

Zika Update: Findings from the U.S. Zika Pregnancy Registry and Updated Clinical Guidance

**Clinician Outreach and
Communication Activity (COCA)
Webinar
May 4, 2017**



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Objectives

At the conclusion of this session, the participant will be able to:

- ❑ **Understand the latest estimates for birth defects associated with Zika virus infection during pregnancy.**
- ❑ **Discuss additional considerations for evaluating and managing infants with possible congenital Zika virus infection.**
- ❑ **Apply the updated recommendations outlined in the additional considerations for the evaluation and management of infants with possible congenital Zika virus infection.**

TODAY'S PRESENTER



Emily Petersen, MD

Medical Officer

Division of Reproductive Health

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Centers for Disease Control and Prevention

TODAY'S PRESENTER



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Director, Division of Public Health Information Dissemination
Editor-in-Chief, *Morbidity and Mortality Weekly Report*
Center for Surveillance, Epidemiology, and Laboratory Services
Centers for Disease Control and Prevention



Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure

U.S. Zika Pregnancy Registry, 2016

Emily Petersen, MD
Centers for Disease Control and Prevention



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

US Zika Pregnancy Registry

Purpose of registry

- » To monitor pregnancy and infant outcomes in pregnancies with laboratory evidence of possible Zika virus infection and to inform clinical guidance and public health response
 - Estimate number of infants with birth defects
 - Provide data to inform phenotype of congenital Zika syndrome
 - Help ensure infants are linked to care



US Zika Pregnancy Registry: Inclusion Criteria

Who is included

- » Pregnant women in the United States with laboratory evidence of possible Zika virus infection (regardless of whether they have symptoms) and their exposed infants
- » Infants with laboratory evidence of congenital Zika virus infection (regardless of whether they have symptoms) and their mothers

US Zika Pregnancy Registry: First Report

Research

JAMA | Original Investigation

Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy

Among pregnancies in the United States with laboratory evidence of possible Zika virus infection

- » **6%** of fetuses or infants had birth defects potentially related to Zika virus
- » Similar proportion of pregnancies with birth defects (**≈6%**) among symptomatic and asymptomatic pregnant women
- » Among women with infection in the 1st trimester of pregnancy, birth defects reported in **11%**

Vital Signs MMWR: Update Previous Estimates

Morbidity and Mortality Weekly Report

Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016

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What is Added by this Report

This report features the latest data from the US Zika Pregnancy Registry

- » Initial estimates were based on 442 completed pregnancies reported to the registry by September 22, 2016
- » This Vital Signs report provides data on 972 completed pregnancies reported to the registry through December 27, 2016
- » Analyzed subgroup of confirmed Zika virus infections

This is the largest series of infant outcomes among pregnant women with laboratory evidence of possible Zika that has been reported

USZPR Definition of Laboratory Confirmed Zika Infection

Zika virus infection can be confirmed by

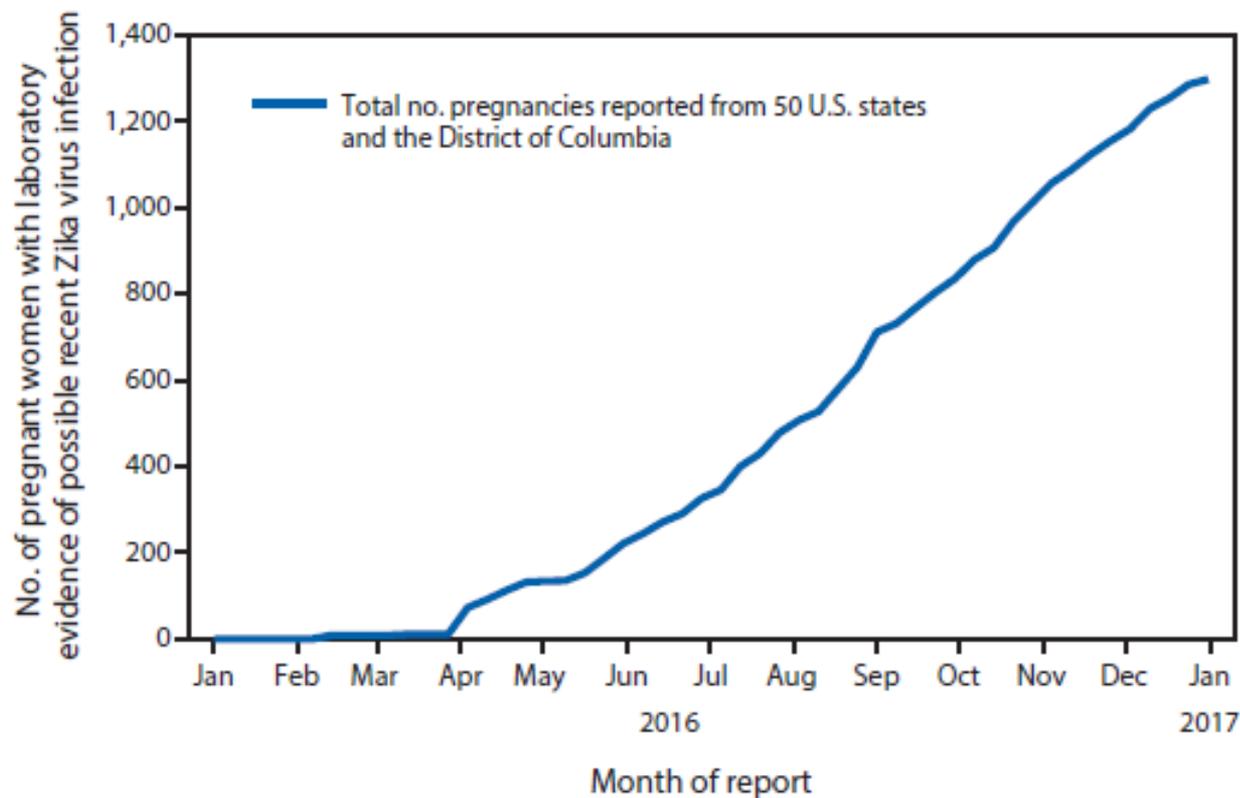
- » Zika virus RNA in any maternal or fetal/infant specimen detected by nucleic acid test (NAT) (e.g., rRT-PCR) OR
- » Positive or equivocal Zika virus IgM with Zika virus plaque reduction neutralization test (PRNT) titer ≥ 10 and dengue virus PRNT < 10

