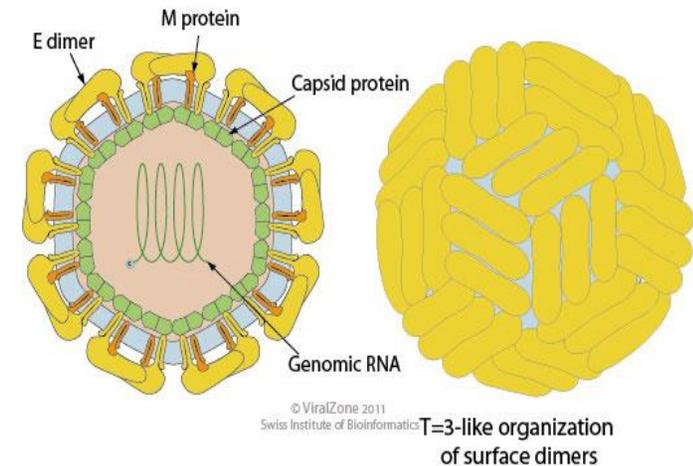


# Zika virus disease:

## What you need to know.

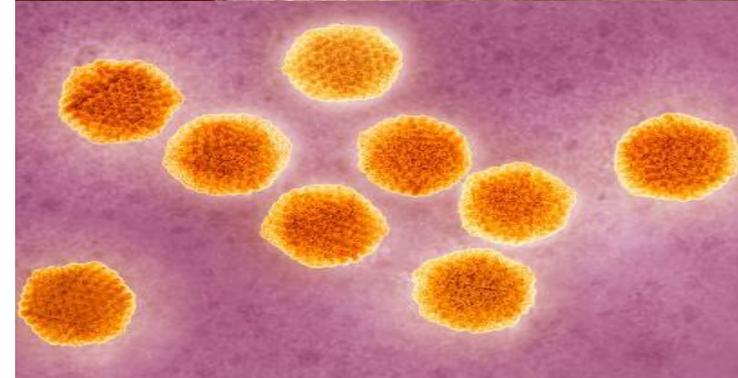
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# Zika: What you need to know.

## Outline:

1. What are viruses v. bacteria?
2. What is Zika virus?
3. Where did Zika virus come from?
4. How is Zika transmitted?
5. What are the symptoms? (Dr. Lopez)  
Complications? (Drs. England & Maupin)
6. How is Zika diagnosed? (Dr. Lopez)
7. Can Zika be treated? Prevented?
8. How can I protect myself & others?
9. What about a vaccine, like polio?
10. What do we not know about Zika?



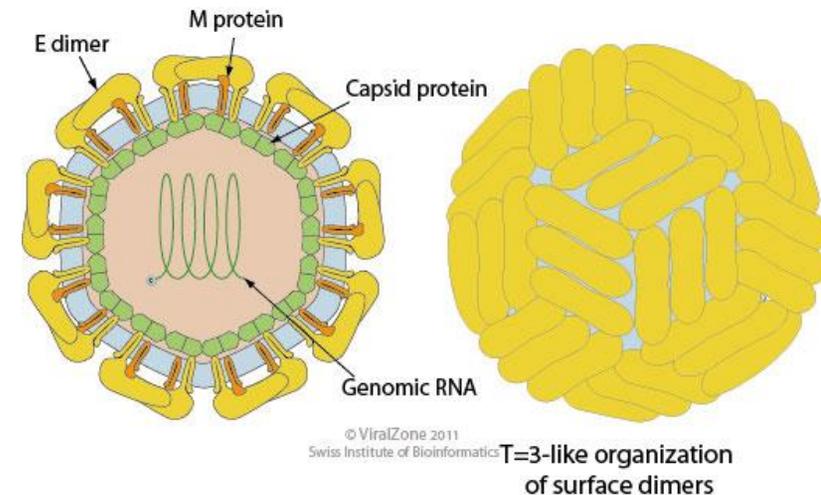
# Zika: What are viruses v. bacteria?

## Infectious pathogens:

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



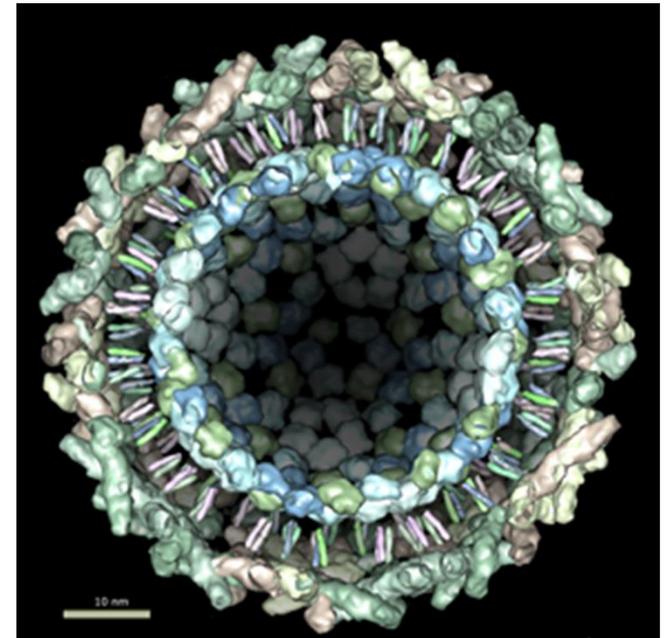
Zika virus



\* Potential prospect for **genetic vector control**.

# What is Zika virus?

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



# Where did Zika virus come from?

1. First discovered in 1947 in a rhesus monkey in the Ziika forest of Uganda, Zika virus was initially dismissed as a cause of a short-term, mild febrile illness with fever, 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 South Pacific island of Yap in 2007.



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



# Zika's Odyssey from Africa to the Americas

How Zika virus spread from Africa



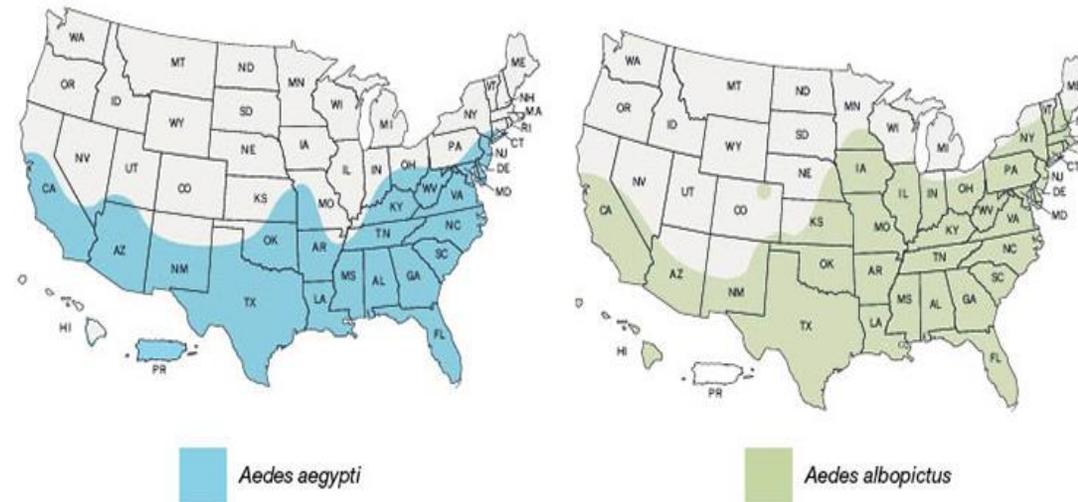
Source: Lancaster University

BBC

1. [Africa, SE Asia, \(1947-1978\)](#) → [Yap \(2007\)](#): fever, rash, joint pain, red eye → 2. [French Polynesia \(2013\)](#): 41 Guillain-Barré (GBS) + 8 microcephaly → 3. [Brazil \(2014\)](#): > ? GBS + 4,000 microcephaly → 4. [Puerto Rico \(2015\)](#) → 1 GBS + 1 microcephaly → 5. [US \(2016\)](#) → 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. coarctatus*, *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.”

