# Yellow Fever Investigation Guideline

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<td>• CDC Specimen Submission Form (CDC 50.34)</td>
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| Supporting Materials found in attachments:      |               |
| • Fact Sheet                                    | 06/2012       |

## Revision History:

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<tr>
<td>07/2012</td>
<td>07/2009</td>
<td>Updated to new format. Added notification section. Updated fact sheet.</td>
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<td>02/2012</td>
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<td>Removed references to KS-EDSS.</td>
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CASE DEFINITION (CDC 1997)

Clinical Description for Public Health Surveillance:
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 Case Classification:
- 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:
Confirmed: a clinically compatible case that is laboratory confirmed.
Probable: a clinically compatible case with supportive serology (stable elevated antibody titer to yellow fever, see examples below). Cross-reactive serologic reactions to other flaviviruses must be excluded, and the patient must not have a history of yellow fever vaccination.
- 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.

LABORATORY ANALYSIS
Warning: Prior consultation with CDC recommended before attempting to collect or send samples. Call the Arbovirus Branch in Ft. Collins, CO at 970-221-6407.

The preliminary diagnosis is based on the patient’s clinical features, places and dates of travel, and activities. Laboratory diagnosis is best performed by:
- Serologic assays to detect virus-specific IgM and IgG antibodies. Because of cross-reactivity between antibodies raised against other flaviviruses, more specific antibody testing, such as a plaque reduction neutralization test, should be done to confirm the infection.
- Virus isolation or nucleic acid amplification tests performed early in the illness for YFV or yellow fever viral RNA. However, by the time more overt symptoms are recognized, the virus or viral RNA is usually undetectable. Therefore, virus isolation and nucleic acid amplification should not be used for ruling out a diagnosis of yellow fever.

Clinicians should call 800-CDC-INFO (800-232-4636) for additional assistance
with diagnostic testing for yellow fever infections and for questions about antibody response to vaccination.

- Call Epidemiologic Services at 877-427-7317 before sending any samples to the Kansas Health and Environment Laboratory (KHEL).

- Serology samples are forwarded to the CDC and must be accompanied by a CDC submission form (CDC 50.34) with the following provided:
  - Date of onset of symptoms
  - Date of specimen collection (Specimen collection within 8 days after the onset of symptoms, requires a convalescent specimen collection.)
  - Pertinent travel history (3 months prior to the date of symptom onset)
  - Patient's name (REQUIRED for submitting specimens)

- Specimen: Blood or serum (3-5 ml). Acute and convalescent specimens, if available, should be sent together.

- Collection: KHEL Serology kit with yellow top blood tubes or any other red topped, clot separator blood tubes.

- Timing of collection for serology: Acute obtained 3 to 10 days after onset of symptoms; convalescent 2-3 weeks after acute sample.

- Test results are normally available 4 to 14 days after specimen receipt. Hard copy of results will take at least 2 weeks after testing is completed.

- For additional information and/or questions, call (785) 296-1620 or refer to online guidance at www.kdheks.gov/labs/lab_ref_guide.htm.

**EPIDEMIOLOGY**

Yellow fever virus is endemic in certain regions of Africa and the Americas located between 15°N and 10°S of the equator. There are 2 types of transmission cycles, a sylvatic or jungle cycle that involves mosquitoes and nonhuman primates, and an urban cycle involving *Aedes aegypti* mosquitoes and humans. Sylvatic transmission is restricted to tropical regions of Africa and Latin America, where a few hundred cases occur annually. Historically, urban yellow fever occurred in many cities of the Americas, although in recent years has only been reported in Nigeria. An outbreak of urban yellow fever has not been reported in the Americas since 1942.
DISEASE OVERVIEW

A. Agent:
Yellow fever virus; flavivirus

B. Clinical Description:
Acute viral infection of short duration and varying severity, characterized by acute onset of fever, chills, headache, backache, generalized muscle pain, prostration, nausea and vomiting. In addition, the pulse may be slow, weak and out of proportion to the elevated temperature (i.e., Faget sign). Most cases improve and recover within 3 - 4 days; however, about 15% enter into a second or toxic phase ≤1 day of initial recovery. Symptoms of the toxic phase include, fever, jaundice, epistaxis, gingival bleeding, hematemesis (i.e., vomiting of blood, usually coffee-ground or black in color), Melina, and liver and renal failure. Twenty to 50% of jaundiced cases are fatal.

