First Reported Human Cases of Leptospirosis in the United States Virgin Islands in the Aftermath of Hurricanes Irma and Maria, September–November 2017

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Objective. Following Hurricanes Irma and Maria, the first case of human leptospirosis ever identified in the US Virgin Islands (USVI) was reported to the Virgin Islands Department of Health. Leptospirosis is a potentially fatal bacterial disease caused by Leptospira species found in animal urine and urine-contaminated water and soil. Outbreaks can occur following extreme weather events.

Method. Additional cases of leptospirosis were identified in the 2.5 months post-hurricanes by reviewing emergency department (ED) records from territorial hospitals for patients demonstrating leptospirosis-consistent symptoms, testing symptomatic patients previously enrolled in the USVI arbovirus surveillance system (VIASS), and adding leptospirosis testing prospectively to VIASS. Available patient sera underwent local rapid diagnostic testing for anti-Leptospira IgM followed by confirmatory microscopic agglutination testing at the US Centers for Disease Control and Prevention. Water was collected from cisterns with epidemiologic links to confirmed cases and tested by real-time PCR (qPCR) for pathogenic Leptospira spp.

Results. Sixteen retrospectively identified symptomatic patients were enrolled in VIASS; 15 with available samples tested negative. Based on review of 5226 ED charts, 6 patients were further investigated; of these, 5 were tested of which 1 was positive. Prospective leptospirosis surveillance tested 57 additional patients; of these, 1 was positive. Water from 1 of 5 tested cisterns was found positive by qPCR.

Conclusions. This investigation documents the first 3 cases of leptospirosis reported in the USVI and demonstrates how VIASS successfully was adapted to establish leptospirosis surveillance. Contaminated cistern water was identified as a potential source for Leptospira spp. transmission, highlighting the need for additional post-hurricane remediation and disinfection guidance.

Key words. cistern water; hurricane response; leptospirosis; syndromic surveillance; US Virgin Islands; zoonotic disease.

INTRODUCTION

Leptospirosis is a life-threatening, reemerging zoonotic infectious disease caused by gram-negative, pathogenic spirochetes of the genus Leptospira [1]. It is recognized as one of the leading global causes of zoonotic disease morbidity and mortality with an estimated 1.03 million cases and 58 900 deaths annually worldwide, 73% of which occur in the tropics [2, 3]. Leptospirosis is endemic in the United States, with the majority of case reports coming from Puerto Rico and Hawaii [4], but no human cases of leptospirosis previously have been identified in the US Virgin Islands (USVI). However, seropositivity in goats (26%) and sheep (32%) has been documented in St. Croix (STX) [5], and leptospirosis causes significant human morbidity and mortality in the Caribbean region [2, 3]. A study testing archived sera from 14 Caribbean countries indicated that out of 3455 suspect cases over a 9-year period, 13.1% tested seropositive [6]. In Jamaica, 12.9% of suspect cases spanning an 18-year period were seropositive [7]. A more recent study found that overall seropositivity among pregnant women across 10 English-speaking Caribbean countries was 18.6 ± 3.6% [8]. Leptospirosis also has been documented in domestic animals throughout the region [9, 10].

Leptospira spp. are maintained in animal host reservoirs and spread through their urine. Among various reservoir animals is
the brown rat (*Rattus norvegicus*), found as an invasive species in USVI [11]. Human infections occur when people are exposed to urine of infected animals or urine-contaminated water and soil. Risk factors for *Leptospira* spp. transmission include water-related recreational activities and gardening [12], as well as occupations like livestock and sugarcane farming, veterinary medicine, and other outdoor professions [13]. Outbreaks can occur after floods and extreme weather events in endemic areas [14, 15].

Clinical diagnosis of leptospirosis can be complicated by the nonspecific and varied range of symptoms that also occur in other acute febrile illnesses. Initial flu-like symptoms (eg, fever, myalgia, headache) can quickly progress to more severe disease including renal or liver failure, pulmonary hemorrhage, and meningitis. However, timely recognition and diagnosis is important, as early antimicrobial treatment can decrease the severity and duration of disease.

