

YELLOW FEVER

REPORTING INFORMATION

- **Class A:** Report immediately via telephone the case or suspected case and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report immediately via telephone to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism:
 - Immediate telephone reporting is required.
 - For the local health department, the case should be entered into the Ohio Disease Reporting System (ODRS) within 24 hours after the telephone report.
 - The ODH [Mosquito-borne Illness Case Investigation Form](#) is available for use to assist in local disease investigation. Information collected from the form should be entered into ODRS and not sent to ODH, unless otherwise requested. If requested, the form can be faxed to ODH at (614) 564-2456 or uploaded to the ODRS record.
- Key fields for ODRS reporting include: import status (whether the infection was travel-associated or Ohio-acquired), date of illness onset, symptoms, all fields in the Epidemiology module, the reason not vaccinated or the vaccine information if previously vaccinated and travel details in the Travel History module (with accurate departure and return dates along with city, province/county, state and country).

AGENT

Yellow fever (YF) virus is an RNA virus that belongs to the genus *Flavivirus* of the family *Flaviviridae*. It cross-reacts serologically with other flaviviruses (e.g., dengue, St. Louis encephalitis, West Nile, Japanese encephalitis, Zika viruses).

Infectious dose: A single bite from an infectious mosquito.

CASE DEFINITION

Clinical Description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria and, in some instances, renal failure, shock and generalized hemorrhages.

Laboratory Criteria for Diagnosis

- Four-fold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded or
- Demonstration of yellow fever virus, antigen or genome in tissue, blood or other body fluid.

Case Classification

Probable: A clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., ≥ 32 by complement fixation; ≥ 256 by immunofluorescence assay; ≥ 320 by hemagglutination inhibition; ≥ 160 by neutralization or a positive serologic result by immunoglobulin M (IgM)-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)

Confirmed: A clinically compatible case that is laboratory confirmed.

Comment

Yellow fever antibodies cross-react extensively with other flaviviruses (e.g., dengue, St. Louis encephalitis, West Nile, Japanese encephalitis, Zika viruses). Travel history may suggest that these other infections be ruled out.

SIGNS AND SYMPTOMS

Most people infected with yellow fever are asymptomatic or have mild disease with complete recovery. The initial illness presents as a sudden onset of fever, chills, headache, severe backache, myalgia, prostration, nausea and vomiting. Most patients improve after the initial presentation, but approximately 15% of cases experience a brief remission for a few hours to a day and then progress to develop a more serious or toxic form of the disease, which is characterized by high fever, jaundice, hemorrhagic symptoms and eventually shock and multi-organ failure. The overall case fatality for cases with jaundice is 20%-50%.

DIAGNOSIS

A presumptive diagnosis of yellow fever is often based on clinical features, places and dates of travel (if patient is from a non-endemic country), activities and epidemiologic history of the location where the presumed infection occurred. In addition to the more common causes of febrile illnesses, arboviruses such as chikungunya, dengue, Eastern equine encephalitis, LaCrosse, Powassan, St. Louis encephalitis, West Nile, Western equine encephalitis and Zika viruses should also be considered in the differential etiology.

Laboratory diagnosis of yellow fever usually includes testing serum to detect virus-specific IgM and neutralizing antibodies. The viremia for yellow fever virus in humans ceases by the time of, or soon after, onset of symptoms, so the virus can sometimes be detected in samples taken very early in the illness. The acute phase blood specimen should be collected immediately upon suspicion of a viral illness and a convalescent sample two or more weeks later. In fatal cases, nucleic acid amplification, histopathology with immunohistochemistry and virus culture of autopsy or biopsy tissues can also be positive. The diagnosis can be supported by the typical lesions in the liver.

Only a few state laboratories, including those at CDC, are capable of performing these specialized tests. Proper protocol is to send the serum or other specimens to CDC through the ODH Laboratory.

For clinical samples being sent to CDC's Arbovirus Diagnostic Laboratory for testing, the [CDC Specimen Submission Form](#) must accompany the samples. Be sure the date of illness onset and travel history fields are completed. Use test order code CDC-10282 for arbovirus serology. Please contact ODH at (614) 995-5599 to arrange for testing at CDC.

EPIDEMIOLOGY

Source

Monkeys serve as vertebrate reservoirs in the sylvatic cycle, and humans serve as the vertebrate reservoir in the urban cycle. *Aedes aegypti* mosquitoes serve as the principal vector in the urban cycle.

