SUPPLEMENT ARTICLE

Cholera in Coastal Africa: A Systematic Review of Its Heterogeneous Environmental Determinants

Stanislas Rebaudet,[1] Bertrand Sudre,[2,3] Benoît Faucher,[1] and Renaud Piarroux[1]

[1]Aix-Marseille University, UMR MD 3, Marseilles 13005, France, [2]European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden; and [3]University of Franche-Comté, UMR 6249 Chrono-environment, Besançon, France

According to the "cholera paradigm," epidemiology of this prototypical waterborne disease is considered to be driven directly by climate-induced variations in coastal aquatic reservoirs of *Vibrio cholerae*. This systematic review on environmental determinants of cholera in coastal Africa shows that instead coastal epidemics constitute a minor part of the continental cholera burden. Most of coastal cholera foci are located near estuaries, lagoons, mangrove forests, and on islands. Yet outbreaks often originate in coastal cities, where cholera is more likely to be imported from distant areas. Cholera outbreaks also may intensify in densely populated slum quarters before spreading to adjacent regions. Frequent seasonality of cholera incidence appears driven by the rainfall-induced contamination of unprotected water sources through latrine overflow and sewage, as well as by the periodicity of human activities like fishing or traveling. Lulls in transmission periods of several years are repeatedly recorded even in high-risk coastal areas. To date, environmental studies have failed to demonstrate a perennial aquatic reservoir of toxigenic *V. cholerae* around the continent. Finally, applicability of the cholera paradigm therefore appears questionable in Africa, although available data remain limited. Thorough surveys with microbiological analyses of water samples and prospective genotyping of environmental and clinical strains of *V. cholerae* are needed to understand determinants of cholera in coastal Africa and better target prevention and control measures.

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

Every year, cholera affects several hundred thousand people globally, with a case fatality rate over 2% [1]. Africa has reported most cases during the current seventh cholera pandemic. Yet the understanding of cholera epidemiology in Africa and notably in its coastal countries still heavily relies on findings from studies performed in Asia and especially around the Bay of Bengal, cholera's historical place of origin. There, autochthonous pathogenic *Vibrio cholerae* have been isolated in the brackish waters of certain estuaries but also thrive in coastal seawaters and tolerate freshwater in rivers, canals, ponds, or lakes, if saline levels are compensated by warmth and organic nutrients [2, 3]. In this aquatic phase, *V. cholerae* can be found as free swimming bacilli or attached to various surfaces as biofilm. In unfavorable environmental conditions, several studies have suggested that *Vibrio* spp could enter a viable but nonculturablecoccoid state and survive during interepidemic periods with intact pathogenic potential [2, 4, 5].

V. cholerae has been associated with numerous environmental components of the marine food chain [6, 7]: cyanobacteria; phytoplankton; plants; free-living amoebae; crustaceans such as copepods (main microscopic and ubiquitous constituents of zooplankton) or blue crabs, whose chitin may feed chitinase-equipped *Vibrio* [8, 9]; bivalves; gut of certain fish, dolphins or aquatic birds; and aquatic sediments. Among these putative reservoirs, copepods remain one of the most demonstrated importance for pathogenic *V. cholerae* O1 and O139

Correspondence: Stanislas Rebaudet, Laboratoire de Parasitologie-Mycologie, Hôpital de la Timone - Assistance Publique-Hôpitaux de Marseille, 264 rue Saint Pierre, 13385 Marseille cedex 05 (stanreb@yahoo.com).

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strains [7]. Each copepod may carry up to 10^4 *V. cholerae*, approaching the infectious dose in susceptible individuals [2, 10]. Along the Bay of Bengal, significant associations have been established between cholera cases and both copepod counts in water samples [11] and phytoplankton blooms directly measured or indirectly estimated by remote satellite sensing of chlorophyll—a concentration [12]. These blooms precede copepod production [2], and their driving by sea surface temperature (SST) or rainfall-induced river discharges of terrestrial nutrients [2, 13] has thus been considered as the source of the frequently observed seasonal patterns of cholera incidence [2, 14, 15]. Cholera incidence in Bangladesh has been correlated with various climatic variables such as rainfall, river discharge, sea level, or SST [11, 12, 16, 17] and SST interannual variability driven by El Niño-Southern Oscillation (ENSO) events [2, 18]. First proposed almost 3 decades ago [19], these relations between this prototypical water-borne disease, the aquatic environment and climate parameters have been called the "cholera paradigm" by Colwell [2, 3].

