Nepalese origin of cholera epidemic in Haiti

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Abstract

Cholera appeared in Haiti in October 2010 for the first time in recorded history. The causative agent was quickly identified by the Haitian National Public Health Laboratory and the United States Centers for Disease Control and Prevention as *Vibrio cholerae* serogroup O1, serotype Ogawa, biotype El Tor. Since then, >500 000 government-acknowledged cholera cases and >7000 deaths have occurred, the largest cholera epidemic in the world, with the real death toll probably much higher. Questions of origin have been widely debated with some attributing the onset of the epidemic to climatic factors and others to human transmission. None of the evidence on origin supports climatic factors. Instead, recent epidemiological and molecular-genetic evidence point to the United Nations peacekeeping troops from Nepal as the source of cholera to Haiti, following their troop rotation in early October 2010. Such findings have important policy implications for shaping future international relief efforts.

Keywords: Cholera, disease transmission, epidemics, epidemiology, Haiti, infectious, *Vibrio cholerae*
Original Submission: 11 January 2012; **Revised Submission:** 10 March 2012; **Accepted:** 12 March 2012
Editor: D. Raoult
Article published online: 14 March 2012
Clin Microbiol Infect 2012; **18:** E158–E163
10.1111/j.1469-0691.2012.03841.x

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Introduction

The cholera epidemic in Haiti has been the world's largest such epidemic during recent decades, with 526 524 suspected cases and 7025 deaths reported by the Haitian government from mid-October 2010 through to January 2012 (Ministry for Public Health and Population (MSPP), Haiti, 20 January 2012). When the outbreak was first observed, immediate focus was on case management, water chlorination and hygiene awareness. Within 2 months, cholera cases were observed throughout the country [1], with dozens of deaths per day, peaking at more than 100 per day by mid-December, 2010 (MSPP, Haiti, 4 January 2011). Cholera had never been reported in Haiti [2] so many wondered where the pathogenic microbe came from.

Some scientists supported a climatic hypothesis for the origin of cholera in Haiti, arguing that *Vibrio cholerae* is primarily an aquatic bacterium, typically living dormant in coastal waters until an event disturbs the local environment and leads to a disease outbreak [3]. Noting that early cholera cases were reported in the Artibonite Valley near the Haitian coast, Professor David Sacks mentioned the climatic hypothesis to a reporter in late October 2010 [4]. According to the reporter, Sacks opined that the most likely explanation for the Haiti cholera outbreak was a rise in temperature and salinity in the river estuaries around the Bay of Saint Marc in the Artibonite Department of Haiti [2]. The climatic hypothesis was also supported by cholera expert Professor Rita Colwell [3,4]. Other people suspected a human source, the pathogen being brought from country where it was endemic, with early focus on United Nations (UN) peacekeeping troops who had recently settled in the country [5,6], and on non-governmental organizations [7]. The human hypothesis was first circulated by reporters from two different international news organizations who noticed serious sanitary problems in a military camp of MINUSTAH, the French abbreviation for the Haiti UN peacekeeping mission

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[5,6]. Although understanding whether the climatic or human hypotheses were true had no impact on the initial management of cholera in Haiti, the consequences of such understanding are vital for future prevention of similar disasters.

Methods

References were identified through searches of PubMed for articles, regardless of language, from October 2010 to December 2011, using the terms, 'origin of cholera in Haiti', 'cholera, Haiti' and 'vibrio cholera Haiti'. For the news articles, we employed Google search using the terms, 'cholera, origin, Haiti' and 'cholera Haiti Nepal' with equivalent words in English, French, Haitian Creole and Spanish. All internet items, searched on a weekly basis starting in December 2010, were computer-archived for subsequent retrieval in case the original citation was deleted.

The bibliographic research also involved the collection of available reports in the field, e-mail exchanges with reporters and scientists having potentially interesting information, direct discussions with physicians, microbiologists and epidemiologists involved in the treatment, diagnosis and investigation of the first cholera cases in Haiti, and meetings with sanitarian and political authorities in Haiti (including the President of Haiti, the Minister of Health, the special representative of the UN Secretary-General in Haiti, and the staff of MINUSTAH).