Occurrence

Enzootic sylvatic (forest-dwelling) yellow fever occurs in Africa south of the Sahara and in South America. Urban outbreaks are still reported. A primary case in Ohio would probably be imported.

Mode of Transmission

Yellow fever virus is spread by the bite of an infected mosquito. The yellow fever mosquito, *Aedes aegypti*, is the principal vector and is not known to be established in

Ohio. However, the Asian tiger mosquito, *Aedes albopictus*, is established in many Ohio counties and may serve as a potential vector. These mosquitoes become infected when they feed on a person infected with yellow fever virus. Infected mosquitoes can then spread the virus to other humans when they bite.

Period of Communicability

Humans are infectious to certain vector mosquito species from symptom onset through day 5.

Incubation Period

3-6 days.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

Investigation should reveal a specific travel history to an endemic area within one week prior to onset of illness. Accurate travel history and confirmation are desirable to document importation of yellow fever from endemic areas into the United States. It should be noted if travelers spent any time in the southeastern Atlantic or Gulf Coastal states, where *Aedes aegypti* is endemic, before returning to Ohio.

Treatment

Supportive. Yellow fever patients should be hospitalized for close observation.

Isolation and Follow-up Specimens

Section 3701-3-13, (EE), of the Ohio Administrative Code states:

"A person with confirmed or suspected yellow fever shall be isolated to prevent access of mosquitoes to the patient for at least five days after onset of disease."

A convalescent sample should be obtained two or more weeks after the acute sample. Autopsy blood and/or tissue samples may also be tested, if indicated. If the CDC laboratory is to be used, proper protocol is to send the sample(s) to CDC via the ODHL (see **DIAGNOSIS** above).

Public Health Significance

High in endemic areas. There is a low probability of endemic transmission of yellow fever in Ohio due to the low prevalence of the vectors and because of the brief period during which the patient is viremic. However, identification of a locally acquired case of yellow fever in Ohio warrants a vector investigation and vector control strategies to prevent an outbreak.

Contacts

No treatment or prophylaxis of contacts is indicated.

Prevention and Control

Vaccination

The yellow fever vaccine is recommended for people ≥ 9 months of age who are traveling to or residing in areas at risk for yellow fever virus transmission. For most travelers, a single dose of yellow fever vaccine provides long-lasting protection and a booster vaccine is not needed; however, some travelers may need a booster dose, and some countries may also require a booster dose of the vaccine before travelers gain entry. Yellow fever vaccine is only available at designated vaccination centers. CDC maintains a website of [yellow fever vaccination clinics](#).

The International Certificate of Vaccination (ICV) against yellow fever is required by many countries to gain entry. Vaccination is highly recommended for travel into infected areas. The ICV is valid for 10 years beginning 10 days after the date of vaccination. For more information, please refer to [CDC's yellow fever vaccine](#) information.

Travelers

Travelers entering endemic areas should be warned to avoid mosquitoes, use mosquito repellents, occupy screened quarters and use mosquito netting over beds.

Vector Investigation

Acutely infected persons must avoid being bitten by *Aedes* mosquitoes during the five days after illness onset, in order to prevent further transmission of the virus. Depending on local resources, environmental assessments around the homes of suspected viremic cases for *Aedes albopictus* mosquitoes may be useful to determine the risk for local transmission of yellow fever. Those jurisdictions with capacity should consider:

- Adult mosquito control:
 - *Ae. albopictus* (and *Ae. aegypti*) are most active during the day and are not effectively controlled by standard ultra-low volume (ULV) applications. Early morning or late evening applications are recommended.
 - Focus ULV barrier applications to the areas where human cases are present to reduce local transmission.
- Larval mosquito control:
 - Remove larval habitats.
 - Encourage the public to participate in efforts by discarding materials or closing containers (e.g., flower pots, buckets, tires, garbage cans).

Mosquito Bite Avoidance

The best way to prevent yellow fever virus infection is to avoid mosquito bites. Prevention tips are similar to those for other viral diseases transmitted by mosquitoes, such as dengue or West Nile virus:

- Use insect repellent [registered with the U.S. Environmental Protection Agency \(EPA\)](#) on exposed skin. Always follow the directions on the package. When using both sunscreen and insect repellent, apply the sunscreen first then the repellent.
- Wear long sleeves, pants and socks if feasible.
- Wear permethrin-treated clothing to repel and kill mosquitoes.
- Use screens on windows and doors to exclude mosquitoes. And, when available, A/C can make households less hospitable to mosquitoes.
- Participation in community and homeowner based vector-control strategies:
 - Ensure that water does not collect in containers around the home and community by emptying water from containers such as flowerpots, buckets, barrels and tires. Change the water in pet dishes, and replace the water in bird baths weekly. Drill holes in tire swings so water drains out. Empty children's wading pools and store on their sides after use.
 - Use chemical or biological control of larvae and adult mosquitoes when necessary.

