# Zika virus disease: <u>What you need to know.</u>

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## Zika: What you need to know.

Outline:

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- 2. What is Zika virus?
- 3. Where did Zika virus come from?
- 4. How is Zika transmitted?
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# Zika: What are viruses v. bacteria?

### **Infectious pathogens:**

- 1. <u>Prions</u>: infectious proteins only, no nucleic acids (human mad cow disease).
- 2. <u>Viruses</u>: inner nucleic acid core, DNA (herpes) or RNA (Zika, HIV) + an outer glycoprotein envelope; reproduce by replication. <u>Mosquito</u> vectors.
- 3. <u>Bacteria</u>: nucleus + intracellular organelles; binary fission. <u>Few mosquito vectors</u>.\*
- 4. <u>Protozoa</u>: nucleus, asexual reproduction (malaria). <u>Mosquito</u> vectors.
- 5. <u>Parasites</u>: sexual reproduction (heartworms). <u>Mosquito</u> vectors.



Zika virus



\* Potential prospect for genetic vector control.

# What is Zika virus?

- 1. Zika virus is a positive, single-stranded <u>RNA flavivirus</u> (Family Flaviviridae) closely related to other <u>flaviviruses</u>, such as yellow fever, dengue, & West Nile virus (WNV).
- 2. Flaviviruses are also known as arboviruses because they are transmitted by <u>arthropods</u>, specifically by mosquitoes.
- 3. Yellow fever, dengue, & Zika viruses are transmitted by <u>Aedes</u> species mosquitoes & WNV by <u>Culex</u> species mosquitoes.



## Where did Zika virus come from?

- First discovered in <u>1947</u> in a rhesus monkey in the <u>Ziika forest of</u> <u>Uganda</u>, Zika virus was initially dismissed as a cause of a <u>short-</u> <u>term, mild febrile illness</u> with <u>fever</u>, joint pain, rash & conjunctivitis confined to 1<sup>st</sup> to Africa & later to Southeast Asia.
- 2. Six decades later Zika erupted suddenly outside of its endemic regions on the <u>South Pacific island</u> of Yap in 2007.



The "Ziika" Forest Research Station, Uganda, abandoned since the early 1970s.



## Zika's Odyssey from Africa to the Americas





1. <u>Africa, SE Asia, (1947-1978)  $\rightarrow$  Yap (2007)</u>: fever, rash, joint pain, red eye  $\rightarrow$  2. <u>French</u> <u>Polynesia (2013)</u>: 41 Guillain-Barré (GBS) + 8 microcephaly  $\rightarrow$  3. <u>Brazil (2014)</u>: > ? GBS + 4,000 microcephaly  $\rightarrow$  4. <u>Puerto Rico (2015)</u>  $\rightarrow$  1 GBS + 1 microcephaly  $\rightarrow$  5. <u>US (2016)</u>  $\rightarrow$  1 GBS + 1 microcephaly (imported Zika only at present).

## How is Zika transmitted?

- 1. Several Aedes species are now confirmed as capable of transmitting Zika virus by RT-PCR: Aedes aegypti, A. africanus, A. coargenteus, A. luteocephalus, A. furcifer, A. vitattus.
- 2. Aedes hensilii was suspected as the vector on Yap Island, 2007.
- 3. Aedes albopictus, a highly competent vector of dengue & chikungunya, is distributed worldwide, & should be considered a competent Zika vector.
- 4. A. polynesiensis, is distributed throughout Oceania & should also be considered a competent Zika vector.





# **Aedes Mosquito Misconceptions**

Ref: Turell M, Lundstrom J. Am J Trop Med Hyg 1990; 43: 543-50.

- I. "The mosquitoes are inactive in our area at this time."
- Research has confirmed that dengue & other virus transmission can occur at temps as low as 50° F., but <u>↑ temps & wide fluctuations in daytime temps</u> (≥ 20 ° F) will ↑ transmission & ↓ extrinsic incubation time (the time for virus to become infective in the mosquito).
- Extrinsic incubation time for dengue is 12 days & around 10 days for Zika. Incubation time for dengue virus is ↓ to 7 days at temps ≥ 89 ° F.
- In short, virus transmission ↑as temps ↑, especially when there is a wide variation in daytime temps.

- II. "The mosquitoes only bite during dawn and dusk."
- 1. Female Aedes mosquitoes are <u>aggressive daytime biters</u>, & prefer to bite people for their blood meals more than animals.
- 2. Aedes mosquitoes prefer to live around homes because of so many potential breeding sites in <u>standing</u> <u>freshwater containers</u> ranging from potted plant saucers to upturned garbage can lids & abandoned tires.





# How else is Zika transmitted?

#### Zika virus transmission cycle



Zika can be transmitted through blood, but this is an infrequent mechanism. The virus has also been isolated in semen, but person-to-person sexual transmission is unconfirmed.

Source: PAHO/WHO

1. <u>Congenital transmission</u>: mother-to-baby. Breastfeeding is OK.