Apart from Latin America in 1991 through 1993, and again in 2010 and 2011, and Asia in 1994 (because of *Vibrio cholerae* O139), sub-Saharan Africa has been the most affected region with regard to cholera over the past 2 decades [1, 20, 21]. Between 2002 and 2011, Africa reported over two-thirds of the 2.2 million worldwide cases. Along African coasts, several areas have suffered from recurrent cholera outbreaks, such as the estuarine cities of Bissau in Guinea-Bissau, Calabar in Nigeria, Douala in Cameroon, Beira in Mozambique, or Dar es Salam in Tanzania. But unlike in the Bay of Bengal, no comprehensive overview of cholera transmission dynamic has ever been proposed for these coastal African hotspots. The present review thus aims at searching for evidence supporting environmental cholera determinants in coastal Africa and at assessing the degree to which this evidence fits the cholera paradigm established for the Bay of Bengal.

MATERIALS AND METHODS

A systematic Pubmed query was conducted using the terms "cholera OR *Vibrio*" AND ("Africa" OR the current or past names of all sub-Saharan African countries) between 1970 and September 2012. Retrieved citations were selected for articles published in English or French, whose title or abstract addressed cholera outbreaks or epidemiology in Africa or *Vibrio* detection in the environment (Supplementary Figure 1). Other articles from nonindexed journals and reports from several agencies were searched using Google, Google Scholar, and reference lists from key textbooks and searched articles (Supplementary Figure 1). ProMED-mail alerts were also investigated using the website's (www.promedmail.org) search archives function with the term "cholera" and the country names. Selected full texts were assessed as eligible provided that 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 outbreak start, peak, and end; population affected; epidemic dynamics; suspected origin and/or underlying risk factors; local environmental isolation of *V. cholerae* and other *Vibrio* species; and genotyping of epidemic strains. In this review, only reports relevant for countries having access to the sea (defined as "coastal countries") and, if available, for regions of seaside countries located on the coast or along an estuary (defined as "coastal regions") were included (Supplementary Figure 1). Links between cholera and environment in inland African countries and inland regions of seaside countries have been addressed in a different review [22].

RESULTS

Cholera Burden in Coastal Africa

Nearly three-quarters of the 1.5 million cholera cases reported in Africa during the past 10 years were located in countries with access to the sea [1] (Table 1). Nevertheless, most of the major outbreaks affecting countries like Nigeria, Cameroon, Democratic Republic of Congo, Kenya, or Sudan actually occurred in their inland part (locations cited in the text are mapped in Figure 2). According to the available subnational data, it has thus been estimated in a separate review dedicated to inland Africa [22] that only less than one-quarter of all cholera cases reported by Sub-Saharan Africa in 2009–2011 actually affected its coastal regions.

Cholera in Estuaries, Lagoons, and Mangrove Areas

Like in the Bay of Bengal, numerous cholera foci in Africa have been located in estuarine areas. For instance, in Guinea-Bissau, cholera epidemics recorded during the past 20 years mainly affected the capital Bissau and the adjacent Biombo region, 2 areas bordering estuaries [43]. In the neighboring Guinea, cholera between 2003 and 2008 frequently struck Kamsar, a city located on the Rio Nunez estuary [23]. In Sierra Leone, Freetown, the capital built at the mouth of a vast estuary, has been among the mostly affected districts of the country [44]. In Nigeria, although most cases have been notified in the Lake Chad Basin and other northern states [45, 46], cholera also has repeatedly stricken coastal southern areas like the estuarine city of Calabar, in the Southeast corner of the country [47]. Similarly in Cameroon, cholera has regularly affected the maritime regions that notified 37% of the 22 762 national cases in 2011, especially around Douala, a port city built on the swampy plain of the Wouri delta [45, 48]. In Mozambique on the east coast of the continent, cholera has recurrently stricken estuarine cities like Maputo, Beira, or Quelimane. In 1997–1998, for instance, a major outbreak of >50 000 cases originated in Maputo City before spreading to Beira City, on the Pungwe River [32, 33].

