KILLER BITES:
Mosquito-Borne Viruses

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Disclosures

• Conflicts of Interest:
  – Pfizer consultant related to Sickle Cell Disease
Presentation Objectives

• Identify at least 3 mosquito-borne viruses potentially transmitted in the Continental U.S.
• Briefly discuss arboviruses and vectors
  – Include review of disease epidemiology
• Discuss West Nile, Dengue and Zika Viruses
ARBOVIRUSES AND VECTORS
Mosquito-Borne Viruses

• West Nile Virus
• Dengue
• Zika Virus
• Chikungunya
• Yellow Fever
• St. Louis Encephalitis

• Jamestown Canyon Virus
• Western Equine Encephalitis
• Eastern Equine Encephalitis
• La Crosse Encephalitis

And many others...
Terms

• Arboviruses:
  – ARthropod-BOrne virus

• Arthropods
  – E.g: mosquitos, ticks, sandflies

• Flaviviridae (family)
  – Flavivirus (genus)
    • Single stranded RNA viruses

Dengue Virus

Arboviruses

- Transmitted by arthropods
- Can have rare person-to-person transmission
  - Blood borne
    - Transfusion, sharing needles
  - Organ transplantation
  - Breast feeding
  - Intrauterine
  - Sexual transmission

Aedes albopictus

en.wikipedia.org/wiki/Aedes_albopictus
Major Arbovirus Viral Families

- **Family Bunyaviridae**
  - Rift Valley, Crimean–Congo hemorrhagic
- **Family Flaviviridae**
  - Dengue, West Nile, Zika, Yellow Fever
- **Family Reoviridae**
  - Equine encephalalosis
- **Family Togaviridae**
  - Chikungunya, Western equine encephalitis
**Flaviviridae: Flavivirus**

**Mosquito-borne viruses**
- Dengue virus group
  - *Dengue virus* (DENV)
- Japanese encephalitis virus group
  - *Japanese encephalitis virus* (JEV)
  - *Murray Valley encephalitis virus* (MVEV)
  - *St. Louis encephalitis virus* (SLEV)
  - *West Nile virus* (WNV)

**Mosquito-borne viruses (cont.)**
- Spondweni group
  - *Spondweni virus*
  - *Zika virus* (ZIKV)
- Yellow fever virus group
  - *Yellow fever virus* (YFV)

**Tick-borne viruses**
- Mammalian tick-borne virus group
  - *Kyasanur forest disease virus* (KFDV)
  - *Tick-borne encephalitis virus* (TBEV)
Vector for:
Dengue virus, Yellow Fever virus, Chikungunya virus, and Zika virus
DENGUE FEVER
# Dengue Fever: “Break-bone Fever”

<table>
<thead>
<tr>
<th><strong>Virus genus</strong></th>
<th>Flavivirus</th>
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<tbody>
<tr>
<td><strong>Transmission</strong></td>
<td>Mosquito-borne (<em>Aedes sp</em>)</td>
</tr>
<tr>
<td><strong>Amplifying host</strong></td>
<td>Humans/primates</td>
</tr>
<tr>
<td><strong>Global Distribution</strong></td>
<td>Primarily tropical and subtropical (similar to Yellow Fever)</td>
</tr>
<tr>
<td><strong>U.S. Continental Distribution</strong></td>
<td>Rarely South Texas (Found in Puerto Rico, the U.S. Virgin Islands, Samoa and Guam)</td>
</tr>
<tr>
<td><strong>Vaccine</strong></td>
<td>None currently available in US</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Symptomatic</td>
</tr>
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</table>
Worldwide Tropical Distribution

https://www.cdc.gov/dengue/epidemiology/index.html
Dengue Viruses

- Four serotypes
  - Provides long-term serotype specific immunity
  - Short-term cross-immunity
- All serotypes can cause severe/fatal disease
- Most important arboviral disease
  - >2.5 billion people at risk globally
  - Dengue hemorrhagic fever (DHF) mortality rate 2%-5%.
    - Untreated- mortality rate as high as 50%
Dengue Fever – Mode of Transmission

Healthy person

Infected mosquito

Infected person

Incubation Period: 3 to 14 days
Most commonly 4 to 7 days

Dengue fever is not spread by contact with infected persons.
Diagnosis of Dengue

• **Good Clinical Acumen**

• First 7 days of illness
  – viral RNA can often be identified in serum
  – RT-PCR is the preferred test
    • Dengue, Zika, Chikungunya

• Virus specific IgM antibodies may be detectable >4 days after onset of illness.
  – strong cross reactivity with other flaviviruses
Dengue Fever - Symptoms

- **High fever:**
  - Continuous for 2 to 7 days

- **Severe headache**
  - Retro-orbital

- **Joint, muscle, and back pain**

- **Nausea, vomiting**

- **Rash**
  - Including maculopapular

- **May worsen into DHF**
  - Leading to internal bleeding, shock, or even death.
Dengue Treatment