- 2. Sexual transmission: is <u>unprecedented for an arbovirus</u>; male-to-female & male-to-male. Zika remains capable of replication in <u>semen</u> from <u>2-8</u> <u>months</u> but only remains viable in <u>blood 7 days</u> & <u>urine 10 days</u>.
- 3. <u>How else?</u> Blood & organ transplant transmission likely, just like WNV.

BBC

# Zika: What are the symptoms? Complications?

- 1. The Zika virus causes <u>no symptoms</u> <u>in most people (80%)</u> who can still transmit the disease by mosquito bite, sex, blood & organ donation, & to their fetuses.
- 2. A <u>few people (20%)</u> will have <u>fever</u>, joint pain, measles-like rash, & red <u>eyes</u>.
- 3. Major neurological complications include <u>microcephaly</u> (small head) & eye abnormalities in fetuses & <u>Guillain-Barré</u> syndrome (an autoimmune-mediated ascending paralysis) in adults. Other neurological complications may occur.



## **Descriptive Epidemiology of Zika in the US Today:**

## Who, What, When, & Where? Source: CDC, May 18,2016

Zika virus disease in US states:

- 1. Imported (travel-associated) cases: <u>544</u>
- 2. Locally acquired, mosquito-borne: **0**
- 3. Among the 544 cases: 157 in pregnant women, 10 sexually transmitted, 1 case of GBS, 1 microcephalic neonate.
- 4. States: <u>NY</u> 114, <u>FL</u> 109, CA 44, TX 35 (LA 4).

Zika virus disease in US territories:

- 1. Imported (travel-associated) cases: 4
- 2. Locally acquired, mosquito-borne: 832
- 3. Of the 836 cases: 122 in pregnant women, 5 with GBS, 1 microcephalic neonate.
- 4. Territories (mostly locally acquired): Puerto Rico 803, US Virgin Is. 15, American Samoa 14.



# All countries & territories (N = 47) with active Zika virus transmission. Source: CDC, May 11,2016.



# How is Zika diagnosed?





1. <u>Serological tests</u>: <u>Screening acute-</u> <u>convalescent serum tests for anti-Zika</u> <u>antibodies</u>: (1) <u>ELISA</u> to detect IgM Abs against Zika; but cross-reacting AB's from dengue, WNV, & possibly chikungunya are problematic; (2) a <u>blood/urine Dip Stix</u> <u>ELISA</u> for anti-Zika IgM AB's is in R&D. Greater sensitivity than specificity.

2. <u>Molecular tests</u>: <u>Confirmatory molecular</u> <u>serum & virology tests</u>: (1) <u>RT-PCR</u> to detect Zika RNA, Quest Diagnostics, May 2016; (2) an <u>improved rapid RT-PCR</u> to differentiate RNA from Zika, dengue, & chikungunya is in R&D at CDC; (3) <u>virus isolation</u> is possible, time-consuming, & only requires a BSL-2; (4) recovery of the entire Zika viral <u>genome</u>. Greater specificity than sensitivity.

# **Can Zika be treated? Prevented?**

- 1. There are <u>no specific antiviral</u> <u>treatments</u> for Zika virus disease.
- The only effective national strategies to immediately prepare the US for the Zika virus invasion are for everyone to undertake (1) <u>vector control measures</u> & (2) <u>personal protection from mosquito</u> <u>bites</u>.
- 3. In addition to a basic knowledge of the Aedes mosquito vectors & their biting behaviors, a constant practice of (1) conducting <u>simple vector control</u> <u>measures</u> & (2) selecting the <u>best</u> <u>chemical & physical mosquito repellents</u> are the major requirements needed to prepare citizens to repel the Zika threat.





### Integrated vector control approach for mosquito











## How can I protect myself, my family, my neighbors?

### What works for Zika & why?

- 1. <u>Anti-larval environmental</u>: small container breeders, empty/cover.
- 2. <u>Anti-larval chemical</u>: also works.
- 3. <u>Adult targeted spraying</u>: also works.
- 4. <u>Personal protection</u>: air conditioning, screens, repellents all work. *Aedes* are daytime biters, prefer humans to animals, & are attracted to dark colors; so wear <u>khakis</u> (Persian-Urdu for "*dusty*", 1<sup>st</sup> uniforms, British cavalry, India 1850s).
- 5. <u>Legislative controls</u>: 个\$\$ fines for abandoned tires & containers.







## How can I protect myself, my family, my neighbors?

What does not work for Zika & why?

- 1. <u>Anti-larval biological</u>: will not work, containers are too small.
- 2. <u>Adult biological</u>: will not work, adults are peri-domestic dwellers.
- 3. <u>Adult open-space spraying</u>: missed targets as larvae become adults in clogged gutters, pot plants, tires, graveyard vases; & not in marshes.
- 4. <u>Adult genetic</u> is attractive, but can <u>backfire</u>. Bird & reptile predators could be infected & killed by introduced pathogens? Irradiated sterile males & endosymbionts (*i.e.*, commensal bacteria in insect's gut) may be the safest genetic controls.



