Unprotected People #44
Yellow Fever

Fatal yellow fever in a traveler returning from Amazonas, Brazil, 2002

On April 19, 2002, the Centers for Disease Control and Prevention (CDC) published "Fatal Yellow Fever in a Traveler Returning from Amazonas, Brazil, 2002" in the Morbidity and Mortality Weekly Report (MMWR, *vol. 51, no. 15). The article describes the case of a previously healthy 47-year-old male who traveled to Brazil for a fishing trip in March of this year, contracted yellow fever, returned to his home state of Texas, became severely ill, and died. The man's death is the third reported death from yellow fever in a U.S. citizen following travel to the Amazon region since 1996, according to the Editorial Note to the article.*

The Immunization Action Coalition (IAC) is republishing this story as the 44th in our series of stories about people who have suffered or died from vaccine-preventable diseases. We usually try to choose stories that are written for a general audience. Sometimes, however, a powerful story appears in a technical medical or public-health source that we think almost all readers will appreciate. Today's MMWR *story about an adult traveler's death from yellow fever infection contains information for clinicians and epidemiologists, but it also provides case details that are useful for all international travelers.*

Many of us in the United States do not even know what yellow fever is; it's a viral disease found in parts of Africa and South America that is transmitted by mosquito bite. The fatality rate for the disease is approximately 20 percent.

Travelers, even if your tour group or company informs you that yellow fever vaccination certification is not required in the country or countries you plan to visit, please consult with a travel medicine specialist and weigh the minor inconvenience and cost of getting vaccinated against the possible cost of serious or even fatal illness. (Please note that the person whose death is documented in this article was given incorrect advice about vaccination from his travel agency, as you will read.) This is a simple, one-dose vaccine that lasts 10 years. It can be received at a designated yellow fever center, typically a local health department. As the Editorial Note to this article states, vaccination should be obtained at least 10 days before departure in order to allow for an adequate immune response.

Yellow fever (YF) is a mosquitoborne viral disease that has caused deaths in U.S. and European travelers to sub-Saharan Africa and tropical South America (1-5). Although no specific treatment exists for YF and the case-fatality rate for severe YF is approximately 20%, an effective vaccine is available (6). This report describes a case of fatal YF in an unvaccinated traveler who had returned from a 6-day fishing trip on the Rio Negro west of Manaus in the state of Amazonas, Brazil. Because information from some commercial outfitters and travel agents might underestimate health risks, health-care providers and travelers should review vaccination and other traveler's health recommendations from public health agencies.

On return from Brazil on March 10, 2002, a previously healthy man aged 47 years from Texas presented to an emergency department (ED) with a 4-day history of crampy abdominal pain and a 1-day history of fever of 102.8 degrees F (39.3 degrees C) and severe headache. At the ED, he received symptomatic treatment and doxycyline for a possible rickettsial disease and was discharged. His fever and headache worsened, and on March 12 he was hospitalized for intractable vomiting.

On admission, physical examination revealed an ill-appearing, febrile man. Laboratory tests documented leukopenia (2,300/mm3 [normal: 4,800-10,800/mm3]), anemia (hemoglobin 10.5 g/dL [normal: 14-18 g/dL]), thrombocytopenia (36,000/mm3 [normal: 150,000-450,000/mm3]), abnormal coagulation (prothrombin time: 29 seconds [normal:

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10.5-13.0 seconds] and INR 6.3), renal failure (creatinine: 5.5 mg/dL [normal: 0.6-1.0 mg/dL] and blood urea nitrogen: 65 mg/dL [normal: 6—20 mg/dL]), and liver failure (ALT: 7,600 U/L [normal: 30—65 U/L], AST: 13,700 U/L [normal: 15—37 U/L], and bilirubin: 3.3 mg/dL [normal: 0—1.0 mg/dL]). The patient was presumptively treated for malaria. Bacterial cultures of blood, urine, and cerebrospinal fluid showed no growth, and a malaria smear of peripheral blood was negative. Three days after admission, the patient developed shock, seizures, and excessive bleeding at venipuncture sites; he died the following day.

Tests performed at CDC on serum samples collected on the second day of illness were negative for IgM and IgG antibody to South American arboviruses (i.e., YF, dengue, St. Louis encephalitis, and Venezuelan equine encephalomyelitis viruses); serum samples collected on days 3-7 also were negative for IgM and IgG antibody to YF virus. Serum specimens collected on days 4, 5, and 7 of illness and a postmortem liver sample were positive for YF virus RNA by RT-TaqMANT PCR tests. Virus isolation was attempted by inoculation of serum samples onto Vero and AP-61 cells in tissue culture, and by inoculation of postmortem plasma onto Vero cells in tissue culture and intracerebrally into suckling mice. No virus was recovered.

