The Buzz on Zika: Should We Still Be Concerned?

Inland Empire Infectious Disease Conferences
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Roadmap

- Is Zika still a thing?
- Do we know where Zika still is?
- What does it mean for pregnancy, and what's up with all these guidelines?
- Do we know any more about pediatric outcomes?
- Do newborns still need testing and followup?

Aedes aegypti

Background

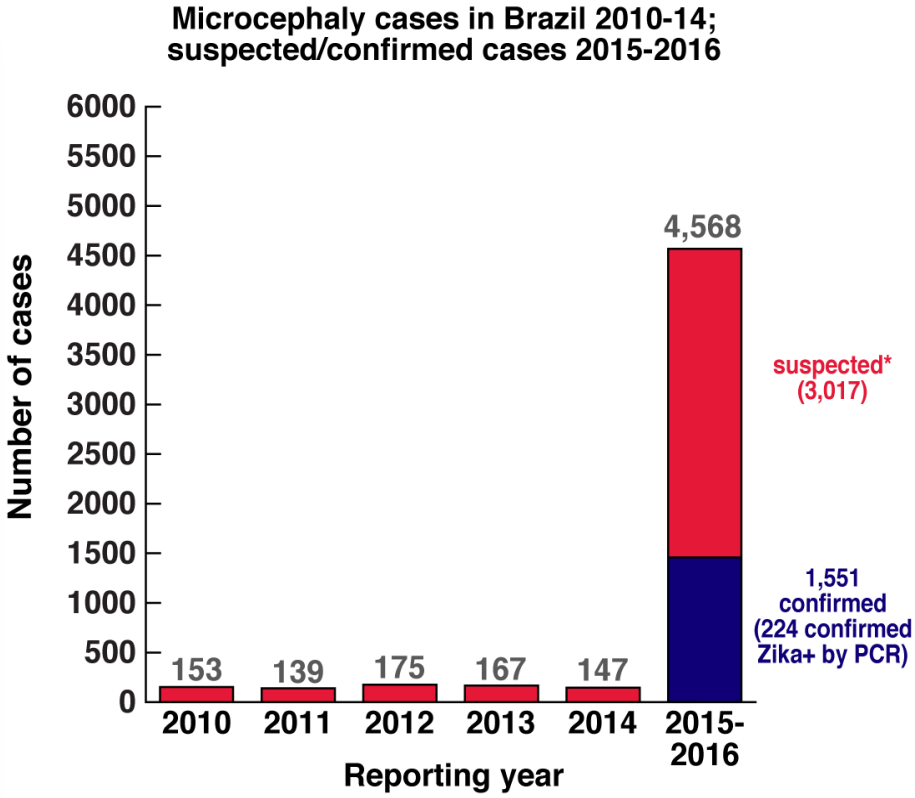
- Zika virus is transmitted to humans primarily through the bite of infected *Aedes* sp. mosquito
  - Nearly all Zika outbreaks due to *aegypti* & *albopictus*
  - These are the same mosquitoes that transmit dengue and chikungunya
    - Dengue and Zika are flaviviruses (YF) ; chikungunya: alphavirus
    - West Nile also arbovirus/flavivirus, but spread by Culex sp.
  - The mosquito vectors typically breed in domestic water-holding containers
  - *Aegypti* -- high "vectorial capacity": feeds primarily on humans, multiple humans in a single meal, lives close to humans , also daytime and nighttime feeders

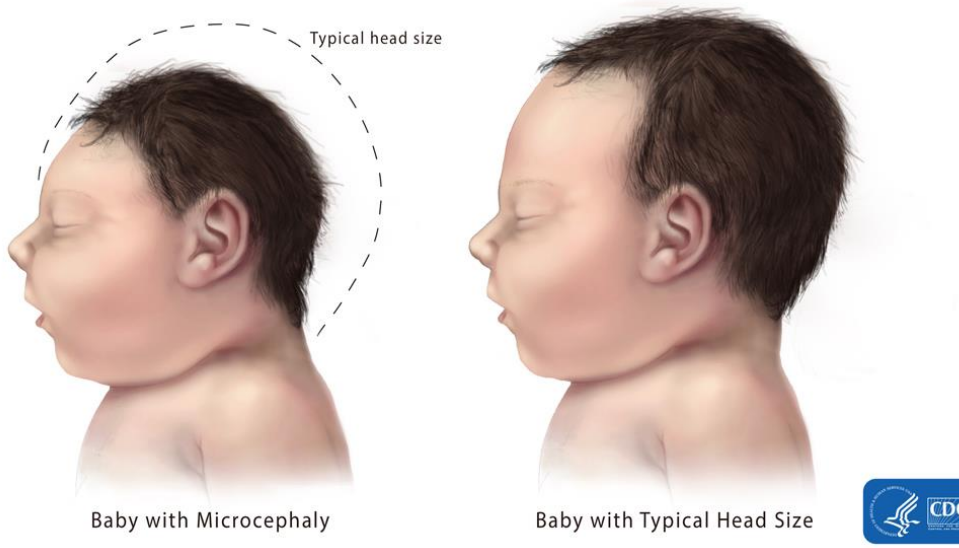
Clinical Disease

- About 20% of people infected with Zika virus become symptomatic
- Among those with clinical illness
  - Symptoms mild, typically develop within 1 week from exposure, lasting several days to a week
  - Characteristic clinical findings: acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis.
  - Severe disease requiring hospitalization is uncommon and fatalities are rare.
- Guillain-Barré syndrome also has been reported at increased rates in patients following Zika infection

Brazil Zika Outbreak

- May 2015: First infection in Brazil
- October 2015: increase in microcephaly





Microcephaly: the tip of the iceberg?

- Microcephaly is a very specific diagnosis, and typically unusual as an isolated finding: initially seen in ***newborns***
  - On ultrasound, defined as **HC < 3 SD** for GA *(SMFM, 2016)**
  - **HC < 2 SD** for GA should trigger more detailed eval and f/u

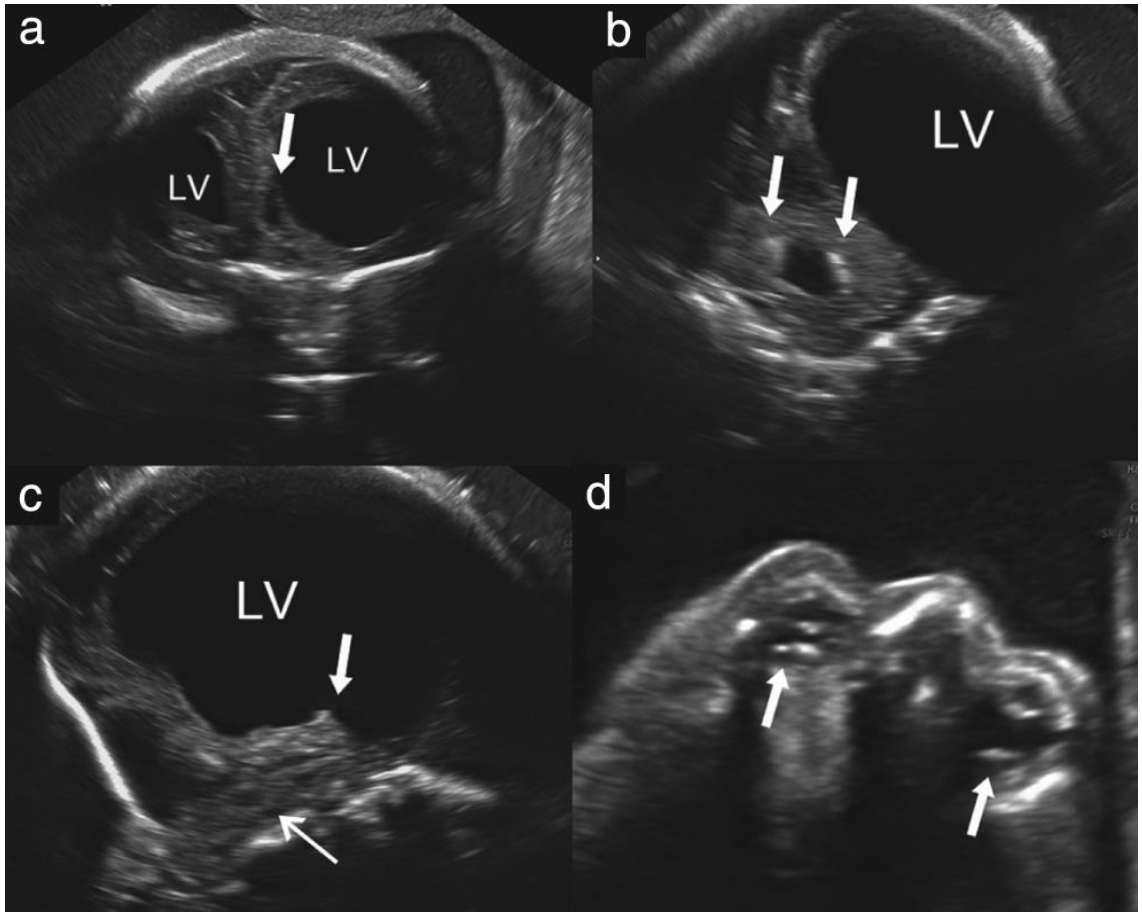
- Microcephaly became an ***early trigger*** to search for Zika association, but spectrum of disease became apparent
  - Microcephaly can occur as a result of a **fetal brain disruption sequence**: this appears to be pathology of Zika infection

** ref: Chervenak FA, et al, AJOG 1984*

Guidance from other Viral Infections?

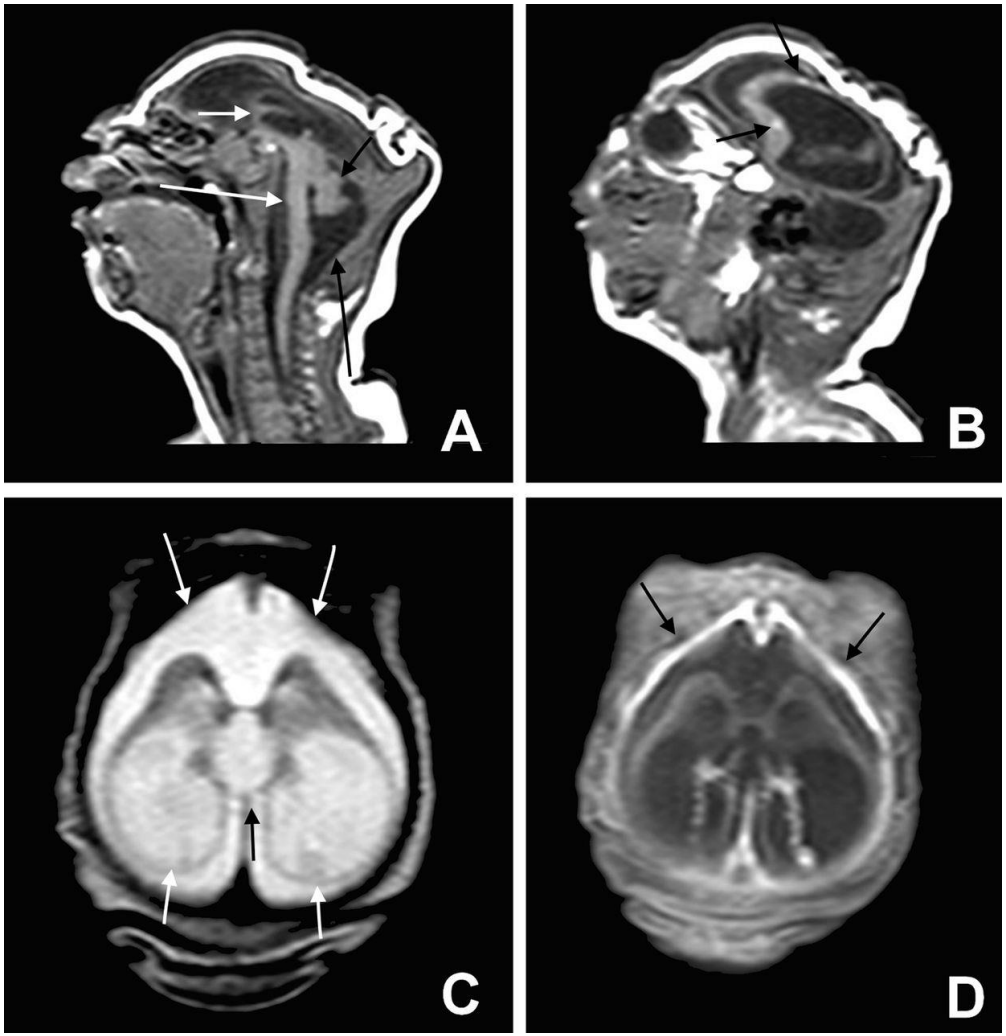
- Well-established risks and effects of maternal infection with rubella and CMV
- Both with greater impact with 1st trimester infection but still impact later
  - Congenital rubella in 90% of 1st Δ infections
  - CMV: 30% infection risk across pregnancy, with greater risk of severe impact with 1st Δ infection
- US prevalence of microcephaly: 6 cases per 10,000 live births (range: 2-12)
  - With Zika, risk of developmental brain abnormalities will be greater than risk of microcephaly

Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg?



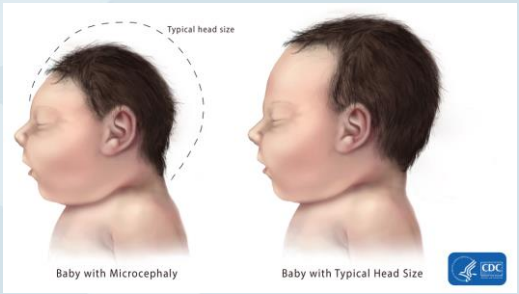
Ultrasound in Obstetrics & Gynecology
Volume 47, Issue 1, pages 6-7, 5 JAN 2016 DOI: 10.1002/uog.15831
http://onlinelibrary.wiley.com/doi/10.1002/uog.15831/full#uog15831-fig-0002

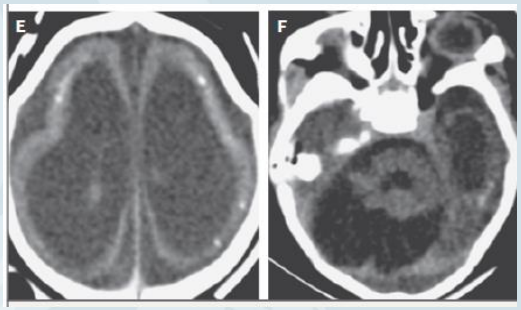
Fig 3 Severe microcephaly.

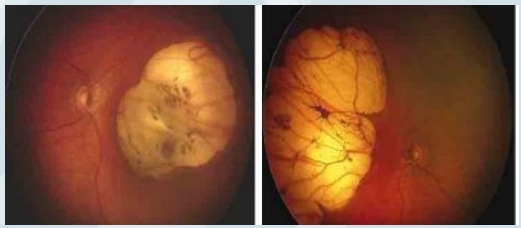


Maria de Fatima Vasco Aragao et al. BMJ 2016;353:bmj.i1901

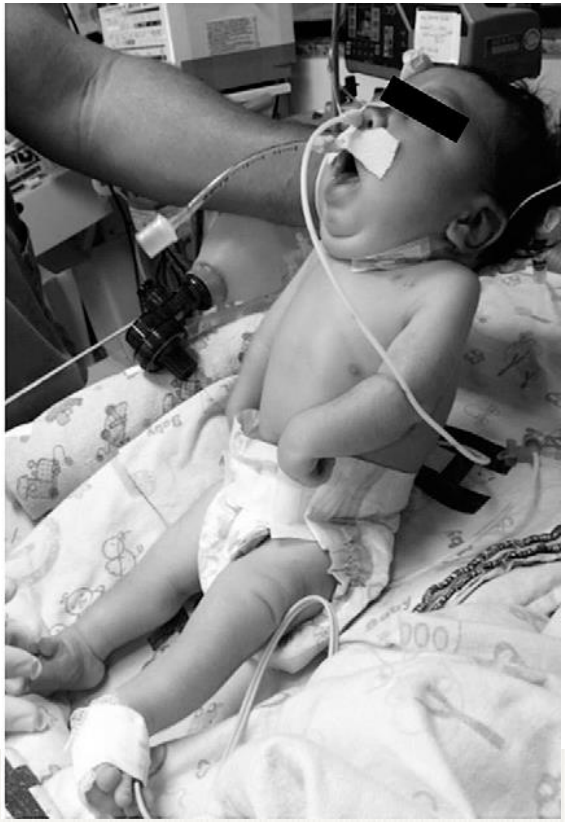
Zika Associated Pregnancy Outcomes







- Fetal loss/miscarriage, stillbirth
- Fetal growth abnormalities
- Fetal brain anomalies
  - Microcephaly
  - Ventriculomegaly
  - Intracranial calcifications
- Eye abnormalities
- Neurologic
  - Hypertonia
  - Arthrogryposis
  - Seizures



Miranda-Filho et al, AJPH April 2016, Vol 106 No. 4

Pregnancy Risk Estimates

- Brasil et al: Rio cohort[1]
  - Prospective study cohort of134 symptomatic pregnant women with confirmed ZKV infection
  - Overall, 49/117 (42%) liveborn ZKV-exposed infants had abnormal findings by 1st month of life [5% in ZKV(-): p< 0.001]
- Adverse outcomes seen regardless of trimester of infx
  - 55% risk if maternal infx in 1st, 52% if in 2nd, 29% if in 3rd
- Updated report from US Zika Pregnancy Registry[2]
  - Birth defects related to Zika in 6%, 21 in live births
  - No risk difference regarding sx; 11% risk if exposure in 1st Δ

1. Brasil et al, NEJM 12/16. 2. Honein M et al, JAMA 12/13/16

Pregnancy Outcomes: Recent French Territorial Data

- Outcome report from French territories in the Americas
  - 546 pregnancies, 555 fetuses/newborns (last delivered 4/17)
  - All mothers were symptomatic & had PCR-confirmed infections
  - 34% of infections n 1st trimester, 46% in 2nd, 20% in 3rd
- Neurologic and ocular abnormalities observed in 7% of fetuses/newborns overall
  - **Risk by trimester: 13%, 4%, 5% for 1st, 2nd, 3rd**
- Findings similar to those from US Registry
- Studies like this continue to be important and underscore need to continue surveillance for all pregnant women at-risk, including the 80% who are asymptomatic

Hoen B, et al. NEJM 3/15/18

Morbidity and Mortality Weekly Report

Health and Development at Age 19–24 Months of 19 Children Who Were Born with Microcephaly and Laboratory Evidence of Congenital Zika Virus Infection During the 2015 Zika Virus Outbreak — Brazil, 2017

Ashley Satterfield-Nash, DrPH[1]; Kim Kotzky, MPH[1]; Jacob Allen, MPH[2]; Jeanne Bertolli, PhD[3]; Cynthia A. Moore, MD, PhD[3]; Isabela Ornelas Pereira[4]; André Pessoa, MD[5]; Flavio Melo, MD[6]; Ana Carolina Faria e Silva Santelli, MD[7]; Coleen A. Boyle, PhD[3]; Georgina Peacock, MD[3]

ZODIAC Study: compiled comprehensive description of children > 12 months of age born with microcephaly (< 3rd %ile at birth) and (+) Zika IgM from Oct 2015-Jan 2016

19 infants, mean age at followup 22 months (range 19-24 months)

15/19 infants had HC ranging from 3.7-8.4 SD below the mean (avg 6.3 SD)
All of these infants were symptomatic and had developmental testing < 6 mos.

4/19 infants had HC within 1 SD of mean, all had testing results for > 6 mos.

TABLE 1. Growth measurements* of children aged 19–24 months with confirmed or probable congenital Zika virus infection†,§ and microcephaly classification at birth¶, — Paraíba, Brazil, August–October 2017**

Growth	No. (%)	
	Male (n = 10)	Female (n = 9)
Head circumference††		
>3 SD below mean for age and sex§§	7 (70)	8 (89)
Length¶¶		
1–3 SD below mean for age and sex***	6 (60)	7 (78)
Weight†††		
1 to >3 SD below mean for age and sex§§§	6 (60)	7 (78)

TABLE 3. Health and developmental outcomes of 19 children aged 19–24 months with confirmed or probable congenital Zika virus infection,[*,†] and microcephaly classification[§,¶] at birth — Paraíba, Brazil, August–October 2017

Outcome	No. (%)
Medical findings	
Seizures[**,††]	11 (58)
Retinal abnormalities[§§]	4 (21)
Hospitalization[**]	8 (42)
Pneumonia/Bronchitis	6 (75)
Intestinal infection	1 (14)
High fever	1 (14)
Failure to thrive/feed	1 (14)
Functional outcomes	
Sleeping difficulties[**]	10 (53)
Feeding difficulties[**]	9 (47)
Impaired response to auditory stimuli (hearing asymmetric or no response)[¶¶]	13 (68)
Impaired response to visual stimuli[¶¶]	11 (58)
Neurologic outcomes[¶¶]	
Severe motor impairment[¶¶]	15 (79)
Cerebral palsy[***]	14 (74)

Summary

What is already known about this topic?

Congenital Zika virus infection has been linked to increased rates of microcephaly and a unique pattern of birth defects among infants. Although children with microcephaly and laboratory evidence of Zika virus infection have been described in early infancy, the subsequent health and development in young children have not been well characterized, constraining planning for the care of these children.

What is added by this report?

The growth and development of 19 children, aged 19–24 months, with laboratory evidence of Zika virus infection were thoroughly assessed. All children had at least one adverse outcome including feeding challenges, sleeping difficulties, severe motor impairment, vision and hearing abnormalities, and seizures, and these outcomes tended to co-occur.

What are the implications for public health practice?

Children with microcephaly and laboratory evidence of Zika virus infection face medical and functional challenges that span many areas of development, some of which become more evident as children age. They will continue to require specialized care from clinicians and caregivers. These data allow for anticipation of medical and social services needs of affected children and families, such as early intervention services, and planning for resources to support these families in healthcare and community settings.

Zika – still here….

