Hydroclimatic influences on seasonal and spatial cholera transmission cycles: Implications for public health intervention in the Bengal Delta

Ali Shafqat Akanda,[1] Antarpreet S. Jutla,[1] Munirul Alam,[2]
Guillaume Constantin de Magny,[3] A. Kasem Siddique,[2] R. Bradley Sack,[4]
Anwar Huq,[5] Rita R. Colwell,[3,4] and Shafiqul Islam[1,6]

[1] Cholera remains a major public health threat in many developing countries around the world. The striking seasonality and annual recurrence of this infectious disease in endemic areas remain of considerable interest to scientists and public health workers. Despite major advances in the ecological and microbiological understanding of *Vibrio cholerae*, the causative agent of the disease, the role of underlying large-scale hydroclimatic processes in propagating the disease for different seasons and spatial locations is not well understood. Here we show that the cholera outbreaks in the Bengal Delta region are propagated from the coastal to the inland areas and from spring to fall by two distinctly different transmission cycles, premonsoon and postmonsoon, influenced by coastal and terrestrial hydroclimatic processes, respectively. A coupled analysis of the regional hydroclimate and cholera incidence reveals a strong association of the space-time variability of incidence peaks with seasonal processes and extreme climatic events. We explain how the asymmetric seasonal hydroclimatology affects regional cholera dynamics by providing a coastal growth environment for bacteria in spring, while propagating the disease to fall by monsoon flooding. Our findings may serve as the basis for "climate-informed" early warnings and for prompting effective means for intervention and preempting epidemic cholera outbreaks in vulnerable regions.

1. Introduction

[2] Cholera broke out as part of a global pandemic in the Bengal Delta region of the Indian subcontinent during the early nineteenth century [*Sack et al.*, 2004]. Two hundred years later, the disease still remains a major threat to public health in the developing world. Cholera is an acute water-borne diarrheal illness caused by two toxigenic strains of the bacterium *Vibrio cholerae*, O1 and O139, which are associated with marine plankton species [*Colwell and Huq*, 2001]. There is agreement on the coastal nature of early outbreaks of this infectious disease [*Huq and Colwell*, 1996; *Worden et al.*, 2006]; however, the striking seasonality and strong interannual variability as well as its annual recurrence and spatial variability in endemic areas remain a mystery to scientists and public health professionals [*Bertuzzo et al.*, 2010; *Jutla et al.*, 2010].

[3] The incidence of cholera in the Bengal Delta region shows distinct seasonal and spatial variations (Figure 1a). In addition to the unique dual-incidence pattern in some regions of the Bengal Delta [*Akanda et al.*, 2009], such as Dhaka and Matlab, we also see single annual peaks in coastal (spring peak in Mathbaria) and inland (fall peak in Chhatak) areas. In this outbreak pattern, the first cholera peak of the year occurs during the dry season in spring, and the second, and usually bigger, peak occurs in fall following the wet season. Other cholera-affected regions in the world, such as Southeast Asia [*Emch et al.*, 2008], sub-Saharan Africa [*Hashizume et al.*, 2008], southern Africa [*Bertuzzo et al.*, 2008], and South America [*Gil et al.*, 2004], typically show single-incidence peaks in a year. A key objective of this study is to show that the biannual cholera peaks in the Bengal Delta region are governed by two spatially distinct seasonal transmission mechanisms, influenced by large-scale hydroclimatic processes.

[4] For the past several decades, cholera research has primarily focused on clinical, microbiological, and ecolog-

[1]Water and Environmental Research, Education, and Actionable Solutions Network, Department of Civil and Environmental Engineering, Tufts University, Medford, Massachusetts, USA.
[2]International Center for Diarrhoeal Disease Research, Dhaka, Bangladesh.
[3]Center for Bioinformatics and Computational Biology, University of Maryland, College Park, Maryland, USA.
[4]Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, USA.
[5]Maryland Pathogen Research Institute, University of Maryland, College Park, Maryland, USA.
[6]Water Diplomacy, Fletcher School of Law and Diplomacy, Tufts University, Medford, Massachusetts, USA.
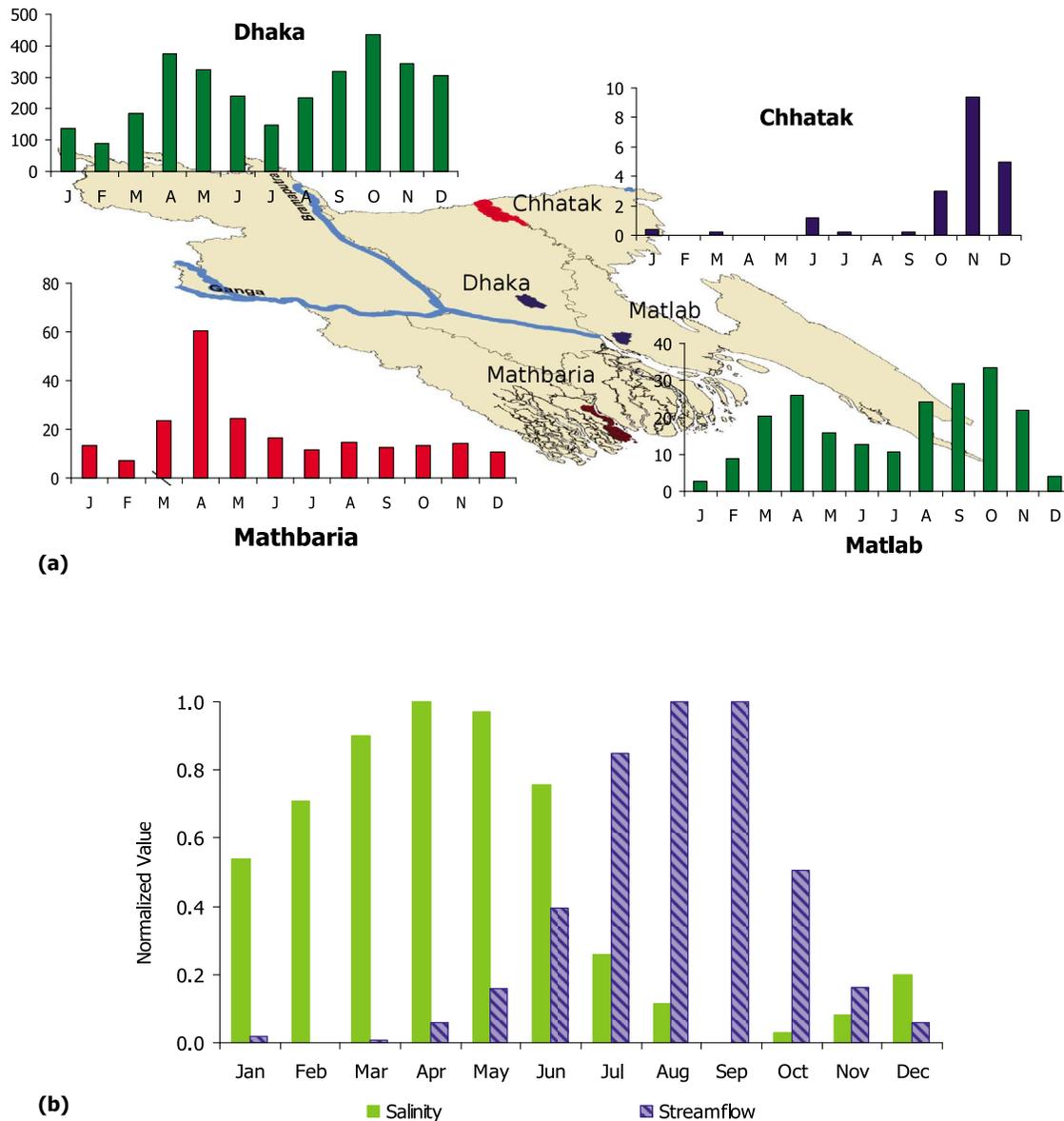
Figure 1. (a) Monthly climatology of cholera incidence recorded at International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) surveillance centers in Dhaka, Mathbaria, Chhatak, and Matlab, Bangladesh (latitude 21°N–26°30′N, longitude 88°E–92°30′E). (b) Observed coastal salinity in Bangladesh (mean monthly salinity recorded at 10 coastal river stations [*Hoque et al.*, 2006]) and monthly climatology of combined Ganges and Brahmaputra streamflow (recorded at the Paksey and Bahadurabad stations, respectively, of the Bangladesh Water Development Board (BWDB)).

