Yellow Fever
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Yellow Fever

Case Definition – https://ndc.services.cdc.gov/case-definitions/yellow-fever-2019/

Overview

- ***Agent*** – Yellow fever (YF) is a viral pathogen. This virus belongs to a group of viruses known as the flaviviruses, the same family of viruses that includes West Nile, dengue, and Zika.
- ***Reservoir*** – In Africa and South America, where YF is endemic, the virus is maintained in urban areas through a human-*Aedes* mosquito cycle. In forest and savannah areas, the virus is maintained through a sylvatic cycle involving non-human primates and mosquitoes. Humans can be infectious with YF and transmit infection to mosquitoes prior to the onset of fever and for the first 3-5 days of illness.
- ***Occurrence*** – YF is endemic throughout several countries in Africa and South America.
- ***Risk Factors –*** Individuals residing in or traveling to YF-endemic areas are at an increased risk of infection. Vaccination against YF is recommended for all travelers to YF-endemic areas and individuals who work or reside in YF-endemic areas that do not have vaccine-acquired or naturally acquired immunity.
- ***Mode of Transmission*** – YF transmission is primarily transmitted through the bite of an infected mosquito. Other possible, though rarer, modes include transmission via breastfeeding, blood or organ donation, health care, or laboratory-associated transmission via needlestick exposures. Vertical transmission (mother to baby during pregnancy) and sexual transmission have not previously been documented, though there has been at least one report of YF viral RNA detected in semen.
- ***Incubation Period*** – Typically 3-6 days.
- ***Clinical Illness*** – The majority (about 55%) of people who become infected are asymptomatic. If symptoms develop, they can range from mild febrile illness to severe illness that includes jaundice and hemorrhaging. Initial symptoms include sudden onset of fever, chills, headache, backache, myalgia, nausea, and vomiting. Pulse may be slow, weak and out of proportion with the patient's elevated body temperature. Leukopenia can occur and is often most pronounced by day 5 of illness, the point at which most other symptoms are resolving. For about 15% of cases, a brief period of symptom resolution or significant improvement will occur, followed by a recurrence of symptoms that are more severe. Severe YF symptoms include high fever, jaundice, shock, hemorrhaging, and organ failure.
- ***Laboratory Testing*** – Testing for YF is not available through the Missouri State Public Health Laboratory (MSPHL) or most commercial laboratories. many commercial laboratories. If YF testing is requested by a provider, specimens can be sent to CDC for testing. YF testing requires pre-approval. Requests for testing through CDC should be coordinated through the Bureau of Communicable Disease Control and Prevention (BCDCP) Zoonotic Disease Program.

- ***Treatment*** – No specific antiviral therapy exists for YF virus infection. Recommended supportive care measures include keeping the patient hydrated and addressing other symptoms, such as fever or pain. Early recognition of symptoms of shock and initiation of intensive supportive therapy may reduce the risk of death if severe YF symptoms develop.
- ***Priority*** **–** Prompt investigation and implementation of control measures are required.

Quick References / Factsheets

- Resources for Yellow Fever (07/25)

- Public Health Professionals:
  - Reviewing Dengue Medical Records: Job Aid (07/25)
  - Response to Dengue Cases in Non-Endemic Areas of the United States (07/25)

Forms

- Disease Case Report (CD-1)
- Yellow Fever Surveillance Worksheet
- Missouri Outbreak Report Form (MORF)

Notifications

- If YF virus infection is suspected, the local public health agency (LPHA) should notify the District Epidemiologists or the Missouri Department of Health and Senior Services (MDHSS) Bureau of Communicable Disease Control and Prevention (BCDCP), phone (573) 751-6113, Fax (573) 526-0235.

Reporting Requirements

- Dengue is a Category 2 (A) disease and shall be reported to the LPHA or to the Missouri Department of Health and Senior Services (MDHSS) within one (1) calendar day of first knowledge or suspicion by telephone, fax, or other rapid communication.
  1. For confirmed and probable cases, complete a Disease Case Report (CD-1) and a Yellow Fever Surveillance Worksheet
  2. Entry of the completed CD-1 into the ShowMe World Care (SMWC) database negates the need for the paper CD-1 to be forwarded to the District Office.
  3. All outbreaks or "suspected" outbreaks must be reported as soon as possible (by phone, fax, or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the Missouri Outbreak Report Form (MORF).
  4. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

Laboratory Testing and Diagnosis

Testing for YF is not available through the Missouri State Public Health Laboratory (MSPHL) or most commercial laboratories. many commercial laboratories. If YF testing is requested by a provider, specimens can be sent to CDC for testing. YF testing requires pre-approval. Requests

for testing through CDC should be coordinated through the Bureau of Communicable Disease Control and Prevention (BCDCP) Zoonotic Disease Program.

Laboratory diagnosis of yellow fever is generally accomplished by testing serum to detect virus-specific immunoglobulin (Ig) M and neutralizing antibodies. It is important to obtain a yellow fever vaccination history, as IgM antibodies to the yellow fever vaccine virus can persist for several years following vaccination, and available tests cannot differentiate antibodies raised against wild-type virus and vaccine. Serologic cross-reactions occur with other flaviviruses (e.g., West Nile or dengue viruses), so positive results should be confirmed with a more specific test (e.g., plaque-reduction neutralization test).

Early in the illness (during the first 3-4 days), yellow fever virus or viral RNA often can be detected in the serum by virus isolation or nucleic acid amplification testing (e.g., reverse transcription-polymerase chain reaction [RT-PCR]). However, by the time overt symptoms are recognized, the virus is not detectable. Viral RNA can be detected a little longer, typically in the first week after illness onset. Because of the transient viremia, negative virus isolation and RT-PCR results do not rule out the diagnosis of yellow fever. Immunohistochemical staining of formalin-fixed material can detect yellow fever virus antigen in histopathologic specimens. In fatal cases, nucleic acid amplification, histopathology with immunohistochemistry, and virus culture of biopsy or autopsy tissues can be positive.

