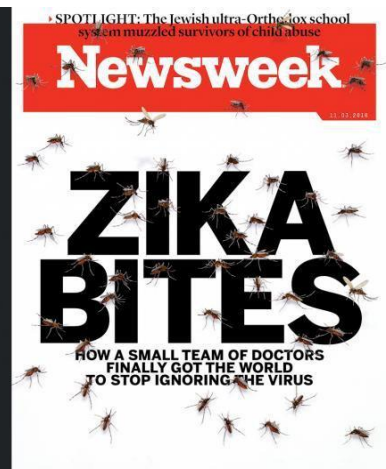
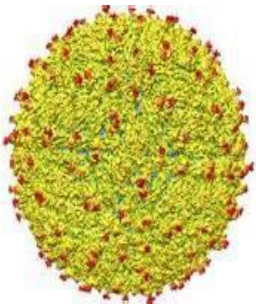




Perinatal ZIKA Infection

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Zika Virus in Pregnancy



- Limited information demonstrates:
 - No evidence of increased susceptibility
 - Infection can occur in any trimester
 - Incidence of Zika virus infection in pregnant women is not known
 - No evidence of more severe disease compared with non-pregnant people

Centers for Disease Control and Prevention, *CDC Health Advisory: Recognizing, Managing, and Reporting Zika Virus Infections in Travelers Returning from Central America, South America, the Caribbean and Mexico*, 2016.

Besnard, M., et al., Evidence of Perinatal Transmission of Zika Virus, French Polynesia, December 2013 and February 2014. *Euro Surveill*, 2014. 19(14): p. 1-5.

Oliveira Melo, A., et al., Zika Virus Intrauterine Infection Causes Fetal Brain Abnormality and Microcephaly: Tip of the Iceberg? *Ultrasound in Obstetrics & Gynecology*, 2016. 47(1): p. 6-7.

Zika Virus – Fetal Brain Abnormalities

- 2016 Brazil study: 42 women with laboratory-confirmed Zika virus infection with prenatal ultrasound
 - 12 (29%) abnormalities detected, including 2 intrauterine fetal deaths
 - 7 (17%) structural brain anomalies (microcephaly, calcifications, cerebellar atrophy, ventriculomegaly)
- 2013-14 outbreak in French Polynesia
 - 8 cases of microcephaly identified
 - Modeling estimated infection with Zika during 1st trimester of pregnancy resulted in microcephaly risk of $\approx 1\%$

Brasil P, Pereira JP Jr, Raja Gabaglia C, et al. Zika virus infection in pregnant women in Rio de Janeiro—preliminary report. N Engl J Med 2016. Published online March 4, 2016. [Link to Brasil et al article](#)

Cauchemez S, Besnard M, Bomopard P, et al. Association between Zika virus and microcephaly in French Polynesia, 2013-15: a retrospective study. Lancet 2016. Published online March 15, 2016. [Link to Cauchemez et al article](#)

Zika Virus and Microcephaly

- **Brazil: >5200 cases of suspected microcephaly temporally linked with current Zika outbreak**
- **French Polynesia: 17 cases of neurologic malformations among fetuses and newborns that were temporally linked to 2013–2014 outbreak**
- **Investigations in Brazil and French Polynesia are ongoing**

Victora CG, Schuler-Faccini L, Matijasevich A, Ribeiro E, Pessoa A, Barros FC. Microcephaly in Brazil: how to interpret reported numbers? *Lancet* 2016 Feb 13;387(10019):621-4.

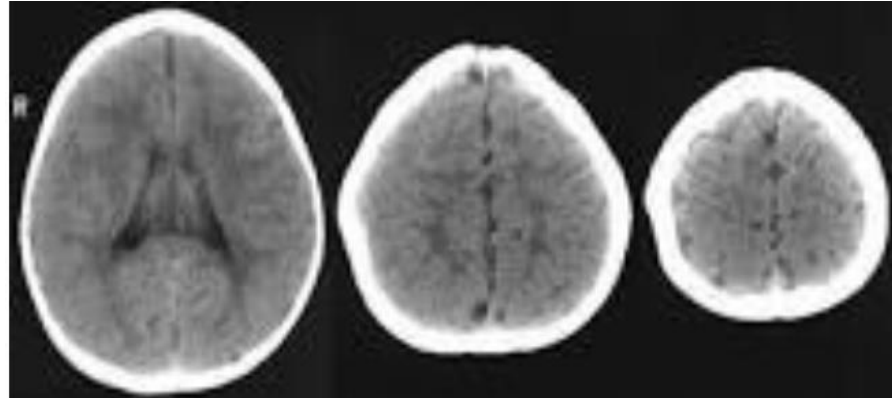
European Centre for Disease Prevention and Control. Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barre syndrome. 21 January 2016. Stockholm: ECDC; 2016.