Zika in the US: as of April 4, 2018

US States/DC (5676 cases)

- 432 cases in 2017; 14 so far in 2018 (all travel)
- Travel-associated Zika virus disease cases reported: 5284 (50 other routes)
- Locally acquired vector-borne cases reported: 225
  - **In 2017: all travel cases,** *except 1 local and 3 sexual*

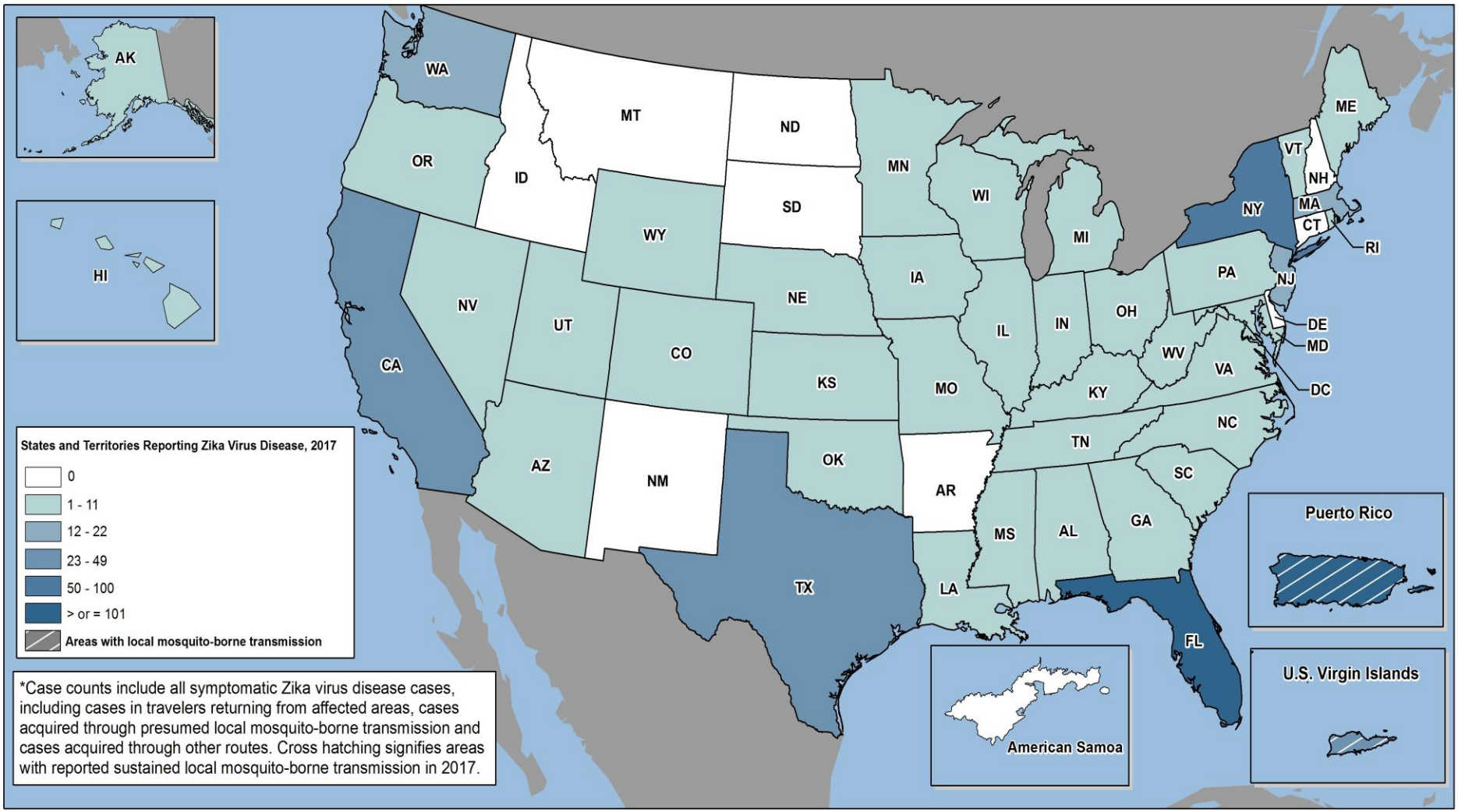
US Territories

- Travel-associated cases reported: 147 (1 in 2017)
- Locally acquired cases reported: 37190 **(including 653 in 2017, 15 so far in 2018)**

Current Zika Statistics (as of 3/20/18)

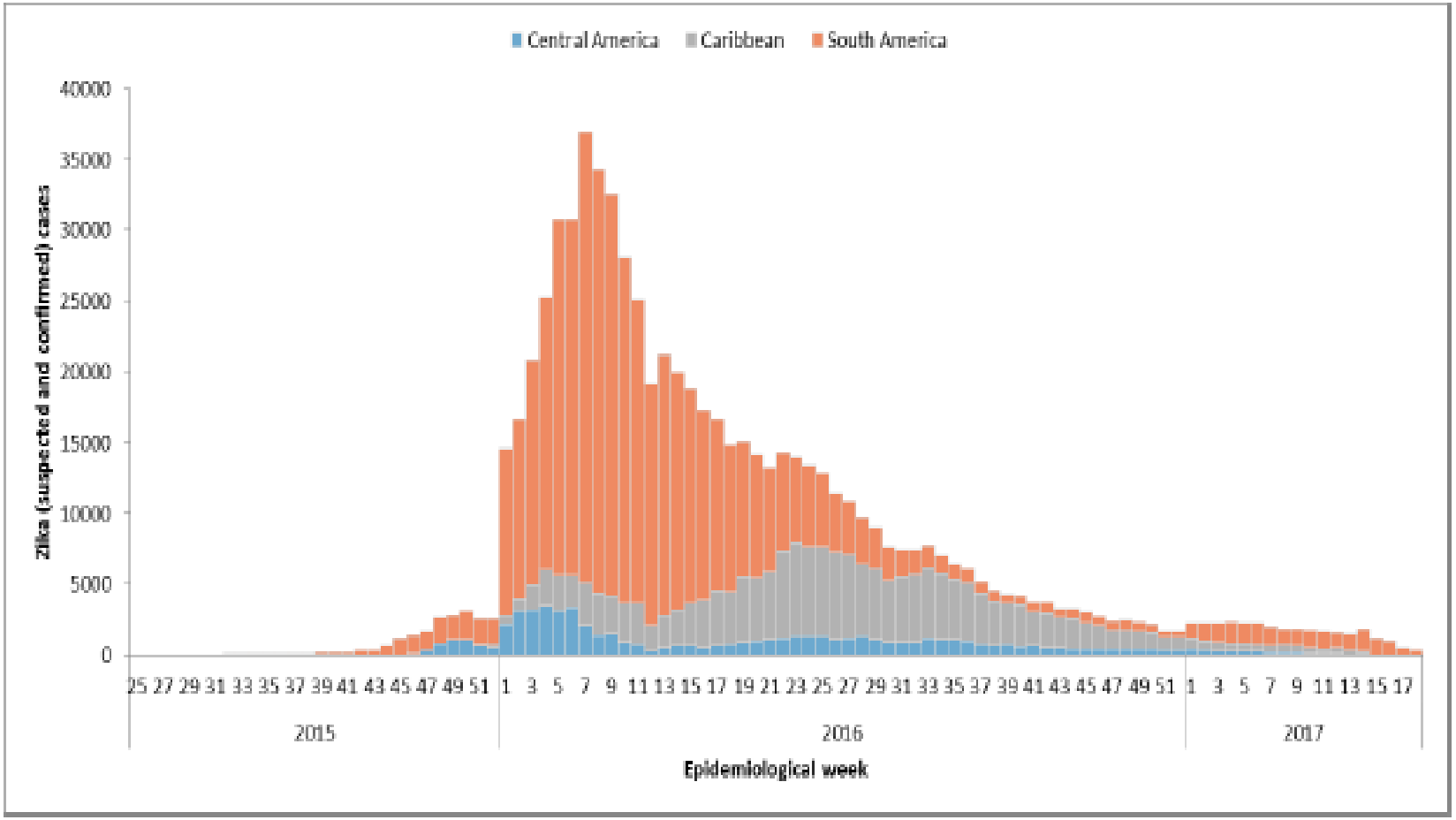
- 2470 **pregnant travelers** with laboratory evidence of Zika virus in US States and DC – vast majority imported/travel-related
  - **52 additional cases** since last report date 2/20/18
  - 2286 completed pregnancies
  - 114 reported liveborn infants and 9 fetal losses with Zika related birth defects (5.3%)
- 4831 **pregnant** cases in US territories (mostly P. Rico) -- 4181 completed, 174 affected (4.2%)
  - **47 additional cases** since 2/20/18

Laboratory-confirmed symptomatic Zika virus disease cases* reported to ArboNET by states and territories— United States, 2017 (Provisional data as of April 4, 2018)



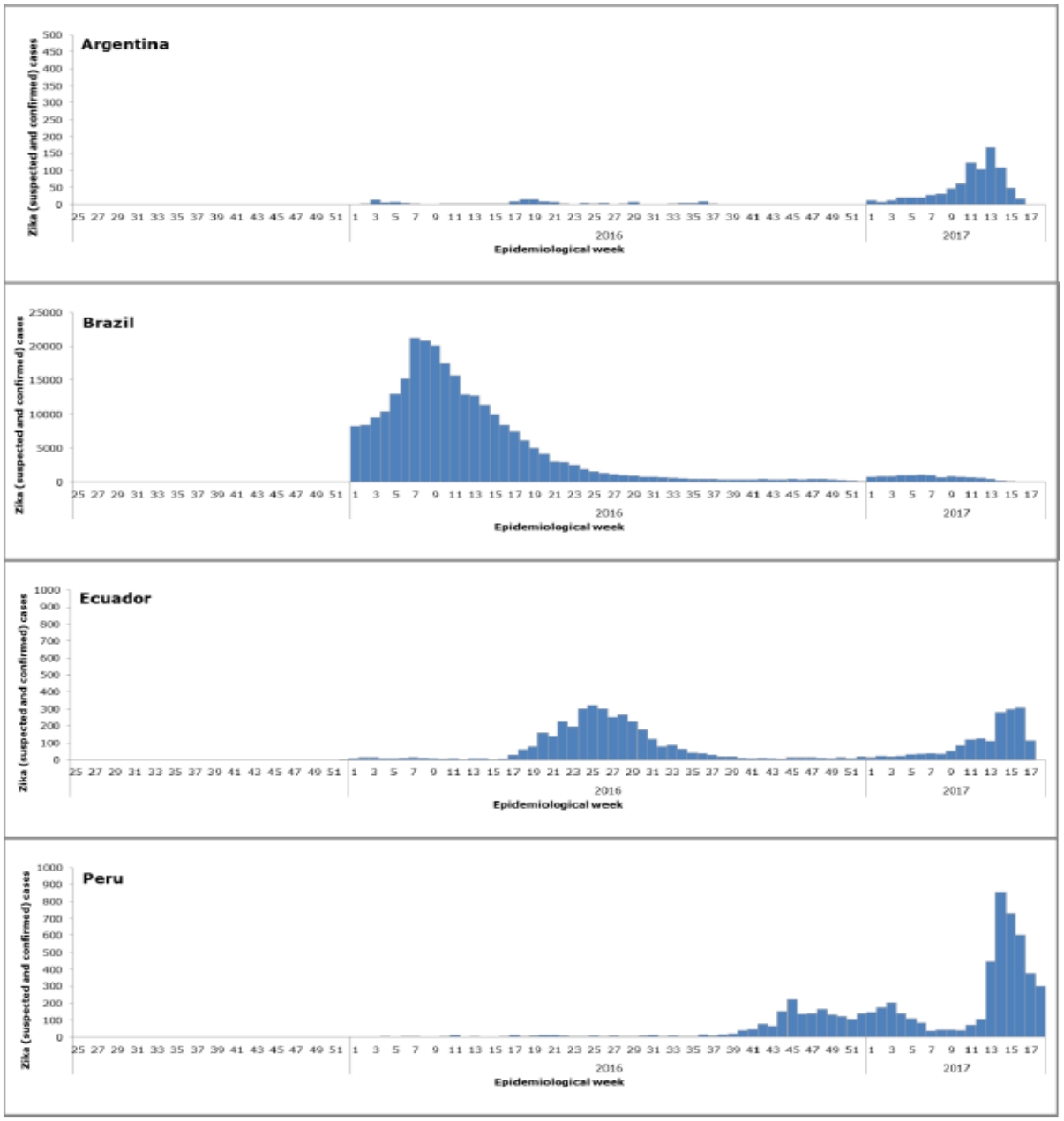
*Case counts include all symptomatic Zika virus disease cases, including cases in travelers returning from affected areas, cases acquired through presumed local mosquito-borne transmission and cases acquired through other routes. Cross hatching signifies areas with reported sustained local mosquito-borne transmission in 2017.

