West Nile Virus: Keep it on your radar!

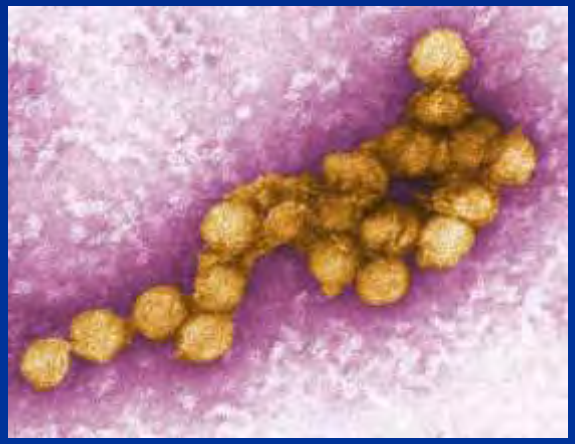
Purpose

(You may click to go to the specific section or proceed through the presentation. Click on the logo at the bottom right corner of each slide to return to this page)

- Briefly review West Nile virus (WNV) ecology and epidemiology
- Update of WNV in California
- Highlight current clinical information
- Address diagnostic testing and reporting issues
  - When to suspect and test for WNV
  - How to test
- Review effective prevention of WNV
- Provide real-life illustrative case studies

WNV Ecology and Epidemiology

What is West Nile virus?



Transmission electron micrograph of WNV particles. Source: CDC

- First identified in Uganda, 1937
- A virus in the Flaviviridae family, related to:
  - Yellow fever
  - Dengue
  - St. Louis encephalitis (SLE)
- Virology
  - Spherical, enveloped capsid
  - Single-stranded, positive-sense RNA

Transmission Cycle

West Nile virus is maintained in nature in a mosquito-bird cycle

- Migratory birds expand the endemic region of WNV

Primary Transmission Cycle

Mosquito <u>vector</u> (*Culex* spp. mostly)

Bird reservoir host

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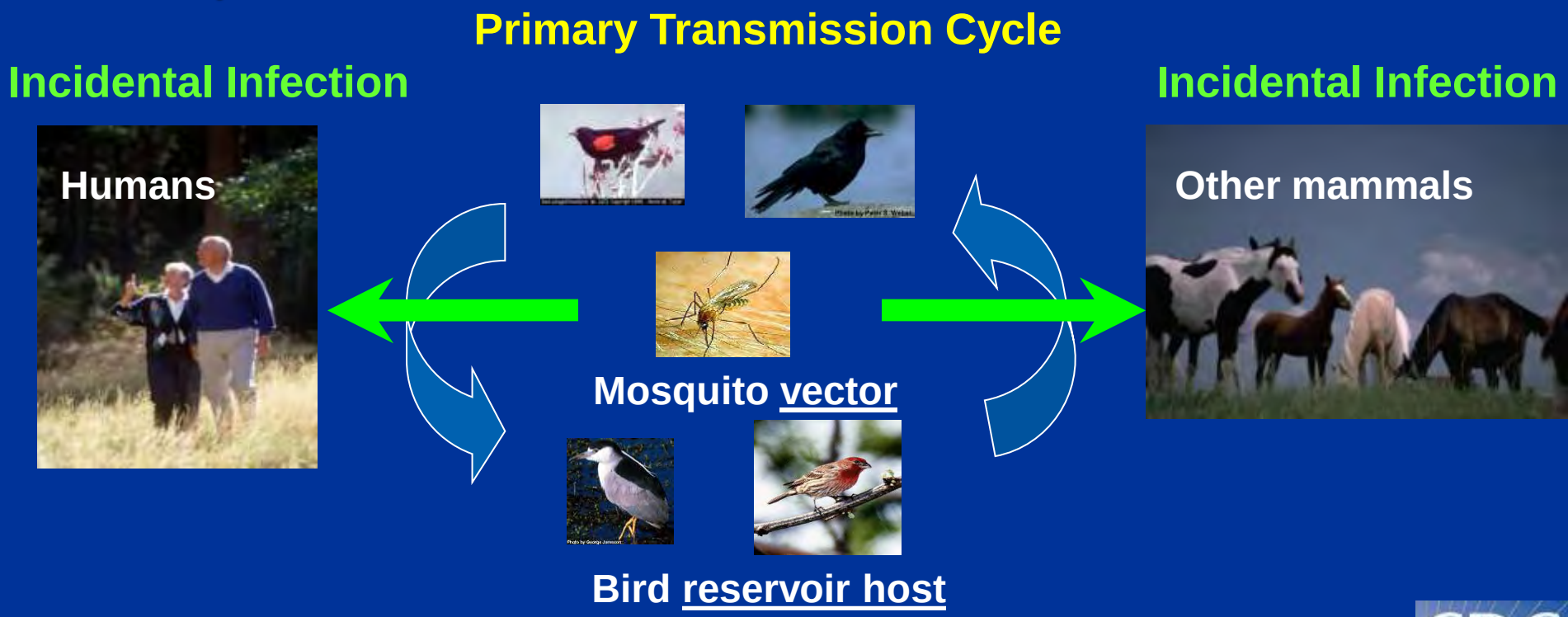
Transmission Cycle

Incidental infections occur when infected mosquitoes feed on humans or other animals.

