CDC'S Response to **Zika**



Zika Virus and Infants: A Primer

Grand Rounds



First time in history...

"Never before in history has there been a situation where a bite from a mosquito could result in a devastating malformation."

– Dr. Tom Frieden, CDC DirectorFortune, April 13, 2016

"...the last time an infectious pathogen (rubella virus) caused an epidemic of congenital defects was more than 50 years ago..."

- New England Journal of Medicine, April 13, 2016



Today's Presentation

- Zika: The Basics
- Zika, Pregnancy, and Congenital Zika Syndrome
- CDC Guidance: Infants with Possible Zika Virus Infection
- Zika Virus and Children
- What is CDC Doing?
- What Can You Do?

Zika: The Basics

What is Zika virus?

- Single-stranded RNA virus
- Closely related to dengue, yellow fever, Japanese encephalitis, and West Nile viruses
- Primarily transmitted by the bite of two Aedes species mosquitoes
 - Aedes aegypti and Aedes albopictus mosquitoes
- Additional modes of transmission
 - Intrauterine and perinatal transmission (mother to fetus)
 - Sexual transmission
 - Laboratory exposure
 - Probable: Blood transfusion



Aedes aegypti mosquito



Aedes albopictus mosquito

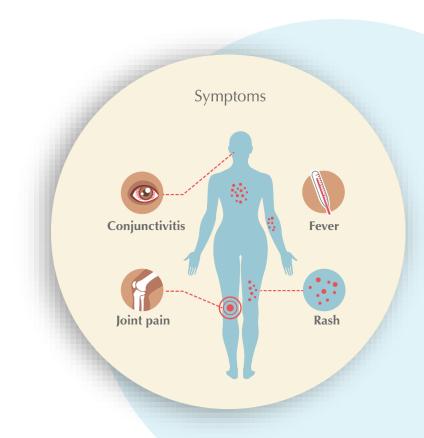
Where is Zika Now?

As of December 14, 2016



Signs and Symptoms

- Clinical illness is usually mild
- Most common symptoms are:
 - Fever
 - Rash
 - Joint pain
 - Conjunctivitis
- Symptoms last several days to a week
- Severe disease is uncommon
- Fatalities are rare
- Once infected, a person is likely to be protected from future infections



Clinical Management

- No vaccine or specific antiviral treatment
- Treat the symptoms
 - Rest
 - Drink fluids to prevent dehydration
 - Take medicine such as acetaminophen to reduce fever and pain
 - Avoid aspirin and other non-steroidal antiinflammatory drugs (NSAIDS) until dengue can be ruled out to reduce the risk of bleeding



Zika, Pregnancy, and Congenital Zika Infection

Zika Virus Infection in Pregnant Women

- Pregnant women can be infected
 - Through the bite of an infected mosquito
 - Through sex without a condom with an infected partner
- If a woman is infected around conception
 - Zika might present risk to fetus
- If infected during pregnancy
 - Zika can be passed to the fetus during pregnancy or around the time of birth



Zika Virus in Pregnancy



- Infection can occur in any trimester
- No evidence of increased susceptibility to Zika virus
- The clinical course is similar in pregnant women and in 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.

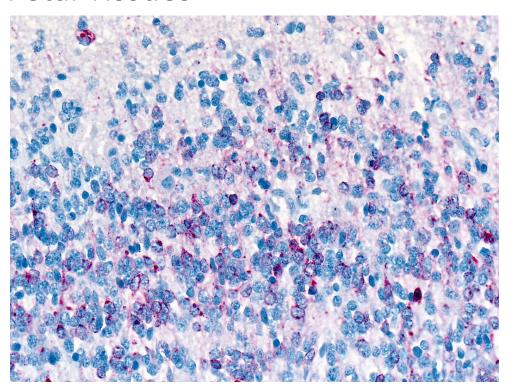
Oliveira Melo, A., et al., Zika Virus Intrauterine Infection Causes Fetal Brain Abnormality and Microcephaly: Tip of the Iceberg? Ultrasound in Obstetrics & Gynecology, 2016. 47(1): p. 6-7.

