

# ZIKA Virus

The information in this presentation is current as of September 14, 2016. For the most updated guidance and information please see <http://bitly.com/zikaoregon>

# ZIKA Virus

HAI “Lunch & Learn”

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September 14, 2016

- \* Margret Oethinger
- \* Nothing to disclose
- \* Working for Providence Health & Services

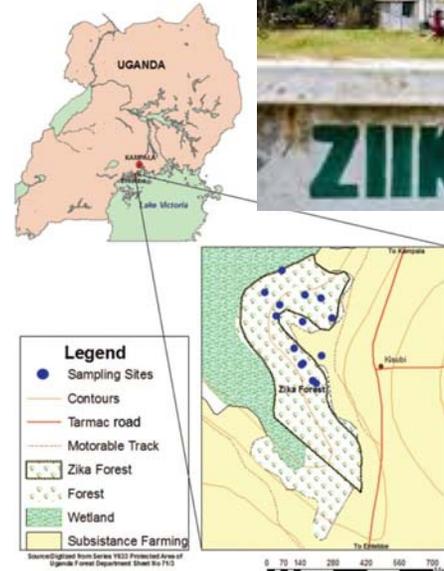


- \* Sarah Humphrey
- \* Nothing to disclose
- \* Working for Oregon State Public Health Laboratory



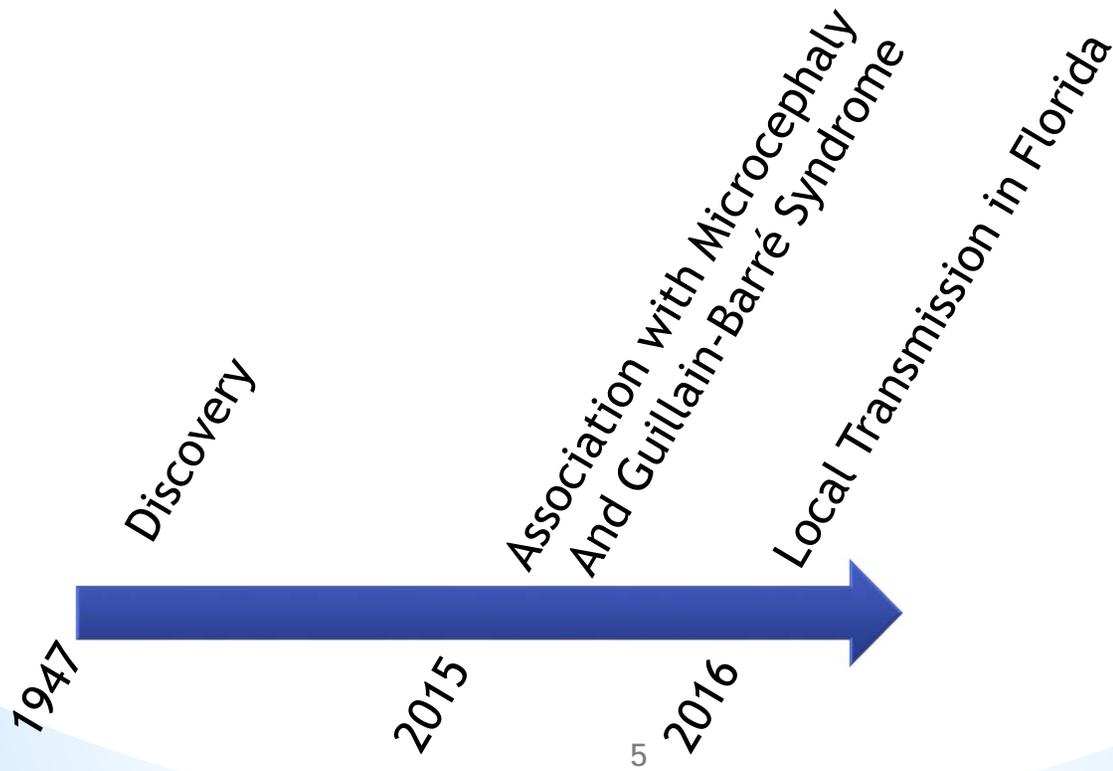
# Disclosures

- \* ZIKA, geographical location. Small forest in Uganda, named for Ziika = “overgrown” in Luganda language
- \* ZIKA Virus (ZIKV): Named after the forest where mosquito studies were carried out at the Yellow Fever Research Institute

