Zika Virus in the Americas

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Rockefeller Foundation dedicated to arbovirus discovery 1947 (sentinel macaque),
1948 (mosquito),
1954 (human)

Zika virus: Discovery

Adapted from National Academy presentations by R. Rosenberg
(platform photo by B. Beard)

And presentation by Scott Weaver

A member of the Flaviviridae family of RNA viruses

Genome is single positive strand of RNA ~ 10,600 nt Transmitted by mosquitoes

**Zika virus: Genetics**

**Sequence:**

A representation of the surface of the Zika virus. Image courtesy of Kuhn and Rossman research groups, Purdue University/Released.

**Zika virus: Genetics**

Zika Virus probably originated in Africa

**ZIKV transmission cycles**

 Sylvatic Cycle
Primates

Urban Cycle

Ae. aegypti
Ae. albopictus
Ae. hensilli

Primates

Vervet monkey
Chlorocebus sabaeus

Gerbils
Tulane indick

Mammals, humans,
Sheep and goats?

**ZIKV Getting to the Americas**

1947 to 2014

**Kansas State University**

Adapted from National Academy presentation by R. Rosenberg, S. Weaver.
Zika virus: Spread

Adapted from National Academy presentation by R. Rosenberg

Yap Island, Federated States of Micronesia
Zika virus: Yap Island

49 confirmed and 59 probable cases of Zika virus disease. Most patients had mild illness.

Rash, fever, arthralgia, and conjunctivitis were common symptoms. No hospitalizations, hemorrhagic manifestations, or deaths due to Zika virus were reported.

Estimated that 73% of Yap residents 3 years of age or older were infected with Zika virus (more than 900 people in total).

The mosquito vector was not identified but Aedes hensilli was the predominant mosquito species identified.
Zika virus: Spread

- Estimated 28,000 (11% population) - clinically similar to Yap, but...
- First suspect association Guillan-Barré syndrome
- 2015 retrospective case review: increase in microcephaly
- 2014 – New Caledonia, Cook Islands, Solomons, Easter Island
- Asian genotype – Yap, Cambodia

Zika virus: South Pacific Outbreaks

- 2013 – French Polynesia
  - Estimated 28,000 (11% population)
  - clinically similar to Yap, but...
  - First suspect association Guillan-Barré syndrome
  - 2015 retrospective case review: increase in microcephaly
  - 2014 – New Caledonia, Cook Islands, Solomons, Easter Island
  - Asian genotype – Yap, Cambodia

Zika virus: Perinatal transmission

- Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014

Zika virus: Guillain-Barre

- Zika virus infection complicated by Guillain-Barré syndrome – case report, French Polynesia, December 2013
2011 Zika virus: Human infections

ZIKV 2016 in US

Probable Non-Vector-borne Transmission of Zika Virus, Colorado, USA

First case in US January 11, 2016

Traveler from El Salvador to Harris County, Houston, Texas

First sexually transmitted case in US February 2, 2016

Texas reports first case in the USA of sexually transmitted Zika virus

Zika virus; First case in US January 11, 2016
Last week, the Centers for Disease Control and Prevention reported something it had been anticipating for months:

New York reports first female-to-male Zika transmission via sex

Published July 15, 2016 - Reuters

Check the facts?

The New York City Health Department on Friday reported the first instance of male-to-male transmission of the Zika virus, which is most typically spread by the bite of an infected mosquito.

472 travel associated cases
0 locally transmitted cases

1,404 travel associated cases
0 locally transmitted cases
Zika Case Distribution by Week: October 12, 2016

3,808 travel associated cases
(66 NC)
128 locally transmitted cases

MOSQUITO INFECTIONS

ZIKV transmission cycles

SYLVATIC CYCLE

URBAN CYCLE

Zika virus: Vectors

The first isolation of Zika virus from mosquito samples was made in 1948 from *Aedes africanus*.