Three field investigations were conducted in Haiti by two of us (RB, RP). The first two were joint French–Haitian investigations, one in November 2010 and the second in April 2011. The third investigation was during the first year of the epidemic by the National Public Health Laboratory and the Department of Epidemic Surveillance of MSPP (i.e. following the epidemic and investigating new cholera foci) assisted by one of us (RB). The laboratory investigations of the Haitian isolates alone were performed by other researchers, and on similarly timed Haitian and Nepalese isolates by one of us (PSK).

Previous publications directly related to the assessment of the origin of cholera in Haiti are summarized in Table 1. Primary information refers to sources extensively addressed in the article, whereas the secondary information contains sources mentioned in the article but described more completely in the Supplementary material, Data S1 section.

TABLE 1. Previous publications on cholera in Haiti

Authors (reference number)	Type of investigation	Location[a]
Primary information		
Cravioto A, Lanata CF *et al.*, (8, S5)	Epidemiological	Haiti
Piarroux R, Barrais R *et al.*, (9, S7)	Epidemiological	Haiti
Hendriksen RS, Price LB *et al.*, (17)	Laboratory	Haiti, Nepal
Secondary information		
LNSP and CDC, (11, S11)	Laboratory	Haiti
Chin C, Sorenson J *et al.*, (12, S12)	Laboratory	Haiti
Ali A, Chen Y *et al.*, (13, S13)	Laboratory	Haiti
Reimer AR, Van Domselaar G, *et al.* (14, S15)	Laboratory	Haiti
Ceccarelli D, Spagnoletti M, *et al.* (15, S14)	Laboratory	Haiti

[a]Location of field investigation or time-similar specimens.
LNSP, National Public Health Laboratory; CDC, Centers for Disease Control.

Results

Background information

Background information is presented in detail in the Supplementary material (Data S1). Briefly, our findings shows that in early October 2010 a Nepalese contingent of UN peacekeepers with 1280 personnel was exposed to a cholera epidemic in Nepal either during the 3-month training period or, more probably, during a 10-day home visit before leaving for Haiti. Once they returned to their battalion to embark for Haiti, the soldiers were not subjected to a medical examination or stool testing. In Haiti, most of the soldiers were housed in a camp near Mirebalais and the remainder in two smaller settlements in neighbouring towns (Fig. 1). Sanitation conditions were assessed in the MINUSTAH camp near Mirebalais by a panel of scientists assembled by the UN to investigate the origin of the epidemic [8]. They reported many important hygiene deficiencies and concluded that the sanitation conditions were not sufficient to prevent faecal contamination of the neighbouring river, the water source for local cooking and drinking. Although the panel of scientists in their review of the camp's early medical records reported no cases of severe diarrhoea and dehydration, they made no mention of mild or moderate diarrhoea. In addition, no review was made of medical records of Nepalese troops assigned to the two other neighbouring camps. Septic wastewater from all three camps was trucked to and deposited in an open septic pit by the camp near Mirebalais, where the panel of scientists reported that the local river flowed 'a short walk down the hill from the pit' (see Fig. 1).

Epidemiological information

Several epidemiological field studies of cholera were conducted in Haiti, notably by investigators at CDC, but they did not address the origin issue, or the cause of the explosive outbreak that followed. There have only been two public documents addressing the origin of cholera in Haiti. One is a report by the panel of scientists appointed by the UN [8], and the other is an article published in a scientific peer-reviewed journal that relates the findings of two field investigations [9]. The first of the two field investigations was made in the Mirebalais region by a team of Haitian epidemiologists during