Besnard M, Mallet H. Increase of cerebral congenital malformations among newborns and fetus in French Polynesia 2014-2015. 15 November 2015. Polynesie Francaise.

Infants with Microcephaly



AP Photos/Felipe Dana



scattered intracranial calcifications

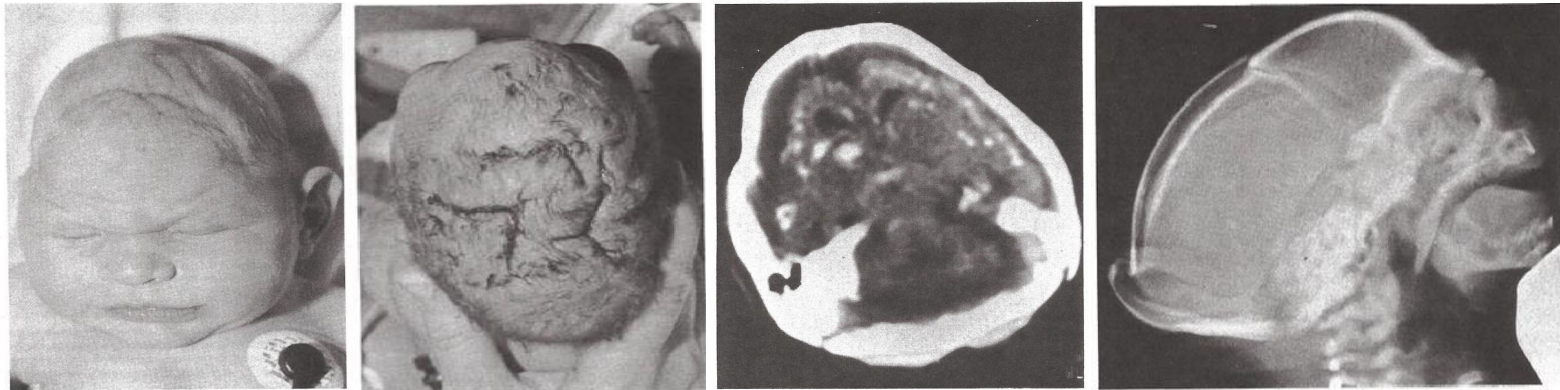


enlarged ventricles and volume loss



Fetal Brain Disruption Sequence

- First described in 1984 but noted in earlier literature
- Brain destruction resulting in collapse of the fetal skull, microcephaly, scalp rugae and neurologic impairment
- Images below from 1990 series; phenotype appears to be present in some affected babies in Brazil (2015—present)



Moore et al., J Peds, 1990

Pregnancy Outcomes and Zika Virus

- **Pregnant woman residing in Brazil**
 - . **Symptoms of Zika virus disease at 10 weeks**
- **Ultrasound findings**
 - . **22 weeks: Fetal mild hypoplasia of cerebellar vermis and head circumference <10th percentile**
 - . **25 weeks: Fetal microcephaly (head circumference <3rd percentile) with severe hypoplasia of cerebellar vermis, enlargement of posterior fossa, normal brain parenchyma**
- **Testing**
 - . **28 weeks: Amniotic fluid positive for Zika virus RNA; serum and urine negative by Zika RT- PCR**
- **Delivery**
 - . **Infant born with severe ventriculomegaly, microphthalmia, cataracts and severe arthrogryposis**

Pregnancy Outcomes and Zika Virus

- Two additional women in Brazil had clinical signs of Zika virus disease during the first trimester
 - Two fetal losses at 11 & 13 weeks gestation
- Zika virus RNA detected in products of conception
- Zika viral antigen detected by immunohistochemistry in one case
- Histopathologic changes in one case
 - ” Calcification and fibrosis in the chorionic villi

Martines RB, Bhatnagar J, Keating MK, et al. *Notes from the Field: Evidence of Zika Virus Infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses — Brazil, 2015*. MMWR Morb Mortal Wkly Rep 2016;65(Early Release):1–2.

