West Nile Virus in California:
Guidelines for Human Testing and Surveillance
Within the Regional Public Health Laboratory Network

California Department of Health Services
Viral and Rickettsial Disease Laboratory
Richmond, California

July 2006
# West Nile Virus in California: Guidelines for Human Testing and Surveillance
## Within the Regional Public Health Laboratory Network

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West Nile Virus in California: Guidelines for Human Testing and Surveillance Within the Regional Public Health Laboratory Network

Diagnostic Testing Guidelines

West Nile virus (WNV) testing within the regional public health laboratory network (i.e., the California Department of Health Services Viral and Rickettsial Disease Laboratory and participating local public health laboratories) is recommended for individuals with the following:

A. Encephalitis
B. Aseptic meningitis (Note: consider enterovirus for individuals ≤ 18 years of age)
C. Acute flaccid paralysis; atypical Guillain-Barré Syndrome; transverse myelitis; or
D. Febrile illness*
   a. Illness compatible with West Nile fever and lasting ≥ 7 days
   b. Must be seen by a health care provider

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

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, local public health laboratories 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 Regional Public Health Laboratory Network 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).

Specimens must be submitted with a completed specimen submittal form (See Appendix A: Instructions for Submitting Specimens; and Appendix B: West Nile Virus Specimen Submittal Form).
Viral and Rickettsial Disease Laboratory Testing Algorithm

- When both serum and CSF are received, enzyme immunoassay (EIA) is done on serum (CSF is stored in case additional confirmatory testing is needed)
- If only CSF is received, EIA is done on CSF (Note: Focus EIA IgM is not currently FDA-approved for use on CSF; if CSF is positive, a confirmatory serum sample will be requested)
- Immunofluorescence assay (IFA) may be done as an adjunct test on serum (IFA is not done on CSF)
- Neutralization testing is done to resolve indeterminate results, or by request
- Enterovirus PCR may also be done on CSF specimens on a seasonal basis, depending on the availability of resources at VRDL - Call 510-307-8606 to find out whether the most current algorithm includes enterovirus PCR
- See Appendix C: VRDL WNV Testing Algorithm – Serum; Appendix D: VRDL WNV Testing Algorithm – CSF; and Appendix E: WNV Laboratory Testing at VRDL

Laboratory Diagnosis and Test Interpretation

- Local public health laboratories are encouraged to perform at least two different assays on each suspect case, e.g. IgM by EIA and IgM by IFA, or IgM and IgG by IFA
- For the first suspect cases of each WNV season, VRDL recommends that local public health labs obtain repeat/confirmatory test results from VRDL
- IFA is a more subjective assay than EIA and should be interpreted with caution
- 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
- In 2004, VRDL did encounter a few specimens where serum was drawn soon after onset (≤ 5 days) and was IgM-negative/IgG-positive, but convalescent serum drawn a few days later was IgM-positive/IgG-positive
- VRDL is always available for consultation on test results with local public health laboratories

<table>
<thead>
<tr>
<th>Tests</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgM</td>
<td>negative</td>
<td>Antibody not detected</td>
</tr>
<tr>
<td>IgG</td>
<td>negative</td>
<td>Infection at undetermined time</td>
</tr>
<tr>
<td>IgM</td>
<td>negative</td>
<td>Possible evidence of recent or current infection; further testing necessary**</td>
</tr>
<tr>
<td>IgG</td>
<td>negative</td>
<td>Evidence of recent or current infection***</td>
</tr>
<tr>
<td>IgM</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>IgM</td>
<td>indeterminate</td>
<td>Inconclusive</td>
</tr>
<tr>
<td>IgG</td>
<td>negative</td>
<td>‡ request convalescent serum</td>
</tr>
</tbody>
</table>

* 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 may have persisting IgM/IgG from the previous WNV season
‡ Paired acute and convalescent serum samples may be useful for demonstration of seroconversion
Case Classification: Regional Public Health Laboratory Network