ical aspects of the bacterium, including vaccines, therapy, and improved treatment. The role of underlying hydrologic, climatic, and other large-scale environmental processes in transporting cholera bacteria through the ecosystem and propagating the disease in different seasons has received less attention [*Jutla et al.*, 2010]. Earlier studies related to Bengal cholera outbreaks have mostly focused on rural areas [*Cockburn and Casanos*, 1960; *Glass et al.*, 1982; *Bouma and Pascual*, 2001]. In fact, an overwhelming fraction of the investigations on cholera outbreaks [*Longini et al.*, 2002; *Ruiz-Moreno et al.*, 2010] and the role of environmental factors [*Koelle et al.*, 2005; *Emch et al.*, 2008;

Constantin de Magny et al., 2008; *Islam et al.*, 2009] have relied on surveillance data from Matlab. Also, these studies did not attempt to explain how large-scale drivers (e.g., precipitation, flood, and temperature) with single annual peaks create dual seasonal peaks in cholera incidence.

[5] *Akanda et al.* [2009] provided a hydroclimatological explanation of the temporal nature of the dual-peak cholera incidence in Dhaka. They associated dry season water scarcity in the region with early cholera outbreaks in spring and suggested a positive role of monsoon water abundance in the fall season outbreaks. However, how these large-scale processes may affect outbreaks beyond individual seasons

and how they may cause single or dual outbreaks in different locations were not explored. We build on these findings to investigate the spatial and temporal nature of cholera outbreaks throughout Bangladesh and the role of regional hydroclimatic processes and extreme events. We argue that the annual transmission process is governed by two separate transmission cycles propagating from spring to fall aided by the asymmetric nature of regional terrestrial and coastal processes. We hypothesize the existence of two distinctly different physical drivers of cholera outbreaks influenced by two hydroclimatic controls, premonsoon and postmonsoon. More specifically, we attempt to answer the following questions: Are cholera outbreaks in consecutive seasons or subsequent years related to or independent of each other? Does the hydroclimatology of the Bengal Delta region contribute to the propagation of cholera outbreaks from one season and one region to another? Are the record outbreaks in different years modulated by the significant hydroclimatic events in those years?

2. Background

[6] *Vibrio cholerae* (henceforth *V. cholerae*), primarily known to be an estuarine aquatic bacterium, is indigenous to the macroenvironment of aquatic ecosystems [*Colwell et al.*, 1981]. Cholera is an ancient disease, occurring almost every year in many parts of the world, including Bangladesh; however, the source of the organisms remained unknown, as the causative agent could not be easily isolated between epidemics. *Huq et al.* [1990] first demonstrated the presence of the pathogen in aquatic environments of Bangladesh during all the months of the year using direct detection methods. The bacteria remain in a nonculturable state for most of the year in aquatic reservoirs, allowing the organisms to survive and multiply [*Huq et al.*, 2005; *Chun et al.*, 2009].

[7] Different ecosystem variables such as water temperature, salinity, and other nutrients (organic carbon, nitrogen, and phosphorus) have been associated with the abundance of plankton and the occurrence and persistence of *V. cholerae* in aquatic environments [*Singleton et al.*, 1982a, 1982b; *Huq et al.*, 1984; *Vital et al.*, 2007]. Phytoplankton serves as the primary food source for zooplankton, also releasing nitrogenous nutrients into the water through disintegration, which aids proliferation of the bacteria [*Lipp et al.*, 2002]. A brackish salinity of 5–20 parts per thousand (ppt) and water temperature above 20°C was found to be optimum for growth of *V. cholerae* in estuarine environments [*Louis et al.*, 2003]. In the Bengal Delta region, a 5°C increase in the water temperature was associated with a 3.3-fold increase (range of 2.4–4.6; median of 3.3) in the risk of cholera outbreaks, with a lag of 6 weeks [*Huq et al.*, 2005]. *Stine et al.* [2008] concluded that cholera outbreaks in different areas were of independent origin, suggesting that the bacteria may be triggered simultaneously by large-scale processes, causing disease outbreaks in multiple locations.

[8] The hydroclimatology of the Ganges-Brahmaputra-Meghna (GBM) basin region is highly seasonal in nature, with most of the annual precipitation occurring during the four monsoon months, June–September [*Chowdhury and Ward*, 2004]. During the prolonged dry season (December–May), lower runoff availability and upstream diversions leave

only a fraction of the combined average flow to reach the Bay of Bengal (BOB) (Figure 1b). As a result, the salinity front in the estuarine region travels toward inland freshwater, as far as 100 km in extreme dry years [*Rahman et al.*, 2000]. Consequently, a large region in coastal Bangladesh exhibits brackish water conditions in spring [*Wahid et al.*, 2007; *Islam and Gnauck*, 2008], providing an optimum environment for *V. cholerae* growth [*Vital et al.*, 2007; *Louis et al.*, 2003].

[9] The situation undergoes drastic changes as monsoons arrive in June; peak streamflow volumes cause substantial inundation along the major riverbanks of Bangladesh and lead to large-scale contamination of water systems such as rivers, canals, and ponds [*Schwartz et al.*, 2006], with the bacteria present in the ecosystem [*Akanda et al.*, 2009]. Open mixing of water with sediment occurs within such systems during floods, and the submerged areas quickly become contaminated with *V. cholerae*. Some areas stay submerged and turbid until November [*Mirza et al.*, 2001], providing an ideal condition for the growth and proliferation of *V. cholerae* due to the availability of rain-flushed nutrients and plankton growth, which act as sources of transmission with the surrounding population [*Islam et al.*, 2006]. This hypothesis is also supported by the significant 3 month lag correlation reported by *Akanda et al.* [2009] between monsoon floods and fall outbreaks, which provides plausible evidence of the delayed response of plankton and vibrio growth in inundated water bodies.

[10] An ecological survey of *V. cholerae* in the coastal ecosystems of the Bay of Bengal provided firm evidence that *V. cholerae* O1 cells are present during epidemics in samples collected from water bodies serving as drinking water sources for two rural areas of Bangladesh. The molecular detection of toxigenic *V. cholerae* between 2004 and 2007 showed the presence of *V. cholerae* in Bakerganj between April and June and between August and December. During this study, *V. cholerae* was not detected in water samples during the winter months or during the peak monsoon months. For Mathbaria, *V. cholerae* was present in water samples mainly between March and June and sporadically in the fall. These preliminary results thus strengthen the hypothesis of a contrasted seasonality of the presence of toxigenic *V. cholerae* in the environment and its potential link with the cholera incidence pattern in these areas [*Alam et al.*, 2006].