Figure 2. Distribution of suspected and confirmed Zika cases by epidemiological week and sub-region. Region of the Americas, 2016 – 2017 (as of EW 18).[16]



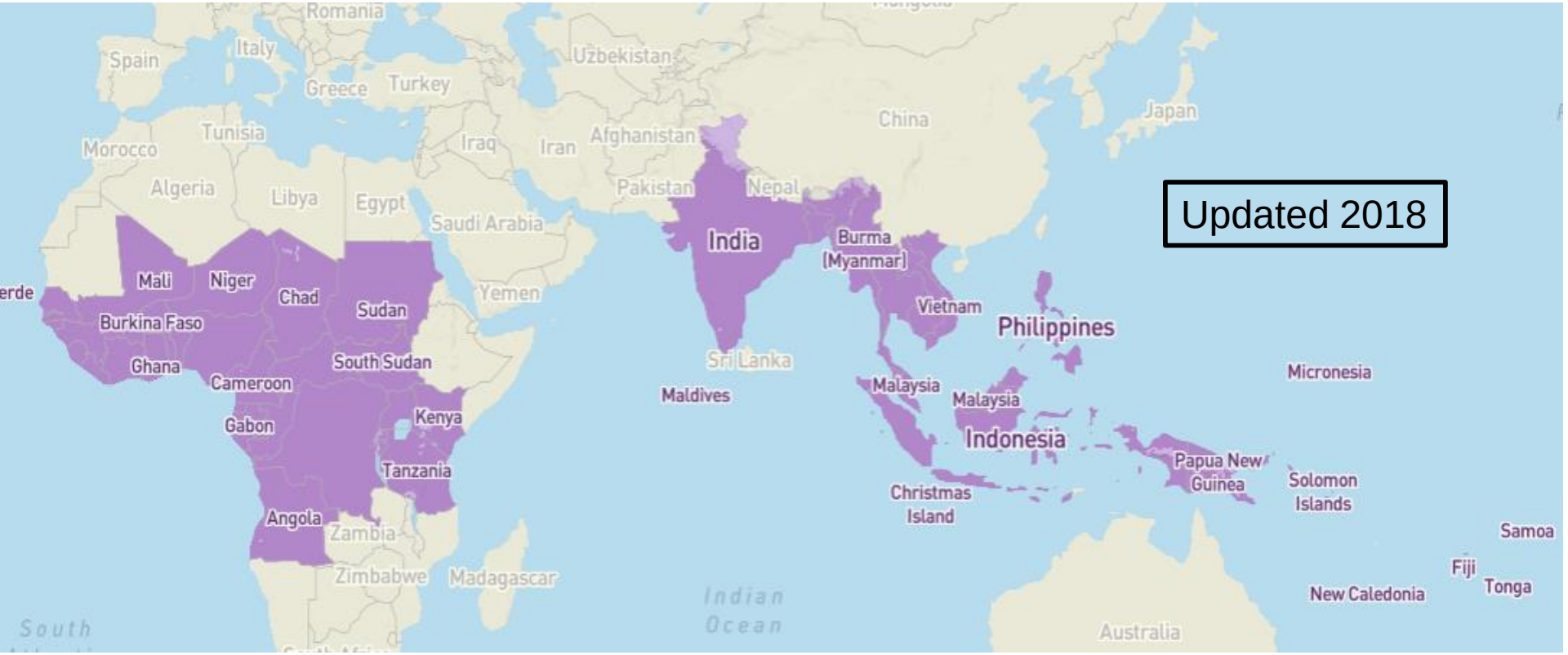
Source: Data provided by countries and territories and reproduced by PAHO/WHO

Figure 3. Distribution of suspected and confirmed Zika cases by EW. Argentina, Brazil, Ecuador, and Peru, EW 25 of 2015 to EW 18 of 2017.



Zika as an Endemic Infection

- Zika virus is considered endemic in some countries, and a large number of local residents are likely to be immune. However, US travelers to endemic areas may not be immune to Zika virus and infections have occurred among travelers to Asia and Africa



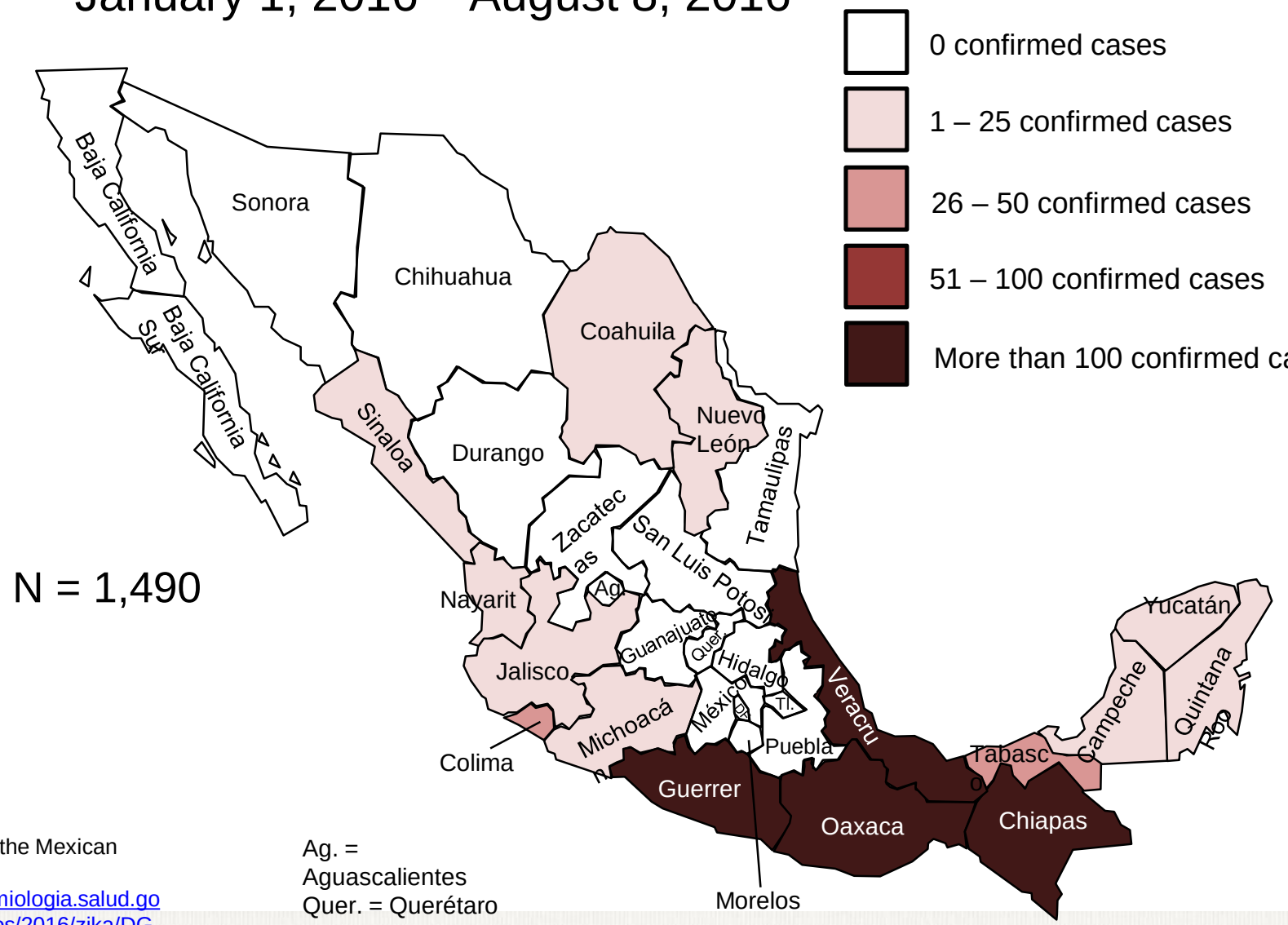
- Zika evolving as an outbreak like other arboviruses : areas of endemicity but high potential (like West Nile and chikungunya) for ongoing sporadic cases and local outbreaks *(Paules C, Fauci A: JAMA 1/12/17)*

Thoughts on Zika's evolution

- Morens/Fauci, JID 2017: the virus, which has existed for years in Asian countries, may have undergone viral mutations that enabled easier spread
- Zika genotyping in Miami showed it came from Caribbean/S America; in S Texas, from Mexico
  - Implications may be that Zika still a risk in Texas and other states, since transmission still occurring in Mexico [1]
- Herd immunity in high-risk countries may have lowered risk in US, but this won't last forever as more nonimmune individuals enter a population[2]
  - This can create a smoldering disease risk with flares

