Dengue and Chikungunya in the Caribbean and Americas

Vector-Borne Diseases: Exploring the Environmental, Ecological and Health Connections

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Global Risk of Dengue Virus Infection
Likelihood of Transmission

## Dengue Burden

Estimated burden of dengue, by continent, 2010

<table>
<thead>
<tr>
<th>Continent</th>
<th>Dengue (Millions (credible interval))</th>
<th>Inapparent Infections (Millions (credible interval))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>15.7 (10.5-22.5)</td>
<td>48.4 (39.3-65.2)</td>
</tr>
<tr>
<td>Asia</td>
<td>66.8 (47.0-94.4)</td>
<td>204.4 (151.8-273.0)</td>
</tr>
<tr>
<td>Americas</td>
<td>13.3 (9.5-18.5)</td>
<td>40.5 (30.5-53.3)</td>
</tr>
<tr>
<td>Oceana</td>
<td>0.18 (0.11-0.28)</td>
<td>0.55 (0.35-0.82)</td>
</tr>
<tr>
<td>Global</td>
<td>96 (67.1-135.6)</td>
<td>293.9 (217.0-392.3)</td>
</tr>
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</table>

Bhatt, S et al Nature 2013; 496: 504-507
Dengue in the Americas
Dengue Incidence in the Americas 1980-2013

Source: Pan American Health Organization (PAHO)
Incidence* of Dengue in the Americas, 1980-2013

adapted from San Martin, JL. Meeting on State of the Art in Dengue Prevention and Control, PAHO May 2014

*per 100,000 population
What are the Causes of the Apparent Expansion of Dengue

- Urbanization and vector expansion due to expansion of vector breeding sites
- Movement of people and viruses – all areas now have all four DENVs circulating
- But how much is under recognition of dengue?
Dengue in Puerto Rico

- Vector and DENV introduced in early post-1492 period
- 1899 - Glennan reported annual recognition of dengue
- 1915 - epidemic reported by King – evidence of previous ongoing disease, also confusion with yellow fever
- ~50 years – no reports of disease, including to PR DOH
- 1963 - 27,000 suspect cases reported to PR DOH
  - 36% attack rate in prospective cohort based on CF testing
  - Affected all age groups
  -Ultimately shown to be DENV-3
- 1969 – epidemic of DENV-2
- 1970 – island-wide passive dengue surveillance begun
Passive Dengue Surveillance System (PDSS)

- Co-operative effort by PR Department of Health and CDC to monitor dengue – established 1970
- Passive syndromic surveillance with laboratory confirmation of dengue
- Reporting mandated by law but no enforcement
- Provides dengue diagnostic testing to reporting physician
- Only captures status of suspect case at point when reported
Variable approaches to diagnostic testing conducted over this period: 2009-present = PCR + IgM; 2000 – 2009 = IgM; 1986 – 2000 = virus culture
Surveillance for Dengue

- **Dengue is a syndrome.** No signs or symptoms differentiate dengue from other illnesses in the differential diagnosis except plasma leakage – but this is a late and relatively uncommon event.

- **Diagnostic testing** can determine the etiology of the syndrome.

- **Dengue can evolve** from dengue fever to severe dengue to death over a 5-7 day period after onset of illness.
Causes of Suspected Dengue Cases
Puerto Rico, 2010

Cases

Month of Illness Onset

January  February  March  April  May  June  July  August  September  October  November  December

Dengue
Leptospirosis
Other
Laboratory vs Clinical Diagnosis of Dengue
Ratchaburi, Thailand, 2006 - 2009

- Acute Febrile Illnesses among cohort of 5-13 y.o.
- Laboratory case definition = fever + DENV viremia = 394 cases
- Clinical Case Definitions = WHO classifications 1997 or 2009

<table>
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<tr>
<th>Severity by WHO Definitions*</th>
<th>Number</th>
<th>Percent</th>
</tr>
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<tbody>
<tr>
<td>Undifferentiated Fever (UF)</td>
<td>210</td>
<td>53.3</td>
</tr>
<tr>
<td>Dengue Fever (DF)</td>
<td>142</td>
<td>36.0</td>
</tr>
<tr>
<td>Dengue Hemorrhagic Fever (DHF)</td>
<td>42</td>
<td>10.7</td>
</tr>
<tr>
<td>Total</td>
<td>394</td>
<td>100</td>
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From Sabchareon, A et al. PLoS NTD 2012; 6: e1732
Dengue Diagnostics – Changes

- **Past**
  - *Complicated* - required acute and convalescent samples for IgM anti-DENV testing
  - *Slow* - not useful clinically, not in clinical labs

- **Today**
  - Single specimen diagnosis
  - FDA approved diagnostic tests
    - DENV 1 - 4 rRT-PCR
    - IgM anti-DENV
  - Testing Recommendations – coming in 2015
Dengue Diagnostics – Today

Day Post Onset of Fever

0 1 2 3 4 5 6 7 8 9 10

Incubation Period

Day Post Onset of Fever

0 1 2 3 4 5 6 7 8 9 10

PCR for DENV

Febrile Phase

VIRUS

NS1 antigen detection
(immunoassay)

IgM
MAC ELISA

CDC DENV-1-4
Real-Time RT-PCR Assay
for detection and serotype identification of Dengue Virus
Diagnostic Testing in the Americas

