Concurrent Outbreaks of St. Louis Encephalitis and West Nile Virus — Arizona, 2015

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Background

- West Nile Virus (WNV) and St. Louis Encephalitis Virus (SLE) are closely-related RNA flaviviruses
  - Transmitted primarily by mosquitoes in the genus *Culex*
Clinical spectrum of human infections with neuroinvasive arboviruses

- Neuroinvasive disease (encephalitis, meningitis, or acute flaccid paralysis)
  - <1%
- Mild febrile illness
  - 10–30%
- Asymptomatic infection
  - 50–80%
Known Clinical Risk Factors for Neuroinvasive Disease

- Age $\geq 65$ years
- Hypertension
- Other chronic medical conditions
A Concurrent Outbreak Begins

- Outbreaks involving co-circulation of WNV and SLE not previously documented in the U.S.

- In Arizona in 2015
  - 116 mosquito pools WNV positive and 85 mosquito pools SLE positive
  - First two suspected human WNV cases were actually SLE
  - Only one human SLE case in 2014, and none since 2006
Enhanced Testing

- Serum and cerebral spinal fluid (CSF) tested at state laboratory and CDC
  - Commercial SLE laboratory test unavailable starting January 2015
  - Antibody cross-reaction between flaviviruses
  - Confirmatory testing using plaque reduction neutralization testing (PRNT)

- Specimens that could not be distinguished between WNV and SLE were categorized as ‘Unspecified Flavivirus’ (U.F.)
  - Includes samples pending confirmatory testing
### Number of Confirmed and Probable Cases

<table>
<thead>
<tr>
<th></th>
<th>WNV</th>
<th>SLE</th>
<th>U.F.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed</td>
<td>38</td>
<td>20</td>
<td>--</td>
<td>58</td>
</tr>
<tr>
<td>Probable</td>
<td>48</td>
<td>3</td>
<td>17</td>
<td>68</td>
</tr>
<tr>
<td>Total</td>
<td>86</td>
<td>23</td>
<td>17</td>
<td>126</td>
</tr>
</tbody>
</table>

*Preliminary results with patient classification based on current testing are presented here. Laboratory testing is ongoing*
Epidemiologic Curve

Number of cases

Epidemiological Week of Symptom Onset

Unspecified Flavivirus
St. Louis Encephalitis
West Nile Virus

May        June          July           Aug          Sept        Oct         Nov      Dec
<table>
<thead>
<tr>
<th>Demographics and Clinical Description</th>
<th>WNV</th>
<th>SLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median</td>
<td>54</td>
<td>66</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>44 (51)</td>
<td>15 (65)</td>
</tr>
<tr>
<td>Neuroinvasive syndrome, n (%)</td>
<td>54 (63)</td>
<td>21 (91)</td>
</tr>
<tr>
<td>Hospitalized, n (%)</td>
<td>64 (74)</td>
<td>19 (83)</td>
</tr>
<tr>
<td>Died, n (%)</td>
<td>6 (7)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Age of patients who died, years, median</td>
<td>75</td>
<td>67</td>
</tr>
</tbody>
</table>
Distribution of WNV and SLE Cases in Arizona in 2015

- Maricopa: 68%
- Pima: 22%
- Cochise: 0.8%
- Yavapai: 0.8%
- Gila: 0.8%
- Apache: 0.8%
- Mohave: 0.8%
- Coconino: 0.8%
- Navajo: 0.8%

Note: The percentages may not add up to 100% due to rounding.
Animal Surveillance for WNV in 2015

- 10 sentinel chicken flocks
- 3 equines
- 1 avian (Poorwill)
WNV Blood Donor Screening in Arizona in 2015

- Number of rejected blood products for WNV = 17
  - Number of asymptomatic viremic blood donors = 14
  - Number of symptomatic viremic blood donors = 3
The Notification — September 2015

- By United Network for Organ Sharing

- Arizona resident tested IgM-positive for St. Louis encephalitis virus (SLE)
  - Recently received an organ transplant 35 days prior

- Objectives
  - To confirm infection in index case
  - To determine infection source
Organ and Blood Transmission

- Organ donors are not universally screened for WNV or SLE because no test specifically optimized
  - Organ transmission documented for WNV, but not SLE

- Blood donors in U.S. are screened for WNV because of documented transmission and available FDA-approved screening test, but not SLE
Case Investigation Revealed Possible Sources of Infection

- Organ transplant?
- Blood transfusion?
- Mosquitoes?
Investigation — Interview and Medical Record Review
Investigation — Interview and Medical Record Review

Organ donor

IL
Investigation — Interview and Medical Record Review

Organ donor

Organ recipients

IL

IL

AZ

AZ

Index case
Investigation — Interview and Medical Record Review

Organ donors

Organ recipients

Blood donors

Index case
Investigation — Interview and Medical Record Review

Nightmare III

Organ recipient

Organ donor

Day 0: Organ transplant in index case

Blood donors

Index case
Investigation — Interview and Medical Record Review

Organ recipients

Blood donors

Transfused to index case

Day 0: Organ transplant in index case

Day 1

Day 2

Day 20

Day 21

Index case
Investigation — Interview and Medical Record Review

Organ recipients

Organ donor

Blood donors

Transfused to index case

Day 1

Day 2

Day 20

Day 21

Index case

Day 0: Organ transplant in index case

Day 35: Illness onset in index case
Specimen Testing

- Serum, plasma, cerebral spinal fluid, or tissues:
  - IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA)
  - Microsphere immunoassay (MIA)
  - Real-time polymerase chain reaction (RT-PCR)
  - Plaque reduction neutralization testing (PRNT)