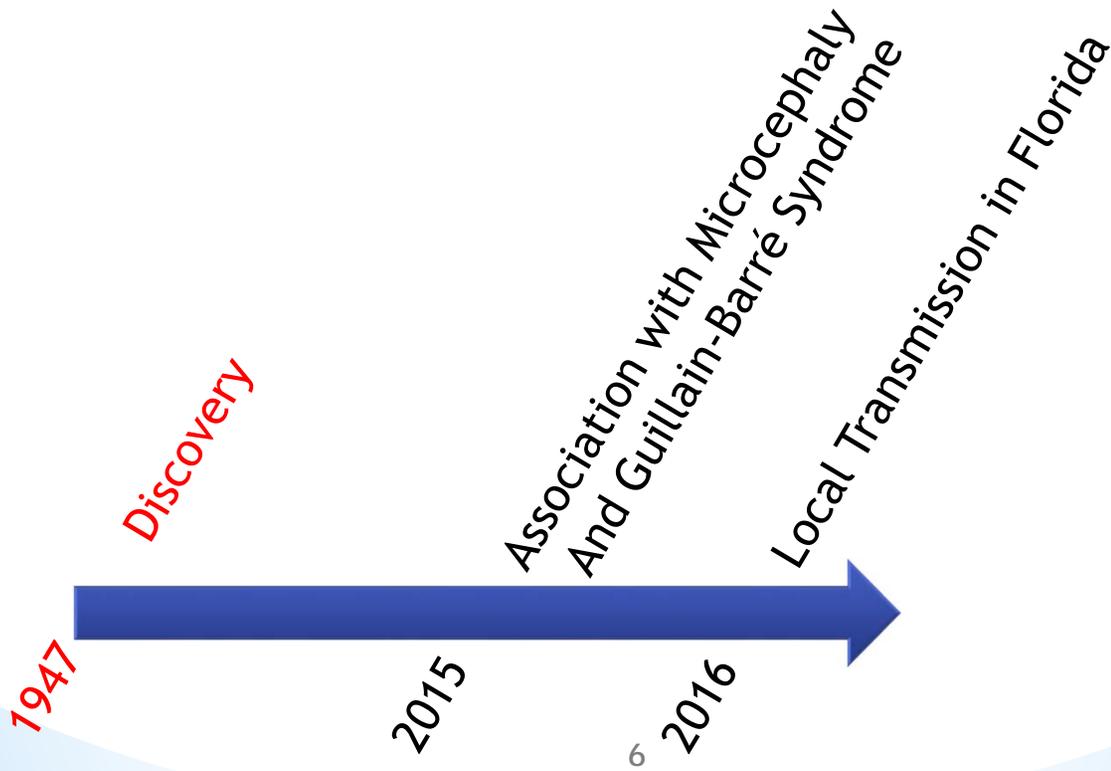


# What is in the name?

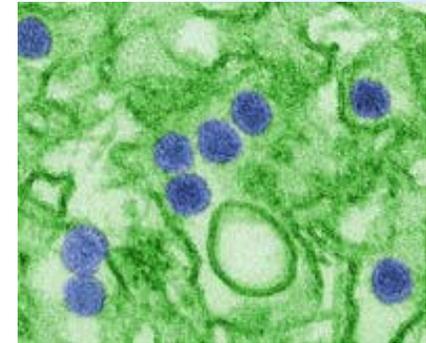
# Timeline



# Timeline

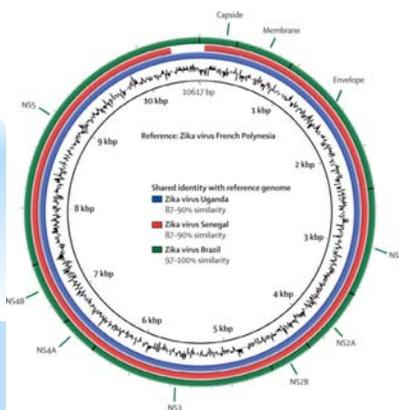


- \* During routine surveillance for Yellow Fever in 1947, the Zika virus was isolated from a Rhesus monkey
- \* Zika virus is taxonomically a Flavivirus, a member of the family of Flaviviridae
- \* Zika virus is also one of the Arboviruses: arthropod-borne infection
- \* Most closely related to Spondweni virus



# What is in the name?

- \* Positive sense, single-stranded RNA virus
- \* 30-45  $\mu\text{m}$  in diameter
- \* The Zika virus genome contains 10,794 nt encoding 3,419 aa
- \* Genome is composed of 2 noncoding regions (5' and 3') that flank an open reading frame, which encodes a polyprotein
- \* Polyprotein is cleaved into the capsid, precursor of membrane, envelope, and 7 nonstructural proteins