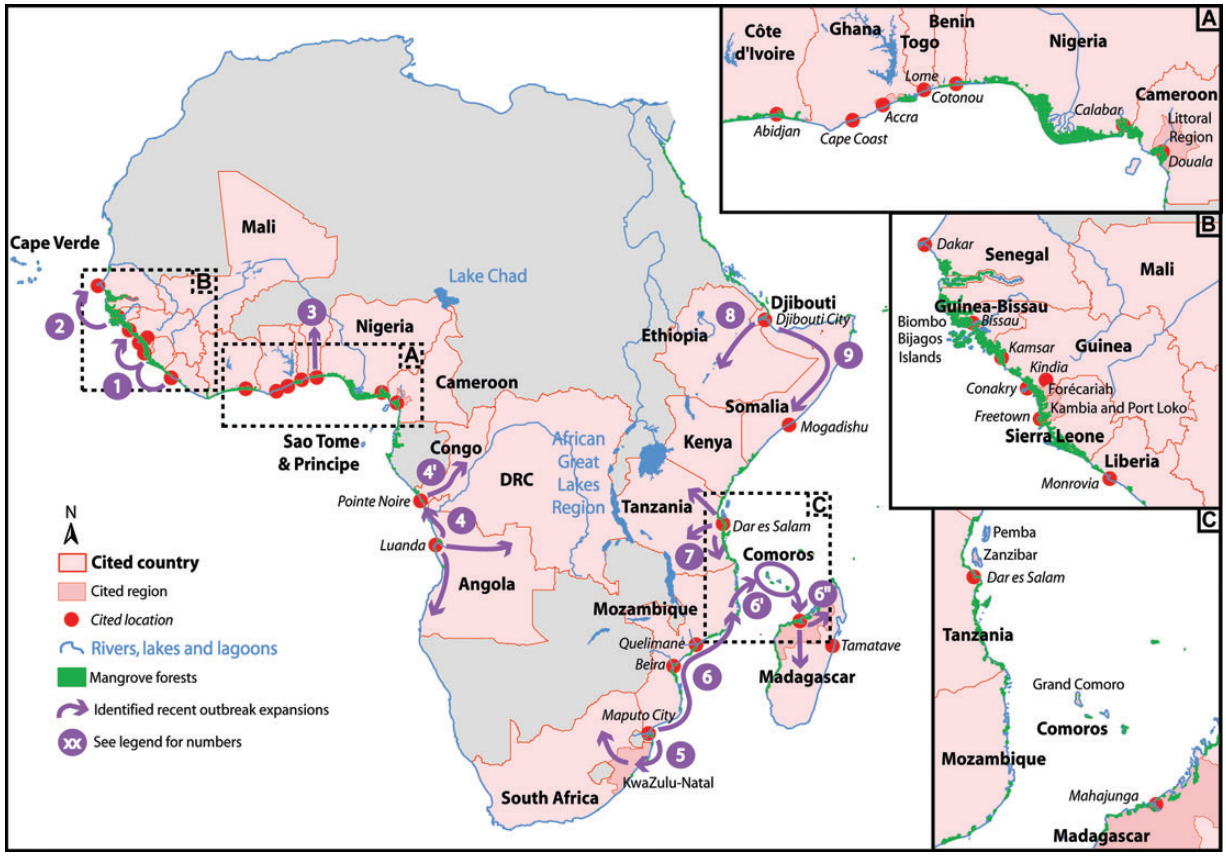

Figure 1. Cholera in coastal Africa. Places cited in the text and identified outbreaks expansions. (DRC, Democratic Republic of the Congo). Global distribution of Mangroves (V3.0, 1997) compiled by UNEP World Conservation Monitoring Centre (UNEP-WCMC) in collaboration with the International Society for Mangrove Ecosystems (ISME). Available at: www.unep-wcmc.org. Information on outbreak expansions (numbers on figure): 1: in 1994, 2003–2007 and 2012, transboundary epidemics from Liberia (uncertain for 2012) and Sierra Leone to Guinea [23–25]. 2: in 1994–1995, from Guinea-Bissau to Senegal [26]. Genetically confirmed (see Table 2). 3: in 1991, from Cotonou to northern Benin [27]. 4: in 2006–2007, from Luanda to whole Angola and probably Congo [28, 29]. 4′: in 2006–2007, from Pointe-Noire (Congo) to Brazzaville [30]. 5: in 1980–1981 and 1997, from Mozambique to KwaZulu-Natal and the rest of South Africa [31]. 6: in 1997, from Maputo to Beira and the rest of Mozambique [32, 33]. 6′: in 1997, from Mozambique to Comoros [34, 35]. 6″: in 1999, from Comoros to Mahajunga and the rest of Madagascar [36–38]. Genetically confirmed (see Table 2). 7: in 1997, from Dar es Salam to the rest of Tanzania [39]. 8: in 1993 and 1998, from Djibouti to Ethiopia [40]. 9: in 1994 and 1999, from Djibouti to Somalia [41, 42].