A case is considered to be WNV positive if the patient has a clinically compatible illness (See Appendix F for case definition) and has the following laboratory results:
- IgM(+) by two different assays (e.g. EIA and IFA); or
- IgM(+) and IgG(+) by EIA; or
- IgM(+) and IgG(+) by IFA; or
- Rising IgG antibodies

Results from Commercial or Reference Laboratories

- Beginning in 2005, commercial labs will no longer be asked to forward IgM(+) specimens for repeat/confirmatory testing (though VRDL has requested that specimens with ambiguous results be forwarded)
- Local health departments will need to follow up on IgM(+) results from commercial labs
  - If patient has clinically compatible illness and is IgM-positive and IgG-positive, the commercial lab results are sufficient to conclude that patient is infected with WNV – however, for the first few cases of the WNV season, it is recommended that positive results from commercial labs be verified by repeat/confirmatory testing at the local public health lab and/or VRDL
  - If patient is IgM-positive and IgG-negative, be aware that IgM can be falsely positive; follow-up testing is suggested
- IgG-positive result only (i.e., IgM-negative) typically indicates previous infection
- When in doubt, try to obtain either the original specimen or a follow-up sample to forward to the local public health lab or to VRDL for repeat/confirmatory testing
- Public health reporting by commercial laboratories is being facilitated by VRDL (see below)
West Nile Virus-Associated Fatalities

Determining whether or not West Nile virus infection has played a causal role in a fatality can be difficult. West Nile virus may not always be listed as a contributory or underlying cause of death on death certificates. Patients often have many underlying conditions and preexisting medical problems that also may 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), a health department may consider designating the patient as a WNV-associated fatality.

Reporting

Since West Nile virus infection is a laboratory diagnosis, and since West Nile surveillance is a multi-component system maintained nation-wide through ArboNet (CDC’s source for WNV data), reporting human cases of West Nile virus to the California Department of Health Services is done through slightly different routes than regular disease reporting. The algorithm below outlines the various paths through which West Nile virus infections may be reported.
Important Issues about Reporting

- West Nile virus infection is reportable both by laboratory and provider
- Fax or mail case history forms to Viral and Rickettsial Disease Laboratory (VRDL) – please indicate, either on form or by phone/email, that individual has tested positive for WNV: Fax (510) 307-8599; VRDL-West Nile, 850 Marina Bay Parkway, Richmond, CA 94804
- Only cases reported to CDHS-VRDL are entered into ArboNET and posted on the California WNV website – If a local agency uses AVSS or another local system for their disease surveillance, they will enter West Nile infections separately into those systems, as well as send a case history form to CDHS-VRDL
  - The following AVSS classifications can be used to enter cases:
    - ENCP-WNV: For West Nile encephalitis cases
    - MENG-WNV: For West Nile meningitis cases
    - WNV-FVR: For West Nile fever cases
    - WNV-AFP: For West Nile acute flaccid paralysis cases
    - WNV-ASYM: For WNV infections detected via blood bank with no accompanying illness
    - WNV-UNK: For cases with unknown or undeterminable clinical status
  - CDHS-VRDL will check AVSS for reported WNV infections that may not have been previously reported
- A line list of locally acquired WNV cases will be maintained and updated biweekly on the California WNV website (http://westnile.ca.gov)
- Report clinical syndrome as West Nile fever, neuroinvasive disease (specify encephalitis, meningitis, acute flaccid paralysis, or other), or unknown
- Report to VRDL if local lab or health department knows of a case that is not on website or ArboNET

Important Issues about VRDL Results

- All VRDL results are faxed/mailed to local health department/lab of patient’s residence (and submitting local health department/lab if different)
- Local health departments need to report West Nile virus results to providers
- VRDL results are routinely reported to local health departments/labs
  - Positive results relayed immediately by phone or email, then followed up with fax/mail
  - Negative results faxed/mailed 1-2 times/week
- Fax requests for results (include patient names and dates of birth) to: (510) 307-8599, Attn: West Nile Virus Project
Contacts

