Update on the status of WNV and DENV infection in the U.S.

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## Arbovirus Classification

<table>
<thead>
<tr>
<th>Virus</th>
<th>Serocomplex</th>
<th>Clade</th>
<th>Cluster</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Nile</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Kunjin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>Japanese encephalitis</td>
<td>XIV</td>
<td>Mosquito-borne</td>
</tr>
<tr>
<td>Murray Valley encephalitis</td>
<td></td>
<td>XI</td>
<td></td>
</tr>
<tr>
<td>St Louis encephalitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dengue-1</td>
<td>Dengue</td>
<td>IX</td>
<td></td>
</tr>
<tr>
<td>Dengue-3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dengue-2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dengue-4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yellow fever</td>
<td>None</td>
<td>VII</td>
<td></td>
</tr>
<tr>
<td>Central European encephalitis</td>
<td>Tick-borne encephalitis</td>
<td>IV</td>
<td>Tick-borne</td>
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<td>Far Eastern encephalitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Powassan</td>
<td></td>
<td>III</td>
<td>No vector</td>
</tr>
<tr>
<td>Dakar bat</td>
<td>None</td>
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</tr>
</tbody>
</table>
WNV spread in the US

- First recognized in the Western Hemisphere in NYC in the summer of 1999
- Became increasingly spread reaching the West Coast in 2002
  - Covering the entire country by 2006
- WNV is now endemic in the US reoccurring each summer for 12 consecutive years
- WNV infections are mostly asymptomatic
Final 1999 WNV: Incidence of Human Neuroinvasive Disease (ND) in the US
Final 2000 WNV Human ND Incidence in the US
Final 2001 WNV Human ND Incidence in the US

Incidence per million

- .01-9.99
- 10-99.99
- >=100
- Any WNV Activity
Final 2002 WNV Human ND Incidence in the US
Final 2003 WNV Human ND Incidence in the US
Final 2004 WNV Human ND Incidence in the US
Final 2005 WNV Human ND Incidence in the US
Final 2006 WNV Human ND Incidence in the US
Final 2007: WNV Human ND Incidence in the US

Activity in 47 states, DC & PR
Human cases in 43 states
Final 2008: WNV Human ND Incidence in the US
Final 2009: WNV Human ND Incidence in the US
Final 2010: WNV Human ND Incidence in the US
WNV Blood Screening in the U.S.

From 2003 to 2010 resulted in:
- Interdiction of >3,000 WNV NAT-reactive units
- Prevention of 3,000 to 9,000 potential WNV transmissions by transfusion

Transmission by Transfusion

<table>
<thead>
<tr>
<th>Year</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAT-Reactive Units</td>
<td>&gt;1,000</td>
<td>224</td>
<td>417</td>
<td>441</td>
<td>511</td>
<td>235</td>
<td>222</td>
<td>~200</td>
</tr>
<tr>
<td>TT Confirmed* (n=32)</td>
<td>6 ‡</td>
<td>1 ‡</td>
<td>0</td>
<td>2 ‡</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1°</td>
</tr>
<tr>
<td>TT Inconclusive+ (n= 26)</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*All seronegative for WNV; + Lack of f/up, sample, recipient loss
‡ Negative in MP-NAT and positive on ID-NAT (low viremia)
° first case of transmission by transfusion of granulocytes
WNV and Blood Safety Summary

- Identification of risk of WNV to blood safety – August 2002
- FDA OBRR/CBER calls for test development – November 2002
- Collaboration among various sectors: government, academia, industry and blood establishments resulted in interdiction of donations with confirmed or suspected WNV infections
- Nationwide implementation of blood screening for WNV under expedited approvals of INDs by FDA June 2003
- Approval of 2 NAT for blood screening

Results of Blood Screening for WNV

<table>
<thead>
<tr>
<th>Year</th>
<th>Interdicted donations</th>
<th>Transf. Transm. Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>2004</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>2006</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2008</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2010</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
WNV in the US 1999-2010

Estimated no. of infections: between 1.9M (1:150) and 4.4M (1:350)
Dengue Virus (DENV) at Risk Areas

Most common vector-borne virus, threatens 2.5 billion people worldwide.
Causes over 50 million infections and over 24 thousand deaths yearly.
Recent Dengue Epidemics in Puerto Rico

Cases occur every week of year. High season begins on first week of June.