1. Peter Hotez, Baylor 2. Amesh Adalja, Hopkins --- Infect Dis News 3/18

Confirmed Zika Cases in Mexico by State
January 1, 2016 – August 8, 2016

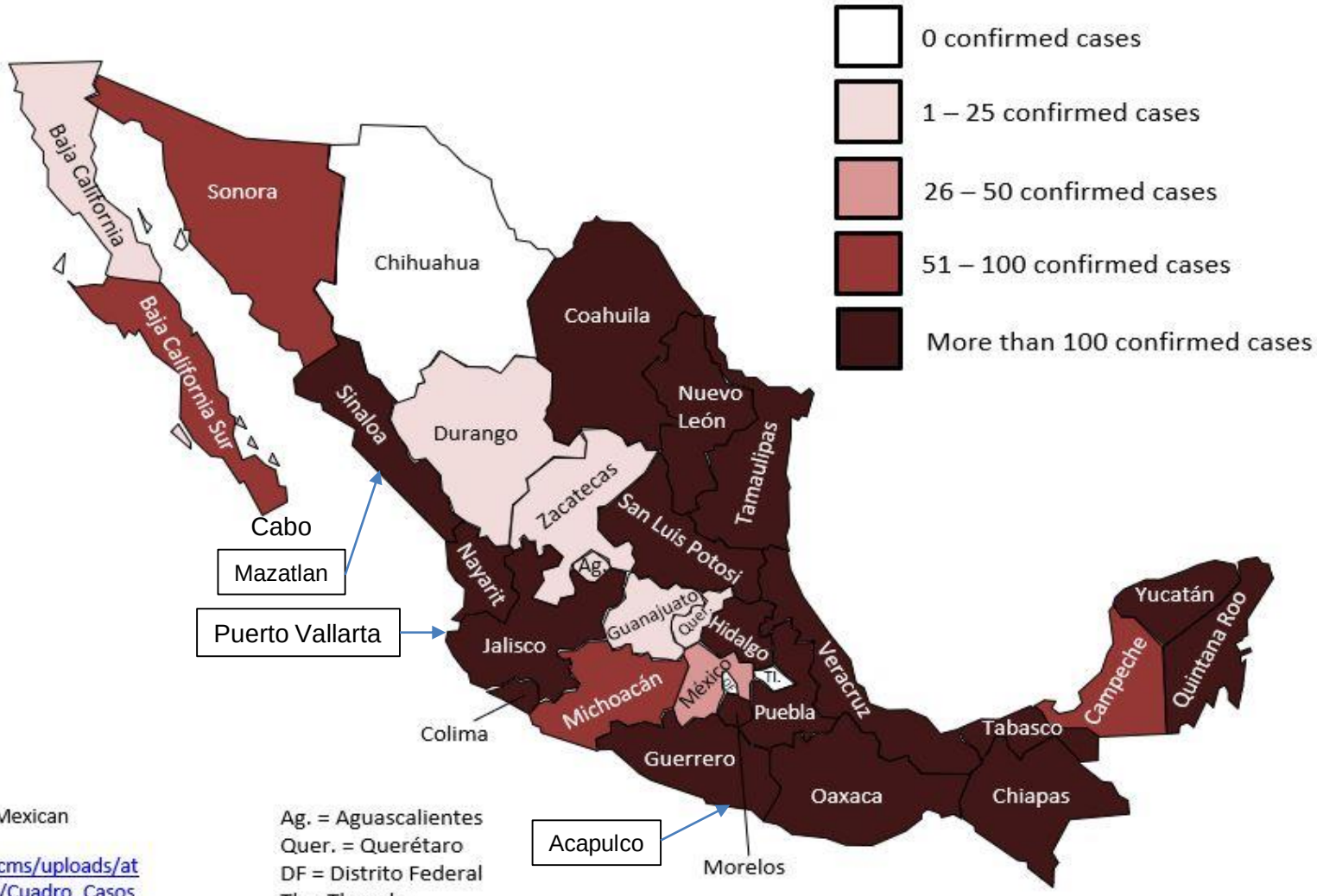


N = 1,490

Data provided by the Mexican Ministry of Health
http://www.epidemiologia.salud.gob.mx/doctos/avisos/2016/zika/DGE_ZIKA_CASOS_SEM028_2016.pdf

Ag. = Aguascalientes
Quer. = Querétaro
DF = Distrito Federal
Tl. = Tlaxcala

Confirmed Zika Cases in Mexico by State
January 1, 2016 – April 2, 2018



Data provided by the Mexican Ministry of Health
https://www.gob.mx/cms/uploads/attachment/file/314604/Cuadro_Casos_ZIKA_y_Emb_SE13_2018.pdf

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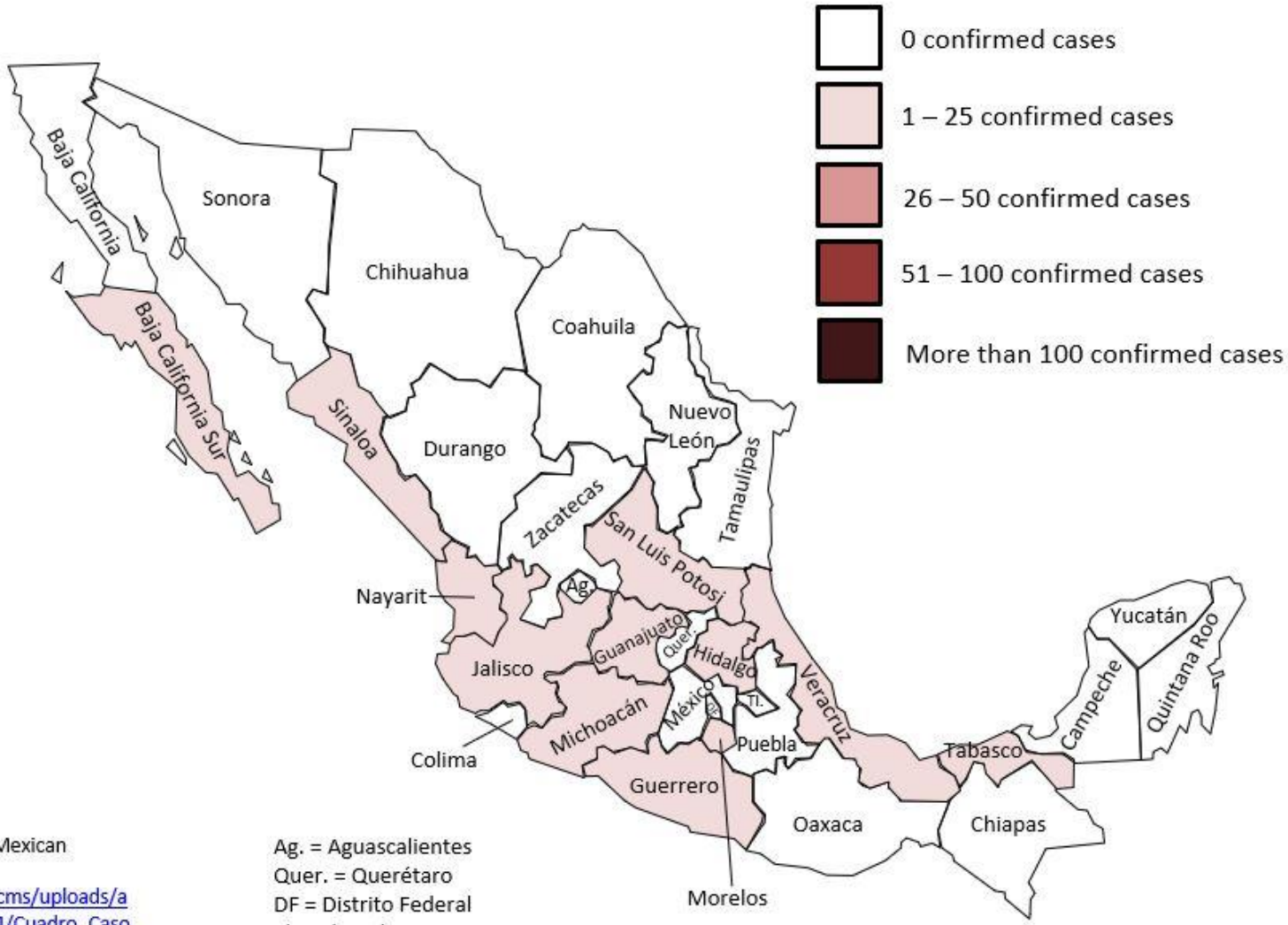
Confirmed Zika Cases in Mexico by State
January 1, 2018 – April 2, 2018



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A_y_Emb_SE13_2018.pdf

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L.A. County officials confirm first case of sexually transmitted Zika virus

Aedes aegypti mosquitoes, responsible for transmitting Zika, sit in a petri dish at the Fiocruz Institute in Recife, Brazil. (Felipe Dana / AP)

By Soumya Karlamangla · Contact Reporter

JANUARY 4, 2018, 12:10 PM

Imported Zika Cases in California, 2015-17

(n = 609, through Nov 3, 2017,
with 101 total in 2017 so far)

Country Traveled To	Number of Imported Cases in California (%)
Mexico	195 (36%)
Nicaragua	61 (11%)
Guatemala	49 (9%)
El Salvador	37 (7%)
Dominican Republic	26 (5%)

These 5 countries account for 68% of travel cases in CA

Median age 35 66% in women

Zika – Education and Testing

What do we tell our pregnant patients?

- How much fetal risk with confirmed maternal infection?
  - Based on current data, **range may be as high as 29%**
  - Rates are derived from methodologically diverse studies
- Despite earlier reports, recent data suggest later GA at infection does not exclude potential adverse impact
- Pregnant women **should not travel** to areas with active local Zika transmission

The role of prevention

- If in an area with transmission, protection and prevention strategies are important – ***and repellent for 3 weeks after return from these areas***
- DEET, picaridin fine for use in pregnancy
  - Consumer Reports (Sept 2017): Deet at 25-30% concentrations works best, picardin 20% (spray, not lotion), oil of lemon eucalyptus 30% (Repel better than Coleman)

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 66
July 24, 2017

Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories), July 2017

Titilope Oduyebo, MD[1]; Kara D. Polen, MPH[1]; Henry T. Walke, MD[1]; Sarah Reagan-Steiner, MD[1]; Eva Lathrop, MD[1]; Ingrid B. Rabe, MBChB[1]; Wendi L. Kuhnert-Tallman, PhD[1]; Stacey W. Martin, MSc[1]; Allison T. Walker, PhD[1]; Christopher J. Gregory, MD[1]; Edwin W. Ades, PhD[1]; Darin S. Carroll, PhD[1]; Maria Rivera, MPH[1]; Janice Perez-Padilla, MPH[1]; Carolyn Gould, MD[1]; Jeffrey B. Nemhauser, MD[1]; C. Ben Beard, PhD[1]; Jennifer L. Harcourt, PhD[1]; Laura Viens, MD[1]; Michael Johansson, PhD[1]; Sascha R. Ellington, MSPH[1]; Emily Petersen, MD[1]; Laura A. Smith, MA[1]; Jessica Reichard, MPA[1]; Jorge Munoz-Jordan, PhD[1]; Michael J. Beach, PhD[1]; Dale A. Rose, PhD[1]; Ezra Barzilay, MD[1]; Michelle Noonan-Smith[1]; Denise J. Jamieson, MD[1]; Sherif R. Zaki, MD[1]; Lyle R. Petersen, MD[1]; Margaret A. Honein, PhD[1]; Dana Meaney-Delman, MD[1]

Adapted for specific usage in CA: July 2017, then in Jan 2018

Definition of Possible Zika Virus Exposure during Pregnancy

- Travel to or living in an area with Zika risk during their pregnancy or up to 8 weeks before conception
  -- (6 weeks prior to last menstrual period)

- Sex without barrier protections (male or female condoms and dental dams) with a male partner who had possible exposure to Zika within 6 months prior to sexual contact, or a female partner who had possible exposure to Zika within 8 weeks of sexual contact.
  - Sexual activity includes vaginal, anal, and oral sex, as well as sharing of sex toys

What informed the new testing guidelines?

- While consequences of Zika infection are better understood, accurate diagnosis continues to be challenging
  - Virus present in body fluids only transiently
  - Serologic testing (IgM) can't always reliably time infection
  - Serology prone to false-positive results and cross-reaction with other flaviviruses
- With declining prevalence of Zika infection, probability of false-positive tests increases
- Changing epidemiology further limits diagnostic capabilities of existing tests

Zika Immunity

- Presumption has been that Zika infection confers immunity after the IgM response
- Based on experience with other flaviviruses, previous Zika infection is likely to confer prolonged, likely lifelong immunity
  - If true, prior infection would prevent risks for a future pregnancy
- However, **no commercially-available IgG testing exists**, and IgM duration limited

New guidelines – what do the changes reflect?

- As many areas in the Americas move into a 2nd or 3rd mosquito season after introduction of Zika virus, testing becomes more complex
- Given the evolving epidemiology and the better-realized limitations of testing, updated testing algorithms for symptomatic and asymptomatic pregnant women emphasize a **shared decision-making model**
- Need for pre-and post-test counseling, with results interpreted in context of limitations

New guidelines: what's the same (mostly)?