- **Incidental hosts cannot infect mosquitoes ("dead-end") hosts**



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Other Modes of Transmission

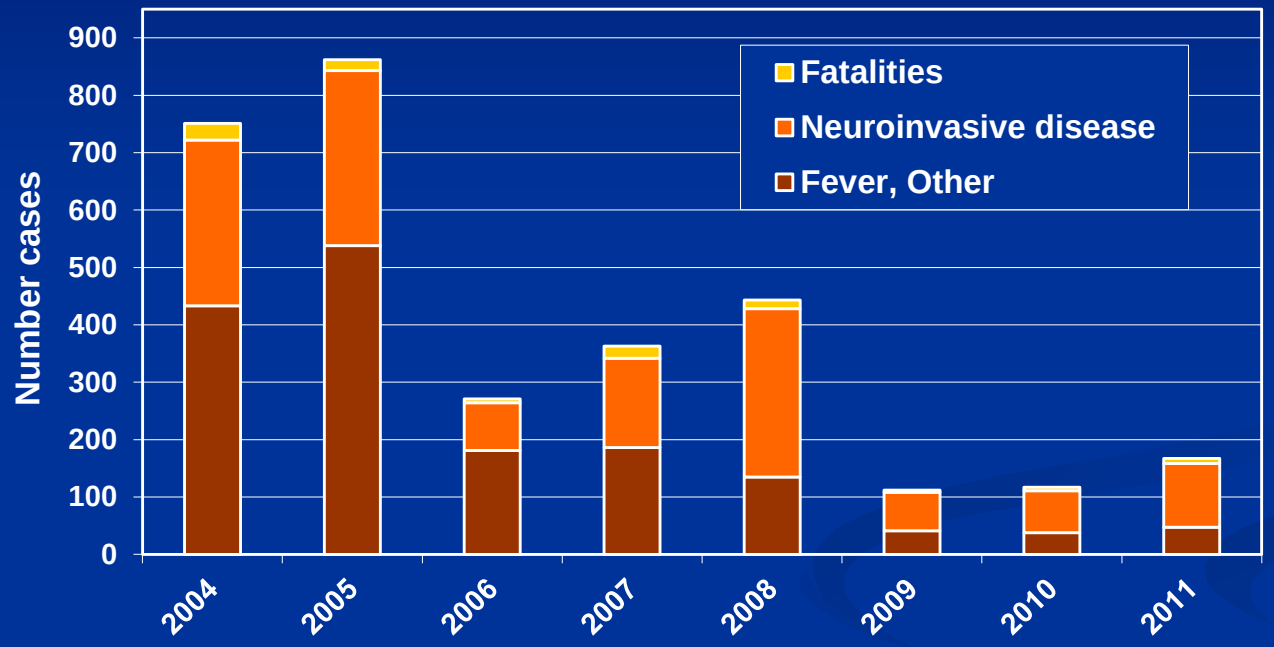
- Blood transfusion (over 2,000 infected donors identified since 1999)
- Less common other modes:
  - Organ transplant (at least 2 implicated donors)
  - Laboratory-acquired (2 reported)
  - Transplacental (1 possible)
  - Breast milk (1 probable)

WNV in the United States

- The most widespread flavivirus in the U.S.
- Human toll in the U.S., 1999-2011
  - 31,414 total symptomatic cases
  - 13,241 (42%) neuroinvasive disease (WNND) cases
  - 1,263 (4%) fatal cases
- Economic toll
  - Louisiana 2002: estimated total epidemic costs (medical and mosquito control) were $20.14 million for 329 cases (Zohrabian A, et al., Emerg Infect Dis. 2004)
  - Sacramento County 2005: $2.98 million for 163 cases ($2.28 million medical costs, $700,000 mosquito control). (Barber LM et al. Emerg Infect Dis. 2010)

