

CD Rounds

# **Zika Virus:** Adapting responses to a rapidly changing epidemic

Thursday, May 5, 2016

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## Objectives

1. The participant will be able to describe the clinical and epidemiologic features of Zika and its prevention;
2. The participant will learn about the biology and distribution of and public agency responses to invasive *Aedes* mosquitoes in California;
3. The participant will learn about the available diagnostic tests for Zika and other arboviruses.

# Case 1: Dianna

- 40-year-old woman, 40 weeks pregnant
- Traveled to Costa Rica at 30 weeks gestation
- Presented to her obstetrician with total body rash 3 days after return; no fever or other symptoms
- Fetal ultrasound at 36 and 40 weeks GA showed normal head circumference
- Serum for Zika virus testing was collected at 36 weeks
- Results received **on her due date** were positive for anti-Zika virus antibodies by PRNT

# Case 1: Dianna

- Baby born at 40 weeks, 6 days gestation
  - Apgar scores 1min 8/ 5min 9
  - Birth head circumference 35cm, 53 percentile
  - Birth weight 9.3lbs, length 55.75cm
- Specimens collected for Zika testing
  - Placenta, cord blood, cord tissue, neonate blood

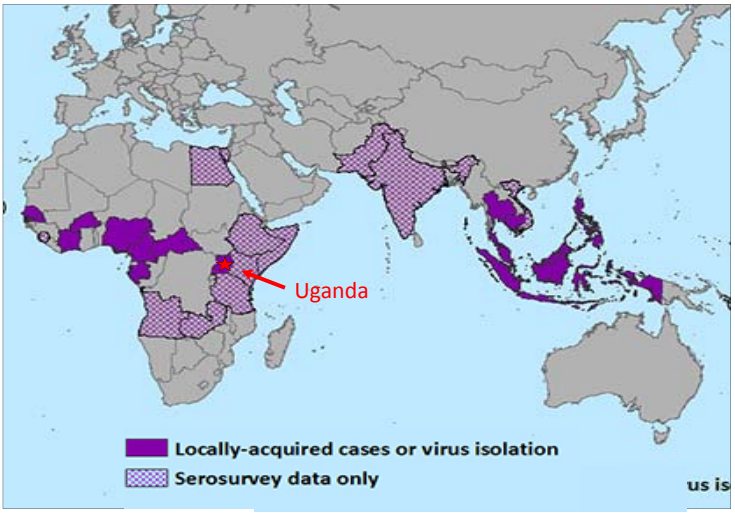
## Overview

- What and where is Zika virus?
- Non-vector-borne Zika virus transmission
- Clinical syndromes and complications
- Laboratory diagnosis of Zika virus infection
- Preventing local Zika virus transmission

## What is Zika Virus?

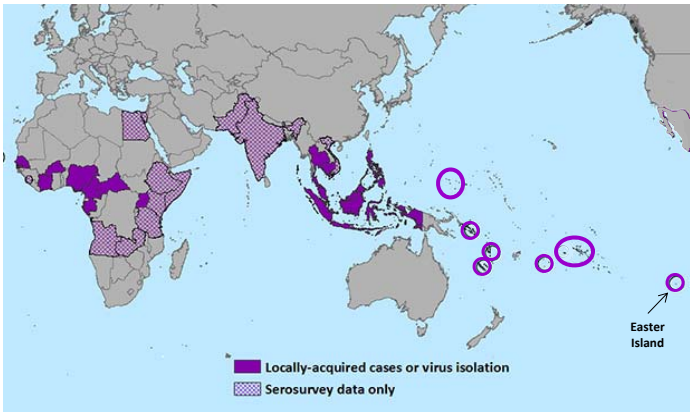
- Zika virus is a mosquito-borne flavivirus similar to dengue, yellow fever, West Nile and Japanese encephalitis viruses
  - *Aedes aegypti* is the primary vector
- First isolated from a sentinel rhesus monkey placed in the Zika Forest of Uganda in 1947
- First isolated from humans in 1952 in Uganda and Tanzania
- Until 2007, only isolated, sporadic cases were reported from Africa and Asia

## Known Geographic Extent of Zika Virus from 1947 through 2006

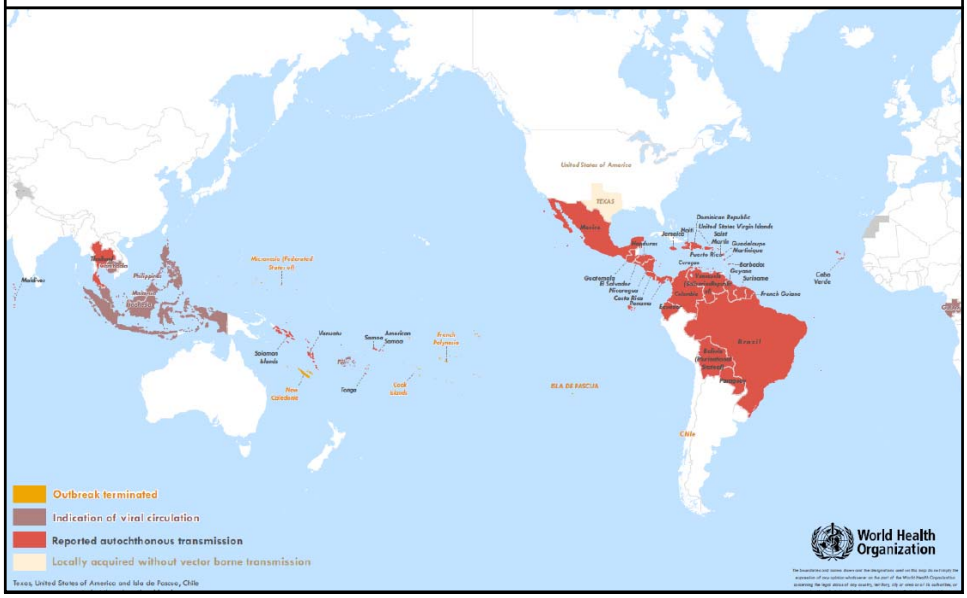



## Zika Spreads to Pacific Islands

- 2007: First major outbreak of Zika on the island of Yap
  - 185 suspect cases
- 2013-2014: Outbreak in French Polynesia
  - 8750 reported cases; 74 with severe neurologic symptoms
- 2014: Cases reported from New Caledonia, Cook Islands, Easter Is.



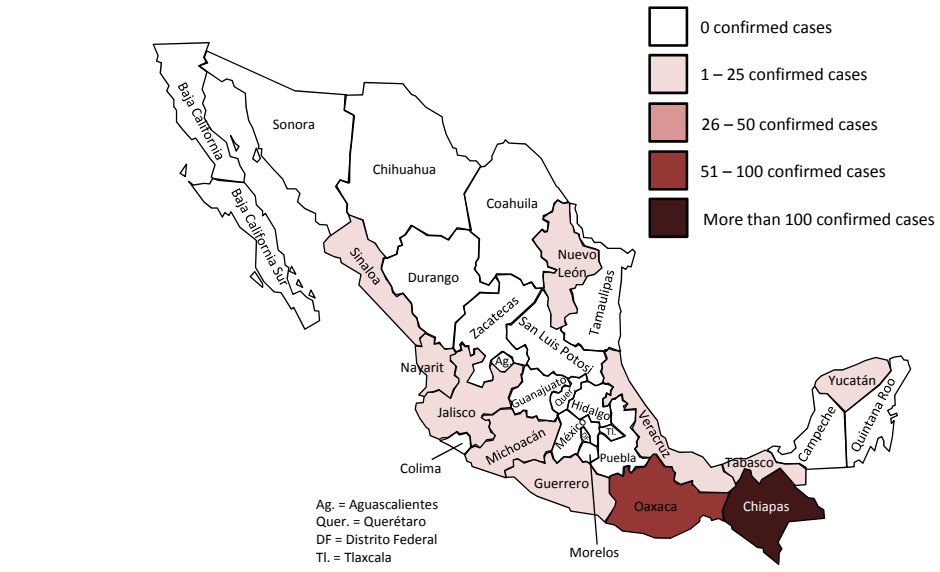
## Countries, Territories and Areas with Autochthonous Zika Virus Circulation (2007-2016)