Laboratory confirmation of leptospirosis is necessary for definitive diagnosis and usually is done by the microscopic agglutination test (MAT), which is the reference standard for serological diagnosis [16], or TaqMan real-time PCR (qPCR), targeting pathogenic *Leptospira* spp. DNA in acute whole blood (preferred) or serum, or a urine sample [17, 18]. *Leptospira* culture rarely is used for clinical diagnosis as it is difficult to isolate due to slow growth (up to 13 weeks), requirement of specialized media, and a low event rate (28–30°C) [12].

The USVI, located between the Atlantic Ocean and the Caribbean Sea, consist of 4 major islands: St. Croix, St. Thomas, St. John, and Water Island (comprising ≈133 square miles combined land area in total). On September 6 and 19, 2017, the USVI were directly struck by Category 5 Hurricanes Irma and Maria, respectively, which generated record-breaking rainfalls and extensive flooding in the following weeks. Six major hurricanes have directly affected the territory since 1956; however, robust disease surveillance programs only have been recently established. Shortly after the 2017 hurricanes, the Virgin Islands Department of Health (VIDOH) reported the first-ever case of leptospirosis detected in USVI.

In November 2017, the VIDOH and the US Centers for Disease Control and Prevention (CDC) launched a public health investigation to identify additional post-hurricane cases of leptospirosis, characterize their exposure history, and establish prospective surveillance in USVI within the pre-existing VIDOH arbovirus syndromic surveillance system (VIASS). VIASS has been in place since 2014 to identify cases of dengue, chikungunya, and Zika by testing serum, with or without urine, from patients with at least 2 of the following symptoms: fever, rash, headache, arthralgia, conjunctivitis, and myalgia. Asymptomatic pregnant women also are enrolled for Zika testing.

**METHODS**

**Epidemiologic Investigation for Leptospirosis**

**Leptospirosis Index Case Identification**

Shortly after Hurricanes Irma and Maria, the VIDOH reported the first-ever case of leptospirosis detected in USVI—a resident of St. Thomas (STT), whose diagnosis was confirmed on October 11, 2017, after medical evacuation and hospitalization in South Carolina (Case Report 1). A timeline of the events described in this manuscript is shown in Figure 1.

**Retrospective Case-Finding Through Medical Record Review**

Emergency Department (ED) patient medical records from the 2 USVI hospitals were reviewed. At Schneider Regional Medical Center (SRMC) in STT, paper medical records were reviewed for September 7, 2017 (1 day post-hurricane Irma), to October 19, 2017 (1 month post-hurricane Maria), and November 12–15, 2017 (the 4-day period before chart abstraction to intercept patients whose blood or serum samples were still at the hospital). At Juan F. Luis Hospital (JFL) in STX, electronic medical records (EMR) were reviewed for September 21–November 22, 2017 (2 days to 2 months post Hurricane Maria, because STX was not severely hit by Hurricane Irma). Records were screened to identify patients presenting with or having a recent history of fever (temperature ≥100.4°F) as well as additional signs and symptoms consistent with leptospirosis, such as jaundice, myalgia, acute kidney injury, transaminis, or conjunctivitis, as defined by the documenting provider. No additional exclusion criteria were used during screening of medical charts. Identified patients had serum samples retrieved for leptospirosis testing from hospital laboratories if available, or newly obtained from the patient. Hospital laboratories in USVI keep patient sera for up to 7 days at 0–4°C.

**Prospective Case-Finding Through VIASS**

Enhanced surveillance for leptospirosis was established and conducted in USVI from November 18, 2017, to May 9, 2018, by revising the existing VIASS questionnaire to include a differential diagnosis and adding leptospirosis testing for patients meeting the VIASS case definition or suspected of having leptospirosis. Testing included a minimum of serum screening for anti-*Leptospira* IgM using a rapid diagnostic test (RDT) locally, followed by confirmatory testing with MAT at the CDC.

Training sessions were held at clinics, urgent care centers, and EDs on leptospirosis clinical signs and symptoms, risk factors, diagnostic testing, and to discuss the updated VIASS.