- **Screen pregnant women for Zika exposure risk and/or symptoms** at every prenatal *and hospital* visit
  - Knowledge of potential exposure before and during pregnancy is critical information for test interpretation
- **Symptomatic** pregnant women with recent possible Zika exposure: testing still recommended
  - Concurrent NAT (blood/urine) and IgM as soon as possible, through 12 weeks post-exposure ***(can consider if > 12 wks, but..)***
- Pregnant women with exposure and u/s findings: **test**
- Asymptomatic women with *ongoing* possible Zika exposure: testing still offered once/trimester
  - ***NAT testing of blood and urine, not IgM (diagnostic limits)***

New guidelines: what's different (mostly)

- Asymptomatic women with recent possible Zika exposure **but not ongoing exposure**
  - Testing now ***not routinely recommended*** for this group
  - BUT: shared-decision making and ***consideration of local/regional epidemiologic risks*** important for this group
  - CDC acknowledges that data indicate that while perinatal Zika risk doesn't differ by maternal symptoms, routine testing in a low-prevalence group increases risk of false-positives in absence of any prevention or therapies
  - If testing done, default to algorithm for symptomatic/no ongoing exposure: **PCR and IgM**
- ***Until recently (Jan/18): CA, FL, TX, NY kept prior guidelines***

State of California—Health and Human Services Agency

California Department of Public Health

KAREN L. SMITH, MD, MPH
Director and State Public Health Officer

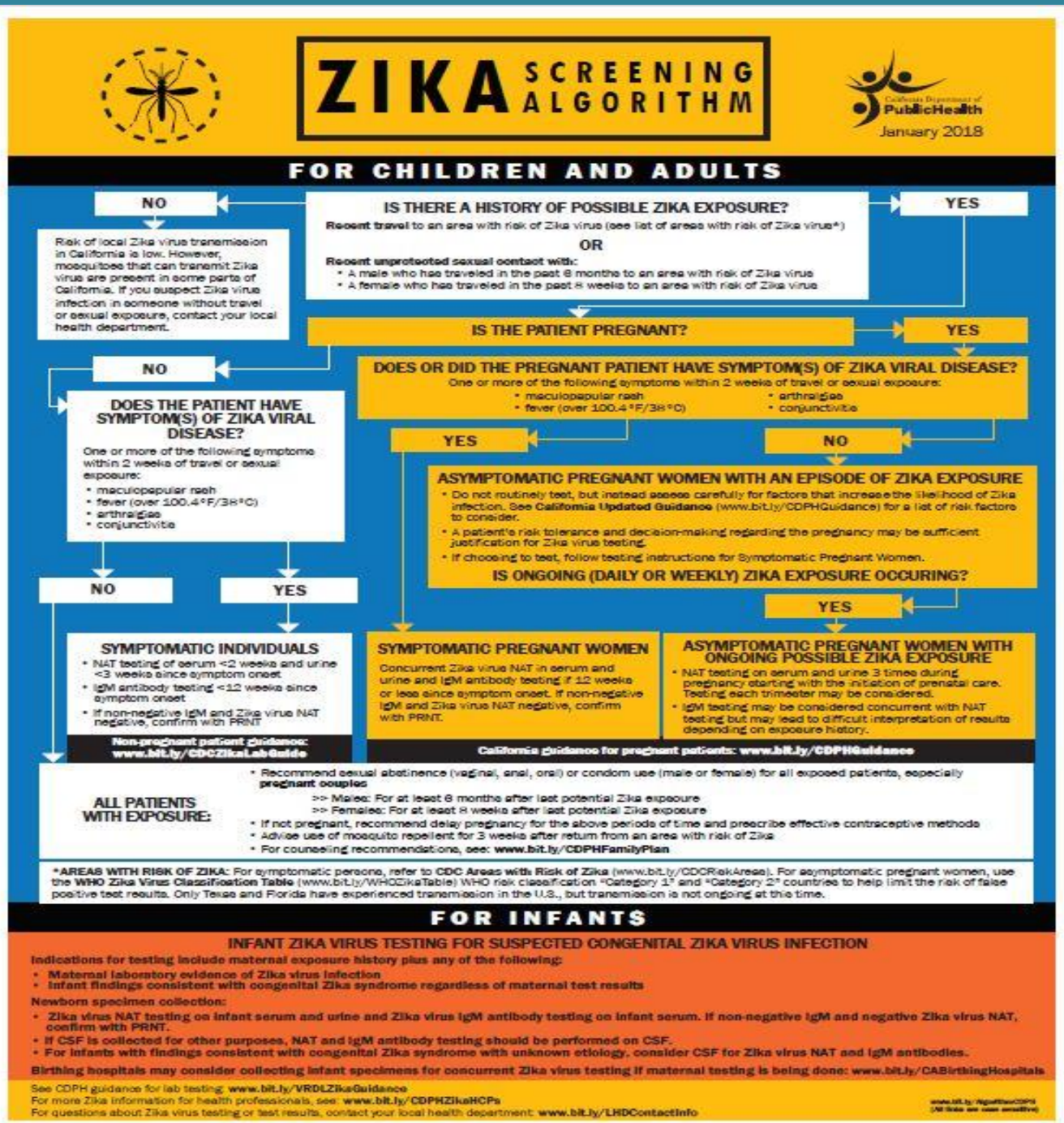
EDMUND G. BROWN JR.
Governor

Date: January 10, 2018

To: California Health Care Providers

C. **Asymptomatic Pregnant Women** with recent *but without ongoing* exposure are not routinely tested **but instead should be assessed carefully** for factors that increase the likelihood of Zika infection. A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification to test for Zika virus infection.

California has substantially declined. These factors together lead to a lower pre-test probability of infection when considering testing pregnant women and their newborns. As of November 24, 2017, 162 pregnant women with travel-associated Zika infection have been reported in California since 2015. Of these, 136 women have had completed pregnancies and 9 infants have been born with microcephaly and other Zika-associated anomalies. More than half of the infants born in California with Zika-associated birth defects were born to Zika-exposed mothers who were asymptomatic for Zika infection.


ZIKA SCREENING ALGORITHM
California Department of PublicHealth
January 2018
FOR CHILDREN AND ADULTS
IS THERE A HISTORY OF POSSIBLE ZIKA EXPOSURE?
Recent travel to an area with risk of Zika virus (see list of areas with risk of Zika virus*)
OR
Recent unprotected sexual contact with:
• A male who has traveled in the past 6 months to an area with risk of Zika virus
• A female who has traveled in the past 8 weeks to an area with risk of Zika virus
NO
Risk of local Zika virus transmission in California is low. However, mosquitoes that can transmit Zika virus are present in some parts of California. If you suspect Zika virus infection in someone without travel or sexual exposure, contact your local health department.
YES
IS THE PATIENT PREGNANT?
YES
NO
DOES THE PATIENT HAVE SYMPTOM(S) OF ZIKA VIRAL DISEASE?
One or more of the following symptoms within 2 weeks of travel or sexual exposure:
• maculopapular rash
• fever (over 100.4°F/38°C)
• arthralgias
• conjunctivitis
NO
YES
DOES OR DID THE PREGNANT PATIENT HAVE SYMPTOM(S) OF ZIKA VIRAL DISEASE?
One or more of the following symptoms within 2 weeks of travel or sexual exposure:
• maculopapular rash
• fever (over 100.4°F/38°C)
• arthralgias
• conjunctivitis
YES
NO
ASYMPTOMATIC PREGNANT WOMEN WITH AN EPISODE OF ZIKA EXPOSURE
• Do not routinely test, but instead assess carefully for factors that increase the likelihood of Zika infection. See California Updated Guidance (www.bit.ly/CDPHGuidance) for a list of risk factors to consider.
• A patient's risk tolerance and decision-making regarding the pregnancy may be sufficient justification for Zika virus testing.
• If choosing to test, follow testing instructions for Symptomatic Pregnant Women.
IS ONGOING (DAILY OR WEEKLY) ZIKA EXPOSURE OCCURING?
YES
NO
YES
SYMPTOMATIC INDIVIDUALS
• NAT testing of serum <2 weeks and urine <3 weeks since symptom onset
• IgM antibody testing <12 weeks since symptom onset
• If non-negative IgM and Zika virus NAT negative, confirm with PRNT
Non-pregnant patient guidance: www.bit.ly/CDCZikaLabGuide
SYMPTOMATIC PREGNANT WOMEN
Concurrent Zika virus NAT in serum and urine and IgM antibody testing if 12 weeks or less since symptom onset. If non-negative IgM and Zika virus NAT negative, confirm with PRNT.
ASYMPTOMATIC PREGNANT WOMEN WITH ONGOING POSSIBLE ZIKA EXPOSURE
• NAT testing on serum and urine 3 times during pregnancy starting with the initiation of prenatal care. Testing each trimester may be considered.
• IgM testing may be considered concurrent with NAT testing but may lead to difficult interpretation of results depending on exposure history.
California guidance for pregnant patients: www.bit.ly/CDPHGuidance
ALL PATIENTS WITH EXPOSURE:
• Recommend sexual abstinence (vaginal, anal, oral) or condom use (male or female) for all exposed patients, especially pregnant couples
>> Males: For at least 6 months after last potential Zika exposure
>> Females: For at least 8 weeks after last potential Zika exposure
• If not pregnant, recommend delay pregnancy for the above periods of time and prescribe effective contraceptive methods
• Advise use of mosquito repellent for 3 weeks after return from an area with risk of Zika
• For counseling recommendations, see: www.bit.ly/CDPHFamilyPlan
*AREAS WITH RISK OF ZIKA: For symptomatic persons, refer to CDC Areas with Risk of Zika (www.bit.ly/CDCRiskAreas). For asymptomatic pregnant women, use the WHO Zika Virus Classification Table (www.bit.ly/WHOZikaTable) WHO risk classification "Category 1" and "Category 2" countries to help limit the risk of false positive test results. Only Texas and Florida have experienced transmission in the U.S., but transmission is not ongoing at this time.
FOR INFANTS
INFANT ZIKA VIRUS TESTING FOR SUSPECTED CONGENITAL ZIKA VIRUS INFECTION
Indications for testing include maternal exposure history plus any of the following:
• Maternal laboratory evidence of Zika virus infection
• Infant findings consistent with congenital Zika syndrome regardless of maternal test results
Newborn specimen collection:
• Zika virus NAT testing on infant serum and urine and Zika virus IgM antibody testing on infant serum. If non-negative IgM and negative Zika virus NAT, confirm with PRNT.
• If CSF is collected for other purposes, NAT and IgM antibody testing should be performed on CSF.
• For infants with findings consistent with congenital Zika syndrome with unknown etiology, consider CSF for Zika virus NAT and IgM antibodies.
Birthing hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done: www.bit.ly/CABirthingHospitals
See CDPH guidance for lab testing: www.bit.ly/VRDLZikaGuidance
For more Zika information for health professionals, see: www.bit.ly/CDPHZikaHCPs
For questions about Zika virus testing or test results, contact your local health department: www.bit.ly/LHDContactInfo

Pregnancy Management

- Microcephaly and intracranial calcifications typically detected during ultrasounds in the late 2nd/early 3rd Δ
  - These birth defects might be detected as early as 18-20 weeks gestation.
  - A recent study of 17 pregnancies with laboratory confirmed Zika virus infection and adverse fetal outcomes reported a ***median of 18 weeks*** from symptom onset to prenatal diagnosis of microcephaly. *(Paara-Saavedra et al, ObGyn 7/17)*
- If early testing negative and 2nd trimester or early 3rd trimester scan normal: usual care
- If confirmed/possible maternal Zika infection, consider serial u/s q 3-4 weeks