# What are <u>endosymbionts</u>? What is their role in <u>genetic vector control</u> for ARBOR-IDs?





# What about a vaccine, like polio?

- 1. Although virologists & vaccinologists have recent experiences with other <u>investigational</u> <u>flavivirus vaccines for West Nile</u> and <u>dengue</u>, a Zika virus vaccine is many months-to-years away for the following reasons.
- 2. A Zika vaccine that is rushed into production for mass-administration prior to trial testing could precipitate <u>Guillain-Barré syndrome</u>; or be inactivated by <u>cross-reacting antibodies</u> from prior flaviviral experiences with dengue, West Nile virus, chikungunya, yellow fever, even, the yellow fever vaccine, up to 10+ years ago.
- 3. A <u>live virus Zika vaccine is contraindicated</u>, especially in pregnant women.



## Prevention of Zika: <u>Topical Insect Repellents</u>

**Ref:** <u>Diaz JH</u>. Chemical and plant-based insect repellents: Efficacy, safety, and toxicity. *Wilderness & Environmental Medicine* 2016 Mar;27(1):153063. Doi:10.1016/j.wem.2015.11.007. Epub 2016 Jan 27.

<u>Repellent</u>	<u>Brands</u>	<u>Strength %</u>	Duration (hrs)	<u>Efficacy against</u>	<u>Comments</u>
DEET (N, N-diethyl-m- toluamide)	Off® Cutter® Sawyer®	5-100% Rec: 20- 35% max	6-12 hrs	Mosquitoes, fleas, chiggers, gnats, flies (< picaridin), ticks (use DEET + permethrin)	≤ 30% for children > 2 months; can damage plastic > clothing
Picaridin	Cutter Advanced® Natrapel 8 Hour® Go Ready®	7% 20%	6-12 hrs	<u>Mosquitoes</u> , fleas, chiggers, flies, ticks	No damage to clothing & plastic
Oil of lemon eucalyptus	Cutter Lemon® Repel Lemon®		6 hrs	Mosquitoes	Children < 3 years old-skin sensitive
Permethrin (apply to clothing)	Sawyer Permethrin® Duranone® Ultrathon® Permanone®	NA	2-4 weeks on clothes	<u>Mosquitoes, ticks</u>	Chemical contact dermatitis
IR3535 (plant derived, comes with sunscreen)	Avon Skin Soft® Bug Guard+® Bull Frog®	7.5% 20%	6 hrs	Mosquitoes, gnats	>10% effective
Citronella	Natrapel, Green Ban	NA	<1 hr	Mosquitoes only	Short-term

## What do we not know about Zika? 1.



- 1. Is there an <u>animal reservoir of Zika virus disease</u> like there is for WNV & sylvancycle YF? Would you recommend eradication of these animals, if identified later?
- 2. How has the <u>Zika viral genome changed itself</u> over time (mutation v. reassortment?) to be able to cross the placenta and cause teratogenic effects, similar to those of toxoplasmosis, rubella, and cytomegalovirus (CMV), specifically microcephaly, intracranial calcifications, & chorioretinal & optic nerve damage?
- 3. Why do <u>some pregnant women infected with Zika have babies with microcephaly</u> & underdeveloped brains & others do not? Would you recommend avoiding pregnancy until 2018 like the Salvadorian MOH has?
- 4. Is the <u>timing of infection during pregnancy</u> critical? Apparently, the earlier the more severe the birth defects, with a <u>critical period at 6-12 weeks of gestation</u>. What would you tell someone who is pregnant and just returned from a Caribbean vacation?

## What do we not know about Zika? 2.



- 1. Does <u>sexual transmission of Zika virus pose different or even greater risks for</u> <u>congenital infections</u> than that of mosquito-borne transmission of Zika virus? What do you recommend for men who have traveled to an area of Zika transmission who have a pregnant sex partner?
- 2. What are the <u>risks of acute post-viral Guillain-Barré syndrome</u> (GBS) in Zika-infected persons, most of whom will be asymptomatic? Like Zika, GBS can occur after dengue, YF, & WNV; or even after the "flu".
- 3. Why is there so much <u>cross-reactivity on serologic screening</u> now? There is an immediate need for better molecular diagnostics to screen for Zika, WNV, dengue, & chikungunya simultaneously. What test would you recommend—the more sensitive one or the more specific one?
- 4. If 4 M persons are anticipated to be infected by the end of 2016, <u>how many</u> <u>microcephalic babies</u> with severe brain damage will be born & require prolonged, expensive medical care? What will the societal burdens & international costs be?
- 5. What <u>flaviviral vaccines are now in use or development</u> that industry can piggyback on to develop a Zika vaccine ASAP? How about the new JE vaccine or the polyvalent dengue vaccine now in R & D? What about the abandoned WNV & Ebola vaccines? How much will this cost? Is \$1.9 billion enough (\$600/person)?