What is yellow fever?

Yellow fever is a disease caused by a virus that is spread to humans by the bite of an infected mosquito.

Where does yellow fever virus occur?

Yellow fever virus is found in tropical and subtropical areas in Africa and South America. Yellow fever virus is a very rare cause of illness in U.S. travelers to these areas. The last case in Ohio was in 1878 in Gallipolis during an epidemic that began in New Orleans.

How is yellow fever transmitted?

Yellow fever is transmitted by the bite of an infected mosquito. Infants and children are at higher risk. There are two cycles of infection: one carried by monkeys and one by humans.

“Jungle yellow fever” is mainly a disease of monkeys in the tropical rain forest. People get it when they are bitten by mosquitoes that have been infected by monkeys. Jungle yellow fever is rare and occurs mainly in persons who work in tropical rain forests.

“Urban yellow fever” is a disease of humans. It is spread by mosquitoes that have been infected by other people. Urban yellow fever is the cause of most yellow fever outbreaks and epidemics.

How soon do people get sick after being bitten by an infected mosquito?

The incubation period (time from infection to illness) is usually 3-6 days.

What are the symptoms of yellow fever?

Initial symptoms of yellow fever include sudden onset of fever, chills, severe headache, back pain, general body aches, nausea and vomiting, fatigue and weakness. Most people will improve after these initial symptoms. However, roughly 15% of people will have a brief period of hours to a day without symptoms and will then develop a more severe form of yellow fever disease. In severe cases, a person may develop high fever, jaundice (a condition that involves yellow discoloration of the skin and the whites of the eyes), bleeding (especially from the gastrointestinal tract) and eventually shock and failure of many organs. Roughly 20%-50% of people who develop severe illness may die.

How is yellow fever diagnosed?

Diagnosis is usually based on blood tests that look for antibodies that a person’s immune system makes against the viral infection.

What is the treatment for yellow fever?

No specific treatments have been found to help patients with yellow fever. If possible, patients with yellow fever should be hospitalized for treatment of their symptoms and close observation by health care workers. Rest, fluids and use of pain medications and fever-reducing medications may relieve symptoms of fever and aching. Certain medications should be avoided, such as aspirin or other non-steroidal anti-inflammatory drugs (such as ibuprofen and naproxen) because these may increase the risk for bleeding.

How can people reduce the chance of getting infected with yellow fever virus?

Yellow fever can be prevented by vaccination. The vaccine is a live but attenuated (less potent) strain of the virus. Travelers should also take actions to prevent mosquito bites when in areas of Africa or South America with yellow fever transmission.

- **Use insect repellent.** When outdoors, use an EPA-registered insect repellent such as those containing DEET, picaridin, IR3535 or oil of lemon eucalyptus on exposed skin. Even a short time outdoors can be long enough to get a mosquito bite.
- **Wear proper clothing to reduce mosquito bites.** When weather permits, wear long sleeves, long pants and socks when outdoors. Mosquitoes may bite through thin clothing, so spraying clothes with repellent containing permethrin or another EPA-registered repellent gives extra protection. Clothing pretreated with permethrin is commercially available. Mosquito repellents containing permethrin are not approved for application directly to the skin.
- **Be aware of peak mosquito hours.** The peak biting times for many mosquito species is dusk to dawn. However, *Aedes aegypti*, one of the mosquitoes that transmits yellow fever virus, feeds during the daytime. Take extra care to use repellent and protective clothing during daytime as well as during the evening and early morning. Staying in accommodations with screened or air-conditioned rooms, particularly during peak biting times, will also reduce risk of mosquito bites.

What should I do if I think a family member might have yellow fever?

If you or anyone in your household has symptoms that are causing you concern, consult a healthcare provider promptly for proper diagnosis.

Who should get yellow fever vaccine?

Yellow fever vaccine is recommended for people age 9 months or older who are traveling to or living in areas at risk for yellow fever virus transmission in South America or Africa. Proof of yellow fever vaccine may be required for entry into certain countries. Country-specific yellow fever risk information, along with vaccine recommendations, can be found in the [Yellow Fever Vaccine Requirements and Recommendations table](#). For some countries, there are only certain areas where there is yellow fever risk; for those countries, more specific information is given in the chart to guide the recommendation for vaccination.