1. Research has confirmed that dengue & other virus transmission can occur at temps as low as 50° F., but ↑ temps & wide fluctuations in daytime temps ( $\geq 20^\circ$  F) will  $\uparrow$  transmission &  $\downarrow$  extrinsic incubation time (the time for virus to become infective in the mosquito).
2. Extrinsic incubation time for dengue is 12 days & around 10 days for Zika. Incubation time for dengue virus is  $\downarrow$  to 7 days at temps  $\geq 89^\circ$  F.
3. In short, virus transmission  $\uparrow$  as temps  $\uparrow$ , especially when there is a wide variation in daytime temps.

## II. “The mosquitoes only bite during dawn and dusk.”

1. Female *Aedes* mosquitoes are aggressive daytime biters, & 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 standing freshwater containers ranging from potted plant saucers to upturned garbage can lids & abandoned tires.

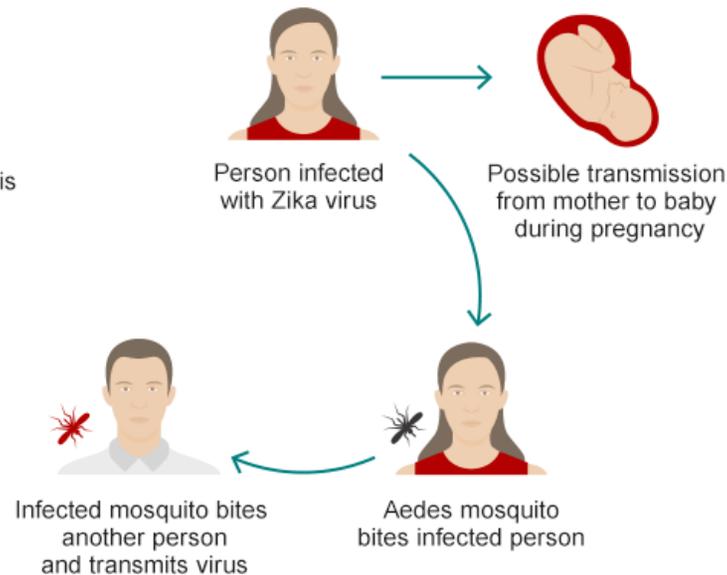


# How else is Zika transmitted?

## Zika virus transmission cycle

### Symptoms

- Fever
- Rash
- Joint pain
- Conjunctivitis (red eyes)



