



## A Cluster of Acute Diarrhea Suspected to Be Cholera in French Travelers in Haiti, December 2010

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A cluster of 21 cases of watery diarrhea suspected to be cholera that involved French military policemen and young volunteers occurring in the context of the Haiti cholera outbreak is described. The attack rate (AR) was higher among young volunteers (71.4%) than among policemen (15.3%) ( $p < 0.0001$ ). There was a significant association between raw vegetables consumption and watery diarrhea in the young volunteer group. If we consider the raw vegetables consumers only, AR was lower among doxycycline-exposed subjects (relative risk: 0.2; 95% confidence interval: 0.1–0.4). The main aspect that is of scientific interest is the potential prophylactic effect of doxycycline used for malaria prophylaxis on the watery diarrhea AR.

On October 21, 2010, the Haitian Ministry of Public Health and Population reported a cholera epidemic caused by *Vibrio cholerae* O1, serotype Ogawa, biotype El Tor. Antimicrobial susceptibility testing of selected *V. cholerae* O1 isolates conducted at the National Laboratory of Public Health and at Centers for Disease Control demonstrated susceptibility to tetracycline (susceptibility to this drug predicts doxycycline susceptibility).<sup>1</sup> This epidemic was surprising, as no cholera outbreak had been reported in Haiti for more than a century.<sup>1</sup> Piarroux et al. strongly suggest that contamination of the Artibonite river and one of its tributaries downstream from a military camp triggered the epidemic.<sup>2</sup> With more than 250,000 cases and 4,000 deaths in the first 6 months, the cholera epidemic in Haiti has been one of the most explosive and deadly in recent history.<sup>3</sup> The Haitian National cholera surveillance system defined a case as profuse, acute, watery diarrhea in a resident of a *département* in which at least one case of cholera had been laboratory-confirmed by isolation of *V. cholerae* from culture of a stool specimen.<sup>1</sup>

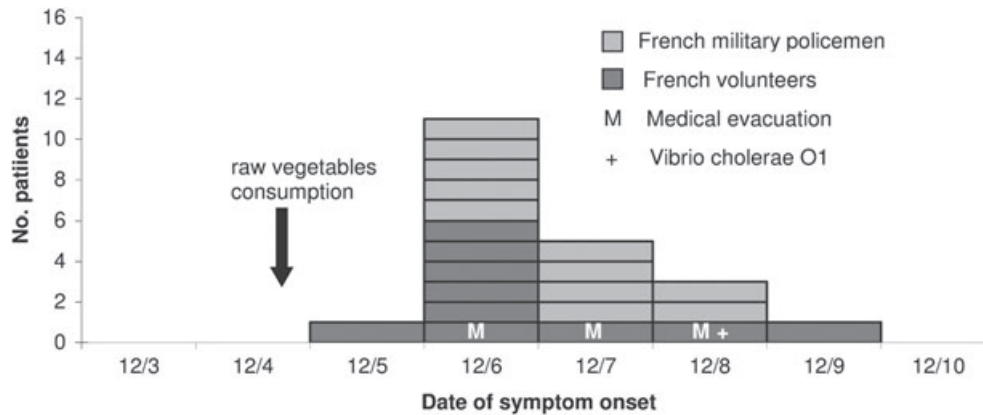
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This study describes an outbreak suspected to be cholera that occurred in Haiti from December 5 to 9, 2010 involving French military policemen and young health care volunteers who had arrived a few months previously in Haiti.

On December 7, 2010, acute cases of diarrhea were notified in a group of young French health care volunteers. This group had been living in the same site in Port au Prince as a squadron of French military policemen, with meals delivered by a Haitian company. Neither of these two populations had been in charge of the care of cholera patients.

A retrospective cohort study was performed on these two groups to determine the source of infection, using a standardized questionnaire asking about symptoms, risk exposure (food consumption and beverages from December 3 to 6), and chemoprophylaxis for malaria (100 mg doxycycline in the French Armed Forces). Due to operational imperatives, the French Armed Forces are liable to move rapidly from one operational theatre to another in case of emergency needs. This is why doxycycline was chosen as the sole antimalarial prophylaxis in the French Armed Forces. A case was defined as a person with acute watery diarrhea from December 3 to 9.

A total of 21 persons met the case definition (attack rate (AR): 24.4%). The AR was higher among the young volunteers [71.4% (10/14)] than among the policemen



**Figure 1** Dates of symptom onset among 11 French military policemen and 10 French health care volunteers with watery diarrhea, Port au Prince, Haiti, December 2010.

[15.3% (11/72)] ( $p < 0.0001$ ). The onset of symptoms occurred between December 5 and 9 (peaking on December 6 in the morning) (Figure 1). Symptoms were profuse watery diarrhea without blood (100.0%), nausea (85.7%), abdominal pain (78.6%), and vomiting (64.3%). The median number of stools per day was 10 (range 3–30). Fever was observed in one person. Three young volunteers were evacuated to Fort de France University hospital because of dehydration. None of the policemen needed hospitalization or medical evacuation. All patients had a favorable outcome.