CDC Lab Confirms Zika In Fetal Tissues

- Zika virus has been shown to be present in fetal tissue
- Evidence of Zika virus has been detected in
 - Amniotic fluid
 - Placenta
 - Fetal brain tissue.
 - Products of conception
- Zika virus has been found to continue to replicate in infants' brains after birth (Bhatnagar et.al., 2017)

Bhatnagar J, Rabeneck DB, Martines RB,Reagan-Steiner S, Ermias Y, Estetter LBC, et al. Zika virus RNA replication and persistence in brain and placental tissue. Emerg Infect Dis. 2017 Mar [Epub ahead of print].

Reference/attribution for image: Ritter JM, Martines RB, Zaki SR. Zika Virus: Pathology From the Pandemic. Arch Pathol Lab Med. 2016 Oct 5. [Epub ahead of print]



Immunohistochemical staining of Zika virus antigen (red stain) in fetal brain tissue. This staining is present in the same areas where neuronal cell death/necrosis was identified by microscopic review of tissue morphology.

Zika is a Cause of Microcephaly

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

Zika Virus and Birth Defects — Reviewing the Evidence for Causality

Sonja A. Rasmussen, M.D., Denise J. Jamieson, M.D., M.P.H., Margaret A. Honein, Ph.D., M.P.H., and Lyle R. Petersen, M.D., M.P.H.

SUMMARY

The Zika virus has spread rapidly in the Americas since its first identification in Brazil in early 2015. Prenatal Zika virus infection has been linked to adverse pregnancy and birth outcomes, most notably microcephaly and other serious brain anomalies. To determine whether Zika virus infection

POTENTIAL RELATIONSHIP BETWEEN
ZIKA VIRUS INFECTION AND BIRTH
DEFECTS

Since the identification of the Zika virus in Brazil in early 2015, the virus has spread rapidly throughout the Americas (www.cdc.gov/zika/geo/active-countries.html). An increase in the

Potential Risk of Birth Defects Related to Zika

- Among pregnant women in the United States with laboratory evidence of possible Zika virus infection:
 - Overall about 6% of fetuses or infants had birth defects potentially related to Zika virus
 - The proportion of pregnancies with birth defects was simila (around 6%) among symptomatic and asymptomatic pregnant women
 - Among women with infection in the 1st trimester of pregnancy, birth defects were reported in 11% of fetuses of infants



Congenital Zika Syndrome

- Pattern of congenital anomalies associated with Zika virus infection during pregnancy that includes
 - Severe microcephaly (small head size) resulting in a partially collapsed skull
 - Thin cerebral cortices with subcortical calcifications
 - Eye anomalies, including macular scarring and focal pigmentar retinal mottling
 - Congenital contractures or limited range of joint motion
 - Marked early hypertonia, or too much muscle tone, and symptoms of extrapyramidal involvement
- Infants with normal head circumference at birth may:
 - Have brain abnormalities consistent with congenital Zika syndrome
 - Develop mirocephaly after birth







Potential Risk of Microcephaly

- 1 13% estimated risk of microcephaly due to Zika virus infection in first trimester
 - Modeling based on current outbreak in Bahia, Brazil
 - Not enough data to estimate 2nd or 3rd trimester risk
- Important to remember
 - Data are limited (infection rates unknown; microcephaly cases still being reported)
 - Microcephaly is difficult to detect prenatally
 - Microcephaly is only one of a range of possible adverse outcomes



Congenital Zika Syndrome without Microcephaly at Birth

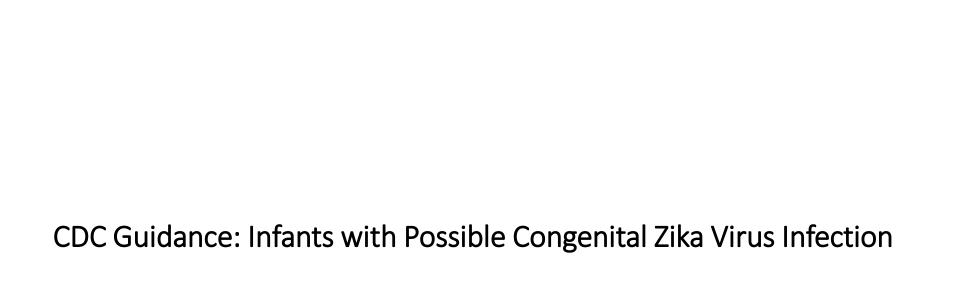
- Microcephaly from congenital infection can occur after birth
- The full spectrum of poor outcomes caused by Zika virus infection during pregnancy remains unknown