**Laboratory Investigation for Leptospirosis**

All serum samples collected or still available in USVI (versus already at the CDC) were screened locally for anti-*Leptospira* IgM antibodies using the Test-it *Leptospira* IgM Lateral Flow Assay (Life Assay Diagnostics, Cape Town, South Africa). Regardless
of the RDT result, all sera then were tested at the CDC with MAT serology [17].

One acute serum sample was selected for additional testing by qPCR targeting the lipL32 gene [18, 19], after initially testing RDT- and MAT-negative, but then testing RDT- and MAT-positive on a convalescent serum sample (Case Report 3).

In accordance with the Council for State and Territorial Epidemiologists’ case definition, a confirmed case of leptospirosis was defined as a patient with a positive qPCR result or a MAT titer of ≥1:800 in a single serum specimen or a 4-fold increase in MAT titers between acute and convalescent sera [20]. Leptospirosis was ruled out in patients with a negative MAT results on serum collected ≥14 days post illness onset.

### Environmental Investigation

Environmental assessments were conducted at properties associated with confirmed cases to look for signs of rodent infestation, presence of other animals, and examine water sources and overall living conditions post-hurricanes. Permanent sources of freshwater are not common in the USVI, and >80% of the population uses rainwater-catchment systems (eg, household cisterns) for various needs, including drinking or bathing. Cisterns associated with confirmed cases were investigated as a potentially contaminated freshwater source. Fifty gallons of water from each cistern were collected and subjected to dead-end ultrafiltration using hollow fiber ultrafilters [21]. Ultrafilters were shipped to the CDC for backflushing and analysis. Backflushed samples were concentrated by centrifugation, followed by nucleic acid extraction [22] and leptospirosis testing with lipL32 qPCR. Testing for total coliforms and E. coli also was performed using Colilert-18 and IDEXX Quanti-Trays (IDEXX, Westbrook, ME). Results were expressed as most probable number (MPN) of coliforms/100 mL.

### RESULTS

#### Medical Record Review

At SRMC, 2358 medical records were reviewed and 100 febrile patients (4.2%) were identified. Four were selected for leptospirosis testing based on additional symptoms and exposure history. Of the 4, 1 was RDT-positive and MAT-confirmed, and 3 tested RDT-negative, with 1 ruled out by MAT and 2 not tested by MAT. The positive patient was the second case of leptospirosis identified in USVI (Case Report 2).

At JFL, 2868 EMRs were reviewed and 206 febrile patients (7.2%) were identified, with 2 of them selected for leptospirosis testing. One was RDT-negative and the other had previously tested anti-Leptospira IgM-negative at a commercial laboratory. Neither were tested by MAT.

#### Retrospective Case-Finding Through the VIASS

In the 2.5 months post-hurricane, VIASS enrolled 125 people, including 16 symptomatic patients. Of the 15 with sera available for leptospirosis testing, all were MAT-negative, including 9 who also were RDT-negative. None of the samples were collected late enough to have leptospirosis ruled out by MAT.

#### Prospective Case-Finding Through VIASS

Adding leptospirosis to the VIASS, combined with targeted healthcare professional education resulted in 57 patients with sera tested for leptospirosis between November 18, 2017, and May 9, 2018. All of the patients except 1 tested negative by RDT and MAT, but only 14 had sera collected late enough to have...
leprospirosis ruled out by MAT. The RDT-positive patient, tested in USVI on December 1, 2017, was confirmed positive by MAT at the CDC—the third confirmed case of leptospirosis identified in USVI (Case Report 3).