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

BBC

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

# Zika: What are the symptoms? Complications?

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



## Descriptive Epidemiology of Zika in the US Today:

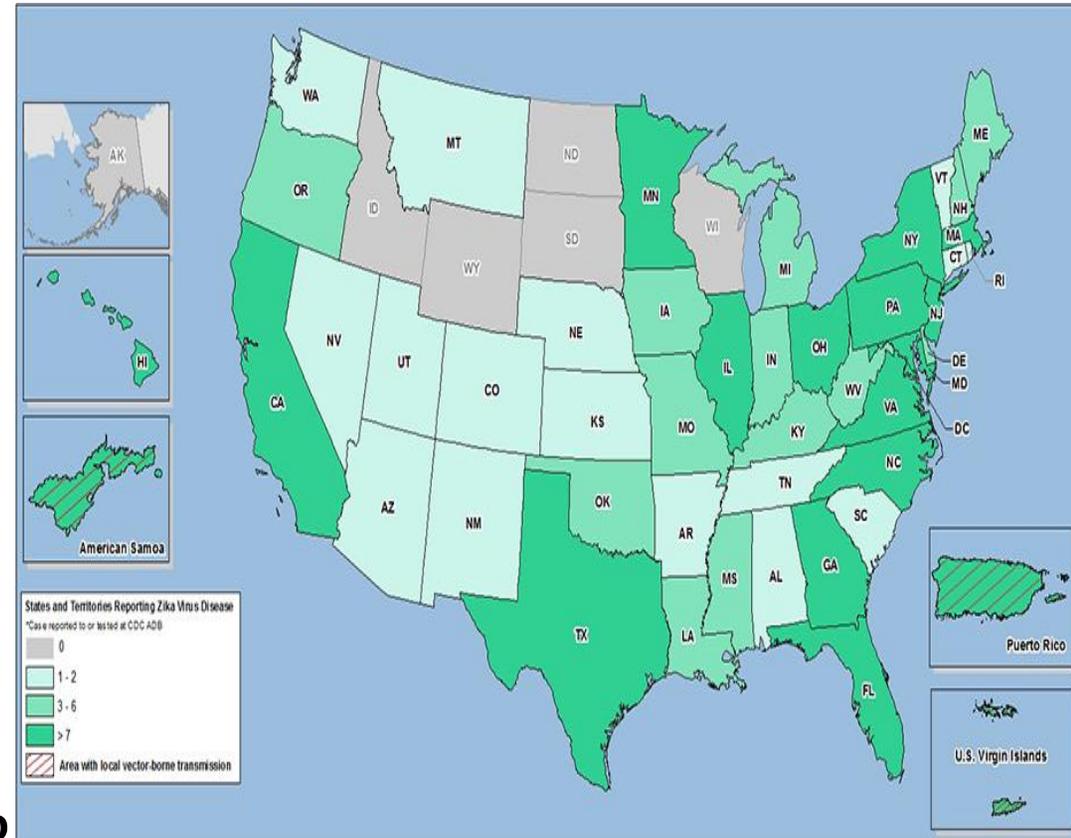
### *Who, What, When, & Where?* Source: CDC, May 18, 2016

#### Zika virus disease in US states:

1. Imported (travel-associated) cases: **544**
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:** **NY** 114, **FL** 109, CA 44, TX 35 (LA 4).

#### Zika virus disease in US territories:

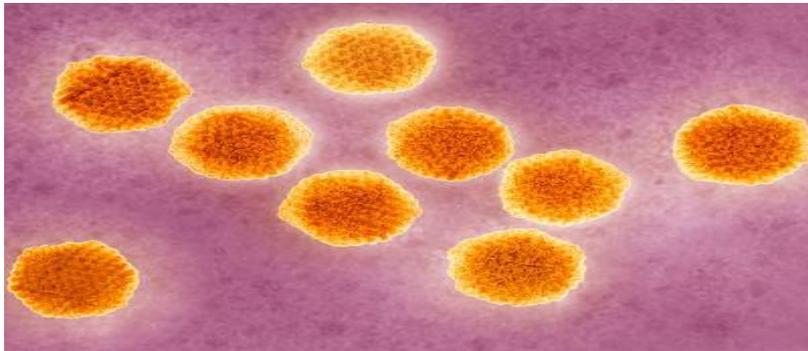
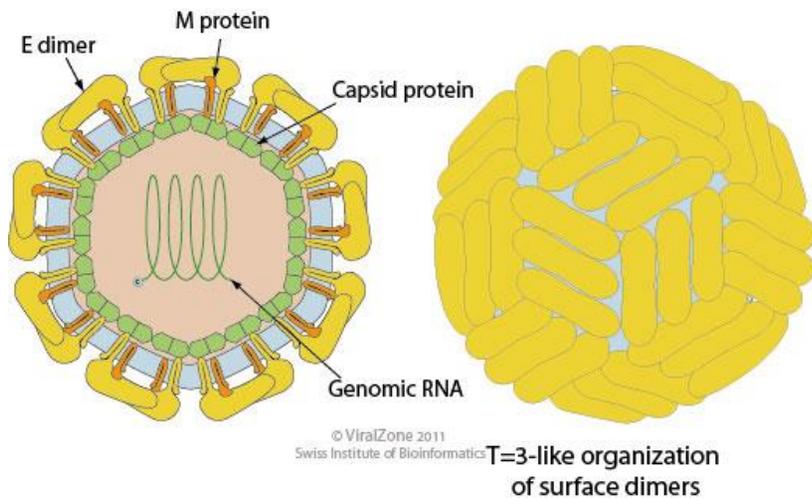
1. Imported (travel-associated) cases: **4**
2. Locally acquired, mosquito-borne: **832**
3. Of the 836 cases: 122 in pregnant women, 5 with GBS, 1 microcephalic neonate.
4. **Territories (mostly locally acquired):** Puerto Rico 803, US Virgin Is. 15, American Samoa 14.



