Emerging Pathogens: Zika, and other things that go bump in the night

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Director, Emerging Pathogens Institute
University of Florida
• Interdisciplinary Research Institute, created in 2006 with appropriation from Florida state legislature, focusing on human, animal, and plant pathogens

• Over 200 faculty members, from 11 UF colleges (including medicine, public health, veterinary medicine, and agriculture)

• Strong global emphasis, driven by Florida’s sub-tropical location, the risk of introduction of new pathogens, and the critical role of trade and tourism in the Florida economy
From goulies and ghosties and long-leggedy beasties
And things that go bump in the night
Good Lord, deliver us!

The Cornish and West Country Litany, 1926

Zika
Chikungunya
Dengue
Ebola
Coronaviruses (SARS, MERS)
Influenza
Mayaro...
and many more
And other viruses....

- **Dengue (serotypes 1, 2, 3, & 4)**
  - Flavivirus, transmission by *Aedes aegypti* and *Aedes albopictus*
  - Serial infection with different serotypes may precipitate dengue hemorrhagic fever

- **Chikungunya**
  - Alphavirus, transmitted by mosquitoes
  - Causes fever, severe joint pain that may persist for weeks to months
  - Epidemics in the Caribbean in 2014, with 459 travel-related cases in Florida, and 11 Florida-acquired cases

- **Mayaro**
  - Alphavirus, first isolated in Trinidad in 1954
  - Transmitted by mosquitoes
  - Produces clinical syndrome very similar to Chikungunya
Phylogenetic tree based on complete genome sequence analysis. This figure illustrates the close genetic relationship between USUV and MVEV, WNV, and JEV. The number at each node is the percentage of 1000 bootstrap replicates. Ashraf U, Ye J, Ruan X, et al. Viruses 2015, 7(1): 219-238
ZIKV full genome ML tree

The spread of the Zika virus

0.02
Physical manifestations of dual dengue-2/Zika infection. A. Fine, erythematous rash on neck and upper chest on day 2 after initial symptom onset. B. Rash on thigh, day 2. C. Resolving conjunctivitis on day 8 after symptom onset.

However – 80% of patients asymptomatic
Clinical/Laboratory Timeline: UF Zika Patient

- **Rash appears** on 1/29/16
- **Malaise starts** on 1/30/16
- **Peak of rash** on 1/31/16
- **Rash resolves** on 2/2/16
- **Arthralgias start** on 2/1/16
- **Conjunctivitis starts** on 2/3/16
- **Rash resolves** on 2/4/16
- **Arthralgias resolve** on 2/5/16
- **Malaise resolves** on 2/6/16
- **Conjunctivitis resolves** on 2/7/16

- **Return to the U.S.** on 2/7/16
- **State DOH testing done +Dengue –Zika** on 2/5/16
- **UF research lab testing done +Dengue +Zika** on 2/6/16
Complications

• Guillain-Barre syndrome
  – Diffuse demyelinating disorder leading to ascending paralysis, often requiring ventilatory support
  – Autoimmune process associated with a wide variety of infectious triggers, including foodborne pathogens

• Birth defects
  – Limited primarily to first trimester
  – Microcephaly
  – Fetal death, placental insufficiency, fetal growth restriction, CNS injury
  – Possible hearing, visual defects
Transmission

• Reservoirs: non-human primates; rodents, sheep, goats?

• Transmission:
  – Insect vectors
    • Mosquitoes: *Aedes aegypti*, other *Aedes* species?
      Other mosquitos?
    • Biting flies, other insects?
  – Sexual transmission
  – Blood supply
Sexual Transmission

• Concept of “protected sanctuaries”
  – Men:
    • Can transmit virus before, during, or after symptoms
    • In semen longer than in blood, but exact risk period not known
  – Women:
    • Initial reports of transmission; mechanism being investigated

• Recommendations (CDC):
  – No unprotected sexual activity for 6 months after onset of symptoms
  – No unprotected sex for 6 months after travel to a Zika-endemic area, even if no symptoms
  – If living in a zika-endemic area, no unprotected sex
Unknowns

• Transmission
  – Impact of dual infection/prior infection?
    • Concept of antibody-dependent enhancement
  – Mosquito vectors
    • More than just *Ae. aegypti* or *Ae. albopictus*? *Culex* species?
    • Role of animal reservoirs?
  – Role of sexual transmission
    • Increased risk of complications?

• Risk of complications
  – Guillain Barre
    • Risk/risk factors?
  – Microcephaly
    • 29% of women with documented infection in Rio study had evidence of fetal injury (*Brasil et al*).
    • But – overall population rates may be much lower
      ‒ French Polynesia: 95 cases/10,000 women infected in first trimester (~1%)
**ZIKV infection in the U.S. (CDC data)**

<table>
<thead>
<tr>
<th>Source</th>
<th>Number of cases (through 10/19/2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>US States</strong></td>
<td></td>
</tr>
<tr>
<td>Locally-acquired mosquito-borne cases</td>
<td>137</td>
</tr>
<tr>
<td>Travel-associated cases</td>
<td>3,878</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>13</td>
</tr>
<tr>
<td><strong>US Territories</strong></td>
<td></td>
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<tr>
<td>Locally-acquired cases</td>
<td>27,314</td>
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<tr>
<td>Travel-associated cases</td>
<td>88</td>
</tr>
<tr>
<td>Guillain-Barre syndrome</td>
<td>40</td>
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## Zika in Florida

<table>
<thead>
<tr>
<th>Zika infections</th>
<th># as of 10/15/2016</th>
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</thead>
<tbody>
<tr>
<td>Travel related cases</td>
<td>813</td>
</tr>
<tr>
<td>Non-travel related cases (Florida)</td>
<td>160</td>
</tr>
<tr>
<td>Non-travel related cases (out of state, Florida acquired)</td>
<td>19</td>
</tr>
</tbody>
</table>

Major Countries of Origin for Travel-Related Cases
- Dominican Republic
- Puerto Rico
- Jamaica
- Colombia
- Nicaragua
- Haiti
- Venezuela
- Honduras
Zika in Florida

- Number of travel-related Zika cases by county (as of 10/15/2016)
  - Miami-Dade 238
  - Broward 120
  - Orange 87
  - Palm Beach 40
  - Osceola 37
  - Polk 27
  - Seminole 22
  - Pinellas 19
  - Alachua 10

- State-acquired cases
  - Miami-Dade 149
  - Palm Beach 7
  - Broward 3
  - Pinellas 1
  - Out-of-state 19
Ongoing Issues

• Modeling by UF/EPI – not unreasonable to expect >400 locally-acquired cases in Florida this year
• Mosquito control is tough
  – *Aedes* is the “cockroach” of mosquitos
  – Aerial spraying of uncertain utility
  – Problems with insecticide resistance
  – Toxicity of insecticides
• Major gaps in our knowledge

WHAT WE NEED

• Major, ongoing research program
• Ongoing public education

Protect those Alachua County/Florida mosquitoes from foreign viruses – and keep them from breeding