



Cholera in Times of Chaos

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Cholera is a deadly, diarrheal disease that has been recognized for millennia. It is caused by a gram-negative, toxigenic organism, *Vibrio cholerae*, which is found in aquatic environments. The disease is characterized by watery diarrhea that is so voluminous that daily fluid losses in adults are measured in liters. Without interventions, this disease can result in profound dehydration, hypovolemic shock and death. Death is most commonly seen in infants and young children, especially those who are malnourished, because of the rapidity with which dehydration and shock can occur.

Although cholera outbreaks have not occurred in the U.S. in the last 100 years, the disease remains a significant global health concern in many countries around the world, which has been enduring its 7th cholera pandemic, since 1961. Recent outbreaks in Haiti provide a clear example of how geopolitical, environmental and anthropological factors can compound to the level of polycrisis and act as key drivers of the disease.



Broad Street pump with handle removed.

Source: [wikimedia Commons](#)

***V. cholerae* Pathogenesis**

How does *V. cholerae* cause such severe diarrhea? The bacterial pathogen colonizes host intestines and produces an enterotoxin (called cholera toxin). That toxin enters enterocytes, where it activates adenylate cyclase, leading to an increased level of cyclic AMP. A major impact of increased cyclic AMP levels is activation of protein kinase A, resulting in an efflux of chloride and bicarbonate ions and water into the lumen of the small intestine.

An additional impact of cholera toxin is the blockage of sodium and potassium ion uptake, which reduces water reabsorption in the small intestine and colon. The efflux of electrolytes and water is responsible for the high volume, watery stools that occur, and the higher the stool volume in relation to body mass, the more severe the clinical disease of cholera becomes.

Mapping Cholera with John Snow

The first recognized cholera pandemic began in India in 1817, and the genesis of the field of epidemiology is a result of Dr. John Snow's observation during a cholera outbreak in 1854 London. Snow mapped each cholera death in the Soho region of London in late summer of 1854. He noticed that the cases were primarily found in areas surrounding the Broad Street pump marked by an "X" on this map. When he removed its pump handle, thereby preventing people from drinking the *V. cholerae* contaminated water, the number of cases declined.

Subsequent studies of other metropolitan London outbreaks



John Snow's cholera map. "X" indicates the location of the Broad Street pump.

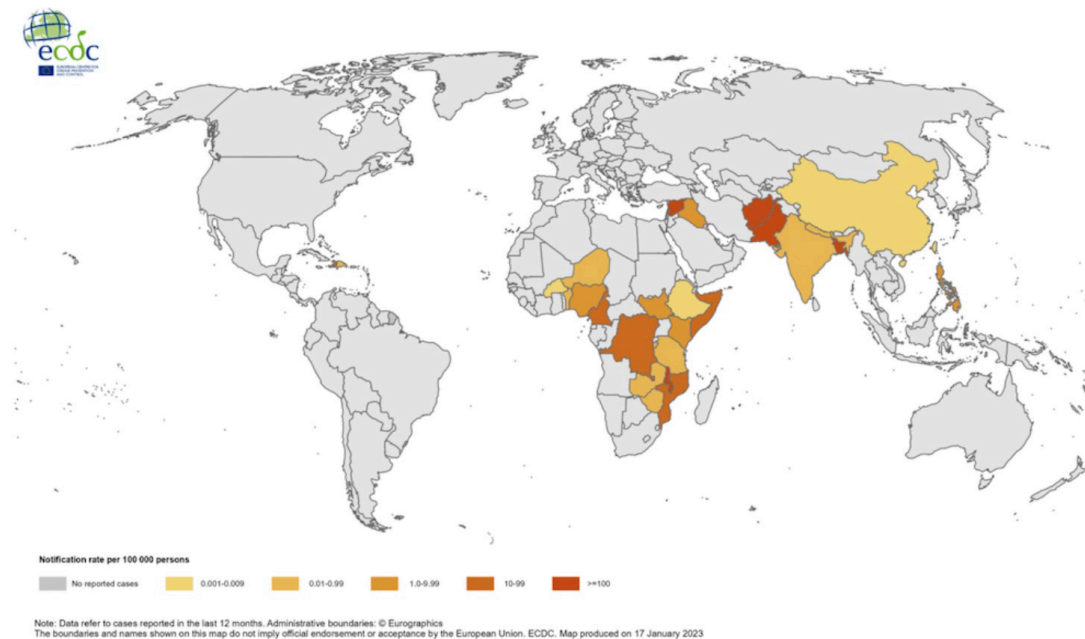
Source: [wikimedia Commons](#)

