboring North Kivu province of Zaire [26]. In the huge refugee camps that burgeoned around Goma on the northern shore of Lake Kivu, *V. cholerae* infected virtually everyone and caused at least 50 000 cholera cases. Together with dysentery, it claimed almost 50 000 lives during July alone. With less intensity, cholera also struck Uganda's capital, Kampala, in 1997–1998. In only 4 months, this lakeside city counted >6000 cases scattered around most of its parishes [27]. On the Kenyan side of Lake Victoria, Nyanza Province has been repeatedly affected and appeared as the origin of important national outbreaks both in 1997 and 2009 [16].

The seventh cholera pandemic hit the Lake Chad Basin in mid-1971 [9] and was imported by patients traveling north from coastal Nigeria and west along the Sahelian belt. While the following 2 decades were marked by occasional flares in the region, there have been several thousand cases of cholera annually since the mid-1990s. Areas surrounding Lake Chad have thus become the most affected regions in its 4 bordering

countries (Figure 3). The situation recently worsened, with a severe outbreak affecting >100 000 people in the region during 2010–2011 [13, 14, 28–31].

Spread of cholera across the African continent has also benefited from human traffic along its main rivers, notably in Sahel. Following the Niger River downstream from Mopti, Mali, cholera struck Niger heavily in 1971, causing almost 10 000 cases in towns and fishing villages of the riverbanks [32]. In 2003–2004 and 2011, new outbreaks spread along the Niger River in Mali (in Bamako, Segou, Mopti, and Timbuktu) [33–35] and Niger (in Tillabery and Niamey provinces) [28]. And in 2005 cholera was also reported in the Senegal River valley in Mali (in Kayes). Further east in Sudan, traffic along the White Nile River obviously contributed to the spread of the 2006 cholera outbreak from the Juba area up to Malakal and Khartoum [36–39], before it moved west and reached Darfur by a passenger train [40]. The same phenomenon has recently been observed in the vast equatorial forest of Central Africa, along the Oubangui River in the Central African Republic, in 1997 [41], and along the Congo River in the Democratic Republic of the Congo. A cholera epidemic started in February 2011 in Kisangani, a major river port within Province Orientale. Descending the Congo River, cholera crossed the downstream provinces of Equateur and Bandundu and eventually traveled 2000 km to the megacity of Kinshasa in only 130 days. On its cruise, it affected >7000 people, including 10% in Kinshasa, and killed >300 individuals [42, 43]. Between 1996 and 2001, Kinshasa had previously been affected by a double-peaked epidemic involving >5000 notified cases and about 300 deaths [43]. In 2011, like a decade earlier, the most affected quarters of the capital were located along the Congo River and one of its tributaries [43, 44].

In 2008–2009, Zimbabwe was struck by a 100 000-case epidemic [8], whose dynamic did not appear to be associated with any lake or river. It originated in Harare and Chitungwiza, 2 urban centers that remained the most affected areas, and then spread to the other provinces and neighboring countries [45, 46]. In Harare, cases clustered in very poor and lowly elevated suburbs, such as areas where people from Chitungwiza arrive daily to work in adjacent informal markets [46, 47].

Seasonal and Climatic Determinants

As in many coastal regions, precipitation patterns have had an important influence on temporal patterns of cholera epidemics in Uganda [48], Zambia [18, 49, 50], and Malawi [51]. In Kinshasa, cases between December 1998 and March 2001 were significantly correlated with rainfalls, with a 7-week time lag [43]. Between 2002 and 2008 in eastern Democratic Republic of the Congo, the impact of rainfall on cholera appeared more profound as the distance from the equator increased [17, 24]. Yet, these seasonal patterns may reflect the seasonal variations of human exposure to contaminated water, as in temporary fishing settlements on the Congolese [17] and Zambian [18]

shores of Lake Tanganyika, and the seasonal variations of human movements, such as those occurring between these fishing camps and the markets of surrounding cities. With regard to the Lake Chad Basin, past observations and field studies conducted during the recent and major 2010 and 2011 epidemics suggest a correlation with the rainy season in this lakeside region, too [9, 29]. In the rest of Sahel, cholera seasonality appears to be complex. Whereas epidemics repeatedly struck drought- and famine-affected areas of Mali during the 1970s and in 1984–1986 [35, 52], the major outbreaks of the last 20 years mainly started during the rainy season [34, 35]. Cholera in Niger was also associated with severe droughts in 2004, but its resurgence in 2006 followed excessive rains [32]. In 2005, cholera affected the Ouagadougou area of Burkina Faso during the rainy season [53]. And while it usually affects Sokoto and other northern states of Nigeria during the rainy season [54], cholera was reported in Katsina at the end of the 1982 dry season in the context of acute water shortage [55] and hit Kano state at the end of several dry seasons, too [56]. Further east, in 2006, 30 000 people from the area that is now Sudan and South Sudan experienced a severe cholera outbreak that started during the dry season and extended throughout the year [57]. Floods have also favored extension of cholera outbreaks in both countries [58, 59]. Conversely, cholera struck Kakuma Camp in 2005 and 2009, despite the very dry climate of this northwestern region of Kenya [60, 61]. Finally, the 2008 outbreak in Zimbabwe was reported long before the beginning of the rainy season [62].