Morbidity and Mortality Weekly Report

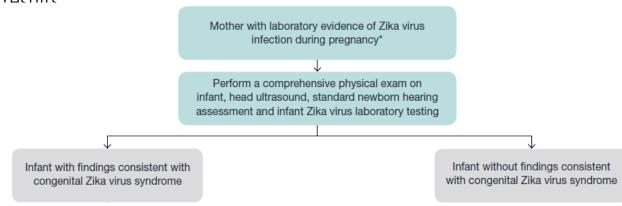
November 22, 2016

Description of 13 Infants Born During October 2015–January 2016 With Congenital Zika Virus Infection Without Microcephaly at Birth — Brazil



Infants with Possible Congenital Zika Virus Infection

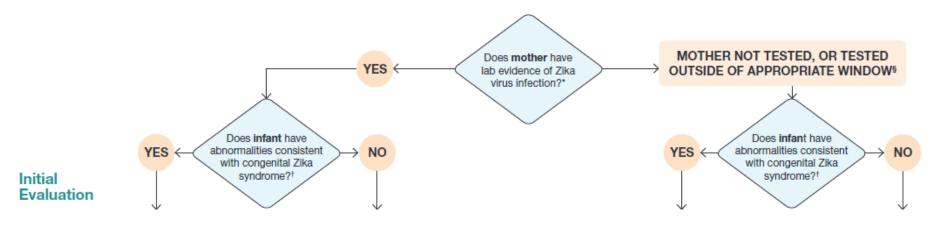
- Testing for Zika virus infection is recommended for infants born to:
 - 1) mothers with laboratory evidence of possible Zika virus infection;
 - 2) infants with findings suggestive of congenital Zika syndrome and a maternal epidemiologic link suggesting possible transmission, regardless of maternal testing results
- Congenital Zika virus infection can be diagnosed by RNA nucleic acid testing (NAT)
- All infants with possible congenital Zika virus infection should have a comprehensive physical exam and head ultrasound before hospital discharge regardless of the presence of abnormalities and prenatal ultrasound results



Link: http://www.cdc.gov/zika/pdfs/zika peds.pdf

Infants with Possible Congenital Zika Virus Infection

Recommendations for follow-up depend on whether the infant has abnormalities consistent with congenital Zika syndrome



Initial Evaluation

Infants with abnormalities consistent with congenital Zika syndrome born to a mother with lab evidence of Zika

- Before hospital discharge:
 - ✓ Routine newborn care: physical exam, including occipitofrontal (head) circumference, weight, length, a neurologic exam, and universal hearing screen
 - ✓ Head ultrasound
 - ✓ Testing for congenital Zika virus infection
 - ✓ Complete blood count, metabolic panel and liver enzyme testing
 - ✓ Consult with multiple subspecialists
 - ✓ Referral for comprehensive eye exam by an ophthalmologist
 - ✓ Referral for auditory brainstem response (ABR) hearing evaluation
 - ✓ Consider advanced cranial imaging (e.g., MRI)
 - ✓ Consider transfer to hospital with specialty care
- Refer for a comprehensive ophthalmologic exam and evaluation of hearing by ABR testing before 1 month of age

Consult with Specialists

Infants with abnormalities consistent with congenital Zika syndrome and lab evidence of Zika

- Neurologist to determine appropriate neuroimaging and additional evaluation
- Infectious disease specialist to evaluate other congenital infections
- Ophthalmologist to examine the eye and evaluate for possible cortical visual impairment prior to discharge from hospital or within 1 month of birth
- Endocrinologist to evaluate for hypothalamic or pituitary dysfunction
- Clinical geneticist to evaluate for other causes of microcephaly or other anomalies if present

Consult with Specialists

Infants with abnormalities consistent with congenital Zika syndrome and lab evidence of Zika

Consultation with the following should also be considered:

- Orthopedist, physiatrist, and physical therapist to manage hypertonia, club foot, or arthrogrypotic-like conditions
- Pulmonologist or otolaryngologist to consult about aspiration
- Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist to manage feeding issues

Outpatient Management

Infants with abnormalities consistent with congenital Zika syndrome and lab evidence of Zika