C. Reservoirs:
In urban areas: humans and Aedes aegypti mosquitoes; in forest areas: vertebrates other than humans and forest mosquitoes. Humans do not have a role in transmission of jungle yellow fever or in maintaining the virus, but are the primary amplifying host in the urban cycle.

D. Mode(s) of Transmission:
Bite of infected mosquitoes. Direct person-to-person spread does not occur.

E. Incubation Period:
3-6 days.

F. Period of Communicability:
No person-to-person transmission. Human blood can infect feeding mosquitoes during first 3-5 days of illness. Mosquitoes can transmit virus 9-12 days after feeding and remain infected for life. Mosquitoes can live weeks to months.

G. Susceptibility and Resistance:
Susceptibility of non-immunized individuals is universal. Individuals who have recovered from a yellow fever infection develop life-long immunity. Transient passive immunity in infants born to immune mothers may persist for up to 6 months.

H. Treatment:
No specific treatments. Supportive care only.

I. Vaccine:
YF-Vax, the only yellow fever vaccine licensed for use in the United States, is manufactured by Sanofi Pasteur. Studies comparing the reactogenicity and immunogenicity of various yellow fever vaccines, including those manufactured outside the United States, suggest that there is no significant difference in the reactogenicity or immune response generated by the various vaccines. Thus, people who receive yellow fever vaccines in other countries should be considered protected against yellow fever.
NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Yellow Fever infections shall be designated as infectious or contagious in their nature, and cases or suspect cases shall be reported within seven days:

1. Health care providers and hospitals: report to the local public health jurisdiction or KDHE-BEPHI (see below)
2. Local public health jurisdiction: report to KDHE-BEPHI (see below)
3. Laboratories: report to KDHE-BEPHI (see below)
4. KDHE-BEPHI will contact the local public health jurisdiction by phone within one hour of receiving any suspected yellow fever report.

Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Informatics (BEPHI)
Phone: 1-877-427-7317    Fax: 1-877-427-7318

- The local public health jurisdiction will report information requested in the Kansas electronic surveillance system, as soon as possible, ensuring that the electronic form is completed within 7 days of receiving a notification of a report.

Further responsibilities of state and local health departments to the CDC:

As a nationally notifiable condition, yellow fever cases require an IMMEDIATE, URGENT report to the Center of Disease Control and Prevention (CDC).

- KDHE epidemiologist will call the CDC EOC at 770-488-7100 within 24 hours of becoming aware of a probable or confirmed case.
- Local public health jurisdiction will report information requested on the disease reporting forms as soon as possible, completing the forms within 7 days of receiving a notification of an yellow fever report.
- KDHE-BEPHI will file an electronic case report the next regularly scheduled electronic transmission.  
  (KDHE-BEPHI files electronic reports weekly with CDC.)

INVESTIGATOR RESPONSIBILITIES

1) Use current, to confirm diagnosis with the medical provider.
2) Conduct a case investigation to identify potential source of infection.
3) Conduct contact investigation to identify additional cases.
4) Identify whether the source of infection is major public health concern.
5) Initiate control and prevention measures to prevent spread of disease.
6) Complete and report all information requested in the Kansas electronic surveillance system and any additional forms requested by the CDC.
7) As appropriate, use the disease fact sheet to notify individuals or groups.
STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

1) Contact the medical provider who diagnosed or ordered testing of the case and obtain the following information. This includes copies of hospital records.

