

PUBLIC HEALTH REFERENCE SHEET

Yellow fever



Name	Yellow Fever Virus (family <i>Flaviviridae</i> and genus <i>Flavivirus</i>)
Reservoir & Transmission	Humans and <i>Aedes</i> mosquitoes (urban areas) Non-human primates and forest mosquitoes (rural areas) Bite of an infected <i>Aedes spp.</i> Mosquito
Incubation Period	3–6 days
Common Symptoms	Fever, headache, nausea, vomiting, jaundice, elevated total bilirubin ≥ 3.0 mg/dl
Gold Standard Diagnostic Test	Serology of IgM and neutralizing antibodies
Risk Groups	Unvaccinated travelers, those who do not have vaccine-acquired or naturally acquired immunity and live near forest areas or in <i>A. aegypti</i> -infested areas
Geographic Significance	Sub-Saharan Africa, tropical South America

What is yellow fever?

Yellow fever is a disease caused by the yellow fever (YF) virus which is a single-stranded RNA virus that belongs to the genus *Flavivirus*.

What is the occurrence of yellow fever?

YF occurs in sub-Saharan Africa and tropical South America, where it is endemic and intermittently epidemic. Most YF disease in humans is due to sylvatic or intermediate transmission cycles. Urban YF occurs periodically in Africa and sporadically in the Americas.

How is yellow fever transmitted?

- Vectorborne transmission of YF virus occurs via the bite of an infected mosquito, primarily *Aedes* or *Haemagogus* spp. Nonhuman primates and humans are the main reservoirs of the virus, and anthroponotic (human-to-vector-to-human) transmission occurs. YF virus has three transmission cycles: sylvatic (jungle), intermediate (savannah), and urban.
- The sylvatic (jungle) cycle involves transmission of virus between nonhuman primates and mosquito species found in forest canopies. Virus is transmitted from monkeys to humans via mosquitoes when occupational or recreational activities encroach into the jungle. In Africa, an intermediate (savannah) cycle involves transmission of YF virus from tree hole—breeding *Aedes* spp. to humans in jungle border areas. YF virus can be transmitted from monkeys-to-humans or from human-to-human via these mosquitoes. The urban cycle involves transmission of virus between humans and peridomestic mosquitoes, primarily *Ae. aegypti*.
- Humans infected with YF virus experience the highest levels of viremia shortly before onset of fever and for the first 3–5 days of illness, during which time they can transmit the virus to mosquitoes. Because of the high level of viremia, bloodborne transmission theoretically can occur via transfusion or needlesticks. One case of perinatal transmission of wild-type YF virus from a woman who developed symptoms of YF 3 days prior to delivery has been documented; the infant subsequently tested positive for YF viral RNA and died of fulminant YF on the 12th day of life (CDC, 2023).

Who is at risk for yellow fever?

In areas of Africa with persistent circulation of YF virus, natural immunity accumulates with age; consequently, infants and children are at greatest risk for disease. In South America, YF occurs

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most frequently in unimmunized young people exposed to mosquito vectors through their work in forested areas.

A traveler's risk for acquiring YF is determined by their immunization status as well as destination-specific (e.g., local rate of virus transmission) and travel-associated (e.g., exposure duration, occupational and recreational activities, season) factors.

What are the signs and symptoms of yellow fever?

Most people infected with YF virus have minimal or no symptoms and are unlikely to seek medical attention. For those who develop symptomatic illness, the incubation period is typically 3–6 days. The initial illness is nonspecific: backache, chills, fever, headache, myalgia, nausea and vomiting, and prostration. Most infected people improve after the initial presentation. After a brief remission of ≤ 48 hours, 12% of infected patients progress to a more serious form of the disease, characterized by hemorrhagic symptoms, jaundice, and eventually shock and multisystem organ failure. The case-fatality rate for severe cases is 30%–60% (CDC, 2023).

How is yellow fever diagnosed?

YF is a nationally notifiable disease. A preliminary diagnosis is based on clinical presentation and exposure details. Laboratory diagnosis is best performed by virus isolation or nucleic acid amplification tests (e.g., reverse transcription PCR (RT-PCR)) or by serologic assays. Perform virus isolation or nucleic acid amplification tests for YF virus or YF viral RNA early in the course of the illness. By the time more overt symptoms are recognized, the virus or viral RNA might no longer be detectable; thus, virus isolation and nucleic acid amplification testing should not be used to rule out a diagnosis of YF. Serologic assays can be used to detect virus-specific IgM and IgG antibodies. Because of the possibility of cross-reactivity between antibodies against other flaviviruses, however, more specific antibody testing (e.g., a plaque reduction neutralization test) should be performed to confirm the infection. Contact your state or local health department or call the Centers for Disease Control and Prevention (CDC) Arboviral Diseases Branch at 970-221-6400 for assistance with diagnostic testing for YF virus infections (CDC, 2023).

How is yellow fever treated?

No specific medications are available to treat YF virus infections; treatment is directed at symptomatic relief or life-saving interventions. Fluids, rest, and use of analgesics and antipyretics might relieve symptoms of aching and fever. Avoid prescribing medications that can increase the risk for bleeding (e.g., aspirin or other nonsteroidal anti-inflammatory drugs). During the first few days of illness, protect infected people from further mosquito exposure by keeping them indoors or under a mosquito net, so they do not contribute to the transmission cycle.

How can yellow fever be prevented?

The best way to prevent mosquito-borne diseases, including YF, is to avoid mosquito bites. YF is preventable by a relatively safe, effective vaccine. All YF vaccines currently manufactured are live attenuated viral vaccines. Only one YF vaccine (YF-VAX, Sanofi Pasteur) is licensed for use in the United States. YF vaccine is recommended for people aged ≥ 9 months who are living in, or traveling to, areas with risk for YF virus transmission in Africa or South America. A single dose of YF vaccine protects most people for life, but a booster dose after 10 years may be recommended for some travelers, as well as some countries may require evidence of YF

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vaccination within the past 10 years. Visit the CDC web site for country-specific YF vaccination recommendations and requirements at <https://wwwnc.cdc.gov/travel/yellowbook/2024/preparing/yellow-fever-vaccine-malaria-prevention-by-country>.

What are some Public Health considerations?

- When reporting cases of YF in the Disease Reporting System Internet (DRSi), document relevant travel and deployment history occurring within the incubation period and note the patient's YF immunization history.
- As proof of vaccination, individuals must possess an International Certificate of Vaccination or Prophylaxis (ICVP), Form CDC 731, that validates with the provider's signature and an official YF vaccination stamp. For all non-operational and leisure travel to endemic areas, follow the Advisory Committee on Immunization Practices, which recommends that a single lifetime dose of YF vaccine is sufficient for most travelers. Consult the DHA Immunization Healthcare Division website at <https://www.health.mil/Military-Health-Topics/Health-Readiness/Immunization-Healthcare/Vaccine-Recommendations/Vaccine-Recommendations-by-AOR> for deployment vaccine recommendations by Area of Responsibility (AOR).

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