- Establish a medical home to facilitate coordination of care
- Provide routine preventive pediatric health care, including immunizations and monthly primary care visits for at least the first 6 months
- Conduct developmental monitoring at each routine visit
- Complete neurologic exam at age 1 and 2 months, then as needed
- Refer patients to developmental specialist and early intervention services
- Repeat ophthalmology exam with retinal assessment at 3 months
- Repeat ABR hearing assessment at age 4–6 months
- Conduct thyroid screening at age 2 weeks and age 3 months
- Provide family support services
- Provide appropriate referrals

Initial Evaluation & Outpatient Management

Infants with lab evidence of Zika and <u>without</u> abnormalities consistent with congenital Zika syndrome

- Before hospital discharge infants should receive
 - Routine care including monitoring of occipitofrontal circumference, length, and weight
- Outpatient management includes routine follow up and
 - Establish medical home
 - Perform vision screening at every well child visit
 - Evaluate hearing: consider repeat ABR testing at 4–6 months or perform behavioral diagnostic testing at age 9 months if ABR is not done at 4-6 months
 - Provide referrals: Any children with identified or suspected delays should be referred to a developmental specialist or early intervention programs
 - Provide family support services, such as counseling, as needed

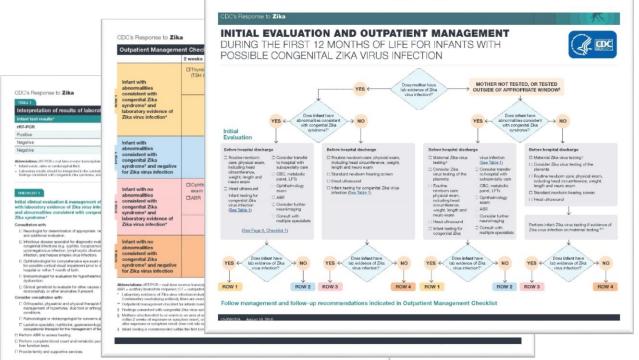
Family and Psychosocial Support

- Families and caregivers of infants with congenital Zika virus infection may require ongoing psychosocial support.
- Families should be empowered to be active participants in their child's monitoring and care.
- Healthcare providers should work closely with parents to ensure that the care plan is consistent with the infant's needs and the family's wishes.
- Families with already limited access to medical care might be affected with a disproportionate burden of Zika virus infection.
- Barriers to care for all affected infants and their families should be addressed by linking them with national, state, and local health programs as well as social services.
- Additional resources for families can be found at: http://www.cdc.gov/zika/parents/families-of-newborns-affected-zika.html

Pediatric Evaluation and Follow-up Tools

Initial Evaluation and Outpatient Management During the First 12 Months of Life for

Infants with Possible Congenital Zika Virus Infection



Download at:

http://www.cdc.gov/zika/pdfs/p ediatric-evaluation-follow-uptool.pdf

Zika Virus and Caring for Infants and Children

Infants with Possible Postnatal Zika Virus Infection

- <u>Guidance for testing and clinical management</u> of infants and children with postnatal Zika virus infection is in line with testing and clinical management recommendations for adults.
- <u>Symptomatic treatment and supportive care</u> are appropriate and usually sufficient to treat Zika. Special considerations to treat children with Zika include
 - Aspirin should never be used to treat children with symptoms of acute viral illness because of the risk of Reye's syndrome.
 - All non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided in children <6 months.
- Patients with suspected Zika virus infections should be evaluated and managed for possible dengue or chikungunya virus infection.
 - Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided until dengue can be ruled out

Zika and Breastfeeding

- Transmission of Zika virus through breast milk has not been documented.
- Benefits of breastfeeding outweigh theoretical risk of Zika virus transmission through breast milk
- CDC and the World Health Organization recommend that infants born to women with suspected, probable, or confirmed Zika virus infection, or who live in or have traveled to areas of Zika, should be fed according to usual infant feeding guidelines.



Tips for Parents and Caregivers

- Dress your child in clothing that covers arms and legs.
- For children older than 2 months, use insect repellent on exposed skin.
 - » Do <u>not</u> use insect repellent on babies younger than 2 months old.
- Cover crib, stroller, and baby carrier with mosquito netting.