by Snow also implicated water as the source of cholera. Ingestion, primarily of water, but also food contaminated with feces from *V. cholerae*-infected individuals, is the major mode of transmission. These observations resulted in infrastructure improvements in potable water treatment and human sewage disposal throughout the industrialized world.

Such improvements have prevented cholera outbreaks in the United States for well over a century, even though the organism is present in U.S. estuarine water sources, and natural disasters, such as flooding associated with tropical storms, are common. For example, in August 2005, after one of the worst hurricanes in U.S. history, which devastated the Gulf Coast of Mississippi, Louisiana and parts of Texas, only 2 cases of cholera were reported, even though *V. cholerae* is found throughout the Gulf Coast estuary.

Cholera Is a Disease of Poverty, Natural Disasters and Political Violence

Although cholera outbreaks have not occurred in the U.S. in the last 100 years, the disease remains a significant global health concern in many countries around the world. The world is now in its 7th cholera pandemic, which started in 1961. The map below shows where cholera outbreaks occurred or were ongoing in 2022.



Geographical distribution of cholera cases from Jan. 2022-Jan2023.

Source: European Center for Disease Control and Prevention

Notably, the number of countries with cholera outbreaks increased from 23 in 2021, to 29 in 2022. This is particularly disheartening since the World Health Organization (WHO) has a 2030 goal to reduce the number of cases of cholera globally by 90%. The outbreaks predominately occur in lower and lower-middle income countries, where large portions of the population have limited or no access to clean water and sewage disposal. The spread of this disease has been exacerbated by flooding due to tropical storms (Malawi and Mozambique), monsoon rains (Pakistan and Bangladesh) and political violence (9 countries primarily in Africa and the Middle East).

Author and reporter, Thomas Friedman, describes the 21st century as being divided into a world of “order” and “disorder.” In the world of order, cholera essentially does not occur because that world has infrastructure that provides clean water, sanitation and civil order. In times of crisis (disorder), such as flooding, tropical storms or earthquakes, resources to provide clean water, sanitation and hygiene (a.k.a. W.A.S.H.) can be quickly supplied by an ordered society and health care workers; and, if necessary, security forces can be deployed.

The 2022 Haitian cholera outbreak is a prime example of what happens when this organism is introduced into the world of disorder. Because of widespread political violence, the poorest portion of the population does not have access to clean water, sanitation hygiene or medical care. As a result, Haiti is in the midst of another deadly cholera outbreak, only months after Haiti was declared cholera-free since the last outbreak that started in 2010.

The Tragedy of Cholera in Haiti

Prior to the catastrophic January 2010 earthquake, Haiti had been cholera free for over a century. However, the earthquake caused catastrophic damage to Haiti’s infrastructure, including water treatment and sewage disposal, leading to consumption of *V. cholerae* contaminated water. During relief efforts following the earthquake, a camp for UN peacekeepers from Nepal was established in early October near the Artibonite River. Within days, cases of cholera were being reported downstream from the camp. Molecular studies showed that a strain common in Nepal was responsible for the cholera outbreak in Haiti. Since *V. cholerae* can be carried asymptotically, the most likely explanation for the source of the outbreak was that the Nepalese peacekeepers carried the organism into Haiti and improperly disposed fecal waste from the camp, contaminating the Artibonite River used as a drinking water source by the population downstream from the camp.

Over the next months, cholera spread throughout Haiti and to its neighbor on the island of Hispaniola, the Dominican Republic. Over the next 9 years, Haiti experienced 820,000 cholera cases and close to 10,000 deaths. This epidemic concluded in January of 2019 and by January 2022, the WHO again judged Haiti to be “cholera-free.”