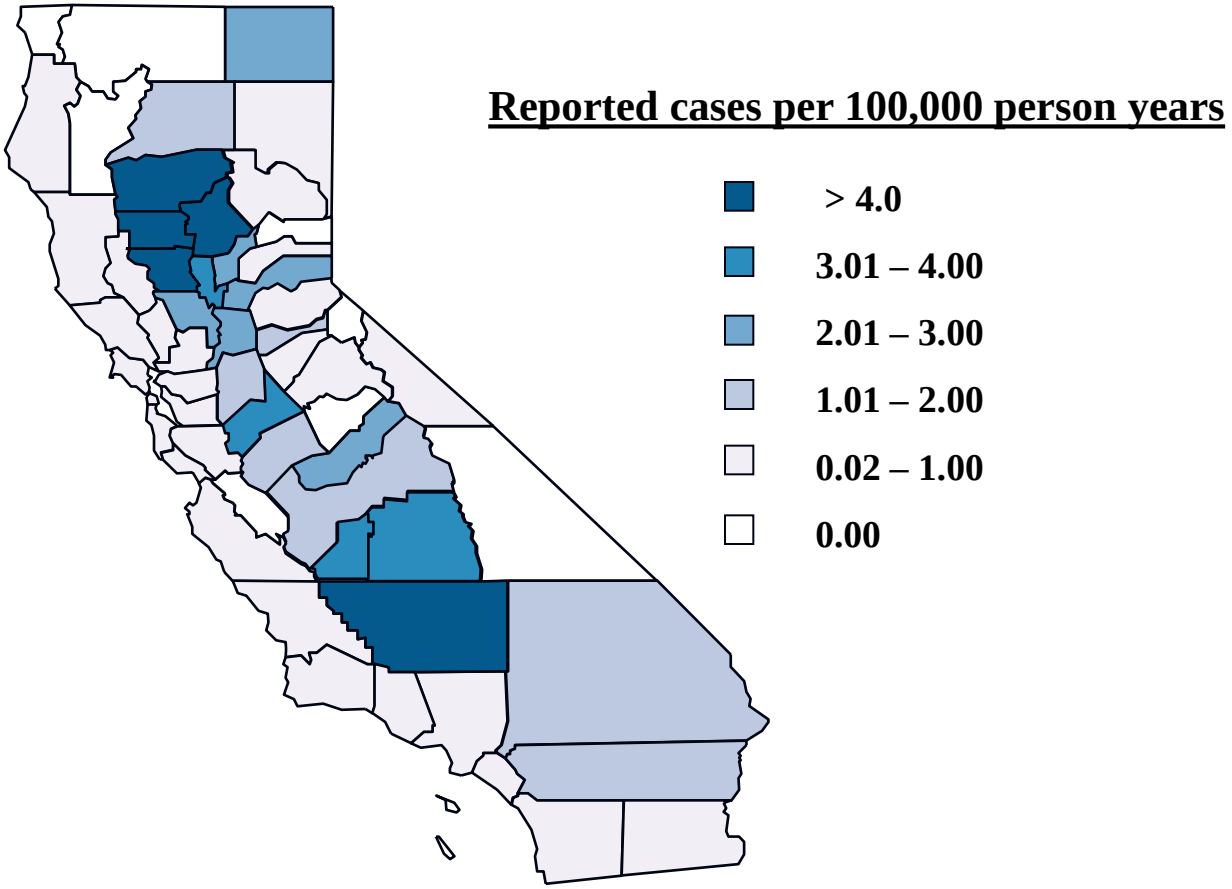
WNV in California

WNV cases and clinical classification 2004 - 2011. Total = 3,143 (110 Fatal)



- Incidence of WNV has decreased since 2004, but WNV remains endemic to California
- Future change in incidence will depend on weather, host immunity, mosquito control, personal protective measures and case detection.
- Neuroinvasive cases make up an increasing proportion of detected West Nile virus cases, likely because less ill cases do not seek medical care or are not tested.