Outbreaks typically in rainy season; cyclic variation of timing and intensity of outbreaks

* Threshold is defined by the 75% variability of the mean. Epidemics are defined by 2 consecutive weeks of above threshold activity.
Dengue in the Continental US

- The last outbreak in Florida prior to 2009 happened in 1934
  - Locally acquired dengue outbreaks in the U.S. were considered rare
- There have been a few confirmed cases along the Texas-Mexico border in recent years but locally acquired dengue in the U.S. is rare
- The number of U.S. hospitalized cases of dengue infection more than tripled between 2000 and 2007
- CDC reported ~5 percent of Key West residents, or about 1,000 people, were exposed to it in 2009
  - 28 confirmed cases in 2009
- Dengue was placed on the CDC list of "reportable diseases" in January 2010
Dengue in the Continental US

- **DENV in Florida 2010** – 491 confirmed cases
  - 65 cases of locally acquired dengue, 2 in mainland and 63 in Key West (63/193 reported)
  - Onset dates ranged from March 17 to November 30, 2010

- **DENV in FL 2011** – 6 confirmed cases
  - 2 locally acquired confirmed cases, by Mar 2, in Miami-Dade area
  - 4 cases of dengue with onset in 2011 have been reported in individuals with travel history to a dengue endemic country as of May 7

- **Will dengue fever spread in the U.S.??**
  - Too soon to tell

http://www.doh.state.fl.us/Environment/medicine/arboviral/Weekly-Summary.html
http://www.doh.state.fl.us/Environment/medicine/arboviral/weeklyreportarchive.html
Epidemiology: Where do cases occur in USA?
Travel-associated cases in USA, 2010 (n=426)

Source: http://www.cdc.gov/ncidod/dvbid/westnile/USGS_frame.html
Will dengue fever spread in U.S.?

Distribution of Aedes aegypti

Source: Chester G. Moore, Dept. Microbiology, Immunology & Pathology, Colorado State University
Will dengue fever spread in U.S.?

*Distribution of Aedes albopictus*

Still too soon to tell!

Source: Chester G. Moore, Dept. of Microbiology, Immunology & Pathology, Colorado State University
Transfusion-related Transmission

Transfusion transmitted DENV has been reported after transfusion of Fresh Frozen Plasma, Red Blood Cells and Platelets
- 3 Donations, 5 Recipients
Two donors were outside the U.S. & one in Puerto Rico

Hong Kong, 2002 (Chuang et al, Hong Kong Med J, 14: 170-7, 2008) RBC component infected, recipient developed DF


USA, 2007 (Stramer et al, Vox Sang, Science Series 2010: 99(S1)3E-S18-02) RBC component infected, recipient developed DHF
The rate of transmissibility by transfusion may be inaccurate due to:

1) The high proportion of asymptomatic infections
2) The high incidence during outbreaks
3) The unknown duration of viremia
4) Lack of a licensed test
5) Lack of recognition by clinicians
6) Lack of surveillance and reporting
Potential Screening Methods for DENV:

- Currently, there are no FDA approved or licensed tests for screening.
- Can be detected by viral isolation, antigen and nucleic acid tests.
- Antibody tests detect past or present infection.
- Nucleic Acid Tests
  - RT-PCR and TMA assays are highly sensitive for detecting viral RNA from all 4 serotypes early in infection.
- Dengue NS1 antigen ELISA
  - NS1 antigen assay is useful for the detection of the virus early in infection.
  - Platelia NS1 assay from BioRad has been used, under FDA approved IND, to screen blood donations in Puerto Rico and Florida.
- Immunoglobulin IgM or IgG ELISA
  - May not reflect an active infection but may confirm a past or present infection.