# Zika Reported from Brazil

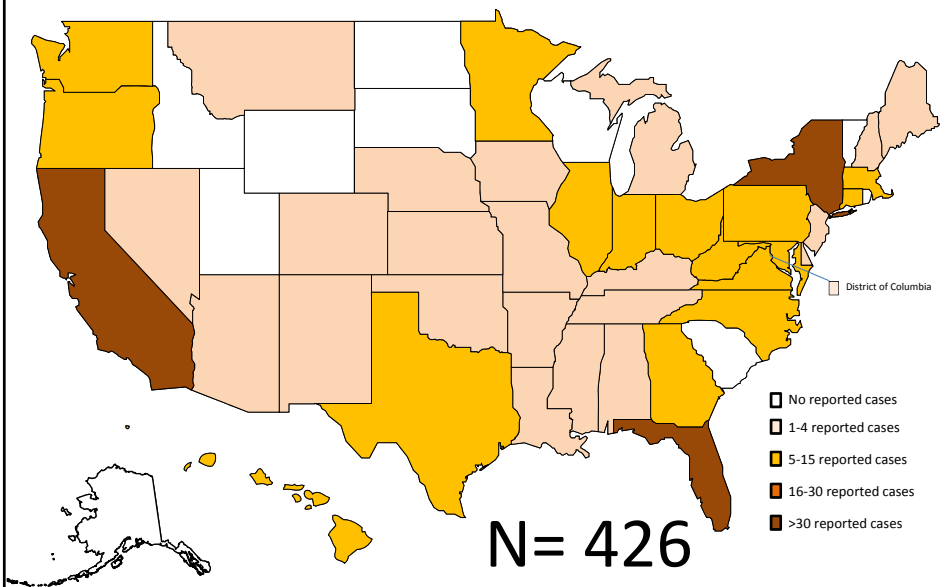
- In May 2015, an outbreak of Zika was identified in several northeastern states of Brazil; by December 2015, Zika had spread to 18 states.
- A retrospective analysis of positive dengue test samples found Zika positive results evident as early as February 2015.
- The virus may have been introduced into Brazil in 2014 by persons attending the World Soccer Cup or by members of a Polynesian team attending an international canoe race.
- *Aedes aegypti* is the primary vector in the Brazilian outbreak, but *Aedes albopictus* may also be playing a role.
- An estimated 1.5 million cases have been reported through January 2016.

## Confirmed Zika Cases in Mexico by State
## January 1, 2016 – May 2, 2016




Data provided by the Mexican Ministry of Health
http://www.epidemiologia.salud.gob.mx/doctos/avisos/2016/zika/DGE_ZIKA_CASOS_SEM015_2016.pdf

## Imported Zika in the United States, 2015-2016

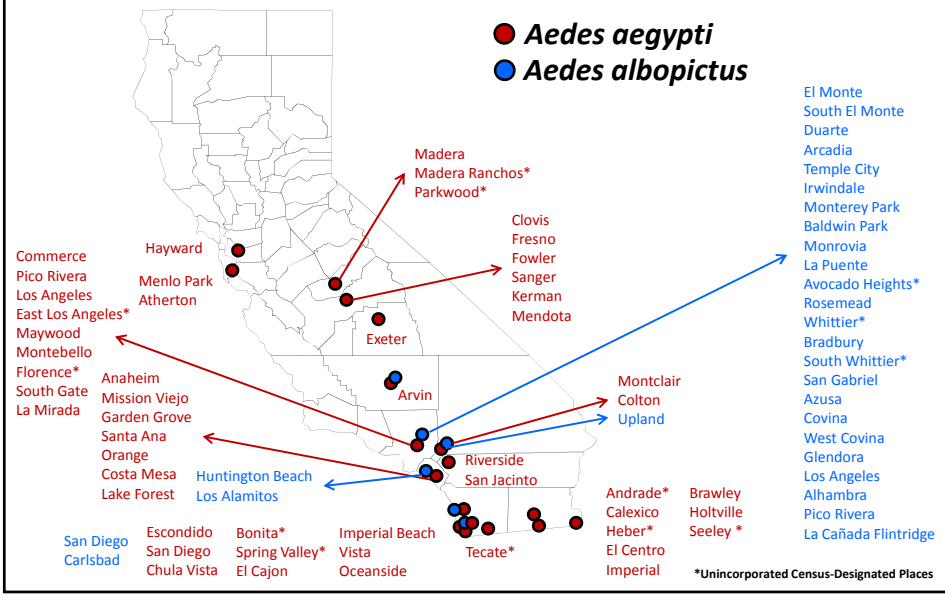


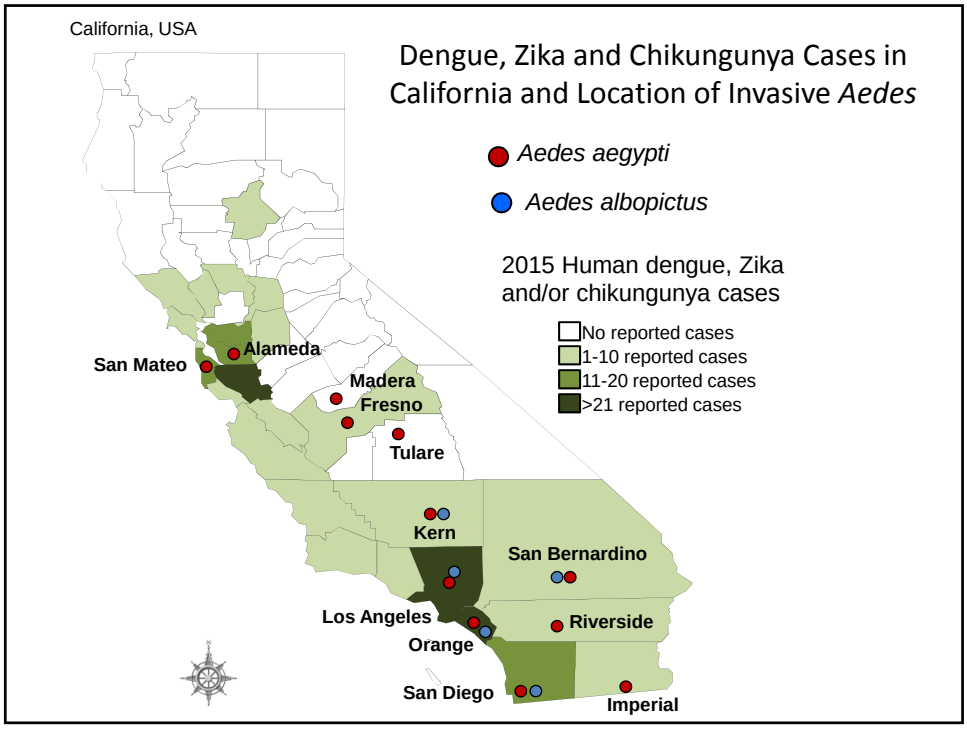
## 43 Travel-Associated Zika Cases in California
(as of April 29, 2016)

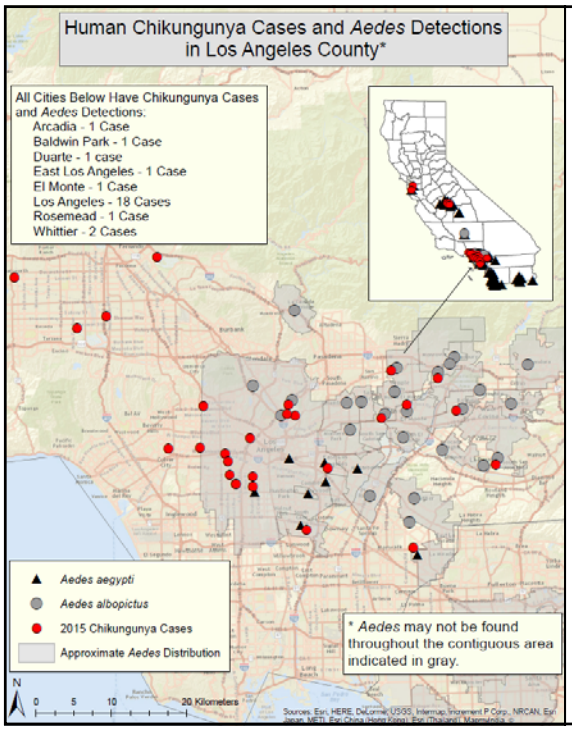
| Year | Confirmed Cases |
|---|---|
| 2013 | 1 |
| 2014 | 3 |
| 2015 | 11 |
| 2016 | 32 |