Cholera incidence fluctuations in inland Africa are also linked to interannual climate variability. In East and West Africa, rainfall levels are deeply influenced by El Niño–Southern Oscillation (ENSO) events, the periodic warming of surface waters across the central equatorial Pacific Ocean [63]. At the continental scale, the strong 1997–1998 ENSO event and its associated higher temperatures and flooding coincided with an increased number of outbreaks reported to ProMED [3]. Between 1978 and 2008 in the African Great Lakes Region, years with a large increase in cholera incidence significantly correlated with abnormally warm ENSO events [17]. In addition, cholera outbreaks over a 30-year period in the Lake Victoria Basin also seemed to coincide with peaks of high river flow during ENSO events [64]. Yet on the Kenyan side of the lake and on a finer time scale, the 1997 outbreak in Nyanza province actually started before the floods, and the 2008 outbreak began almost 1 year after the ENSO rains [65].

Human-Related Determinants

Apart from spatial and temporal determinants, several human-related factors have been associated with cholera transmission in inland Africa. Numerous outbreaks have affected slums of inland cities, such as Ouagadougou [53]; Kumasi, in Ghana [66]; Bauchi and other northern Nigerian urban centers [9];

Kinshasa [43]; Addis Ababa, in Ethiopia [67, 68]; Nairobi, in Kenya [69]; and Lusaka, in Zambia [70, 71]. Markets and other trading areas have been pointed out as possible sources in Kumasi [72], northern Central African Republic [41], Kinshasa [43], the Lubango area in Angola [73], Harare [46], and a refugee camp in Malawi [74]. Several such camps populated by refugees and internally displaced persons have been stricken [75], not only in Goma [26], Malawi [76, 77], and Zimbabwe [78] during the Mozambican civil war, but also in Kenya, in 2005 [60] and 2009 [61], and in Darfur, in 2006 [39]. Cholera has sometimes taken advantage of other social and geopolitical events, like the Touba Pilgrimage in Senegal in 2005 [79, 80], the economical collapse of Zimbabwe [45, 81], and conflicts in Rwanda [26] or Sudan [39]. The severity of outbreaks may sometimes have been exacerbated by impaired nutrition and immunity among affected populations, as suggested during the 1970s and 1980s Malian famines [52] or in the Goma camps [26]. Yet cholera transmission in these situations has mainly benefited from promiscuity, a significant risk factor reported in a rural Senegalese area in 1996 [82]; in Kumasi, between 1999 and 2005 [66, 72, 83]; in the Lake Chad Basin, between 2003 and 2010 [9]; or in Kinshasa, in 1998–1999 [43].

As suggested by the drought-associated epidemics in Sahel in the early 1970s and in 1984, when refugees had to crowd around limited water supplies [52], deprivation of clean water is another key factor of cholera transmission, which has been frequently incriminated in various report and in ecological, case-control, and microbiological studies (Supplementary Table 2). In Zimbabwe, for instance, a comparison between 2 outbreaks in 1992 suggested that access to a protected water supply and a population density per borehole were both important factors in explaining the spatiotemporal distribution of cholera cases [78]. More recently, in 2008, the outbreak in Chitungwiza was clearly enhanced by a breakdown in the water supply, which compelled people to rely on shallow wells for drinking water [45, 81]. Drinking from or bathing in lakes or rivers contaminated with *V. cholerae* have been associated with cholera transmission in several places, including Burundi [25, 84], Tanzania [85], and South Africa [86]. In this latter country, some people have been reported to prefer drinking fresh river water instead of water from safer sources [87].

