

West Nile Virus: Guidelines for Human Testing and Surveillance

Marin County Department of Health & Human Services, July 2006

Diagnostic Testing Guidelines

West Nile Virus (WNV) cases are reportable within one working day in Marin County (see Reporting section below).

WNV testing within the regional public health laboratory network [i.e., the California Department of Health Services (CDHS) Viral and Rickettsial Disease Laboratory (VRDL) and participating local public health laboratories such as the Marin County Health & Human Services (HHS) Public Health Lab (PHL)] is recommended on individuals with the following:

A. Encephalitis

- Encephalopathy (depressed or altered level of consciousness, lethargy, or personality change), and one or more of the following: Fever ($T \geq 38C$), seizure(s), focal neurologic findings, CSF pleocytosis, abnormal EEG, abnormal neuroimaging.

B. Aseptic meningitis (Note: Consider enterovirus workup for individuals ≤ 18 years of age, e.g. CSF PCR, throat or stool isolation)

- Fever ($T \geq 38C$), headache, stiff neck and/or other meningeal signs
- CSF pleocytosis

C. Acute flaccid paralysis; atypical Guillain-Barré Syndrome; transverse myelitis; or

- Fever ($T \geq 38C$), altered mental status, and/or CSF pleocytosis

D. Febrile illness compatible with West Nile fever and lasting ≥ 7 days (must be seen by health care provider):

- The West Nile fever syndrome can be variable and often includes headache and fever ($T \geq 38C$). Other symptoms may include rash, swollen lymph nodes, eye pain, nausea or vomiting. After initial symptoms, the patient may experience fatigue and lethargy for several days or longer.

Diagnostic Categories:

- WNV Neuro-invasive Disease (WNND): (See A, B, C above). Most cases (99%) will be IgM positive by day 5 of illness.
- West Nile Fever (WNF): (See D above). Not all cases will be IgM positive by 7 days.
- Asymptomatic (testing not recommended).

Identification of human cases is important early in the West Nile virus season to assess the burden of human illness and target mosquito control and public education activities to reduce exposure risk. However, depending on the volume of tests requested and laboratory capacity, the Marin County Health & Human Services (HHS) Public Health Lab (PHL) may need to consider limiting testing to individuals in categories A – C (encephalitis, meningitis, acute flaccid paralysis) once West Nile virus is established in a given area.

Submitting Specimens to Private Labs for Testing

Clinicians utilizing private labs should consult with the individual laboratories for instructions. Note: For the first few suspect cases of the season that are IgG and IgM positive at a commercial lab, it is recommended that the Marin PHL obtain a specimen to verify the commercial lab results.

Submitting Specimens to the Marin County HHS PHL for Testing

Required specimens:

- Acute serum: ≥ 2cc serum
- Cerebral Spinal Fluid (CSF): 1-2cc CSF if lumbar puncture is performed

If West Nile virus is highly suspected and acute serum is negative or inconclusive, request:

- 2nd serum: ≥ 2cc serum collected 3-5 days after acute serum

Paired acute and convalescent serum specimens are useful for demonstration of seroconversion to WNV. Paired samples should be collected whenever WNV is suspected. Although a single acute serum may provide evidence of recent WNV infection, a negative acute serum does not necessarily rule out infection. Occasionally, a specimen may be collected too soon to show antibody related to a current illness (e.g. with immunocompromised individuals).

The PHL is open Monday-Friday 8AM-5PM for receipt of specimens. After hours and on weekends, refrigerate specimens until delivery. All specimens must be accompanied by a completed specimen submittal form, **WEST NILE VIRUS SPECIMEN SUBMITTAL FORM – Marin County HHS Public Health Laboratory**. For testing questions please contact the Marin County HHS PHL at 415- 499-6849 or -507-4133.

For encephalitis cases, the **California Encephalitis Project** at the CDHS VRDL also provides an extensive battery of testing to rule out WNV and other etiologic agents. For information on the California Encephalitis Project, please contact Shilpa Gavali, MPH, (510) 307-8608. Also the encephalitis project specimen submittal form is available at the website www.ceip.us (click on “Projects” and then “California Encephalitis Surveillance Project”).

Laboratory Diagnosis and Interpretation

- Marin County PHL will perform IgM and IgG by the IFA method and IgM by the EIA method.
- IgG(+) result only (i.e., negative for IgM) typically indicates previous infection of a flavivirus
 - Check case history for travel to flavivirus-endemic areas, early onset date in relation to specimen collection, vaccination history, etc.
 - If current infection still suspected, obtain convalescent serum to test for seroconversion

Interpretation of West Nile virus antibody test results*

| Tests | Results | Interpretation |
|------------|---------------------------|---|
| IgM IgG | negative negative | Antibody not detected |
| IgM IgG | negative positive | Infection at undetermined time |
| IgM IgG | positive negative | Possible evidence of recent or current infection; further testing necessary** |
| IgM IgG | positive positive | Evidence of recent or current infection*** |
| IgM IgG | indeterminate negative | Inconclusive ‡request convalescent serum |

* Due to heterotypic antibody responses and/or cross-reactions, serologic results should be interpreted on the basis of clinical and epidemiological information

** Note possibility of false positive IgM result (EIA)

*** Note that some individuals infected in 2004 may have persisting IgM/IgG in 2005

‡ Paired acute and convalescent serum samples may be useful for demonstration of seroconversion

Case Classification:

A patient is considered a WNV case if clinically compatible and has one of the following lab results:

- IgM(+) by two different assays (e.g. EIA and IFA)
- IgM(+) and IgG(+) by EIA
- IgM(+) and IgG(+) by IFA
- Rising IgG antibodies

(Reference: ***West Nile Virus: Revised National Surveillance Case Definition – Domestic Arboviral Disease***. This document is also available on the Marin County HHS WNV webpage.)

Reporting:

Clinicians must report WNV cases, and laboratories must report positive WNV lab results, to the Marin County HHS Communicable Disease Unit **within one working day** by fax (415-473-6002) or phone (415-473-7805). In reporting, clinicians should complete and submit a **WNV Case History Form**; this form can be downloaded from the Marin County WNV webpage (www.co.marin.ca.us – keyword “West Nile”) or be obtained by phoning 415-473-7805. NOTE: Clinicians using a private lab should also complete and submit the **WNV Case History Form**, along with the positive lab report, to report a WNV case. WNV related deaths should also be reported within one working day by fax or phone.

West Nile Virus-Associated Fatalities

Determining whether or not a fatality is associated with West Nile virus can be difficult. West Nile virus may not always be listed as a contributory or underlying cause of death on death certificates. Also, patients often have many underlying conditions and preexisting medical problems that may also be related to the immediate causes of death. In general, if a patient was diagnosed with West Nile virus and never recovered from the sequelae (e.g. was discharged to convalescent hospital until date of death), Marin County HHS may consider designating the patient as a WNV-associated fatality.