Yellow Fever

Signs and Symptoms	• Acute onset fever, headache, muscle aches, nausea, vomiting, and jaundice • Pulse may be relatively slow for fever • ~15% progress after 24 hour remission to hemorrhage, hepatorenal failure, and shock marked by jaundice, albuminuria, and leukopenia with 30-60% mortality	
Incubation	3-9 days	
Case classification	**Clinical criteria**: acute illness with fever, jaundice, or elevated total bilirubin ≥3mg/dl	
	Confirmed: Clinically consistent illness with ≥4-fold rise or fall in yellow fever antibody titer OR demonstration of yellow fever virus antigen or genome in tissue, blood or other body fluid OR IgM positive with virus-specific neutralizing antibodies, without recent yellow fever vaccine	**Probable**: Clinically consistent illness and epi-linked with IgM positive AND negative IgM for other arboviruses AND no history of yellow fever vaccination
Differential diagnosis	Other flavivirus infection, viral hemorrhagic fever (e.g., Ebola, Lassa, dengue, Congo-Crimean), viral hepatitis, arenavirus, louse-borne relapsing fever, toxic hepatitis	
Treatment	Supportive; may require intensive care	
Duration	About a week if uncomplicated, weeks if hemorrhagic disease	
Exposure	Mosquito-borne in sub-Saharan Africa and South America, including Brazil in 2018	
Laboratory testing	Local health jurisdiction (LHJ) and Office of Communicable Disease Epidemiology (CDE) arrange testing if suspected based on illness and travel – **urgent** • Washington State Public Health Laboratories can forward specimens to CDC • **Best specimens**: serum (acute and convalescent), biopsy tissue, autopsy specimen *Specimen shipping (Section 4):* • Hospital to keep all specimens **cold, ship cold** with Serology form https://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf	
Public health actions **URGENT**	LHJ immediately contacts CDE 877-539-4344 for diagnosis • Yellow fever is internationally notifiable • Obtain serum for testing at CDC • Interview for risk exposure, particularly travel to an endemic area • Sequester from mosquitoes (*Aedes*) • Identify others who travelled with the case and interview for symptoms • Determine if case donated blood, tissues, or body fluids and notify agency *Infection Control:* standard precautions	

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) Office of Communicable Disease Epidemiology (CDE) (206-418-5500 or 1-877-539-4344).

C. Local Health Jurisdiction Investigation Responsibilities

1. Alert CDE about possible cases.
2. Facilitate transport of specimens to the Washington State Department of Health Public Health Laboratories (PHL) if initial testing or confirmatory testing is needed. Please call CDE prior to submitting specimens (206-418-5500).
3. Report all *confirmed* and *probable* cases to CDE (see definitions below). Complete the Yellow Fever case report form (https://www.doh.wa.gov/Portals/1/Documents/5100/210-064-ReportForm-Yellow.pdf) and enter the data into the Washington Disease Reporting System (WDRS) as "Yellow Fever."

2. THE DISEASE AND ITS EPIDEMIOLOGY

Background

Yellow fever is a very rare cause of illness among travelers arriving in the United States. The disease is known to occur only in tropical and subtropical Africa and South America. CDC recommended vaccine for some areas of Brazil due to an outbreak beginning in 2017.

A. Etiological agent

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

B. Description of Illness

Symptoms typically begin with fever, chills, headache, muscle aches, nausea and vomiting. The pulse may be slow and out of proportion to the fever (Faget's sign). Jaundice is moderate early in the disease and increases later. Albuminuria often helps to distinguish yellow fever from other causes of viral hepatitis. Leukopenia appears early

and peaks about the fifth day of illness. Although up to 85% of illnesses resolve at this stage, after a 2-24 hour remission others progress to severe disease. During this stage, patients develop liver failure, renal failure, and hemorrhagic symptoms characterized by epistaxis, gingival bleeding, hematemesis (coffee-ground or black vomit), and melena (black stool). Up to 60% of cases that progress to severe disease are fatal.

C. Yellow fever in Washington State

No cases of wild-type yellow fever disease have ever been reported in Washington. One case of yellow fever vaccine-associated viscerotropic disease was reported in 2002, and one case of yellow fever vaccine-associated neurologic disease was reported in 2018.

D. Vectors and Reservoirs

There are three transmission cycles for yellow fever virus – a *sylvatic* (or *jungle*) cycle involving mosquitoes and non-human primates; an *intermediate* cycle involving various *Aedes* mosquito species and humans or nonhuman primates in African savannahs; and an *urban* cycle involving *Aedes aegypti* and humans. The sylvatic cycle is restricted to tropical regions of Africa and South America with a few hundred cases annually, usually 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.

Reinfestation with *Ae. aegypti* in many areas (including the southern United States) would raise the risk of urban yellow fever transmission should a yellow fever-viremic person arrive in 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. The virus can be transmitted through blood, body fluid, or tissue.

California reported transfusion-associated transmission of the attenuated yellow fever vaccine strain in 2009 (https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5902a2.htm). Despite serologic evidence of transmission, no adverse events in blood recipients were attributed to the transfused virus. Also in 2009, a breast-fed, three-week-old infant had confirmed yellow fever vaccine-associated meningoencephalitis after maternal vaccination.

F. Incubation Period

Three to nine 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 strain transmission.