Viral and Rickettsial Disease Laboratory

West Nile Virus Surveillance Project:
Cynthia Jean, MPH ........................................... (510) 307-8606
Shilpa Gavali, MPH.............................. (510) 307-8608
Carol Glaser, DVM, MD (for clinical consultation)......... (510) 307-8613
West Nile Virus Surveillance Project Fax ............... (510) 307-8599

California Encephalitis Project:
Somayeh Honarmand, MS............................. (510) 307-8607
California Encephalitis Project Fax ............... (510) 307-8599

Vector Borne Disease Section

West Nile Virus Hotline .................................. (877) 968-2473

Links

California West Nile Virus Website ............... http://westnile.ca.gov
CDC West Nile Virus Website ............... http://www.cdc.gov/ncidod/dvbid/westnile/

Appendices

A. Instructions for Submitting Specimens
B. West Nile Virus Specimen Submittal Form
C. Viral and Rickettsial Disease Laboratory West Nile Virus Testing Algorithm – Serum
D. Viral and Rickettsial Disease Laboratory West Nile Virus Testing Algorithm – CSF
E. West Nile Virus Laboratory Testing – Viral and Rickettsial Disease Laboratory
G. West Nile Virus Case History Form
Instructions for Submitting Specimens

- Refrigerated specimens should be sent on **cold pack** using an overnight courier
  - If CSF needs to be stored ≥ 48 hours before submittal, freeze at -20°C
  - Ship frozen specimens on dry ice
- Each specimen should be clearly labeled with **patient name**, **specimen type**, and **date of specimen collection**
- Specimens must be submitted with a specimen submittal form. The following information is asked for on the specimen submittal form because it is important for accurate interpretation of results:
  - Onset date
  - Unusual immunological status of patient, if any
  - County of residence
  - Travel history in flavivirus-endemic areas
  - History of prior vaccination against flavivirus disease
  - Brief clinical summary including clinical diagnosis
- Please include local public health laboratory IFA/EIA results, if applicable
  - Local laboratory results affect VRDL testing algorithm (e.g. heterophile subtract procedure done on all specimens that screen positive for IgM)
- **Do not send specimens on Fridays** (VRDL Specimen Receiving Hours M-F 8-5)
- Address specimens for VRDL to:
  Specimen Receiving/ West Nile
  850 Marina Bay Parkway
  Richmond, CA  94804
Appendix B: Specimen Submittal Form (version for use by local public health labs)

West Nile virus testing is recommended on individuals with the following:

A. Encephalitis
B. Aseptic meningitis (Note: Consider enterovirus for individuals ≤ 18 years of age)
C. Acute flaccid paralysis; atypical Guillain-Barré Syndrome; transverse myelitis; or
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 > 38°C). Other symptoms include rash, swollen lymph nodes, eye pain, nausea or vomiting. After initial symptoms, the patient may experience several days of fatigue and lethargy.

1. **Required specimens:**
   - **Acute Serum:** ≥ 2 cc serum
   - **Cerebral Spinal Fluid (CSF):** 1-2 cc CSF if lumbar puncture is performed

2. If West Nile virus is highly suspected and acute serum is negative or inconclusive:
   - **2nd Serum:** ≥ 2 cc serum collected 3-5 days after acute serum

   - Refrigerated specimens should be sent on cold pack using an overnight courier
   - If CSF is frozen, send on dry ice (all specimens may be sent on dry ice)
   - Each specimen should be labeled with **date of collection, specimen type, and patient name**
   - Please do not send specimens on Fridays (Specimen Receiving Hours: M-F 8-5)
   - Send specimens to CDHS VRDL: Specimen Receiving – West Nile
     850 Marina Bay Parkway
     Richmond, CA 94804

   - Local Public Health Laboratory West Nile **IFA/EIA IgM results** (or attach copy of results):

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Date Collected</th>
<th>IgM Assay Method</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>IFA EIA</td>
<td>Negative Reactive Indeterminate Not Tested</td>
</tr>
</tbody>
</table>