Pregnancy Outcomes and ZIKV Isolation

- **Finnish woman on vacation in Mexico, Guatemala and Belize at 11 weeks gestation November 25, 2015. Later return to Finland**
- **Acute symptoms at 12 weeks gestation**
- **Normal sonograms at 13 and 16 weeks**
- **ZIKV RNA & serum IgM/IgG positive at 16 weeks**
- **20 weeks gestation abnormal fetal CNS findings & amniotic fluid sample + ZIKV RNA**
- **Pregnancy termination**
 - **High viral titers of ZIKV RNA in fetal brain, placenta membranes and cord**
 - **ZIKV isolated in neural tissue**

Driggers et al. NEJM Brief Report April 13, 2016



Morbidity and Mortality Weekly Report

Update: Interim Guidance for Health Care Providers Caring for Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016

Emily E. Petersen, MD¹; Kara N. D. Polen, MPH²; Dana Meaney-Delman, MD³; Sascha R. Ellington, MSPH¹; Titilope Oduyebo, MD^{1,4}; Amanda Cohn, MD⁵; Alexandra M. Oster, MD⁶; Kate Russell, MD^{4,7}; Jennifer E. Kawwass, MD^{1,8}; Mateusz P. Karwowski, MD^{4,9}; Ann M. Powers, PhD¹⁰; Jeanne Bertolli, PhD⁶; John T. Brooks, MD⁶; Dmitry Kissin, MD¹; Julie Villanueva, PhD¹¹; Jorge Muñoz-Jordan, PhD¹⁰; Matthew Kuehnert, MD¹²; Christine K. Olson, MD¹; Margaret A. Honein, PhD²; Maria Rivera, MPH¹; Denise J. Jamieson, MD¹; Sonja A. Rasmussen, MD¹³


On March 25, 2016, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

CDC has updated its interim guidance for U.S. health care providers caring for women of reproductive age with possible Zika virus exposure (1) to include recommendations on coun-

partners (3,5,7–10). Based on data from a previous outbreak, most persons infected with Zika virus are asymptomatic (11). Signs and symptoms, when present, are typically mild, with the most common being acute onset of fever, macular or papular rash, arthralgia, and conjunctivitis (11).

Updated Recommendations

Testing of PREGNANT Women With Possible Zika Virus Exposure Who DO NOT Reside in An Area With Active Zika Virus Transmission

- If one or more signs/symptoms of Zika virus disease within 2 weeks of travel, serum testing should be performed
 - Testing can be offered to asymptomatic pregnant women with possible exposure
 - History of travel to an area with active Zika virus transmission or
 - Sex without a condom with a symptomatic male
 - Testing is not currently recommended for pregnant women with possible sexual exposure to Zika virus if both partners are asymptomatic
- 