Associated impaired sanitation has also been involved in numerous contexts (Supplementary Table 2). Cholera has repeatedly benefited from the scarcity of pit latrines in areas with very poor living conditions, such as slums and camps, locations where rocky volcanic soils make digging difficult, and regions where there is a cultural preference for open defecation. In the over crowded Goma camps, for instance, most refugees had to defecate in open spaces. And because overwhelmed relief organizations could only provide a mere liter of purified water to each person per day, cholera was related to the practice of drinking untreated water from subsequently contaminated ponds

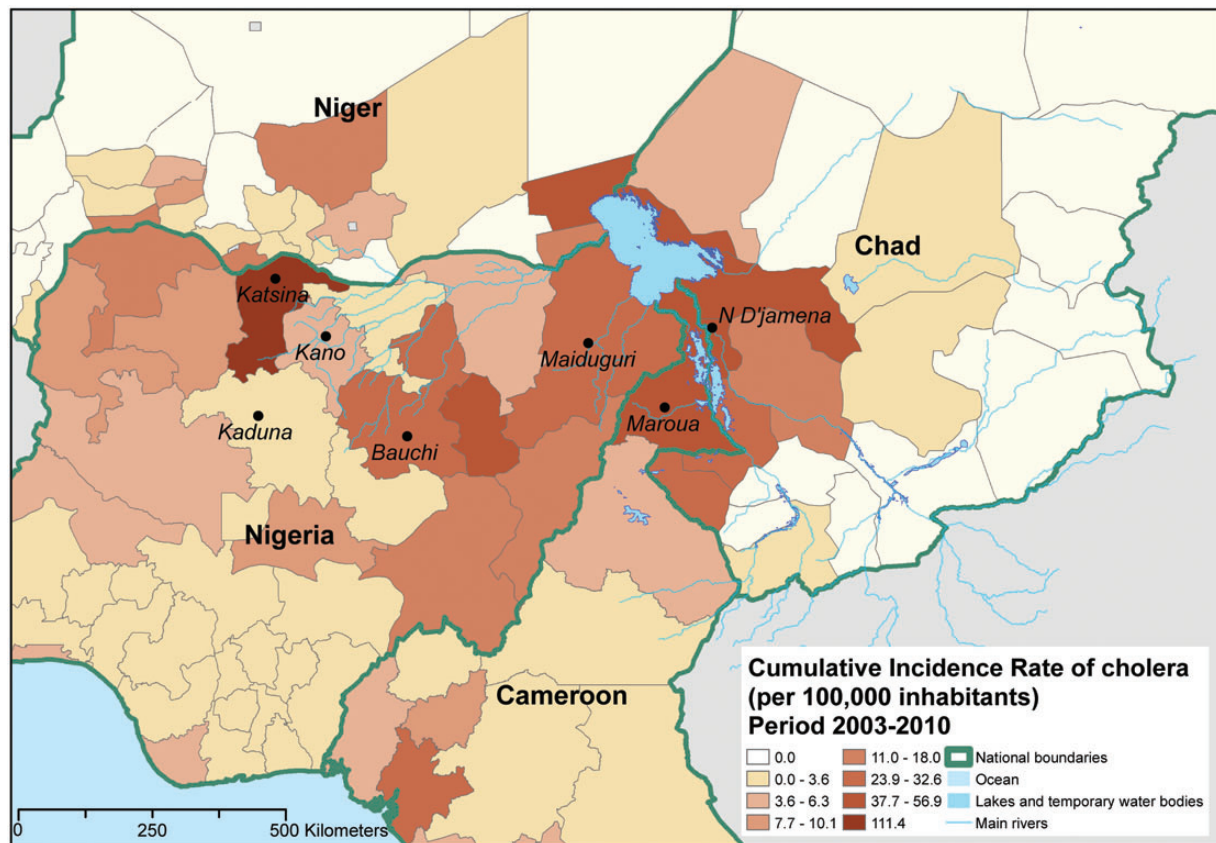


Figure 3. Incidence of cholera in countries of the Lake Chad Basin between 2003 and 2010.

and Lake Kivu [26, 88]. In addition to the lack of latrines [70], the cholera incidence in Lusaka was also statistically associated with insufficient drainage networks [50]. In Kumasi, it was significantly correlated with the concentration of and proximity to refusal dumps [66, 83]. Together, the frequently observed influence of rainfall levels may thus be related to latrine overflow and flushing of human waste, as proposed in urban areas like Kumasi [66], Juba [89], Lusaka [50], and Harare [47] or rural areas like southern Malawi [90, 91].

Cholera transmission in Africa has also been exacerbated by bad domestic storage conditions and lack of efficient treatment of water (Supplementary Table 2). Numerous epidemics have been related to unhygienic practices, including the lack of soap use after defecation and before meals and hand eating from common plates (Supplementary Table 2). Attendance at funeral feasts has been repeatedly described as risk factor, especially when individuals used bowel enemas to clean the body of cholera victims prior to preparing the meal as reported in Tanzania for example [92].