Sexual Transmission: What We are Learning

- Maximum duration of virus in semen/vaginal fluids to infect a sexual partner
  - *Lancet* 6/7/16: transmission through semen 34-41 d after infection
  - *Lancet* 8/2016: Zika RNA found in semen after 90 days
  - *Eurosurveillance* 8/11/16: RNA (+) in urine up to 91 days and in semen 134 days after sx
- If Zika can be transmitted through saliva or other body fluids
- Transmission risk/duration after ***asymptomatic*** infection

Sexual Partner concerns/guidelines

- Sexual transmission of Zika virus can occur
  - Male/female, female/male, male/male all reported
- Pregnant women whose male partners have or are at risk for Zika virus infection should consider using condoms or abstaining from sexual intercourse – ***duration of pregnancy***
- Zika has recently been shown to cause testicular damage in mouse models *(Govero J, et al. Lancet Dec 15, 2016)*
  - ZKV persistence in testis/epididymis→ tissue injury resulting in diminished testosterone and inhibin B levels and oligospermia

Zika "waiting periods" – not just pregnancy

- Timeframes to wait to get pregnant after travel to an area with a CDC travel notice ***(CDC 7/17)***
  - Women -- 8 weeks Men -- 6 months
  - If both partners traveled, wait 6 months + condoms

- Egg and sperm donors ***(ASRM, 3/16)***
  - Wait period ***6 months*** after infx, travel, or contact

- Blood donors ***(FDA, 2/16)***
  - 4 week waiting period

Zika Shedding in Zika-Infected Men

- Prospective CDC study of 184 symptomatic men with confirmed Zika infection
  - Semen and urine samples obtained 2x/month for 6 months after illness onset
  - Tested by PCR for ZIKV RNA and a ***plaque assay for infectious ZIKV***
  - Total of 1327 semen samples and 1038 urines obtained
- Zika less common in urine (4%) than semen (33%) when tested by PCR -- 61% in semen within 30 days
- Zika shedding decreased during 3 months post illness but continued for 281 days in 1 man (11% > 4 months)
- Infectious ZIKV isolated from 3/78 samples (3.8%), all within 30 days from illness, all with high viral titers
  - None of the samples with VL < 7 log 10 yielded infectious ZIKV

Mead PS, et al. NEJM 4/12/18

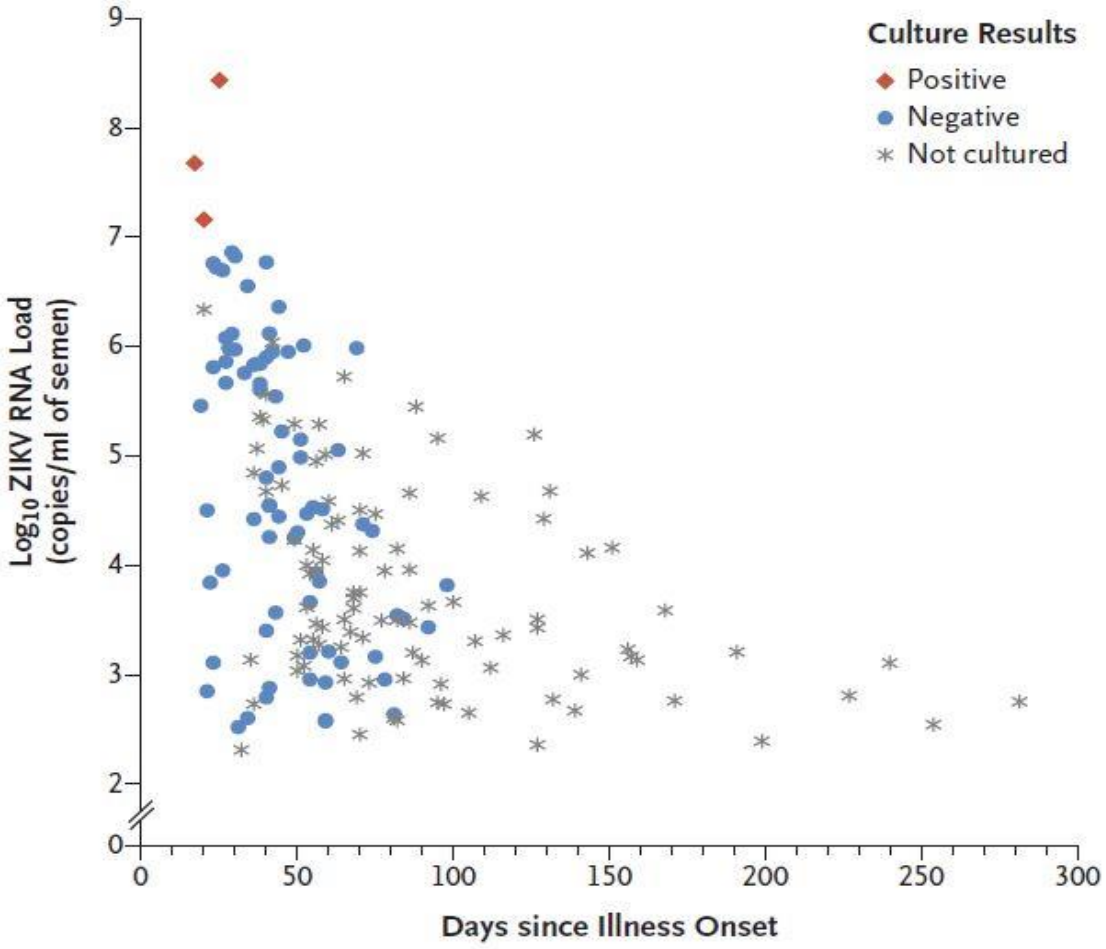


Figure 1. Estimated Viral RNA Load and Culture Results in Semen Samples from 184 Men, 2016–2017.

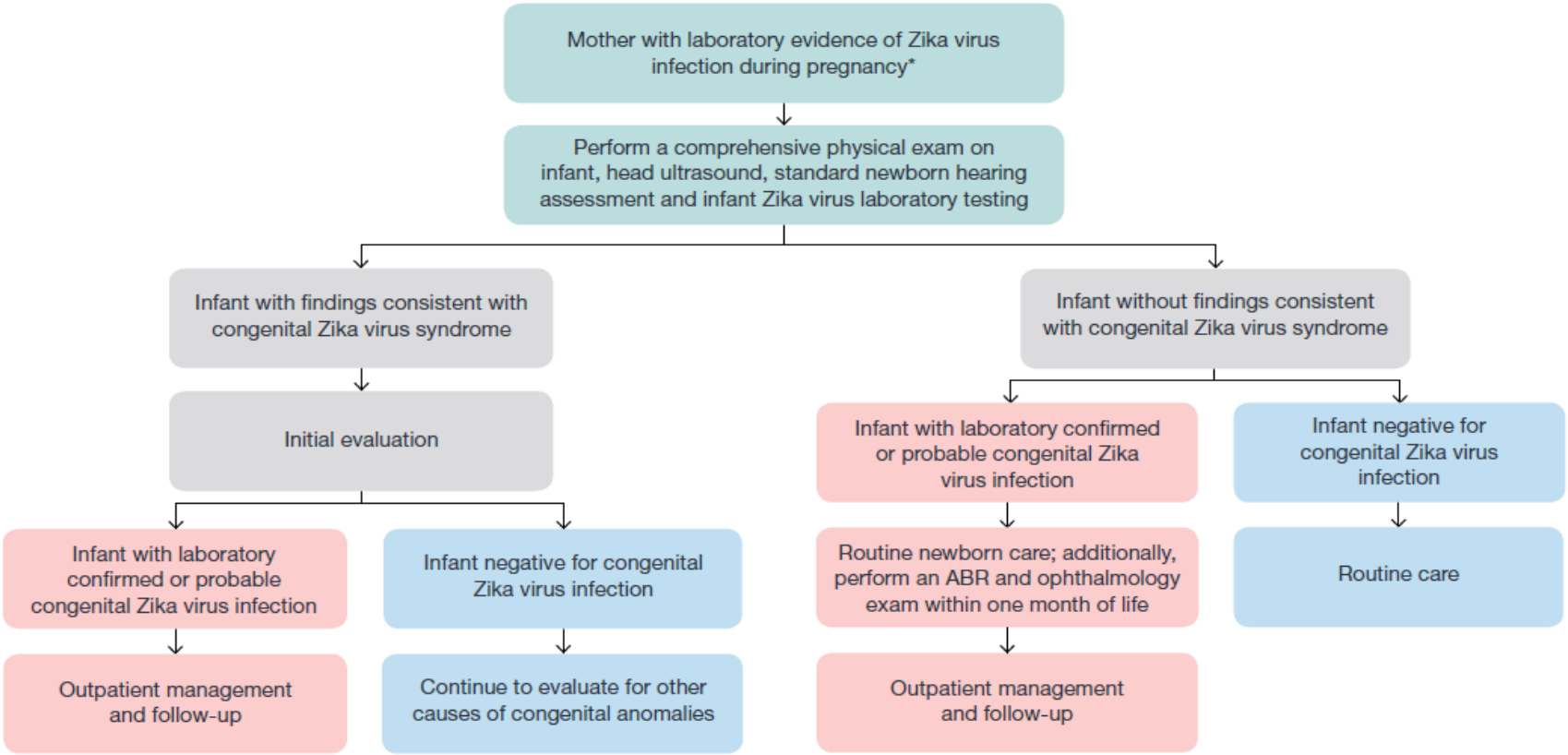
Shown is the estimated viral RNA load and culture results for semen samples with Zika virus (ZIKV) RNA detected by reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay, according to days since illness onset, among 184 enrolled U.S. residents with symptomatic ZIKV infection in the 2016–2017 period.

CDC's Response to **Zika**

INTERIM GUIDANCE

Neonatal coordination is Critical!

Evaluation and testing of infants with possible congenital Zika virus infection



*Laboratory evidence of maternal Zika virus infection includes: (1) Zika virus RNA detected by real-time reverse transcription-polymerase chain reaction (rRT-PCR) in any clinical specimen; or (2) positive Zika virus immunoglobulin M (IgM) with confirmatory neutralizing antibody titers. Mother's should be tested by rRT-PCR within 2 weeks of exposure or symptom onset, or IgM within 2-12 weeks of exposure or symptom onset. Due to the decline in IgM antibody and viral RNA levels over time, negative maternal testing 12 weeks after exposure does not rule out maternal infection.

Abbreviation: ABR = auditory brainstem response.

More information on the evaluation, management, and follow-up of infants with possible congenital Zika virus infection is available at www.cdc.gov/zika/hc-providers/infants-children.html.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Need for Neonatal Followup & Deficits

- Recent report on 2549 completed pregnancies (1/16-4/17)
  - 5% of fetuses/newborns of women in Puerto Rico with confirmed Zika infection had likely Zika-associated birth defects [1]
  - Of liveborns without birth defects, only 52% had postnatal neuroimaging and 78% had hearing screens
- Recent US Pregnancy Registry Data worse (MMWR, 4/7/17) [2]
  - Among 895 liveborns with maternal infection: postnatal neuroimaging reported for 25%, Zika testing of at least 1 infant specimen 65%
- While 98% of pregnant women in P.R. in a recent survey took at least 1 measure to avoid Zika infection, use of repellents (45%) and condoms (40%) during pregnancy overall low [3]

1. Shapiro-Mendoza CK, et al, MMWR 6/8/17. 2. Reynolds M et al, MMWR 4/7/17.
3. D'Angelo DV et al, MMWR 6/9/17

Which newborns need Zika surveillance?

