



Merlin disease code: 06090 Yellow Fever

[Paper case report form](#)

Specimens for all cases must be sent to the Bureau of Public Health Laboratories

Merlin extended data required

Clinical criteria for case classification

One or more of the following, in the absence of a more likely etiology: fever, jaundice, or bilirubin ≥ 3.0 mg/dL.

Laboratory criteria for case classification

Confirmatory:

One or more of the following:

- Both of the following:
 - Isolation of virus or detection of specific viral antigen or nucleic acid in tissue, blood, cerebrospinal fluid (CSF), or other body fluid (e.g., culture, immunohistochemistry [IHC], polymerase chain reaction [PCR]),
 - **And** no history of yellow fever vaccination within 30 days before illness onset, unless there is molecular evidence of infection with wild-type yellow fever virus,
- **Or** both of the following:
 - Fourfold or greater change in virus-specific neutralizing antibody titers in paired sera (e.g., plaque reduction neutralization [PRNT]),
 - **And** no history of yellow fever vaccination within 30 days before illness onset,
- **Or** all of the following:
 - Virus-specific IgM antibodies in serum or CSF (e.g., enzyme immunoassay [EIA], microsphere immunoassay [MIA], immunofluorescence assay [IF]),
 - **And** confirmatory virus-specific neutralizing antibodies in the same or a later specimen (e.g., PRNT),
 - **And** no history of yellow fever vaccination.

Presumptive:

All of the following:

- Virus-specific IgM antibodies in serum or serum (e.g., EIA, MIA, IF),
- **And** negative, equivocal, or indeterminate result for IgM antibodies in serum or CSF for arboviruses endemic to the region where exposure occurred (e.g., EIA, MIA, IF),
- **And** no history of yellow fever vaccination.

Supportive:

One or more of the following:

- Both of the following:
 - Isolation of virus from or detection of specific viral antigen or nucleic acid in tissue, blood, CSF, or other body fluid (e.g., culture, IHC, PCR)
 - **And** yellow fever vaccination within 30 days before illness onset with molecular evidence of infection with the vaccine strain;

- **Or** both of the following:
 - One or more of the following:
 - Isolation of virus from or detection of specific viral antigen or nucleic acid in tissue, blood, CSF, or other body fluid (e.g., culture, IHC, PCR);
 - **Or** fourfold or greater change in virus-specific neutralizing antibody titers in paired sera (e.g., PRNT);
 - **Or** both of the following:
 - Virus-specific IgM antibodies in serum or CSF (e.g., EIA, MIA, IF)
 - **And** confirmatory virus-specific neutralizing antibodies in the same or a later specimen (e.g., PRNT);
 - **Or** both of the following:
 - Virus-specific IgM antibodies in serum or CSF (e.g., EIA, MIA, IF)
 - **And** negative, equivocal, or indeterminate result for IgM antibodies in serum or CSF for arboviruses endemic to the region where exposure occurred (e.g., EIA, MIA, IF);
 - **And** yellow fever vaccination within 30 days before illness onset where vaccine-associated illness could not be ruled out

Epidemiological criteria for case classification

One or more of the following:

- Resides in or recent travel to an area with known yellow fever virus transmission,
- **Or** epidemiologically linked to a confirmed or probable case,
- **Or** likely vector exposure in an area with suitable seasonal and ecological conditions for potential local vector-borne transmission,
- **Or** receipt of blood or blood products within 30 days before illness onset,
- **Or** receipt of organ or tissue transplant within 30 days before illness onset.

Case classification

Confirmed:

A clinically compatible illness in a person with confirmatory laboratory criteria and epidemiological criteria.

Probable:

A clinically compatible illness in a person with presumptive laboratory criteria and epidemiological criteria.

Suspect:

One or more of the following:

- A clinically compatible illness in a person with supportive laboratory criteria
- **Or** a person with confirmatory or presumptive laboratory criteria and epidemiological criteria.

Criteria to distinguish a new case from previous reports

Not applicable.

Comments

Cross-reaction with related flaviviruses (e.g., dengue, West Nile, yellow fever, Japanese encephalitis viruses) on serological tests is common and results may be difficult to interpret. Due to this cross reactivity, it is important to ask if there has been any lifetime travel to a flavivirus-endemic country or vaccination for Japanese encephalitis virus.

Yellow fever vaccination history is essential to properly interpret yellow fever diagnostic test results. Following routine vaccination, yellow fever vaccine viral RNA can be detected in serum for up to 14 days, and IgM and neutralizing antibodies can persist for years. In addition, yellow fever vaccine-associated viscerotropic disease is a rare serious adverse event in which vaccine virus proliferates in multiple organs within weeks after vaccination; viral RNA and antigen can be detected in serum and tissues and may be indistinguishable from wild-type disease without additional testing.

Arboviral IgM antibodies may be detected in some patients months or years after their acute infection or vaccination. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a fourfold or greater change in virus-specific antibody neutralizing titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient's recent illness. Clinical and epidemiologic history also should be carefully considered.

Clinicians should also consider testing for dengue, chikungunya, and Zika viruses for suspected yellow fever cases. As testing capacity allows, specimens meeting the requirements for yellow fever virus PCR testing at the Bureau of Public Health Laboratories (BPHL) will also be tested for dengue, chikungunya, and Zika viruses as appropriate