- Samples from one organ recipient not available for testing

- Mosquito data gathered from RT-PCR testing already performed during the SLE outbreak
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Presumptive: IgM antibody capture enzyme-linked immunosorbent assay (MAC-ELISA), Microsphere immunoassay (MIA)

Confirmatory: Real-time polymerase chain reaction (RT-PCR), Plaque reduction neutralization testing (PRNT)
Results of Potential Human Sources of Infection

Organ donors

Blood donors
Transfused to index case
Day 1
Day 2
Day 20
Day 21

Organ recipients

Index case

Day 0: Organ transplant in index case

Day 35: Illness onset in index case
Results of Potential Human Sources of Infection

- **Organ donors**
  - Day 0: Organ transplant in index case
  - Day 1
  - Day 2
  - Day 20
  - Day 21
  - Transfused to index case
  - Asymptomatic

- **Blood donors**
  - Transfused to index case
  - Asymptomatic

- **Index case**
  - Day 35: Illness onset in index case
**Culex spp. Mosquito Surveillance Results for July – Aug 2015**

- 5-mile radius per location
- 30 days prior to index case’s symptom onset

- Index case location
- Index case hospital location
- Positive AZ blood donor location
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Index case location

1/45 (2%) mosquito traps
2 SLE-positive mosquitoes

Index case hospital location

Positive AZ blood donor location
**Culex spp. Mosquito Surveillance Results for July – Aug 2015**

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- **Index case hospital location**
  - 1/33 (3%) mosquito traps
  - 3 SLE-positive mosquitoes

- **Positive AZ blood donor location**
Culex spp. Mosquito Surveillance Results for July – Aug 2015

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- 30 days prior to index case’s symptom onset

Index case location

1/45 (2%) mosquito traps
2 SLE-positive mosquitoes

Index case hospital location

1/33 (3%) mosquito traps
3 SLE-positive mosquitoes

Positive AZ blood donor location

12/53 (23%) mosquito traps
104 SLE-positive mosquitoes
Hypothetical Mechanisms

- Change in bird hosts?
- Change in the mosquitoes?
- Change in the viruses?

Concurrent WNV-SLE outbreak
Change in the Bird Hosts?

- Avian reservoir studies performed Fall 2015
- CDC Team collected birds by mist net at 40+ sites
- Birds were identified and bloods collected
- Serologic testing was performed by PRNT
- Thirteen avian species were represented
- Five species tested IgG (+) for SLEV and ten species tested IgG (+) for WNV
- WNV (+) - 116/305 (38%)
- SLEV (+) - 28/305 (9%)
- Flavivirus (+) - 10/305 (3%)
SLE and WNV Positive Birds

- **SLEV (+) Species**
  - Starlings
  - House Sparrows
  - Eurasian Collared Doves
  - Mourning Doves
  - Chickens

- **WNV (+) Species**
  - Starlings
  - House Sparrows
  - Eurasian Collared Doves
  - Mourning Doves
  - Chickens
  - Great-tailed Grackles
  - Red Wing Blackbirds
  - House Finches
  - Brown-headed Cowbirds
  - White Wing Doves
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- **Five bird species = IgM(+) for SLEV & WNV**
Change in the Viruses?

- 2005 Argentina epidemic SLE strain detected (genotype III) in 2015 Arizona outbreak

- Co-circulation of SLE and WNV detected in an equine serosurvey in Argentina in 2012

- House sparrows in Argentina inoculated with epidemic strain developed higher and longer viremias than those inoculated with non-epidemic strain
  - Viral amplification was enhanced when they had previous flavivirus immunity
Change in the Mosquitoes?

- Since 2012, Maricopa County Vector Control tests mosquito pools for WNV by PCR
- >750 CO$_2$ traps set weekly
- *Culex sp* mosquitoes are pooled & tested
- Mosquito surveillance data are used to guide vector control efforts
- 116 mosquito pools WNV (+) and 85 mosquito pools SLE (+) in 2015
Mosquito testing for SLE

- PCR testing of mosquito pools for SLE at the end of June 2015
- All negative mosquito pools collected/tested prior to June had been discarded
- All WNV(+) samples had been retained and were re-tested for SLE
- 39 WNV(+) pools were also SLE(+)
- Pools sizes ranged from 2 to 50 mosquitoes
Treatment and Prevention

- Supportive care and management of complications
- No proven antiviral or adjunctive therapy
- No vaccine licensed or undergoing clinical trials
- Community mosquito control programs
- Household and personal protective measures
Prevention Recommendations

- Wear insect repellent when outdoors
- Wear long sleeves and pants
- Empty and clean containers holding water
- Use window and door screens
Conclusions

- The first concurrent outbreak of both WNV and SLE in the United States occurred in Arizona in 2015
  - Both flaviviruses can circulate simultaneously

- First reported SLE case by possible blood transfusion transmission in U.S.
  - Outbreak of SLE in general population led to possible transfusion-associated case
Conclusions

- SLE is still present
  - Surveillance and control infrastructure should be maintained

- Clinicians and public health officials should consider West Nile and SLE in cases with compatible symptoms
Acknowledgments

The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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