Histopathologic examination of a postmortem percutaneous needle sample of the liver demonstrated massive acidophilic hepatocellular necrosis with minimal inflammation. Immuno-histochemistry (IHC) tests using a cross-reactive, polyclonal flavivirus antibody and a polyclonal YF-virus—specific antibody were positive. IHC tests for New World arenaviruses (Machupo, Guanarito, and Sabia viruses), spotted fever rickettsiae, dengue virus, and Leptospira spp. were negative. A postmortem serum sample was negative for IgM and IgG antibody to Leptospira spp. and New World arenaviruses, and negative for Machupo virus by ELISA antigen capture. A blood sample collected on day 2 was negative for malaria by PCR test.

The deceased traveler was one of 15 U.S. citizens who visited the Amazon as part of a fishing trip. The patient slept aboard an air-conditioned fishing boat and wore DEET-impregnated clothing while fishing. Before traveling to the Amazon, the traveler had not received medical consultation, YF vaccine, or malaria prophylaxis. Information on the outfitter's website stated, "The International medical community suggests yellow fever and malaria prophylaxis for the Amazon region. This is not a requirement to enter Brazil, but merely a suggestion." A brochure from the group's travel agent stated, "We do not suggest any inoculations of any kind for this trip.... But to make sure you are worry free, consult with your personal physician."

The 15 U.S. citizens living aboard this fishing boat (including the patient) were interviewed or investigated by the Texas Department of Health. Other than the patient, none reported febrile illnesses. Eight (53%) were appropriately vaccinated for YF according to World Health Organization (WHO) guidelines (i.e., within the preceding 10 years and 10 or more days before arrival in Manaus). Of the seven that were not appropriately vaccinated, one had received YF vaccine 11 years earlier, one had been vaccinated 5 days before arrival in Manaus, and one was unsure whether he had been vaccinated in the military >30 years earlier. Of the four persons (including the patient) who were never vaccinated, three stated that they had been "unconcerned" about the risk for YF. Three (20%) of the 15 reported taking malaria prophylaxis.

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Editorial Note:

This case represents the third reported YF death in a U.S. citizen following travel to the Amazon region since 1996 (1,2). YF can initially manifest as fever, headache, myalgias, arthralgias, epigastric pain, or

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vomiting (6). Illness can progress to liver and renal failure, and thrombocytopenia and abnormal coagulation can cause hemorrhagic symptoms and signs. Definitive diagnosis is made by viral culture of blood or tissue specimens or by identification of YF virus antigen or nucleic acid in tissues (especially liver) using IHC, ELISA antigen capture, or PCR tests. Although antibodies are not always present in the first week of illness, detection of YF-specific IgM antibody by capture ELISA with confirmation of >4-fold rise in neutralizing antibody titers between acute- and convalescent-phase serum samples also is diagnostic.

On returning home, viremic travelers can establish new foci of YF transmission where susceptible vectors are present. The geographic range of Aedes aegypti, a mosquito that transmits YF virus among humans, includes the southern United States. Patients with suspected or confirmed YF should be isolated from contact with mosquitoes during at least the first 5 days of illness, and local or state health departments must be notified immediately (7). YF is one of three diseases (along with cholera and plague) designated by the International Health Regulations as internationally quarantinable and requires international reporting of all suspected and confirmed cases within 24 hours (8).

Commercial outfitters and travel agents should ensure that health information provided to travelers is consistent with CDC and WHO YF vaccination and malaria prophylaxis recommendations. Undervaccination of travelers at risk for YF might be an increasing problem. Using a mathematical model based on U.S. arrivals to countries where YF transmission occurs and on YF vaccine doses sold to U.S. civilians, overall coverage among U.S. travelers to regions where YF is endemic might have declined 50% from 1992 to 1998 (9). The degree to which inaccurate health information contributes to apparently decreasing coverage is unknown.

Because of the severity of YF illness, the potential for epidemics, and the availability of an efficacious vaccine, CDC recommends vaccination of persons aged 9 months or greater traveling to nonurban areas where YF is endemic (i.e., sub-Saharan Africa and tropical South America, including Amazonas states in Brazil and Venezuela). To allow for an adequate immune response, vaccination should be completed at least 10 days before travel. Some countries, other than the United States, require YF vaccination for travelers returning from countries where YF is endemic and may impose quarantine if the traveler does not have official vaccination documentation or a written medical waiver. Although recent reports described occurrence of severe systemic illness potentially related to recent YF vaccination (10), the rarity of these events does not warrant changes in YF vaccination recommendations. Before international travel, persons should review CDC recommendations (http://www.cdc.gov/travel) for prevention of vectorborne and other travel-related diseases.

To see the Centers for Disease Control and Prevention (CDC) Comprehensive Yellow Fever Vaccination Requirements web page, which includes a list of the countries for which vaccination is required or recommended, go to: http://www.cdc.gov/travel/yfever.htm

For general information on yellow fever, go to the CDC Yellow Fever Disease and Vaccine web page at: http://www.cdc.gov/ncidod/dvbid/yellowfever/index.htm

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