Emerging Mosquito-Borne Diseases

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Basic Patterns of Mosquito-Borne Arbovirus Transmission

Scenario one: Humans are the primary hosts

Scenario two: Humans are incidental hosts
West Nile virus transmission

- *Culex* spp mosquitoes
- Virus overwinters in adult female hibernating mosquitoes in temperate climates
- Infected mosquitoes emerge in spring and start transmission cycle
- Birds amplifying host – many passerine species develop enormous viremias (>10⁷ PFU/ml)
- Cycle continues throughout spring and summer
- Humans and horses are dead-end hosts
Climate/Weather and Anthropogenic Factors Affect Nearly All Factors Influencing Arboviral Transmission

- Food
- Breeding sites
- Predators

Prevention
Behavioral interaction

Adults

Virus replication
Vector genetics
Virus genetics

Breeding site abundance and suitability
Predators

Terrestrial
Aquatic

Eggs

Larvae

Pupae
Scenario One: Humans Serve as the Primary Vertebrate Host

- Dengue
- Chikungunya
- Zika
Dengue

- Caused by four flaviviruses
- No known important animal reservoir
- Causes fever, rash, severe pain ("break bone fever"), shock, hemorrhage
- 400 million infections per year
- Subsequent infections increases likelihood of severe disease
- Spread by the *Aedes aegypti* mosquito
- *Aedes albopictus* can also sustain transmission
Dengue Incidence is Rapidly Increasing in the Americas

Source: Pan American Health Organization (PAHO)
Dengue Incidence in Latin America and the Caribbean, 1980-2010

Source: PAHO
Aedes aegypti

- Adapted to urban habitats
- Preferentially feeds on humans
- Can bite multiple humans in a single blood meal
- Feeds indoors
- Breeds in small containers
- Present throughout the tropical world
Reinfestation of *Aedes aegypti* after Cessation of Control Efforts from 1947-1970*

*Continental plan for eradication of the *Aedes aegypti*. PAHO Resolution–CD1.R1*
Rapidly Increasing Human Population and Urbanization

- **Population**
  - 6.1 Billion in 2000
  - ~9.4 to 11.2 Billion in 2050

- **Percent world population urban**
  - 1950: 29%
  - 2007: 49%
  - 2030: 60%
  - Increase largely due to 3X increase in Asia and Africa
Can Dengue Reemerge in Temperate Climates?

*Dengue in the Continental USA*

- Dengue epidemics in US from 1700s until first half of the 1900s
- 807 returning travelers with dengue reported in 2013
- 8 outbreaks in Texas since 1980
- 2 outbreaks in Florida since 2009

*Maps of Aedes aegypti and Aedes albopictus in North America*
A Tale of Two Cities: 
Dengue Outbreak on the US-Mexico Border

<table>
<thead>
<tr>
<th></th>
<th>Brownsville</th>
<th>Matamoros</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive serology</td>
<td>4%</td>
<td>32%</td>
</tr>
<tr>
<td>Breteau index</td>
<td>16</td>
<td>28</td>
</tr>
<tr>
<td>Air conditioning</td>
<td>85%</td>
<td>29%</td>
</tr>
<tr>
<td>Screens</td>
<td>61%</td>
<td>65%</td>
</tr>
<tr>
<td>Lot size (m²)</td>
<td>1070</td>
<td>307</td>
</tr>
</tbody>
</table>

No air conditioning was a major risk factor for infection in Matamoros: OR 6.6 (1.9-17.9)

Lot size smaller than median was a risk factor for infection in Brownsville: OR 14.6 (1.2-172.3)

Chikungunya Virus

- Single-stranded RNA virus
- Genus *Alphavirus*, Family *Togaviridae*
- Closely related to Mayaro, O’nyong-nyong, and Ross River viruses
- Three major genotypes
  - West African
  - East/Central/South African (ECSA)
  - Asian

*Organization of the chikungunya virus genome from: Expert Rev. Vaccines 11(9), (2012)*
*Cryo-EM from: Mukhopadhyay S et al., Structure 2006*
Chikungunya Virus Infection

- Most (72%–97%) infected people develop clinical symptoms
- Incubation period usually 3–7 days (range 1–12 days)
- Primary clinical symptoms are fever and polyarthralgia
Chikungunya Transmission Cycles

Sylvatic CHIKV Transmission Cycle

Urban CHIKV Transmission Cycle

History of Outbreaks

• Discovery in 1953 in febrile woman in Tanzania
• First major documented emergence
  – Large urban outbreaks in India and Southeast Asia due to introduction of ECSA genotype in or around early 1950s
  – Resultant “Asian” genotype persisted in SE Asia
  – Numerous outbreaks documented in Africa and SE Asia subsequently
History of Outbreaks

• Second major emergence of ECSA genotype virus
  – Started in coastal Kenya in 2004
  – Spread to Comoros and then to La Reunion Island
    • Outbreaks of unprecedented size
    • Acquires E1-A226V mutation that increases fitness in *Aedes albopictus*
  – Spread to other islands in Indian Ocean and India where it has caused >1 million illnesses
  – Outbreaks in Italy and France initiated by travelers from India. Vectored by *Aedes albopictus*. 
Chikungunya Infections – As of 2007