   Note: If the physician submitted samples to CDC, the CDC submission form (CDC 50.34) may already be completed or started – try to obtain a copy for valuable epidemiological data

   • Identify if the patient was ill with symptoms of yellow fever:
     − 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.
     − Record onset date of symptoms.
   • Examine any laboratory testing that was done; if not yet reported:
     − Record date serum specimen(s) and/or tissue (specify) were collected.
     − Record or obtain copies of serology results and virus isolation and PCR tests, if done.
   • Record information about the patient’s receipt of yellow fever vaccine.
   • Collect case’s demographic data and contact information (Full name, birth date, county, sex, race/ethnicity, home address, occupation and work address, and phone number(s))
   • Record hospitalizations: location, admission and discharge dates
   • Record outcomes: recovered or date of death and/or complications,

2) Interview the case or proxy to determine source, risk factors and on potential vectors of disease transmission; focus on incubation period usually 3-6 days prior to illness onset.

   Note: Travel to an endemic Yellow fever area or some connection to a Yellow fever area is a crucial element. With no travel to areas endemic for Yellow fever or other obvious risk factors, refer to Managing Special Situations – Unusual Circumstances.

   1) Immunization history and/or a previous history of yellow fever.
   2) Travel history, including dates and places for travel during the incubation period.
      − List countries and cities, dates of stay.
      − Record all places the case visited before onset including forested areas.
   3) Exposure to mosquitoes, include dates and places during incubation period.
   4) With no travel to areas endemic for yellow fever prior to onset:
      − Obtain assistance to search the case’s work and places visited for any mosquitoes possible of transmitting yellow fever and eradicate them.
      − Investigate febrile illness reports or unexplained deaths in the area.

   • Refer to Managing Special Situations.
   • Travel history:
      − Travel outside of KS; list states visited; dates visited
      − Travel outside of U.S.; list country; date of departure and return to U.S.
• Case’s occupation – note laboratory or blood and body fluid exposures
• Exposure to mosquitoes, ticks, rodents, primates or livestock of African origin: include dates and places.
• Household members or close contacts with recent travel to endemic areas in the last 3 months.
• Collect information from case for the Contact Investigation. (See below).

3) Investigate epi-links among cases (clusters, household, co-workers, etc).
• For suspected outbreaks to Managing Special Situations section.

**Contact Investigation**

1) Contacts are those with possible exposure to the source of infection. Contacts are not persons in close proximity to a case only.
2) Individuals living in the same household, co-workers, and anyone who might be exposed to the same vector as the case are considered at risk.

**Isolation, Work and Daycare Restrictions**

5) Follow blood and body fluid precautions.
6) Prevent access of mosquitoes to case for at least 5 days after onset of symptoms through the use of screened sickrooms, spraying with insecticides and using bed nets.

**Case Management**

None required.

**Contact Management**

1) If indicated, recommend yellow fever vaccine.

**Environmental Measures**

Mosquito control is an important part of preventing virus transmission. Although the *A. aegypti* mosquito is relatively rare in the United States they have been found in the following areas: Alabama, Arkansas, Delaware, Florida, Georgia, Illinois, Kansas, Kentucky, Louisiana, Maryland, Mississippi, Missouri, New Mexico, New York, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia and Washington, D.C..

**Education**

1) Instruct travelers to endemic areas on the risks and the need for immunizations and to minimize contact with mosquitoes through the use of nets and repellents.
2) Information for travelers to endemic areas can be found at the CDC Traveler’s Health website. (http://wwwnc.cdc.gov/travel/)
MANAGING SPECIAL SITUATIONS

A. Outbreak Definition:
   - One or more cases for which a known risk factor (i.e., recent travel to an endemic area) cannot be identified should be considered a potential outbreak and adequate resources applied to the investigation.

B. No Recent Travel to Endemic Areas:
   - A single diagnosed or suspected case of yellow fever with no travel history should be reported and investigated immediately. Contact the on-call epidemiologist (local) and KDHE (1- 877-427-7317) immediately.
   - A locally acquired case of yellow fever would be an unusual occurrence in the United States.
   - Environmental measures such as investigating local areas visited by the case to locate the source of infection and surveillance of other people for illness may be necessary.

C. Intentional Contamination
   Yellow fever is a potential bioterrorism weapon. If the case has no remarkable travel history, a bioterrorism event should be considered. If a natural etiology cannot be established by a prompt, vigorous investigation; the situation is considered a bioterrorist act until proven otherwise.