Tips for Parents and Caregivers

Adults applying insect repellent for babies and children

- Do not apply repellent onto hands, eyes, mouth, and cut or irritated skin.
- Spray onto your hands and then apply to a child's face.
- Do not use products containing oil of lemon eucalyptus or para-menthane-diol on children younger than 3 years old.

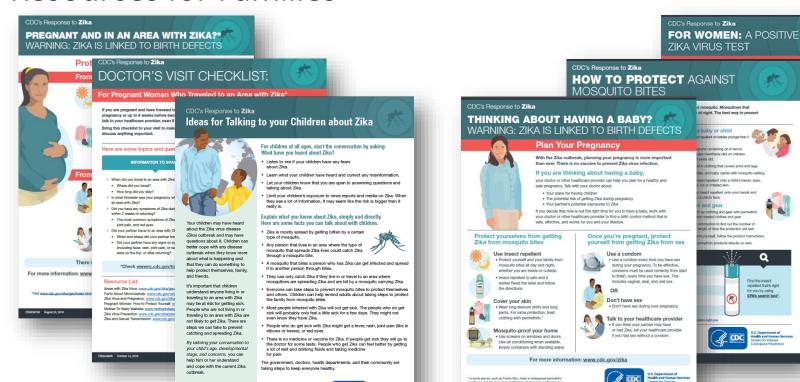


Resources for Healthcare Providers

- Caregivers of children with Zika-related complications are often overwhelmed and may need support, guidance, and help establishing a medical home.
- Healthcare providers should work closely with and empower parents and families to monitor their infant's development and determine what choices are available and how to best care for their infant's condition and needs.
- Resources and guidance for healthcare providers caring for infants affected by Zika virus are available on the CDC website.

Resources for Families

www.cdc.gov/zika



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What is CDC Doing?

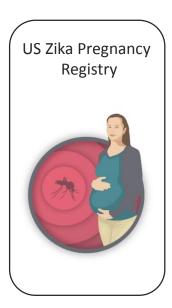
Many Questions Remain

- What is the level of risk from a Zika virus infection during pregnancy?
- When during pregnancy does Zika virus infection pose the highest risk to the fetus?
- What is the full range of potential health problems that Zika virus infection may cause?
- What other factors (e.g., co-occurring infection, nutrition, symptomatic vs. asymptomatic) might affect the risk for birth defects?
- What is the risk for later health problems in an infant who is infected or who has had exposure to Zika virus but is born without abnormalities?



Collecting Data for Action

Surveillance of Zika and its Effects on Pregnant Women, Infants, & Children











Sharing Up-to-Date Information

- Providing updated clinical guidance
- Responding to your inquiries:
 - Email: ZikaMCH@cdc.gov
 - Zika Pregnancy Hotline: 770-488-7100
 - <u>CDC-INFO</u>: (800-232-4636)



http://www.cdc.gov/zika



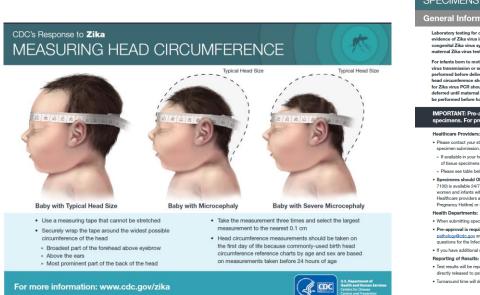
Morbidity and Mortality Weekly Report

July 25, 2016

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

Titilope Oduyebo, MD¹; Irogue Igbinosa, MD²; Emily E. Petersen, MD¹; Kara N.D. Polen, MPH²; Satish K. Pillai, MD³; Elizabeth C. Ailes, PhD²; Julie M. Villanueva, PhD³; Kim Newsome, MPH²; Marc Fischer, MD⁴; Priya M. Gupta, MPH²; Ann M. Powers, PhD¹; Margaret Lampe, MPH⁴; Susan Hills, MBB5⁴; Kathryn E. Arnold, MD²; Laura E. Rose, MT5³; Carrie K. Shapiro-Mendoza, PhD¹; Charles B. Beard, PhD⁴; Iorge L. Muñoz, PhD³; Carol Y. Rao, ScD²; Dana Meaney-Delman, MD³; Denise J. Jamieson, MD¹; Margaret A. Honein, PhD²