Besides estuaries, cholera has repeatedly affected lagoon areas like Abidjan in Côte d'Ivoire. Between 2001 and 2005, 60% of the 11 874 Ivorian cases were reported from this 6-million-inhabitant port city built on either side of the brackish Ebrié lagoon [49, 50]. In Benin, the 1991 outbreak was reported to originate close to the lagoonal Lake Nokoué before spreading northward from ponds and rivers to wells and cisterns [27]. Located on its southern shores, the capital Cotonou and its surroundings recorded over half of national cases in 2008 [51], and over one-third in 2011 [52].

Remarkably, almost all these cholera-affected areas are lowlands forested with more or less saline mangrove swamps (Figure 2). They often form complex networks of channels and islets with important fishing-related activities and population movements, as observed between Liberia and Guinea-Bissau. Hence, all cholera epidemics in Guinea except in 1994 [25] have started in such ecosystems in Forecariah or Boke prefectures close to the Sierra Leone and Guinea-Bissau borders, respectively [23, 53]. Epidemics have affected mainly these mangrove lowland areas, especially Conakry, the 2-million-inhabitant capital that lies on a peninsula, and they have shown a limited inland spread. During late 2011 and early 2012, an important outbreak emerged in Kambia and Port Loko, 2 coastal districts of Sierra Leone, before spreading through fishing activities northward across the Guinean border to the Forecariah Prefecture, then Conakry, and southward to the capital Freetown [24, 54, 55].

Cholera on Islands

Cholera outbreaks, often related to fishing activities, have also repeatedly affected wider groups of islands such as the Bijagos Islands in Guinea-Bissau [43, 56] or the Tanzanian

Table 1. Cholera Cases Notified by African Coastal Countries

Coastal country[a]	Total cases[b] 1970–2011	Total cases[b] 2002–2011	Main location of cholera burden	Environment type in coastal cholera foci
Algeria	12 729	0		
Angola	182 875	101 503	Coastal > inland	Urban
Benin	28 835	4983	Coastal > inland	Lagoonal, urban
Cameroon	72 551	46 053	Inland > coastal	Estuarine, urban
Cape Verde	14 144	0		
Comoros	17 866	3183	Coastal	Insular
Congo	17 385	9010	Coastal > inland	Urban
Côte d'Ivoire	23 389	7093	Coastal > inland	Lagoonal, urban
Democratic Republic of the Congo	391 524	217 569	Inland	
Djibouti	19 553	3384	Coastal	Urban
Egypt				
Equatorial Guinea	6962	6450		
Eritrea	120	120		
Gabon	649	637		
Gambia	252	227		
Ghana	128 525	24 510	Coastal > inland	Urban
Guinea	62 635	17 750	Coastal > inland	Estuarine, insular, urban
Guinea-Bissau	91 609	40 916	Coastal	Estuarine, insular, urban
Kenya	99 022	21 831	Inland > coastal	
Liberia	84 999	55 454	Coastal and inland	
Libya				
Madagascar	46 531	32	Coastal and inland	Insular, urban
Mauritania	17 765	4320		
Mauritius	0	0		
Mayotte	12	0		
Morocco	63	0		
Mozambique	315 295	106 842	Coastal > inland	Estuarine, urban
Namibia	3854	3854		
Nigeria	264 119	105 648	Inland > coastal	Estuarine, urban
Sao Tome and Principe	7861	3101		
Senegal	69 841	38 590	Coastal > inland	Urban
Seychelles	178	178		
Sierra Leone	38 343	5360	Coastal	
Somalia	255 788	142 563	Coastal and inland	Urban, refugee camps
South Africa	186 462	34 602	Coastal and inland	
Sudan + South Sudan	80 634	75 315	Inland	
Togo	15 820	4956		
Tunisia	60	0		
United Republic of Tanzania	204 569	57 822	Coastal and inland	Estuarine, urban, island
Total cases in Africa	3 589 002	1 568 701		
Total cases in coastal countries	2 762 819	1 143 856		
(%)	(77%)	(73%)		

Abbreviation: ND, no data.

[a] Any African country with access to the sea.