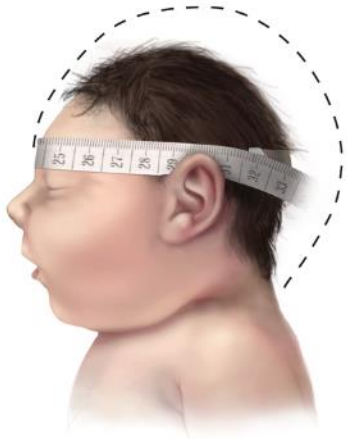
- Zika testing for in 1st two days after birth for infants at risk: serum and urine for PCR, serum for IgM – NOT cord blood
  - Mothers with lab-confirmed infection
  - Abnormal clinical findings suggestive of congenital Zika and potential maternal epidemiologic link, regardless of maternal test results
  - Birthing hospitals may consider collecting infant specimens for concurrent Zika virus testing if maternal testing is being done at delivery.
  - If infant testing is being conducted but maternal infection is not yet confirmed, consider concurrent maternal testing to inform infant Zika test result interpretation.
- All infants born to women with lab-confirmed Zika infection should get:
  - Zika testing, comprehensive exam, head ultrasound, and standard hearing assessment, and formal eye exam

Possible Limitations of Infant Laboratory Testing

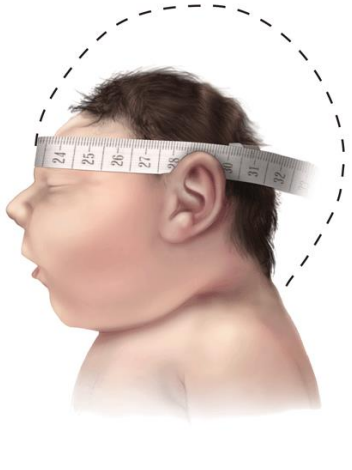
- Optimal tests, types of specimens to test, and timing to test for congenital Zika virus infection are not entirely established.
  - Recent studies have described a small number of infants with clinical findings consistent with congenital Zika syndrome in whom results of laboratory testing for Zika virus infection were negative.
- Negative test results might occur in an infant with clinical findings of possible congenital Zika virus syndrome for several reasons:
  - The clinical findings are due to another cause
  - Testing was incomplete (e.g., RNA testing without antibody testing), performed on suboptimal specimens (e.g., cord blood rather than blood obtained from the infant), or performed too late (e.g., after RNA and IgM antibodies had cleared or waned)
  - The fetus did not mount an IgM antibody response

Measuring head circumference for microcephaly

Baby with typical head size



Baby with Microcephaly



Baby with Severe Microcephaly

- Use a measuring tape that cannot be stretched
- Securely wrap the tape around the widest possible circumference of the head
  - Broadest part of the forehead above eyebrow
  - Above the ears
  - Most prominent part of the back of the head

Take the measurement three times and select the largest measurement to the nearest 0.1 cm

Optimal measurement within 24 hours after birth.

- Commonly-used birth head circumference reference charts by age and sex based on measurements taken before 24 hours of age

http://www.cdc.gov/zika/pdfs/microcephaly_measuring.pdf

Recommended consultation for initial evaluation and management of infants affected by Zika

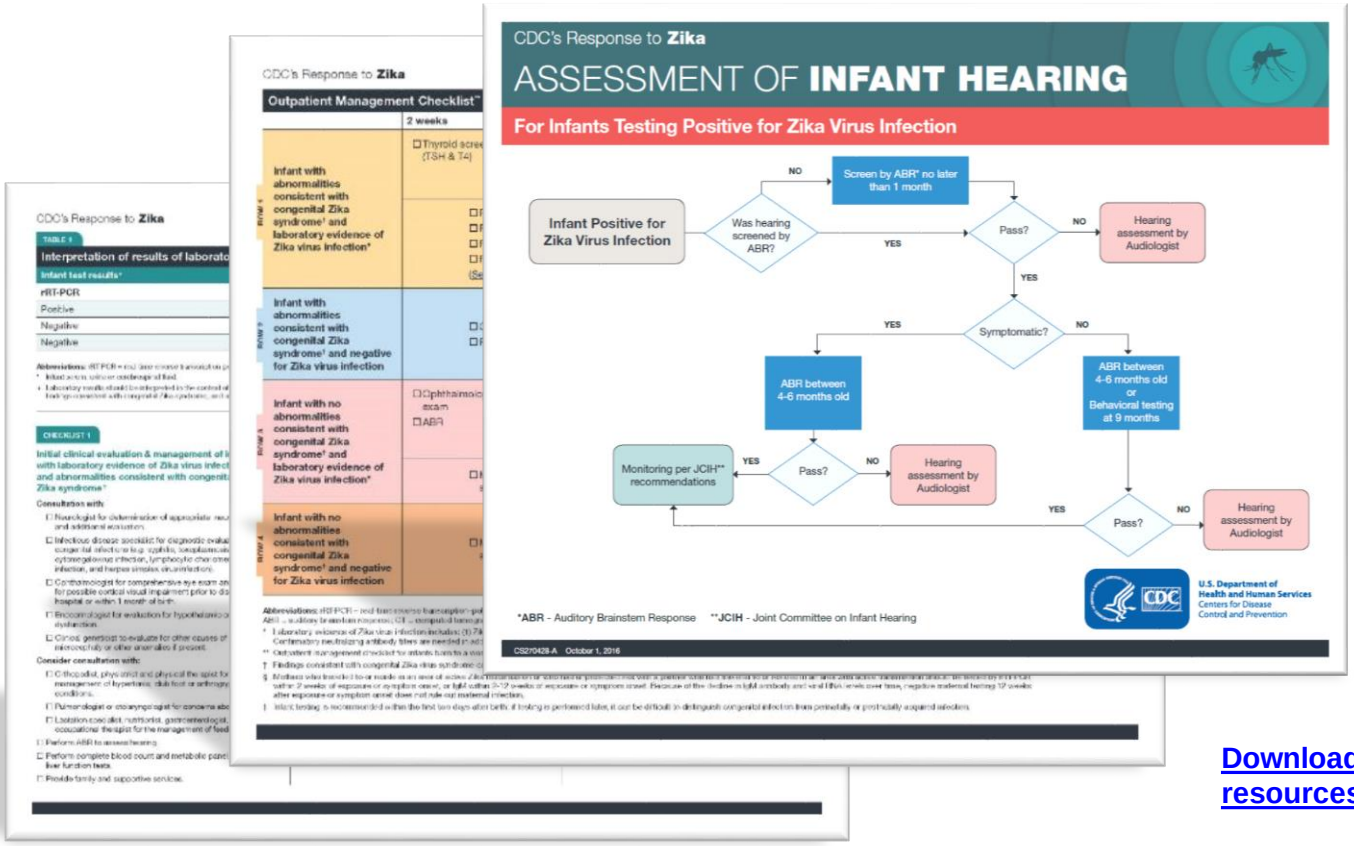
- **Neurologist** - determination of appropriate neuroimaging and evaluation
- **Infectious disease specialist** - diagnostic evaluation of other congenital infections
- **Ophthalmologist** - comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from hospital or within 1 month of birth

Infants with clinical findings consistent with congenital Zika syndrome require a multidisciplinary team and an established medical home for coordination of care to ensure abnormal findings are addressed.

Outpatient management checklist

	2 weeks	1 mo.	2 mo.	3 mo.	4-6 mo.	9 mo.	12 mo.
Infant with abnormalities consistent with congenital Zika syndrome and laboratory evidence of Zika virus infection	❑ Thyroid screen (TSH & free T4)	❑ Neuro exam	❑ Neuro exam	❑ Thyroid screen (TSH & free T4) ❑ Ophthalmology exam	❑ Repeat audiology evaluation (ABR)	❑ Developmental screening	
	❑ Routine preventive health care including monitoring of feeding, growth, and development ❑ Routine and congenital infection-specific anticipatory guidance ❑ Referral to specialists as needed ❑ Referral to early intervention services						
Infant with abnormalities consistent with congenital Zika syndrome and negative for Zika virus infection	❑ Evaluate for other causes of congenital anomalies ❑ Further management as clinically indicated						
Infant with no abnormalities consistent with congenital Zika syndrome and laboratory evidence of Zika virus infection	❑ Ophthalmology exam ❑ ABR				❑ Consider repeat ABR	❑ Developmental screening ❑ Behavioral audiology evaluation if ABR was not done at 4-6 mo	
	❑ Monitoring of growth parameters (Head circumference, weight, and height), developmental monitoring by caregivers and health care providers, and age-appropriate developmental screening at well-child visits						
Infant with no abnormalities consistent with congenital Zika syndrome and negative for Zika virus infection	❑ Monitoring of growth parameters (Head circumference, weight, and height), developmental monitoring by caregivers and health care providers, and age-appropriate developmental screening at well-child visits						

Pediatric evaluation and follow-up tools



[Download these print resources]

ZIKA

OUTREACH AND EDUCATION TOOLS

The California Department of Public Health

California Department of PublicHealth

NEW Outreach & Education Tools

Don't Bring Zika Home

CDPH has developed NEW Zika education materials for the travel season.

Materials to download and share include:

- *Web posters*
- *Social media graphics*
- *Website ads*
- *Video PSA (watch now)*

To view and order all education materials, visit www.zikafreeca.com or www.sinelzikaca.com (in Spanish) for more information.

Patient Education & Clinical Resources

Encourage all Californians to help prevent the spread of Zika virus!

To view and order, visit www.cdph.ca.gov/zika .

CDPH ONLINE TOOLKITS:

Toolkits include: posters, social media messages, talking points and website graphics.

Zika + Pregnancy Toolkit
For those who provide services to women who are pregnant or planning pregnancy.

Zika + Travel Toolkit
For those who provide pre-travel health guidance and services to people going to areas with risk of Zika (including Mexico).

ORDER TODAY!

Zika + Men Toolkit NEW!
For those who provide services to men going to areas with risk of Zika.

Zika + Sex Education Toolkit
For health educators who provide sex education to groups and classrooms.

Zika + Family Planning Toolkit
For those who serve women and their partners in the family planning process.

CLINICAL TOOLS

- Zika Screening Algorithm
- Patient Exposure Self-Assessment

CLINICAL RESOURCES

- CDPH Updated Zika Guidance for Providers Caring for Pregnant Women
- Comprehensive Zika Information for Healthcare Providers
- CDPH Information for California Birthing Hospitals
- CDPH Zika Virus Testing Information
- Insect Repellent Guide for Pregnant Women
- Current CDC Guidance
- Recorded Webinars and Webcasts




Zika Resources

- CDC Zika website: www.cdc.gov/zika
- ACOG's Zika webpage: www.acog.org/zika
- CDC Zika Pregnancy Hotline for Healthcare Providers: 770-488-7100 or email ZikaPregnancy@cdc.gov for concerns related to clinical mgmt or the Zika Pregnancy Registry
- CA Dept of Public Health webpage for health care professionals
  - www.cdph.ca.gov/zika

This is
my
thank you
dance!