



Department of Health

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TO: Healthcare Providers, Hospitals, and Local Health Departments (LHDs)

**FROM: New York State Department of Health (NYSDOH)
Bureau of Communicable Disease Control (BCDC)**

**INFORMATIONAL MESSAGE: TESTING AND REPORTING OF
MOSQUITO-BORNE ILLNESS - YELLOW FEVER**

Please distribute to the Infection Control Department, Emergency Department, Infectious Disease Department, Family Medicine, Travel Medicine Service, Pediatrics, Director of Nursing, Medical Director, Laboratory Service, Pharmacy, and all patient care areas.

NYSDOH is advising health care providers on the procedures to test and report suspected cases of yellow fever virus. There is an ongoing outbreak of yellow fever in Brazil and a shortage of yellow fever vaccine (YF-Vax) licensed for use in the U.S.

SUMMARY

- The CDC has issued a Level 2 Travel Alert because of an ongoing yellow fever outbreak in Brazil¹. The first cases were reported in the State of Minas Gerais in December 2016, but confirmed cases have since been reported in the neighboring states of Espirito Santo, São Paulo, and Rio de Janeiro (not Rio de Janeiro City). In response, Brazilian health authorities have recently expanded the list of areas in which yellow fever vaccination is recommended and are recommending enhanced precautions when traveling to Brazil. Additional information is available at <https://wwwnc.cdc.gov/travel/notices/alert/yellow-fever-brazil>.
- Health care providers should consider yellow fever in the differential diagnosis of any adult or pediatric patient with clinical evidence of fever, nausea, vomiting, epigastric pain, jaundice, renal insufficiency, and cardiovascular instability along with recent travel to Brazil or an area with risk of yellow fever virus transmission. A map of these areas is available at <https://www.cdc.gov/yellowfever/maps/index.html>
- All cases of suspected yellow fever should be reported immediately to the Local Health Department (LHD) where the patient resides. Upon approval, NYSDOH can provide testing for yellow fever, which is only available at the Department's Wadsworth Center and a limited number of specialized laboratories nationally.
- Providers whose patients are planning travel to areas with risk of yellow fever virus transmission and to whom vaccination is recommended need to be aware of the yellow fever vaccine shortage in the U.S. Updates regarding yellow fever vaccine supply are available on CDC's Travelers' Health website at <https://www.cdc.gov/yellowfever/vaccine/>.

EPIDEMIOLOGY AND CLINICAL FEATURES

Yellow fever virus is an RNA virus that belongs to the genus *Flavivirus* and is transmitted to people primarily through the bite of infected mosquitoes. Mosquitoes acquire the virus by feeding on infected primates (human or non-human) and then can transmit the virus to other primates (human or non-human). People infected with yellow fever virus are infectious to mosquitoes shortly before the onset of fever through several days after onset.

In its mildest form, yellow fever is a self-limited infection characterized by sudden onset of fever and headache without other symptoms. Other patients experience an abrupt onset of a high fever (up to 104°F [40°C]), chills, severe headache, generalized myalgias, lumbosacral pain, anorexia, nausea, vomiting, and dizziness. The patient is usually viremic during this period, which lasts for several days. Many patients have an uneventful recovery, but in approximately 15% of infected persons, the illness recurs in more severe form within 48 hours following the viremic period. Symptoms include fever, nausea, vomiting, epigastric pain, jaundice, renal insufficiency, and cardiovascular instability. Viremia generally is absent during this phase of symptom recrudescence. A bleeding diathesis can occur, with hematemesis, melena, metrorrhagia, hematuria, petechiae, ecchymoses, epistaxis, and oozing blood from the gingiva and needle-puncture sites. Physical findings include scleral and dermal icterus, hemorrhages (e.g., hematemesis, melena, petechiae, ecchymoses), and epigastric tenderness without hepatic enlargement.

Multiple laboratory abnormalities can be observed in patients with yellow fever; these can vary depending on the severity and stage of illness. In the first week of the illness, leukopenia might occur; however, leukocytosis also can occur during the second week of the disease. Bleeding dyscrasias also can occur, together with elevated prothrombin and partial thromboplastin times, decreased platelet count, and presence of fibrin-split products. Hyperbilirubinemia might be present as early as the third day but usually peaks toward the end of the first week of illness. Elevations of serum transaminase levels occur in severe hepatorenal disease and might remain elevated for up to 2 months after onset.

DIAGNOSIS AND TESTING

Preliminary diagnosis is based on the patient's clinical features, vaccination status, and travel history. Diagnosing yellow fever based on signs and symptoms can be difficult because early in its course, the infection can be easily confused with malaria, typhoid, dengue fever and other viral hemorrhagic fevers.

