Zika Virus Introduction and Overview

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Zika Virus.
I. Isolations and Serological Specificity

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Virus first isolated from a monkey in the Zika forest of Uganda in 1947
Zika Virus Background

- Belongs to Genus *Flavivirus*
- family *Flaviviridae*
- Enveloped icosahedral
- Single stranded RNA virus
- Two lineages:
  - African and Asian

Tick-borne encephalitis virus
  - West Nile Virus
  - Murray Valley Encephalitis Virus
  - Japanese Encephalitis Virus
  - St. Louis Encephalitis Virus
  - DENV 1
  - DENV 3
  - DENV 2
  - DENV 4
  - Yellow Fever Virus
  - Zika Virus
Zika Virus Spread, 1947-2016

1952: First human cases described
1947: Discovered in Uganda
1977-78: Pakistan, Malaysia, Indonesia
2007: Yap, Micronesia
2009: Hawaii
2013: French Polynesia
2015: Brazil
2016: Texas
2016: Florida
2016: Florida

Source: Lancaster University
Clinical Presentation of rash syndrome in Northeast Brazil, May 2015

Rash, swollen joints, and conjunctival hyperemia

Microcephaly Attributed to Zika

Normal infant brain and head size

Microcephaly, Colombia 2015

Source: Research team of the São Luís/MA municipal health office - From a presentation by the Ministry of Health of Brazil, 2015
Guillain-Barré Syndrome Outbreak Associated with Zika Virus Infection in French Polynesia: A Case-Control Study

VM Cao-Lormeau, F Ghawché et al.

- 98% of 42 pts with GBS had anti-Zika virus IgM or IgG, and all (100%) had neutralizing antibodies against Zika virus compared with 56% of 98 pts in control group w/nAbs (p<0.0001)

- 88% of 42 patients with GBS reported symptoms of Zika virus infection ~6 days before onset of neurological symptoms

- Based on attack rate for Zika virus of 66% in French Polynesia, risk of GBS in the general population during the outbreak was 24 /100,000 infections
Potential for Imported Cases of Zika in the United States

~216 million passenger journeys to U.S. annually from areas with local Zika virus transmission

- 34 M by air
- 173 M by land
- 9 M by sea

Chikungunya Cases in the United States, 2014-2015

50 states
- Travel-associated cases: 3,478
- Locally-transmitted cases: 12

Source: CDC. Cases reported to ArboNET as of 1/12/2016.

Dengue Cases in the United States, 2010-2015

50 states
- Travel-associated cases: 3,572
- Locally-transmitted cases: 292

Source: ArboNet. Includes provisional data for 2015.
Modalities of Transmission of Zika Virus

- Mosquito bites
- Sexual transmission
- Blood transfusion
Zika At-A-Glance

Pregnant Women with Any Lab Evidence of Zika Virus Infection*

- US States and DC: 1,246
- US Territories: 2,701

*Source: Pregnancy Registries as of December 13, 2016

Zika Virus Disease Cases Reported to ArboNET*

- US States and DC: 4,809
- US Territories: 34,973

*Source: ArboNET as of December 28, 2016
Zika Cases in Texas

Zika cautionary area in Brownsville, TX

Pregnant women should consider postponing travel to these areas.
Zika Vaccine Development Timeline

- **DNA vaccine candidate (NIAID VRC)**
  - Preclinical Discovery
  - 2016 Q1: Phase 1
  - 2017 Q1: Phase 1
  - 2017 Q2: Phase 2/2b
  - 2018 Q4: Long term follow up

- **Whole-particle inactivated virus (NIAID/WRAIR/BARDA and corporate partner)**
  - Preclinical Discovery
  - 2016 Q1: Phase 1
  - 2017 Q1: Phase 1
  - 2017 Q2: Phase 1
  - 2017 Q3: Phase 2/2b
  - 2018 Q4: Long term follow up

- **Live-attenuated Zika/dengue chimeric virus (NIAID intramural/Butantan)**
  - Preclinical Discovery
  - 2016 Q1: Phase 1
  - 2017 Q1: Phase 1
  - 2017 Q2: Phase 2/2b
  - 2018 Q3: Phase 2
  - 2018 Q4: Phase 3

- **Vesicular Stomatitis Virus vectored vaccine (NIAID extramural)**
  - Preclinical Discovery/ Tech Transfer
  - Phase 1

- **mRNA vaccine candidate (NIAID VRC)**
  - Preclinical Discovery
  - Phase 1

- **Intramural NIAID and partnerships**
- **Extramural NIAID and partnerships**
- **Preparation for clinical trials**
A healthy volunteer receives the NIAID Zika virus investigational DNA vaccine as part of an early-stage trial to test the vaccine’s safety and immunogenicity. This encounter pictured above was the first administration of this vaccine in a human.
DNA Vaccine Approach

Gene encoding surface protein from Zika virus

Inject DNA containing Zika gene

Body’s cells produce virus-like particles, the basis of the vaccine
DNA Vaccine Development Timeline

**2016**
- Pilot scale manufacturing (NIAID Vaccine Research Center Pilot Plant, Frederick MD)
- Small animal testing
- Non-human primate testing

**2017**
- Initial safety and immunogenicity data
- Phase 1 US multi-center settings (Zika naïve)

**2018**
- Long term follow up
- Phase 2/2b (multiple sites in Southern US, Caribbean, Central and S. America, age range 18-35)
- Long term follow up
Vaccination for Congenital Infections: Lessons from Rubella

- 1964-65 U.S. rubella epidemic
  - 11,000 miscarriages, 2,100 newborn deaths, 20,000 babies born with congenital rubella syndrome (CRS)
- CRS causes deafness, cataracts, heart defects, often microcephaly
- With MMR vaccine, CRS eliminated in U.S. in 2004

National Library of Medicine
Prevent mosquitos breeding in and near your home and neighborhood
References

- www.everbridge.com/wp.../1The-Zika-Virus-An-Emergency-Management-Panel.pptx
- Interim CDC Zika Response Plan, October 2016
- https://www.texastribune.org/tribpedia/texas-mexico-border/