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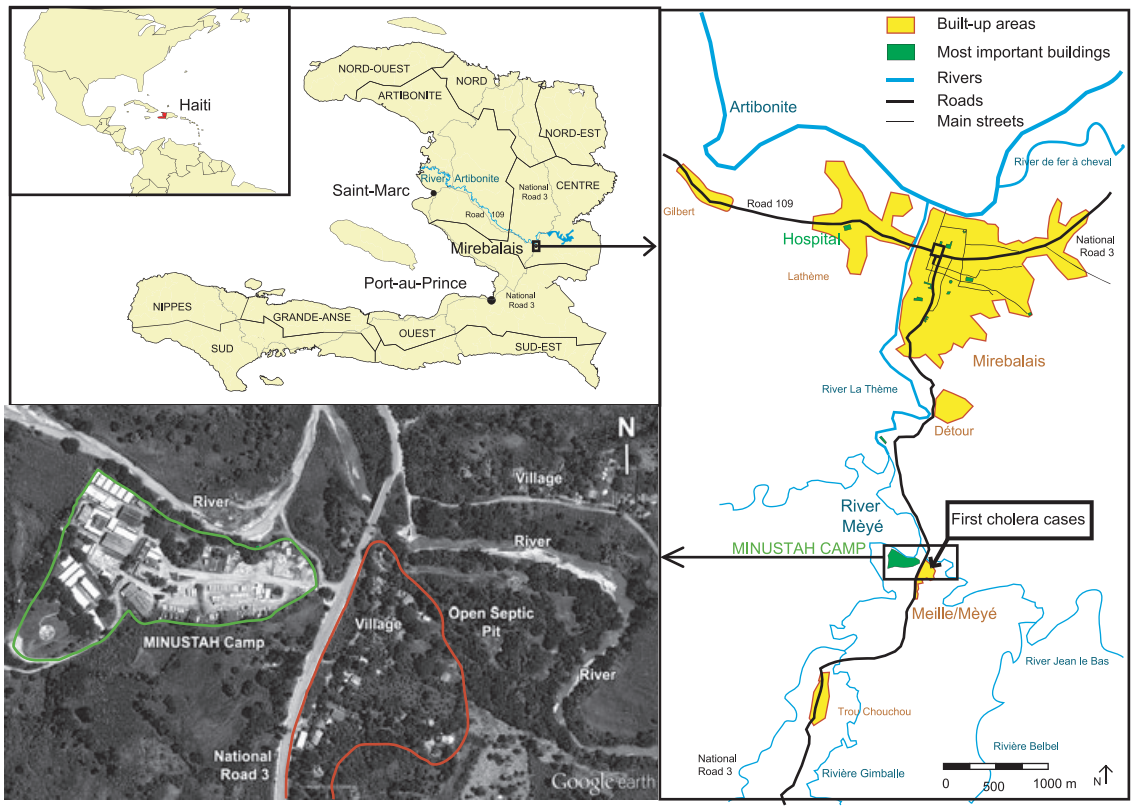


FIG. 1. Location of first cholera cases and Nepalese MINUSTAH camp near Mirebalais with villages, rivers and open septic pit (Google earth; Image © 2011 GeoEye; 8 September 2010).

19–24 October 2010. The second field investigation was conducted from 7 to 27 November 2010 by a joint research team from France and Haiti who travelled to the most affected areas of the country. The second team also performed spatiotemporal analyses that identified five significant cholera clusters. The first cluster was near Mirebalais (occurring 16–19 October). The second was along the lower Artibonite River (occurring 20–28 October). The third, fourth and fifth clusters, which will not be discussed here, were some distance north and south of the Artibonite River, caused by the centrifugal epidemic spread during November 2010 [9].

First cluster. On 18 October Cuban doctors working at the Mirebalais community hospital in central Haiti (see Fig. 1) reported an increase of acute watery diarrhoea (61 cases treated in Mirebalais during the preceding week) to MSPP. That same day, the situation worsened, with 28 new admissions and two deaths. MSPP immediately sent a Haitian investigation team [9]. This Haitian Investigation team formally identified the first cases, reporting that the epidemic began on 14 October 2010 (i.e. 5 days after the arrival of the first group of Nepalese troops). The first hospitalized patients were members of a family living in Meille (also spelled Mèyé), a small village 2 km south of Mirebalais (Fig. 1). On 19 October the investigators identified ten other cases in the 16 houses near the index family's house. Five of the six samples collected in Meille from these outpatients, who became sick during 14–19 October yielded *V. cholerae* O1, serotype Ogawa, biotype El Tor [9].

