Imported Case of Marburg Hemorrhagic Fever—Colorado, 2008

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MARBURG HEMORRHAGIC FEVER (MHF) is a rare, viral hemorrhagic fever (VHF); the causative agent is an RNA virus in the family Filoviridae, and growing evidence demonstrates that fruit bats are the natural reservoir of Marburg virus (MARV). On January 9, 2008, an infectious disease physician notified the Colorado Department of Public Health and Environment (CDPHE) of a case of unexplained febrile illness requiring hospitalization in a woman who had returned from travel in Uganda. Testing of early convalescent serum demonstrated no evidence of infection with agents that cause tropical febrile illnesses, including VHF. Six months later, in July 2008, the patient requested repeat testing after she learned of the death from MHF of a Dutch tourist who had visited the same bat-roosting cave as the patient, the Python Cave in Queen Elizabeth National Park, Uganda. The convalescent serum tested positive for anti-MARV immunoglobulin M (IgM) and IgG ELISA. The patient was discharged on January 19 and had a prolonged recovery over the following year because of persistent abdominal pain, fatigue, and "mental fog," but had no long-term sequelae such as chronic hepatitis or chronic renal disease. She received a blood transfusion for persistent anemia after she was discharged.

In July 2008, the patient requested repeat testing after she learned of the fatal case of MHF in a Dutch tourist who recently had visited the same cave she had visited in Uganda, the Python Cave. The Colorado patient had visited the cave on December 25, 2007, 10 days before onset of her initial symptoms. Serum collected on July 15 tested positive for anti-MARV IgG by ELISA, prompting additional testing of the archived day 10 serum. Traditional reverse-transcriptase polymerase chain reaction (RT-PCR) was negative, but real-time (Taqman) RT-PCR was equivocal; however, nested RT-PCR* confirmed the presence of MARV RNA fragments in the day 10 sample.

Public Health Response
On January 22, 2009, CDC notified the World Health Organization and Uganda Ministry of Health of the imported MHF.
What is already known on this topic?

Marburg hemorrhagic fever (MHF) is a rare viral hemorrhagic fever caused by Marburg virus (a filovirus in the same family as Ebola virus), which is endemic in tropical areas of Africa and likely is maintained in nature by cave-dwelling bats.

What is added by this report?

The case described in this report, the first imported case of a filoviral hemorrhagic fever in the United States, adds further support to the epidemiologic link between MHF and exposure to caves inhabited by bats in Africa.

What are the implications for public health practice?

Health-care providers should advise travelers to endemic areas of Africa to avoid entering caves inhabited by bats, should consider the diagnosis of viral hemorrhagic fever among severely ill travelers returning from endemic areas, and should rapidly report, isolate, and test patients with suspected cases.

The Python Cave had already been closed to visitors in July 2008, during the response to the Dutch MHF case. CDPHE and CDC conducted a public health investigation during January-February 2009. Interviews were conducted with the patient and her spouse, the patient’s medical records were reviewed, and a retrospective contact investigation was conducted to identify possible secondary transmission. A contact was defined as a person who had physical contact with the patient, her body fluids, or contaminated materials or was in the same room as the patient during her acute illness (January 4-19, 2008). Contacts included health-care workers (including health-care providers, housekeeping staff, and hospital laboratory staff), commercial laboratory staff, and social contacts.

To limit the effect of recall bias and to identify secondary cases of MHF, a contact-tracing protocol was modified for retrospective use to identify contacts who had a high-risk exposure to the patient’s body fluids (through splash, percutaneous, or nonintact skin exposure), or prolonged absenteeism of ≥7 days as indicated by review of health and payroll records. The contact investigation identified approximately 260 contacts: 220 health-care workers, approximately 30 commercial laboratory workers from five laboratories, and 10 social contacts. No high-risk exposure or severe febrile illness was identified.

The patient and her spouse reported spending approximately 15-20 minutes in the cave and recalled seeing bats flying overhead. Neither remembered her having contact with a bat or sustaining an injury in the cave. However, the patient reported touching guano-covered rocks while climbing into the cave and surmised that she might have covered her mouth and nose with her hands once inside because of the unpleasant smell.

CDC, with assistance from public health agencies in Illinois, Uganda, Belgium, and the United Kingdom, conducted an investigation of the eight tour companions who accompanied the patient when she visited the Python Cave. During February-July 2009, participants were interviewed using a standardized questionnaire by telephone or e-mail and were offered serologic testing by anti-MARV IgG ELISA. Questionnaires were completed for all eight tour companions. All eight reported having entered the cave (at least under the cave ceiling), and six reported climbing over a crop of boulders further inside as the patient had done; however, none reported direct contact with bats or bat guano/urine. Serum samples were provided by six of the tour companions; none had evidence of prior MARV infection by anti-MARV IgG.

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CDC Editorial Note: Before the case described in this report, the only human cases of VHF imported into the United States were single cases of Lassa fever (an arenaviral hemorrhagic fever) in Chicago, Illinois, in 1989 and in Trenton, New Jersey, in 2004. No previous cases of imported filovirus (MARV or Ebola virus) infections have been reported in the United States, making this the first imported case of a filoviral hemorrhagic fever in the United States.