**IMPORTANT: THE INFORMATION BELOW MUST BE COMPLETED AND SUBMITTED WITH SPECIMENS**

<table>
<thead>
<tr>
<th>Patient’s last name, first name:</th>
<th>Patient Information</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Address ______________</td>
</tr>
<tr>
<td></td>
<td>City _______________ Zip_______ County ____________</td>
</tr>
<tr>
<td></td>
<td>Phone Number (_____) ___________________</td>
</tr>
<tr>
<td></td>
<td>Other information (immunocompromised, travel hx, hx of flavivirus infection, etc.):</td>
</tr>
</tbody>
</table>

**This section for Laboratory use only.**

<table>
<thead>
<tr>
<th>Specimen type and/or specimen source</th>
<th>Date Collected</th>
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<tbody>
<tr>
<td>1st</td>
<td></td>
</tr>
<tr>
<td>2nd</td>
<td></td>
</tr>
<tr>
<td>3rd</td>
<td></td>
</tr>
</tbody>
</table>

Questions? Call Cynthia Jean at (510) 307-8606
California Department of Health Services Viral and Rickettsial Disease Laboratory

Submitting Facility ________________________________ Phone Number (_____) ____________________
Appendix C: Viral and Rickettsial Disease Lab West Nile Virus Testing Algorithm - Serum

**SERUM**

**LOCAL RESULT:**
NEGATIVE/ NOT TESTED

- EIA
  - Focus IgM
  - In-house IgG

  - Focus M(-)
  - In-house G(-)
  
  - Report (Neg)

  - Repeat EIA
    - Focus IgM w/heterophile

  - Focus M(-)
  - In-house G(-)
  
  - Review*

  - Focus M(-)
  - In-house G(+)

  - Focus M(+)
  - In-house G(+)

  - Call LHD

  - Focus M(+)
  - heterophile(-)
  - In-house G(-)

  - Review*

  - Focus M(+)
  - heterophile(+)
  - In-house G(+/-)

  - Focus M(-)
  - heterophile(-)
  - In-house G(+)

  - Review*

  - Focus M(-)
  - heterophile(-)
  - In-house G(-)

  - Review*

**LOCAL RESULT:**
POSITIVE

- EIA
  - Focus IgM w/heterophile†
  - In-house IgG

  - Focus M(-)
  - heterophile(-)
  - In-house G(-)

  - Report (Pos)

  - IFA and/or Neut
  - Request conv sample

  - Focus M(+)
  - heterophile(-)
  - In-house G(+)†

  - Review*

  - Focus M(+)
  - heterophile(+)
  - In-house G(+/-)

  - Review*

  - Focus M(-)
  - heterophile(-)
  - In-house G(+)

  - Review*

  - Focus M(-)
  - heterophile(-)
  - In-house G(-)

  - Review*

† Heterophile antibodies are “interfering” antibodies that can cause false positive IgM EIA results

* Review the following information:
  - onset date?
  - travel history?
  - old flavivirus?
  - vaccine?
Appendix D: Viral and Rickettsial Disease Lab West Nile Virus Testing Algorithm - CSF

CSF

EIA
- Focus IgM
- If IgM(+), in-house IgG

Focus M(-) [In-house G(-)]

Report (Neg)

ANY POSITIVE RESULT:
- Focus M(+)/ In-house G(+)
- Focus M(+)/ In-house G(-)
- Focus M(-)/ In-house G(+)

Request serum
Laboratory diagnosis of human West Nile virus (WNV) infection is a multi-step process. In some cases, physicians send specimens to private commercial laboratories for WNV diagnostic testing. More commonly, specimens are sent to the local or state health department for diagnostic laboratory testing.