Chikungunya Appears in the Western Hemisphere

• First cases reported:
  • St. Martin in December 5, 2013
  • Onsets actually in October 2013
• Asian genotype (recent outbreaks in Yap, Philippines, Indonesia, China)
  • Lacks E1-A226V mutation

Source: PAHO
Chikungunya: December 2013

New locations
St. Martin
Martinique
Guadeloupe
St. Barthelemy
Sint Maartin

Source: PAHO
New locations
Br. Virgin Islands
Dominica
Anguilla

Source: PAHO
Chikungunya: Feb 2014

New locations
St. Kitts and Nevis
French Guiana
Chikungunya: March 2014

New locations
Dominican Republic
Chikungunya: April 2014

New locations
St. Vincent & Grenadines
Antigua & Barbuda
New locations
St. Lucia
Haiti
Puerto Rico
Guiana

Source: PAHO
Chikungunya: June 2014

New locations
- Aruba
- El Salvador
- Grenada
- Suriname
- Turks and Caicos
- U.S. Virgin Islands
- Venezuela

Source: PAHO
Chikungunya: July 2014

New areas
Bahamas
Barbados
Cayman Islands
Trinidad and Tobago
Panama
Costa Rica
United States

Countries with autochthonous transmission
Sub-national areas with autochthonous transmission

Source: PAHO
Chikungunya: August 2014

New Areas
Curacao
Jamaica

Countries with autochthonous transmission
Sub-national areas with autochthonous transmission

Source: PAHO
Chikungunya: September 2014

New areas
Brazil
Colombia
Guatemala
Honduras
Nicaragua

Countries with autochthonous transmission
Sub-national areas with autochthonous transmission

Source: PAHO
Countries with autochthonous transmission

Sub-national areas with autochthonous transmission
CHIK in the Americas
December 2013 – May 2015

44 countries
1,427,005 reported cases
222 deaths

Chikungunya in the United States

(As of March 24, 2015)

**Historically, from 2006–2013:**
- An average 28 people/year with positive tests for recent CHIKV infection
- (Range 5–65 per year)

**Current Outbreak, CONUS**
- 47 states reporting cases, and the District of Columbia
- 2,549 travel-associated cases
  - 18% from FL
  - 30% from NY
- 12 locally-acquired cases (FL)

http://www.cdc.gov/chikungunya/geo/index.html
Zika Virus

- Mild dengue-like illness
- Human-mosquito-human transmission
- *Aedes aegypti* primary vector
- Discovered in Zika Forest in Uganda
- Circulating in Western Pacific in recent years
- First detected in Western Hemisphere in Brazil in 2015; spreading
Scenario Two:
Humans are Incidental Hosts

- West Nile virus
West Nile Virus

- Flavivirus
- Birds are vertebrate hosts; *Culex* mosquitoes vectors
- Introduced into New York City area in 1999
- No means of natural transport to Western Hemisphere
- Emergence during a heat wave
- Genetics suggests separate introductions in Europe and USA of lineage 1 WNV from Africa
- At least two sequential genetic mutation events of consequence
  - NY99 strain: NS3 T249P mutation increases viremia and mortality in birds
  - WN02 strain: E-V159A mutation changes viral transmission dynamics in birds and mosquitoes
- Continued co-evolution: Birds becoming less susceptible to illness and death, but viruses creating higher viremia
Clinical spectrum of human WNV infections

- 70 - 80% Asymptomatic
- 20 - 30% “West Nile Fever”
- <1% WNND

Neuroinvasive Disease: Meningitis, Encephalitis, Acute flaccid paralysis

~ 10% of WNND are fatal
Estimated Number of West Nile Infections and Illnesses, 1999-2014

• 18,788 neuroinvasive disease cases reported
• For every reported neuroinvasive disease case,
  – 30 - 70 non-neuroinvasive disease cases
    • 560,000 - 1.3 million non-neuroinvasive disease cases
  – 150 - 300 infections
    • 2.8 - 5.6 million infections
Average annual incidence of WNV severe neurological disease by county – United States, 1999–2013
Average annual **number** of WNV neuroinvasive disease cases by county – United States, 1999-2013
Average annual incidence of WNV neuroinvasive disease – United States, 1999–2013
Increasing Temperature Does Two Bad Things to Infected Mosquitoes

- Shortens time from infection to infectiousness (extrinsic incubation period)
- Increases viral replication in mosquitoes, making them more infectious

- E-V159A mutation in WN02 strain may augment this effect
Conclusions

- Climate and weather affect many factors that influence viral amplification, and hence outbreaks.
  - Heat waves appear to promote West Nile outbreaks
- Anthropogenic factors – travel and trade, land use, lifestyle, urbanization – are the major contributing factors to mosquito-borne disease emergence
  - Influence of climate change unclear
  - Models that consider climate change impacts on mosquito-borne disease emergence must consider anthropogenic factors that promote or prevent emergence
The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention.