Zika Virus Outbreak in the Americas

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Learning Objectives

• Understand the pathogenesis of West Nile virus infection in human cases of acute encephalitis.
• Obtain a basic understanding of the emerging field of Zika virus epidemiology and pathogenesis research.
• Describe the basic principles and interactions between viral life cycles, environment, and novel host interactions that drive the emergence of novel viral pathogens.
Outline

• Emerging Infections
  – Evolution of viruses
• Zika Virus history
• Zika Virus Clinical features
• Next steps for Zika virus
  – Vaccine development
West Nile Virus Transmission Cycle

West Nile virus

Mosquito vector

Bird reservoir hosts

Incidental infection

Incidental infection

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Zika Virus Transmission Cycles

Sylvatic (jungle) cycle

Epidemic (urban) cycle
Zika Forest, Uganda
Concept for EID

• RNA viruses are engineered by evolution to adapt to changing environments

• As humans continue to encroach on or change established RNA virus niches, the world of RNA viruses will continue to adapt to new niches that sometimes involve humans.
Zika virus

- **Arthropod-borne virus (arbovirus)**

- *Flavivirus* viral genus in *Flaviviridae* viral family
  - Includes dengue, West Nile, and yellow fever viruses
  - Positive-sense, single-stranded, enveloped, icosahedral, ribonucleic acid (RNA) viruses

- Transmitted primarily by certain *Aedes* spp. mosquitoes

- Zika virus “disease” is when infection with Zika virus causes clinical symptoms
A lot of viruses

Family Flaviviridae contains over 70 viruses!
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Origins of Zika virus

- Small forest between swamp and Kampala-Entebbe road
Zika Forest, Uganda
Zika Virus Identified

- Yellow fever virus researchers built tree platforms in canopy of Zika Forest.
- Put “sentinel” rhesus monkeys on platforms.
- Measured temperature of rhesus monkeys daily.
- Rhesus 766 had a temperature of 39.7 on April 18, 1947.
- Isolated a novel virus from serum which they named “Zika virus”.

**FIG. 1**

TEMPERATURE RECORD

Rhesus 766
Zika virus 1947-2006

- Only 14 human cases of Zika virus disease were documented
  - One Zika Forest worker in Uganda in 1964
  - Five children in Nigeria during 1968–1975
  - A laboratory accident infecting one researcher in 1973
  - Seven inpatients in Indonesia during 1977–1978

- All with self-limited, acute febrile illnesses

- Likely many more undiagnosed
Zika Virus Disease Outbreak-Yap State, 2007

- First documented human outbreak of Zika virus disease
- 185 with acute onset of rash, arthralgia, or conjunctivitis
  - 49 confirmed, 59 probable, 72 suspected Zika virus infections*

*Five people were ruled out for Zika virus infection
Zika Virus Disease Outbreak- Yap State 2007

- All age groups and both sexes were affected
- Household and seroprevalence survey performed
- Estimated 73% (95% CI: 68–77%) of Yap residents infected
- Estimated 19% of those infected had symptoms attributable to Zika virus infection
- No reports of microcephaly or other neurologic conditions

How the Zika virus spread

- **Active transmission**
- **Known previous transmission**
- **Antibodies also detected**

### 2013
**Epidemic on French Polynesia**

### 2014-16
Zika appears in northern Brazil and spreads through the Americas

### 1960
First human cases in Nigeria

### 1947
First documented in monkeys in Uganda

### 2007
Epidemic on island of Yap, Micronesia

### 1970s
Cases in Pakistan, India, Malaysia, and Indonesia

**SOURCE:** WHO and Lancaster University, Feb.1
Zika virus in Florida
Zika virus Disease

- **Cases in US (CDC)**
- Locally acquired mosquito-borne cases: 128
- Travel associated cases: 3,807
- All Cases: US and DC: 3,936
  - Sexually transmitted: 32
    - GBS: 13
  - Pregnant women: 878

- **US Territories**: Locally acquired cases: 25,871
  Pregnant Women: 1,806

- **Pregnancy Outcomes**: US- 23 birth defects, 5 pregnancy losses

Mosquito Transmission by *Aedes* sp.