- Cases reported from 13 counties
  - Including 6 counties with invasive *Aedes* mosquitoes
- 2015-2016 cases traveled to: El Salvador (13), Guatemala (7), Brazil (3), Colombia (3), Puerto Rico (3), Mexico (2), Honduras (3), Venezuela (2), Haiti (2), Costa Rica (2), Kiribati (1), Samoa (1), and Dominican Republic (1)
  - Two case-patients traveled to more than one location
- Case numbers updated every Friday on CDPH Zika webpage

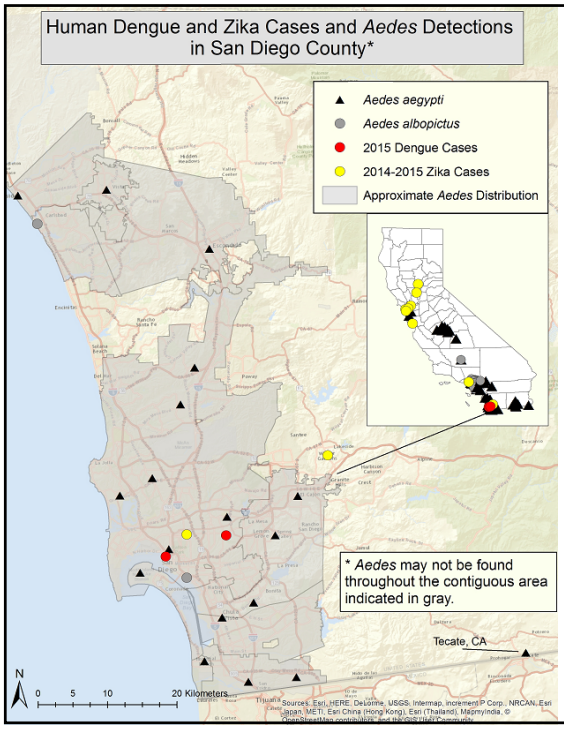
## *Aedes aegypti* and *Aedes albopictus* Mosquitoes Detection Sites in California






- 85 cases of chikungunya were reported in residents of Los Angeles in 2015
- 51% of those cases returned to Los Angeles potentially viremic (within 7 days of symptom onset)
- 26 potentially viremic cases reside in a city with known invasive *Aedes*
- 36% (31) of chikungunya cases from Los Angeles reported travel/exposure in Mexico




- 11 cases of dengue were reported in residents of San Diego in 2015
- 91% of those cases returned to San Diego potentially viremic (within 5 days of symptom onset)
- 2 potentially viremic cases reside in a city with known invasive *Aedes*
- 27% (3) of dengue cases from San Diego reported travel/exposure in Mexico
- San Diego has reported 1 Zika case that was potentially viremic who resides in a city with known invasive *Aedes*

# Potential for local transmission is low

- A viremic person would need to return to a region where there are *Aedes* mosquitoes and be bitten by an *Aedes* that would live long enough to be come infectious and bite another person who then becomes infected
- Mitigating factors:
  - Patchy *Aedes aegypti* and *albopictus* distribution in CA
  - Use of AC, window and door screens
  - Better water management than in other countries
  - Good mosquito control!
- If an outbreak were to occur, it would likely be limited in scope and duration
- Outbreaks of dengue and chikungunya elsewhere in the US have been contained
- Therefore the US is unlikely to experience the same extensive outbreaks currently being experienced in Latin America

## Case 2: Phillip

- 29-year-old male, no past medical history
- Traveled to Colombia in January
- 1 week before returning home developed maculopapular rash, headache, and joint pain.
- Had unprotected vaginal sex with his girlfriend day 9 and day 11 after symptom onset
- Serum collected on day 9 after symptom onset for Zika virus tested positive for anti-Zika antibodies by PRNT

## Case 3: Robyn

- 30-year-old female, no past medical history
- No history of travel or blood transfusion
- Unprotected vaginal sex with her boyfriend, who just returned from Colombia with a rash
- Developed symptoms 5 days after sexual exposure: maculopapular rash, fever, arthralgia, conjunctivitis, headache.
- Serum collected 8 days after symptom onset tested positive for anti-Zika antibodies by PRNT

Sexual Transmission of Zika Virus


# Signs and Symptoms

- Similar to other arboviruses
- About 20% estimated to experience symptoms
- Onset 3-12 days after exposure
- Usually last up to one week

By Eddie314 at the English language Wikipedia, CC BY-SA 3.0

## Clinical Characteristics of 31 Patients with Confirmed Zika Virus Disease on Yap Island during the Period from April through July 2007.

**Table 1. Clinical Characteristics of 31 Patients with Confirmed Zika Virus Disease on Yap Island during the Period from April through July 2007.**

| Sign or Symptom | No. of Patients (%) |
|---|---|
| Macular or papular rash | 28 (90) |
| Fever* | 20 (65) |
| Arthritis or arthralgia | 20 (65) |
| Nonpurulent conjunctivitis | 17 (55) |
| Myalgia | 15 (48) |
| Headache | 14 (45) |
| Retro-orbital pain | 12 (39) |
| Edema | 6 (19) |
| Vomiting | 3 (10) |

* Cases of measured and subjective fever are included.

Duffy MR et al. N Engl J Med 2009;360:2536-2543.

# DDx of Acute Infection

- Other mosquito-borne diseases: **dengue, chikungunya**, malaria
- Other viruses: rubella, measles, parvovirus, acute HIV infection
- Bacterial infections: leptospirosis, rickettsia, GAS infections, syphilis

| Features | Zika | Dengue | Chikungunya |
|---|---|---|---|
| Fever | ++ | +++ | +++ |
| Rash | +++ | + | ++ |
| Conjunctivitis | ++ | - | - |
| Arthralgia | ++ | + | +++ |
| Myalgia | + | ++ | + |
| Headache | + | ++ | ++ |
| Hemorrhage | - | ++ | - |
| Shock | - | + | - |

*Table courtesy of Dr. Ingrid Rabe, CDC*

# Management of Symptomatic Infection

- No antiviral treatment available
- Supportive care: rest, fluids, and acetaminophen
- Avoid aspirin and NSAIDs
- Protect others:
  - Avoid mosquito bites
  - Prevent sexual transmission
  - Defer blood donation

## Guillain-Barré Syndrome (GBS)

- Autoimmune neurologic disease causing weakness and/or paralysis
  - Respiratory weakness needing ventilatory support in 10-30%
  - Autonomic dysfunction in 70%; can lead to sudden death
- 1-2 cases/100,000 per year worldwide
- Surveillance is difficult
- Treatment can be expensive and hard to access

## GBS and Zika

- French Polynesia 2013–2014 (8,752 cases)
  - 42 of these diagnosed with GBS (20x increase)
- Brazil January–July 2015 (500,000-1.5mil cases)
  - 121 cases of neurological manifestations including GBS, all with history of rash and travel to areas with known Zika outbreaks
- El Salvador December 1, 2015-January 30, 2016
  - 104 cases of GBS
- Venezuela:
  - 252 cases of GBS
- Puerto Rico November 2015–January 2016 (155 cases)
  - 1 case hospitalized for GBS

