

Yellow Fever



Public Health Branch

1. Case Definition

1.1 Laboratory-Confirmed Case:

Clinical illness* with laboratory confirmation of infection:

- Isolation of yellow fever virus (non-vaccine strain)
OR
- Detection of yellow fever virus nucleic acid in body fluids or tissue (non-vaccine strain)
OR
- A significant (i.e., fourfold or greater) rise in antibody titre (using the plaque reduction neutralization test) to the yellow fever virus in the absence of yellow fever vaccination
OR
- A single elevated yellow fever virus IgM antibody titre in the absence of yellow fever vaccination within the previous two months (1).

1.2 Probable Case:

Clinical illness* with laboratory evidence of infection:

- A stable elevated antibody titre to yellow fever virus with no other known cause
AND
- Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination (1).

*Clinical illness is characterized by acute onset of fever 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 (1). Illness must occur in an individual with a compatible

travel history, i.e., travel to an area of South America or Africa endemic for yellow fever in the past 14 days.

Note: The Manitoba Health Surveillance Unit monitors naturally acquired yellow fever disease only, not illness resulting from yellow fever vaccination. Post-vaccination illnesses are captured by the AEFI (Adverse Events Following Immunization) reporting.

2. Reporting and Other Requirements

Laboratory:

- All positive laboratory results are reportable to the Public Health Surveillance Unit (204-948-3044 secure fax).

Health Professional:

- Probable (clinical) cases of yellow fever are reportable to the Public Health Surveillance Unit by telephone (204-788-6736) during regular hours (8:30 a.m. to 4:30 p.m.) AND by secure fax (204-948-3044) on the **same day** that they are identified. After hours telephone reporting is to the Medical Officer of Health on call at (204-788-8666). The *Clinical Notification of Reportable Diseases and Conditions* form https://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0013.pdf should be used.
- Adverse events following immunization (AEFI) should be reported by health care professional by completing and returning the form available at: http://www.gov.mb.ca/health/publichealth/cdc/docs/aeFI_form.pdf.

Regional Public Health or First Nations Inuit Health Branch (FNIHB):

- Once the case has been referred to Regional Public Health or FNIHB, the *Communicable Disease Control Investigation Form* https://www.gov.mb.ca/health/publichealth/cdc/protocol/mhsu_0002.pdf should be completed and returned to the Public Health Surveillance Unit by secure fax (204-948-3044).

3. Clinical Presentation/Natural History

The majority of infected persons are asymptomatic (2). Clinical disease varies from mild febrile illness to severe disease with jaundice and hemorrhage (2). When symptomatic, initial symptoms may include sudden onset of fever, chills, headache, backache, general muscle pain, prostration, nausea, and vomiting (2). The pulse may be slow and weak and out of proportion to the elevated temperature (Faget sign) (2). Leukopenia occurs early in the course of the illness (2). Resolution of this stage of the infection usually concludes the illness (3). However, in approximately 15% of cases, there is a brief remission of hours to a day, followed by recurrence of initial symptoms with progression to jaundice and hemorrhagic symptoms, including epistaxis, gingival bleeding, hematemesis, or melena (2). Among the 15% of cases who develop severe illness, the case fatality rate is 20% to 60% (4). Recovery from yellow fever results in lifelong immunity (2).

YEL-AND and YEL-AVD

Rare serious adverse events may follow immunization. Yellow fever virus vaccine-associated neurotropic disease (YEL-AND)

occurs as a result of vaccine virus invasion of the central nervous system (CNS) (5). It is a group of clinical syndromes that includes meningoencephalitis, acute disseminated encephalomyelitis, Guillain Barré syndrome and acute bulbar palsy (5). Autoimmune manifestations may result in CNS or peripheral nerve damage (5). YEL-AND typically occurs 4 to 23 days post-vaccination (5). The clinical course is usually brief with full recovery (5). Yellow fever vaccine-associated viscerotropic disease (YEL-AVD) resembles wild-type yellow fever virus infection with onset 2 – 5 days following vaccination (5). It is characterized by severe illness with multi-organ failure (5), and can be fatal (6).

4. Etiology

Yellow fever is caused by a RNA virus from the family *Flaviviridae* (5).

5. Epidemiology

5.1 Reservoir and Source:

In urban areas: humans and mosquitoes (*Aedes aegypti*); in areas of rainforest: monkeys and mosquitoes; and in savannah areas: humans, monkeys and mosquitoes (7).