The patient described in this report was first diagnosed by convalescent serology because initial testing of the day 10 sample was negative by virus isolation, antigen-detection, and IgM and IgG ELISA. After the Dutch patient was diagnosed with MHF, retesting of the archived specimen with more sensitive molecular methods was performed, including a nested RT-PCR assay that detected viral RNA. This, along with the positive convalescent serology and compatible clinical course, confirmed the diagnosis. To obtain a rapid diagnosis during the acute illness, patients with suspected VHF should have paired acute blood specimens (ideally collected during days 0-4 and days 4-9 of the acute illness) tested at a World Reference Laboratory (e.g., CDC) with biosafety level 4 capability using multiple methods as appropriate for the timing of the sample, including virus isolation, RT-PCR, and IgM and IgG ELISA. Because the incubation period for MARV is 2-21 days, daily contact tracing is recommended to contain outbreaks. This involves following all contacts of patients suspected of having MHF, and isolating and testing those that experience fever within 21 days after their last contact.

Other sporadic cases of MHF have been reported outside of Africa: two laboratory-acquired cases in Russia and two cases imported from endemic areas.3,6 These imported cases occurred in a patient hospitalized in South Africa who likely acquired the disease while camping in Zimbabwe in 1975 and the second in the previously described Dutch patient hospitalized in the Netherlands who died of MHF after
visiting the Python Cave in Uganda in 2008.³ Case-fatality rates of 83%-90% have been reported for widespread outbreaks of MHF in Africa.¹,²

Virologic and serologic evidence of MARV infection has been documented among cave-dwelling bats, particularly the Egyptian fruit bat Rousettus aegyptiacus;¹ this evidence has implicated bats as the likely natural reservoir for MARV. R. aegyptiacus bats have a wide range covering most of Africa, indicating that risk for zoonotic infection might exist beyond areas with previously documented cases. The precise route of MARV transmission from the putative bat reservoir to humans has not been determined and might include direct or indirect exposure to bat excretions and secretions. MHF outbreaks have resulted from exposure to caves or mines inhabited by bats¹,³ and subsequent human-to-human transmission through direct contact with infectious body fluids and contaminated materials, primarily affecting caregivers and health-care workers.⁵ Isolation of suspected patients and implementation of droplet and contact precautions are recommended to prevent person-to-person spread.†

Although the Python Cave is closed and no additional MHF cases have been reported, travelers should be aware of the risk for acquiring MHF in endemic areas in Africa and should avoid entering caves or mines inhabited by bats in these areas.¹⁰ Health-care providers should have a low threshold of suspicion for VHF among travelers returning from endemic areas, promptly implement appropriate infection control measures, and rapidly report suspected cases. Suspected cases of VHF are nationally notifiable and should be reported immediately to local and state health departments and to CDC’s Special Pathogens Branch at 404-639-1115 (770-488-7100 after hours) to obtain guidance on testing, management, and response. Additional information regarding Marburg hemorrhagic fever,‡ travelers’ health,§ and VHF infection-control guidelines∥ are available online.

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REFERENCES
10 Available.

*Nested RT-PCR is more sensitive and specific than traditional RT-PCR. A portion of the product produced from the first round of amplification is used in the second round of amplification along with a different set of primers.
‡Available at http://www.cdc.gov/ncidod/dhqp/bp_vhf_interimguidance.html.
§Available at http://www.cdc.gov/travel/
∥Available at http://www.cdc.gov/ncidod/dhqp/bp_vhf_interimguidance.html.

Idiopathic Granulomatous Mastitis in Hispanic Women—Indiana, 2006-2008

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IDIOPATHIC GRANULOMATOUS MASTITIS (IGM) is a rare inflammatory breast lesion of unknown etiology that occurs in women of childbearing age, only a few hundred cases have been reported worldwide.¹,² A breast cancer mimic, IGM also is diagnosed by breast biopsy.³ On December 12, 2008, a physician in Indianapolis, Indiana, reported a cluster of seven IGM diagnoses in multigravid Hispanic women, an unusually high number. To evaluate the etiology of the breast masses and characterize associated epidemiologic and clinical features, the Indiana State Department of Health and CDC conducted a multidisciplinary investigation. This report describes the results of that investigation. A total of nine cases of IGM were confirmed during 2006-2008 in Indianapolis, for an annual prevalence of IGM of 2.4 per 100,000 women aged 20-40 years. The prevalence was 12 times higher among Hispanic women. Among IGM patients at the hospital, a median of 5 months elapsed between symptom onset and diagnostic biopsy. Histopathologic evaluations confirmed IGM. In a case-control study of all seven cases and 21 controls from the hospital, case-patients were significantly more likely than controls to have less than a sixth-grade education (odds ratio [OR] = 12.7), a positive tuberculin skin test (OR = undefined), or a medication allergy (OR = 15.0). No other risk factors were significantly associated with case status. Barriers to accessing health care, including low education level, resulted in delayed care for breast masses. Future research could provide more complete descriptions of the epidemiology and etiology of IGM.

The hospital is a university-associated, county medical center that emphasizes care of vulnerable populations. * Before this cluster, the reporting physician had never seen a case of IGM in 15 years of practice. All seven women had sought medical care for painful breast masses and received a diagnosis of IGM based on pathologic findings during biopsies to rule out malignancy. The masses were palpable (ranging from 1 x 1 cm to 6 x 4 cm in size) and unilateral in the left breast in six cases and bilateral in one case. All seven patients reported at least two pregnancies and had breastfed at least one of their children. Symptoms occurred a median of 34 months (range: 10-62 months) after last pregnancy and 26 months (range: 4-46 months) after cessation of breastfeeding. The median time between symptom onset and biopsy was 5 months (range: 3-6 months); the patients attributed the delays to barriers in accessing health care, including concerns about financial implications, occupational repercussions, and/or child care obligations. After symptom onset, case-patients missed or cancelled 23% of their appointments. One patient was deported before completing treatment.

All seven biopsy specimens were sent to CDC for additional histopathologic evaluation. † This testing confirmed IGM in all seven patients, each with noncausing granulomas, acute and chronic.