Because of poor laboratory resources, no stool samples could be analyzed in Haiti. Stool samples from the three young volunteers evacuated were collected a few days after the onset of symptoms by the bacteriology laboratory in Fort de France University hospital in Martinique (a French overseas *département* in the eastern Caribbean). Culture by plating on selective media following hyperalkaline peptone water enrichment enabled the isolation of bacterial colonies suggestive of *V. cholerae* from one of the three samples. This presumptive identification was later confirmed by bacteriological, serological, and molecular methods by the National Reference Centre for Vibrios and Cholera as a variant of *V. cholerae* biotype El Tor, serogroup O1, serotype Ogawa. Susceptibility to tetracycline was confirmed by MIC determination (MIC 2 mg/L) using Etest (AB bioMérieux, Solna, Sweden) according to the Clinical and Laboratory Standards Institute procedures and interpretative standards for *V. cholerae*.<sup>4</sup> This positive case was a nurse from the young volunteer group evacuated to Fort de France hospital, and she had treated the other sick volunteers a few days before becoming symptomatic (onset on December 8) (Figure 1). The two other samples were negative for *V. cholerae* serogroup O1 but they were collected after antibiotic treatment received in Haiti. No sample was collected from policemen in Haiti.

Raw vegetables delivered by a Haitian company were served on the evening of December 4 (Figure 1). AR was higher among consumers of raw vegetables (81.8%) than

among nonconsumers (0.0%) ( $p = 0.07$ ) in the young volunteer group. There was no association between illness and raw vegetables consumption in the police group (AR: 16.0 vs 17.6%,  $p = 0.6$ ). Drinking water for the two groups was bottled, in packs. The young volunteer group also used a water cooler, and during the week before the onset of symptoms they had probably used bottled water having broken seals. But this mode of transmission could not explain the AR in the police group. No analysis of food, water, or food preparation processes was performed.

Regarding doxycycline prophylaxis, 91.0% of the policemen were fully compliant. None of the young volunteers was receiving chemoprophylaxis against malaria. If we consider the raw vegetables consumers only, AR was higher among young volunteers (81.8%) than among policemen (16.0%) (relative risk: 5.1; 95% CI: 2.6–10.2) and lower among doxycycline-exposed subjects (14.9%) than among nonexposed subjects (71.4%) (relative risk: 0.2; 95% CI: 0.1–0.4). Furthermore, the diarrhea AR was lower among doxycycline compliant policemen (14.9%) than among nondoxycycline-compliant policemen (33.3%) ( $p = 0.4$ ).

These study results suggest a food-borne disease suspected to be cholera, and the role of doxycycline in the prevention of this outbreak. According to the Haiti surveillance case definition for cholera, a cluster of acute watery diarrhea cases with at least one laboratory-proven case is sufficient to count them as cholera cases. This means that the cases reported here would be counted as cholera cases. However, the evidence seems insufficient to consider them as confirmed cholera cases because of the lack of accurate information on the causative agent(s). If this cluster was proven to be a cholera attack, it would be the largest cluster ever recorded in a population of travelers (including volunteers).

Travelers to epidemic countries may be at an increased risk of contracting cholera if they consume contaminated food or water.<sup>5–6</sup> Doxycycline was one of the first antibiotics to be studied and to show effectiveness due to its broad spectrum coverage of

the pathogens that cause traveler's diarrhea.<sup>7,8</sup> The use of prophylactic antibiotics to prevent cholera is debatable.<sup>9</sup> Although it may reduce the risk of the disease, mass antibiotic prophylaxis is not recommended against cholera outbreaks, because it does not prevent contamination and is limited by contraindications, costs, and modes of administration.<sup>9</sup> Moreover, it increases the risk of developing resistance. Chemoprophylaxis can contribute to the widespread emergence and dissemination of antimicrobial resistance, as observed in Madagascar in 2000, where resistance to tetracycline developed following extensive use of the drug.<sup>10</sup> Tetracycline-resistant *V. cholerae* O1 isolates are being increasingly reported worldwide.<sup>11</sup> The value of selective chemoprophylaxis during a cholera epidemic depends on local circumstances and may be useful for members of a household, under the same roof and eating the same food as a cholera patient.<sup>12</sup> The role of chemoprophylaxis in limiting cholera epidemics is difficult to ascertain. Large-scale prophylaxis should be selective and limited to close contacts, in accordance with WHO recommendations, with strict application and monitoring of both integrated prevention procedures and antibiotic susceptibility. Nevertheless, antibiotics were extensively used, both for curative and prophylactic purposes, to prevent an explosive spread of the 2004 cholera epidemic in Douala.<sup>13</sup> Despite the risks of massive and prolonged use of antibiotics, strictly prescribed and controlled, no resistance developed in the identified strain. Chemoprophylaxis must follow rigorous protocols and be continuously monitored.<sup>13</sup> A recent systematic review<sup>14</sup> assesses the effects of chemoprophylaxis in preventing cholera among exposed contacts. Their findings suggest that chemoprophylaxis has a protective effect among household contacts of people with cholera, but the results are based on studies with a high likelihood of bias. Hence, there is a need for reliable research evaluating the effects of chemoprophylaxis, enabling a balance to be found between harm and benefit.

In conclusion, this study underlines the interest of investigating food-borne outbreaks even in settings with poor laboratory resources, and the potential dual efficacy of doxycycline chemoprophylaxis against malaria.

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### Declaration of Interests

The authors state they have no conflicts of interest to declare.

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