**Case Reports**

**Case 1**

On October 11, 2017, the VIDOH and the CDC were notified of a confirmed case of leptospirosis—a 53-year-old man from STT who was at that time receiving treatment in a South Carolina hospital (Figure 1). The index case-patient reported symptom onset on September 29, 2017, and presented at SRMC on October 3, 2017, with abdominal pain, vomiting, jaundice, and arthralgia. Lab testing revealed thrombocytopenia and evidence of acute kidney injury. He was medically evacuated to South Carolina on October 4, 2017, treated with ceftriaxone, and had his blood tested by qPCR for pathogenic *Leptospira* spp., with a positive test result at a commercial laboratory. The index case-patient recovered and returned to USVI. On October 13, 2017, the VIDOH conducted an environmental assessment of the property where the partially undomiciled index case-patient lived in a tent in the yard. Several dogs were present as well as rodent traps and some free-standing receptacles for rainwater collection that were reportedly used by the individual for bathing and drinking. On November 17, 2017, a follow-up assessment and water testing was conducted. The yard rainwater receptacles were no longer available, but water from the household cistern (Figure 2), which was reportedly not used by the index case-patient, was collected as representation of possible environmental contamination. It tested qPCR-positive for pathogenic *Leptospira* spp. and positive for total coliforms (114 MPN/100 mL) and *E. coli* (15 MPN/100 mL).

**Case 2**

Medical record review identified a 57-year-old woman from STT who presented to SRMC on September 28, 2017, with a 9-day history of fever, vomiting, fatigue, sensitivity to noise and light, jaundice, bilateral conjunctivitis, and dark, cloudy urine. Lab testing revealed leukocytosis and elevated liver enzymes. Investigation triggered by medical record review discovered the patient then sought care and was hospitalized in Virginia, where she tested positive for anti-*Leptospira* IgM by ImmunoDot (Cambridge Biomedical, Boston, MA) at a commercial laboratory and initially was treated with ampicillin-sulbactam, followed by doxycycline. The patient eventually recovered and was discharged. A convalescent serum sample collected by the investigation team on November 18, 2017, tested RDT-positive in USVI. Leptospirosis was confirmed by MAT at the CDC on the same sample with highest titer against *Leptospira interrogans* serovar Mankarso (1:12 800).

The patient worked at a veterinary clinic where she cleaned flood water after Hurricane Irma in the week before symptom onsets.
onset. On November 18, 2017, an environmental assessment at her work place and residence found evidence of rodents at the veterinary clinic—staff reported increased rodent presence due to hurricane damage to the building. The patient’s home was uninhabitable after the hurricanes due to lack of electricity and mold growth, but she visited regularly. Cistern water from both the patient’s home and veterinary clinic tested negative for *Leptospira* spp. and *E. coli*. However, 68 MPN/100 mL total coliforms were detected in the veterinary clinic cistern.

**Case 3**
On November 17, 2017, a 47-year-old woman from STX presented to her primary care physician with a 1-day history of fever, chills, headache, eye pain, myalgia, and arthralgia. An acute serum sample was submitted for arbovirus testing and also was tested for leptospirosis as part of the prospective case-finding through VIASS. Leptospirosis testing by RDT, MAT, and qPCR was negative. On November 24, 2017, the patient presented again with fever now lasting 8 days, hemorrhages (petechiae and ecchymoses), myalgia, chills, headache, conjunctivitis, anorexia, abdominal pain, rash, cough, and jaundice. Lab testing revealed thrombocytopenia and evidence of renal failure. A second serum sample collected that day was submitted for follow-up leptospirosis testing through VIASS and outpatient treatment with doxycycline was prescribed. An initial RDT-positive result in USVI was confirmed by MAT at the CDC, with a higher titer against *Leptospira interrogans* serovar Mankarso (1:6400).

An environmental assessment at the patient’s property, including water collection from 2 available cisterns, was conducted on January 18, 2018. The patient reported direct contact with flood water, wet soil, and rodent feces in her home post-hurricanes. She owned an indoor dog that was allowed to roam and drink water outside. A urine sample from the asymptomatic dog, collected on the same day, tested negative for leptospirosis by qPCR whereas MAT on serum showed titers of 1:400 against several *Leptospira interrogans* serovars. The dog’s veterinary records showed leptospirosis vaccination administered on December 22, 2017. Water from both household cisterns tested negative for *Leptospira* spp. and *E. coli*, but positive for total coliforms (>80.5 and >74.1 MPN/100 mL, respectively).