Lately, many other *Aedes* species have been surveyed for the detection of Zika virus, and thus far, Zika virus has been detected by RT-PCR or isolated from many mosquito species, human beings, and non-human primates.
Zika virus: Vectors

Adapted from National Academy presentation by T. Monath

Aedes aegypti
the Yellow Fever Mosquito (photo S. Higgs)

Aedes albopictus
the Asian Tiger Mosquito (photo S. Higgs)

Zika Virus in Gabon (Central Africa) – 2007: A New Threat from Aedes albopictus?

Abstract

Aedes albopictus and dengue cases increased in Gabon in 2007 with large infected areas affecting the different regions of the country. The increase of Aedes albopictus population and dengue cases raised the question about the origin of this invasion. In this work, we present the results of a study aimed at understanding the way the Asian tiger mosquito invaded the Gabonese territory. Our results show that the Aedes albopictus invasion is due to the introduction of the species in many regions of Gabon. The study was conducted using the GIS (Geographic Information System) and satellite imagery. The results show that the Aedes albopictus invasion is not only limited to the coastal areas but also extends to the inland regions of the country. The study also highlights the need for more research on the role of climate change in the spread of this mosquito species. The results are relevant for the development of strategies to control dengue fever in Gabon and other countries in the region. The study was published in the journal *Journal of Vector Ecology*.
What about Culex species?

October 10, 2016

Culex pipiens quinquefasciatus

October 27, 2016

Culex pipiens and Aedes triseriatus Mosquito susceptibility to Zika Virus.

Dr. D. Vanlandingham

Dr. S. Huang

CVM

None became infected

Also tested: Cx. pipiens from Mercer Count, NJ, F7 and Cx. pipiens from Anderson, CA, F15. None became infected.

Vero Beach is 140 miles from Miami Beach.
Zika virus replication in the mosquito Culex quinquefasciatus in Brazil.

New vectors in the Americas
New control (RIDL, Wolbachia)
Insecticides
Repellants
Reagents
Detection
Diagonostics (differential)
New Vertebrates
(WV primates, rodents, livestock)
Animal Models

ZIKV transmission cycles in the Americas?

Viral genetics: Asian vs African infectivity/pathogenicity
Disease: Guillain-Barre, microcephaly, sexual transmission, persistence
Treatments: Vaccines, reagents, detection, diagnostics (differential)

New World Primates (135 spp.)

<table>
<thead>
<tr>
<th>FAMILY</th>
<th>COMMON NAME</th>
<th>NUMBER OF SPECIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family Callitrichidae</td>
<td>Marmosets and Tamarins</td>
<td>20 marmosets, 22 tamarins</td>
</tr>
<tr>
<td>Family Cebidae</td>
<td>Capuchins and Squirrel monkeys</td>
<td>9 capuchins, 5 squirrel</td>
</tr>
<tr>
<td>Family Aotidae</td>
<td>Night/Owl monkeys</td>
<td>11</td>
</tr>
<tr>
<td>Family Pitheciidae</td>
<td>Tits, Sakis and Uakaris</td>
<td>29 tits, 10 sakis, 5 uakari</td>
</tr>
<tr>
<td>Family Atelidae</td>
<td>Howler, Spider, Wooly spider &amp; Wooly</td>
<td>10 howler, 7 spider, 2 wooly spider, 5 wooly</td>
</tr>
</tbody>
</table>

ZIKV: WHAT IS LEFT TO DO?

Surveillance
Predictive models

ENVIRONMENT
VECTORS
ZIKA VIRUS
HOST

Viral genetics:
Disease:
Treatments:
Animal Models

INFECTIONS of "OTHER" VERTEBRATES
Results

Over all prevalence rates were highest for WN, DEN and JE viruses (3.2% to 7.8%) followed by ZIKA (2.4%) and the other four viruses (Table I). CF titres were high (1:16 and/or 1:32) for certain samples of each virus except CHIK (Table II). All ZIKA and RF titres were 1:8 or higher. Between 60% and 79% of the WN, JE, SIN, and UGS titres were 1:8. In rodent sera, 72% (18 of 25) reacted to one virus and 28% (7 of 25) reacted to two or more (mostly two) viruses. High CF titres (1:16 and/or 1:32) were obtained with WN, JE, SIN, ZIKA, and RF viruses (Table III).