USZPR Definition of Possible Recent Zika Infection

Laboratory evidence of possible recent Zika virus infection

- » Recent Zika virus infection detected by a Zika virus RNA nucleic acid test (NAT, e.g., [RT-PCR]) on any maternal, placental, or fetal/infant specimen or
- » Detection of recent Zika virus infection or recent unspecified flavivirus infection by serologic tests on a maternal or infant specimen
 - Either positive or equivocal Zika virus IgM AND Zika virus PRNT titer ≥ 10 , regardless of dengue virus PRNT value; or
 - Negative Zika virus IgM, AND positive or equivocal dengue virus IgM, AND Zika virus PRNT titer ≥ 10 , regardless of dengue virus PRNT titer

FIGURE 1. Cumulative number of pregnant women with laboratory evidence of possible recent Zika virus infection reported to the U.S. Zika Pregnancy Registry, by month of report — United States, January–December 2016 (n = 1,297)



Box. Birth Defects Potentially Related to Zika Virus Infection During Pregnancy and Monitored by the US Zika Pregnancy Registry for Enhanced Surveillance

Brain Abnormalities With and Without Microcephaly

Confirmed or possible congenital microcephaly^a

Intracranial calcifications

Cerebral atrophy

Abnormal cortical formation (eg, polymicrogyria, lissencephaly, pachygyria, schizencephaly, gray matter heterotopia)

Corpus callosum abnormalities

Cerebellar abnormalities

Porencephaly

Hydranencephaly

Ventriculomegaly/hydrocephaly (excluding "mild" ventriculomegaly without other brain abnormalities)

Fetal brain disruption sequence (collapsed skull, overlapping sutures, prominent occipital bone, scalp rugae)

Other major brain abnormalities including intraventricular hemorrhage in utero (excluding postnatal intraventricular hemorrhage)

Neural Tube Defects and Other Early Brain Malformations

Neural tube defects including anencephaly, acrania, encephalocele, spina bifida

Holoprosencephaly (arhinencephaly)

Eye Abnormalities

Microphthalmia/anophthalmia

Coloboma

Cataract

Intraocular calcifications

Chorioretinal anomalies involving the macula (eg, chorioretinal atrophy and scarring, macular pallor, gross pigmentary mottling and retinal hemorrhage; excluding retinopathy of prematurity)

Optic nerve atrophy, pallor, and other optic nerve abnormalities

Consequences of Central Nervous System Dysfunction

Congenital contractures (eg, arthrogryposis, clubfoot, congenital hip dysplasia) with associated brain abnormalities

Congenital deafness documented by postnatal audiological testing

^a Live births: measured head circumference (adjusted for gestational age and sex) less than the third percentile at birth or, if not measured at birth, within first 2 weeks of life. Pregnancy loss: prenatal head circumference more than 3 SDs below the mean based on ultrasound or postnatal head circumference less than the third percentile. Birth measurements are evaluated using the intergrowth-21st standards (<http://intergrowth21.ndog.ox.ac.uk/>) based on measurements within 24 hours of birth.

TABLE 1. Pregnancy outcomes* for 972 women with completed pregnancies† with laboratory evidence of possible recent Zika virus infection, by maternal symptom status and timing of symptom onset or exposure—U.S. Zika Pregnancy Registry, United States, December 2015–December 2016

Characteristic	Brain abnormalities and/or microcephaly (No.)	NTDs and early brain malformations, eye abnormalities, or consequences of CNS dysfunction without brain abnormalities or microcephaly (No.)	Total with ≥1 birth defect (No.)	Completed pregnancies (No.)	Proportion affected by Zika virus-associated birth defects, % (95% CI) [§]
Any laboratory evidence of possible recent Zika virus infection[¶]					
Total	43	8	51	972	5 (4–7)
Maternal symptom status					
Symptoms of Zika virus infection reported	18	3	21	348	6 (4–9)
No symptoms of Zika virus infection reported	24	4	28	599	5 (3–7)
Unknown	1	1	2	25	—
Timing of symptoms or exposure^{**}					
First trimester ^{††,§§}	13	1	14	157	9 (5–14)
Multiple trimesters including first	22	6	28	396	7 (5–10)

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Maternal symptom status					
Symptoms of Zika virus infection reported	8	3	11	141	8 (4–13)
No symptoms of Zika virus infection reported	10	2	12	102	12 (7–19)
Unknown	0	1	1	7	—
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First trimester ^{††,§§}	8	1	9	60	15 (8–26)
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Postnatal Neuroimaging and Testing