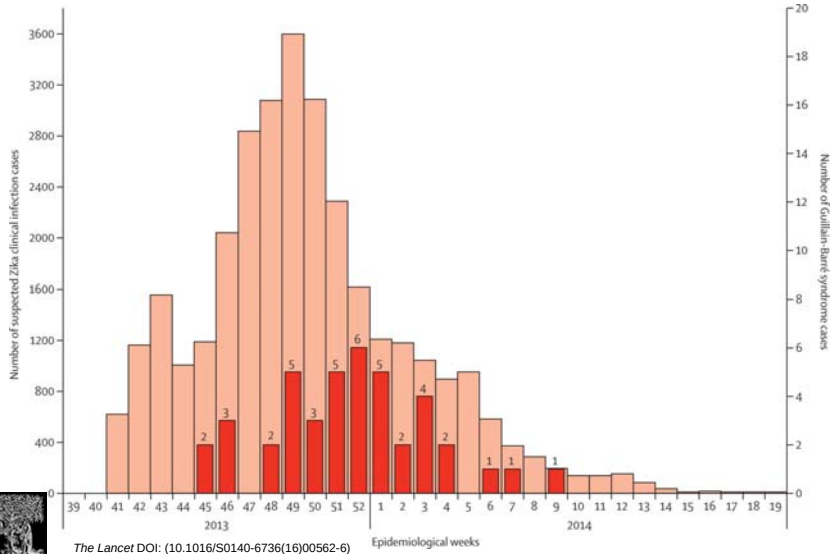
# GBS and Zika

## Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study

Van-Mai Cao-Lormeau*, Alexandre Blake*, Sandrine Mons, Stéphane Lastère, Claudine Roche, Jessica Vanhomwegen, Timothée Dub, Laure Baudouin, Anita Teissier, Philippe Larre, Anne-Laure Vial, Christophe Decam, Valérie Choumet, Susan K Halstead, Hugh J Willison, Lucile Musset, Jean-Claude Manuguerra, Philippe Despres, Emmanuel Fournier, Henri-Pierre Mallet, Didier Musso, Arnaud Fontanet*, Jean Neil*, Frédéric Ghawché*

- GBS cases were **significantly more likely** to have evidence of recent Zika infection than matched controls
- GBS can occur **after asymptomatic Zika** virus infection
- Patients with GBS and Zika may be have **axonal type** of GBS, rapid plateau, lasting deficits
- Rate of GBS after Zika may be 0.24/1000 cases
  - Similar to estimated rate for Campylobacter infection

**Cao-Lormeau, Blake, et al:** Weekly cases of suspected Zika virus infections and Guillain-Barré syndrome in French Polynesia between October, 2013, and April, 2014




*The Lancet* DOI: (10.1016/S0140-6736(16)00562-6)

## Zika Virus Associated with Meningoencephalitis and ADEM


Carteaux G et al. N Engl J Med 2016. DOI: 10.1056/NEJMc1602964

The NEW ENGLAND JOURNAL of MEDICINE

# Microcephaly and Zika

**Definition:** Head circumference at birth <2 standard deviations below mean for gestational age and sex

Causes:
- Congenital infection: e.g. syphilis, rubella, toxoplasmosis
- Genetic disorders and inherited mutations
- Other brain injury: hypoxia, drugs, toxins, FAS

Outcomes:
- Range from normal to severe, including death
- Can include seizures, visual or hearing deficits
- Correlate with severity of microcephaly

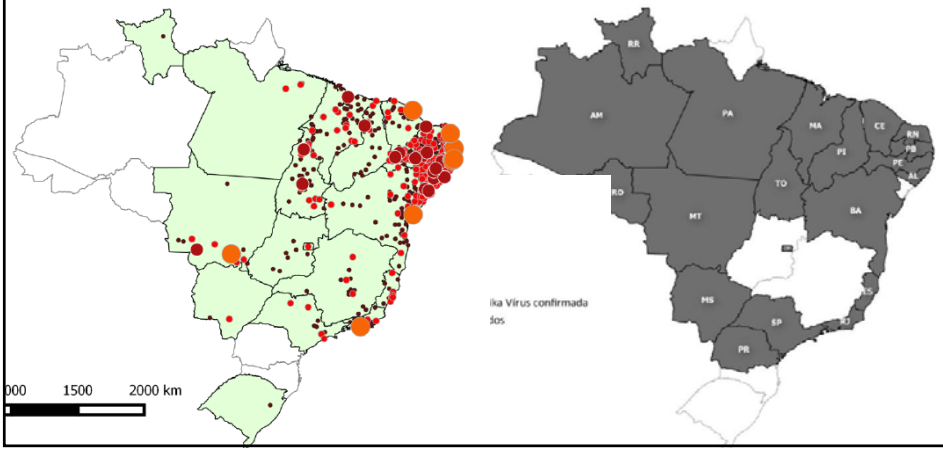
Epidemiology:
- 2-12/10,000 live births in US, 2/10,000 in California


Baby with Microcephaly

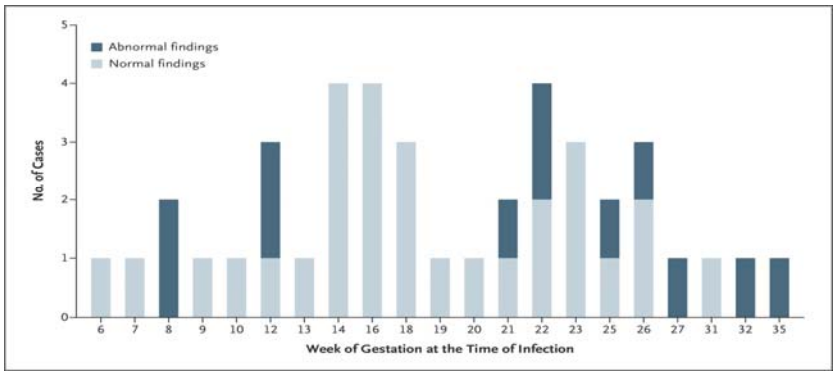
# Microcephaly and Zika

Location of Microcephaly Cases

States with Local Zika Cases




**Week of Gestation at the Time of ZIKV Infection and Abnormal Ultrasonographic and Doppler Findings.**

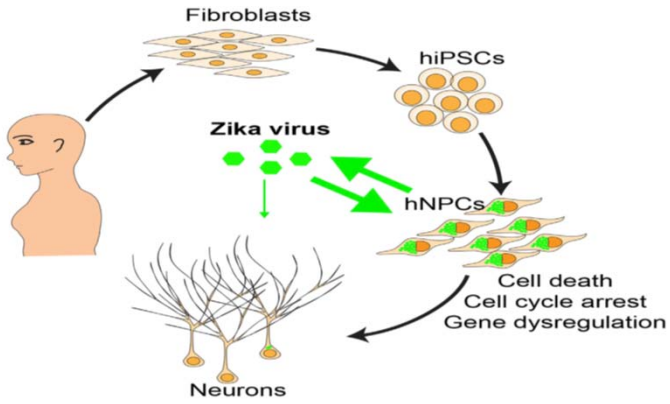



- 88 pregnant women with rash enrolled 9/15-2/16.
  - 72 (82%) positive for ZIKV in blood, urine, or both.
  - 12(29%) of 42 with Zika had US abnormality vs 0% women without Zika

Brasil P et al. N Engl J Med 2016. DOI: 10.1056/NEJMoa1602412

The NEW ENGLAND JOURNAL of MEDICINE

## Zika Virus (ZIKV) Infects Human Cortical Neural Progenitors (hNPCs) and Attenuates Their Growth*




*Tang et al. Cell Stem Cell (2016), http://dx.doi.org/10.1016/j.stem.2016.02.016*

## Neonatal Zika

- Two cases in French Polynesian outbreak documenting perinatal transmission
  - One infant with thrombocytopenia and rash
  - Both recovered fully without known sequelae

RAPID COMMUNICATIONS

**Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014**

M Besnard[1], S Lastère[1], A Teissier[2], V M Cao-Lormeau[2], D Musso (dmusso@ilm.pf)[2]
1. Centre hospitalier de Polynésie française, Hôpital du Taaone, Tahiti, French Polynesia
2. Institut Louis Malardé, Tahiti, French Polynesia

Citation style for this article:
Besnard M, Lastère S, Teissier A, Cao-Lormeau VM, Musso D. Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014 . Euro Surveill. 2014;19(13):pii=20751. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=20751