The space–time distribution of the early cholera cases is presented in Fig. 2. The first cluster of cases from 16 to 19 October is shown in the top row of Fig. 2, with all cases remaining in the Mirebalais region. During their field investigation, the Haitian epidemiologists also observed sanitary deficiencies at the MINUSTAH camp, including a pipe discharging sewage from the camp into the river. This finding is similar to what was reported by reporter Katz during his 27 October visit to the same location [6]. Both the Haitian epidemiologists and the reporter Katz noted that the villagers regularly used water from the River Meille/Mèyé for cooking and drinking. The Meille/Mèyé becomes the River La Thème and flows north into the Artibonite River at Mirebalais (see Fig. 1).

Following statistical analyses of the spatiotemporal clusters, the French and Haitian researchers wrote, 'Our epidemiologic study provides several additional arguments confirming an importation of cholera in Haiti. There was an exact correlation in time and places between the arrival of a Nepalese battalion from an area experiencing a cholera outbreak and the

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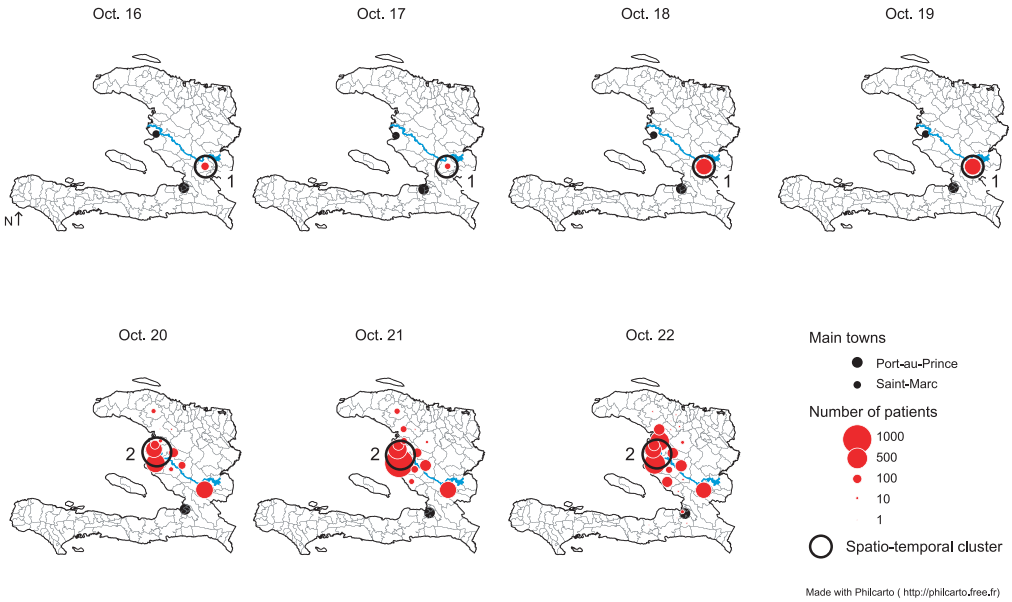


FIG. 2. Evolution of cholera cases during the first week of the Haitian cholera epidemic.

appearance of the first cases in Meille a few days after. The remoteness of Meille in central Haiti and the absence of report of other incomers make it unlikely that a cholera strain might have been brought there another way' [9]. The UN Panel, in their later investigation, agreed with the French and Haitian investigators on the epidemic's starting point when they concluded: 'the evidence overwhelmingly supports the conclusion that the source of the Haiti cholera outbreak was the result of contamination of the Meye Tributary of the Artibonite River with a pathogenic strain of current South Asian type *V. cholerae* as a result of human activity [8].'