# Structure of Zika Virus

TABLE 1. *Continued*

Virus	Vector <sup>a</sup>	Principal vertebrate host	Geographic distribution	Human disease	Animal disease
Tyuleniy	Tick	Bird	Asia, NA		
Uganda S	Mosquito	Bird	Afr.		
Usutu	Mosquito	Bird	Afr.		
Wesselsbron	Mosquito (Tick)	?Rodent, sheep	Afr., Asia	+	Sheep
West Nile	Mosquito (Tick)	Bird	Afr., Eur., Asia	+	Horse
Yacunde	Mosquito	Rodent, bird	Afr.		
Yellow fever	Mosquito (Tick)	Monkey	Afr., SA	+	
Zika	Mosquito	Monkey	Afr., Asia	+	

<sup>a</sup>Parentheses indicate isolation from alternate vector but uncertain role in natural transmission cycle.

<sup>b</sup>Viruses closely related or identical to Russian spring-summer encephalitis.

<sup>c</sup>Laboratory infection only.

<sup>d</sup>Disease following experimental infection for cancer therapy.

Afr., Africa; Austr., Australia-New Guinea; CA, Central America; Eur., Europe; ME, Middle East; NA, North America; SA, South America; WW, world-wide.

Modified from ref. 345, with permission.

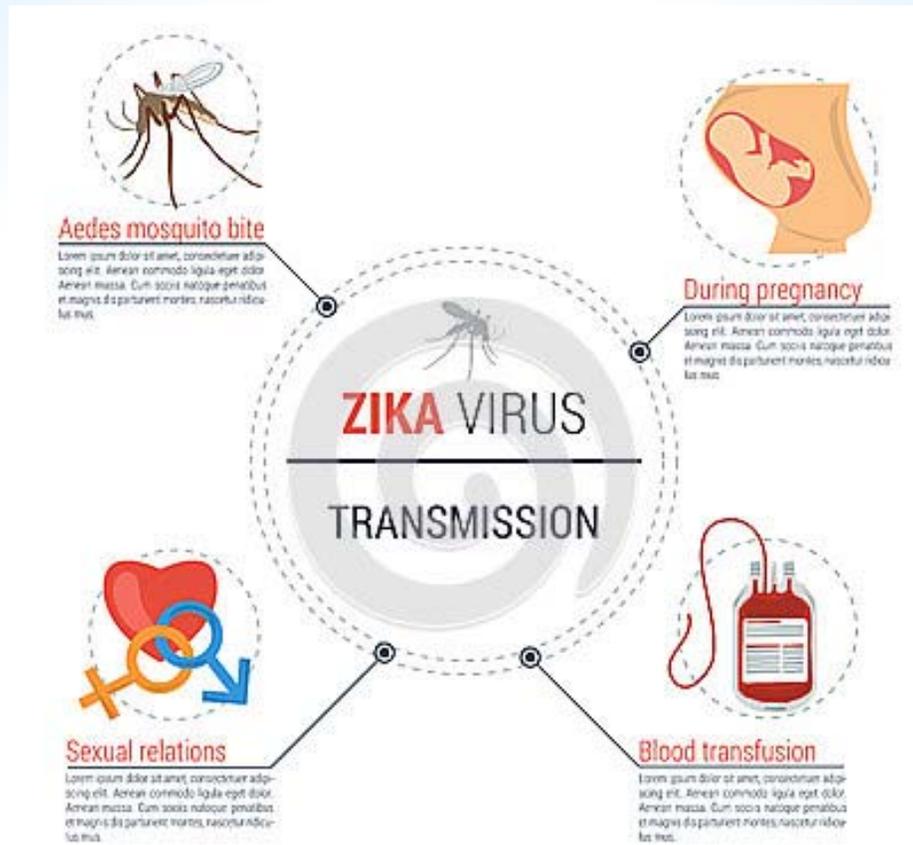
Fields Virology Textbook, 4<sup>th</sup> edition, 2001

# Taxonomy

- \* Zika is spread mostly by the bite of an infected Aedes species mosquito (Ae. africanus, Ae. aegypti and Ae. albopictus)
- \* These mosquitoes are aggressive daytime biters and can also bite at night
- \* Spread also by sexual contact with infected person during viremia



## What We Know



[dreamstime.com](http://dreamstime.com)

# Transmission

## ZIKA Infection

- \* Produces viremia in monkeys but no illness in monkeys
- \* Similarly, infections in humans are asymptomatic in most cases (about 80%)
- \* Prevalence of human infection up to 50% in many areas of Africa and in parts of Asia
- \* In contrast, human disease had been rarely reported:
  - \* First case was described by a researcher who fell ill in 1964
  - \* By 2001, only 14 human cases had been reported