Article submitted on 20 March 2014 / published on 3 April 2014

# Laboratory testing indications

- Individuals with symptoms of acute Zika virus infection that occur within 2 weeks of exposure*
- Asymptomatic pregnant women 2-12 weeks after exposure during pregnancy or up to 8 weeks prior
- Infants with microcephaly or intracranial calcifications after maternal exposure or with confirmed maternal infection
- Other considerations:
  - sexual partners of case-patients with no travel history
  - GBS after potential Zika virus exposure

*Symptoms of acute Zika virus infection are defined as 1 or more of the following: fever, maculopapular rash, arthralgia, or conjunctivitis

# VRDL Arbovirus Testing

- The VRDL has maintained a large number of assays to test for a broad array of arboviruses.
- VRDL has been actively working on laboratory testing for Zika and other exotic mosquito borne diseases such as dengue and chikungunya over the last two years building upon experience with West Nile virus testing.
- Diagnosis of specific arboviral diseases is complex and often requires a combination of rule in and rule out of several arboviruses.

| Family | Virus | Sample type | EIA IgM | EIA IgG | IFA IgM | IFA IgG | RT-PCR | Western Blot | PRNT |
|---|---|---|---|---|---|---|---|---|---|
| Flaviviridae | WNV | Serum | X | X | X | X | X | X | X |
| | | CSF | X | | | | X | | |
| | Dengue | Serum | X | X | X | X | X* | X | X |
| | SLE | Serum | X | | | | X | X | X |
| | Yellow Fever | Serum | | | | | | | X |
| | Zika | Serum | X | | X | | X** | | X |
| Togaviridae | WEE | Serum | X | X | | | | X | X |
| | Chikungunya | Serum | X | | X | X | X* | X | X |
| Bunyaviridae | Jamestown Canyon | Serum | X | | | | | | X |
| | CA encephalitis | Serum | | | | | | | X |

*RT-PCR also can be performed for CSF **RT-PCR also can be performed for CSF, urine and amniotic fluid

## How VRDL Can Assist in Confirming an Arbovirus Case

**Why lab confirm a case?**

- Most commercial assays screen for IgM in a single serum

**Problems with this approach are:**

- **Lack of specificity**: There is a high degree of serologic cross-reactivity between Flaviviruses* (WNV *vs* SLE *vs* Dengue *vs*...another flavivirus)
- **Timing:** Flavivirus IgM may persist for months and confound interpretation; IgM may not distinguish from last year's infection

➡ Therefore, detection of IgM antibodies to a flavivirus in CSF or serum ***with no other testing*** = ***Probable*** case

➢ **Serologic specificity** requires the Plaque Reduction Neutralization Test (PRNT)
  – PRNT detects neutralizing Ab, is best on paired sera, and takes ~ one week to perform

➢ To establish ***timing*** of infection: Test paired A/C samples or perform PCR or other method of direct detection

* similar issues exist within other arbovirus families

## 2015 CSTE Arbovirus Case Definition: Laboratory criteria for diagnosis

**What is needed from the lab to help confirm an arbovirus case?**

**Answer: Evidence of *recent* infection with a *specific* arbovirus**

- **Direct Detection of the virus establishes both *timing* and *specificity*:**
  - Detect viral nucleic acid (PCR)
  - Isolate the virus
  - Detect viral antigen

  **By any of these methods *OR***

- **Serological evidence of *recent* infection with a *specific* arbovirus**
  - 4-fold rise in antibody titers in paired sera (e.g., IgM, IgG, or Neut Ab by EIA, IFA, or PRNT), or
  - IgM(+) serum *and* PRNT (+) in the same or a later specimen or
  - IgM(+) CSF* *and* IgM(-) CSF for other endemic arboviruses

# Studies from previous outbreaks of Zika Virus were the basis for guidance on diagnostic testing

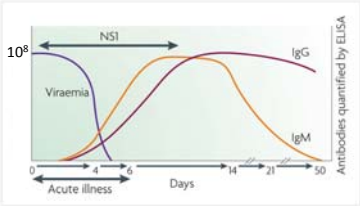
*Prior to Yap Island outbreak, only 14 confirmed human cases had been described*

| Outbreak (Study Reference) | Year | Study size: # cases lab tested | # PCR(+)/ tested | % PCR (+) § | # IgM+/ tested | % IgM+ | PRNT ZIKA ≥ 4X |
|---|---|---|---|---|---|---|---|
| Yap Island (Lanciotti, 2008) | 2007 | 185 | **17/157** | **10.8%** | **108/108** | **100%** | **49/108** |
| French Polynesia (Musso, 2015) | 2013-2014 | 885 | **210/748 serum** | **28.1%** | | | |
| | | | **182/319 saliva** | **57.1%** | | | |
| New Caledonia (Gourinat, 2015) | 2014 | 6 | **4/6 serum** | | | | |
| | | | **6/6 urine** | | | | |
| Easter Island (Tognarelli, 2016) | 2014 | 89 | **51/89** | **57.3%** | | | |
| Pernambuco, Brazil (Pessoa, 2016) | 2015 | 77 | **31/77** | **40.2%** | | | |

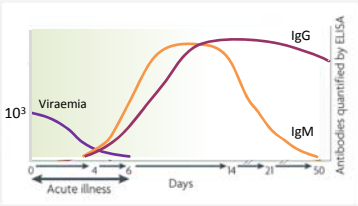
§ Consistently, mean time point of illness to detect Zika virus RNA by RT-PCR = 3.5 days

# Diagnostic Testing for Zika Virus Rationale for the Testing Guidance

Acute dengue virus infection




Acute Zika virus infection




from Guzman, M. G. *et al.* Dengue: A continuing global threat. *Nature Reviews Microbiology* **8,** S7–S16 (2010)

- Zika viraemia is lower and of shorter duration
  - Viral loads estimated to be 2 - 3.5 X $10^3$ viral particles/ml (*Lanciotti et al., 2008*)
  - Viral loads for dengue and chikungunya are estimated to be ~$10^7$ - $10^8$
  - Studies indicate virus is no longer detectable at or shortly after symptom onset
  - Most detections of Zika virus by RT-PCR are within the first 3 days of illness onset
  - Clinical sensitivity of RT-PCR can be poor
- Zika-specific IgM can appear later in course of infection
  - Samples collected <7 days after onset can be falsely negative
  - It is not known, but it is believed that Zika virus IgM can persist as long as dengue virus IgM (~12 weeks)
  - For individuals with no symptoms (no onset date), 2 weeks after exposure was chosen to ensure that IgM should be detectable if infected with Zika virus.

# Flavivirus-specific antibodies cross-react: the need for confirmatory testing

- Flavivirus antibodies directed against the highly immunogenic envelope protein contain both flavivirus cross-reactive and virus-specific epitopes
- Yap Island outbreak initially indicated to be dengue based upon IgM test results
  - Neutralization studies from Yap outbreak illustrate the complexity of the immune response in primary versus secondary flavivirus exposures