Second cluster. Regarding the explosion of cases corresponding to the second significant cluster, the investigators reported that there no cholera cases were reported in the lower Artibonite River communes until after 19 October 2010 [9]. Field investigations showed that contamination of the seven communes of the lower Artibonite River occurred simultaneously (see bottom row of Fig. 2, 20–22 October). Their regression model indicated that the spread of cholera was strongly linked to the Artibonite River and not to the proximity to Mirebalais, as would be expected for road-dependent propagation. They also noted that the numbers of new cases and deaths dropped dramatically after only 2 days, suggesting a rapid decrease of the level of cholera contamination in the river [9]. These findings were also confirmed by members of the UN panel who stated 'This contamination [of the Meille/Mèyé tributary of the Artibonite River] initiated an explosive cholera outbreak downstream in the Artibonite River Delta, and eventually, throughout Haiti' [8].

As to what might have caused such a cholera-contaminated sewage plume in the Artibonite River, Piarroux *et al.* [9] were cautious in their interpretation, but noted that an explosive pattern was compatible with rumours that held the dumping of a septic tank responsible for the epidemic [10]. Yet they pointed out that the exact event that provoked the massive contamination of Lower Artibonite could not be definitively deduced from an epidemiological study.

Molecular-genetic evidence

Several tools were used to characterize the isolates collected during the Haitian cholera epidemic and to compare them with isolates of other epidemics. These tools were either pulse-field electrophoresis, or analysis of variable-number tandem-repeats also called multiple-locus variable-number tandem-repeat analysis (MLVA), or partial genome sequencing or whole genome sequence typing (WGST). Most of the published analyses were performed only for isolates from Haiti. A detailed review of these Haiti-only analyses is presented in the Supplementary material (Data S1) but briefly summarized here. Overall, the microbial studies of the Haitian isolates exhibited very few polymorphisms, showing that the cholera was likely to have been brought to Haiti by a single source or event [8], probably from South Asia [11–14]. In addition, one study reported that the Haitian isolates were similar, but not totally identical, to an altered El Tor *V. cholerae* variant which was first isolated during an epidemic in north India in 2007 [15]. Time-similar isolates from both Haiti and Nepal were included in two studies, one published and the other not, and are presented in the following section.

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Isolates from Nepal and Haiti

Cravioto A et al., Kim DW 2011. In their unpublished report on the 2010 Haiti cholera epidemic, the panel of scientists appointed by the UN included a section entitled 'recent preliminary data from Nepal strains' [8]. They wrote of their correspondence with Dr Dong Wook Kim of the International Vaccine Institute in Korea on the availability in Korea of Nepal strains from 2007 to 2010 of *V. cholerae* O1. In this group of specimens they mentioned two Ogawa strains isolated in Nepal in 2010, and stated that they were being compared with seven Ogawa strains isolated in Haiti in 2010, but the more definitive whole genome sequence analysis is still 'in process'. The panel of scientists did state, however, that in the interim a simpler genetic typing method was used, namely MLVA. They wrote, 'A careful analysis of the MLVA results and the *ctxB* gene indicated that the strains isolated in Haiti and Nepal during 2009 were a perfect match.' This information was widely circulated in the news media, as evidence that the cholera organisms in the two countries were genetically linked. One of us (RRF) wrote to Dr Dong Wook Kim to confirm this statement.

Dr Kim clarified in his email that the 'perfect match' was with strains isolated in Haiti and Nepal in 2010, not 2009 as stated in the UN report (R. Frerichs, personal communication, 19 July 2011). Hence this represents the first acknowledged comparative analysis of a 2010 cholera specimen from Nepal time-linked with a 2010 specimen from Haiti, although not published. He further stated that the MLVA method used in the analysis is described by Choi *et al.* [16].