Various foods been associated with cholera transmission in Africa (Supplementary Table 2) and around the world [93]. Consumption of cooked but nonreheated leftover food was a

significant risk factor in several case-control studies. Conversely, cooking with acidic ingredients, such as lemon, tomato, or curled milk, seems protective (Supplementary Table 2). The impact of Ramadan is equivocal and barely studied: whereas collective meals with raw vegetables and fruits have been suspected to favor cholera transmission in Nigeria [56], fasting may limit the consumption of leftover food and the number of water sources accessed.

According to Mintz et al [93], direct person-to-person transmission of cholera is “not expected.” Except for limited documented outbreaks in a gold mine and several pediatric wards (Supplementary Table 2), this transmission route does not seem to have played a prominent role in the spread of cholera in Africa.

***V. cholerae*–Related Determinants and Environmental Reservoirs**

Whatever its route, transmission of cholera implies sufficient survival or multiplication of toxigenic *V. cholerae* outside the human gut, as reviewed elsewhere [93, 94]. In particular, vibrios proved able to grow in a few African foods, like millet gruel or peanut sauce (Supplementary Table 2). The role of at-risk lakes

and rivers has been explored by only a few environmental microbiological studies, and toxigenic *V. cholerae* has scarcely been isolated from water samples in inland African settings (Supplementary Table 2): rivers, canals, and a trough in South Africa [86, 87]; a well in Mali [52]; Lake Tanganyika, in Burundi [25]; a river in Tanzania [85]; and several previously identified but nonspecified foci in Sudan [95]. In South Africa, Mali, Burundi, and Tanzania the positive specimens were obtained only during epidemic periods; in Lake Tanganyika *V. cholerae* could not be isolated 2 months later; the time since the previous outbreak was not mentioned in the Sudanese study. Overall, a perennial presence of *V. cholerae* in inland African environments has therefore never been expressly confirmed so far.

Several putative environmental reservoirs of *V. cholerae* have been proposed [96], such as copepods (ie, ubiquitous microscopic crustaceans and main constituents of zooplankton), chironomids (ie, nonbiting midges abundant in freshwater habitats such as African lakes), and water hyacinths. But caution is required in interpreting these data. On the Congolese shores of Lake Tanganyika, the temporal correlation between cholera incidence and satellite-estimated concentration of chlorophyll *a*, a remote surrogate marker of copepod population, may only be a synchronous consequence of rainfall: a plankton bloom induced by an increase in terrestrial nutrients and a fecal contamination of lake waters induced by the overflow of latrines [17]. Despite interesting experiments, chironomid egg masses and flying adults have to date been found to harbor and carry only nonpathogenic strains of *V. cholerae* [97, 98], and the rough correspondence between the directions of dominant winds and cholera spread in Africa during 1970–1971 and 2005–2006 remains weak support for the iconoclastic hypothesis of anaeroplanktonic transport of *V. cholerae* [99]. A positive association between the number of cholera cases and the yearly water-hyacinth coverage has been exhibited only in Nyanza Province in the Kenyan section of Lake Victoria [65]. Finally, *V. cholerae* has been associated with *Acanthamoeba* in Sudanese samples [95], suggesting that this free-living amoebae may enhance the survival of vibrios, as previously described [96]. Yet these hypotheses have not been confirmed anywhere else in Africa.

Spread of Cholera Epidemics

Rather than emerging from such putative environmental reservoirs, several cholera epidemics in inland Africa have been historically described as the spread of distant epidemics, as illustrated by the initial course of the seventh pandemic in Africa during 1970–1971 [100, 101], when cholera traveled from Abidjan to Mopti and then to Niger, and from coastal Nigeria and Sahel to the Lake Chad Basin. Other diffusions of cholera in inland Africa more recently described in the literature are illustrated in Figure 2.