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



# How is Zika diagnosed?



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

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

# Can Zika be treated? Prevented?

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



# Integrated vector control approach for mosquito

## Mosquito Control Measures

### Anti larval measures

1. Environmental control
2. Chemical control
3. Biological control

### Anti adult measures

1. Space sprays
2. Residual sprays
3. Genetic control

### Protection against mosquito bites

1. Mosquito nets
2. Screening
3. Repellents

### Legislative control

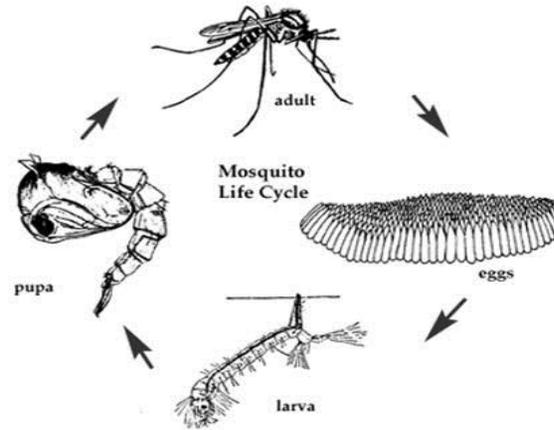
Civic laws



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

## What **works** for Zika & why?

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



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

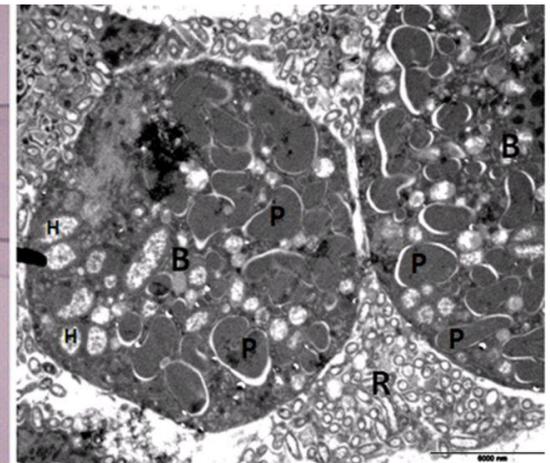
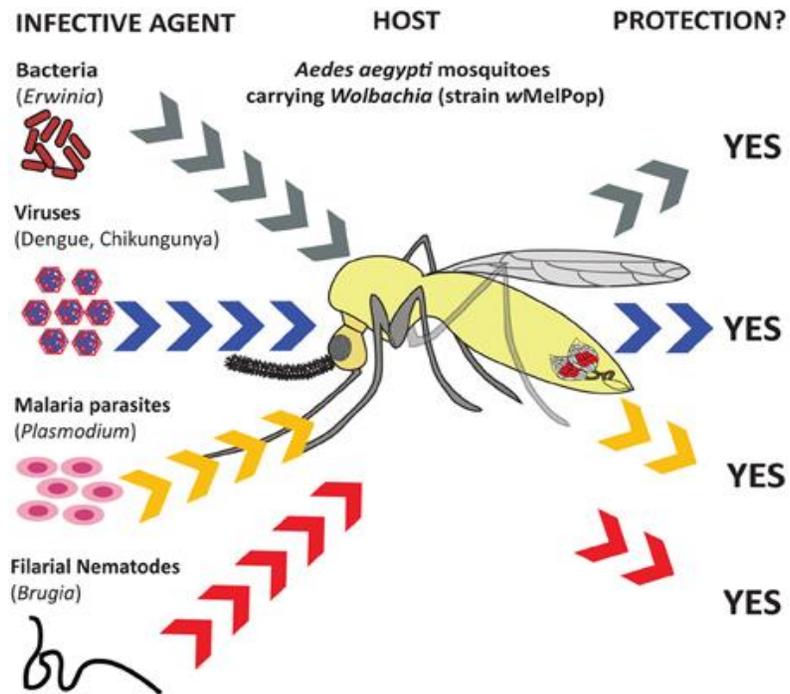
## What does **not work** for Zika & why?

