

Yellow Fever

1. DISEASE REPORTING

A. Purposes of Reporting and Surveillance

1. To identify cases of yellow fever associated with travel
2. To prevent further spread of the disease within the United States.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction.**
2. Health care facilities: **immediately notifiable to local health jurisdiction.**
3. Laboratories: isolation of yellow fever virus, or detection of viral antigen, antibody or nucleic acid **immediately notifiable to local health jurisdiction of the patient's residence**; specimen submission is required – serum (2 business days).
4. Local health jurisdictions: **suspected and confirmed cases are immediately notifiable** to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) (1-877-539-4344).

C. Local Health Jurisdiction Investigation Responsibilities

1. Alert CDES about possible cases.
2. Facilitate transport of specimens (e.g., serum) to the Washington State Department of Health Public Health Laboratories (PHL) if initial testing or confirmatory testing is needed. Please call CDES prior to submitting specimens (206-418-5500).
3. Report all *confirmed* and *probable* cases to CDES (see definitions below). Complete the Yellow Fever case report form (<http://www.doh.wa.gov/notify/forms/yellow.pdf>) and enter the data into the Public Health Issues Management System (PHIMS) as “Yellow Fever.”

2. THE DISEASE AND ITS EPIDEMIOLOGY

Background

Yellow fever is a rare cause of illness among travelers arriving in the United States. The disease is known to occur only in certain regions of Africa and South America.

A. Etiological agent

The etiologic agent is an RNA virus of the genus *Flavivirus* and family Flaviviridae.

B. Description of Illness

The disease typically begins with fever, headache, muscle aches, nausea and vomiting. The pulse may be slow and out of proportion to the elevated temperature (Faget's sign). Jaundice is moderate early in the disease and is intensified later. Albuminuria often helps to distinguish yellow fever from other types of viral hepatitis. Leukopenia appears early and is most pronounced about the fifth day of illness. Although up to 85% of illnesses resolve at this stage, others progress into an ominous “stage of intoxication” following a

brief 2-24 hour remission of symptoms. During this stage, patients develop liver failure, renal failure, and hemorrhagic symptoms characterized by epistaxis, gingival bleeding, hematemesis (coffee-ground or black), and melena. Up to 50% of cases that progress to intoxication are fatal.

C. Yellow fever in Washington State

No cases of yellow fever have been reported in Washington in over 50 years.

D. Vectors and Reservoirs

There are three transmission cycles for yellow fever virus – a *sylvatic* (or *jungle*) cycle that involves mosquitoes and non-human primates; an *intermediate* cycle involving various non-aegypti *Aedes* mosquito species and humans in African savannahs; and an *urban* cycle involving *Aedes aegypti* mosquitoes and humans. Sylvatic transmission is restricted to tropical regions of Africa and South America, where a few hundred cases occur annually, usually among young adult males who work in forested areas. The intermediate cycle occurs in the humid savannah of Africa, where infected mosquitoes feed on both monkeys and humans.

Except for a limited urban outbreak during 1997 in Santa Cruz, Bolivia, urban yellow fever has not occurred in the western hemisphere since the 1950s. Still, urban growth and reinfestation with *Ae. aegypti* in many areas (including the southern United States) raise the risk urban yellow fever transmission should a yellow fever-viremic person return to those areas. Humans are not essential for maintaining the jungle cycle but are the primary amplifying host in the urban cycle.

E. Modes of Transmission

Except on very rare occasions, yellow fever is acquired through the bite of an infected mosquito.

In 2009, multiple cases of transfusion-associated transmission of the attenuated yellow fever vaccine strain occurred. Despite serologic evidence of transmission, no adverse events attributable to the transfused virus were noted in the blood recipients. Also in 2009, a confirmed case of yellow fever vaccine-associated meningoencephalitis occurred in a breast-fed, three-week-old infant following maternal vaccination.

F. Incubation Period

Three to six days.

G. Period of Communicability

Yellow fever is not directly transmitted person-to-person, but can be indirectly transmitted among persons via a mosquito vector as described above in the intermediate and urban transmission cycles. The disease is readily transmitted where many susceptible people and abundant vector mosquitoes coexist. Viral concentration in blood is adequate to infect mosquitoes from shortly before fever onset through the fifth day of illness. Once infected, mosquitoes remain so for life. See above for vaccine transmission.

H. Treatment

Treatment is supportive, often involving hospitalization with intensive care therapy.

3. CASE DEFINITION

A. Clinical Description

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

B. Laboratory Confirmation Criteria for Diagnosis

1. Fourfold 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
2. Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

C. Case Definition (1997)

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-capture enzyme immunoassay]).

Note: 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.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

Laboratory diagnosis is often made by demonstrating the presence of yellow fever-specific RNA by PCR, specific immunoglobulin M (IgM) in early sera, or a rise in yellow fever-specific antibody titer in paired acute and convalescent samples. Serologic cross-reactions occur with other flaviviruses. Positive complement fixation tests can often distinguish a recent infection from immunity due to vaccination. Laboratory diagnosis can also be made by demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid.