[b] Notification data extracted from the WHO yearly cholera overviews [1].

archipelago of Zanzibar [57]. African islands more distant from the continent have intermittently been affected. Since 1971, Sao Tome and Principe has experienced only 2 major epidemics: in 1989–1990 and 2005–2006 with 4 757 and 2 892 reported cases, respectively [1, 58]. Cape Verde had remained cholera-free since 1976, until a major epidemic occurred in late 1994. On this archipelago where the volcanic soil makes water supply inadequate and latrine construction difficult, the

epidemic produced nearly 13 000 cases in 1995 [1, 59]. Similarly, a severe outbreak hit the volcanic Comoros archipelago in 1998 after a 2-decades lull period. The highest attack rates were observed in lowland areas of Grand Comoro, a rocky island with chronic and severe water scarceness, where many people still have to rely on unprotected collective wells or watering places close to the sea and filled with brackish water [34, 35]. From Comoros, cholera crossed over to Madagascar where it landed in March 1999 in Mahajunga, an estuarine and port city with close commercial exchange with Comoros; from there it spread throughout the Red Island within a few months [36, 37].

Cholera in Coastal Cities

Whether estuarine, lagoonal, insular, or not (like Accra and Cape Coast in Ghana [60], Pointe Noire in Congo [30], or Luanda in Angola [28, 29, 61]), main cholera transmission foci along African coasts have often been localized to densely populated urban settings. More precisely, cases within these coastal cities have been commonly clustered in slum quarters with limited safe water access and low sanitation standards, like in the ancient inner-city neighborhoods of Calabar in 1989 [47], in Luanda in 2006 [61, 62], or in Dar es Salam in 2006 and 2008 [63]. In Douala in 2004, cholera spared quarters well connected to the water distribution network and mostly struck those relying on traditional shallow and poorly protected wells [64]. In Quelimane, Mozambique, during the civil war in the early 1990s, the outbreak mostly affected quarters overcrowded with recently arrived displaced people [65, 66]. In chronically war-torn Somalia, suspected cholera outbreaks have also recurrently affected congested displaced persons camps, especially in the Mogadishu area. The country declared over 41 000 cases in 2007, nearly 78 000 in 2011, and 11 478 cases had been recorded in 2012 by late April [1, 67, 68].

Associated lowland location and particular hydroecological characteristics have been pointed out in many of these highly affected overcrowded quarters. Affected areas of Lome [69], Douala [64, 70, 71], Djibouti [72–74], Beira [75], and Tamatave [76] have all been situated in floodable areas prone to contamination of surface waters, unprotected wells, or shallow boreholes. In Conakry in 2007 [23, 77], in Abidjan during the 1996 outbreak [78], or in Cotonou in 2008 [51], cholera mostly affected areas neighboring inlets, backwaters, or lagoons. A high and sometimes brackish groundwater table feeding the wells and marshes was identified in several high-risk urban neighborhoods like Bandin in Bissau [79], Bépanda in Douala [70, 71], in Beira [75], or in Quelimane [65, 66].

Overall, certain African coastal cities, especially ports of estuarine or lagoonal locations, may thus constitute favorable repositories and amplifiers for cholera. Large population movements—by sea, road, rail, or air—can favor cholera importation. The combination of factors such as high human density, lack of adequate safe water supplies due to urban expansion, and vulnerability of surface and ground water resources to fecal contamination can favor onset and propagation of outbreaks. These outbreaks may subsequently spread to surrounding regions and countries.

Cholera Spreading from Coastal Urban Foci

All documented cholera pandemics have spread inland into the African continent from its coastal belt, sometimes through identified importation events [80–83]. Notably, the current Seventh Pandemic (1961-) first reached Guinea in August 1970 probably through a flight coming from Crimea [83]. Spreading southeast along the coast, cholera arrived in Ghana a few months later possibly with a Togolese person coming from Conakry who collapsed in the transit area of the Accra airport, and with the corpse of a Ghanaian person who died from cholera while fishing in Togo, Liberia, and Guinea [84].

Since then, numerous inward and cross-border epidemics have been identified that followed terrestrial, maritime, and aerial routes from coastal urban transmission foci (Figure 2). Often suspected by epidemiology but rarely confirmed by biology, some epidemic routes have been traced by molecular comparison of *V. cholerae* strains (Table 2), like from Guinea-Bissau to Senegal in 1995 [26], or from Comoros to Madagascar in 1999 [36]. Similarly, genetic comparisons of cholera strains from Africa and different countries worldwide [85–88] have demonstrated several waves of cholera importation into Africa (Table 2). In recent years, epidemics in coastal African countries all proved to be caused by new and atypical strains of *V. cholerae* El Tor, secreting the classical toxin, which obviously emerged in the early 1990s in the Bay of Bengal [95] (Table 2).