   If suspected:
   - Contact the local Health Officer, the on-call epidemiologist (local) and KDHE (1-877-427-7317) immediately. Notify local law enforcement and state public health officials.
   - Implement “Chain of Custody” procedures for all samples collected, as they will be considered evidence in a criminal investigation.
   - Work to define population at risk which is essential to guide response activities. Public health authorities will play the lead role in this effort, but must consult with law enforcement, emergency response and other professionals in the process. The definition may have to be re-evaluated and redefined at various steps in the investigation and response.
   - Once the mechanism and scope of delivery has been defined, the identification of the symptomatic and asymptomatic exposed individuals can be completed and recommendations for the treatment and/or chemoprophylaxis made.
   - Establish and maintain a detailed line listing of all cases and contacts with accurate identifying and locating information.

Safety Considerations:
   - By the time the first cases are identified the risk of exposure is dependent on the number of infected mosquitoes remaining at the exposure site. Appropriate protective clothing and repellents should be used.

Vaccination:
   - Yellow fever vaccine is a live virus vaccine which has been used for several decades. A single dose confers immunity lasting 10 years or more. If a
person is at continued risk of yellow fever infection, a booster dose is needed every 10 years. Adults and children over 9 months can take this vaccine.

**Treatment:**
- No specific therapy. Patients who develop severe illness may require anticonvulsant and supportive care to maintain fluid and electrolyte balance, for ventilation, and to prevent secondary bacterial infections.

**Postexposure prophylaxis (PEP):**
- No post-exposure prophylaxis is associated with this group of diseases; however, vaccination may be an option for some of the arboviruses.

**Environmental decontamination:**
- The viruses do not persist in the environment for long periods of time. No environmental decontamination necessary.
- A release in areas populated with appropriate animal host and/or appropriate arthropod vectors could initiate both an epizootic and epidemic trends.
- Integrated pest management at the presumed infected site, including insecticide fogging, may be a reasonable approach.

**DATA MANAGEMENT AND REPORTING TO THE KDHE**

**A.** Organize and collect data.
- The CDC Specimen Submission Form (CDC 50.34) can assist with data collection.

**B.** Report data via the state electronic surveillance system.
- Especially data that collected during the investigation that helps to confirm or classify a case.
ADDITIONAL INFORMATION / REFERENCES


C. Case Definitions: CDC Division of Public Health Surveillance and Informatics, Available at: www.cdc.gov/osels/ph_surveillance/nndss/casedef/case_definitions.htm

D. Kansas Regulations/Statutes Related to Infectious Disease: www.kdheks.gov/epi/regulations.htm


F. Community Containment Standard Operation Guide: www.kdheks.gov/cphp/operating_guides.htm#CommunityDiseaseContainmentSOG

G. Guidelines for Arbovirus Surveillance Programs in the United States (CDC 1993). Available at: www.cdc.gov/ncidod/dvbid/Arbor/arboguid.pdf

H. ASTO Mosquito Control Resources: www.astho.org/Programs/Environmental-Health/Natural-Environment/Vector-Borne-and-Zoonotic-Diseases/Vector-Borne-and-Zoonotic-Disease-Resources/Main/

I. Additional Information (CDC): www.cdc.gov/health/default.htm
   • CDC Arboviral Specimen Submission Instructions: www.cdc.gov/ncezid/dvbd/specimensub/index.html
**LABORATORY EXAMINATION(S) REQUESTED:**
- ☐ ANtimicrobial Susceptibility
- ☐ ISolation
- ☐ Histology
- ☐ SErology (Specific Test)
- ☐ IDentification
- ☐ OTher (Specify)

**CATEGORY OF AGENT SUSPECTED:**
- ☐ BActerial
- ☐ Rickettsial
- ☐ Viral
- ☐ PArasitic
- ☐ FUngal
- ☐ OTher (Specify)

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**SPECIFIC AGENT SUSPECTED:**