1. **Anti-larval biological**: will not work, containers are too small.
2. **Adult biological**: will not work, adults are peri-domestic dwellers.
3. **Adult open-space spraying**: missed targets as larvae become adults in clogged gutters, pot plants, tires, graveyard vases; & not in marshes.
4. **Adult genetic** is attractive, but can **backfire**. 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.



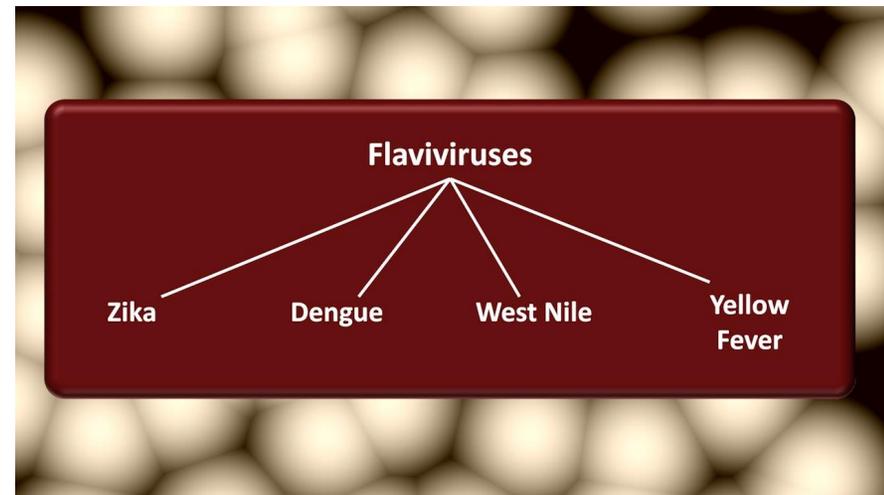
# What are endosymbionts?

# What is their role in genetic vector control for ARBOR-IDs?



# What about a vaccine, like polio?

1. Although virologists & vaccinologists have recent experiences with other **investigational flavivirus vaccines for West Nile** and **dengue**, 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 **Guillain-Barré syndrome**; or be inactivated by **cross-reacting antibodies** from prior flaviviral experiences with dengue, West Nile virus, chikungunya, yellow fever, even, the yellow fever vaccine, up to 10+ years ago.
3. A **live virus Zika vaccine is contraindicated**, especially in pregnant women.



# Prevention of Zika: Topical Insect Repellents

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

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



1. Is there an animal reservoir of Zika virus disease like there is for WNV & sylvan-cycle YF? Would you recommend eradication of these animals, if identified later?
2. How has the Zika viral genome changed itself over time (mutation v. re-assortment?) 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 some pregnant women infected with Zika have babies with microcephaly & underdeveloped brains & others do not? Would you recommend avoiding pregnancy until 2018 like the Salvadorian MOH has?
4. Is the timing of infection during pregnancy critical? Apparently, the earlier the more severe the birth defects, with a critical period at 6-12 weeks of gestation. 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 sexual transmission of Zika virus pose different or even greater risks for congenital infections 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 risks of acute post-viral Guillain-Barré syndrome (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 cross-reactivity on serologic screening 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, how many microcephalic babies with severe brain damage will be born & require prolonged, expensive medical care? What will the societal burdens & international costs be?
5. What flaviviral vaccines are now in use or development 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)?