[11] In summary, the life cycle of *V. cholerae* is intricately linked to both microenvironmental and macroenvironmental processes, with vastly different space and time scales of interacting variables [*Jutla et al.*, 2010]. Here we define micro as microbiological and genetic processes, while macro refers to hydrological, ecological, and climatic processes. We recognize the importance of microenvironmental understanding to develop vaccines and treatment protocols. However, as *V. cholerae* may survive and thrive in a wide range of natural conditions and since evidence of new biotypes is emerging, it is unlikely that this disease will ever be eradicated. Consequently, we need a new approach to minimize the impact of this devastating disease by predicting where it may occur and initiating effective intervention strategies. Our approach in this study thus attempts to identify the macroenvironmental processes and variables that have longer temporal and larger spatial "memory" to

Table 1. Intra-annual and Interannual Correlation between Seasonal Cholera Prevalence for the Period 1980–2007[a]

Beginning Season	Ending Season	Correlation ($n = 28$)
Spring	summer (same year)	0.70**
Summer	spring (next year)	0.23
Spring	fall (same year)	0.73**
Fall	spring (next year)	0.33
Summer	fall (same year)	0.76**
Fall	summer (next year)	0.37

[a]Spring is March–April–May, summer is June–July–August, and fall is September–October–November. Statistical significance indicators are as follows: **, $p < 0.01$.

allow the development of an early warning system for cholera outbreaks.

3. Analysis and Results

3.1. Data and Methodology

[12] Cholera incidence data for the period 1980–2007 were collected from the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B), located in Dhaka, Bangladesh. The incidence data are recorded as the number of people infected with *V. cholerae* among a statistical subset of the patients visiting the hospital each month. We use prevalence rate, a population-corrected measure of incidence, for our analyses by normalizing the incidence data by the number of patients tested and reporting it as a percentage number. We separate out the mean cholera prevalence rate of the two outbreak seasons, spring (March–April–May, MAM) and fall (September–October–November, SON), as well as summer (June–July–August, JJA) and winter (December–January–February, DJF) seasons to examine the intra-annual and interannual variability of outbreaks. Mean streamflow values for dry (January–April, JFMA) and wet (July–October, JASO) seasons were used to develop low and high streamflow time series, respectively. Flood-affected area (FAA) is an annual measure based on flood surveys conducted through the high-flow (JASO) season. For the sea surface temperature (SST), rainfall, and chlorophyll data sets, we developed similar seasonal time series (DJF, MAM, JJA, and SON) for effective seasonal lead-lag comparisons with cholera outbreaks.

[13] For this study, we use the Sea-viewing Wide Field-of-view Sensor (SeaWiFS)–measured chlorophyll *a* (Chl *a*) concentration as a surrogate of phytoplankton abundance for the coastal zone of the GBM rivers in the BOB (areas north of 21°N between 86°E and 93°E). This zone was chosen on the basis of available bathymetric and active production zone information [*Chamarthi et al.*, 2008]. The Reynolds 1° × 1° SST database [*Reynolds and Smith*, 1994] was used to extract SST information for the BOB. Gridded rainfall time series data (2.5° × 2.5° spatial resolution) for the GBM catchment areas were obtained from the National Centers for Environmental Prediction/National Center for Atmospheric Research (NCEP/NCAR) Reanalysis Project atmospheric data sets. Daily river discharge records for the Ganges and the Brahmaputra rivers, which were aggregated to monthly scales, and the FAA information, a measure of annual extent of flood inundation in Bangladesh, were obtained from the Bangladesh Water Development Board (BWDB).

3.2. Fall to Spring or Spring to Fall?

[14] Previous studies on the nature of cholera outbreaks in rural Bengal [*Cockburn and Casanos*, 1960; *Glass et al.*, 1982] reported outbreaks in fall closely followed by those in spring. *Pascual et al.* [2000] and *Bouma and Pascual* [2001] reiterated a fall-spring transmission cycle, with the annual monsoon rainfall providing a "dilution" effect between the two major outbreak seasons [*Ruiz-Moreno et al.*, 2010]. This notion of a fall-spring transmission pattern, however, appears inconsistent with recent observations: A careful analysis of the spring (March–April–May), summer (June–July–August), and fall (September–October–November) cholera outbreaks for the last 3 decades of records from Dhaka, Bangladesh, in fact, suggests the opposite. Table 1 shows intra-annual and interannual cross-correlation values between mean seasonal cholera prevalence rates for 1980–2007. An intriguing observation from Table 1 is that same-year seasonal cholera outbreaks are strongly correlated, but the correlation breaks down between successive years. These results imply that summer and fall prevalences are dependent on the preceding spring outbreaks. However, fall outbreaks do not have an impact on subsequent spring prevalence, suggesting a winter break in the annual transmission process.

[15] *Akanda et al.* [2009] argue that lower discharge volumes during the dry season (from January through April) and associated saltwater and plankton intrusion may initiate early cholera outbreaks in the GBM basin. On the other hand, as streamflow direction is predominantly southward in regional rivers during and after the wet season (from June through November) [*Mirza et al.*, 2001], there is no realistic way for coastal plankton to reach estuarine rivers during these months. If coastal plankton abundance, salinity, and associated bacteria affect inland water resources only during spring and if summer and fall prevalences are dependent on the preceding spring outbreaks (Table 1), one would expect to see a physically consistent pattern of prevalence between years of high and low coastal intrusion. Figure 2a shows a consistent progression pattern in cholera outbreaks from spring (MAM) to fall (SON) months during strong and weak drought years (i.e., years with higher and lower coastal intrusion in spring, respectively). We see a clear demarcation of higher and lower cholera prevalence in all months between these years, suggesting the influence of coastal and brackish plankton abundance. However, a similar progression pattern is not observed between the years with the highest and lowest flood events. Flood-induced contamination appears to have an impact on cholera prevalence during the immediate fall months but not during the following winter or spring months (Figure 2b). These results suggest an asymmetric role of regional hydroclimatology and provide secondary evidence of a break in the annual transmission process in winter.