Conducting the Investigation

- **Verify the diagnosis**. Obtain demographic, clinical and laboratory information on the case from the health care provider, hospital, and/or laboratory. Obtain other epidemiological information necessary to complete the Disease Case Report (CD-1) and the Yellow Fever Surveillance Worksheet from the patient or a knowledgeable family member. Key pieces of information to obtain include: patient demographics (age, sex, race/ethnicity, occupation, or any characteristic that may inform seasonal, geographic, and demographic pattern), date of illness onset, hospitalization status and outcome, and history of vaccination against YF (including dates, place, product name, etc.).

- **Establish the extent of illness.** Determine if household, traveling companions or other close contacts are, or have been, ill by contacting the health care provider, patient, or family members. Strongly urge persons with a YF-like illness to contact their physician for a medical evaluation. These persons should also be watched for warning signs of severe YF infection that can occur after a brief period of symptom resolution or significant improvement. Persons with a YF-like illness should go immediately to an emergency room or the closest health care provider if any of the following warning signs appear: high fever, jaundice, hemorrhaging, or signs of shock or organ failure.

- **Establish the source of infection.** For all cases, please obtain the following information from the patient, patient's family, or health care provider:
    - Travel history:

    - Determine the start and end dates of the trip and the location(s) of travel. Start and end dates will be requested for all locations if the patient visited multiple cities or countries.
    - If there is no history of foreign travel consistent with exposure to YF, please contact your District Epidemiology team and/or the Zoonotic Disease Program.
- Vaccination history for YF
    - Information related to the vaccination (date of administration, where the vaccine was obtained, product name, etc.) should be obtained.
    - Rare but serious adverse events can follow YF vaccination, including anaphylaxis, vaccine-associated neurologic disease, and vaccine-associated viscerotropic disease.
    - Encourage health care providers to report cases of adverse events possibly caused by vaccination to the CDC/FDA Vaccine Adverse Events Reporting System (VAERS). For more details, go to: https://www.cdc.gov/yellow-fever/hcp/vaccine-adverse-events/index.html.
- Do any of the following situations apply to the case:
    - Works in a laboratory or clinical setting?
    - Pregnant or breastfeeding at time of exposure/onset?
    - Known to have contacts with a similar illness or a similar illness reported in the area of exposure?
    - Known to be a recent organ, tissue, bone marrow, or blood donor or recipient?
        - If yes, the blood or tissue bank will need to be notified and asked to determine if any donated blood components or tissues remain and whether any products have been disseminated to other individuals.
        - Identification of other possibly exposed patients through these routes will be required.
        - If assistance is needed with this tracing process, please contact the Zoonotic Disease Program for guidance.

Control Measures

Primary prevention for persons potentially exposed to YF-infected mosquitoes is by vaccination. The YF vaccine is a live-virus vaccine that has been used for several decades. More information about the YF vaccine and current recommendations, adverse reactions, and contraindications can be found here: https://www.cdc.gov/yellow-fever/vaccine/index.html.

Efforts should be made to promote YF awareness among international travelers and persons visiting family and friends in other countries. For more information about international travel and

YF risk, visit CDC's pages about Travel Health Notices and Yellow Fever Vaccine and Malaria Prevention Information, where recommendations can be searched by country.

There are no specific antiviral medications to treat YF virus infections. This makes personal protective behaviors to avoid mosquito bites the most important prevention measure. Key prevention measures include the following:

- Protect your home against mosquitoes! Identify and eliminate sources of standing water that mosquitoes need to reproduce.
- Avoid mosquito-prone areas and all mosquito bites for at least 1 week following return from international travel to YF-endemic areas.
    - Be aware of peak mosquito exposure times (typically around dawn and dusk).
    - The *Aedes* mosquitoes that transmit YF are known to be daytime biters and can be active all day long.
- Apply insect repellent to all exposed skin when planning to spend time outdoors.
    - The American Academy of Pediatrics has recommended that repellents containing up to 30% DEET are safe to use on children over 2 months of age.
    - For other active repellent ingredients, check the product label for minimum age requirements before applying to children.
    - EPA offers an insect repellent search tool that the public can use to identify repellent products that work best for their needs.
- Wear long sleeves and pants when weather permits to help reduce the amount of exposed skin and easy places for mosquitoes to bite.
- Consider using bed nets and/or choosing accommodations with air conditioning or tight, well-fitting window and door screens to prevent mosquitoes from entering sleeping or living areas.
- Mosquito control measures may need to be considered, especially if a locally acquired case of YF infection is identified. Vector control activities are the responsibility of the county, city, or municipal jurisdiction. For more information about this, please reach out to the Zoonotic Disease Program.

Resources

1. American Public Health Association. [Yellow Fever]. In: Heymann DL, ed. *Control of Communicable Diseases Manual*. 21st ed. Washington, DC: American Public Health Association; 2022 [712-719].
2. American Academy of Pediatrics. [Arboviruses]. In: Kimberlin DW, Barnett, ED, Lynfield, R, Sawyer, MH, eds. *Red Book: 2021 Report of the Committee on Infectious Diseases*. 32nd ed. Itasca, IL: American Academy of Pediatrics; 2021: [202-209].
3. Centers for Disease Control and Prevention. Yellow Fever. https://www.cdc.gov/yellow-fever/index.html (07/25)