CDC Recommendations: Diagnostic testing

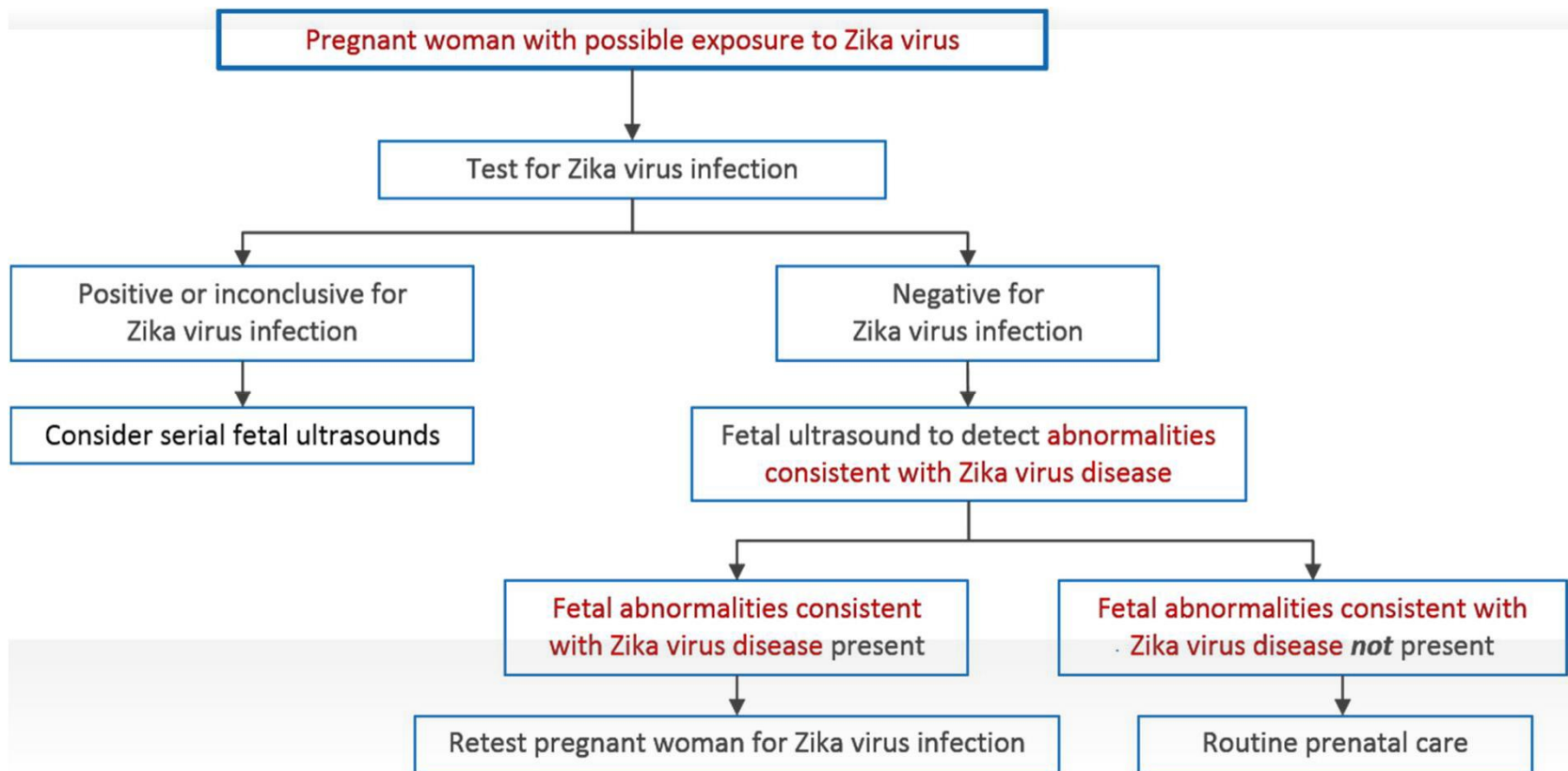
- **Reverse Transcription-Polymerase Chain Reaction (RT-PCR) for viral RNA in serum collected ≤ 7 days after illness onset**
- **Serology for Immunoglobulin M (IgM) in serum collected ≥ 4 days after illness onset**
 - “ **Cross-reactivity can occur among related flaviviruses**
 - “ **Plaque Reduction Neutralization Test (PRNT) can be performed to measure virus-specific neutralizing antibodies**

CDC Recommendations: Testing for Asymptomatic Pregnant Women with Possible Zika Virus Exposure

- **Serologic (IgM) testing can be offered to asymptomatic pregnant women**
- **Negative IgM result could suggest a recent infection did not occur and obviate need for serial ultrasounds**
- **Information about performance of testing of asymptomatic persons limited**

Interim Guidelines (3/25/16):

Pregnant Women With Possible Zika Virus Exposure NOT Residing in an Area With Active Zika Virus Transmission



Zika and Pregnancy: Clinical Management

- **Confirmed maternal or fetal infection:**
 - **Antepartum:**
 - “ **Consider serial ultrasounds every 3-4 weeks**
 - “ **Consider referral to specialist with expertise in pregnancy management**
 - **Peripartum:**
 - “ **Histopathologic examination of the placenta and umbilical cord;**
 - “ **Testing of frozen placental tissue and cord tissue for Zika virus RNA**
 - “ **Testing of cord serum for Zika and dengue virus IgM and neutralizing antibodies**

