Epidemiology and Clinical Impact of West Nile in Texas

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Emerging Arboviruses in Texas:

• **Dengue**
  - First recognized outbreak of dengue-like illness in 1895-1896: more than 16,000 cases in Austin area*
  - 1922: more than 500,000 cases (“Galveston outbreak”)*

• **St. Louis encephalitis virus**
  - First identified in 1933, first recognized outbreak in Texas in 1964

• **West Nile virus**
  - Introduced to US in 1999 and Texas in 2002

• **Chikungunya virus**
  - 1st locally acquired case reported 2016

• **Zika virus**
  - 1st locally acquired case reported 2016

*Beaumier et al. Current Tropical Medicine Reports, 2014*
West Nile Virus

• Natural transmission → mosquito vector
  - Houston: *Culex quinquefasciatus*
  - Birds are reservoir host

• Newly discovered means of transmission with WNV in humans (2002)
  - Transplant
  - Transfusion
  - Transplacental
  - Breastfeeding
  - Laboratory acquired
  - Sexual?
West Nile Virus
Clinical Features in Humans

• Incubation 2 to 15 days
• ~ 80% infected persons asymptomatic
• ~ 20% infected persons flu-like symptoms
• < 1% (1 out of 150) “neuroinvasive disease”
  • WNM: Meningitis
  • WNE: Encephalitis or meningoencephalitis
  • Acute flaccid paralysis
  • 10 % case fatality ratio for those with severe disease
West Nile Virus
Clinical Cases by Year, 1999-2016

Total no. of clinical cases > 46,000
Total no. of deaths > 2,000

Decade of WNV Transmission in Texas

Nolan et al. *Emerging Infectious Diseases*, 2013
Total no. of clinical cases = 1,868
Total no. of WNND = 844
Total no. of deaths = 89

Total estimated acute care and loss of productivity costs: $47 million
48% of cases from Tarrant, Dallas, Collin, and Denton counties

Murray et al., EID 2013
Houston 2014 WNV Outbreak

Martinez et al., in press, *Emerging Infectious Diseases*
2018 Activity as of mid-September
Study Methods

• Study initiated in 2002 following introduction to Houston
• Cases of WNV identified through local surveillance
• Medical chart abstractions completed on all cases (n=302)
• Cases invited to enroll in 10 year prospective, longitudinal cohort study, 267 cases currently enrolled
  - Interviews and blood draws q. 6 mos
  - Subjective symptoms
  - Objective measurements: CES-D, Barthel Index, MMSE
  - Other studies using the cohort: risk factors for encephalitis and death, clinical predictors for death, genetic susceptibility, immune functioning
# Sequelae following Infection

<table>
<thead>
<tr>
<th>Year</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>60.1%</td>
</tr>
<tr>
<td>2 years</td>
<td>46.4%</td>
</tr>
<tr>
<td>3 years</td>
<td>40.6%</td>
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<tr>
<td>4 years</td>
<td>38.9%</td>
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<tr>
<td>5 years</td>
<td>41.9%</td>
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- **Most commonly reported sequelae:** depression/personality change, weakness, fatigue, difficulty walking, blurred vision, paralysis, memory loss, confusion, headaches, tremors

- **Depression:** 31% new onset depression; 75% have CES-D scores indicative of clinical depression. Can continue up to 8 yrs (Murray et al, EID 2007 and Nolan et al, J Clin Psych 2012)
West Nile encephalitis

West Nile fever

West Nile meningitis

Kaplan-Meier Survival Curve: Percentage of Study Participants Continuing to Report West-Nile Virus-related Symptoms by Days Post-Infection based on Initial Diagnosis

<table>
<thead>
<tr>
<th>CKD Prevalence</th>
<th>All WNV participants n=139 (%)</th>
<th>Neuroinvasive WNV n=67 (%)</th>
<th>Mild WNV n=44 (%)</th>
<th>Asymptomatic WNV n=28 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD, All Stages</td>
<td>55 (40)</td>
<td>32 (48)</td>
<td>12 (27)</td>
<td>11 (39)</td>
</tr>
<tr>
<td>CKD Stages 3-5</td>
<td>13 (10)</td>
<td>9 (13)</td>
<td>3 (7)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>CKD Stage 1-2</td>
<td>42 (30)</td>
<td>23 (34)</td>
<td>9 (20)</td>
<td>10 (36)</td>
</tr>
<tr>
<td>CKD Indicators</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td>36(26)</td>
<td>21(31)</td>
<td>9(20)</td>
<td>6(21)</td>
</tr>
<tr>
<td>Hematuria</td>
<td>32(23)</td>
<td>18(27)</td>
<td>7(16)</td>
<td>7(24)</td>
</tr>
<tr>
<td>Anemia</td>
<td>80(60)</td>
<td>40(60)</td>
<td>23(58)</td>
<td>17(63)</td>
</tr>
</tbody>
</table>
West Nile Persistence