## ZIKA Fever

- \* Incubation Time: around 3-12 days
- \* Mild symptoms, lasting < 7 days (self-limiting):
  - \* Fever
  - \* Malaise
  - \* Headache
  - \* Conjunctivitis
  - \* Joint pain
  - \* Maculopapular rash
- \* Closely resembles symptoms of Dengue and Chikungunya



# Symptoms

## Several Decades

- Sporadic cases or small outbreak clusters
- No association with birth defects reported

## 2007

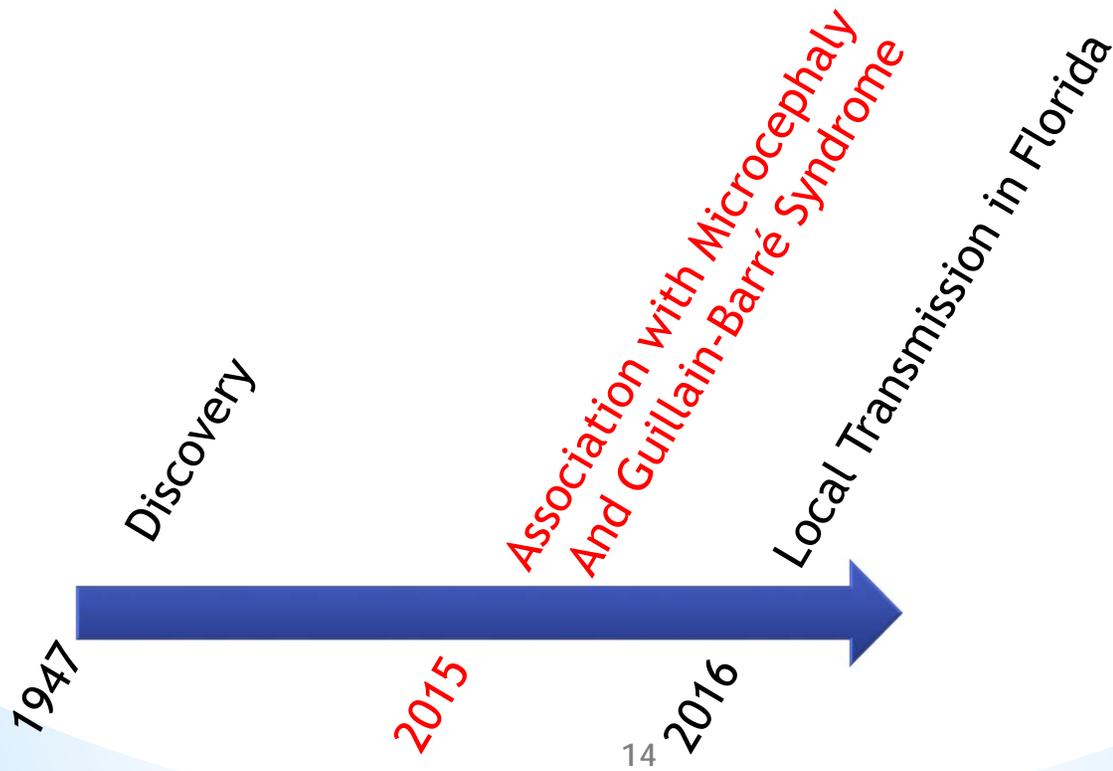
## First Large Outbreak

- First large Zika outbreak in humans (Micronesia)
- An estimated 73% of Yap residents are infected with Zika virus
- About 18% developed Zika disease
- Lack of immunity in the island's population (no herd immunity)
- Underreporting, due to the clinical similarities of (mild) illness symptoms associated with Zika, Dengue, and Chikungunya infections might also account for previous Zika outbreaks being overlooked



Credit: United States Air Force

# Timeline



## ZIKA and Pregnancy

- \* Infections during first trimester and early second trimester can cause fetal abnormalities in some babies
- \* Most prominent feature is microcephaly, a smaller-than-normal head size
- \* Infection during third trimester is associated with birth defects other than microcephaly
- \* Some babies develop a constellation of severe birth defects, called fetal brain disruption syndrome



## Fetal Brain Disruption Syndrome

## Rapid Spread of Zika Virus in the Americas:

- \* Other birth defects even without microcephaly:
  - \* Seizures
  - \* Developmental delay
  - \* Contractures
  - \* Abnormal eye exams