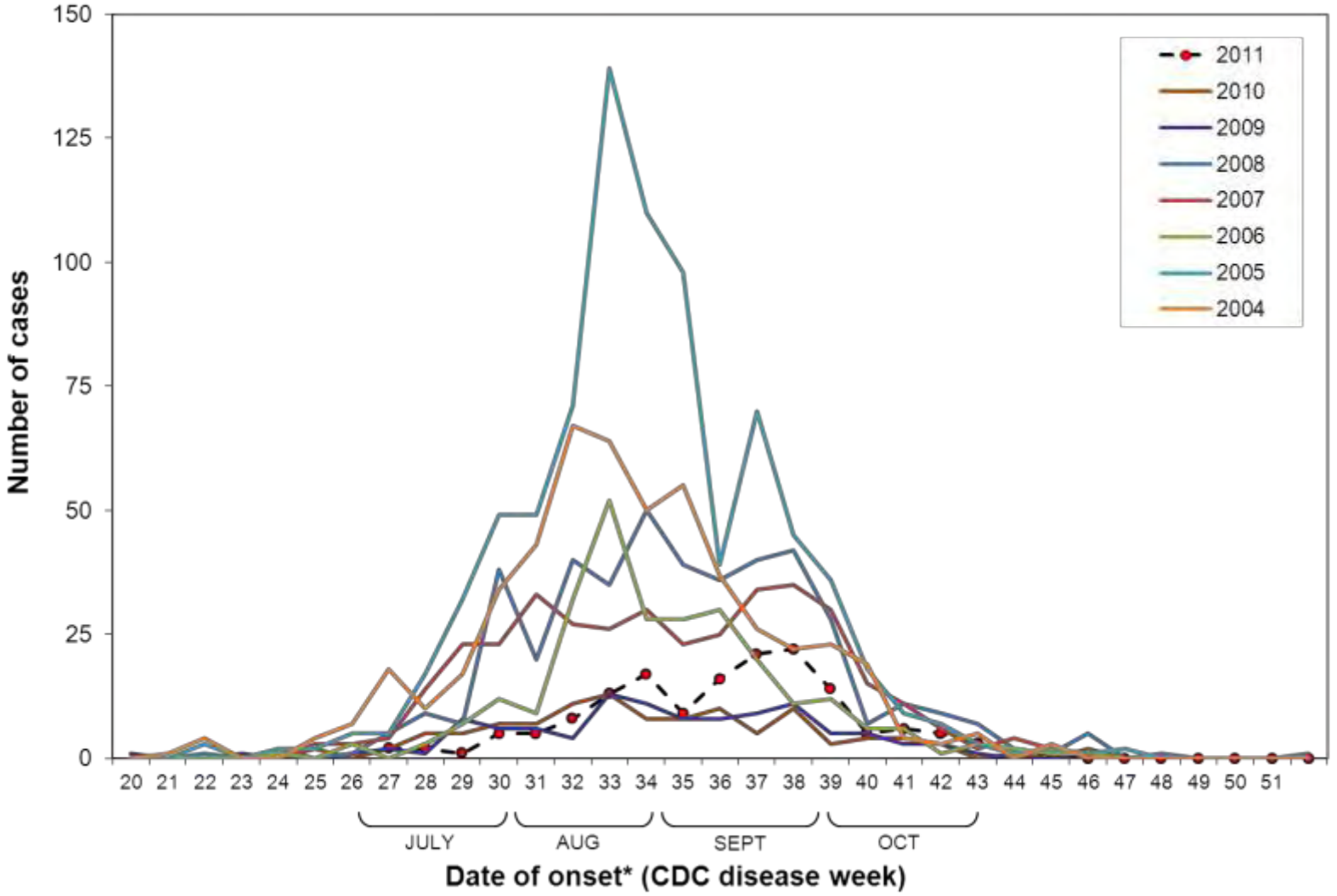
Reported incidence of West Nile virus, by county of residence, California 2004 - 2011



Incidence of WNV tends to be higher in the Central and San Joaquin Valley areas of California where prolonged high summer temperatures increase the rate and amount of viral replication within the natural cycle.