• Symptomatic treatment
• Hydration
• Avoid aspirin and non-steroidal
  – Use acetaminophen
• Monitor hematocrit and platelets
**DHF Criteria**

- Fever lasting 2-7 days
  - May be biphasic
- Hemorrhagic tendencies
  - Positive tourniquet (aka Rumpel-Leede) test
  - Petechiae, ecchymosis or purpura
  - GI bleeding
- Thrombocytopenia (<100,000/mm$^3$)
- Evidence of plasma leakage
  - Increase in hematocrit >20% above age/sex normal
  - Decrease in hematocrit >20% after volume replacement
  - Signs of plasma leakage
    - e.g. pleural effusions, ascites, hypoproteinemia
DKF Treatment

• Supportive Care

• Careful fluid management
  – Aggressively hydrate if dehydrated
  – Slow/stop intravenous fluids if adequate hydration is present

• Proactive treatment of hemorrhage
  – Platelet and fresh frozen plasma transfusions
**Flaviviridae: Flavivirus**

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[West Nile Virus](www.cdc.gov/vhf/virus-families/flaviviridae.html)
Vector for:
West Nile virus, Japanese encephalitis, St. Louis encephalitis, and Western and Eastern Equine Encephalitis.

Culex pipiens

Photo from https://cameronwebb.wordpress.com/tag/culex-pipiens/
WEST NILE VIRUS
# West Nile Virus

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<table>
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</thead>
<tbody>
<tr>
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<td>Flavivirus</td>
</tr>
<tr>
<td><strong>Transmission</strong></td>
<td>Mosquito-borne (<em>Culex sp.</em>)</td>
</tr>
<tr>
<td><strong>Amplifying host</strong></td>
<td>Birds</td>
</tr>
<tr>
<td><strong>Global Distribution</strong></td>
<td>Worldwide</td>
</tr>
<tr>
<td><strong>U.S. Continental Distribution</strong></td>
<td>Through-out</td>
</tr>
<tr>
<td><strong>Vaccine</strong></td>
<td>No human vaccines</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Symptomatic</td>
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West Nile Virus

West Nile virus first identified in the West Nile Region of Uganda, Africa in 1937

First cases in the US in 1999...
States with Laboratory Confirmed West Nile Virus In Animals or People, 1999
States with Laboratory Confirmed West Nile Virus In Animals or People, 2000

The map shows the states in red that had confirmed West Nile Virus cases in 2000. The states include those in the Northeastern United States.
WNV in Humans

• **Incubation:** 2 to 14 days
  – Many WNV infections asymptomatic
  – Two forms of clinical disease

• **West Nile fever**
  – Most common form
  – Resembles influenza
  – Most infections resolve within a week
  – Some symptoms, such as fatigue, can persist
Clinical Spectrum of WNV

- Neuroinvasive (<1%)
- Febrile illness (20%-30%)
- Asymptomatic infection (70%-80%)
WNV Neuroinvasive Disease

- Occurs rarely (<1%)
  - Progression of West Nile fever
- Can be severe and life-threatening
  - Most cases require hospitalization
- Three syndromes
  - Encephalitis, Meningitis, Acute flaccid paralysis
- Persistent neurological dysfunction may occur
  - 50%-70% need assisted living or rehabilitation
- Case fatality- 10%
Symptoms of Neuro WNV

- Headache
- High fever
- Neck stiffness
- Disorientation
- Coma
- Tremors
- Seizures
- Paralysis

www.nature.com/nrneurol/journal/v2/n5/fig_tab/ncpneuro0176_F4.html
Risk Factors for Severe Disease

• Age >60 y/o
• Hypertension
• Diabetes
• Cancer
• Kidney disease
• H/O organ transplant
WNV Diagnosis in Humans

- **Good clinical acumen**
- **Serology**
  - Serum or CSF
  - IgM capture ELISA
    - Cross reactions possible
  - Plaque reduction neutralization test
- **Detection of virus, antigen, or nucleic acids**
  - RT-PCR
  - Immunohistochemistry
WNV Treatment

• Supportive care
• Manage complications
• No proven antiviral or adjuvant therapy
**Flaviviridae: Flavivirus**

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  - Yellow fever virus group
    - *Yellow fever virus* (YFV)
What is the common name for the *Aedes albopictus* mosquito?

- Common house mosquito
- Southern house mosquito
- That @#$@# mosquito
- Flying tiger mosquito
- Asian tiger mosquito
ZIKA VIRUS
# Zika Virus

<table>
<thead>
<tr>
<th>Description</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virus genus</td>
<td>Flaviviruses</td>
</tr>
<tr>
<td>Transmission</td>
<td>Mosquito-borne (Aedes sps.)</td>
</tr>
<tr>
<td>Amplifying host</td>
<td>Humans/primates</td>
</tr>
<tr>
<td>Global Distribution</td>
<td>Tropical</td>
</tr>
<tr>
<td>U.S. Continental Distribution</td>
<td>Rarely South Texas, Florida</td>
</tr>
<tr>
<td></td>
<td>(found in Puerto Rico, the U.S. Virgin Islands)</td>
</tr>
<tr>
<td>Vaccine</td>
<td>None available</td>
</tr>
<tr>
<td>Treatment</td>
<td>Symptomatic</td>
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How the Zika Virus Enters the Human Population

The virus originates with nonhuman primates in tropical rainforests but can infect humans. Warm, urban environments with standing pools of water attract mosquitoes, and can lead to the virus's spread.