*First insect-borne disease with a proven link to serious birth defects*

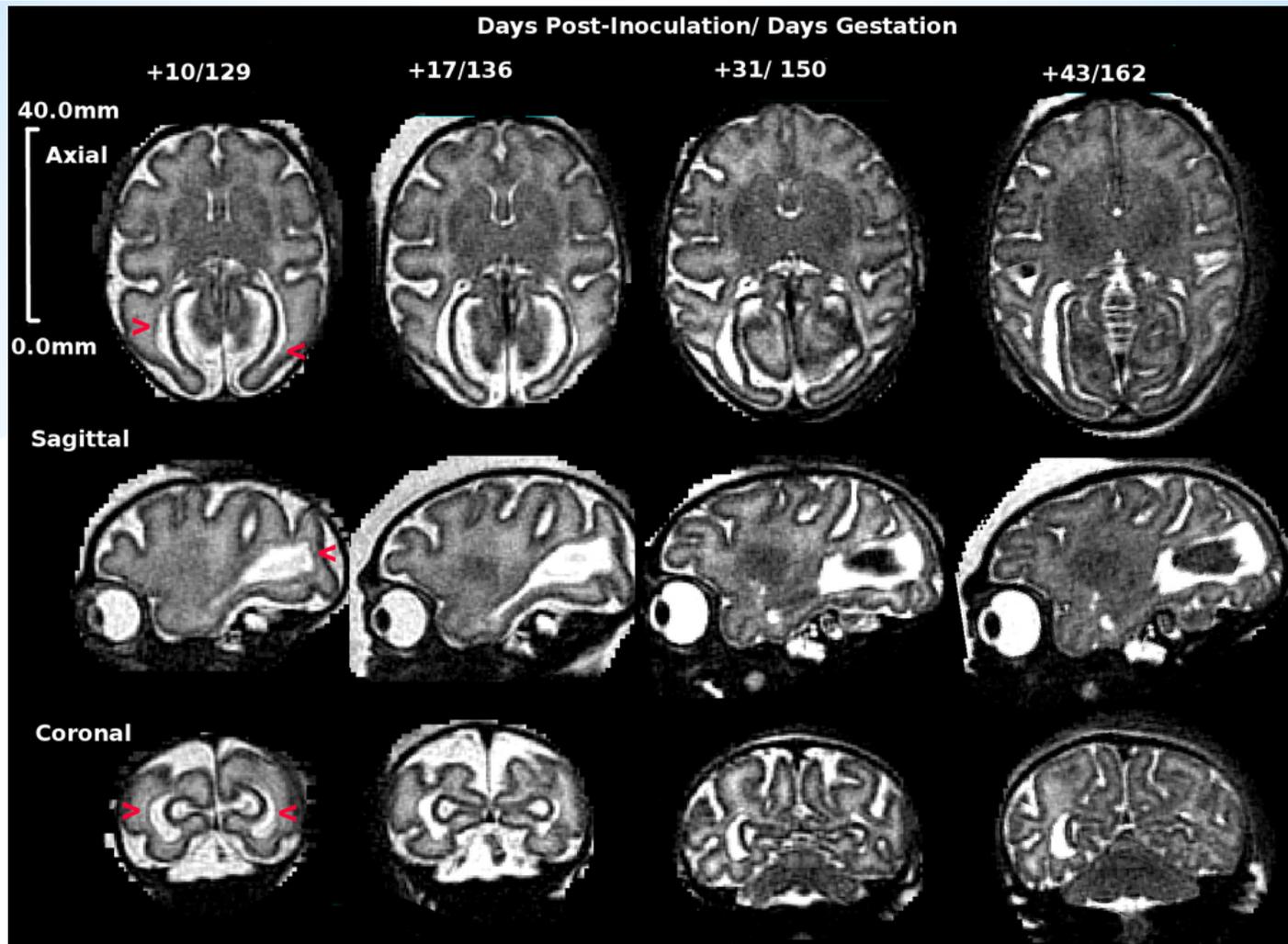
Sonja A. Rasmussen *et al.* Zika Virus and Birth Defects – Reviewing the Evidence for Causality. *N Engl J Med* 2016; 374:1981-1987

# Congenital Zika Infection

- \* In March 2015, scientists at UW launched an experiment that infected a pregnant, 9-year-old macaque with the Zika virus
- \* The monkey mother showed no signs of illness, but very quickly – within 10 days of infection – the fetus developed brain damage similar to that seen in human babies affected by Zika

Nature Medicine, September 12, 2016

**Evidence**



*Brain damage in a pigtail macaque monkey fetus from 10 days (left column) to 43 days (right column) after its mother was infected with Zika virus. The arrows point to the white-matter lesions – the areas outside the white areas at the back of the skull – also seen in human babies infected with Zika in utero. (Courtesy of Nat Med, 9/12/2016)*