Seasonality of Cholera in Coastal Africa

Like in Asia, influence of the rainy season on cholera epidemics has been repeatedly suggested by observations, temporal correlations, or time-series analyses along West, East, and Austral African coasts. For example, in Conakry, the earlier the first cases recorded within the rainy season, the larger the epidemics that followed [77]. Increased spread of cholera during the rainy season was also observed in Guinea-Bissau [43]; in Sierra Leone, and Liberia [44, 100, 101]; in Côte d'Ivoire [49]; in Angola [61, 102]; in KwaZulu-Natal, a South African province [103]; on the Mozambican coast [32, 65, 66, 104]; in the Tanzanian archipelago of Zanzibar and Pemba [57, 105]; and in Somalia [106]. Conversely, some other cholera epidemics have emerged during the dry season, as observed in Guinea in 1986 [53], 2007 [23], and 2012 [24], in Benin in 1991 [27], in Côte d'Ivoire in 2001, 2003, and 2004 [49], in Calabar in 1989, concomitantly with an increase of estuary's salinity [47], in Grand Comoro Island in 1998 [34, 35], or in Madagascar during the first phase of the 1999 epidemic [37]. In Douala, outbreaks usually start during the dry season [71] and may recede with the onset of

Table 2. Genetic comparisons of *Vibrio cholerae* strains sampled in Africa

Sampling country (year)	Strains' origins[a] (no.)	Genotyping method	Conclusions	References
Guinea-Bissau (1987)	C (5)	Ribotyping	Distinct origin for the two consecutive epidemics	[89]
Guinea-Bissau (1994–1995)	C (14)			
Senegal (1978; 1988)	C (2)	Ribotyping	The last Senegalese epidemic originated in Guinea-Bissau	[26]
Senegal (1995–1996)	C & E (117)			
Guinea-Bissau (1994)	C (7)			
Comoros (1998–1999)	C (N/A)	Ribotyping	Epidemic spread from Comoros to Madagascar	[36]
Madagascar (1999)	C (N/A)			
South Africa (1980)	C (15)	PFGE	Second epidemic due to the introduction of a new strain, likely from Mozambique	[31]
South-Africa (2001–2002)	C (112)			
Djibouti, Kenya, Mozambique, Sudan and Tanzania (1968–2009)	C (30)	Genome-wide SNP analysis	Cholera importation in Africa through 3 independent waves arisen from the Bay of Bengal	[88]
Worldwide (1910–2010)	C (127)			
Algeria, Chad, Comoros, Guinea, Kenya, Malawi, Morocco, Mozambique, Senegal and Sierra Leone (1970–2004)	C (13)	SNPs analysis, MLVA	African strains dispatched in several groups without clear geographical and temporal systematization	[86, 87]
Worldwide (1937–2002)	C (56)			
Goma in DRC (1994)	C (9)	MLVA	Separate clustering of congolese and guinean strains	[85]
Equatorial-Guinea (N/A)	C(3)			
Worldwide (1910–2005)	C & E (130)			
Angola (2006), Mozambique (2004–2005) Zambia (1996–2004) Nigeria & Cameroon (2009) Zimbabwe (2008) Ghana (2006) Kenya (2009–2010)	C	Classic PCR +/- Southern blot, gene sequencing, MAMA PCR, MLSA	Recent importation in Africa of two types of atypical/variant El Tor strains secreting the classical toxin: hybrid El Tor (Mozambique, Zimbabwe, Zambia . . .) and altered El Tor (Angola, Zimbabwe, Ghana . . .)	[90–99]
Kenya (2009–2010)	C (170)	MLVA	Multiple simultaneous outbreaks: numerous importations or local reemergences?	[99]

Abbreviations: MAMA, Mismatch Amplification Mutation Assay; MLSA, MultiLocus Sequence Analysis; MLVA, MultiLocus-Variable no. of tandem repeats (VNTRs) Analysis; PFGE, Pulse Field Gel Electrophoresis; SNP, Single-Nucleotide Polymorphisms.

[a] Clinical (C) or environmental (E)

heavy rains, whose collection may provide a safer source of water to the population [64].

Climate Influences on Cholera Transmission

Beside its seasonal variations, the burden of cholera has exhibited important interannual fluctuations in numerous costal African countries. According to the cholera paradigm, these fluctuations could be attributed to global climate interannual variability. Indeed, rainfalls in East and West Africa appear deeply influenced by Pacific ENSO, and African climates may be even more impacted by the Atlantic ocean's SST variations [107]. For instance, early 1990s cholera epidemics in Ghana, Togo, Benin, and Nigeria showed a significant synchrony with rainfall and Indian Oscillation Index [108]. Cholera incidence between 1971 and 2006 in southeastern African countries appeared significantly impacted by SST anomalies at hemispheric scales [109]. Finally, the 2001–2002 outbreaks in the KwaZulu-Natal province of South Africa presented a strong temporal association with local SST, and a 6-month lagged association with marine chlorophyll-a concentration estimated by satellite-sensing [103].