The testing available at the California State Health Department includes:

**Serologic tests**

**Enzyme Immunoassay (EIA) testing:** The immunoglobulin M (IgM) EIA is the frontline test for WNV diagnosis. The EIA is the ideal test because it is both simple and sensitive (i.e., highly likely to find true-positives) and it can be used with both serum and cerebrospinal fluid (CSF) specimens. EIA testing can be completed in 1 to 2 days from the time samples arrive at the laboratory. Generally several specimens are done on each EIA run.

The immunoglobulin G (IgG) EIA test is used as an adjunct test—a single IgG result cannot differentiate between old and new infection; however, paired sera showing significant change in IgG antibody levels can be helpful.

**Immunofluorescence Assay (IFA) testing:** IFA tests for WNV can also test for IgM and IgG antibodies. The advantages of these tests are that they are rapid and amenable to just a few samples. However, the IFA is a more subjective assay than the EIA.

**Molecular tests**

Molecular methods for WNV testing can be used as an adjunct to the serologic tests. For diagnosis of clinical disease, serological tests are more accurate than molecular tests. Reverse Transcriptase - Polymerase Chain Reaction (RT-PCR) is a process that uses nucleic acid amplification techniques. While these tests can be useful in diagnosis, they have low sensitivity for a variety of reasons for WNV, making them inappropriate as the sole test for laboratory diagnostic testing of possible human WNV infections. An advantage of this method is the relatively rapid turn around time. RT-PCRs may be useful for immunocompromised individuals that have a delay in antibody response and prolonged viremia. Additionally, VRDL uses molecular methods to rule out enterovirus.

**Confirmation of results**

**Plaque reduction neutralization test (PRNT)**

Once VRDL has an initial positive result, further testing may be done to confirm that the infection detected is West Nile. WNV is a flavivirus, which can be problematic as far as cross-reactivity. The flaviviruses include St. Louis encephalitis (SLE) and Japanese encephalitis (JE) viruses, both of which are closely related to West Nile, yellow fever (YF) and dengue (DEN) viruses. People who have been recently vaccinated for JE or YF, or who have a recent exposure to JE, YF, SLE, or DEN viruses may have a positive MAC-ELISA for WNV, even though they have not actually been exposed to WNV.

Additional laboratory testing may be required to rule out the false-positive reactions that result from an exposure to a related flavivirus. The PRNT is the most specific test available for distinguishing between and among the arthropod-borne flaviviruses. Because exposure to other flaviviruses is possible in many areas of WNV activity, initial IgM-capture Enzyme Linked Immunosorbtant Assays (MAC-ELISA) positive results may need to be confirmed by PRNT. The PRNT usually takes up to 8 days if testing for both WNV and SLE viruses is required. The process may take even longer if testing with YF or Dengue viruses is necessary. This additional testing (e.g., the PRNT) may require growth of the virus and may take a week or more (plus shipping time) to conduct.

**Tests in development**

The VRDL is in the process of developing tests for more rapid confirmation of WNV, e.g. the Western Blot. Additionally, VRDL hopes to provide avidity testing in order to ascertain the binding strength of antibodies.
West Nile virus infection (neuroinvasive disease, fever, and asymptomatic infection) is reportable to DHS under Title 17 of the California Code of Regulations. Below is the summary statement by the Council of State and Territorial Epidemiologists (available at http://www.cste.org/ps/2004pdf/04-ID-01-final.pdf) including the case definition for West Nile neuroinvasive disease, followed by the case definitions for West Nile fever and West Nile infection.

**CASE DEFINITION: Neurotropic Domestic Arboviral Diseases**

**Clinical description**
Arboviral infections may be asymptomatic or may result in febrile illnesses of variable severity sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes include aseptic meningitis, myelitis and encephalitis, which are clinically indistinguishable from similar syndromes caused by other viruses. Arboviral meningitis is usually characterized by fever, headache, stiff neck, and pleocytosis in cerebrospinal fluid. Arboviral myelitis is usually characterized by fever and acute limb paresis or flaccid paralysis. Arboviral encephalitis is usually characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction. Less common neurological syndromes can include cranial and peripheral neuritis/neuropathies, including Guillain-Barré syndrome.