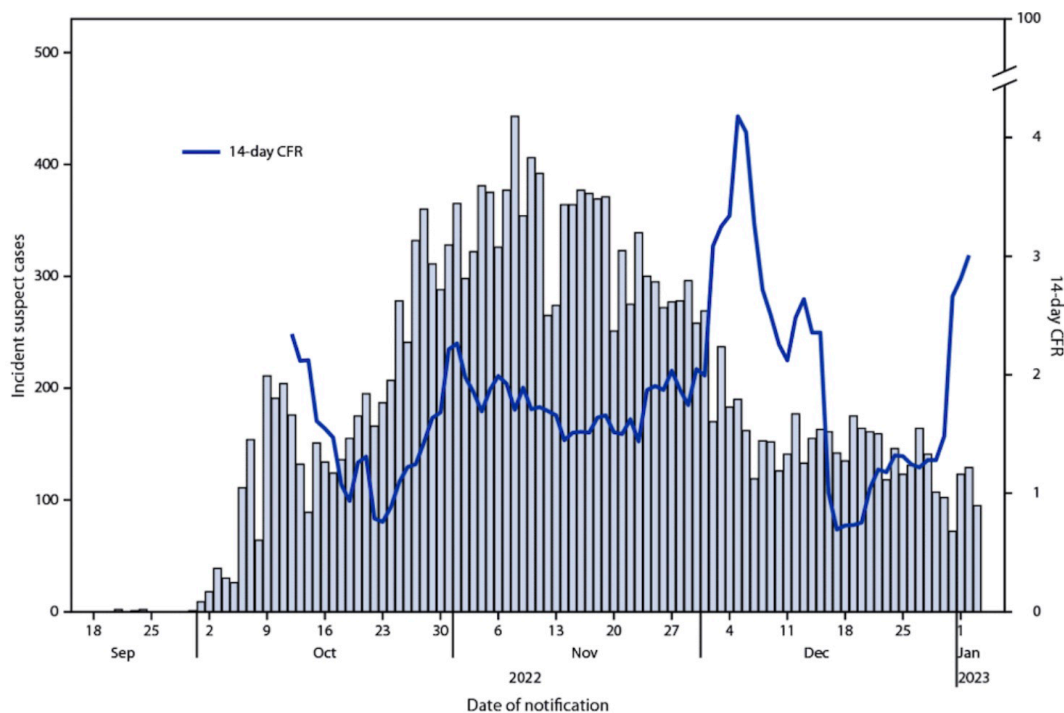
Why the 2022 Resurgence of Cholera in Haiti?

Sadly, that period of being cholera-free only lasted for a little more than 7 months before new cases of cholera were reported in late September 2022 in the impoverished Citi Soleil neighborhood in the capital, Port au Prince. Molecular studies showed that the strain responsible for the current outbreak was genetically highly related to the strain responsible for the 2010-2019 epidemic.

The event that triggered this resurgence was the assassination of the Haitian President, Jovenel Moïse, in July 2021. Since then, the capital, Port-au-Prince has been wracked with violence centered around the large town of Citi Soleil, where 200,000-400,000 individuals live in extreme poverty without clean water or sanitation. Furthermore, political unrest and violence resulted in blockage of the major fuel depot in Port-au-Prince for several weeks during the onset of the epidemic. Since public hospitals in Port-au-Prince depended on electricity provided by generators, fuel shortages shuttered hospitals, limiting access to care.

Today, citizens in Citi Soleil still have very limited access to clean water and sewage disposal, inadequate food supplies and mountains of trash. It is estimated that over half of the Haitian population is facing “acute hunger,” and an ever-increasing number of children are facing “catastrophic hunger/famine,” especially those living in Cite Soleil. Children suffering from malnutrition due to catastrophic hunger have compromised innate immunity, making them highly vulnerable to cholera.

Ongoing violence makes it impossible to access health care at night, or to establish local cholera treatment centers because health care workers fear being killed or kidnapped. As a result, the most vulnerable do not have access to care that is taken for granted in much of the world where cholera is endemic.