- Most common method of Zika virus transmission
- Primarily *Aedes aegypti*; secondarily *Aedes albopictus*
- “Domesticated” mosquitoes; evolved to live near humans
Aedes aegypti Predicted Geographic Range

Aedes albopictus Predicted Geographic Range

Zika Virus-Mosquito Transmission Cycles

Zika Virus Transmission Cycles

Sylvatic (jungle) cycle

Epidemic (urban) cycle
Other Mechanisms of Transmission

• Sexual Transmission
• Maternal-Fetal Transmission (not breastfeeding)
• Blood Transfusion
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Symptomatic Rate and Incubation Period

- Symptomatic rate of 20% estimated from Yap outbreak
- May be higher in different settings with different populations
- Unknown incubation period, but likely a few days to up to two weeks

Zika virus Disease

- Cases in US (CDC)
- Locally acquired mosquito-borne cases: 43
- Travel associated cases: 3,314
- All Cases: US and DC: 3,358
  - Sexually transmitted: 28
    - GBS: 8
  - Pregnant women: 749

- US Territories: Locally acquired cases: 19,706
  - Pregnant Women: 1,348
- Pregnancy Outcomes: US-20 birth defects, 5 pregnancy losses
  - US Territories: unknown (only 1 reported)
Zika clinical features in Adults

- Only ~20% of infected adults develop symptoms
- Fever 101-103F
- Rash
- Conjunctivitis
- Body and joint aches
- Symptoms last about 1 week
- Complications: Guillain-Barre Syndrome, sexual transmission, vertical transmission (Fetal infection)
**CDC’s Response to Zika**

**PREGNANT and living in an area with Zika?**

**What we know about Zika**

- Zika can be passed from a pregnant woman to her fetus.
- Infection with Zika during pregnancy is linked to birth defects in babies.
- Zika is spread mostly by the bite of an infected Aedes species mosquito.
  - These mosquitoes are aggressive daytime biters. They also bite at night.
- There is no vaccine to prevent or medicine to treat Zika.
- Zika can be spread by a man to his sex partners.

**What we don’t know about Zika**

- When during pregnancy Zika might cause harm to the fetus.
- How likely it is that Zika infection will affect your pregnancy.
- If your baby will develop birth defects from the infection.

**Symptoms of Zika**

Most people with Zika won’t even know they have it. The illness is usually mild with symptoms lasting for several days to a week.

The most common symptoms of Zika are

- Fever
- Rash
- Joint Pain
- Red eyes
Zika Virus and Microcephaly: Examples

Photos of microcephalic infants in Brazil courtesy of AP Photo/Felipe Dana and Ueslei Marcelino/Reuters
Zika Virus and Microcephaly: CT Findings

- Photos show CT images of microcephalic infants.
Zika Virus and Ophthalmologic Birth Defects

- Case series of infants born to mothers with presumed Zika virus infection

Zika Virus and Guillain-Barré Syndrome (GBS)

- Increase in GBS incidence in French Polynesia, Brazil, Colombia, and El Salvador during outbreaks

- Case-control series from French Polynesia showed 100% cases with Zika virus neutralizing antibodies versus 56% controls (odds ratio = 34)

- Study results based on antibody testing

- Predominantly acute axonal motor neuropathy (AMAN)

Reverse Transcription-Polymerase Chain Reaction (RT-PCR)

- Zika virus nucleic acid usually detectable in serum 0–7 days post symptom onset by RT-PCR
- May be detected longer in urine, saliva, and semen
- RT-PCR can also be used on CSF and amniotic fluid
- Very specific test for Zika virus presence
- Trioplex RT-PCR for dengue, chikungunya, and Zika viruses

Antibody Testing and Limitations

- Zika virus infection usually results in IgM production by 7 days

- Flavivirus antigen cross-reactivity common with IgM tests
  - Positive Zika virus IgM = recent flavivirus infection (may not be Zika)

- Neutralizing antibody tests (e.g., PRNTs) more specific
  - Dilute patient’s serum to see how well it neutralizes each virus
  - Less useful in flavivirus endemic areas due to original antigenic sin

- Paired acute and convalescent samples recommended
  - Allows for detection of a 4-fold change in titers


Need for a Zika vaccine - 2016

The good

- There are licensed vaccines against other flaviviruses
  - Yellow fever
  - JE
  - Dengue
- Expertise on flavivirus research and vaccine development

Challenges

- Many unknowns
  - Animal models, assays
- Safety concerns
  - Possibility of GBS, enhancement and neurovirulence
- Fast moving epidemiology
- Small percentage of symptomatic infections
  - Efficacy endpoints

Adapted from C. Cassetti, NIAID
Acknowledgements

**Laboratory**
Katie Shives
Aaron Massey
Erica Beatman
Mastooreh (Massi) Chamanian
Karla Hedman

**Collaborators**
Greg Ebel – CSU
Mike Gale – UW
Mike Diamond – WashU
Aaron Brault – CDC
Jeff Kieft- UCO
Patrik Brundin - VAI
Pei-Yong Shi - UTMB

**Funding:**
CU SOM, DOM, Center for Neuroscience
UC AMC Light Microscopy & Imaging Core