Non-neuroinvasive syndromes caused by these usually neurotropic arboviruses can rarely include myocarditis, pancreatitis, or hepatitis. In addition, they may cause febrile illnesses (e.g., West Nile fever [WNF]) that are non-localized, self-limited illnesses with headache, myalgias, arthralgias, and sometimes accompanied by skin rash or lymphadenopathy. Laboratory-confirmed arboviral illnesses lacking documented fever can occur, and overlap among the various clinical syndromes is common.

**Clinical criteria for diagnosis**
Cases of arboviral disease are classified either as neuroinvasive or non-neuroinvasive, according to the following criteria:

**Neuroinvasive disease** requires the presence of fever and at least one of the following, as documented by a physician and in the absence of a more likely clinical explanation:
- Acutely altered mental status (e.g., disorientation, obtundation, stupor, or coma), or
- Other acute signs of central or peripheral neurologic dysfunction (e.g., paresis or paralysis, nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, or abnormal movements)
- Pleocytosis (increased white blood cell concentration in cerebrospinal fluid [CSF]) associated with illness clinically compatible with meningitis (e.g., headache or stiff neck)

**Non-neuroinvasive disease** requires, at minimum, the presence of documented fever, as measured by the patient or clinician, the absence of neuroinvasive disease (above), and the absence of a more likely clinical explanation for the illness. Involvement of non-neurological organs (e.g., heart, pancreas, liver) should be documented using standard clinico-laboratory criteria.
Laboratory criteria for diagnosis
Cases of arboviral disease are also classified either as confirmed or probable, according to the following laboratory criteria:

Confirmed case:
• Fourfold or greater change in virus-specific serum antibody titer, or
• Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, CSF, or other body fluid, or
• Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or
• Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).

Probable case:
• Stable (less than or equal to a twofold change) but elevated titer of virus-specific serum antibodies, or
• Virus-specific serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.

Case definition
A case must meet one or more of the above clinical criteria and one or more of the above laboratory criteria.

Comment
Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic tests using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in areas where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization tests using an appropriate battery of closely related viruses. This is essential, for example, in determining that antibodies detected against St. Louis encephalitis virus are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur. Because dengue fever and West Nile fever can be clinically indistinguishable, the importance of a recent travel history and appropriate serologic testing cannot be overemphasized. In some persons, West Nile virus-specific serum IgM antibody can wane slowly and be detectable for more than one year following infection. Therefore, in areas where West Nile virus has circulated in the recent past, the coexistence of West Nile virus-specific IgM antibody and illness in a given case may be coincidental and unrelated. In those areas, the testing of serially collected serum specimens assumes added importance.

The seasonality of arboviral transmission is variable and depends on the geographic location of exposure, the specific cycles of viral transmission, and local climatic conditions. Reporting should be etiology-specific (see below; the six diseases printed in bold are nationally reportable to CDC):

• St. Louis encephalitis virus disease
• West Nile virus disease
• Powassan virus disease
• Eastern equine encephalitis virus disease
• Western equine virus disease
• California serogroup virus disease (includes infections with the following viruses: La Crosse, Jamestown Canyon, snowshoe hare, trivittatus, Keystone, and California encephalitis viruses)
**West Nile Fever:** West Nile fever is reportable in California. The following definition is used:

West Nile fever syndrome can be variable and often includes headache and fever (T $\geq$ 38C or 100.4F). Other symptoms include rash, swollen lymph nodes, eye pain, nausea or vomiting. After initial symptoms, the patient may experience several days of fatigue and lethargy. For the purposes of surveillance, an individual is considered to be a West Nile fever case if he or she has a febrile illness compatible with West Nile fever, and laboratory confirmation (as described above).

**Asymptomatic WN Infection:** Asymptomatic infection with WNV may be detected through routine blood bank screening where the Nucleic Acid Test (NAT) is used. Donors who are confirmed viremic or NAT positive will not necessarily be ill, nor will they initially have positive IgM or IgG WNV tests. Local health departments should report blood donors who test positive for WNV to the California DHS, Viral and Rickettsial Disease Laboratory (VRDL.)