3.3. Coastal to Inland Areas or Inland to Coast?

[16] *Siddique et al.* [1994] was perhaps the first study to suggest plausible pathways of the progression of cholera outbreaks from the coastal regions of Bangladesh to inland areas of the country during major epidemics. *Bouma and Pascual* [2001] provided historical evidence of a coastal link to cholera mortality. A more recent study by *Sack et al.* [2003] showed that spring peaks are more common in
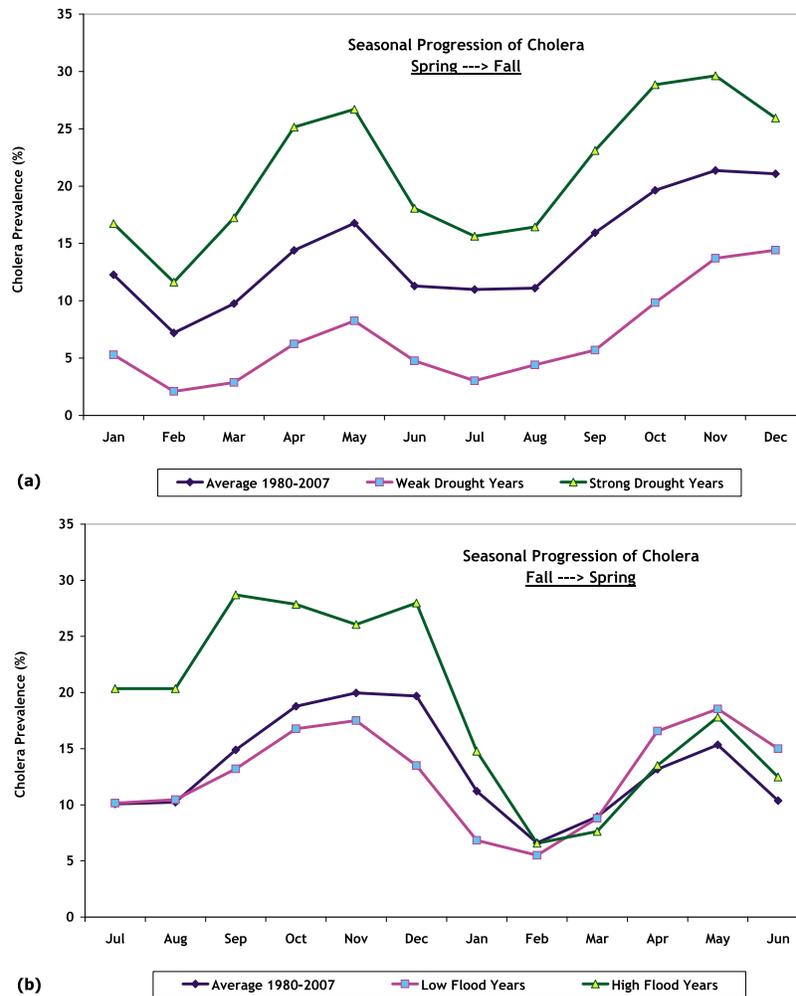
Figure 2. Comparison of seasonal progression of cholera prevalence from (a) spring to fall seasons between strong and weak drought years and from (b) fall to spring seasons between high- and low-flood years, classified on the basis of combined Ganges and Brahmaputra streamflow (BWDB) and cholera surveillance from Dhaka (ICDDR,B).

locations closer to the coast, while the inland locations are affected mostly by fall outbreaks. Taken together, these studies suggest a spatial heterogeneity of cholera outbreaks across the Bengal Delta region. However, these studies did not specifically investigate the spatial signatures with any climatic, ecological, or environmental processes.

[17] If the understanding of the seasonal and spatial processes and their asymmetric role is to be physically consistent, we should expect to see a spatial signature of these processes across a larger section of Bangladesh. To explore and validate this possibility, we investigate the seasonal nature of recently recorded cholera cases in four locations of Bangladesh. These four locations are distinctly different in their geographical and meteorological settings, as well as in their seasonal outbreak patterns. Dhaka is a freshwater ecosystem in central Bangladesh, surrounded by several distributaries of the GBM rivers. Mathbaria is a coastal area located in estuarine southwestern Bangladesh, close to the BOB coast. Mathbaria is not typically affected by floods; however, it is prone to freshwater scarcity during the dry spring months because of the reduced amount of streamflow

from upstream regions. Chhatak is located in northeastern Bangladesh and is the farthest away from the coast among the four locations; it is, however, prone to rainfall-driven flash floods in the Meghna basin region. Matlab is a well-reported cholera-endemic area frequented by floods, located near the confluence of the three major rivers of the region. However, Matlab is less than 150 km from the BOB coast and thus belongs to the coastal floodplains in our classification.

[18] Figure 1a shows the monthly average number of cholera cases recorded at each of these four locations. We find that coastal hydroclimatic processes primarily modulate the first outbreak season in spring, whereas inland processes exhibit a strong influence on the second cycle of outbreaks. Mathbaria (data period: 2003–2007), a coastal location close to the BOB, shows cholera outbreaks only during the spring season. On the other hand, Chhatak (1997–2001), which is an inland location that is the farthest away from the coast, shows outbreaks only during fall months. Dhaka (1980–2007) and Matlab (1998–2007), located in the floodplains of the GBM rivers, appear to be affected by both waves of

Table 2. Seasonal Cross Correlation Between Hydroclimatic Variables and Cholera Prevalence in Dhaka, Bangladesh, for the Period 1980–2007[a]

Hydroclimatic Variable	Seasonal Cholera Prevalence 1980–2007 ($n = 28$)				
	Spring (Same Year)	Summer (Same Year)	Fall (Same Year)	Winter (Year End)	Spring (Next Year)
Flow					
JFMA	−0.47*	−0.41*	−0.30	−0.12	−0.08
JASO	-	0.51*	0.45*	0.16	0.01
FAA, JASO	-	0.66**	0.43*	−0.09	0.05
Rainfall					
DJF	−0.60**	−0.40*	−0.39	−0.50*	−0.48*
MAM	−0.49*	−0.44*	−0.28	−0.32	−0.29
JJA	-	0.35	0.38	0.07	−0.07
SON	-	-	−0.19	−0.12	−0.17
SST					
DJF	−0.60**	−0.54*	−0.46*	−0.32	−0.40*
MAM	0.11	0.22	0.26	0.07	−0.16
JJA	-	0.41*	0.56**	0.13	−0.01
SON	-	-	0.34	−0.05	−0.10
Chl a[b]					
DJF	0.14	0.30	0.07	0.20	0.67*
MAM	−0.01	0.12	0.21	0.45	0.41
JJA	-	0.11	−0.19	0.11	−0.09
SON	-	-	0.46	0.01	0.87**

[a]Source is the International Center for Diarrhoeal Disease Research, Bangladesh. Spring is March–April–May (MAM), summer is June–July–August (JJA), fall is September–October–November (SON), and winter is December–January–February (DJF). Statistical significance indicators are as follows: **, $p < 0.01$; *, $0.05 > p > 0.01$. JFMA, January–April average; JASO, July–October average; FAA, flood-affected area; SST, sea surface temperature; Chl a, chlorophyll a.
[b]For 1998–2007 ($n = 10$).

outbreaks. Thus, the two transmission cycles show distinctive seasonal and spatial signatures with respect to their coastal or terrestrial origins.

3.4. Intra-annual Variability: Asymmetric Influence of Seasonal Hydroclimatology

[19] A contrasting influence of GBM streamflow and BOB SST on intra-annual or seasonal cholera outbreaks in Dhaka, Bangladesh, was presented by *Akanda et al.* [2009]. However, how these variables contribute to infection beyond individual seasons was not explored in their study. In addition, how related hydroclimatic variables such as rainfall and coastal plankton abundance affect the seasonal outbreaks was not quantified. The goal of this analysis is to identify if these macroscale drivers contribute to cholera outbreaks in subsequent seasons. If the correlations between seasonal cholera prevalence in the same and successive years (Table 1) were to be physically meaningful, one would expect to see the manifestations of these results in underlying physical processes. We hereby investigate seasonal lead-lag relationships between coastal and terrestrial hydroclimatic processes in the region and cholera outbreaks during the spring, summer, winter, and fall seasons of one particular year as well as the spring season of the subsequent year. Table 2 shows the cross-correlation coefficients between mean seasonal cholera prevalence in Dhaka and regional hydroclimatic variables. We calculate Pearson and nonparametric Kendall correlation values and perform statistical significance tests for all time series pairs (the Pearson coefficients are reported in Table 2).

