June 2017

Yellow Fever

Surveillance Protocol

Summary Paragraph about the Disease

Yellow fever is a viral hemorrhagic fever caused by *Flavivirus* that is transmitted to humans by the bites of infected mosquitoes in the *Aedes and Haemogogus* family. Forty-seven countries in Africa and Central and South America are either endemic for or have regions that are endemic for yellow fever. Yellow fever is the most severe arbovirus ever to circulate in the Americas, and although vaccination campaigns and vector-control efforts have eliminated it from many areas, sylvatic (jungle) transmission cycles continue to occur in endemic tropical regions. The most common symptoms are: jaundice, muscle pain, nausea, vomiting, and fatigue. **Cases of yellow fever must be reported within 24 hours to the local health department in the patient's home county.**

Healthcare Provider Responsibilities

1. Report suspected or confirmed cases to your local health department within one week. Supply requested clinical information to the local health department to assist with case ascertainment.
2. Collect appropriate specimens for detection of virus, antigen, or genome (see *Case Definition* section).
3. Report any positive laboratory results pertaining to yellow fever to the local health department located in the patient's home county within 24 hours.

Laboratory Responsibilities

1. Perform appropriate testing for patients with suspected yellow fever. This involves testing serum to detect virus-specific immunoglobulin M (IgM) and neutralizing antibodies.
2. Forward copies of any positive yellow fever test results to the local health department located in the patient's home county within 24 hours.

Local Health Responsibilities

1. Conduct an appropriate case investigation.
    a. Contact the healthcare provider that ordered the laboratory test to obtain the clinical information on the West Virginia's Electronic Disease Surveillance System (WVEDSS) form.
    b. Contact the patient to obtain information regarding travel history. Inquire if the patient donated blood in the recent past. Identify others who traveled with the case and interview to determine exposure and symptoms.
    c. Report all case data using WVEDSS.

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2. Educate the public about yellow fever, especially regarding mosquito bite prevention measures when traveling.
3. Educate providers, laboratories, and infection control practitioners about diagnosis and reporting of yellow fever.

State Health Responsibilities

1. Forward specimens for yellow fever testing to the Centers for Disease Control and Prevention. Review completed case reports from local health departments within one week.
2. Report all confirmed and probable cases to CDC using WVEDSS.
3. Provide consultation to local health departments regarding case ascertainment.
4. Conduct mosquito pools to monitor for the presence of *Aedes aegypti* (currently not present in West Virginia).

Disease Control Objectives

1. Practice mosquito bite measures when traveling to countries where yellow fever is endemic.

Disease Prevention Objectives

1. Administer yellow fever vaccine prior to traveling to an area where yellow fever is endemic.
2. Mosquito control in areas with a population of *Aedes aegypti* mosquitoes.

Disease Surveillance Objectives

1. Identify and monitor the epidemiologic characteristics of yellow fever cases in West Virginia.
2. Conduct mosquito surveillance in the event that *Aedes aegypti* populations may be present in West Virginia.
3. Identify and characterize instances of local transmission if they occur.

Occupational Health

One of the main priorities for yellow fever case investigations is the prevention of local transmission in the United States. There are many states that have an established population of *Aedes aegypti* mosquitoes. Patients should be discouraged from traveling while they are infectious to mosquitoes, from 3- 5 days after onset of illness. It is important to prevent exposure to mosquito-borne diseases while outdoors. Individuals should cover their skin as much as possible. Wear long sleeved shirts, long pants, socks, and a hat. Shirt should be tucked

into pants and pants should be tucked into socks. In addition to covering exposed skin, repellants with DEET (at least 20%) oil of lemon eucalyptus, IR3535, or picaridin (≥20%) should also be used. If repellant is not worn during mosquito surveillance, permethrin-treated shirts should be considered.

Public Health Significance

From 1793-1822 yellow fever was one of the most dreaded diseases in US port cities. In the 1780s, yellow fever outbreaks in Philadelphia were responsible for killing one tenth of the city's population. The disease may have played a part in shaping the decision to move the nation's capital from Philadelphia to Washington D.C. In the early 20th century, Carlos Findlay and Walter Reed's discovery of *Aedes aegypti* as a source of yellow fever transmission led to the eradication of yellow fever in parts of Latin America. Isolation of the virus and later development of the 17D vaccine by Max Theiler helped to eliminate *Aedes aegypti* and yellow fever from countries in Africa and the Americas during the mid-20th century.