• Persistent symptoms, persistent IgM, abnormal cytokine response, progressive kidney disease
  • Persistent infection of kidneys with shedding of viral RNA

• What about CNS persistence?
• 86% of encephalitis cases, 25% of meningitis, and 20% fever cases had abnormal neurological exams after acute infection
• Anomalies: abnormal motor strength, vibratory sensory loss, tandem gait and balance abnormalities, hearing loss, and postural or intention/action tremors
• 63% of encephalitis cases had impaired tandem gait, suggesting vestibular-cerebellar and/or dorsal column dysfunction
• At the time of the second assessment 7 years later, 57% of WNF, 33% of WNM, and 36% of WNE had developed new neurological complications.
• Cortical Thinning:
  - posterior cingulate cortex, superior frontal cortex, medial-orbito frontal region, anterior cingulate cortex, inferior frontal cortex, cuneus and para hippocampal region, middle and inferior temporal cortex, supramarginal region, inferior frontal region and insular cortex

• Regional atrophy
Use of Testing for West Nile Virus and Other Arboviruses

Jakapat Vanichanan, Lucrecia Salazar, Susan H. Wootton, Elizabeth Aguilera, Melissa N. Garcia, Kristy O. Murray, Rodrigo Hasbun

• 751 patients in Houston area diagnosed with meningitis or encephalitis, 2005-2010
  - 281 (37%) were tested for WNV; only 25% of children tested
  - 220/470 (47%) not tested for WNV had onset June-Oct
  - 518 had an unknown etiology (69%)

• Similar study ongoing at TCH: 1,699 meningitis/encephalitis cases diagnosed 2009-2014; 1,192 unknown etiology (70%); only 10% tested for WNV

Vanichanan et al. 2016, Emerging Infectious Diseases
Risk of Arboviruses in Houston: the Perfect Storm

- Proximity to endemic areas
- Vast shipping; both air and ship travel entry points; NAFTA
- High proportion of its ~6 million residents who routinely travel to and from endemic areas
- Dense urban population
- Abundance of \textit{Aedes} sp.
- Mild winters and year-round survival of mosquitoes
- Passive surveillance, lack of diagnostic testing available
What’s next?
Zika Virus: an arbovirus and a flavivirus

FLAVIVIRUSES (ss +RNA)
• Dengue Virus
• Yellow Fever Virus
• Japanese Encephalitis Virus
• West Nile Virus
• St. Louis Encephalitis Virus
• Zika Virus

TRANSMITTED BY AEDES MOSQUITOES
• Dengue, Yellow Fever, but NOT WNV

SEXUAL TRANSMISSION

Zika autochthonous transmission, as of Aug. 8, 2016

>811,000 cases in 48 countries
>3,600 confirmed Zika congenital syndrome cases in 26 countries
Challenges and Needs

• Best approach to combat Zika?
  - Mosquito bite prevention (Integrated Mosquito Control Management)
  - Educate on sexual transmission risk
  - Surveillance strategies
  - No treatment available…..need a vaccine!!!

• Diagnostic tests to detect exposure

• Research to better understand risks for microcephaly, virus shedding/infectivity, clinical outcomes
Dengue Virus

- **Flavivirus**
- Four serotypes
  - DEN-1, DEN-2, DEN-3, DEN-4
- Lifelong immunity
- Complicated illness with secondary infection of different serotype
- Three classifications of disease
  - Dengue Fever (DF)
  - Dengue Hemorrhagic Fever (DHF)
  - Dengue Shock Syndrome (DSS)

Epidemiology

Epidemic Curve of Dengue IgM Positive Cases

Month and Year of Symptom Onset

* = History of travel to Mexico;  X = Fatal Case
Chikungunya

• Vector: *Aedes* species mosquitoes

• “that which bends up”
  - Fever, headache, fatigue, rash, nausea, vomiting, muscle pain, severe joint pain
  - Fatality rare

Speaking of Medicine, 2014.
Introduced Western Hemisphere in 2013

By 2015:
44 countries/territories reporting autochthonous cases

> 1.25 million cases reported in Western Hemisphere
Murine Typhus Cases in Texas, 2003-2013

Year of Onset

Number of Cases


0 50 100 150 200 250
Prevention of Emerging Vector-borne Diseases

• Surveillance, surveillance, surveillance
  - Humans (active + “enhanced” passive), sentinel species, mosquitoes
  - Multidisciplinary “One Health” approach is critical

• Public education

• Prevention of bites

• Vaccine, diagnostic, and therapeutic development

• Did I mention surveillance?
Barriers to Public Health Surveillance

- Patient is infected
- Patient develops symptoms?
- Patient seeks medical care?
- Clinician suspects vector-borne disease?
- Clinician submits samples for testing?
- Laboratory testing in a timely manner?
- Clinician reports case to public health

Additional Cases Prevented
- eReporting; reduce burden to provider

Case is MISSED
- Large capacity for timely testing, automated electronic reporting to both medical provider and public health

- Diagnostic tests available, provider knows what tests to order, and patient can afford testing
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