Local health departments should follow up with the donor after two weeks of the date of donation to assess if the patient subsequently became ill.

- If the donor did become ill as a result of WNV infection, a case history form should be sent to VRDL so that the case may be classified appropriately
- Additional serological testing is not required

Note: Due to the continued risk of unintentional or intentional introduction of exotic arboviruses into the United States (e.g., Venezuelan equine encephalitis virus), or the reemergence of indigenous epidemic arboviruses (e.g., St. Louis encephalitis and western equine encephalitis viruses), physicians and local public health officials should maintain a high index of clinical suspicion for cases of potential exotic or unusual arboviral etiology, and consider early consultation with arboviral disease experts at state health departments and CDC.
Appendix G: West Nile Virus (WNV) Infection Case Report

Patient Information:
Last Name: __________________________ First Name: __________________________ DOB: _____/____/____ Medical Rec #: __________________________
Address: __________________________ City: __________________________ Zip Code: __________________________
Phone: Home ( _____) Work ( _____) Occupation: __________________________
Sex: □ Male □ Female □ Unknown
Ethnicity: □ Hispanic □ Non-Hispanic □ Unknown
□ White □ Asian/Pacific Islander □ Black □ American Indian/Alaskan Native □ Other: __________________________

Physician Information (Mandatory):
Name: __________________________
Facility: __________________________
Pager/Phone: ( _____) Fax: ( _____)
Email: __________________________

Date of first symptom(s): _____/____/____ □ Hospitalized or □ ER / Outpatient
If hospitalized, admit date: _____/____/____ Discharge date: _____/____/____ If patient died, date of death: _____/____/____

Clinical syndrome:
Encephalitis .................... □ Yes □ No □ Unk
Aseptic meningitis ............. □ Yes □ No □ Unk
Acute flaccid paralysis ....... □ Yes □ No □ Unk
Febrile illness .................. □ Yes □ No □ Unk
Asymptomatic .................. □ Yes □ No □ Unk
Other __________________________

Do the following apply anytime during current illness:
In ICU: □ Yes □ No □ Unk
Fever ≥38° .......... □ Yes □ No □ Unk
Headache .......... □ Yes □ No □ Unk
Rash ............... □ Yes □ No □ Unk
Stiff neck .............. □ Yes □ No □ Unk
Muscle pain/weakness .... □ Yes □ No □ Unk
Altered consciousness .... □ Yes □ No □ Unk
Seizures .............. □ Yes □ No □ Unk

Other lab results (MRI/CT, LFTs, etc.): __________________________

Exposures/Travel within 4 wks of onset (specify details):
Mosquito bites/exposure: □ Yes □ No □ Unk
Traveled outside of California: □ Yes □ No □ Unk
Traveled outside the U.S.: □ Yes □ No □ Unk
Ever traveled outside the U.S.: □ Yes □ No □ Unk

Other pertinent information (specify details):
Immunocompromised patient: □ Yes □ No □ Unk
Yellow fever vaccination:
Date: _____/____/____

Donated blood:
Date: _____/____/____

Donated organ:
Date: _____/____/____

Received blood:
Date: _____/____/____

Received organ:
Date: _____/____/____

Current pregnancy:
Week of gestation: _____

If infant, breast fed?: □ Yes □ No □ Unk

Knowledge of WNV prior to illness:
Did patient do anything to
avoid mosquito bites? □ Yes □ No □ Unk
- used insect repellent? □ Yes □ No □ Unk
- drained standing water near home? □ Yes □ No □ Unk

Other specific history (social, family, etc.):
______________________________________________________

For questions regarding testing or specimens, call Cynthia Jean (510) 307-8606
Fax this form to (510) 307-8599 or mail to CDHS VRDL – West Nile Virus, 850 Marina Bay Parkway, Richmond CA  94804

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