

# Yellow Fever

## **DISEASE REPORTABLE WITHIN 24 HOURS OF DIAGNOSIS**

Per NJAC 8:57, health care providers and administrators shall report by mail or by electronic reporting within 24 hours of diagnosis, confirmed cases of Yellow fever to the health officer of the jurisdiction where the ill or infected person lives, or if unknown, wherein the diagnosis is made. A directory of local health departments in New Jersey is available at <http://www.state.nj.us/health/lh/directory/lhdselectcounty.shtml>.

If the health officer is unavailable, the health care provider or administrator shall make the report to the Department by telephone to 609.826.5964, between 8:00 A.M. and 5:00 P.M. on non-holiday weekdays or to 609.392.2020 during all other days and hours.



## 1 THE DISEASE AND ITS EPIDEMIOLOGY

### A. Etiologic Agent

Yellow fever is a mosquito-borne viral illness. It is caused by the yellow fever virus, which is in the genus *Flavivirus* and family *Flaviviridae*.

### B. Clinical Description and Laboratory Diagnosis

Many cases of yellow fever are so mild they go undetected. In typical cases of recognized illness, the patient experiences a sudden onset of fever, chills, headache, backache, generalized muscle pain, prostration, nausea, and vomiting. Jaundice, albuminuria (the presence of protein in the urine), and anuria (absence of urine) may occur. Most infections resolve at this stage. However, in more severe cases of illness, after a brief remission of hours to a day, there is progression to liver and kidney failure and to hemorrhagic symptoms, including nosebleeds, bleeding gums, bloody vomiting, and bloody stools. Twenty to fifty percent of severe cases with jaundice are fatal. The overall case-fatality rate in endemic regions is about 5%. Lifetime immunity follows yellow fever recovery. Laboratory diagnosis is made by isolation of the virus from blood, by demonstration of viral antigen in the blood by enzyme-linked immunosorbent assay (ELISA) or liver tissue by immunohistochemistry, by demonstration of viral genome in blood and liver tissue by polymerase chain reaction, by demonstration of specific immunoglobulin M (IgM) antibodies in early sera, or by demonstration of a rise in titer of specific antibodies in paired acute and convalescent sera.

### C. Reservoirs

Monkeys and mosquitoes are the primary reservoirs in jungle areas of Africa and South America. Humans and *Aedes aegypti* mosquitoes are involved in the infective cycle in urban areas.

### D. Modes of Transmission

Yellow fever has two different transmission cycles that affect humans: the jungle cycle and the urban cycle. In the jungle cycle, several species of mosquitoes are vectors and transmit

virus from monkey to monkey. Humans are involved in the jungle cycle accidentally if they are bitten by infected mosquitoes. In the urban cycle, the virus is transmitted among humans by the bite of an infected house-dwelling *Ae. aegypti* mosquito. In the urban cycle, monkeys play little or no role as a reservoir. Direct person-to-person spread of yellow fever does not occur.

### **E. Incubation Period**

The incubation period for yellow fever is three to six days following the bite of an infected mosquito.

### **F. Period of Communicability or Infectious Period**

Yellow fever is not transmitted from person to person. Patients with yellow fever may be viremic (have virus in their blood) from shortly before onset of fever until three to five days of illness, meaning the virus can be spread by *Ae. aegypti* mosquitoes that have been infected by other people.

### **G. Epidemiology**

Yellow fever is endemic in tropical regions of South America and Africa only. Jungle yellow fever is rare and occurs mainly in persons who live or work in tropical rain forests. Urban yellow fever is the cause of most yellow fever outbreaks and epidemics. In many towns and villages in South America and Africa, *Ae. aegypti* have adapted to living among humans and mosquito larvae grow in discarded tires, flower pots, and water storage containers close to human dwellings. The case-fatality rate for yellow fever is highly variable and ranges from an overall 5% to 20% in more high-risk areas. Infants and children are at the greatest risk of severe illness.

Yellow fever does not occur naturally in New Jersey and any cases in New Jersey are probably due to recent travel abroad. Overall, yellow fever is a rare cause of illness in U.S. travelers. The last yellow fever epidemic in the United States was in New Orleans in 1905.

## **2 NEW JERSEY DEPARTMENT OF HEALTH AND SENIOR SERVICES CASE DEFINITION**

### **A. 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, in some instances, renal failure, shock, and generalized hemorrhages.

## B. Laboratory Criteria and Case Classification

### CONFIRMED

A clinically compatible case AND

- Four-fold 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.