TABLE 2. Postnatal neuroimaging* and infant Zika virus testing results for 895 liveborn infants in the U.S. Zika Pregnancy Registry — 50 U.S. states and the District of Columbia, 2016

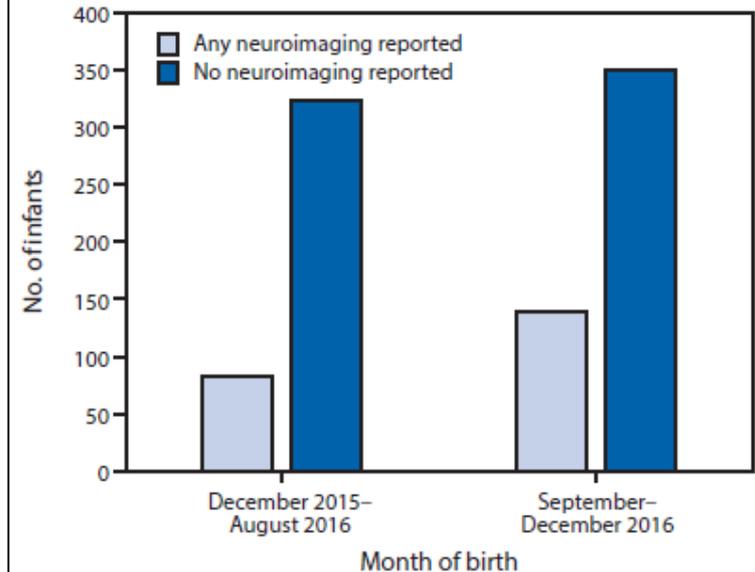
Testing	No (%) liveborn infants		
	With birth defects	Without birth defects	Total
Total	45	850	895
Neuroimaging			
Any neuroimaging reported to USZPR	29 (64)	192 (23)	221 (25)
Infant Zika virus testing			
Positive test result on an infant specimen ^{†,5}	25 (56)	69 (8)	94 (11)
Negative infant test results among infants with ≥1 infant specimen reported as tested	17 (38)	474 (56)	491 (55)
No infant specimen test results reported to USZPR	3 (7)	307 (36)	310 (35)

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FIGURE 2. Postnatal neuroimaging for infants reported to the U.S. Zika Pregnancy Registry, by month of birth — United States, December 2015–December 2016



Postnatal Neuroimaging and Testing

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Baseline Prevalence of Birth Defects Observed with Zika

- » Used data from birth defects surveillance systems in Massachusetts, North Carolina, and Atlanta, Georgia, during pre-Zika outbreak years (2013–2014)
- » Prevalence of Zika-related birth defects before Zika outbreak in the Americas:

3 out of every 1,000 births

- » Proportion of infants with birth defects among completed pregnancies with confirmed Zika infection (2016):

24 out of every 250 completed pregnancies

Estimated

**30-fold
increase**

in Zika-related birth defects in pregnancies with confirmed Zika infection compared with pre-Zika years

Key Vital Signs Findings

44

States reported pregnant women with evidence of Zika in 2016

about
1 in 10

Pregnant women with confirmed Zika had a fetus or baby with birth defects

only
1 in 4

Babies with possible congenital Zika infection were reported to have received brain imaging after birth



Vital^{CDC}signs™

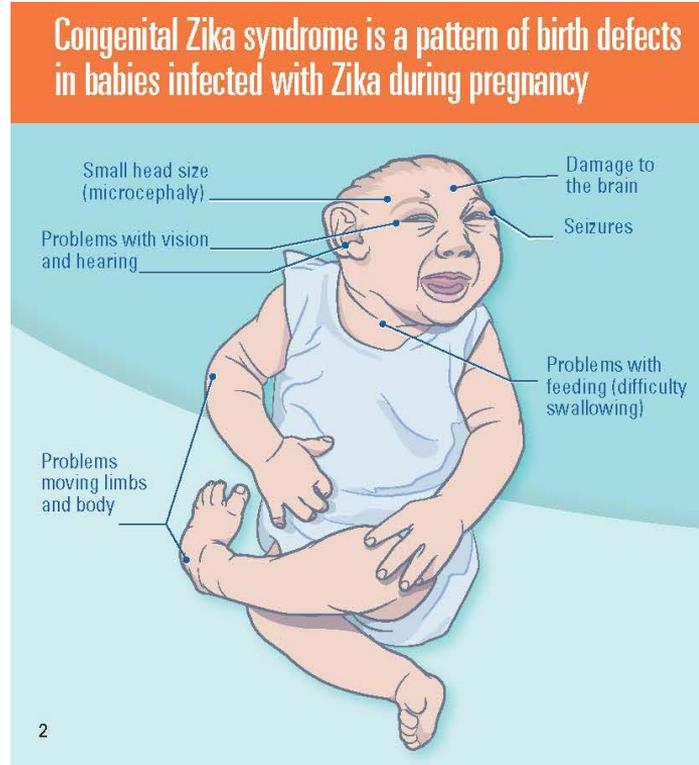
www.cdc.gov/vitalsigns/zika-babies



Key Vital Signs Findings

972 pregnant women with evidence of Zika completed their pregnancies in 2016, and some had babies with Zika-related birth defects:

- » **5%** with possible Zika had birth defects
- » **10%** with confirmed Zika had birth defects
- » **15%** with confirmed Zika in the first trimester had birth defects