## Treatment

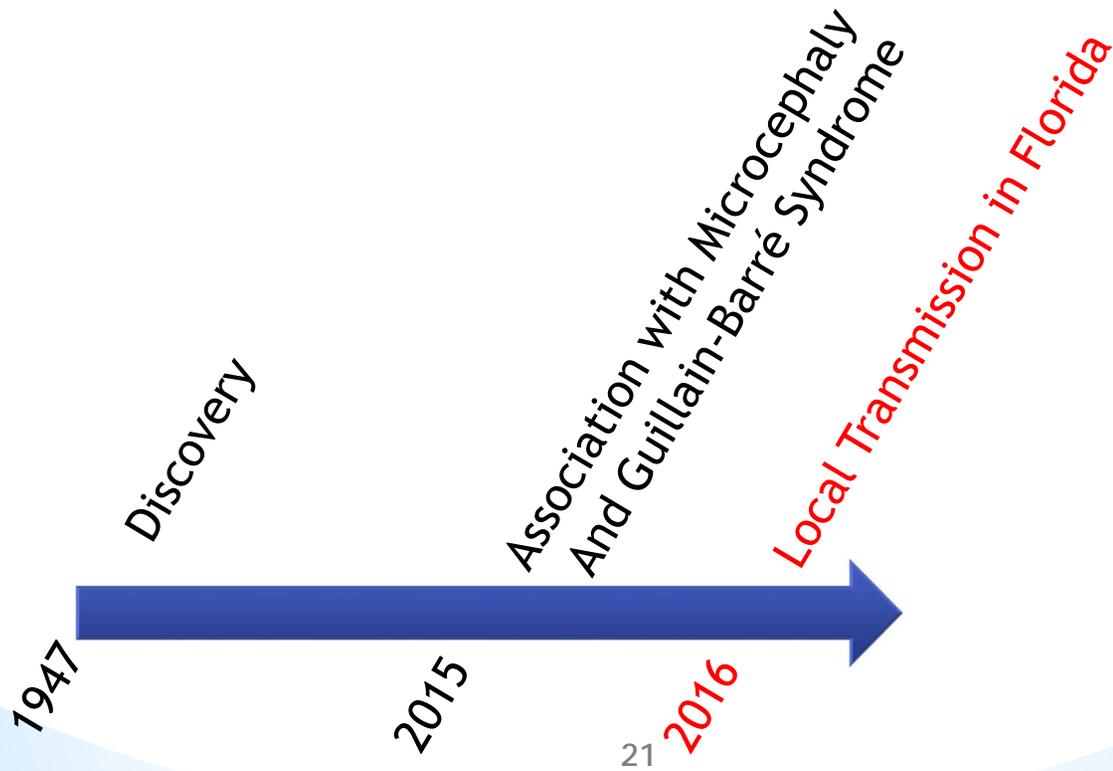
- \* No virostatic drugs are yet available
- \* No specific treatment
- \* Supportive therapy:
  - \* Rest
  - \* Fluids
  - \* Antipyretics
  - \* Analgesics

# Treatment

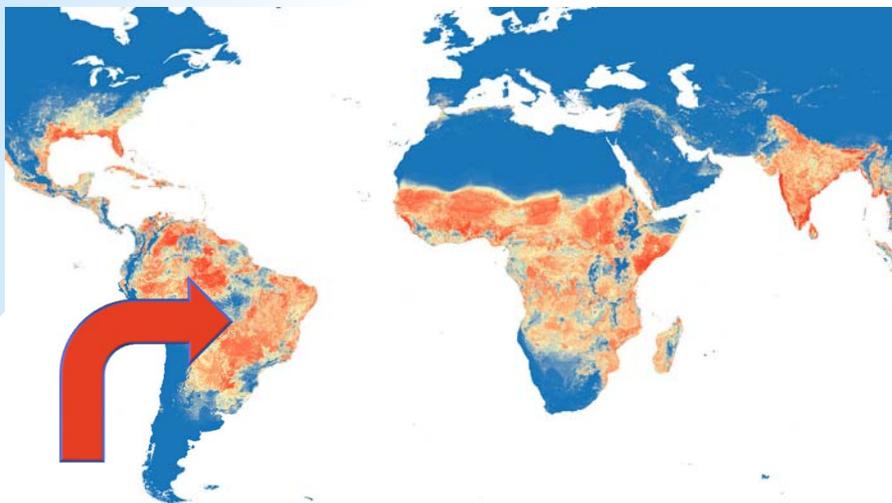
- \* Prevention is key!
- \* Currently no vaccine is available yet but a Phase 1 clinical vaccine study is underway at NIAID
- \* Avoidance of mosquito bites (insect repellents, travel restrictions, etc.)
- \* No unprotected sex with persons who traveled to endemic area
- \* Blood supply in the US:
  - \* Starting in November 2016, blood products in all states need to be screened for Zika virus
    - \* By end of August 2016, testing required in Florida and Puerto Rico
    - \* By end of September 2016, testing required in Alabama, Arizona, California, Georgia, Hawaii, Louisiana, Mississippi, New Mexico, New York, South Carolina and Texas
    - \* <http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMissues/ucm485199.htm#blood>