[20] An important observation from Table 2 is the consistent asymmetric influence of dry and wet season processes on same-year spring and fall cholera outbreaks, respectively: negative correlation in spring and positive

values in fall. Winter (DJF) SST in coastal BOB, dry season (DJF and MAM) rainfall in Bangladesh, and low-flow (JFMA) values in GBM rivers have all shown strong negative influences on spring cholera prevalence ($r = −0.60$ for DJF SST and $r = −0.60$ for DJF rainfall, both values significant at $p < 0.01$, and $r = −0.49$ for MAM rainfall and $−0.47$ for JFMA rainfall, both significant at $p < 0.05$). These variables also show consistent negative correlation values over subsequent summer and fall seasons (Table 2), suggesting that freshwater scarcity in upstream rivers and resulting saltwater and plankton intrusion as well as the environmental changes during and following the first peak may have an influence on the cholera outbreaks in subsequent seasons of the year.

[21] On the other hand, GBM streamflow in JASO months, FAA inside Bangladesh, and summer (JJA) SST in BOB all suggest a strong positive influence on summer and fall cholera prevalence ($r = 0.51$, 0.66, and 0.54 for summer and $r = 0.45$, 0.43, and 0.56 for fall, respectively, with all values significant at $p < 0.05$, except $r = 0.66$ at $p < 0.01$). Unlike the dry season, none of the wet season variables show a significant relationship with cholera prevalence in subsequent winter or spring seasons. These results indicate that water abundance during summer and a warmer BOB may contribute to large-scale water contamination and atmospheric conditions conducive to cholera outbreaks in summer and fall. However, *V. cholerae* contamination in one particular monsoon season does not appear to persist over winter or impact cholera prevalence beyond fall. These observations thus provide plausible physical explanations of the correlations reported in Table 1 and strengthen the hypothesis of an annual transmission process beginning each spring and ending in winter.

[22] Coastal phytoplankton, known to be a major source of bacterial abundance in estuarine areas, exhibits a positive

Table 3. Progression of Seasonal Cholera Outbreaks Associated With Significant Hydroclimatic Events During 1980–2007[a]

Year	Dry Season Processes			Spring Cholera	Wet Season Processes			Fall Cholera
	SST	Chl a[b]	Flow		SST	Flood	Flow	
Five Highest Cholera Burden Years								
1987	avg		low	avg	high	high	high	high
1997	low		low	high	high	high	avg	avg
1998	low	high	low	high	high	high	high	high
1999	avg	high	low	high	high	avg	high	high
2005	avg	high	low	high	avg	avg	high	avg
Five Lowest Cholera Burden Years								
1981	avg		high	low	avg	low	low	low
1989	high		high	low	low	low	low	low
1990	high		high	low	avg	low	low	low
1993	avg		high	low	avg	avg	avg	low
2007	low	Low	high	low	avg	low	avg	low
Years With One Significant Outbreak								
1982	high		low	low	avg	high	high	high
1986	avg		low	avg	avg	avg	avg	high
1988	avg		avg	avg	high	high	high	high
1991	high		avg	avg	avg	avg	high	high
2006	avg		avg	avg	avg	avg	high	high

[a]The categories low, average (avg), and high are based on terciles (bottom 33rd percentile, 33rd to 66th percentiles, and above the 66th percentile) of individual seasonal hydroclimatic or cholera time series.
[b]Chl a data are available only for 1998–2007.

relationship in fall (SON) and winter (DJF) seasons, with subsequent spring prevalence levels. Chl a values for the SON and DJF seasons show a strong relationship with following-year spring cholera (SON: $r = 0.87$ and 0.67, significant at $p < 0.01$ and $p < 0.05$, respectively). None of the other seasons show any meaningful relationship with cholera outbreaks. These results suggest that a coastal reservoir of the bacteria in southern Bangladesh, aided by fall and winter plankton abundance, plays a strong role in cholera outbreaks in the following year.

[23] Monsoon rainfall in the region also shows a consistently positive, albeit weaker, relationship with summer and fall cholera prevalence ($r = 0.35$, $p = 0.09$, and $r = 0.38$, $p = 0.06$, respectively). As streamflow is an aggregated measure of rainfall, we expect to see a positive influence of precipitation similar to that of streamflow [*Akanda et al.*, 2009]. However, as the arrival, duration, and intensity of monsoon rainfall, as well as the terrain and topography, widely vary over the 1.5×10^6 km^2 GBM basin [*Ahmed and Karmakar*, 1993] and as the vast majority of water arrives from upstream regions [*Chowdhury and Ward*, 2004; *Mirza et al.*, 2001], the role of monsoon rainfall in the contamination of water resources inside Bangladesh may be limited compared to that of associated flood inundation ($r = 0.66$, $p < 0.01$).

3.5. Interannual Variability: Role of Extreme Hydroclimatic Events

[24] The goal of this analysis is to determine whether the year-to-year variability of seasonal cholera outbreaks is associated with the hydroclimatic signatures of those years. In other words, the physical mechanisms behind each seasonal outbreak should appear plausible and physically consistent under different hydroclimatic scenarios, including the extreme events. For example, if a particular year begins with anomalous low-flow conditions in the GBM rivers during the dry season, it is likely elevated cholera outbreaks

will be observed in spring. Cooler winter SST and higher plankton abundance in coastal BOB may also contribute to larger outbreaks in spring and subsequent seasons. On the other hand, if a particular year experiences strong monsoon rainfall, high river discharge, and associated floods in summer, the likelihood of strong fall outbreaks also rises considerably. In the event of these conditions occurring within the same year, the region is likely to observe epidemic outbreaks in both spring and fall. To understand these relationships better, we discuss the seasonal emergence of cholera outbreaks and the spatial nature of the mechanisms for record high or low years.

[25] In this analysis, 15 years were selected and categorized on the basis of their total annual cholera burden (average prevalence for the entire year), the presence of significant outbreaks, and also the lack of major outbreaks. Table 3 illustrates the seasonal progression of cholera outbreaks in Dhaka for the high cholera burden years, low cholera burden years, and years with high outbreaks in at least one season and the relative state and contribution of coastal dry (plankton, SST, and low flow) and terrestrial wet (high flow, SST, and floods) season processes in those years. Seasonal mean values for hydroclimatic variables and cholera prevalence are converted to terciles (bottom 33rd percentile, the 33rd to 66th percentiles, and above the 66th percentile) on the basis of individual time series for the years analyzed (1980–2007) and are then grouped within three categories (low, average, and high).