B. Tests Available at the Washington State Public Health Laboratories (PHL)

PHL does not perform testing for yellow fever but will forward specimens to the Centers for Disease Control and Prevention (CDC) for testing. Please contact the Communicable Disease Epidemiology Section for approval prior to submitting specimens. Patient history must include recent travel to a known endemic area to be eligible for testing.

Note that PHL requires all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Specimen Collection

Serum should be refrigerated and transported cold. Frozen serum is also acceptable. It is

strongly recommended to collect both acute and convalescent (2 weeks later) specimens.

Specimens should be submitted with a completed PHL Serology Submission form available at: <http://www.doh.wa.gov/EHSPHL/PHL/Forms/SerVirHIV.pdf>

Please call PHL for instructions for shipping specimens other than serum.

5. ROUTINE CASE INVESTIGATIONS

Since yellow fever rarely occurs in the United States, call Communicable Disease Epidemiology Section to discuss the case investigation. Interview the case and others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

If the case tests positive for yellow fever at a laboratory other than a public health laboratory or CDC, facilitate transport of the specimen to Washington State Public Health Laboratories for further testing.

B. Identify Potential Sources of Infection

Obtain a travel history and ask about mosquito exposures during the likely exposure period.

C. Identify Potentially Exposed Persons

Identify other persons who traveled with the case. Determine if the patient donated blood during the communicable period. If the patient donated blood, inform the blood bank of the potential exposure.

6. CONTROLLING FURTHER SPREAD

A. Infection Control / Case Management

1. Hospitalized patients should be cared for using standard precautions.
2. Patients being treated for yellow fever in the United States should be sequestered from mosquitoes while viremic to avoid urban transmission. Given that *Ae. aegypti*, the principle mosquito vector, is not endemic to Washington State, the risk of the case infecting mosquitoes which could subsequently infect other humans is very low. This is not true in many other areas in the United States.

B. Contact Management:

None, since yellow fever is not directly transmitted from person-to-person.

C. Management of Other Exposed Persons:

If other persons who traveled with the case have symptoms consistent with yellow fever, refer them to a health care provider and arrange for laboratory testing.

7. MANAGING SPECIAL SITUATIONS

Not applicable

8. ROUTINE PREVENTION

See <http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/yellow-fever.aspx> and http://www.cdc.gov/ncidod/dvbid/yellowfever/YF_Prevention.html

A. Immunization Recommendations

For information about yellow fever vaccine recommendations, please see the 2002 Yellow Fever Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2002 at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5117a1.htm>.

Note that some countries have entry requirements that include yellow fever vaccination.

As a precautionary measure, vaccination of nursing mothers should be avoided because of the small risk for the transmission of vaccine strain virus to the breast-fed infant. When travel of nursing mothers to high-risk yellow fever-endemic areas cannot be avoided or postponed, such persons can be vaccinated.

B. Other Prevention Recommendations

When traveling in areas where yellow fever occurs (i.e., areas of Africa and South America), persons should avoid mosquito bites by:

- **Using mosquito repellent.** The most effective mosquito repellents contain the EPA approved active ingredients DEET (N, N-diethyl-m-toluamide), picaridin, oil of lemon eucalyptus, or IR3535. These products come in lotions, creams, gels, sprays, and towelettes. Read and follow instructions on the label. Do not over use repellents. Take special care when using repellent on children.
 - Additional information regarding the use of mosquito repellents can be found on the CDC website at: http://www.cdc.gov/ncidod/dvbid/westnile/ga/insect_repellent.htm and <http://www.cdc.gov/ncidod/dvbid/westnile/RepellentUpdates.htm>
- **Wearing 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 will give extra protection. Don't apply repellents containing permethrin directly to skin.
- **Be Aware of Peak Mosquito Hours.** *Aedes aegypti*, the main vector of yellow fever virus, feeds during the daytime. Repellent and protective clothing should be used during the daytime as well as evening and early morning. In addition, one may consider avoiding outdoor activities during these times in areas where yellow fever is a risk. Bed nets can reduce the number of mosquito bites from other mosquito species that transmit communicable diseases other than yellow fever and should be used for hospitalized persons with yellow fever viremia to prevent nosocomial transmission.

ACKNOWLEDGEMENTS

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UPDATES

March 2008: In Section 1C, the guideline for timeliness of initiating an investigation was removed.

July 2008: In Section 8B, IR3535 was added as a safe and effective mosquito repellent.

June 2009: In Section 4D, updated laboratory submission requirements.

January 2010: In Section 2D and G, the intermediate transmission cycle was added and in Section 4C, the laboratory form link was updated.

June 2010: In Sections 2 (vaccine transmission) and 4 were updated.

January 2011:

The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision.