



Colorado Department  
of Public Health  
and Environment

## **Guidelines for West Nile Virus Human Case Investigation**

### **Colorado Department of Public Health and Environment**

### **Communicable Disease Epidemiology Program**

### **June 20, 2013**

The following procedures will be used for the investigation of West Nile virus (WNV) human cases in Colorado in 2013. A system for tracking and reporting cases should be defined in each county or region with specific duties and responsibilities assigned to an individual or team. In many counties there will be a substantial caseload to manage and a systematic approach will be essential.

#### **CASE ASCERTAINMENT**

WNV is a seven-day reportable condition by all laboratories in Colorado. Cases are reported to either the state health department or local public health agencies, and are entered into the Colorado Electronic Disease Reporting System (CEDRS) under the diagnosis "West Nile Virus". Some laboratories and hospitals enter cases directly into CEDRS.

The CDPHE laboratory will be performing WNV IgM tests, along with numerous private clinical laboratories. Test results from private clinical laboratories will be accepted and cases should be investigated without subsequent verification at the CDPHE laboratory. We will not be confirming all private lab tests this season. However, if during the investigation there is reason to suspect a false positive test result (incompatible illness, onset during off-season, test being attributed to past illness, no other WNV activity in the area, etc), then specimens should be submitted for confirmatory testing at CDPHE. Please note on the lab submission form that the specimen is part of a public health investigation to waive the laboratory fee.

*Note on WNV IgM testing:* In neuroinvasive disease (meningitis or encephalitis), specimens collected within 7 days of onset usually test IgM positive. In milder cases of WNV infection, seroconversion may take up to two weeks or longer in some patients. If specimens collected within a week of onset are IgM negative, but the diagnosis of WNV infection is still being considered, a second specimen collected 3-4 weeks post-onset should be tested. WNV IgM antibody levels have been shown to persist in some patients for greater than 500 days. Positive serologic tests must be correlated with clinical presentation, season, and potential exposure to WNV.

**Due to low test specificity, a single positive IgG antibody test result on serum or CSF, either alone or in conjunction with a negative IgM test, is NOT diagnostic for acute infections and is NOT considered a case of WNV.** Cross-reactions can occur from past infection with St. Louis encephalitis (SLE), dengue fever, and several other viruses. In some parts of Colorado 5-10% of the population, especially older patients, may have antibody against SLE from prior

exposure to this endemic virus. Documentation of a seroconversion from negative to positive IgG antibody status on paired sera (i.e. acute and convalescent) would be diagnostic.

## **CLINICAL DESCRIPTION**

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purpose of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: neuroinvasive disease and non-neuroinvasive disease.

### ***Neuroinvasive Disease***

Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with stiff neck, altered mental status, seizures, limb weakness, cerebrospinal fluid (CSF) pleocytosis, or abnormal neuroimaging. AFP may result from anterior (“polio”) myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barre syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

### ***Non-neuroinvasive Disease***

Most arboviruses are capable of causing an acute systemic febrile illness (e.g., West Nile fever) that may include headache, myalgias, arthralgias, rash, or gastrointestinal symptoms. Rarely, myocarditis, pancreatitis, hepatitis, or ocular manifestations such as chorioretinitis and iridocyclitis can occur.

## **CLINICAL CRITERIA FOR DIAGNOSIS**

A clinically compatible case of arboviral disease, with onset during WNV transmission season (May – Oct)\*, defined as follows:

### ***Neuroinvasive Disease***

- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurological dysfunction, as documented by a physician,  
-AND-
- Absence of a more likely clinical explanation.

### ***Non-neuroinvasive Disease***

- Fever or chills as reported by the patient or a health-care provider,  
-AND-
- Absence of neuroinvasive disease,  
-AND-
- Absence of a more likely clinical explanation.

\* Exceptions to criteria of “onset during WNV transmission season (May – Oct)” are: if transmission occurred during travel outside of Colorado where transmission season is longer or different (e.g. tropical areas such as Florida, South America) OR transmission to patient was through non-mosquito-borne routes such as through blood product, tissue, or organ.

## **CASE CLASSIFICATION**

## **CONFIRMED:**

### ***Neuroinvasive Disease***

A case that meets the above clinical criteria for neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in tissue, blood, CSF, or other body fluid,  
- OR -
- Four-fold or greater change in virus-specific quantitative<sup>⊛</sup> antibody titers in paired sera,  
- OR -
- Virus-specific IgM antibodies in serum with *confirmatory virus-specific neutralizing antibodies*<sup>†</sup> in the same or a later specimen,  
- OR -
- Virus-specific IgM antibodies in CSF and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

### ***Non-neuroinvasive disease***

A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid,  
- OR -
- Four-fold or greater change in virus-specific quantitative<sup>⊛</sup> antibody titers in paired sera,  
- OR -
- Virus-specific IgM antibodies in serum with *confirmatory virus-specific neutralizing antibodies*<sup>†</sup> in the same or a later specimen.

## **PROBABLE:**

### ***Neuroinvasive Disease***

A case that meets the above clinical criteria for neuroinvasive disease and the following laboratory criteria:

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

### ***Non-neuroinvasive Disease***

A case that meets the above clinical criteria for non-neuroinvasive disease, onset during WNV transmission season (May – Oct)\* and the laboratory criteria for a probable case:

- Virus-specific IgM antibodies in serum but with no other testing.

<sup>⊛</sup>quantitative antibody titers are not provided through optical density results such as 0.9 or 1.2 with no units expressed. Examples of quantitative results include serum dilutions (e.g. 1:80) or neutralizing antibody potency expressed in international units (e.g. IU/mL).

<sup>†</sup> “*confirmatory virus-specific neutralizing antibodies*”: confirmatory testing involves the detection of arboviral-specific neutralizing antibodies utilizing assays such as a plaque reduction neutralization test (PRNT). Assays for the detection of IgM and IgG antibodies commonly include enzyme linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed, as described above if confirmation is needed.

Only confirmed and probable cases will be included in state and national case counts. Suspect cases will not be included. To avoid confusion for the public and media, we will not make a distinction between confirmed and probable cases in publicly released information.

## **CASE INVESTIGATION AND INTERVIEW**

**All information required for case verification and counting must be entered into the CEDRS record.** Local public health agencies can choose to use CDPHE's standardized human case investigation form that corresponds to required information for CEDRS entry or a more detailed form developed in house to gather additional information on cases in their jurisdiction.

All reported cases of WNV should be investigated promptly. The regional epidemiologists will work with the local agencies to ensure that proper follow up takes place shortly after the case was reported. Agencies may choose to interview the case's health care provider, the patient or both depending on information needs and resources. At the minimum, the following information should be gathered and entered into the CEDRS record:

- Verify the diagnosis (asymptomatic blood donor, fever, meningitis, encephalitis or meningoencephalitis); meningitis, meningoencephalitis and encephalitis cases will be reported as neuroinvasive to the CDC.
- Obtain an illness onset date.
- Verify if the patient survived or died.
  - **IF DIED** - obtain the date of death and notify CDPHE.
- Is the patient diagnosed with physician diagnosed acute flaccid paralysis?
- Is the patient an organ donor or a transplant recipient in the four weeks prior to onset?
  - **IF YES** - notify CDPHE.
- Did the patient donate blood in the four weeks prior to onset?
  - **IF YES** - obtain the date and place of the donation and notify CDPHE.
- Did the patient receive a blood transfusion in the four weeks prior to onset?
  - **IF YES** - obtain the date and place of the transfusion and notify CDPHE.
- Is the patient pregnant?
  - **IF YES** - obtain the expected delivery date. Determination of whether an infant was infected in-utero will be made later as part of a special study by CDC.
- If the patient is an infant or toddler, is he/she breastfed? This question does not pertain to infected women who are currently breastfeeding their infant.

## **CEDRS / CASE VERIFICATION AND COUNTING**

A reported case will be verified and officially counted if the following criteria are met:

- 1) The patient has a compatible illness and a positive IgM test on serum and/or CSF.
- 2) The case has been entered into CEDRS and classified by syndrome (uncomplicated fever, meningitis, encephalitis, or meningoencephalitis).
- 3) The following variables have been entered into the CEDRS record: county, age, sex, onset date and serum and/or CSF test result.

If any of these variables are missing information, including onset date, the case will not be counted until that information is available. If a county does NOT want to officially count a case, one of the required variables should be left blank in the CEDRS record (such as onset date or syndrome). This insures that the posted summary statistics, epi-curve, map of human cases, and

local, state and national totals agree. When a reported case has met the above criteria for verification and counting, it will be added to the state and national official totals and will be included in the website summary data. This will be done automatically without a subsequent call to the county! The website is located at:

<http://www.cdphe.state.co.us/dc/Zoonosis/wnv/index.html>

Cases will be counted and the website updated Monday through Friday by 4:00 pm during the WNV season. In order to have a case counted, the data must be entered into CEDRS by 3:00 pm. Any case information entered after this time will be added to the following day's count.

**All other CEDRS variables are not required for case verification and counting at the state level. However, many of these variables are required by CDC. All variables in the Extended Record section should be completed in a timely manner to insure comprehensive reporting of required data to CDC.**

### **FLAGGING CEDRS RECORDS**

Two indicators in the CEDRS record will serve as flags for local public health agencies to determine which cases have been included in the official case count:

- 1) CDPHE will enter "WNV13" in the "Outbreak Name" field in the Case Information section of the CEDRS record
- 2) CDPHE will enter "YES" in the "Case Counted" field and the date the case was added to the official case count in the "Date Case Counted" field on the Extended Record section of the CEDRS record.

Agencies can run a line list in CEDRS that lists the cases that have been officially counted:

- Go to the CEDRS Main Menu
- Under "Reports/Queries", click on "Line Listing of Cases by Selected Variables".
- At the "Outbreak Name" field, select "Is Exactly" and type in WNV13 (no spaces).
- Enter any other search parameters you would like, and then click on "Create Line Listing" at the bottom of the page.

The generated line list will contain those cases that have been officially counted. This list can be compared against all reported cases in the county to determine which cases have not been officially counted.

### **SUMMARY - STEPS FOR HUMAN CASE INVESTIGATION**

- 1) Upon receiving a case or laboratory report, verify that the patient has a positive IgM antibody test on serum or CSF. If the IgM test is negative, no further action is necessary. If the medical provider still feels WNV infection is the diagnosis, advise them to submit another specimen.
- 2) If the test result is IgM positive, consider the person a case, enter the case into CEDRS under the diagnosis "West Nile Virus", and proceed with case investigation. If during the investigation a false positive test result is suspected attempt to obtain the original or a second specimen for verification at CDPHE or CDC. The original or second specimen should be sent to CDPHE with a notation that this is a confirmation specimen that is part of a public health investigation so that a lab fee will not be charged. Clinically compatible

cases during WNV transmission season with a positive IgM antibody test of illness onset do not need further laboratory confirmation.

- 3) Interview the physician and/or patient and complete the required fields in the CEDRS record (age, sex, county, onset date, case status, lab/medical testing information, and clinical syndrome).
- 4) Complete all other fields in CEDRS in a timely manner, especially those in the Extended Record section.
- 5) If the patient provides a history of donating or receiving blood or an organ, being pregnant, has been breastfed, or dies notify CDPHE immediately.

For questions or additional information, please contact your regional epidemiologist or CDPHE.