[26] An important observation in Table 3 is that the years showing the highest cholera burden all began with low discharge and thus high saline conditions, reinforcing the role of coastal processes in spring. Except for 1987, all high cholera burden years had large outbreaks in the spring season. Among these years, we also see very large fall outbreaks in 1987 and 1998 in the wake of record flood events. Years such as 1982 and 1988 began with low to average spring outbreaks but showed significant flood-

Table 4. Multivariate Regression Analysis Results With Seasonal Mean of Hydroclimatic Variables and Seasonal Cholera Prevalence as Predictors[a]

Predictor Variables	r^2	Adjusted r^2	Predicted r^2	PRESS	p
Spring Cholera Prevalence (MAM)					
JFMA flow	22.9	20.0	6.4	2216	0.01
JFMA flow + DJF SST	60.1	56.9	50.5	1173	0.01
JFMA flow + DJF SST + DJF rainfall	72.3	68.8	62.3	893	0.03
JFMA flow + DJF SST + DJF rain + previous fall cholera	73.1	68.4	60.4	938	0.01
Fall Cholera Prevalence (SON)					
JASO flow	41.1	38.9	34.0	1485	0.01
JASO flow + JJA SST	59.4	55.3	44.4	1276	0.006
JASO flow + JJA SST + previous spring cholera	78.0	75.3	68.0	720	0.001

[a]MAM, March–April–May (spring); JJA, June–July–August (summer); SON, September–October–November (fall); JFMA, January–April (dry season); JASO, July–October (wet season); r^2, coefficient of determination; PRESS, prediction sum of squares; p, p–value/statistical significance value.

induced fall outbreaks later in those years. In sharp contrast, no large outbreaks and unusually low cholera burden were observed in 1989, 1990, and 1993 because there were no major hydroclimatic events.

3.6. Evidence of Large-Scale Transmission Cycles

[27] If the cholera transmission mechanisms proposed in sections 3.4 and 3.5 are to be plausible, a multivariate regression technique, using the seasonal hydroclimatic controls as predictors, is expected to explain a significant fraction of the variance of seasonal cholera prevalence values. We have thus used a linear multivariate regression analysis technique with a forward variable selection criterion, where we have incrementally added relevant hydroclimatic variables on the basis of the seasonal correlation values and included them in the regression model if they are statistically significant. Table 4 outlines the results of the multivariate regression analysis for seasonal cholera outbreaks in Dhaka during the study period (1980–2007) with the stepwise selection of variables from two separate sets of hydroclimatic controls during the spring and the fall season outbreaks and the corresponding statistical significance.

[28] In Table 4, we find that the dry and wet season processes can explain 69% and 55% of the interannual variability of the spring and fall cholera outbreaks in Dhaka (predicted r^2 of 62% and 44%), respectively. For spring, JFMA flow only explains 20% of the variance for MAM cholera prevalence. However, the inclusion of DJF SST significantly increases the explained variance to 57% (predicted r^2 of 50%), confirming the role of the coastal processes in spring cholera transmission. The addition of dry season rainfall (DJF) marginally increases the explained variance to 69% (predicted r^2 of 62%).

[29] For the fall season, GBM monsoon flow (JASO) explains 39% (predicted r^2 of 34%) of the variability of SON cholera prevalence, while adding BOB SST (JJA) increases the performance of the regression model to 55%, with a predicted r^2 of 44%. However, using spring prevalence as a predictor variable strongly increases the predictability of the fall peak (adjusted r^2 jumps from 55% to 75%, and predicted r^2 increases from 44% to 68%). On the other hand, using the previous fall prevalence to predict outbreaks in following spring shows no improvement (adjusted r^2 of 69% versus 68% and predicted r^2 of 62% versus 60%).

[30] The above results, taken together, assert the role of an annual cholera transmission process consisting of two seasonal cycles, spring and fall, as shown by strong asymmetric correlations within the same year, and combined influences of hydroclimatic variables in extreme years. The prediction sum of squares goodness of fit statistics also show consistent increased skill for combined models (Table 4), suggesting the influence of multiple hydroclimatic controls behind each seasonal peak. The strong inverse relationship of dry season processes with cholera in spring and subsequent seasons (Table 2) and the dependence of the fall peak on preceding spring peak (Table 1) signify the role of a spring-to-fall, coastal-to-inland transmission pattern.

4. Discussion and Conclusion

4.1. A Dual Space-Time Transmission Paradigm

[31] The foregoing results and observations, taken together, strongly suggest the role of two spatially distributed and distinct seasonal physical processes together modulating annual cholera transmission in the Bengal Delta. The first cholera outbreaks are initiated in spring near coastal areas as northward movement of the plankton-rich seawater and increased salinity of the estuarine environment favor increased growth and abundance of the cholera bacteria in river corridors. The ubiquitous use of this river water for irrigation, sanitation, and consumption exposes the riverine societies to the infectious disease. A second cholera transmission environment becomes dominant in summer and leads to fall cholera outbreaks through floods. Open mixing of water bodies, channels, and sediments with dormant *V. cholerae* in heavy monsoon rainfall leads to breakdown in sanitation; submerged areas are enriched with bacteria already present in the ecosystem. Figure 3a is a proposed schematic diagram of the two seasonal transmission cycles progressing in a spring-fall sequence with five hypothesized components: The first is initiation (point A); spring cholera outbreaks start when coastal plankton and bacteria move into brackish estuarine areas facilitated by low-flow conditions. For transmission (point B), aided by increased salinity, coastal water containing zooplankton and *V. cholerae* moves farther inland, and cholera outbreaks are seen in many areas, including Dhaka and its surroundings. During progression (point C), floods inundate vast areas of Bangladesh and contaminate water resources across the country. During transmission (point D), cholera bacteria
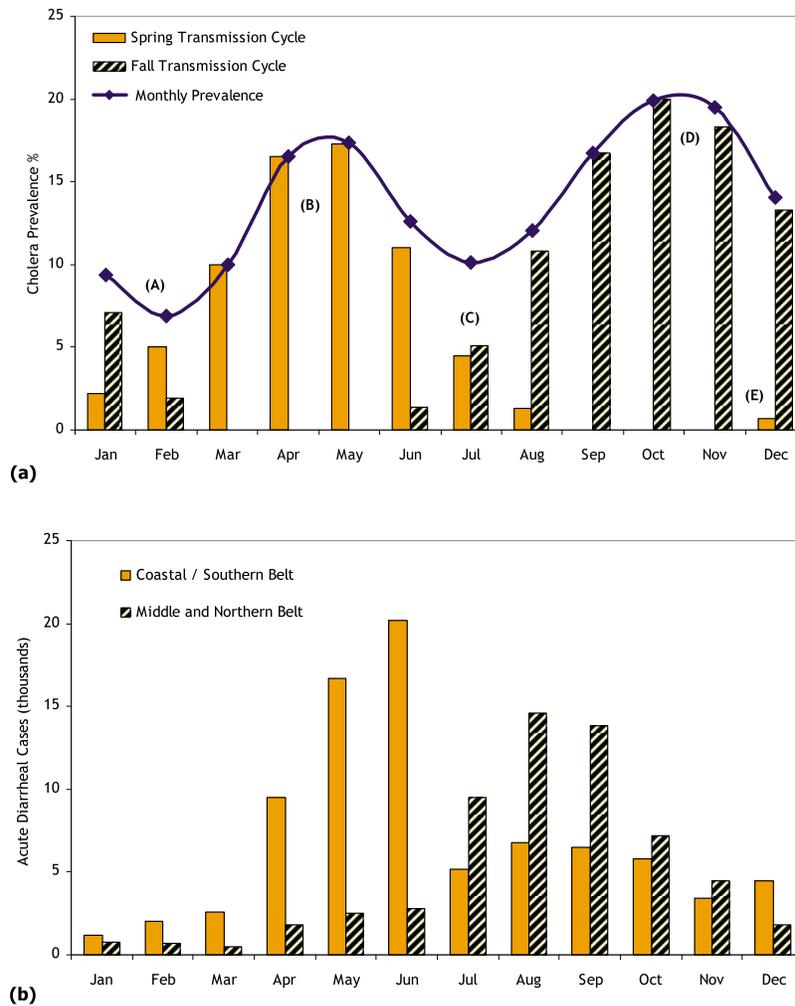
Figure 3. (a) A hypothesized schematic of two seasonal cholera transmission cycles observed in Bangladesh during the spring and fall seasons along with monthly prevalence rates for two separate transmission cycles. (b) Average monthly acute diarrheal infections observed in southern (coastal) and northern (middle and inland) areas of Bangladesh, 1995–2000.

proliferate in water-logged areas after floods recede and cause fall outbreaks. Finally, for termination (point E), winter temperatures, fewer nutrients, and the settling of sediment in inland water help end the fall outbreaks.