5.2 Transmission:

Yellow fever virus is transmitted to humans through the bite of an infected mosquito, mainly the *Aedes* and *Haemagogus* species (5). There are three transmission cycles for yellow fever: sylvatic (jungle), intermediate (savannah), and urban (6). The sylvatic cycle involves transmission of the virus between nonhuman primates and mosquito species found in the forest canopy (6). The virus is transmitted via mosquitoes from monkeys to humans when the humans encroach into the

jungle during occupational or recreational activities (6). An intermediate cycle that occurs only in Africa involves transmission of the yellow fever virus from tree hole-breeding *Aedes* spp. to humans living or working in jungle border areas (6, 7). In this cycle, the virus may be transmitted from monkeys to humans or from human to human via these mosquitoes (6). The urban cycle involves transmission of the virus between humans and peridomestic mosquitoes, primarily *Ae. aegypti* (6) and occurs in both Africa and South America (7). Transfusion-related transmission of yellow fever vaccine virus has been reported (8). The probable transmission of the vaccine strain of the yellow fever virus to an infant through breastfeeding has also been reported (9).

5.3 Occurrence:

General: The yellow fever virus is endemic in tropical areas of Africa and the Americas (6). Refer to <https://wwwnc.cdc.gov/travel/yellowbook/2020/travel-related-infectious-diseases/yellow-fever> for countries with risk of yellow fever virus transmission. The World Health Organization estimates that approximately 200,000 yellow fever cases occur annually with up to 30,000 deaths (5). Approximately 90% of cases occur in Africa, and about 10% in South America (10). The rate of transmission of yellow fever virus is lower in South America than in Africa, in part because of mass immunization campaigns in response to outbreaks of the disease (11). In Africa, peak transmission occurs in the rainy season and early dry season from July through October (10). Outbreaks have recently been identified in Angola, Nigeria and Brazil (12-14).

Canada: The first reported case of yellow fever in Canada (since reporting began in

1930) occurred in 2008 (15). Three cases were reported in 2015 and two in 2016 (15).

Manitoba: One case of yellow fever was reported in a male in 2016.

5.4 Incubation Period:

The incubation period is three to six days (5).

5.5 Host Susceptibility and Resistance:

People of all ages are equally susceptible, but in epidemics those too young to have been immunized during previous epidemics are more vulnerable (10). Infancy and older age are associated with increased severity and lethality of infection with yellow fever virus (11). Recovery from yellow fever results in lifelong immunity (2). Transient passive immunity in infants born to immune mothers may persist for up to six months (2). In 2014, the WHO Strategic Advisory Group of Experts on Immunization concluded that a single dose of yellow fever vaccine provides sustained immunity and lifelong protection against yellow fever disease and that a booster dose is not needed (6). This change came into force legally in June 2016 (16). The CATMAT (Committee to Advise on Tropical Medicine and Travel) statement does not recommend the use of a booster dose of the yellow fever vaccine for travellers to endemic regions, except for certain groups at increased risk and for whom it is safe to administer the vaccine. Refer to statement <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/use-booster-doses-yellow-fever-vaccine.html>.

5.6 Risk Factors:

The risk of acquiring yellow fever in South America is lower than in Africa, because the

mosquitoes that transmit the virus between monkeys in the forest canopy in South America do not often come into contact with humans (6). The risk for infection in South America is highest in the rainy season and is highest during the end of the rainy season and the beginning of the dry season in West Africa (6).

5.7 Period of Communicability:

Once infected, mosquitoes remain infected for life (2). The blood of patients is infective for mosquitoes shortly before onset of fever and for the first 3 – 5 days of illness (2, 5).

6. Diagnosis

Laboratory diagnosis is made by isolation of virus from blood (early in the illness) or molecular detection of yellow fever virus by polymerase chain reaction (PCR). Yellow fever virus RNA has been detected in the blood as well as the urine (17-19) and semen of infected humans (17, 18).

Serologic diagnosis is made by a fourfold or greater rise in neutralizing antibody titre between acute and convalescent serum or by demonstrating specific IgM in early sera, in the absence of yellow fever vaccination in the previous two months. Specimen testing is not available at Cadham Provincial Laboratory. Testing is referred out. Please note, this is a containment level 3 organism, thus arrangements must be made with CPL prior to shipping samples.

7. Key Investigations for Public Health Response

- Travel history.
- Immunization history.

8. Control

8.1 Management of Cases:

- Management is supportive.

Treatment:

- There is no specific treatment.

Infection Prevention and Control:

- Routine Practices.

8.2 Management of Other Potentially Exposed Individuals:

- Regional Public Health will advise fellow travelers of infected persons to report and investigate any signs and symptoms compatible with yellow fever infection.

8.3 Preventive Measures:

- Immunization according to recommendations by CATMAT. Refer to the Statement on the Use of Booster Doses of Yellow Fever Vaccine <https://www.canada.ca/en/public-health/services/publications/diseases-conditions/use-booster-doses-yellow-fever-vaccine.html> .
- For travelers who cannot be immunized and for whom travel is unavoidable, using protective clothing and permethrin-treated clothes and bednets, staying in locations with air-conditioning, screens and bednets and using mosquito repellents (day-time and night-time application) may help lower the risk of disease (2).
- A four-week blood donation deferral in Canada, following yellow fever vaccination to prevent transfusion-related vaccine virus transmission (20).

- Vector surveillance and control (e.g., eliminating potential mosquito breeding sites) in endemic areas (21).

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