### PROBABLE

A clinically compatible case AND

- Stable elevated antibody titer to yellow fever virus (equal or greater than 1:32 by complement fixation, 1:256 by immunofluorescence assay, 1:320 by hemagglutination inhibition, or 1:160 by neutralization), OR
- Positive IgM ELISA in a single specimen.

### POSSIBLE

Not used.

**NOTE: Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.**

## C. Differences from Centers for Disease Control and Prevention Case Definition

New Jersey Department of Health and Senior Services (NJDHSS) and Centers for Disease Control and Prevention (CDC) case definition are the same.

# 3 LABORATORY TESTING AVAILABLE

Laboratory diagnosis of yellow fever is generally accomplished by testing of serum (blood) or cerebrospinal fluid to detect virus-specific IgM and neutralizing antibodies. During an acute infection, the yellow fever virus can be isolated through culture or detected by nucleic acid amplification. In fatal cases, laboratory diagnosis may be based on nucleic acid amplification, histopathology with immunohistochemistry, and virus culture of autopsy tissues.

The NJDHSS Public Health and Environmental Laboratories does not provide testing for yellow fever. Arrangements must be made through the NJDHSS Infectious and Zoonotic Diseases Program (IZDP) for specimens to be sent to the CDC. Specimens will be sent only if cases are clinically compatible cases with appropriate travel history.

# 4 PURPOSE OF SURVEILLANCE AND REPORTING AND REPORTING REQUIREMENTS

## A. Purpose of Surveillance and Reporting

- To identify imported cases of yellow fever to understand the global epidemiology of endemic and epidemic yellow fever
- To ensure that imported cases are appropriately contained to prevent the introduction of virus into New Jersey mosquito populations
- To identify locally acquired cases, if they occur, so appropriate active surveillance and mosquito control interventions can be taken
- To identify cases that may be part of a larger, worldwide outbreak
- To provide travelers with appropriate preventive health information

## B. Laboratory Reporting Requirements

The New Jersey Administrative Code (NJAC 8:57-1.6) stipulates that laboratories report (by telephone, by confidential fax, or over the Internet using the Communicable Disease Reporting and Surveillance System [CDRSS]) all cases of yellow fever to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. The report shall contain, at a minimum, the reporting laboratory's name, address, and telephone number; the age, date of birth, gender, race, ethnicity, home address, and telephone number of the person tested; the test performed; the date of testing; the test results; and the healthcare provider's name and address.

## C. Healthcare Provider Reporting Requirements

The New Jersey Administrative Code (NJAC 8:57-1.4) stipulates that healthcare providers report (by telephone, confidential fax, or in writing) all cases of yellow fever to the local health officer having jurisdiction over the locality in which the patient lives or, if unknown, to the health officer in whose jurisdiction the healthcare provider requesting the laboratory examination is located. The report shall contain the name of the disease; date of illness onset; and name, age, date of birth, race, ethnicity, home address, and telephone number of the person they are reporting. In addition, the name, address, institution, and telephone number of the reporting official should be reported.

## D. Health Officer Reporting

The New Jersey Administrative Code (NJAC 8:57-1.7) stipulates that each local health officer must report the occurrence of any case of yellow fever within 24 hours of receiving the report. Written or electronic copies of the reports must be made to NJDHSS and may be submitted over the Internet using the confidential and secure CDRSS.

# 5 CASE INVESTIGATION

## A. Forms and Laboratory Reports

It is requested that the local health officer complete a CDS-1 reporting form, which can be found online at <http://www.state.nj.us/health/forms/cds-1.pdf>, by interviewing the clinician, patient, and others who may be able to provide pertinent information. Much of the information required on the form can be obtained from the patient’s healthcare provider or the medical record. It is important to collect information about travel history and yellow fever vaccination status to accurately classify cases.

## B. Entry into CDRSS

The mandatory fields in CDRSS include disease, last name, county, municipality, gender, race, ethnicity, case status, and report status.