4.2. Implications for Public Health Intervention

[32] An important finding of this study is that GBM cholera outbreaks are propagated from spring to fall and from coastal to inland regions through macroscale drivers. This finding has significant policy implications as the intrusion of plankton-laden water and the brackish estuarine environment early in the year has a significant impact on subsequent outbreaks throughout the year. Limited intrusion of coastal plankton and lower salinity in estuarine rivers thus may lead to lower cholera burden for the entire year. Future research needs to focus on a detailed characterization of estuarine salinity in the region, which will be helpful for early intervention and targeted mitigation of spring outbreaks. Also, maintaining higher dry season discharge in specific rivers (for example, through the Gorai, the main distributary of the Ganges into southwestern Bangladesh)

may have significant beneficial impacts on public health in later seasons of the year. *Schwartz et al.* [2006] reported that *V. cholerae* strains isolated during peak monsoon months are identical to the strains detected in subsequent fall outbreaks, strengthening our hypothesis of a second transmission cycle beginning in summer and continuing into fall. An early prediction of flood extent using spatial hydrodynamic modeling will thus provide much-needed lead time to predict the magnitude and location of fall outbreaks.

[33] Our findings are further corroborated by the available evidence of waterborne disease infection data from the Director General of Health Survey records (1995–2000) in Bangladesh. Figure 3b clearly shows a pattern of two distinctly different outbreak seasons of diarrheal infections in Bangladesh, which affect the coastal belt during the premonsoon months and affect the northern and middle floodplain belt during and after the monsoon months. It is worthwhile to note that the transmission mechanisms hypothesized in Figure 3a and the observed outbreaks in Figure 3b show affirming similarities in their progression. Further investigation of the regional hydroclimatology and

associated transmission cycles may thus provide important insight into the seasonal patterns of other diarrheal diseases in the coastal and inland areas of the Bengal Delta.

[34] In this study, we have reported consistent relationships between macroscale environmental processes and cholera outbreaks in spring and fall. Our results show how major cholera outbreaks were linked to significant hydroclimatic events during the last 3 decades. An understanding of the hydroclimatic influences on cholera dynamics is also crucial in light of changing climate patterns in this region. Projected runoff decrease in the Ganges basin and increasing monsoon runoff in the Brahmaputra basin may cause extreme events such as prolonged droughts and record floods in South Asia [*Goswami et al.*, 2006; *Milly et al.*, 2005], causing waterborne epidemics and introducing new biotypes of the bacteria [*Siddique et al.*, 2010].

[35] This study provides a basis for using available hydrologic, meteorological, and satellite remote sensing data sources to monitor the coastal and terrestrial processes influencing the two distinct seasonal and spatial cholera transmission cycles. It also provides a guideline for initiating preemptive efforts at intervention on the basis of the environmental signatures associated with the macroscale processes before cholera breaks out in potentially vulnerable areas. In addition, the study outlines a new scope for using dry season water management as a tool for preventing cholera and other diarrheal diseases in specific areas, which may yield significant and widespread public health benefits throughout the year, thus creating useful actionable knowledge for water management and public health officials in Bangladesh.

References

Ahmed, R., and S. Karmakar (1993), Arrival and withdrawal dates of the summer monsoon in Bangladesh, *Int. J. Climatol.*, *13*, 727–740, doi:10.1002/joc.3370130703.

Akanda, A. S., A. S. Jutla, and S. Islam (2009), Dual peak cholera transmission in Bengal Delta: A hydroclimatological explanation, *Geophys. Res. Lett.*, *36*, L19401, doi:10.1029/2009GL039312.

Alam, M., et al. (2006), Seasonal cholera caused by *Vibrio cholerae* serogroups O1 and O139 in the coastal aquatic environment of Bangladesh, *Appl. Environ. Microbiol.*, *72*, 4096–4104, doi:10.1128/AEM.00066-06.

Bertuzzo, E., S. Azaele, A. Maritan, M. Gatto, I. Rodriguez-Iturbe, and A. Rinaldo (2008), On the space-time evolution of a cholera epidemic, *Water Resour. Res.*, *44*, W01424, doi:10.1029/2007WR006211.

Bertuzzo, E., et al. (2010), On spatially explicit models of cholera epidemics, *J. R. Soc. Interface*, *7*, 321–333, doi:10.1098/rsif.2009.0204.

Bouma, M. J., and M. Pascual (2001), Seasonal and interannual cycles of endemic cholera in Bengal 1891–1940 in relation to climate and geography, *Hydrobiologia*, *460*, 147–156.

Chamarthi, S., P. Ram, and L. Josyula (2008), Effect of river discharge on Bay of Bengal circulation, *Mar. Geod.*, *31*, 160–168, doi:10.1080/01490410802265476.

Chowdhury, M. R., and M. N. Ward (2004), Hydro-meteorological variability in the greater Ganges-Brahmaputra-Meghna basins, *Int. J. Climatol.*, *24*, 1495–1508, doi:10.1002/joc.1076.

Chun, J., et al. (2009), Comparative genomics reveals short-term and long-term clonal transitions in pandemic *Vibrio cholerae*, *Proc. Natl. Acad. Sci. U. S. A.*, *106*(36), 15,442–15,447, doi:10.1073/pnas.0907787106.

Cockburn, T. A., and J. G. Casanos (1960), Epidemiology of endemic Cholera, *Public Health Rep.*, *75*(9), 791–804, doi:10.2307/4590925.

Colwell, R., and A. Huq (2001), Marine ecosystems and cholera, *Hydrobiologia*, *460*, 141–145.

Colwell, R., et al. (1981), Occurrence of *V. cholerae* serotype O1 in Maryland and Louisiana estuaries, *Appl. Environ. Microbiol.*, *41*, 555–558.

Constantin de Magny, G., et al. (2008), Environmental signatures associated with cholera epidemics, *Proc. Natl. Acad. Sci. U. S. A.*, *105*(46), 17,676–17,681, doi:10.1073/pnas.0809654105.

Emch, M., et al. (2008), Local environmental predictors of cholera in Bangladesh and Vietnam, *Am. J. Trop. Med. Hyg.*, *78*(5), 823–832.

Gil, A. I., et al. (2004), Occurrence and distribution of *Vibrio cholerae* in the coastal environment of Peru, *Environ. Microbiol.*, *6*, 699–706, doi:10.1111/j.1462-2920.2004.00601.x.

Glass, R. I., et al. (1982), Endemic cholera in rural Bangladesh: 1966–1980, *Am. J. Epidemiol.*, *116*(9), 959–970.

Goswami, B., et al. (2006), Increasing trend of extreme rain events over India in a warming environment, *Science*, *314*, 1442–1445, doi:10.1126/science.1132027.

Hashizume, M., et al. (2008), The effect of rainfall on the prevalence of cholera in Bangladesh, *Epidemiology*, *19*(1), 103–110, doi:10.1097/EDE.0b013e31815c09ea.