Preventing Zika in Pregnant Women

What You Can Do to Help

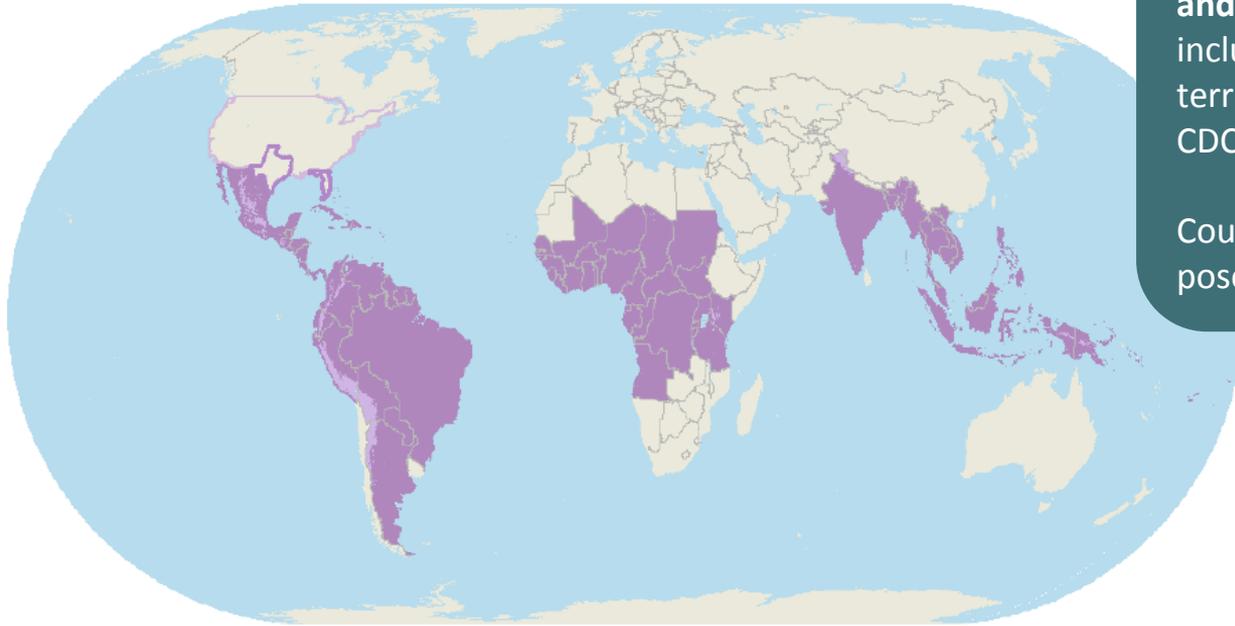
- 1 Educate families on Zika prevention
- 2 Ask about Zika
- 3 Provide all needed tests and follow-up care
- 4 Support infants and families

Do Not Travel to Areas with Risk of Zika

- » Pregnant women should **not** travel to areas with risk of Zika



World Map of Areas with Risk of Zika



There are currently **63 countries and territories worldwide**, including 49 countries and territories in the Americas, with a CDC Zika Travel Notice.

Countries with endemic Zika also pose a risk.

Domestic areas

State Reporting Zika: 

No Known Zika: 

International areas

Zika Travel Recommendation:  Low elevation

 High elevation

No Known Zika: 

As of April 24, 2017

Do Not Travel to Areas with Risk of Zika

If a pregnant woman *must* travel, she should

- » Talk with her healthcare provider before she goes
- » Strictly follow steps to prevent mosquito bites during the trip
- » Take steps to prevent sexual transmission
- » Talk with her healthcare provider after she returns, even if she doesn't feel sick



Prevent Mosquito Bites

If a pregnant woman lives in or travels to an area with Zika, she should

- » Wear long-sleeved shirts and long pants
- » Stay and sleep in places with air conditioning or that use window and door screens
- » Use EPA-registered insect repellents with one of the following active ingredients:
 - DEET, picaridin, IR3535, oil of lemon eucalyptus, para-menthane-diol, or 2-undecanone
- » Once a week, empty and scrub, turn over, cover, or throw out items that hold water, such as trash containers, tires, buckets, toys, planters, flowerpots, birdbaths or pools



Prevent Sexual Transmission of Zika Virus

A pregnant woman whose partner lives in or has traveled to an area with risk of Zika should

- » Use condoms correctly every time they have sex, or
- » Not have sex

For the duration of the pregnancy, even if the pregnant woman's partner does not have symptoms or feel sick.



Healthcare Providers Caring for Pregnant Women and Infants Should Ask about Zika Exposure during Pregnancy

Have you traveled to an area with risk of Zika during pregnancy or just before you became pregnant?

Have you had sex without a condom with a partner who lives in or traveled to an area with risk of Zika?

Do you live in or do you frequently travel (daily or weekly) to an area with risk of Zika?



Who Should Be Tested for Zika?