The following table can be used as a quick reference guide to determine which CDRSS fields need to be completed for accurate and complete reporting of yellow fever. The “Tab” column includes the tabs that appear along the top of the CDRSS screen. The “Required Information” column provides detailed explanations of what data should be entered.

| CDRSS Screen           | Required Information  |
|------------------------|---|
| <b>Patient Info</b>    | Enter the disease name (“YELLOW FEVER”), patient demographic information, illness onset date, and the date the case was reported to the local health department (LHD). There are no subgroups for yellow fever.   |
| <b>Addresses</b>       | Enter any alternate address (e.g., rehabilitation facility). Use the “COMMENTS” section in this screen to record any pertinent information about the alternate address (e.g., length of stay at rehabilitation facility). Entering an alternate address will allow other disease investigators access to the case if the alternate address falls within their jurisdiction.   |
| <b>Clinical Status</b> | Enter any treatment that the patient received and record the names of the medical facilities and physician(s) involved in the patient’s care. If the patient received care from two or more hospitals, be sure that all are entered so the case can be accessed by all infection control professionals (ICPs) covering these facilities. If the patient died, date of death should be recorded under the “MORTALITY” section. |

| CDRSS Screen           | Required Information   |
|------------------------|--|
| <b>Signs/Symptoms</b>  | Check appropriate boxes for signs and symptoms and indicate their onset. Make every effort to get complete information by interviewing the physician, family members, ICP, or others who might have knowledge of the patient’s illness. Also, information regarding the resolution of signs and symptoms should be entered.  |
| <b>Risk Factors</b>    | Enter complete information about risk factors (i.e., travel history) and yellow fever vaccination status.  |
| <b>Laboratory Eval</b> | For all IgM-positive tests, select “YELLOW FEVER VIRUS AB.IGM” for ELISA, EIA, or IFA. In “TEST RESULT” field select “POSITIVE/REACTIVE.” If available, titers should be placed in the “VALUE” field. For all IgG-positive tests, select “YELLOW FEVER VIRUS AB.IGG” for ELISA, EIA, or IFA. In “TEST RESULT” field select “POSITIVE/REACTIVE.” If available, titers should be placed in the “VALUE” field. The “REFERENCE RANGE” field should be completed for all ELISA, EIA, and IFA tests. In addition, the “PAIRED SERA” field should be completed by selecting “ACUTE” or “CONVALESCENT.” For virus isolation, select “YELLOW FEVER VIRUS RNA.” In “TEST RESULT” field select “POSITIVE/REACTIVE.” |
| <b>Contact Tracing</b> | Information regarding contacts is not required for this disease.   |
| <b>Case Comments</b>   | Enter general comments (i.e., information that is not discretely captured by a specific topic screen or drop-down menu) in the “COMMENTS” section. <b>NOTE:</b> Select pieces of information entered in the “COMMENTS” section CANNOT be automatically exported when generating reports. Therefore, whenever possible, record information about the case in the fields that have been designated to capture this information; information included in these fields CAN be automatically exported when generating reports.  |
| <b>Epidemiology</b>    | Record name of and contact information for case investigators from other agencies (e.g., CDC, out-of-state health departments). Document communication between investigators in the “COMMENTS” section.  |

| CDRSS Screen                                    | Required Information   |
|---|--|
| <p><b>Case Classification Report Status</b></p> | <p>Case status options are “REPORT UNDER INVESTIGATION (RUI),” “CONFIRMED,” “PROBABLE,” “POSSIBLE,” and “NOT A CASE.”</p> <ul style="list-style-type: none"> <li>• All laboratory positives entered by NJDHSS will be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”</li> <li>• Cases still under investigation by the LHD should be assigned a case status of “REPORT UNDER INVESTIGATION (RUI).”</li> <li>• Upon completion of the investigation, the LHD should assign a case status on the basis of the case definition. “CONFIRMED,” “PROBABLE,” and “NOT A CASE” are the only appropriate options for classifying a case of yellow fever (see section 2B).</li> </ul> <p>Report status options are “PENDING,” “LHD OPEN,” “LHD REVIEW,” “LHD CLOSED,” “DELETE,” “REOPENED,” “DHSS OPEN,” “DHSS REVIEW,” and “DHSS APPROVED.”</p> <ul style="list-style-type: none"> <li>• Laboratory positive cases entered by NJDHSS will be assigned a report status of “PENDING.”</li> <li>• Once the LHD begins investigating a case, the report status should be changed to “LHD OPEN.”</li> <li>• The “LHD REVIEW” option can be used if the LHD has a person who reviews the case before it is closed (e.g., health officer or director of nursing).</li> <li>• Once the LHD investigation is complete and all the data are entered into CDRSS, the LHD should change the report status to “LHD CLOSED.”</li> <li>• “LHD CLOSED” cases will be reviewed by DHSS and be assigned one of the DHSS-specific report status categories. If additional information is needed on a particular case, the report status will be changed to “REOPENED” and the LHD will be notified by e-mail. Cases that are “DHSS APPROVED” cannot be edited by LHD staff (see section 5C below).</li> </ul> <p>If a case is inappropriately entered (e.g., a case of yellow fever vaccine accidentally entered as yellow fever infection) the case should be assigned a report status of “DELETE.” A report status of “DELETE” should NOT be used if a reported case of yellow fever simply does not meet case definition. Rather, it should be assigned the appropriate case status, as described above.</p> |