**OTHER ORGANISM(S) FOUND:**

**ISOLATION ATTEMPTED?**
- YES
- NO

**NO. OF TIMES ISOLATED:**

**NO. OF TIMES PASSED:**

**SPECIMEN SUBMITTED IS:**
- Original Material
- Mixed Isolate
- Pure Isolate

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**DATE SPECIMEN TAKEN:**

**SOURCE OF SPECIMEN:**
- Blood
- CSF
- Wound (Site)
- Gastric
- HAir
- EXudate (Site)
- SErum
- Skin
- SEPutum
- STool
- TSkin (Specify)
- URine
- Throat
- OTher (Specify)

**ORIGIN:**
- Food
- Animal
- Human
- Soil
- (Specify)

**CRITICAL INFORMATION:**

**EPIDEMIOLOGICAL DATA:**

**IMMUNIZATIONS:**

**SERUM INFORMATION:**

**TREATMENT:**

**DRUGS USED**
- None

**DATE BEGUN**

**DATE COMPLETED**

**SIGN AND SYMPTOMS:**
- FEVER
  - Maximum Temperature:
  - Duration: __________ Days
- CHills
- MAculopapular
- HEmorrhagic
- VEscular
- Erythema Nodosum
- Erythema Marginatum
- OTher

**RESPIRATORY:**
- RHinitis
- PLumonary
- PHaryngitis
- CAlcifications
- OTitis Media
- PNeumonia (type)
- OTher

**CARDIOVASCULAR:**
- MYocarditis
- PEricarditis
- ENdocarditis
- OTher

**GASTROINTESTINAL:**
- Diarrhea
- BLood
- MUCous
- COntipation
- ABnormal Pain
- VOmiting
- OTher

**STATE OF ILLNESS:**
- SYmptomatic
- ASymptomatic
- SUbacute
- CHronic
- DT disseminated
- LEukemia
- MXtraordinary
- OTher

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**PREVIOUS LABORATORY RESULTS/OTHER CLINICAL INFORMATION:**

**CDC NUMBER**

---

**UNIT**

**FY**

**NUMBER**

**SUF.**
Justification must be completed by State health department laboratory before specimen can be accepted by
CDC. Please check the first applicable statement and when appropriate complete the statement with the *
.
1. Disease suspected to be of public health importance. Specimen is:
   (a) from an outbreak. (b) from uncommon or exotic disease.
   (c) an isolate that cannot be identified, is atypical, shows multiple antibiotic resistance, or from a
   normally sterile site(s) (d) from a disease for which reliable diagnostic reagents or expertise
   are unavailable in State.
2. Ongoing collaborative CDC/State project.
3. Confirmation of results requested for quality assurance.
   *Prior arrangement for testing has been made.
   Please bring to the attention of:
   ________________________________________________
   ________________________________________________
   ________________________________________________
   ________________________________________________
   ________________________________________________

Name, Address and Phone Number of Physician or Organization:

FOR CDC USE ONLY

CDC NUMBER

UNIT YY NUMBER SUP

DATE RECEIVED MO DA YR

ASSOCIATED ILLNESS:

DATE OF ONSET: MM/DD/YYYY

DETAL?

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Center for Disease Control
Center for Infectious Diseases
Atlanta, Georgia 30333

The Centers for Disease Control (CDC), an agency of the Department of Health and Human Services, is authorized to collect this information, including the Social Security number (if applicable), under provisions of the Public Health Service Act, Section 301 (42 U.S.C. 241). Supplying the information is voluntary and there is no penalty for not providing it. The data will be used to increase understanding of disease patterns, develop prevention and control programs, and communicate new knowledge to the health community. Data will become part of CDC Privacy Act system 09-20-0106, “Specimen Handling for Testing and Related Dat a” and may be disclosed: to appropriate State or local public health departments and cooperating medical authorities to deal with conditions of public health significance; to private contractors assisting CDC in analyzing and refining records; to researchers under certain limited circumstances to conduct further investigations; to organizations to carry out audits and reviews on behalf of HHS; to the Department of Justice in the event of litigation, and to a congressional office assisting ... their records. An accounting of the disclosures that have been made by CDC will be made available to the subject indi- vidual upon request. Except for permissible disclosures expressly authorized by the Privacy Act, no other disclosure may be made without the subject individual’s written consent.
Fact Sheet

Fact Sheet is available under attachments:

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