# Prevention

# Timeline



\* Active transmission of Zika virus now in 50 countries



In Brazil, as many as 1.3 mio patients were infected

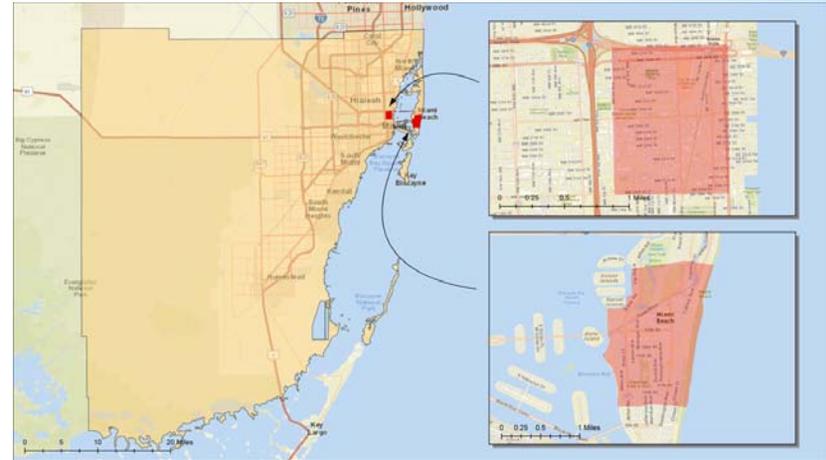
\* September 12, 2016

\* Countries with confirmed local transmission: Chile, Brazil, Colombia, Suriname, El Salvador, Mexico, Panama, Venezuela, Honduras, French Guiana, Martinique, Puerto Rico, Bolivia, Saint Martin, Haiti, Barbados, U.S. Virgin Islands, Dominican Republic, Nicaragua, Jamaica, Curacao, Costa Rica, Republic of Trinidad and Tobago, Aruba, Bonaire, Saint Vincent and the Grenadines, France\*, Canada\*, New Caledonia, Sint Maarten, Laos, Philippines, Italy\*, Cuba, Dominica, Bangladesh, Vietnam, Saint Lucia, Belize, Papua New Guinea, Portugal\*, Republic of Nauru, Grenada, Peru, Saint Barthélemy, Germany\*, Argentina, Anguilla, Spain\*, Guinea-Bissau, Sint Eustatius, Saba, Turks and Caicos, Antigua and Barbuda, United States, Cayman Islands, The Bahamas, Singapore, British Virgin Islands, Malaysia, Netherlands\*

# Worldwide Epidemic



- \* In July this year, the Florida Department of Health has identified two areas where Zika is being spread by mosquitoes:
- \* Both are in Miami-Dade County
  - \* One in Wynwood, and
  - \* One in Miami Beach
- \* As of yesterday, 70 Floridians have been infected



# Spreading to the US

- \* Anticipation that Zika will be found in areas that saw Chikungunya in 2015
- \* Recent outbreaks in the continental US of Chikungunya and Dengue, which are spread by the same type of mosquito, have been relatively small and limited to a small area
- \* Endemic transmission of Zika in any part of the continental U.S. is therefore not expected
- \* Influence of climate change remains to be seen

## Estimated Risk of Zika in the US

	US States	US Territories
Locally acquired mosquito-borne cases	43	15,809
Travel-associated cases	2,920	60
Laboratory acquired cases	1	0
Sum	2,964	15,869
Guillain-Barré syndrome	7	31

Reported to ArboNET for January 01, 2015 - September 7, 2016

# Disease Burden in US

- \* Almost 90% of the 1,709 confirmed cases of congenital microcephaly or birth defects in Brazil are reported from the Northeast of the country. Are other factors contributing?
- \* Virus has not changed - why haven't we seen these severe birth defects before?
- \* What are the virus's vectors and reservoirs, pathogenesis, genetic diversity, and potential synergistic effects of co-infection with other circulating viruses?