**DISCUSSION**
Leptospirosis cases had not been detected in USVI prior to Hurricanes Irma and Maria, and diagnostic tests for leptospirosis were not available locally on the islands. Here, we reported the first 3 cases of the disease identified in USVI through a combination of retrospective investigation methods and setting up prospective surveillance. The extreme weather conditions generated by these storms and the resulting flooding and disruption of water sanitation practices likely contributed to case occurrences. However, serologic evidence of infection in animals in USVI [5], in addition to confirmed reports and endemnicity in other Caribbean islands [3, 4, 6–10] suggest that undetected human cases of leptospirosis might have previously occurred in USVI.

The results of our investigation raised an important concern about the safe use of household cisterns, especially after storms and hurricanes. The detection of pathogenic *Leptospira* spp. in the household cistern water associated with the index case suggested that its use, if untreated, may pose a serious risk of infection. Although we could not directly link the human infection to the *Leptospira* spp.-positive water because the person reportedly did not utilize the household cistern and the water was sampled almost 2.5 months after illness onset, we confirmed environmental contamination on the property. Cisterns usually are filled with rainwater, which can be contaminated with urine from rodents or other animals and, therefore, potentially with *Leptospira* spp. This risk likely increases during severe storms and floods due to rainwater and floodwater runoff and displacement of rodents from their habitats. The *Leptospira*-negative test results of the cistern water epidemiologically linked to the second and third leptospirosis cases did not rule out the presence of the pathogen in the cisterns, as *Leptospira* spp. are generally distributed heterogeneously in water [23]. Of note, the *Leptospira*-positive water source associated with the index case also was positive for *E. coli*, usually indicating fecal contamination and which in high concentrations significantly can improve the recovery of leptospiral DNA by serving as a carrier which cosediments with leptospires (to generate larger pellets) that are less prone to be washed away during DNA extraction [24].

The need for education on and practice of practical and effective remediation of cistern water after floods and heavy rains in USVI is emphasized by the detection of pathogenic *Leptospira* spp. in 1 cistern as well as total coliforms (expected for untreated water) detected in 4 of 5 tested cisterns. The current CDC recommendations for cistern cleaning and disinfection include complete draining, removing debris, scrubbing the interior, and refilling with clean water. However, in emergency situations this may not be feasible and direct disinfection with bleach at the point-of-use may be the only option available.

In addition to cistern water use, the leptospirosis cases reported other possible exposures, including exposure to flood water (reported by all 3 cases) and occupation of buildings with evidence of rodent infestation.

The laboratory tests used to confirm the leptospirosis cases do not have the capacity to definitively identify the infecting serogroup/serovar, which could help indicate the original animal source of infection. TaqMan real-time PCR (index case confirmation) was limited to confirming pathogenic *Leptospira* spp. presence, but not the specific species or serovar. The highest reacting serovar on MAT (Mankarso in the second...
and third cases) might have a low correlation with the actual infecting serovar due to cross-reaction between serovars [25, 26]. Additionally, and pertaining to the dog associated with the third leptospirosis case, MAT cannot distinguish between titres from vaccination and recent *Leptospira* spp. infection, especially with recent vaccination.

The collaboration between the VIDOH and the CDC during and after the investigation led to the identification of 2 additional cases of leptospirosis in USVI after the hurricanes. However, due to limited time and resources, not all medical records from the period between Hurricane Irma and the investigation were searched, and not all patients that had clinical signs and symptoms consistent with leptospirosis were selected for testing. Additionally, 78.2% (61 of 78) of all patients tested were unable to have leptospirosis ruled in or out as they either were not tested by MAT, were unable to have convalescent serum collected, or were missing onset dates to determine the time from onset to testing. The investigation only would have identified patients seeking medical care at healthcare facilities in USVI. These limitations might have led to some post-hurricane cases of leptospirosis being missed in the retrospective and prospective investigations.

The results of our epidemiological and laboratory investigation demonstrated the suitability of a syndromic surveillance network, such as the existing VIASS, to be used as a platform for the development of leptospirosis surveillance based on the often nonspecific and overlapping clinical signs and symptoms with other diseases, such as those caused by arboviruses. The use of a system that already was well-known among the local medical providers in combination with the extensive educational campaign on leptospirosis facilitated successful surveillance and led to the detection of the third case.

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