Developing Tools for Healthcare Providers



CDC's Response to Zika ZIKA VIRUS: COLLECTION AND SUBMISSION OF SPECIMENS FOR ZIKA VIRUS TESTING AT TIME OF BIRTH

General Information

Laboratory testing for congenital Zika virus infection is recommended for infants born to mothers with laboratory evidence of Zika virus infection during pregnancy, and for infants who have abnormal clinical findings suggestive of congenital Zika virus syndrome and a maternal epidemiologic link suggesting possible transmission, regardless of maternal Zika virue teet regulte

For infants born to mothers with risk factors for maternal Zika virus infection (travel to or residence in an area of Zika virus transmission or sex with a partner with travel to or residence in such an area) for whom maternal testing was not performed before delivery, assessment of the infant, including comprehensive physical exam and careful measurement of head circumference should be performed. Maternal diagnostic testing should be performed and testing of the placenta for Zika virus PCR should be considered. If an infant appears clinically well, further evaluation and infant testing can be deferred until maternal test results are available. However, if there is concern about infant follow-up, infant testing should be performed before hospital discharge.

IMPORTANT: Pre-approval is required prior to submission of any placental or other tissue specimens. For pre-approval please contact pathology@cdc.gov and eocevent189@cdc.gov.

- . Please contact your state, tribal, local, or territorial health department to facilitate laboratory testing and pathology
- » If available in your hospital/institution, please consult surgical pathology to ensure appropriate collection and processing of tissue specimens for 7ika virus testing
- » Please see table below for information on collection of specimens for Zika virus testing
- . Specimens should ONLY be sent to CDC directly from health departments. CDC's Zika Pregnancy Hotline (770-488-7100) is available 24/7 to healthcare providers and health departments for consultation regarding management of pregnant women and infants with possible Zika virus. This hotline can also assist with guestions regarding specimen submission. Healthcare providers and state and local health officials can call our CDC Watch desk at 770-488-7100 (ask for CDC Zika Pregnancy Hotline) or email zikapregnancy@cdc.gov.
- . When submitting specimens, please submit CDC Form 50.34 with all specimens. For test order name, write "Zika virus". . Pre-approval is required prior to submission of all tissue specimens (i.e., placenta, umbilical cord). Please contact
- pathology@cdc.gov and socayent189@cdc.gov to discuss the case and obtain pre-approval. If you have additional questions for the Infectious Diseases Pathology Branch, please call 404-639-3133.
- If you have additional questions for the Arboviral Diseases Branch, please call 970-221-6400.

- Test results will be reported to the state health department and the submitting healthcare provider. Results will not be directly released to natients
- . Turnaround time will depend on testing volume and established reporting systems



www.cdc.gov/Zika

*Free materials available in English, Spanish and other languages

What Can You Do?

Report Confirmed or Probable Cases of Zika

- Zika virus infection and disease are nationally notifiable conditions.
- Healthcare providers should report laboratoryconfirmed and symptomatic cases of Zika to the local, state or territorial health department which in turn should report the case ArboNET.



Report Cases to US Zika Pregnancy Registry

 Healthcare providers are encouraged to report and actively monitor pregnancies and congenital outcomes among symptomatic and asymptomatic women with laboratory evidence of possible Zika virus infection

More information

- Available on the <u>US Zika Pregnancy Registry website</u> (http://www.cdc.gov/zika/hc-providers/registry.html)
- To contact CDC Registry staff, call the CDC Emergency Operations Center watch desk at 770-488-7100 and ask for the Zika Pregnancy Hotline or emai <u>ZIKApregnancy@cdc.gov</u>
- For non-urgent requests, call 800-CDC-INFO (800-232-4636)

In Summary

- Know the basics about Zika transmission in your community
- Diagnose and test for Zika for those with symptoms in your community
- Understand the assessment and management of Zika among pregnant women and infants
- Recommend Zika prevention behaviors
- Provide support for families of infants affected by Zika
- Inform your local or state health department to help keep ArboNET and the US Zika Pregnancy Registry up-to-date

More Information about Zika

More information on caring for pregnant women, infants, or children with Zika virus infection is available at CDC's Zika website.



www.cdc.gov/zika

Thank you!

More information on Zika: www.cdc.gov/zika

For more information, contact CDC 1-800-CDC-INFO (232-4636)

TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