### C. Other Reporting/Investigation Issues

1. Case report forms (CDS-1 and labs) DO NOT need to be mailed to NJDHSS as long as mandatory fields in CDRSS indicated in section 5B are completed.
2. Once the LHD completes its investigation and assigns a report status of “LHD CLOSED,” NJDHSS will review the case. NJDHSS will approve the case by changing the report status to “DHSS APPROVED.” At this time, the case will be submitted to the CDC and the case will be locked for editing. If additional information is received after a case has been placed in “DHSS APPROVED,” you will need to contact NJDHSS to reopen the case. This should be done only if the additional information changes the case status of the report.
3. Every effort should be made to complete the investigation within three months of opening a case. Cases that remain open for three months or more and have no investigation or update notes will be closed by NJDHSS and marked as not a case.

## 6 CONTROLLING FURTHER SPREAD

### A. Isolation and Quarantine Requirements (NJAC 8:57-1.10)

#### Minimum Period of Isolation of Patient

Because yellow fever is not transmitted from person to person, there are no restrictions for case-patients or contacts of case-patients. However, to avoid transmitting yellow fever to local mosquitoes, case-patients should avoid and protect against mosquito bites when symptoms are present.

**NOTE: The *Ae. aegypti* mosquito has been found in New Jersey but has not become established in the state. A potential vector of yellow fever, *Aedes albopictus*, has become established in New Jersey. Concerns over local transmission should be small, however.**

### B. Protection of Contacts of a Case

There are no restrictions of contacts.

### C. Managing Special Situations

#### Locally Acquired Case

A locally acquired case of yellow fever would be an unusual occurrence as the *Ae. aegypti* mosquito has not become established in New Jersey. However, in recent years a resurgence of *Ae. aegypti* has occurred in South America and has increased the potential for reemerging

urban yellow fever. In addition, the Asian tiger mosquito, *Ae. albopictus*, has become established in many areas of North America and New Jersey and is considered to be a potential vector of yellow fever. If a local health officer determines during the course of an investigation that a case-patient or suspect case-patient does not have a recent travel history to an endemic country, contact the NJDHSS IZDP at 609.588.7500 as soon as possible. Environmental measures such as investigating local areas visited by the case-patient to locate the focus of infection and surveillance of other people for illness may be necessary. State and county mosquito control agencies would need to conduct mosquito surveillance and, if necessary, mosquito control immediately.

### **Reported Incidence Is Higher Than Usual/Outbreak Suspected**

If an outbreak is suspected, contact the NJDHSS IZDP at 609.588.7500. A common exposure to or association with *Ae. aegypti* mosquitoes (e.g., travelers returning from endemic countries) should be sought and applicable preventive or control measures should be instituted. The NJDHSS IZDP staff helps determine a course of action to prevent further cases and can perform surveillance for cases across jurisdictions and that would be difficult to identify at a local level.

## **D. Preventive Measures**

### **International Travel and Vaccination**

- A live attenuated vaccine is recommended and required by international regulations for all individuals over nine months old who will be living in or traveling to South America or Africa. Pregnant women should not be vaccinated in the first trimester except in high-risk areas.
- Without a valid certificate of immunization against yellow fever, many countries require a six-day quarantine of travelers coming from or going to recognized yellow fever zones of Africa and South America.
- Travelers to yellow fever endemic countries are encouraged to protect themselves from mosquitoes by using repellents, wearing protective clothing, and using mosquito nets when rooms are not screened. Unlike other mosquitoes, the principal mosquito vectors of yellow fever bite during daytime hours.

Additional information regarding international travel and the yellow fever vaccine can be found at the CDC's Traveler Health Office at <http://wwwn.cdc.gov/travel/>

### **Additional Information**

A Yellow Fever Fact Sheet can be obtained at the NJDHSS Web site at <http://www.state.nj.us/health/cd/>.

Additional information can also be found on the CDC Web site at <http://www.cdc.gov/ncidod/dvbid/yellowfever/>.

## References

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