## Remaining Questions

# Zika Lab Testing

Sarah M. Humphrey, CHES  
Oregon State Public Health Laboratory  
Public Health Division

- \* Generally, testing is recommended for:
  - \* Symptomatic individuals, including pregnant women, with possible Zika exposure via travel to a Zika-affected area or unprotected sex with a partner who traveled to a Zika-affected area
  - \* Individuals who are diagnosed with Guillain-Barré syndrome with possible Zika exposure
  - \* Pregnant or post-partum women with evidence of Zika-compatible abnormalities upon ultrasound or delivery

**Who should be tested  
for Zika virus?**

- \* Testing is also available for asymptomatic pregnant women with possible Zika exposure and infants born to a mother with Zika infection
- \* Time frames for testing after possible exposure or symptom onset apply.

**Who should be tested  
for Zika virus?**

- \* Commercial Laboratories
  - \* RT-PCR and/or MAC-ELISA
  - \* Enquire with your reference labs about services offered and processes.
- \* Oregon State Public Health Laboratory (OSPHL)
  - \* RT-PCR and MAC-ELISA
  - \* Testing must be approved by the Local Public Health Authority of the patient's residence, who may consult with State Acute and Communicable Disease Prevention (ACDP)
- \* Testing authorizations require labs to follow CDC testing guidance and algorithms.

**Who is performing  
Zika virus testing?**

- \* OSPHL uses Trioplex RT-PCR
  - \* Results for: Zika virus, Dengue virus, and Chikungunya virus
- \* Commercial labs have ability to test Dengue IgM, but OSPHL does not.

## What about Dengue and Chikungunya?

1. Review “whom to test” and “information to collect.”
  - \* Available at: <http://bitly.com/zikaoregon>
2. Contact the Local Public Health Department of the patient’s residence to review symptoms and risk factors.
  - \* In Oregon: [www.healthoregon.org/lhddirectory](http://www.healthoregon.org/lhddirectory)
3. If approved, collect specimens and transport to the OSPHL.
  - \* Include two required forms.
  - \* Specimen criteria available at: <http://bitly.com/zika-lab>
  - \* Check with your central or referral lab - they may want specimens transferred through their labs.

# Public Health Testing Process

## Symptomatic Patient

Time From Symptom Onset	What to Collect	What Tests to Expect
< 14 days	3mL each of urine AND serum	PCR If needed: <ul style="list-style-type: none"> <li>dengue IgM and Zika IgM</li> <li>PRNT*</li> </ul>
14 days to 12 weeks	3mL of serum	Zika IgM If needed, OSPHL to coordinate PRNT
	3mL of serum	Chikungunya IgM, dengue IgM If needed, PRNT

\*PRNT - Plaque reduction neutralization test

# What Specimens to Collect and When?

## Symptomatic Pregnant Patient

Time From Symptom Onset	What to Collect	What Tests to Expect
< 14 days	3mL each of urine AND serum	PCR If needed: <ul style="list-style-type: none"> <li>dengue IgM, Zika IgM</li> <li>PRNT</li> </ul>
14 days to 12 weeks	3mL of urine AND serum	Zika IgM If needed: <ul style="list-style-type: none"> <li><u>PCR</u></li> <li>PRNT</li> </ul>
	3mL of serum	Chikungunya IgM, dengue IgM If needed, PRNT

**What Specimens to Collect and When?**  
(Cont'd)

## Asymptomatic Pregnant Patient

Time From Most Recent Exposure	What to Collect	What Tests to Expect
< 14 days	2mL of urine AND serum	PCR on serum and urine If needed: <ul style="list-style-type: none"><li>• Zika MAC-ELISA on serum</li><li>• PRNT on serum</li><li>• Second specimen if negative PCR</li></ul>
14 days to 12 weeks	2mL of urine AND serum	Zika MAC-ELISA on serum If needed: <ul style="list-style-type: none"><li>• PCR on serum and urine</li><li>• PRNT on serum</li></ul>

## What Specimens to Collect and When? (Cont'd)

- \* Work with local or state public health department for:
  - \* Cases that don't fit these categories
  - \* Testing due to neonatal death or infants

## Other Specimens

- \* Zika virus Information for Oregon Healthcare Providers  
<http://bitly.com/zikaoregon>
- \* Oregon Local Health Department Contact Information  
[www.healthoregon.org/lhddirectory](http://www.healthoregon.org/lhddirectory).
- \* OSPHL specimen collection and submission instructions  
<http://bitly.com/zika-lab>

## All Website Links