Human West Nile Virus Cases by Week of Onset, California, 2004-2011

WNV is a disease of summer: most cases occur between July and October

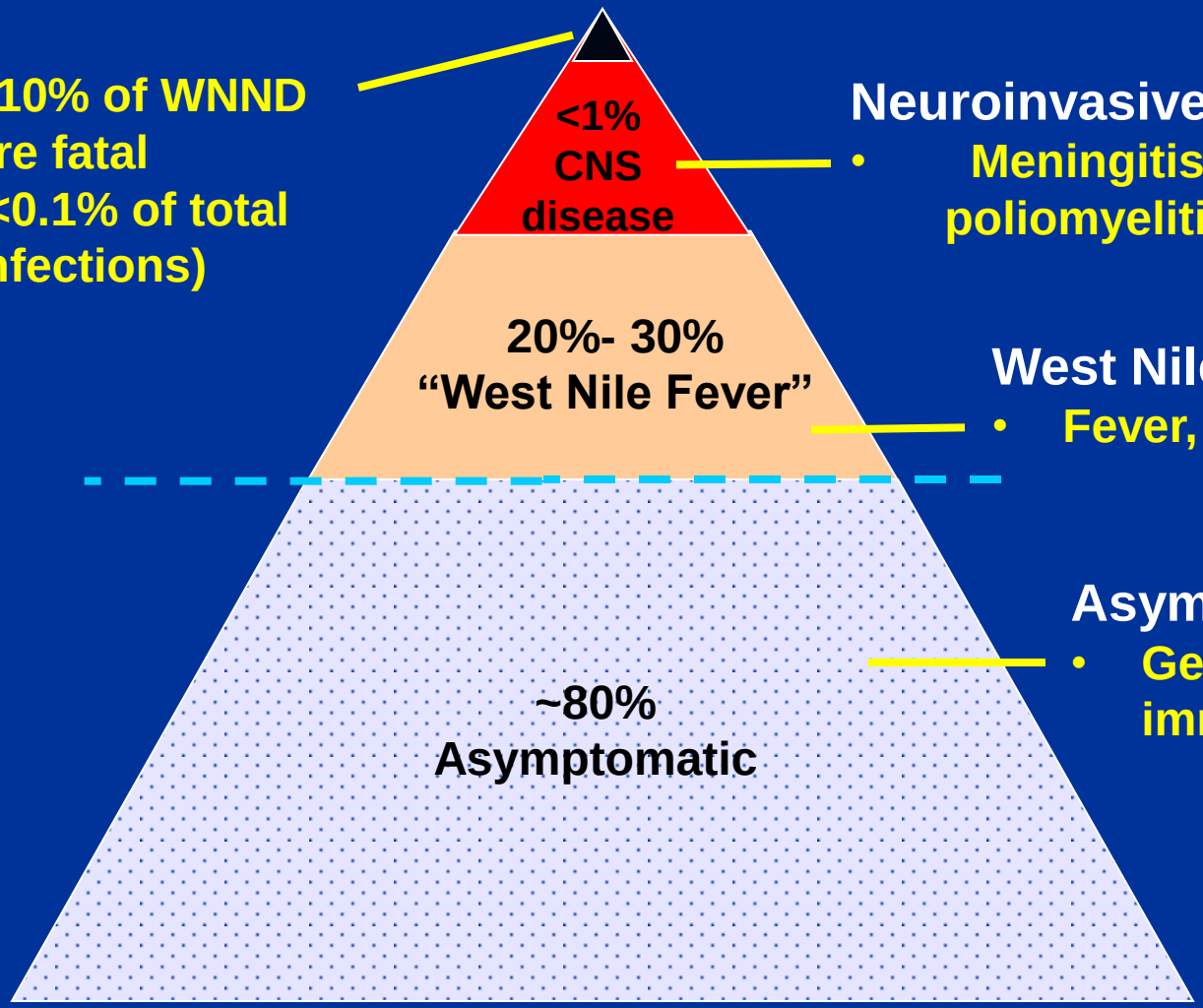


* Onset dates known for 2,783 (89%) cases

West Nile Virus Clinical Information

"We're pretty sure it's the West Nile virus..."

Three General Clinical Categories of WNV Disease



~10% of WNND are fatal (<0.1% of total infections)

Neuroinvasive Disease (WNND)
- Meningitis, encephalitis, poliomyelitis

West Nile Fever (WNF)
- Fever, headache, rash, fatigue

Asymptomatic Infection
- Generation of life-long immunity (presumed)

Incubation period of 2 – 15 days

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Risk for severe illness and death

- Established risk factors for severe illness
  - Advanced age, immunosuppression [a,b]
- Conditions significantly associated with severe illness:
  - Hypertension, cardiovascular disease, and diabetes[b,c]
- Possible risk factors for serious disease
  - Alcohol and drug abuse[d]
  - Chemokine receptor CCR5 gene[e]

[a] Nash et al., NEJM, 2001
[b] Murray et al., EID, 2006
[c] Jean et al., EID, 2007
[d] Bode et al., CID, 2006
[e] Lim et al., JID, 2010

Long-term complications of WNV disease

Suggestion of persistent symptoms or new complications of WNV disease, regardless of initial disease presentation, e.g.

- Slow return to pre-morbid condition (≥ 6 months)
- On-going fatigue
- New-onset depression

  Loeb et al, Ann Int Med 2008; Voelker et al JAMA 2008; Carson et al CID 2006; Watson et al, Ann Int Med 2004
- Long-term neurocognitive impairment

  Sejvar J, J Neuropsychol 2008
- Persistent limb weakness or paralysis
- Persistent movement disorders

  Sejvar J, CID, 2007

Long-term complications of WNV disease

- Persistent infection suggested by polymerase chain reaction detection of WNV in one study of WN encephalitis patients with chronic symptoms

  Murray et al, J Inf Disease, 2010

Treatment

- No specific treatment is currently available
- Primarily supportive care: hospitalization, respiratory support, etc.

Testing and Reporting WNV

When to suspect West Nile virus

- West Nile virus should be considered in patients with compatible clinical presentation
  - Unexplained encephalitis or meningitis in persons of all ages
  - Local presence of activity or cases
  - Recent travel to area with WNV activity
  - Onset during West Nile virus “season”
    - In California, ~July through September

Are We Missing Patients Who Should Be Tested?