All pregnant women (regardless of symptoms) who

- » Live in or recently traveled to an area with risk of Zika that has a CDC Zika travel notice, or
- » Had unprotected sex with a partner who lives in or traveled to an area with risk of Zika that has a CDC Zika travel notice

Pregnant women who live in or recently traveled to an area with risk of Zika but without a CDC Zika travel notice

- » If they develop symptoms of Zika, or
- » If their fetus has abnormalities on an ultrasound that may be related to Zika infection



Testing Infants for Zika

CDC recommends laboratory testing for

- » All infants born to mothers with laboratory evidence of Zika virus infection during pregnancy
- » Infants who have abnormal clinical or neuroimaging findings suggestive of congenital Zika syndrome and a mother with a possible exposure to Zika virus, regardless of maternal Zika virus testing results



Pediatric Evaluation and Follow-Up: The First 12 Months

CDC's Response to Zika

TABLE 1

Interpretation of results of laboratory tests*

rRT-PCR	Positive	Positive
	Negative	Negative

Abbreviations: rRT-PCR = real-time reverse transcription PCR
 * Infant serum, urine or cerebrospinal fluid.
 † Laboratory results should be interpreted in the context of findings consistent with congenital Zika syndrome, as appropriate.

CHECKLIST 1

Initial clinical evaluation & management of infants with laboratory evidence of Zika virus infection and abnormalities consistent with congenital Zika syndrome†

Consultation with:

- Neurologist for determination of appropriate treatment and additional evaluation.
- Infectious disease specialist for diagnostic evaluation of congenital infections (e.g. syphilis, toxoplasma, cytomegalovirus infection, lymphocytic choriomeningitis, and herpes simplex virus infection).
- Ophthalmologist for comprehensive eye exam for possible cortical visual impairment prior to hospital or within 1 month of birth.
- Endocrinologist for evaluation for hypothalamic dysfunction.
- Clinical geneticist to evaluate for other causes of microcephaly or other anomalies if present.

Consider consultation with:

- Orthopedist, physiatrist and physical therapist for management of hypertension, clubfoot or arthralgia conditions.
- Pulmonologist or otolaryngologist for concerns.
- Lactation specialist, nutritionist, gastroenterologist, occupational therapist for the management of feeding difficulties.
- Perform ABR to assess hearing.
- Perform complete blood count and metabolic panel liver function tests.
- Provide family and supportive services.

CDC's Response to Zika

Outpatient Management Checklist**

2 weeks	<input type="checkbox"/> Thyroid screen (TSH & T4)
ROW 1	<input type="checkbox"/> Routine <input type="checkbox"/> Referral <input type="checkbox"/> Refer to (See Page 2)
ROW 2	<input type="checkbox"/> Continue <input type="checkbox"/> Further
ROW 3	<input type="checkbox"/> Ophthalmology exam <input type="checkbox"/> ABR
ROW 4	<input type="checkbox"/> Months and age

Abbreviations: rRT-PCR = real-time reverse transcription-polymerase chain reaction; ABR = auditory brainstem response; CT = computed tomography; M = maternal; LFTs = liver function tests.
 * Laboratory evidence of Zika virus infection includes: (1) Zika virus confirmed by neutralizing antibody titers are needed in addition to laboratory evidence of Zika virus infection.
 ** Outpatient management checklist for infants born to a woman with laboratory evidence of Zika virus infection can include:
 † Mothers who traveled to or reside in an area of active Zika transmission within 2 weeks of exposure or symptom onset, or IGM within 2-12 weeks after exposure or symptom onset does not rule out maternal infection.
 ‡ Infant testing is recommended within the first two days after birth.

INITIAL EVALUATION AND OUTPATIENT MANAGEMENT DURING THE FIRST 12 MONTHS OF LIFE FOR INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION

Initial Evaluation

Before hospital discharge

- Routine newborn care: physical exam, including head circumference, weight, length and neuro exam
- CBC, metabolic panel, LFTs
- Standard newborn hearing screen
- Head ultrasound
- Infant testing for congenital Zika virus

Before hospital discharge

- Routine newborn care: physical exam, including head circumference, weight, length and neuro exam
- Head ultrasound
- Infant testing for congenital Zika virus

Before hospital discharge

- Maternal Zika virus testing†
- Consider Zika virus testing of the placenta
- Routine

Before hospital discharge

- Maternal Zika virus testing†
- Consider Zika virus testing of the placenta
- Routine newborn care: physical exam, including head circumference, weight, length and neuro exam

Morbidity and Mortality Weekly Report

Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016

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On August 19, 2016, this report was posted as an MMWR ongoing psychosocial support and assistance with coordina-

Link to updated infant guidance (April 2017): <https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-and-management.html?permalink=https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-and-management.html>

Contribute to the US Zika Pregnancy Registry

Notify health department of pregnant women and/or infants with Zika virus infection

- » More information available on the [U.S. Zika Pregnancy Registry website](#)
- » 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 email ZIKApregnancy@cdc.gov.
- » For non-urgent requests, call 800-CDC-INFO (800-232-4636)



Thank you!

For more information, please visit:

www.cdc.gov/vitalsigns/index.html

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.



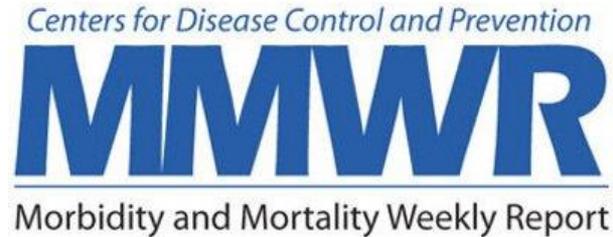


Additional Considerations for Evaluation and Management of Infants with Possible Congenital Zika Virus Infection

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Evaluation and Management of Infants with Possible Congenital Zika Virus Infection



Update: Interim Guidance for the Evaluation and Management of Infants with Possible Congenital Zika Virus Infection — United States, August 2016

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http://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mm6533e2_w