- **US**
  - most testing performed in private reference labs, none routinely perform molecular DENV diagnostics
  - some public health laboratories now perform molecular and immunodiagnostic testing
  - CDC - APHL recommendations under development

- **PAHO**
  - Network of Dengue Diagnostic Laboratories (RELDA)
  - Train-the-trainer Dengue Diagnostic Workshop for RELDA
Dengue in Non-Endemic Areas
Dengue in US Travelers

- ~38 million Americans traveled to dengue endemic destinations in 2012
- Dengue is leading cause of acute febrile illness in returning travelers from the Americas, Caribbean and Asia\(^1\)
- Dengue-related hospitalizations increased 3-fold 2000-2007 \(^2\)

\(^1\)Freeman et al., NEJM 2006
\(^2\)Streit et al., EID 2011
Potential for DENV Transmission
Distribution of Vectors, 2009

Aedes aegypti

Aedes albopictus

Locally Acquired Dengue
Florida, 2010 - 2013

2010
- Key West = 63 (DENV 1) – all closely related genetically
- Broward = 1 (DENV 3); Miami-Dade = 1 (DENV 1)

2011
- Miami-Dade = 3; Palm Beach = 2; Hillsborough and Martin = 1 each

2012
- Miami-Dade = 2; Seminole = 1; Osceola = 1

2013
- Martin – St. Lucie = 20 (DENV 1)
  - June 16 – present
  - Ages 4 – 63 (median 48)
- Miami-Dade = 1

Data: CDC Dengue Branch, Florida Department of Health
DENV Genetic Relatedness
A Way to Determine Source of Cases

Key West 2009-2010
Martin-St. Lucie -2013

CDC Dengue Branch & Florida Department of Health
Chikungunya
Virus and the Vector

- Single stranded RNA
- Genus: *Alphavirus*; Family: *Togaviridae*
- Related to Mayaro, O’nyong-nyong and Ross River viruses
- The same mosquitoes that transmit dengue, transmit CHIKV: *Aedes aegypti* and *Aedes albopictus*
Chikungunya in the Western Hemisphere

Countries and territories in the Americas with reported autochthonous chikungunya cases (as of September 9, 2014).
Differential Diagnosis

- Dengue
- Leptospirosis
- Malaria
- Rickettsia
- Parvovirus
- Enterovirus
- Group A Streptococcus
- Rubella
- Measles
- Adenovirus
- Post-infectious arthritis
- Rheumatologic conditions

- Other alphavirus infections (e.g., Mayaro, Ross River, Barmah Forest, O’nyong-nyong, and Sindbis viruses)
What does it look like?

Edematous polyarthritis

Blanching erythema

Maculopapular rash - including palms

Bullous lesions – infant with in utero infection
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<th>Clinical Comparison CHIK vs. Dengue</th>
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<tr>
<td><strong>Clinical Comparison CHIK vs. Dengue</strong></td>
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<tr>
<td><strong>Fever (&gt;39°C)</strong></td>
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<tr>
<td>+++</td>
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<tr>
<td><strong>Arthralgia</strong></td>
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<tr>
<td><strong>Bullous rashes</strong></td>
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<tr>
<td><strong>Arthritis</strong></td>
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<tr>
<td><strong>Headache</strong></td>
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<tr>
<td><strong>Myalgia</strong></td>
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<tr>
<td><strong>Hemorrhagic manifestations</strong></td>
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<td><strong>Shock</strong></td>
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# Optimal Timing for Diagnostic Testing

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<th>Diagnostic Assay</th>
<th>Days post-illness onset</th>
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<tr>
<td>RT-PCR</td>
<td>≤ 8 days</td>
</tr>
<tr>
<td>IgM Antibody Tests</td>
<td>≥ 5 days</td>
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Treatment in face of Dengue

- Supportive care with rest and fluids
- Acetaminophen to relieve fever / pain
- Non-steroidal anti-inflammatory drugs (NSAIDs) for pain after dengue is ruled out
- Narcotics can be used in patients with severe joint pain not relieved by NSAIDs
- Short-term corticosteroids can be used after evaluating risk-benefit
Treatment-Sub Acute and Chronic

- Convalescence can be prolonged
  - In some patients up to 1 year or longer

- Persistent joint pain may require pain management and benefit from long-term anti-inflammatory treatment
  - use of NSAIDs, corticosteroids, or physiotherapy

- Disabling peripheral arthritis, if refractory to other agents may occasionally respond to short-term corticosteroids
  - To limit use of corticosteroids local injections (intra-articular) or topical NSAID therapy can be used
Cases of Chikungunya in Puerto Rico 2014

Reported cases

Source: Puerto Rico Department of Health, Brenda Rivera DVM and Jomil Torres, MS
Municipalities with Confirmed Chikungunya Cases
Puerto Rico, through Epidemiologic Week 33, 2014

Source: Puerto Rico Department of Health, Brenda Rivera DVM and Jomil Torres, MS
Concerns – Americas

- No immunity to CHIK in the Americas / Caribbean
- Will likely take several epidemic cycles in large populations (e.g., Puerto Rico, Dominican Republic, Colombia)
- The vector mosquitoes are not controlled
  - “CHIK may be best surrogate for effectiveness of vector control”
- CHIK travels with people (planes, ships)