Review of hospital records from 2009 and 2010 West Nile Virus season (April 1-October 31)

Study population:

- Hospitals from counties likely to see WNV cases
  - Sacramento – Sutter, UC Davis
  - Yolo – Woodland
  - Riverside – Corona
  - Kern – Mercy
- Records pulled for all patients with arbovirus neuroinvasive-like disease in top three discharge diagnoses (as determined by ICD-9 Codes)

Are We Missing Patients Who Should Be Tested?

Data collection:

- Identified if any cases had WNV test request in same time period

Results:

Number of neurologic cases tested for WNV, 2009 - 2010				
Year*	All Neurologic cases	Encephalitis only	Meningitis only	Paralysis
2009	46/229 (20%)	13/48 (27%)	33/175 (19%)	0/6
2010	32/162 (20%)	6/30 (20%)	26/132 (20%)	0/0

* Percentages are not significantly different between years or conditions, p >0.05.

Are We Missing Patients Who Should Be Tested?

Conclusions:

- From April 1-Oct 31, in both 2009 and 2010, 80% of patients who had clinically compatible arbovirus neuroinvasive-type disease were not tested for WNV. Testing may have identified etiology of disease.

Recommendation:

- Patients with compatible clinical presentation with history of exposure to WNV endemic areas, should be tested for WNV

Why test if there is no treatment?

- Testing will differentiate WNV from other conditions (enterovirus, other arboviral diseases). Appropriately including WNV on differential may speed diagnosis.
- Testing offers anticipatory guidance—with potential lingering symptoms associated with WNV infection, knowing the underlying etiology is helpful for the patient and family members.
- Mosquito control and public health agencies can institute proper control measures to prevent further cases

WNV Diagnostic Testing

- WN IgM and IgG antibody (serum)
  - Enzyme immunoassay (EIA)
  - Immunoflurescent Antibody Test (IFA)
  - 99% samples positive for IgM at 5 days of onset for neuroinvasive disease
- Plaque reduction neutralization test (PRNT) considered confirmatory, but is not often used as default test
  - Only a few labs perform it
  - Longer turnaround time
  - Not as helpful for IgG-negative specimens

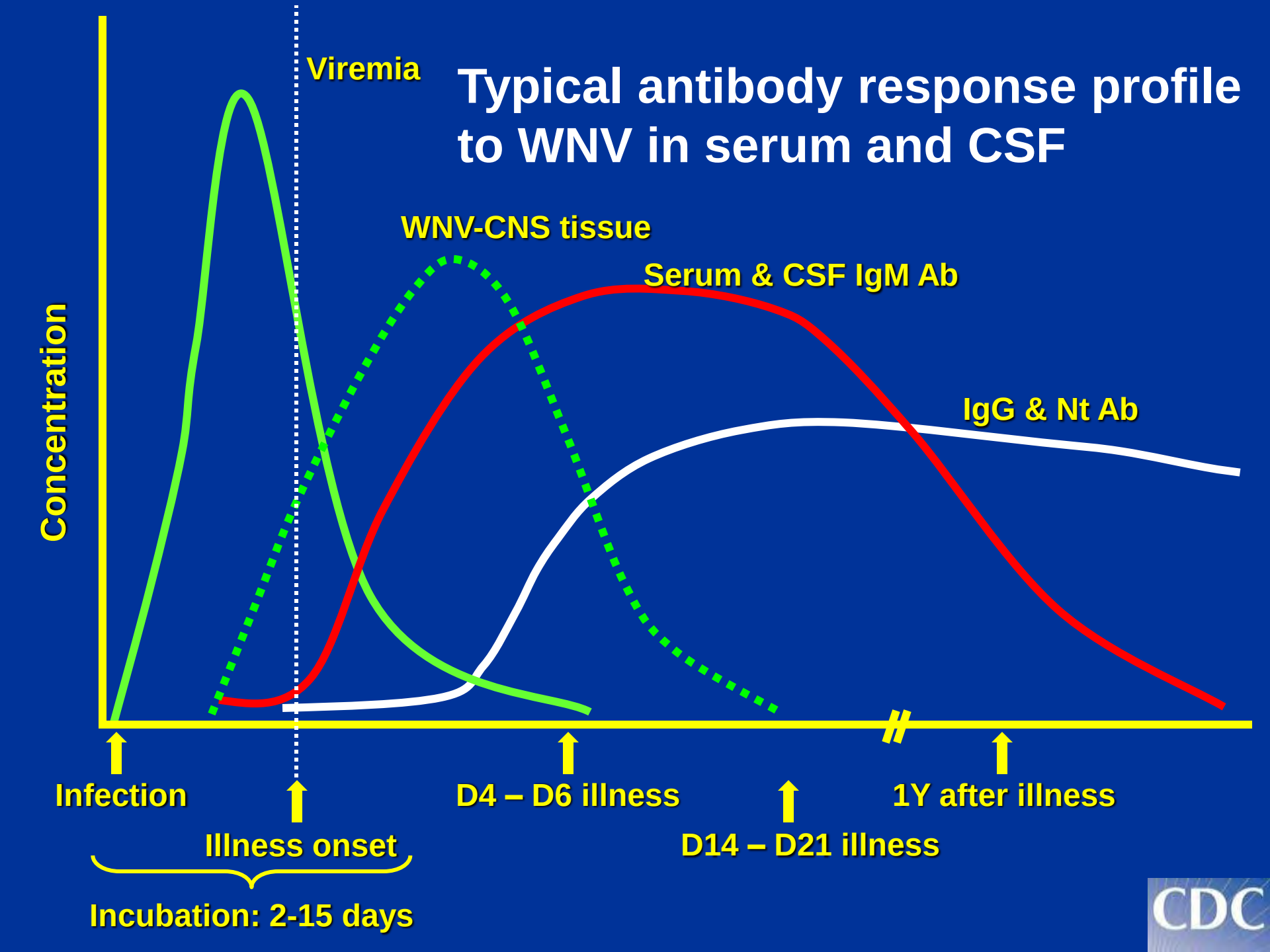
How to test for WNV

- Contact your local health department for details
- Generally an acute serum specimen (≥ 2cc) and, if lumbar puncture performed, 1-2 cc cerebrospinal fluid are required for testing.
  - Many public health laboratories offer free testing, check with your local health department.

How to test for WNV

- If West Nile virus is highly suspected and acute serum is negative or inconclusive, a 2nd serum sample may be requested 3-5 days after acute serum
  - Paired acute and convalescent serum specimens can demonstrate sero-conversion to WNV.
  - 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 immuno- compromised individuals).

Typical antibody response profile to WNV in serum and CSF



CDC

Interpretation of WNV antibody results

Results should be interpreted along with clinical and epidemiological information

Test	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 of current infection; further testing necessary*
IgM IgG	Positive Positive	Evidence of recent or current infection**
IgM IgG	Indeterminate Negative	Inconclusive- request convalescent serum***

* Note the possibility of a false-positive IgM result

** Note that some individuals may have persisting antibodies from the previous WNV season

*** Paired acute and convalescent serum samples may help demonstrate seroconversion

WNV is a reportable disease

- Contact your local health department if you suspect West Nile virus

- Laboratories required to report positive test results
- Public Health preventive measures (mosquito control, education) can be implemented quickly when human cases are reported in a timely fashion