It appears that Zika can be transmitted through sexual intercourse, blood transfusion, and in utero.
Zika Virus Symptoms

- Most common symptoms
  - Fever
  - Rash
  - Muscle and joint pain
  - Conjunctivitis (pink eye)
  - Headache

  Occur 2-14 days after insect bite

- Most illnesses are mild
- Symptoms last 5 days
- Death is rare
Zika Virus Complications

- Guillain-Barre Syndrome (GBS): muscle weakness/paralysis; can affect breathing
  - Lasts weeks to months
  - 1 in 20 die
- Meningoencephalitis
- Myelitis
- Peripheral neuropathy
Congenital Zika Syndromes

• Microcephaly (small head)***
• Other defects
  – Hearing/vision problems
  – Seizures
  – Developmental delay/cognitive impairment/absent or poorly developed brain structures
  – Intracranial calcifications
  – Miscarriage, stillbirth
  – Limb abnormalities,
  – Impaired growth
• A lifelong problem!
Zika Diagnosis & Treatment

- No currently available commercial test
- RT-PCR during first week of illness
- Treatment is symptomatic and supportive
Zika Virus – The next big thing?

"Zika is not contagious in the way that Ebola is, nor is it as lethal (fever, rash, joint pain) but it appears to strike in an especially cruel way – depressing brain growth in babies born to infected mothers. And like so many other pathogens that preceded it, the Zika virus has seemingly whirled out of nowhere, reinforcing how difficult it is to predict confidently which ones will go rogue. It only appeared in Brazil last May and is forecast to affect up to four million across the Americas by the end of this year."

“The World Health Organization announced Thursday it will hold an emergency meeting next week on how to confront the Zika virus, which it said is spreading explosively in the Americas.”
World Health Organization
Public Health Emergency of International Concern

• Extraordinary event which is determined:
  – to constitute a public health risk to other States through the
    international spread of disease; and
  – to potentially require a coordinated international response

• Implies a situation that
  – is serious, unusual or unexpected
  – carries implications for public health beyond the affected State’s
    national border
  – may require immediate international action
WHO Declaration of PHEIC

• April 2009
  When the H1N1 pandemic was still in Phase Three
• May 2014
  With the resurgence of polio after its near-eradication
• August 2014
  In response to the outbreak of Ebola in Western Africa
• February 2016
  Amid fears the mosquito-borne Zika virus is linked to birth defects and spreading rapidly
# Arboviruses

<table>
<thead>
<tr>
<th></th>
<th>Distribution</th>
<th>Main Complications</th>
<th>Treatment</th>
<th>Main Vector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue</td>
<td>Tropical/Subtropical</td>
<td>Hemorrhagic Fever</td>
<td>Supportive</td>
<td>Aedes sps.</td>
</tr>
<tr>
<td>West Nile</td>
<td>Throughout the US</td>
<td>Neurologic</td>
<td>Supportive</td>
<td>Culex sps.</td>
</tr>
<tr>
<td>Zika</td>
<td>Tropical/Subtropical</td>
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<td>Supportive</td>
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VECTOR BORNE VIRUSES: PREVENTIVE MEASURES
Prevention Measures: Travelers

• If traveling to an endemic area
  – Wear pants and long sleeved shirts
  – Use approved mosquito repellants
  – Stay in places with screening/air-conditioning

• Pregnant women should avoid travel to Zika endemic areas
Preventive Measures: Sexual Partners

• For patients at risk for sexual transmission
  – Abstain from sex or use a barrier method
    • At least 8 weeks after illness onset if a female partner is likely to have Zika
    • At least 6 months after illness onset if a male partner is likely to have Zika
I KILL 1.5 MILLION PEOPLE A YEAR AND I STILL CAN’T GET YOUR PRESS. WHO’S YOUR AGENT?
• jhirshon@acep.org
• jhirshon@umaryland.edu
• Twitter:@DrJonMark
# Chikungunya

<table>
<thead>
<tr>
<th>Virus family/genus</th>
<th>Togaviridae/Alphavirus</th>
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<tr>
<td>Transmission</td>
<td>Mosquito-borne (<em>Aedes</em> sps)</td>
</tr>
<tr>
<td>Amplifying host</td>
<td>Humans</td>
</tr>
<tr>
<td>Global Distribution</td>
<td>Multiple countries</td>
</tr>
<tr>
<td>U.S. Continental Distribution</td>
<td>Florida (also found in Puerto Rico and US Virgin Islands)</td>
</tr>
<tr>
<td>Vaccine</td>
<td>None available</td>
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# Yellow Fever

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