Epidemiology of cholera in Haiti. September 2022–January 2023.

Source: CDC

As of January 2023, there have been an estimated 26,000 cases and over 500 cholera-associated deaths, resulting in a mortality rate of 2%, which is twice the rate that is expected in a cholera outbreak globally. Those numbers are likely much higher, but getting accurate data is next to impossible due to the ongoing violence.

Oral Rehydration Therapy to Treat *V. cholerae*

Both the epidemiology and pathogenesis of *V. cholerae* are well understood, and that understanding has led to the development of strategies to control and treat cholera.

The recognition that glucose-mediated sodium and fluid absorption occurred by a cAMP-independent pathway was central to the development of oral rehydration solution (ORS) to treat cholera. This therapy is also effective against enterotoxigenic *Escherichia coli* (ETEC), which produces a heat labile enterotoxin that has similar structure and mechanism of action to that of cholera toxin. ETEC is an important cause of diarrheal disease in children globally.

The current WHO recommendation for oral rehydration therapy is to use fluids made from rehydration packets containing table salt (NaCl), potassium chloride, sodium citrate and glucose dissolved in water. If rehydration packets are not available, a

solution of table salt and sugar can be used. ORS is inexpensive, easily administered and widely available globally.

Preventing Further Cholera Outbreaks

Taking measures to prevent further outbreaks is key to addressing the ongoing pandemic. There are 3 basic strategies that are applied to combating cholera outbreaks:

1. Establishing local cholera treatment centers.
2. W.A.S.H.—providing clean water, sanitation and hygiene for the affected population.
3. Providing oral cholera vaccine (OCV) to prevent cholera in the at-risk population.

Unfortunately, many of these solutions are not currently available to the poorest regions in the world, including Haiti. All 3 of the above strategies are extremely challenging to implement in the Haitian outbreak, but limits to OCV supply have been especially impactful. OCV is typically given in 2 doses and is found to have good efficacy for at least 2 years. However, because of the large number of 2022 global cholera outbreaks, and concerns about exhausting the global ORV stockpile, WHO and global partners took the unprecedented step in October 2022 of recommending that only 1 dose of vaccine be given in outbreak settings. This is a drastic step, given the fact that 1-dose efficacy is known to be much shorter, perhaps offering no more than 1 year of protection. The Haiti Ministry of Public Health and Population, working with Doctors without Borders, is distributing 1.2 million doses of OCV in the most impacted regions.

What Is the Global impact of Haitian Outbreak?

The Haiti outbreak is a quintessential example of a polycrisis, a recent term coined by social scientists. The combination of several crises in Haiti, including political violence, lack of potable water, widespread malnutrition, inadequate sanitation, medical supply chain disruption and lack of personal security for medical personnel and patients, have resulted in the current cholera polycrisis. By definition, a polycrisis has global impact, and the tragedy in Haiti is no exception.

Meanwhile, in Syria, a February 2023 earthquake impacted a region where a cholera outbreak was ongoing, and had already caused 70,000 cases, due to destruction of water and sanitary infrastructure during its 2019 civil war. The specter of an epidemic widening to impact the neighboring earthquake-stricken area of Turkey is of concern. The outbreak in Haiti has required the use of the current global supply of OCV. If the

Syrian outbreak widens, an essential tool for controlling this outbreak will not be available.

Furthermore, the crisis brought on by the political violence and cholera outbreak in Haiti has increased Haitian migration to the Mexican/U.S. border. As a result, the U.S. has doubled the number of Haitian citizens who may apply for temporary protected status (TPS). Under TPS, individuals cannot be deported and may apply for work permits, but they are not permanent residents of the U.S. They must leave the U.S. if it is judged that it is safe to return to their country of origin. For those who wish to become permanent residents, they must apply by leaving the U.S. and re-entering legally. It is expected that by the end of the program in 2024, TPS will be granted to 220,000 people.

Our scientific understanding of cholera has given humanity in the world of order effective strategies for prevention, treatment and control of cholera, but, when chaos is afoot, cholera continues to be a formidable foe.

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