Who should not get yellow fever vaccine?

Infants younger than 6 months of age should not get the vaccine. In addition, anyone with a severe allergy to any part of the vaccine, including eggs, chicken proteins or gelatin should not get the vaccine. Anyone who has had a severe reaction to a previous dose of yellow fever vaccine should not be vaccinated again.

If you have any of the following conditions, your healthcare provider can help you decide whether you can safely receive the vaccine:

- HIV/AIDS or other disease that affects the immune system
- Weakened immune system as a result of cancer or other medical conditions, transplant or drug treatment (such as steroids, chemotherapy or others that affect immune function)
- Thymus disorder
- Adults 60 years of age and older
- Infants 6-8 months of age
- Pregnant women and nursing mothers

How long does yellow fever vaccination last?

For most people, one dose of the vaccine provides long-lasting protection. Certain people may benefit from another dose of the vaccine either because they have problems with their immune system or they are in higher risk settings.

Will I have to go to a special clinic to get a yellow fever vaccination?

Yes. Yellow fever vaccine is regulated by International Health Regulations, so only authorized providers can administer the vaccine. Most providers of yellow fever vaccine can also give you other vaccines or medicines for travel. To find an authorized yellow fever vaccination clinic, see the CDC list of providers at [Yellow Fever Vaccination Clinics](#).

Is yellow fever vaccine recommended for people over age 60 traveling to areas with risk for yellow fever?

People aged ≥ 60 years may be at increased risk for serious adverse events (serious disease or, very rarely, death) following vaccination compared with younger persons. This is particularly true if they are receiving their first yellow fever vaccination. Travelers aged ≥ 60 years should discuss with their healthcare provider the risks and benefits of the vaccine given their travel plans. In addition to considering the vaccine, travelers to endemic areas should protect themselves from yellow fever and other vector-borne diseases. Preventive measures include wearing clothes with long sleeves and long pants and using an effective insect repellent such as those with DEET, picaridin, IR3535 or oil of lemon eucalyptus.

What are the side effects of yellow fever vaccination?

Reactions to yellow fever vaccine are generally mild. They can include mild headaches, muscle aches and low-grade fevers. There have been reports of extremely rare but serious events following yellow fever vaccination.

I think I got sick from the vaccine, what should I do?

Consult with your healthcare provider. Ask your healthcare provider to report your case to the Vaccine Adverse Events Reporting System (VAERS) if he or she thinks the vaccine has made you sick.

I just got the yellow fever vaccine. Do I need to avoid contact with my immunocompromised family member?

No. There is no evidence that people who receive yellow fever vaccine shed the vaccine virus. Therefore, there is no need to avoid people whose immune systems do not work well.

Does the yellow fever vaccine contain thimerosal?

No, the FDA-approved yellow fever vaccine does not contain thimerosal.

How long should a woman wait to conceive after receiving a yellow fever vaccination?

Yellow fever vaccination has not been known to cause any birth defects when given to pregnant women. Yellow fever vaccine has been given to many pregnant women without any apparent adverse effects on the fetus. However, since yellow fever vaccine is a live virus vaccine, it poses a theoretical risk. While a two week delay between yellow fever vaccination and conception is probably adequate, a one month delay has been advocated as a more conservative approach. If a woman is inadvertently or of necessity vaccinated during pregnancy, she is unlikely to have any problems from the vaccine and her baby is very likely to be born healthy.

Medical waivers

Most countries will accept a medical waiver for persons with a medical reason for not receiving the vaccination. CDC recommends obtaining written waivers from consular or embassy officials before departure. Travelers should contact the embassy or consulate for specific advice. Typically, a physician's letter stating the reason for withholding the vaccination and written on letterhead stationery is required by the embassy or consulate. The letter should bear the stamp used by a health department or official immunization center to validate the International Certificate of Vaccination.

For more information, visit these websites:

- WHO Yellow Fever Fact Sheet: <http://www.who.int/mediacentre/factsheets/fs100/en/>
- CDC Yellow Fever Information: <http://www.cdc.gov/yellowfever>
- CDC Traveler's Health Yellow Fever Information:
<http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/yellow-fever>
- CDC Yellow Fever Vaccination Clinics: <http://wwwnc.cdc.gov/travel/yellow-fever-vaccination-clinics/search>