Prevention of WNV

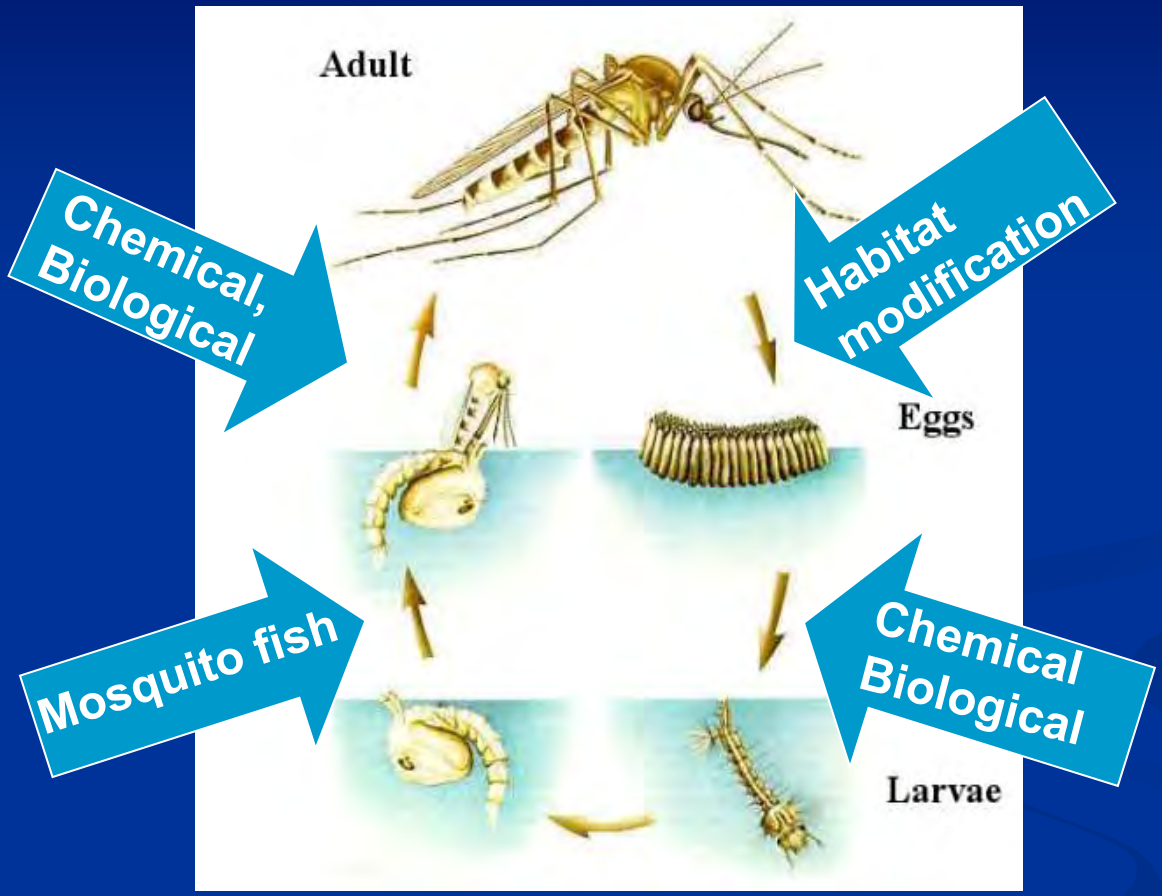
Vaccine Development

- No human vaccine currently available
- Vaccines undergoing clinical trials include:
  - ChimeriVax-WN02. A live, attenuated recombinant vaccine based on infectious clones of yellow fever and West Nile virus. Phase I complete, Phase II in process. (Sanofi-Aventis)
  - Recombinant DNA Plasmid Vaccine. Phase I complete (Sponsored by NIAD -National Institute of Allergy and Infectious Diseases)
  - Live attenuated chimeric virus, derived from the DEN4 dengue virus and wild-type WN serotypes. In Phase I (Sponsored by NIAD and Johns Hopkins School of Public Health)

Prevention:
Personal Protection: The 3 D's

- **DRAIN:** Mosquitoes lay their eggs on standing water. Young mosquitoes grow in the water. Get rid of standing water around the home. Empty water out of buckets, old tires, flower pots, and toys.
- **DEFEND:** Use an EPA-registered insect repellent with DEET, picaridin, IR3535 or oil of lemon eucalyptus in it. Put the repellent on your skin that is not covered by clothes. Follow the directions carefully.
- **DUSK and DAWN:** Mosquitoes that transmit West Nile virus bite in the early morning and early evening hours, and sometimes throughout the night. When outside in the early morning or evening hours, wear long pants and a long sleeved shirt.

Mosquito Control



Local mosquito and vector control agencies use multiple approaches to control mosquitoes following the California Mosquito-borne Virus Surveillance and Response Plan

West Nile Virus Resources

Case studies

Case study #1:

Clinical presentation is not the whole story

- 78-year-old male presenting in January with fever, altered consciousness, encephalopathy
- Hospitalized
- No lumbar puncture performed
- Day 1 – serum collected
  - WNV EIA IgM(+), IgG(+)
  - IgM weakly positive

Case study #1, continued

- Epidemiologic data - one positive dead bird; no other activity
- No history of travel or other exposures
- Day 26 – convalescent serum collected
  - No change in titers

- Ultimately, determined to be likely an old infection; patient was not reported as an acute case. Cause for clinical presentation undetermined

Case study #2
Travel adds wrinkle to diagnosis

- 39-year-old male presenting with fever, headache, muscle weakness, diarrhea, chills
- Day 8 – serum sample collected
  - WNV EIA IgM(+) and IgG(+)
- County health department submitted West Nile virus case report form to CDPH

Case study #2, continued

- Case report form noted travel to Guatemala in October
- Additional testing on serum
  - Dengue IFA IgM(+) and IgG(+)
  - Dengue PRNT = 1:320
  - WNV PRNT = 1:20

- Patient had dengue infection. Check history for travel to areas with other flavivirus activity

Case study #3

Some cases we may never know

- 58-year-old male presenting with febrile illness
- History of dengue fever, malaria
- Received yellow fever vaccine
- No recent travel, but lived in various parts of Africa, Haiti, and Australia, from 1980s through 2000
- Epidemiologic data - very little WNV activity in county of residence

Case study #3, continued

- Received serum samples collected Day 3, Day 7, Day 20, Day 75
- All WNV and dengue results for all samples positive

- Not confirmable if WNV, dengue or both. Cases with prior flavivirus infection and/or vaccination can be difficult to diagnose

Thank you for your attention

- For more information:
  - Visit: www.westnile.ca.gov
  - Call Cynthia Yen, MPH: (510) 620-3987