Table 2. Neutralization testing with heterologous flaviviruses of patients infected with ZIKV, Yap State, Micronesia, 2007*

| Patient | Days after onset | PRNT$_{90}$ titer | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ZIKV | DENV1 | DENV2 | DENV3 | DENV4 | JEV | YFV | WNV | SLEV | MVEV |
| Primary flavivirus ZIKV | | | | | | | | | | | |
| 822a | 5 | 320 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 |
| 822b | 10 | 2,560 | 10 | 10 | 10 | 10 | <10 | <10 | <10 | <10 | <10 |
| 822c | 24 | 5,120 | 10 | 10 | 10 | 10 | <10 | <10 | <10 | <10 | <10 |
| 830a | 2 | <10 | <10 | NT‡ | NT | NT | NT | NT | NT | NT | NT |
| 830b | 21 | 2,560 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 |
| 849a | 3 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 |
| 849b | 18 | 10,240 | <10 | <10 | <10 | <10 | <10 | 20 | <10 | <10 | <10 |
| 862a | 6 | 320 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 | <10 |
| 862b | 20 | 2,560 | 10 | 10 | <10 | <10 | <10 | <10 | <10 | 10 | <10 |
| Secondary flavivirus ZIKV (probable) | | | | | | | | | | | |
| 817a | 1 | 80 | 80 | 160 | 320 | 160 | <10 | <10 | <10 | 40 | 40 |
| 817b | 19 | 10,240 | 2,560 | 20,480 | 5,120 | 5,120 | 20 | 320 | 160 | 1,280 | 640 |
| 833a | 1 | 160 | 320 | 80 | 40 | 20 | <10 | <10 | <10 | <10 | <10 |
| 833b | 19 | 81,920 | 20,480 | 5,120 | 5,120 | 1,280 | <10 | <10 | 80 | 320 | 320 |
| 844a | 2 | 20 | 1,280 | 640 | 320 | 160 | <10 | <10 | 5 | 20 | 20 |
| 844b | 16 | 10,240 | 40,960 | 10,240 | 5,120 | 1,280 | 5 | <10 | 160 | 640 | 640 |
| 955a | 1 | 40 | 1,280 | 640 | 160 | 320 | <10 | <10 | <10 | 20 | 20 |
| 955b | 14 | 163,840 | 81,920 | 20,480 | 10,240 | 5,120 | 10 | <10 | 640 | 2,560 | 1,280 |
| 968a | 1 | 80 | 320 | 320 | 80 | 40 | <10 | <10 | <10 | 40 | 20 |
| 968b | 3 | 10,240 | 640 | 640 | 160 | 160 | <10 | <10 | 10 | 40 | 20 |
| 839a | 3 | <10 | <10 | 10 | <10 | <10 | <10 | 40 | <10 | <10 | <10 |
| 839b | 20 | 10,240 | 40 | 320 | 80 | 80 | <10 | 640 | 40 | 80 | 80 |
| 847a | 5 | <10 | <10 | <10 | <10 | <10 | <10 | 640 | <10 | <10 | <10 |
| 847b | 8 | 2,560 | 40 | 320 | 160 | 40 | <10 | 1,280 | 80 | 320 | 320 |

*PRNT$_{90}$ titer, 90% plaque reduction neutralization test titer; ZIKV, Zika virus; DENV, dengue virus, JEV, Japanese encephalitis virus; YFV, yellow fever virus; WNV, West Nile virus; SLEV, St. Louis encephalitis virus; MVEV, Murray Valley encephalitis virus; NT, not tested (sample depleted).

from Lanciotti et al. 2008. EID 14(8):1232-9

# Availability of recommended tests for the detection of Zika virus

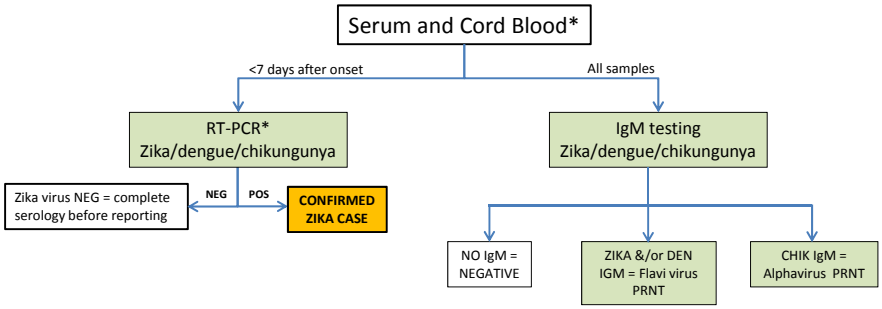
| Type of Test | CDC | VRDL |
|---|---|---|
| **PCR**<br>• *Preferred* test in acute samples<br>• ≤ 7 days post onset | RT-PCR panel<br>• Serum<br>• CSF<br>• Urine<br>• Amniotic fluid<br>• Placenta and fetal tissues | RT-PCR panel – *validated Feb 23rd*<br>EUA Trioplex RT-PCR‡ – *adopted April 18th*<br>• Serum<br>• CSF<br>• Urine<br>• Amniotic fluid |
| **Serology**<br>• IgM<br>• >3 days post onset | IgM MAC ELISA†<br>• Serum<br>• CSF<br>• Amniotic fluid | IgM IFA§ – *validated March 4th*<br>IgM MAC ELISA – *TBD*<br>• Serum only |
| **Serology**<br>• Neutralizing Ab<br>• PRNT confirmation | PRNT<br>• Serum<br>• CSF<br>• Amniotic fluid | PRNT – *validated March 25th*<br>• Serum only<br>• Validated for Zika virus |

† Approved for EUA on February 26, 2016
‡ Approved for EUA on March 17, 2016
§ IgM EIA – under evaluation to increase surge testing capacity

# Zika Testing Algorithms

Symptomatic with International /Specific US Travel

*Serum must be collected ≤ 12 weeks after symptom onset*

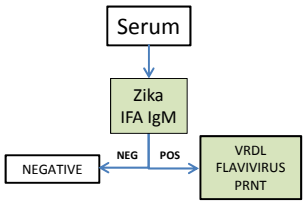



*Negative PCR does not rule out Zika virus infection

# Zika Testing Algorithms

Asymptomatic Pregnant women with International /Specific US Travel

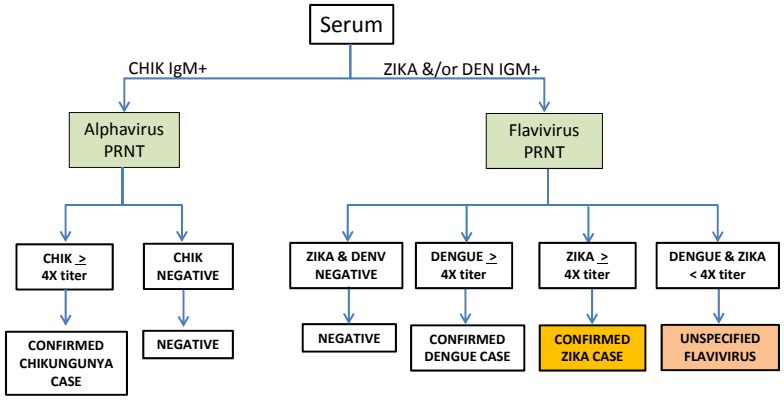
*Serum must be collected ≥ 2 and ≤ 12 weeks after potential exposure**




*Exposure includes travel to an area with ongoing Zika virus transmission or unprotected sex with a symptomatic male partner with relevant travel history.