Hoque, M. A., M. S. Sarkar, S. A. Khan, M. A. Moral, and A. K. Khurram (2006), Present status of salinity rise in Sundarbans area and its effect on Sundari species, *Res. J. Agric. Biol. Sci.*, *2*(3), 115-121.

Huq, A., and R. R. Colwell (1996), Vibrios in the marine and estuarine environment: Tracking *Vibrio cholerae*, *Ecosyst. Health*, *13*(9), 198–214.

Huq, A., et al. (1984), Influence of water temperature, salinity, and pH on survival and growth of toxigenic *Vibrio cholerae* serovar O1 associated with live copepods in laboratory microcosms, *Appl. Environ. Microbiol.*, *48*, 420–424.

Huq, A., et al. (1990), Detection of *Vibrio cholerae* O1 in the aquatic environment by antibody and culture, *Appl. Environ. Microbiol.*, *56*, 2370–2373.

Huq, A., et al. (2005), Critical factors influencing the occurrence of *Vibrio cholerae* in the environment of Bangladesh, *Appl. Environ. Microbiol.*, *71*, 4645–4654, doi:10.1128/AEM.71.8.4645-4654.2005.

Islam, M. S., et al. (2006), Faecal contamination of drinking water sources of Dhaka city, *J. Appl. Microbiol.*, *103*, 80–87.

Islam, M. S., et al. (2009), Effects of local climate variability on transmission dynamics of cholera in Matlab, Bangladesh, *Trans. R. Soc. Trop. Med. Hyg.*, *103*(11), 1165–1170, doi:10.1016/j.trstmh.2009.04.016.

Islam, S. N., and A. Gnauck (2008), Mangrove wetland ecosystems in Ganges-Brahmaputra Delta in Bangladesh, *Front. Earth Sci. China*, *2*(4), 439–448, doi:10.1007/s11707-008-0049-2.

Jutla, A. S., A. S. Akanda, and S. Islam (2010), Tracking cholera in coastal regions using satellite observations, *J. Am. Water Resour. Assoc.*, *46*(4), 651–662.

Koelle, K., X. Rodo, M. Pascual, M. Yunus, and G. Mostafa (2005), Refractory periods and climate forcing in cholera dynamics, *Nature*, *436*, 696–700.

Lipp, E. K., A. Huq, and R. R. Colwell (2002), Effects of global climate on infectious disease, *Clin. Microbiol. Rev.*, *15*(4), 757–770, doi:10.1128/CMR.15.4.757-770.2002.

Longini, I. M., M. Yunus, K. Zaman, A. K. Siddique, R. B. Sack, and A. Nizam (2002), Epidemic and endemic cholera trends over a 33-year period in Bangladesh, *J. Infect. Diseases*, *186*, 246–251, doi:10.1086/341206.

Louis, V., et al. (2003), Predictability of Vibrio cholerae in Chesapeake Bay, *Appl. Environ. Microbiol.*, *69*, 2773–2785.

Milly, P. C. D., K. A. Dunne, and A. V. Vecchia (2005), Global pattern of trends in streamflow and water availability in a changing climate, *Nature*, *438*, 347–350, doi:10.1038/nature04312.

Mirza, M., R. Warrick, N. Ericksen, and G. Kenny (2001), Are peak flows getting worse in Ganges, Brahmaputra and Meghna?, *Environ. Hazards*, *3*, 37–48, doi:10.3763/ehaz.2001.0305.

Pascual, M., X. Rodo, S. P. Ellner, R. R. Colwell, and M. J. Bouma (2000), Cholera dynamics and El Niño-Southern Oscillation, *Science*, *289*, 1766–1769, doi:10.1126/science.289.5485.1766.

Rahman, M., et al. (2000), Environmental impact assessment on water quality deterioration caused by decreased Ganges flow, *Environ. Geol.*, *40*, 31–40, doi:10.1007/s002540000152.

Reynolds, R., and T. Smith (1994), Improved global sea surface temperature analyses using optimum interpolation, *J. Clim.*, *7*, 929–948, doi:10.1175/1520-0442(1994)007<0929:IGSSTA>2.0.CO;2.

Ruiz-Moreno, D., et al. (2010), Spatial clustering in the spatio-temporal dynamics of endemic cholera, *BMC Infect. Dis.*, *10*, 1–12, doi:10.1186/1471-2334-10-51.

Sack, R., et al. (2003), A 4-year epidemiology study of *Vibrio cholerae* in four rural areas of Bangladesh, *J. Infect. Dis.*, *187*, 96–101, doi:10.1086/345865.

Sack, D. A., et al. (2004), Cholera, *Lancet*, *363*, 223–233, doi:10.1016/S0140-6736(03)15328-7.

Schwartz, B., et al. (2006), Diarrheal epidemics in Dhaka, Bangladesh, during three consecutive floods: 1988, 1998, 2004, *Am. J. Trop. Med. Hyg.*, *74*(6), 1067–1073.

Siddique, A. K., et al. (1994), Emergence of a new epidemic strain of *Vibrio cholerae* in Bangladesh, *Trop. Geogr. Med.*, *46*(3), 147–150.

Siddique, A. K., et al. (2010), El Tor cholera with severe disease: A new threat to Asia and beyond, *Epidemiol. Infect.*, *138*(3), 347–352, doi:10.1017/S0950268809990550.

Singleton, F. L., et al. (1982a), Influence of salinity and organic nutrient on survival and growth of *Vibrio cholerae*, *Appl. Environ. Microbiol.*, *43*, 1080–1085.

Singleton, F. L., et al. (1982b), Effects of temperature and salinity on *Vibrio cholerae* growth, *Appl. Environ. Microbiol.*, *44*, 1047–1058.

Stine, O., et al. (2008), Seasonal cholera from multiple small outbreaks, rural Bangladesh, *Emerging Infect. Dis.*, *14*(5), 831–833, doi:10.3201/eid1405.071116.

Vital, M., H. Fuchslin, F. Hammes, and T. Egli (2007), Growth of *Vibrio cholerae* O1 Ogawa Eltor in freshwater, *Microbiology*, *153*, 1993–2001, doi:10.1099/mic.0.2006/005173-0.

Wahid, S., M. Babel, and A. Bhuiyan (2007), Hydrologic monitoring and analysis in Sundarbans mangrove ecosystem, Bangladesh, *J. Hydrol.*, *332*, 381–395, doi:10.1016/j.jhydrol.2006.07.016.

Worden, A. Z., et al. (2006), Trophic regulation of *Vibrio cholerae* in coastal marine waters, *Environ. Microbiol.*, *8*, 21–29, doi:10.1111/j.1462-2920.2005.00863.x.

A. S. Akanda, S. Islam, and A. S. Jutla, Water and Environmental Research, Education, and Actionable Solutions Network, Department of Civil and Environmental Engineering, Tufts University, Medford, MA 02155, USA. (shafiqul.islam@tufts.edu)

M. Alam and A. K. Siddique, International Center for Diarrhoeal Disease Research, GPO Box 128, Dhaka 1000, Bangladesh.

R. R. Colwell and G. C. de Magny, Center for Bioinformatics and Computational Biology, University of Maryland, College Park, MD 20742, USA.

A. Huq, Maryland Pathogen Research Institute, University of Maryland, College Park, MD 20742, USA.

R. B. Sack, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD 21205, USA.