Sometimes, these global climatic forces have provoked local hydrometeorologic disasters, which have been contemporaneous with several cholera epidemics. Examples include floods

and the 2005 outbreak in Dakar [110, 111], floods and the 1994 and 1997 outbreaks in Djibouti city [72, 73]; or cyclones, which were associated with the 1998 Mozambican [32] and with the 2000 Madagascan [112] epidemics. However, according to these reports, these natural disasters did not initiate the cholera outbreak but rather contributed to outbreak expansion particularly in densely populated areas.

Lull Transmission Periods

Cholera around coastal Africa has exhibited repeated lull transmission periods of several years [1], even in high-risk and often designated "endemic" countries like Guinea-Bissau [56], Guinea [113], Côte d'Ivoire [50], Benin [114], Cameroon [115], or Angola [29, 61]. For reasons yet unexplained by the cholera paradigm as described in Southeast Asia, cholera has failed to settle in Cape Verde, Sao Tome and Principe, Comoros [34, 35], Madagascar [37], or Djibouti City [72] in the aftermaths of explosive outbreaks. Cholera has also spared numerous impoverished and overcrowded areas near estuaries or lagoons, including Gambia, Casamance in Senegal, or Gabon. WHO reports and various articles have repeatedly deplored a widespread underreporting of cholera cases [112, 116, 117], notably in Africa where observed lull periods may thus be the consequence of poorly functioning surveillance systems. However, the systematic national surveillance program implemented in Guinea after the 2004–2007 major epidemics [1, 23] identified only 42 cholera cases in 2009 and none in 2010 and 2011. Similarly, Beira City in Mozambique barely recorded cholera cases in 2010 and 2011 despite an enhanced surveillance scheme [104] and irrespective of the vaccination campaign that in late 2003 vaccinated only 10% of its population [118]. On a finer timescale, no study has ever described a continuous cholera transmission in a given area, whatever its location along the African coasts. Conversely, multiyear time-series available for Guinea-Bissau, Guinea [23], Côte d'Ivoire [49], or Mozambique [104] all exhibit numerous periods apparently free from cholera cases.

Environmental Reservoirs of *Vibrio cholerae*

To further explore determinants of cholera transmission along African coasts, several microbiological investigations, summarized in Supplementary Table 1, have searched for evidence of environmental reservoirs of *V. cholerae* or other *Vibrio* species. Most of these 36 identified studies focused on water, aquatic sediment, plankton, or shellfish sampled from brackish estuaries or lagoons in Calabar, Douala, or Côte d'Ivoire. A few others targeted lagoonal waters in Ghana, Togo, and Benin, estuarine waters in Ghana, Luanda, and Beira, city effluents (Douala), fresh water from water tanks, wells, lakes, dams, or rivers (Yaounde, Kenya, Djibouti City), sea water (Ghana, Togo, Benin, Kenya), or marine fish or shellfish (Senegal, Monrovia, Togo, Cameroun, Kenya). Although only 2 studies aimed at identifying viable but nonculturable *Vibrio* through adequate techniques (sensitive membrane antigen rapid test [SMART], cholera direct fluorescent antibody [DFA], polymerase chain reaction [PCR]), all but 2 articles reported *Vibrio* detection in the environment, reaching sometimes high concentrations. *V. cholerae* was isolated in 25 studies, including *V. cholerae* O1 strains in 11 cases. Three studies reported results of El Tor biotyping, and/or Ogawa/Inaba serotyping. Four studies reported the capacity to produce cholera toxin, 3 of which exclusively isolated non-O1 non-O139 *V. cholerae* strains in Côte d'Ivoire. When performed, genotyping always exhibited a clonal similarity with concomitant clinical strains [26, 133, 137]. In most cases, environmental *V. cholerae* O1 strains were either isolated during cholera epidemics, like in Monrovia in 2007–2008 [120], Abidjan in 1996 [78], Calabar in 2006 [128], Douala in 2005–2007 [133], or Luanda in 1992 [102, 137], or during unspecified periods. Sampling organized during lull periods either were negative for *Vibrio* like in Cameroon in 2007 [135], or, like in Côte d'Ivoire, isolated only non-*cholerae Vibrio* [122], unserotyped *V. cholerae* [123], or non-O1/non-O139 V. *cholerae* [126]. *V. cholerae* O1 identified from Beira's estuary water in 2005–2007 [140], and *V. cholerae* O1 Ogawa cultured from an Ebrié Lagoon's alevin in 1991 (cited by [123]), both during interepidemic periods, were not tested for toxin production. In most cases, it was therefore impossible for us to determine if the presence of *Vibrio* in the environment preceded and thus potentially caused a cholera outbreak or if it was the consequence of a human waste contamination secondary to the outbreak. Consequently, the perennial presence of pathogenic *V. cholerae* in coastal African environments seems to have never been confirmed until now.