Update Posted April 2017: Additional Considerations

- Additional Considerations for Evaluation and Management of Infants with Possible Zika Virus Infection
 - » Neuroimaging
 - » Zika virus testing

<https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-and-management.html>

Infants with Possible Congenital Zika Virus Infection

- Born to mothers with laboratory evidence of possible Zika virus infection
- With abnormal clinical or neuroimaging findings suggestive of congenital Zika syndrome and a maternal epidemiologic link*

*An epidemiologic link includes travel to or residence in an area with risk of Zika, or sex without a condom with a partner who traveled to or lived in such an area



Initial Evaluation of Infants with Possible Congenital Zika Virus Infection

- Comprehensive physical exam
 - » Head circumference, weight, length measurements
 - » Neurologic assessment
- Standard newborn hearing assessment
- Head ultrasound
- Zika virus laboratory testing



Initial Evaluation of Infants with Possible Congenital Zika Virus Infection

- Comprehensive physical exam
 - » Head circumference, weight, length measurements
 - » Neurologic assessment
- Standard newborn hearing assessment
- **Head ultrasound**
- Zika virus laboratory testing



Congenital Zika Syndrome

- Distinct pattern of birth defects in fetuses and infants of women infected during pregnancy
- Birth defects that make up the congenital Zika syndrome
 - » Severe microcephaly with partially collapsed skull
 - » Thin cerebral cortex with subcortical calcifications
 - » Macular scarring and focal pigmentary retinal mottling
 - » Congenital contractures
 - » Marked early hypertonia and symptoms of extrapyramidal involvement



Baby with Severe Microcephaly



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

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Early Release / Vol. 65

November 22, 2016

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

New Vital Signs Report

Zika Virus: Protecting Pregnant Women and Babies

44

States reported pregnant women with evidence of Zika in 2016

about

1 in 10

Pregnant women with confirmed Zika had a fetus or baby with birth defects

only

1 in 4

Babies with possible congenital Zika infection were reported to have received brain imaging after birth



Vitalsigns™
CDC

www.cdc.gov/vitalsigns/zika-babies



Infants with Possible Congenital Zika Virus Infection: Neuroimaging

Current Interim Guidance

- A head ultrasound is recommended before hospital discharge for infants with possible Zika virus infection

Infants with Possible Congenital Zika Virus Infection: Neuroimaging

Current Interim Guidance

- A head ultrasound is recommended before hospital discharge for infants with possible Zika virus infection

Additional Considerations

- For an infant with a small or absent anterior fontanelle and poor visualization of the intracranial anatomy on ultrasound, other imaging should be considered

Initial Evaluation of Infants with Possible Congenital Zika Virus Infection

- Comprehensive physical exam
 - » Head circumference, weight, length measurements
 - » Neurologic assessment
- Standard newborn hearing assessment
- Head ultrasound
- **Zika virus laboratory testing**



Laboratory Testing of Infants with Possible Congenital Zika Virus Infection

Current Interim Guidance

Testing for Zika virus infection is recommended for infants

- Born to mothers with laboratory evidence of possible Zika virus infection
- With clinical or neuroimaging findings suggestive of congenital Zika syndrome and a maternal epidemiologic link*

*An epidemiologic link includes travel to or residence in an area with risk of Zika, or sex without a condom with a partner who traveled to or lived in such an area

Laboratory Testing of Infants with Possible Congenital Zika Virus Infection

Current Interim Guidance

Testing for Zika virus infection is recommended for infants

- Born to mothers with laboratory evidence of possible Zika virus infection
- With clinical or neuroimaging findings suggestive of congenital Zika syndrome and a maternal epidemiologic link*

Additional Considerations

Testing for Zika virus infection should be considered for infants

- Born to mothers with an epidemiologic link for whom
 - » There is concern about infant follow-up care
 - » Maternal testing was not performed before delivery and exposure was >12 weeks before delivery, or
 - » Maternal testing was negative but was performed on a specimen obtained >12 weeks after maternal exposure

*An epidemiologic link includes travel to or residence in an area with risk of Zika, or sex without a condom with a partner who traveled to or lived in such an area

Timing of Laboratory Testing of Infants with Possible Congenital Zika Virus Infection

Current Interim Guidance

- CDC recommends testing specimens collected from infants within 2 days after birth.
 - » If specimens are collected later, it may be difficult to distinguish congenital from postnatally acquired infection in areas with risk of Zika.

Timing of Laboratory Testing of Infants with Possible Congenital Zika Virus Infection

Current Interim Guidance

- CDC recommends testing specimens collected from infants within 2 days after birth.
 - » If specimens are collected later, it may be difficult to distinguish congenital from postnatally acquired infection in areas with risk of Zika

Additional Considerations

- Testing specimens collected within the first few weeks to months after birth may still be useful in the evaluation for infants with possible congenital Zika virus infection, particularly among infants born in areas without risk of Zika

Testing of Cerebrospinal Fluid (CSF)

Current Interim Guidance

- If cerebrospinal fluid (CSF) is obtained for other studies, Zika NAT (nucleic acid testing) for Zika virus RNA and Zika virus IgM should be performed on CSF



Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study



Thalia Velho Barreto de Araújo, Laura Cunha Rodrigues, Ricardo Arraes de Alencar Ximenes, Demócrito de Barros Miranda-Filho, Ulisses Ramos Montarroyos, Ana Paula Lopes de Melo, Sandra Valongueiro, Maria de Fátima Pessoa Militão de Albuquerque, Wayner Vieira Souza, Cynthia Braga, Sival Pinto Brandão Filho, Marli Tenório Cordeiro, Enrique Vazquez, Danielle Di Cavalcanti Souza Cruz, Cláudio Maierovitch Pessanha Henriques, Luciana Caroline Albuquerque Bezerra, Priscila Mayrelle da Silva Castanha, Rafael Dhalia, Ernesto Torres Azevedo Marques-Júnior, Celina Maria Turchi Martelli, on behalf of investigators from the Microcephaly Epidemic Research Group, the Brazilian Ministry of Health, the Pan American Health Organization, Instituto de Medicina Integral Professor Fernando Figueira, and the State Health Department of Pernambuco*

Summary

Lancet Infect Dis 2016;
16: 1356–63
Published Online
September 15, 2016

Background The microcephaly epidemic, which started in Brazil in 2015, was declared a Public Health Emergency of International Concern by WHO in 2016. We report the preliminary results of a case-control study investigating the association between microcephaly and Zika virus infection during pregnancy.

Testing of Cerebrospinal Fluid (CSF)

Current Interim Guidance

- If cerebrospinal fluid (CSF) is obtained for other studies, NAT testing for Zika virus RNA and Zika virus IgM should be performed on CSF

Additional Considerations

- Testing CSF for Zika virus RNA and IgM antibody should be considered for infants with clinical findings of possible congenital Zika syndrome but whose initial laboratory tests are negative on serum and urine

Interpretation of Laboratory Test Results of Infants with Possible Congenital Zika Virus Infection

CDC's Response to **Zika**

TABLE 1

Interpretation of results of laboratory testing of infant's blood, urine and/or cerebrospinal fluid for evidence of congenital Zika virus infection

Infant test results*		Interpretation
rRT-PCR	IgM	
Positive	Positive or Negative	Confirmed congenital Zika virus infection
Negative	Positive	Probable congenital Zika virus infection ⁺
Negative	Negative	Negative for congenital Zika virus infection ⁺

Abbreviations: rRT-PCR = real-time reverse transcription-polymerase chain reaction; IgM = Immunoglobulin M

* Infant serum, urine or cerebrospinal fluid.

+ Laboratory results should be interpreted in the context of timing of infection during pregnancy, maternal serology results, clinical findings consistent with congenital Zika syndrome, and any confirmatory testing with plaque reduction neutralization testing (PRNT).

<https://www.cdc.gov/zika/pdfs/pediatric-evaluation-follow-up-tool.pdf>

Laboratory Testing for Infants with Possible Congenital Zika Virus Infection

- Plaque Reduction Neutralization Test (PRNT) can be performed at 18 months to confirm a congenital Zika virus infection after maternal IgG has waned

Possible Limitations of Infant Zika Virus Laboratory Testing

- Case reports of infants with clinical findings consistent with possible congenital Zika virus syndrome in whom Zika virus lab results were negative
- Potential explanations include
 - » The clinical findings are due to another cause
 - » Testing was incomplete, performed on suboptimal specimens, or performed too late
 - » The fetus failed to mount an IgM antibody response

The image shows a screenshot of a research article. The top part is from JAMA Neurology, and the bottom part is a preprint from medRxiv.

JAMA Neurology | Original Investigation
Congenital Zika Virus Infection Beyond Neonatal Microcephaly
Adriana Suely de Oliveira Melo, MD, PhD; Renato Santana Aguiar, PhD; Melania Maria Ramos Amorim, MD, PhD; Monica B. Arruda, PhD; Fabiana de Oliveira Melo, MD; Suellem Tais Clementino Ribeiro, MD; Alba Gean Medeiros Batista, MD; Thales Ferreira, MD; Mayra Pereira dos Santos, MD; Virginia Vilar Sampaio, MD; Sarah Rogéria Martins Moura, MD; Luciana Portela Rabello, MD; Clarissa Emanuelle Gonzaga, MD