Until the early 1990s yellow fever remained only very sporadically active in the countries that benefited from those campaigns. On April 23, 2016, the Democratic Republic of the Congo's (DRC's) Ministry of Health declared a yellow fever outbreak. As of May 24, 2016, approximately 90% of suspected yellow fever cases were reported in a single province, Kongo Central Province, that borders Angola, where a large yellow fever outbreak had begun in December 2015. Two yellow fever mass vaccination campaigns were conducted in Kongo Central Province during May 25–June 7, 2016 and August 17–28, 2016. In June 2016, the DRC Ministry of Health requested assistance from CDC to control the outbreak. Concurrently, recent manufacturing problems resulted in a shortage of the only U.S.-licensed yellow fever vaccine. This shortage is expected to lead to a complete depletion of yellow fever vaccine available for the immunization of U.S. travelers by mid-2017. In order to avoid a lapse in the availability of the vaccine, puplic health officials and private partners are pursuing the importation of the Stamaril yellow fever vaccine into the United States. Domestic production of yellow fever vaccine in the United States should resume in 2018.

Clinical Description

Most people infected with yellow fever have either no illness or only mild illness. The initial symptoms include sudden onset of fever, chills, severe headaches, back pain, general body aches, nausea and vomiting, fatigue, and weakness with these symptoms lessening after initial presentation. After a brief remission of hours to a day, roughly 15% of cases progress to develop a more severe form of the disease. The severe form is characterized by high fever, jaundice, bleeding, and eventually shock and failure of multiple organs.

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Etiologic Agent

Yellow fever is a virus in the genus *Flavivirus* of the family *Flaviviridae*

Reservoir

Nonhuman and human primates are the main reservoirs of the virus, with anthroponotic (human-to-vector-to-human) transmission occurring.

Mode of Transmission

Yellow fever is transmitted to people via *Aedes* or *Haemagogus* species mosquitoes. Mosquitoes acquire the virus by feeding on infected primates (human or non-human) and then can transmit the virus to other primates (human or non-human). People infected with yellow fever virus are infectious to mosquitoes (referred to as being "viremic") shortly before the onset of fever and up to 5 days after onset.

Yellow fever has three types of transmission cycles:

1. **Sylvatic (or jungle) yellow fever**: In tropical rainforests, monkeys bitten by wild mosquitoes which pass the virus on to other monkeys. Occasionally humans working or travelling in the forest are bitten by infected mosquitoes and develop yellow fever.
2. **Intermediate (savannah) yellow fever**: Semi-domestic mosquitoes (those that breed both in the wild and around households) infect both monkeys and people. Increased contact between people and infected mosquitoes leads to increased transmission and many separate villages in an area can develop outbreaks at the same time. This is the most common type of outbreak in Africa.
3. **Urban yellow fever**: Large epidemics occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected mosquitoes transmit the virus from person to person.

Incubation Period

The incubation period for yellow fever is 3 to 6 days.

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Period of Communicability

Humans can transmit the *Flaviviridae* virus to mosquitoes shortly before the onset of fever and for 3-5 days afterwards. Mosquitoes become infectious 9-12 after a blood meal and remain infectious for life.

Outbreak Recognition

One case of locally transmitted yellow fever would be considered an outbreak.

Case Definition

The 1997 case definition is the most current (CSTE Position Statement Number 09-ID-09)

Clinical Description

A mosquito-borne viral illness characterized by acute onset and constitutional symptoms followed by a brief remission and a recurrence of fever, hepatitis, albuminuria, and symptoms and, in some instances, renal failure, shock, and generalized hemorrhages.

Laboratory Criteria for Diagnosis

- Fourfold or greater rise in yellow fever antibody titer in a patient who has no history of recent yellow fever vaccination and cross-reactions to other flaviviruses have been excluded, **OR**
- Demonstration of yellow fever virus, antigen, or genome in tissue, blood, or other body fluid

Case Classification

Probable

A clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever virus [e.g., greater than or equal to 32 by complement fixation, greater than or equal to 256 by immunofluorescence assay, greater than or equal to 320 by hemagglutination inhibition, greater than or equal to 160 by neutralization, or a positive serologic result by immunoglobulin M-capture enzyme immunoassay]. Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.)

Confirmed

A clinically compatible case that is laboratory confirmed

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Case Classification Comments

The 1997 case definition appearing on this page was originally published in the 1990 *MMWR* and re-published in the 2009 CSTE position statement 09-ID-09.[1,2] Thus, the 1990, 1997, and 2010 versions of the case definition are identical.

Preventive Interventions

For information on how to prevent yellow fever while traveling, visit the CDC's traveler's health page: https://wwwnc.cdc.gov/travel/diseases/yellow-fever. Individuals traveling to an area where yellow fever transmission occurs should receive the yellow fever vaccine.

There are many ways to prevent mosquito bites during travel. Mosquitoes that transmit yellow fever are active daytime biters:

- Picaridin (≥20%).
- Cover exposed skin by wearing long-sleeved shirts, long pants, and hats.
- Wear clothing that has been treated with permethrin (or another pyrethroid).
- Use a bed net when you are not sleeping in a sealed air-conditioned room.

Treatment

There is no specific treatment for a patient who has yellow fever. Treatment is symptomatic

Surveillance Indicators

1. Proportion of cases with complete clinical, laboratory, and epidemiologic information including clinical symptoms, testing, and risk factor information (e.g. travel history, outdoor activities).

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