In several instances, molecular typing of strains indicated that outbreaks corresponded to the importation of new *V.*

cholerae strains. Ribotyping suggested that the 1997 epidemic in the Central African Republic corresponded to simultaneous cholera importation from Chad in the north and the Democratic Republic of the Congo in the south [41]. Similarly, multilocus variable tandem repeat analysis of Kenyan strains sampled in 2009–2010 identified 5 concurrent clonal complexes, which were not randomly distributed [102] and may have been imported from surrounding foci. Emergence of new atypical El Tor strains secreting the classical cholera toxin has been recently confirmed in Zambia [103] and Kenya [102, 104]. This may explain the severe epidemics that affected Zimbabwe in 2008–2009 [105] and the Lake Chad Basin in 2010 [9, 106]. Conversely, some other inland outbreaks have been characterized as locoregional resurgences of previous outbreaks. In the Lake Chad Basin, the 2010 epidemic emerged, after an interepidemic period of several months, from residual epicenters in northeastern Nigeria [9]. In the African Great Lakes Region between 2002 and 2008, all hotspots exhibited noncompletely synchronous lull periods, after which they were likely recolonized from other lakeside areas still undergoing cholera outbreaks [17].

DISCUSSION AND CONCLUSION

The major finding of our review is that most of the cholera cases recently recorded in Africa concerned inland areas, while maritime and estuarine locations represented only a minority of the total recorded cases. Moreover, these inland African cholera foci appear to a great extent to be unrelated to coastal affected areas. Such a development of cholera in regions distant from the coasts was previously notified in the Americas during the 1990s. Indeed, even if cholera mostly affected the coastal regions of Peru [107, 108], Brazil [109, 110], Ecuador [107, 111], or Mexico [112], epidemics also deeply struck inland in areas such as Bolivia, the Peruvian Amazon basin [107], northern parts of Argentina [113], and central Mexico [112]. Yet, unlike in Africa, cholera did not take root on this continent. In Asia, it has also recurrently attacked inland countries, such as Nepal and Afghanistan [11].

In inland Africa, the cholera distribution exhibits an important spatial heterogeneity. It particularly affects the African Great Lakes Region and the Lake Chad Basin, 2 hotspots that have notified cases every year during the past decade. Its spread generally follows natural communication routes, such as the Niger, the Congo, and the White Nile rivers, as well as major roads or railways [23, 101]. Currently, only a few inland cholera epidemics seemed to originate in coastal areas, and such inward diffusions have rarely been reported, even in Cameroon and Nigeria, where cholera regularly affects both coastal and Lake Chad Basin areas [9]. Conversely, numerous outbreaks in the Lake Chad Basin and the African Great Lakes Region obviously emerged locally before spreading within the continent.

Despite the remoteness from potential coastal and estuarine environmental reservoirs, cholera outbreaks in inland Africa frequently concur with the rainy season [17, 24], a phenomenon that was also observed at the worldwide scale [114]. In addition to the seasonal variability in cholera incidence, our review shows that interannual variations also occur in inland Africa and have partly been correlated with climate variability, being sometimes exacerbated by ENSO-related floods and severe droughts. By analogy with South Asian estuaries, cholera flares in lakeside African regions during the rainy season have been proposed as the consequence of plankton blooms induced by the increase in levels of terrestrial nutrients. Yet they could instead reflect the fecal pollution of shallow wells and surface waters induced by the overflow of latrines and the washing of waste. Conversely, epidemics during the dry season may be enhanced by scarce and easily contaminated water sources and by prolonged storage of domestic water in unsafe conditions.

Overall, cholera in inland Africa appears to be a highly dynamic process in which the strains probably move from one area to another, through a fecal-oral route, following trade and human population displacements. Unfortunately, very few studies have genotyped and compared *V. cholerae* strains to confirm this hypothesis on the basis of epidemiological observations. Similarly, very few environmental microbiological studies have addressed the potential role of perennial aquatic reservoirs of *V. cholerae* in inland Africa. Consequently, the source of outbreak recurrences in inland Africa is still debatable. In accordance with the cholera paradigm, they could be due to the persistence of toxigenic *V. cholerae* strains in some lakes' ecosystems. More likely, they may be due to asynchronous local outbreaks circulating between neighboring areas, as described in the African Great Lakes Region [17].

In conclusion, inland cholera is emerging as a relevant and major epidemiological entity in Africa. Proximity to possible coastal environmental reservoirs appears less important than other environmental determinants, such as proximity to lakes, as well as social determinants, like population density and movements and access to safe water and sanitation. Although inland cholera represents most of the cases currently reported in Africa, this fact is rather unrecognized. Thorough dynamic reports of outbreaks; ecological studies of water bodies; systematic collecting, genotyping, and comparison of environmental and clinical strains; as well as social and economical studies should be implemented. Their achievement could help direct efforts in surveillance, prevention, and control to reservoirs of *V. cholerae* or to population-movement-associated facilities in order to get rid of this persisting scourge.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (<http://jid.oxfordjournals.org/>). Supplementary materials consist of

data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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