Other Modes of Transmission

- Maternal-fetal
 - Intrauterine
 - Perinatal
- Other
 - Sexual*
 - Blood transfusion
 - Laboratory exposure
- Theoretical
 - Organ or tissue transplantation
 - Breast milk





Centers for Disease Control and Prevention
MMWR

Morbidity and Mortality Weekly Report

Early Release / Vol. 65

February 5, 2016

Interim Guidelines for Prevention of Sexual Transmission of Zika Virus — United States, 2016

Alexandra M. Oster, MD¹; John T. Brooks, MD¹; Jo Ellen Stryker, PhD¹; Rachel E. Kachur², MPH; Paul Mead, MD³; Nicki T. Pesik, MD⁴; Lyle R. Petersen, MD³

Zika virus is a mosquito-borne flavivirus primarily transmitted by *Aedes aegypti* mosquitoes (1,2). Infection with Zika virus is asymptomatic in an estimated 80% of cases (2,3), and when Zika virus does cause illness, symptoms are generally mild and self-limited. Recent evidence suggests a possible association between

The following recommendations, which apply to men who reside in or have traveled to areas with active Zika virus transmission (<http://wwwnc.cdc.gov/travel/notices/>) and their sex partners, will be revised as more information becomes available.

ZIKV – Sexual Transmission

- “ 24 year old French women in Paris
 - “ Acute fever, rash, arthralgia, myalgia – 2/20/2016
 - “ No travel to tropical or ZIKV endemic regions
 - “ Sexual contact 2/10 & 2/20/2016 with male who stayed in Brazil in 12/11/15 thru 2/9/2016
 - “ Male partner with fever/myalgia and rash 2/7 thru 2/9/2016
- “ Both individuals – ZIKV+ RNA in urine
 - “ Woman - neg serum PCR but +ZIKV IgM, + saliva RNA
 - “ Male - +ZIKV RNA and +ZIKV culture in semen day 24
 - “ Salivary/Semen genomic sequencing congruence

Ortenzio et al. NEJM April 13, 2016 - Letter

Sexual Transmission of Zika Virus: What We Know and What We Do Not Know

What we know:

- Zika virus can be sexually transmitted by a man to his sex partners, and this is of particular concern during pregnancy.
 - All reported cases of sexual transmission involved sex without a condom with men who had or developed symptoms.
- Sexual transmission of many infections, including those caused by other viruses, is reduced by consistent and correct use of latex condoms.

What we do not know:

- Whether infected men who never develop symptoms can transmit Zika virus to their sex partners.
- How long Zika virus persists in the semen.
 - One report found the virus in semen at least two weeks after symptoms of infection began.
 - Another report found the virus in semen at least 62 days after symptoms of infection began.
- Whether women with Zika infection can transmit Zika virus to their sex partners.
- Whether Zika can be transmitted from oral sex.
 - It is known that Zika is infectious in semen.
 - It is unknown if Zika is infectious in other body fluids exchanged by oral sex, including saliva and vaginal fluids.

Sexual Transmission of Zika Virus: CDC Recommendations for Men Who Live in or Traveled to an Area of Active Zika Virus Transmission

Men and their pregnant sex partners:


- Should abstain from sexual activity or consistently and correctly use condoms during sex (i.e., vaginal intercourse, anal intercourse, or fellatio) for the duration of the pregnancy.
- Pregnant women should discuss their male partner's potential exposures to mosquitoes and history of Zika-like illness with their healthcare provider; providers can consult CDC's guidelines for evaluation and testing of pregnant women.

Men and their nonpregnant sex partners:

- If concerned about sexual transmission of Zika virus, might consider abstaining from sexual activity or using condoms consistently and correctly during sex. Couples should take several factors into account:
 - Most infections are asymptomatic, and when illness does occur, it is usually mild.
 - Severe disease requiring hospitalization is uncommon.
 - Risk for acquiring vector-borne Zika virus in areas of active transmission depends on the duration and extent of exposure to infected mosquitoes and the steps taken to prevent mosquito bites.
 - After infection, Zika virus might persist in semen when it is no longer detectable in blood.
- At this time, testing of men for the purpose of assessing risk for sexual transmission is not recommended.