Laboratory diagnosis generally is accomplished by testing serum to detect virus-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies by serologic assays. It is important to obtain a yellow fever vaccination history, as IgM antibodies to yellow fever vaccine virus can persist for several years following vaccination. Serologic cross-reactions occur with other flaviviruses, so positive results should be confirmed with a more specific test (e.g., plaque-reduction neutralization test). Early in the illness (during the first several days), yellow fever virus or yellow fever virus RNA often can be detected in the serum by virus isolation or nucleic acid amplification testing (e.g., reverse transcription-polymerase chain reaction [RT-PCR]). However, by the time overt symptoms are recognized, the virus or viral RNA usually is undetectable. Therefore, negative virus isolation and RT-PCR results cannot rule-out the diagnosis of yellow fever. Immunohistochemical staining of formalin-fixed material can also detect yellow fever virus antigen in histopathologic specimens.

RT-PCR and serological testing for yellow fever is available through NYSDOH's Wadsworth Center. Specimens should not be sent to NYSDOH for yellow fever virus testing without first obtaining approval from the LHD of the patient's county of residence or the NYSDOH BCDC. LHD contact information is available at: https://www.health.ny.gov/contact/contact_information/. If you are unable to reach the LHD, please contact the NYSDOH BCDC at 518-473-4439 during business hours or 866-881-2809 evenings, weekends, and holidays.

REPORTING CASES OF YELLOW FEVER

Under NYS Public Health Law 2012 and 10NYCRR 2.10, health care providers must ***immediately report*** by telephone any patient with suspected yellow fever virus. The report should be made to the LHD of the patient's county of residence. LHD contact information is available at: https://www.health.ny.gov/contact/contact_information/.

YELLOW FEVER VACCINE INFORMATION—CURRENT SHORTAGE

Yellow fever vaccine is recommended for anyone nine months or older who travels to high-risk areas. Yellow fever vaccine may be required for entry into certain countries. For most travelers, a single dose of yellow fever vaccine provides long-lasting protection and booster doses are no longer recommended by the CDC. However, a booster dose may be given to travelers who received their last dose of yellow fever vaccine at least 10 years ago and who are planning travel to areas with ongoing outbreaks or to highly endemic areas such as West Africa during peak transmission season or who plan to spend a prolonged period in high-risk areas. In addition, booster doses of yellow fever vaccine are recommended for certain populations (i.e., women who were pregnant when first vaccinated, hematopoietic stem cell transplant recipients, and HIV-infected persons) who might not have a robust or sustained immune response to the vaccine. Additional information on the yellow fever vaccine can be found at <https://www.cdc.gov/yellowfever/healthcareproviders/vaccine-info.html>

Recent manufacturing problems have resulted in a shortage of the only U.S.-licensed yellow fever vaccine (YF-VAX). This shortage is expected to lead to a complete depletion of yellow fever vaccine available for the immunization of U.S. travelers by mid-2017. CDC, the Food and Drug Administration (FDA) and Sanofi Pasteur are collaborating to ensure a continuous yellow fever vaccine supply in the U.S. As part of this collaboration, Sanofi Pasteur submitted an expanded access investigational new drug (eIND) application to FDA in September 2016 to allow for the importation and use of an alternative yellow fever vaccine manufactured by Sanofi Pasteur France, with safety and efficacy comparable to the U.S.-licensed vaccine; the eIND was accepted by FDA in October 2016. CDC and Sanofi Pasteur will continue to communicate information to the public and other stakeholders. A list of locations that will be administering the replacement vaccine (Stamaril) can be found at: <https://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search>
Additional information on the shortage can be found at https://www.cdc.gov/mmwr/volumes/66/wr/mm6617e2.htm?s_cid=mm6617e2_e.

ADDITIONAL INFORMATION

Related links and additional information on mosquito-borne disease, yellow fever can be found at:

- http://www.health.ny.gov/diseases/communicable/yellow_fever/fact_sheet.htm
- <https://www.cdc.gov/yellowfever/index.html>
- <https://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/yellow-fever>
- <https://wwwnc.cdc.gov/travel/notices>
- <https://www.cdc.gov/yellowfever/healthcareproviders/vaccine-info.html>
- <https://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search>
- <https://www.cdc.gov/yellowfever/maps/index.html>

If you have any questions regarding this information, please contact your LHD or the NYSDOH BCDC at (518) 473-4439 or via email at bcdc@health.ny.gov

¹ Travel notices are designed to inform travelers and clinicians about current health issues related to specific destinations.