Hendriksen RS et al., 2011. This is the only analysis of time-related specimens from both Nepal and Haiti that has appeared in a peer-reviewed scientific publication [17]. The authors analysed 24 *V. cholerae* isolates from five different districts in Nepal, provided by officials of the Nepalese National Public Health Laboratory. The cases occurred in Nepal from 30 July to 1 November 2010. The investigators compared the 24 genomes of the Nepal isolates with 10 genomes of previously sequenced *V. cholerae* isolates, including three from the Haitian outbreak. Using WGST, a powerful tool that provides an almost complete picture of genetic polymorphisms, they showed that all 24 *V. cholerae* isolates from Nepal belonged to a single monophyletic (i.e. sharing a common ancestor) group that also contained isolates from Bangladesh and Haiti. The 24 Nepalese isolates were then phylogenetically divided into four closely related genotypic clusters. One such cluster contained three Nepalese isolates (collected on 1 and 30 August 2010 in the Banke and Rupandehi districts of south-central Nepal), and three Haitian isolates collected by CDC and provided by National Center for Biotechnology Information. All six isolates were almost identical, with only one or two base-pair differences [17]. The investigators emphasized that these findings, the first of Haiti–Nepal isolates using the powerful WGST method, are consistent with Nepal as the origin of the Haitian outbreak.

However, the authors offered some words of caution. They stated, 'Attribution of outbreak sources based upon WGST alone requires comprehensive geographic strain collections. The current conclusion that Nepal is the source of the Haitian cholera outbreak can be reached only if both classical epidemiology and highly suggestive WGST are used together' [17]. As presented here, such 'classical epidemiology' now exists [9], along with background information provided by journalists and others, all pointing to Nepalese UN peacekeepers as the initial source of cholera in Haiti.

Discussion

The UN Panel assigned to investigate the origin of the Haiti cholera epidemic wrote in their May 2011 report, 'the evidence overwhelmingly supports the conclusion that the source of the Haiti cholera outbreak was due to contamination of the Meye Tributary of the Artibonite River with a pathogenic strain of current South Asian type *V. cholerae* as a result of human activity' [8]. We agree, but feel our findings support more specific conclusions.

The evidence that the Nepalese UN peacekeeping troops brought cholera to Haiti appears particularly strong, based on background events and published epidemiological and molecular genetic investigations. The soldiers came from Nepal where a cholera outbreak had just occurred. The soldiers were not tested for cholera, either before they left Nepal or when arriving in Haiti. A few days after they arrived, cases of cholera appeared in the village next to the UN camp housing the new Nepalese troops. Local people had complained to journalists that pipes from the camp leaked faecal waste into the river, and the Haitian company responsible for waste disposal at the UN camp was seen dumping waste from its truck outside the usual location (see the Supplementary material, Data S1). Finally, a waste septic pit on a hilltop near the UN camp was found to allow waste fluids to seep down into the nearby river.

The laboratory-based analyses comparing specimens obtained from both Nepal and Haiti gave clear results. After correcting the typographic date error, the report from the UN panel reads, 'the strains isolated in Haiti and Nepal during 2010 were a perfect match'. Nevertheless these preliminary results were further confirmed using the 'most powerful molecular approach imaginable … setting a new standard for

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infectious disease epidemiology [17].' As stated by Hendriksen RS *et al.*, 'this molecular phylogeny reinforces the previous epidemiological investigation—of Piarroux *et al.* [9]—that pointed towards UN peacekeepers from Nepal as the source of the Haitian cholera epidemic' [17].

At this juncture, there is no more scientific evidence to be gleaned. The only missing findings would have been cholera tests of the Nepalese UN troops at the onset of the epidemic. An attempt to do such testing was made on 21 October 2010, but was unsuccessful. During their initial investigation of the Mirebalais outbreak, the Haitian public health team met the doctor of the UN camp by Meille. He told them that none of the peacekeepers showed symptoms of cholera, but the Haitian public health team was not allowed to examine the soldiers.

In conclusion, the onset of cholera in Haiti was not the result of climatic factors and was not the direct consequence of the January 2010 earthquake. All of the scientific evidence shows that cholera was brought by a contingent of soldiers travelling from a country experiencing a cholera epidemic. Understanding what triggered the epidemic is important for preventing future occurrences, and acknowledges the right of Haitians to understand the events that led to their cholera devastation [18].

Acknowledgement

The authors wish to thank Martine Piarroux for creating Figures 1 and 2.

Transparency Declaration

The authors declare no conflict of interest of any nature.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Data S1. Context and circumstantial evidences.

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