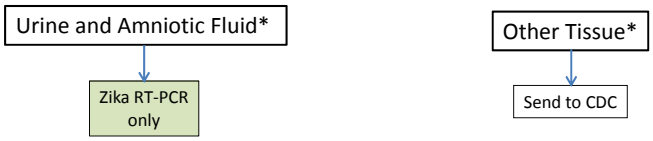
# Zika Testing Algorithms

ANY IgM detection → PRNT



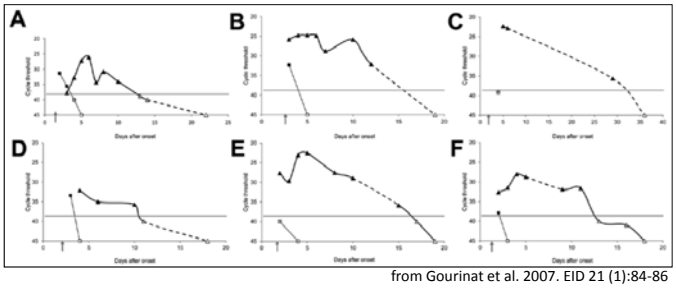

# Zika Testing Algorithms

Other sample types



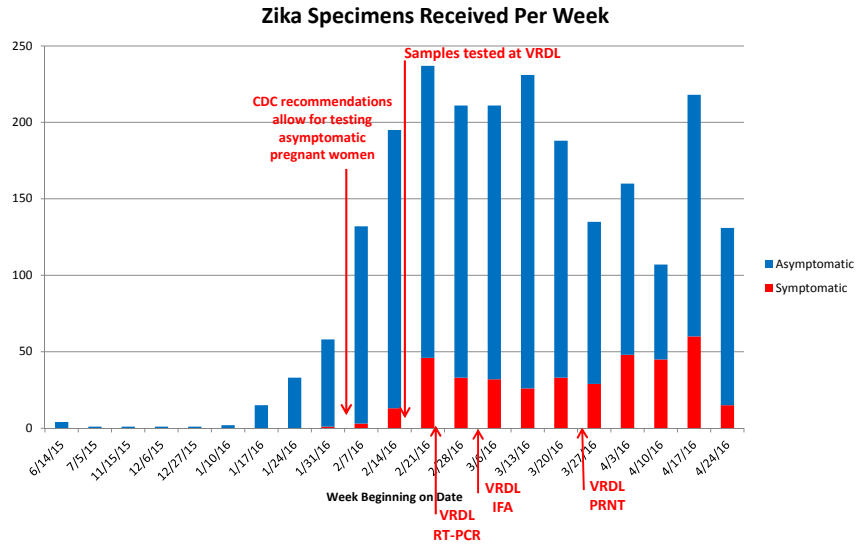

**Urine must be collected < 30 days after onset. Other samples determined on case by case basis.*

Detection of Zika virus RNA in blood and urine specimens




from Gourinat et al. 2007. EID 21 (1):84-86

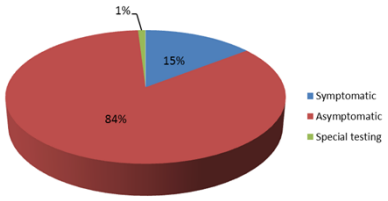
# Zika Virus Testing at VRDL
# Test Volume



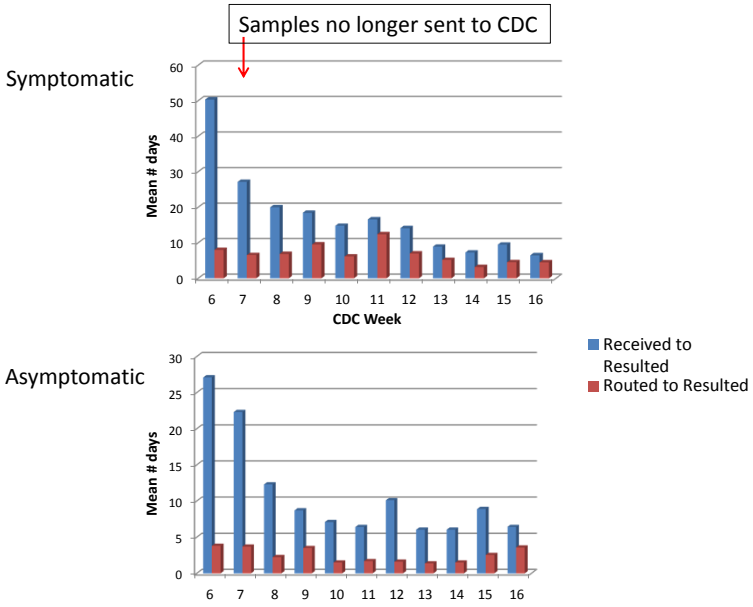

# Zika Virus Testing Volume

| | Week 11 | Week 12 | Week 13 | Week 14 | Week 15 | Week 16 | Week 17 |
|---|---|---|---|---|---|---|---|
| **Total # patients received VRDL** | 1,170 | 1,333 | 1,446 | 1,586 | 1,678 | 1,847 | 1,972 |
| **# patients received/week** | 215 | 187 | 130 | 148 | 90 | 172 | 108 |
| **Total # patients tested @ VRDL** | 848 | 994 | 1,086 | 1,314 | 1,442 | 1,512 | 1,654 |
| **# patients tested/week** | 368 | 247 | 107 | 287 | 177 | 89 | 158 |

- 91.3% patients tested are female
- 84% of samples tested – asymptomatic pregnant women
- ~20% of symptomatic cases tested are pregnant



## Turnaround times (TAT) improved as testing algorithms evolved

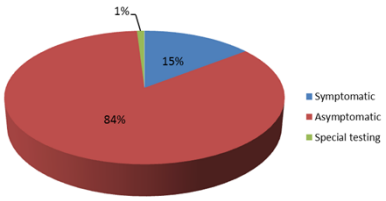



# Test Results Summary

As of April 15th: 1,442 patients tested

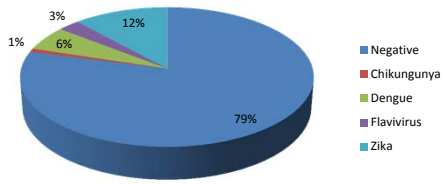
Zika virus lab confirmed cases: 34 cases
(43 cases as of April 29th)

Percentage of Zika virus lab confirmed cases:
- Asymptomatic pregnant women: <0.2%
- Symptomatic cases: 15.7%




Viruses detected in symptomatic cases:

- 34 Zika virus
- 24 dengue virus
- 3 chikungunya
- 9 flavivirus (DEN:ZIKA titers < 4X difference)



# Diagnostic testing for Zika virus is evolving

- **RT-PCR**
  - Among 35 confirmed Zika cases tested at VRDL,
    - 17 sera collected ≤7 days post onset (po)
    - 4 urines collected <30 days po
  - 6/17 (35%) sera positive
  - 3 of 4 (75%) urines positive

**Clinical sensitivity of PCR is low**

| Days PO | Serum PCR | Urine PCR | IgM /PRNT |
|---|---|---|---|
| 0 | POS | NT | NEG |
| 1 | POS | NT | NEG |
| 1 | POS | NT | POS |
| 3 | POS | NT | NEG |
| 5 | POS | NT | NEG |
| 7 | POS | POS | NEG |
| 7 | Equiv | POS | NEG |
| 7 | NEG | POS | POS |
| 9 | NT | NEG | POS |

- **IgM**
  - Within 7 days po, 12/17 IgM+ (70.6%)
  - ~30% false NEG
  - ~10% of patients tested have POS IgM
    - Symptomatic: 86% will be confirmed
    - Asymptomatic: 6% will be confirmed

**Clinical sensitivity of IgM problematic < 7 days; lack of specificity requires PRNT**

- **PRNT confirmation**
  - 6 patients with POS Zika IgM & 3 with POS DEN IgM were unresolved – unspecified flavivirus
    - ZIKA PRNT titers were POS but <4X

**PRNT specificity is high with primary exposures; low with secondary exposures**

# Public Health Surveillance in California

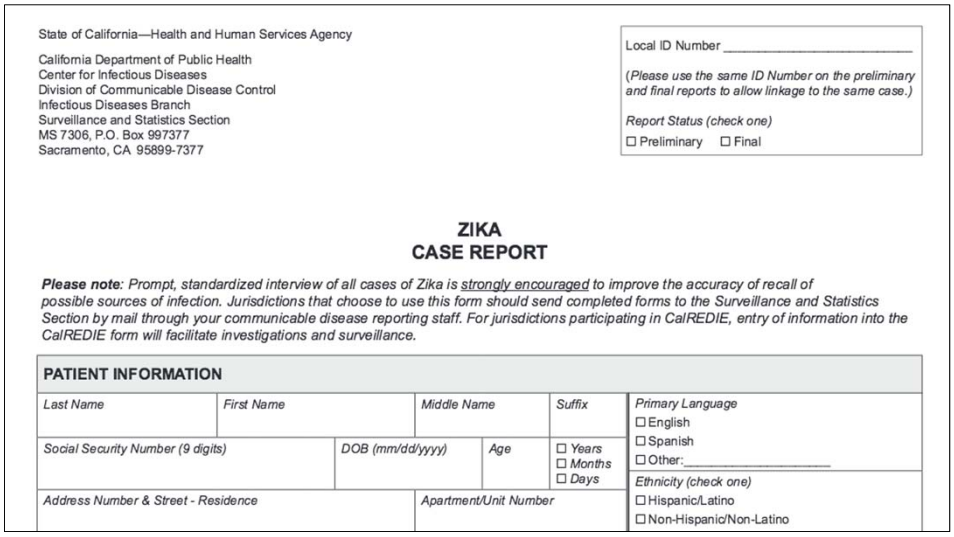
Reporting of notifiable diseases is mandated by state law (Title 17 CCR) Chikungunya, dengue, and Zika are reportable.