DISCUSSION AND CONCLUSION

Numerous locations along the African coasts are repeatedly affected by cholera outbreaks. Like in the Bay of Bengal, this coastal cholera exhibits strong links with environmental factors. Main foci are located along estuaries, lagoons, close to mangrove forests, and in island areas where people often neighbor brackish water expanses used for drinking, cooking, and washing. In various areas, cholera incidence appears related to the rainy season and may be influenced by global climatic trends and concomitant hydrometeorologic disasters. These links with marine ecosystems and rainfall are often highlighted to express the role of the environment as an initiator of cholera in African coastal areas. Toxigenic *V. cholerae* has been cultured from water and seafood samples in several occurrences.

Conversely, links between cholera and coastal environments in Africa appear highly heterogeneous. Some epidemics occur during both the dry and cool seasons, and cholera's frequent concurrence with rainfall may reflect processes independent from planktonic reservoirs of *V. cholerae*. Most cholera foci are

located in densely urbanized areas deprived of clean water and proper sanitation, where seasonal rains can periodically favor contamination of wells and surface water resources by washing out waste and excrements from open defecation or by overflowing latrines. This phenomenon was observed in Kindia (Guinea) [23] but also in various areas distant from the coasts like eastern DRC [145] or Lusaka in Zambia [146]. Periodicity of human activities has also been pointed out to explain cholera seasonality, like fishing in Calabar estuary [47] or, in the 19th century, the sailing trade driven by the monsoon winds along the eastern African coast [80–82].

Interepidemic transmission periods are repeatedly observed, even in high-risk coastal locations of endemic African countries. No cholera serosurveys have been published to question the hypothesis of periodic waning of immunity. Evidence remains also insufficient to attest the perennial presence of toxigenic *V. cholerae* in aquatic ecosystems and its implication in sustaining cholera over the long term in a given place and in the emergence of outbreaks in coastal Africa. Available data have thus not allowed definitive determination of whether cholera outbreaks are the consequence of a proliferation of environmental *V. cholerae* in brackish water expanses or if they are due to the importation of strains by travelers. Indeed, coasts, especially port cities and fishing areas, constitute intense exchange zones prone to cholera importations, which are sometimes genetically confirmed. Along coastal Africa, new atypical El Tor strains likely originating in the Bay of Bengal have replaced previous strains in a matter of a few years. This phenomenon is still not completely understood [95] and raises public health concern because those strains have been associated with more severe outcome [94, 147].

Overall, the temporo-spatial distribution and environmental determinants of cholera outbreaks in coastal Africa exhibit complex particularities, which so far remain incompletely explained by the cholera environmental paradigm. Currently, the hypothesis of an environment-to-human genesis of cholera epidemics in coastal Africa lacks the demonstration of perennial aquatic reservoirs of toxigenic strains. Therefore, the understanding of cholera dynamics in this part of the world would highly benefit from interdisciplinary surveys combining prospective ecological and microbiological analyses of water bodies, dynamic temporo-spatial descriptions of epidemics, and genotyping of clinical and environmental *V. cholerae* isolates. Such data would be invaluable to improve cholera preparedness and response plans implemented in Africa. The evidence of an environmental origin of cholera would indeed justify a careful monitoring of *V. cholerae* aquatic reservoirs and prevention policies specifically targeting their related human activities such as fishing. In contrast, human-borne cholera outbreaks related to imported strains would urge to develop cross-border epidemiological collaboration and to target control efforts on transport facilities and highly mobile populations. It is all the more important to address these key issues in the near future as the spread of recent epidemics has demonstrated the ongoing threat of cholera in Africa, in which the economic context renders it crucial to focus limited resources on the most relevant strategies.

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.

Note

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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