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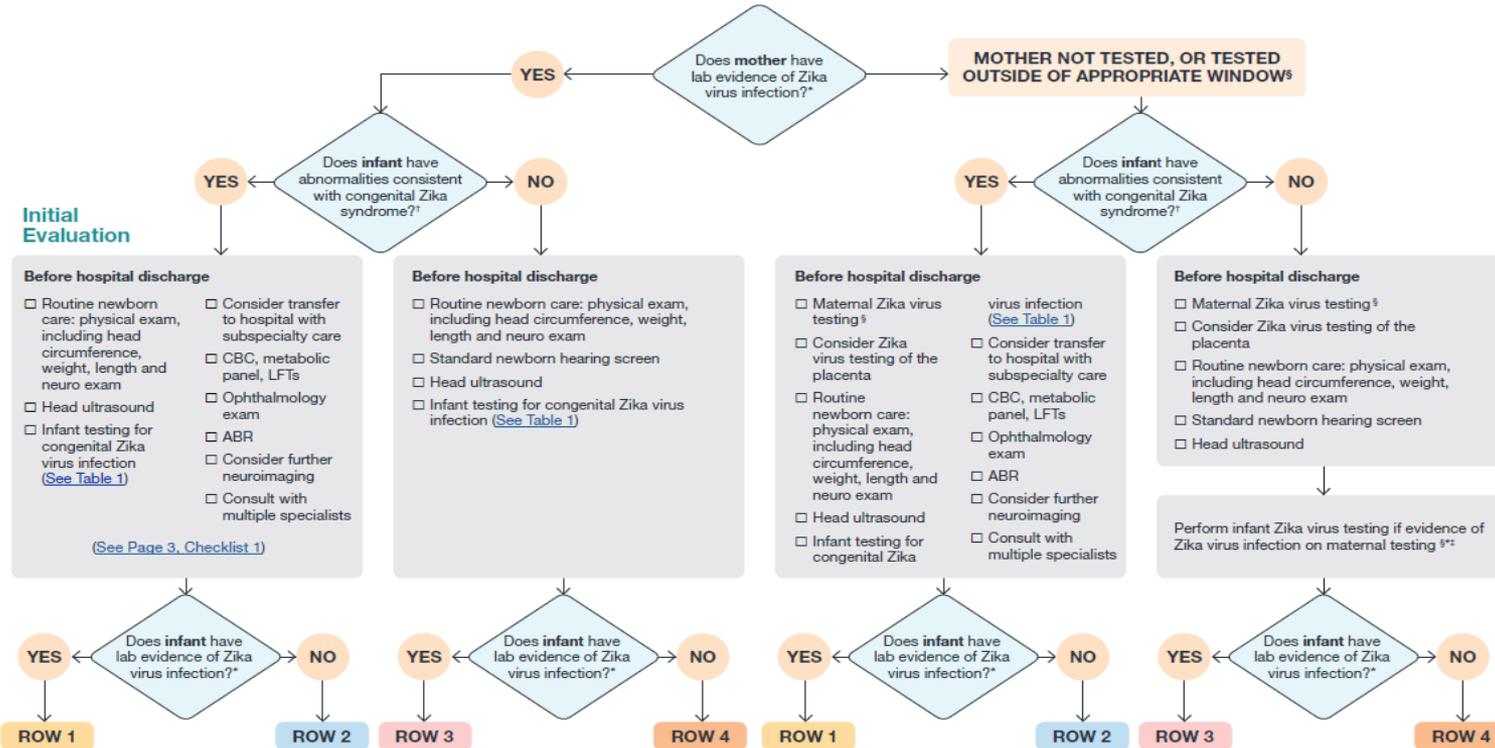
Lancet Infect Dis 2016; 16: 1356-63
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September 15, 2016

Maintain a Level of Suspicion

- For infants without laboratory evidence of Zika virus infection but for whom suspicion for congenital Zika virus infection remains, HCPs should
 - » Evaluate for other causes of congenital infection
 - » Consider an ophthalmology exam and auditory brainstem response (ABR) hearing test
 - » Consider performing other evaluation and follow up in accordance with CDC interim guidance for the evaluation and management of infants with possible congenital Zika syndrome



INITIAL EVALUATION AND OUTPATIENT MANAGEMENT DURING THE FIRST 12 MONTHS OF LIFE FOR INFANTS WITH POSSIBLE CONGENITAL ZIKA VIRUS INFECTION



Follow management and follow-up recommendations indicated in Outpatient Management Checklist

Zika Care Connect: Improving Access to Clinical Services

- Provider Network for Families Affected by Zika
 - » Maternal-fetal medicine, mental health services, audiology, radiology, pediatric ophthalmology, pediatric neurology, developmental pediatrics, infectious disease, and endocrinology
- Laboratory Testing Web Portal for Healthcare Providers
 - » Identify laboratories offering Zika testing



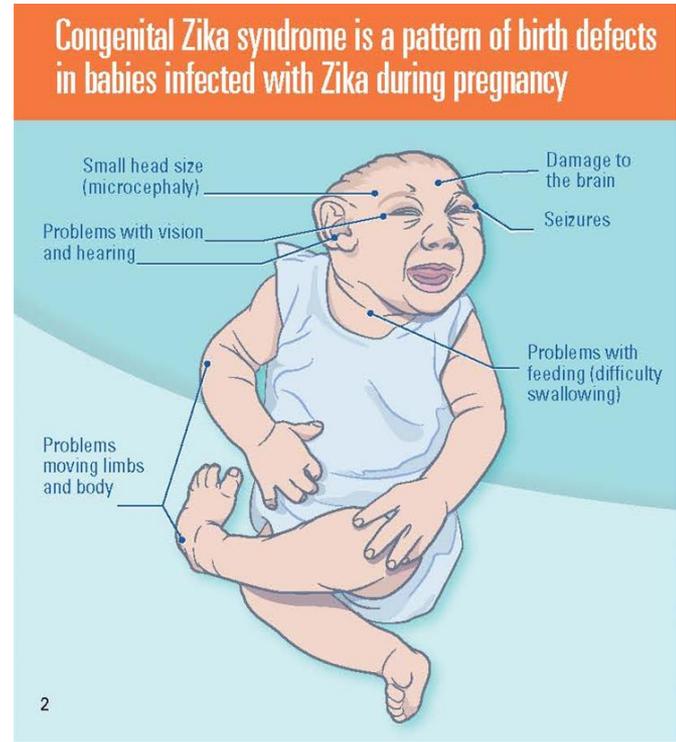
HelpLine: 1-844-677-0447 (toll-free)

Website: www.zikacareconnect.org

ZIKAcareconnect
in collaboration with the **March of Dimes**

Summary

- Infants with possible congenital Zika virus infection
 - » Neuroimaging
 - » Criteria, timing, and specimens for Zika testing
 - » Possible limitations



Thank you!

For more information, please visit:

www.cdc.gov/vitalsigns/index.html

www.cdc.gov/zika

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

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