Suspect dengue, chikungunya and Zika cases are reported by physicians or laboratories to their local health department (LHD). LHD follows up and reviews cases (who, what, where, when).

LHD reports to California Department of Public Health (CDPH). Case is reviewed by subject matter expert and classification finalized.

CDPH reports confirmed and probable cases to CDC

# Reporting: Zika cases



State of California—Health and Human Services Agency

California Department of Public Health
Center for Infectious Diseases
Division of Communicable Disease Control
Infectious Diseases Branch
Surveillance and Statistics Section
MS 7306, P.O. Box 997377
Sacramento, CA 95899-7377

Local ID Number _____

*(Please use the same ID Number on the preliminary and final reports to allow linkage to the same case.)*

*Report Status (check one)*
☐ Preliminary ☐ Final

**ZIKA**
**CASE REPORT**

***Please note**: Prompt, standardized interview of all cases of Zika is strongly encouraged to improve the accuracy of recall of possible sources of infection. Jurisdictions that choose to use this form should send completed forms to the Surveillance and Statistics Section by mail through your communicable disease reporting staff. For jurisdictions participating in CalREDIE, entry of information into the CalREDIE form will facilitate investigations and surveillance.*

**PATIENT INFORMATION**

| *Last Name* | *First Name* | *Middle Name* | *Suffix* | *Primary Language* ☐ English ☐ Spanish ☐ Other:_____ |
|---|---|---|---|---|
| *Social Security Number (9 digits)* | *DOB (mm/dd/yyyy)* | *Age* | ☐ *Years* ☐ *Months* ☐ *Days* | *Ethnicity (check one)* ☐ Hispanic/Latino ☐ Non-Hispanic/Non-Latino |
| *Address Number & Street - Residence* | | *Apartment/Unit Number* | | |

https://www.cdph.ca.gov/pubsforms/forms/Pages/CD-Report-Forms.aspx

# Reporting: Birth Defects

CA.GOV California Department of PublicHealth CDPH

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Home > Programs > California Birth Defects Monitoring Program

## California Birth Defects Monitoring Program

MO-07-0128 CBDMP

The California Birth Defects Monitoring Program (CBDMP) has been an active ascertainment, population based registry since 1982 when the California State Legislature authorized the California Birth Defects Monitoring Program (CBDMP) to collect data on birth defects, stillbirths, and miscarriages. CBDMP currently monitors over 150,000 births in 10 counties—approximately 30% of the births in California, which represents the state's geographic, environmental and racial/ethnic diversity. The CBDMP registry data are used for ongoing surveillance to monitor rates and trends of select birth defects and to provide outcome data for the pregnancy blood samples included in the California Biobank Program. The Program receives funding from the California Birth Defects Monitoring Fund.

### Mission

The California Birth Defects Monitoring Program (CBDMP) collects and analyzes data to identify opportunities for preventing birth defects and improving the health of babies.

### Program Goals

Increase the quality and quantity of California-based birth defect data available for purposes of public health monitoring and investigator-led research

Increase communication of birth defects information

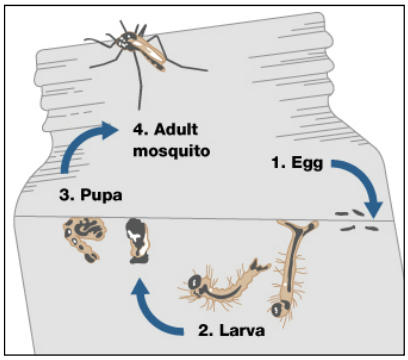
Monitor public health and safety concerns relating to birth defects

http://www.cdph.ca.gov/programs/CBDMP/Pages/default.aspx

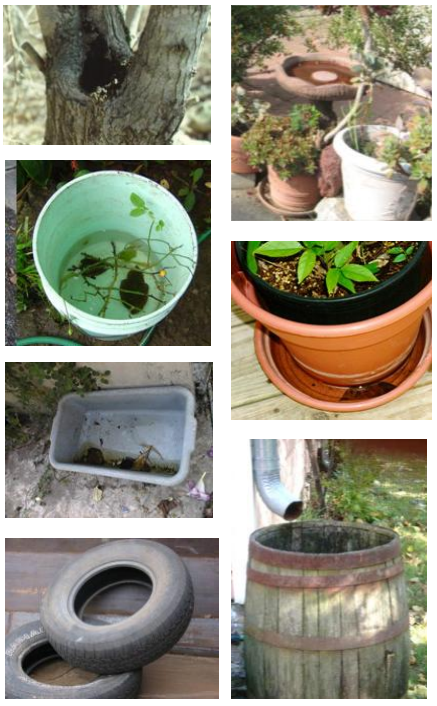
# Challenges

- Some Zika patients (similar to dengue and chikungunya patients) are potentially viremic after return from travel
- Lag-time in testing and reporting may delay detection of potential local transmission
- Need coordination of local health departments and vector control agencies to reduce risk
- As commercial laboratories begin Zika testing, these challenges will be increased, although turn around time may improve for patients

## Mosquito Control




- **Container Breeders**
- **Peridomestic**
- **Cryptic larval sources**
- **Egg to adult in 6-10 days**
- **Desiccation-resistant eggs**



# Prevention

No vaccine exists to prevent Zika virus infection
Prevent Zika by avoiding mosquito bites
Mosquitoes that spread Zika virus bite mostly during the daytime

**Protect yourself from mosquito bites**

- Use insect repellents
- When weather permits, wear long-sleeved shirts and long pants.
- Use air conditioning or window/door screens to keep mosquitoes outside. If you are not able to protect yourself from mosquitoes inside your home or hotel, sleep under a mosquito bed net.
- Help reduce the number of mosquitoes inside and outside your home or hotel room by emptying standing water from containers such as flowerpots or buckets.

**If you have Zika, follow these steps to protect others from getting sick**

- During the first week of infection, Zika virus can be found in the blood and passed from an infected person to another mosquito through mosquito bites. An infected mosquito can then spread the virus to other people.
- To help prevent others from getting sick, avoid mosquito bites during the first week of illness.

# Guidance for those pregnant or seeking pregnancy

- Postpone travel and avoid mosquito bites
- Breast feeding still recommended
- Prevent sexual transmission from male partners: condoms or abstinence
- Delay conception for 8 weeks after exposure or illness

# Prevention of sexual transmission

- Men exposed to Zika virus* with **no symptoms** should:
  - Abstain or use condoms for **8 weeks** after exposure with all partners
  - Abstain or use condoms with any pregnant partner for the **remainder of the pregnancy**
- Men exposed to Zika virus* who develop symptoms or have confirmed Zika virus infection should:
  - Abstain or use condoms with all partners for **6 months** after exposure
  - Abstain or use condoms with any pregnant partner for the **remainder of the pregnancy**
- Testing for the purpose of assessing risk for sexual transmission is **not recommended**.

# Transfusion and Transplant Safety

- AABB and FDA: www.redcross.org
  - Wait 28 days before donation
  - Report illness within 14 days
  - Endemic areas: use pathogen reduction or outsourcing
- Sperm donation:
  - wait 6 months before donation
- OPTN/UNOS: www.optn.transplant.hrsa.gov
  - Zika should not exclude donors
  - Exercise caution in pregnant recipients

# Conclusions

1. Mosquito-borne Zika virus has been spreading through Latin America and the Caribbean causing microcephaly and GBS, and imported cases and rare sexual transmission have been reported in the continental US.
2. Public and provider education, mosquito vector control, and prevention of sexual and blood-borne transmission are important public health responses to Zika virus.
3. Zika laboratory testing is rapidly evolving. More data are needed to guide clinicians in interpreting results and providing prognoses.
4. While the risk of local transmission is still low in California, the potential exists for a local outbreak to occur and enhanced surveillance of human cases and *Aedes* mosquitoes are important to protect the public health in California.