Recommendations for Women and Men Interested in Conceiving Who DO NOT Reside In an Area With Active Zika Virus Transmission

For **Women** With Possible Exposure to Zika Virus

- Health care providers (HCPs) should discuss signs and symptoms and potential adverse outcomes associated with Zika
 - If Zika virus disease diagnosed, wait **at least 8 weeks after symptom onset** to attempt conception
 - If NO symptoms develop, wait **at least 8 weeks after last date of exposure** before attempting conception
- 

Recommendations for Women and Men Interested in Conceiving Who DO NOT Reside In an Area With Active Zika Virus Transmission

For **Men** With Possible Exposure to Zika Virus

- If Zika virus disease diagnosed, wait **at least 6 months** after symptom onset
 - If NO symptoms develop, wait **at least 8 weeks** after exposure
 - Discuss contraception and use of condoms
- 

Preventing Mosquito Bites

- Use EPA- registered insect repellent
- EPA- registered repellents including DEET are considered safe to use in pregnant and lactating women, and children
- Wear long-sleeved shirts and long pants to cover exposed skin
- Wear Permethrin-treated clothes
- Stay and sleep in screened-in or air-conditioned rooms
- Aedes mosquitoes that transmit Zika virus bite mostly during the daytime
- Practice mosquito prevention strategies throughout the entire day


Zika Virus and Blood Safety

- As of March 31, 2016, there have not been any confirmed blood transfusion transmission cases in the United States.
- There have been suspected cases of Zika transmission through blood transfusion in Brazil. These reports are currently being investigated.
- During the previous French Polynesian outbreak, 2.8% of blood donors tested positive for Zika and in previous outbreaks, the virus has been found in blood donors.
- Zika virus currently poses a low risk to the US blood supply, but this could change depending on how many people in the United States become infected with the virus.
- Zika virus may be transmitted through blood transfusions. Because 80% of people infected with the Zika virus don't show any symptoms, they may not know they have been infected.

Zika Virus and Blood Safety

- **February 16th – FDA released “Recommendations for Donor Screening Deferral and Product Management to Reduce the risk of Transfusion – Transmission of Zika Virus”**
- **March 30, 2016 – FDA Announced the availability of an investigational test to screen blood donations for Zika virus**

CDC Recommendations: Zika Virus Disease in Labor and Delivery Settings

- Zika virus has been detected in blood, amniotic fluid, urine, saliva, and semen
 - No reports to date of transmission of Zika virus transmission from infected patients to HCP or other patients
 - Healthcare personnel (HCP) working in these settings must adhere to Standard Precautions
- 

Infection Control and Zika Virus: Considerations for Labor and Delivery Units

- **MMWR- “Infection Control and Zika Virus: Considerations for Labor and Delivery Units” – report emphasizing the infection control practices to prevent spread of infectious diseases such as Zika virus**
- **Standard Precautions - CDC recommends basic measures to prevent infections**
- **No difference between recommendations for labor and delivery setting versus other healthcare settings**
- **Standard precautions can help prevent the spread of infectious diseases**
 - “ Zika virus
 - “ HIV
 - “ Hepatitis C

Zika Pregnancy Surveillance

- In collaboration with state and territorial health departments, CDC has established two surveillance systems for pregnant women with Zika virus infection
 - “ US Zika Pregnancy Registry
 - “ 50 U.S. States & Washington, DC
 - “ Zika Active Pregnancy Surveillance System (ZAPSS)
 - “ Puerto Rico
 - “ Data collected via medical record abstraction
- Surveillance systems will facilitate public health response for pregnant women with Zika virus infection

U.S. Zika Pregnancy Registry

- **Purpose of registry:** To monitor pregnancy and infant outcomes following Zika virus infection during pregnancy and to inform clinical guidance and public health response
- **How it works:** The registry is a supplemental surveillance effort coordinated by CDC and dependent on the voluntary collaboration of the state, tribal, local, and territorial health departments



U.S. Zika Pregnancy Registry

- **Who is included:** Pregnant women with laboratory evidence of Zika virus infection and exposed infants born to these women; infants with laboratory evidence of congenital Zika virus infection and their mothers
- **How can you support the registry?** Spread the word about the US Zika Pregnancy Registry and assist with health department follow-up for pregnant women and infants who are part of the registry