Zika virus in animals: 1983

372 sera: 157 rodents, 172 domestic animals, 43 humans
Complement fixation tests for 8 viruses
Zika virus antibodies in animals: 1983

RESULTS

3.8% rodents positive (n=6/157)
- 3/47 Tatera indica
- 2/33 Meriones hurrianae
- 1/2 Bandicota bengalensis

1.2% domestic animals (n=2/172)
- 1/46 sheep
- 1/48 goat

2.3% humans (n=1/43)

The reaction of all positive sera with JE antigen was monospecific except that one rodent (T. indica) serum was simultaneously positive for another Flavivirus (Zika virus). All other positive sera reacted monospecifically with the respective Flavivirus except from one rodent (T. indica) and one human (40-year-old female); these two sera reacted with both Zika and Uganda S viruses.

Antibodies against ZIKA virus were detected in sera from rodents, sheep, goats and one person (without antibodies to other flaviviruses).

These data are the first indication of ZIKA virus infection in rodents and domestic animals.

The natural history of this agent should be investigated in more detail.

Gerbils, Tatera indica, and jirds, Meriones hurrianae, may be reservoirs of JE, WN and ZIKA viruses.

Rattus rattus and R. norvegicus are also potential sources of human infection by these viruses, especially in rural areas with dense mosquito populations.

Zika virus in animals: 1983 Conclusions

Zika virus in animals: 2016 (unpublished)
Zika virus in animals: 2016 (unpublished)

- Zika Virus strains
  - PRV-BCS9: Puerto Rico December 2015
  - FSS13025: Cambodia 2010
- Inoculation dose: 10^5 PFU/mL subcutaneous and intradermal

- The study
  - Challenged at day 0 and maintained animals for 28 days
  - Recorded clinical signs, temperatures
  - Collected sera at days post infection 0-5, 7, 14, 21, 28
  - Collected tissues at necropsy

- Serology
  - Plaque reduction neutralization assay
    - PRNT 90
- Virus Isolation
  - Plaque assay on sera and tissues
  - Real Time RT-PCR on sera
- Histopathology and Immunohistochemistry

Results:
- No clinical signs or febrile state detected
- Viremia detected in frogs
- Real time RT-PCR on sera
  - In progress
  - Detection of RNA in frogs and an armadillo

No antibodies in
Armadillo, Pigeon, Chicken, Snake, Hamster, Mink, Ground Hog, Calf, Deer, Mouse, Sparrow
Antibodies detected in goats, cottontail rabbits, ducklings, pigs, and frogs

Antibodies detected in:
- Puerto Rican strain elicited stronger immune response than Cambodian strain
- No difference in susceptibility between young and adult animals
- No birth defects noted in newborns during study
  - Rabbits, deer mice

Zika virus in animals: 2016 (unpublished)

- Future work:
  - Additional species
    - Horses, dogs, cats, guinea pigs, pregnant sows, domestic mice, bats,
  - Immunohistochemistry and histopathology
  - Real time RT-PCR
  - Developing pregnancy model in animals

“Alternative Approaches to Control Dengue and Chikungunya”

Release of Insects carrying a Dominant Lethal gene (RIDL)
Wolbachia spp – infected mosquitoes. Intracellular bacteria that infects multiple tissues including ovaries and salivary glands.

Photo: © Public Library of Science / Scott O’Neill

Wolbachia spp – infected mosquitoes.
Many of the slides in this presentation were obtained from open source material and PowerPoints from the National Academies website. Slides were from presentations by Albert Ko, Richard Kuhn, Tom Monath, Ron Rosenberg (some original pictures by Ben Beard), and Scott Weaver. Refer to website for original images.

Many journals have provided open access to articles about Zika virus, for example Lancet, and Trans. R.S.T.M.H.