

Zika Virus, Still a Threat Updates and Implementation

AAP Webinar Series on Zika Virus Syndrome
Wednesday, December 13, 2017
4:00pm ET/3:00pm CT

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN®



OBJECTIVES

The webinar will address updated recommendations for the diagnosis, clinical evaluation, and management of infants:

1. With clinical findings consistent with congenital Zika syndrome born to mothers with possible Zika virus exposure in pregnancy.
2. Without clinical findings consistent with congenital Zika syndrome born to mothers with laboratory evidence of possible Zika virus infection during pregnancy.
3. Without clinical findings consistent with congenital Zika syndrome born to mothers with possible Zika virus exposure in pregnancy but without laboratory evidence of possible Zika virus infection during pregnancy.



OBJECTIVES

By the end of this webinar, participants will be able to:

1. Understand the new recommendations for the screening, diagnosis, evaluation, and management of infants with possible congenital Zika virus infection, including:
 - A. Interpretation of infant laboratory testing results
 - B. Guidance for vision and hearing screening
 - C. Which screenings are no longer recommended
2. Describe the need for physicians to be vigilant in screening infants who are relocated to the United States from hurricane-impacted areas with Zika outbreaks.
3. Identify how to find the latest AAP and CDC resources.



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Q & A

- Submit questions at any time through the chat box
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Zika Virus, Still a Threat – Updates and Implementation

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December 13, 2017



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

Overview

- Background
 - » Review of what's known about congenital Zika virus infection
 - » Updated Zika virus pregnancy guidance
 - » Emerging data on clinical findings
 - » Forum on the Diagnosis, Evaluation, and Management of Zika Virus Infection among Infants
- Updated interim guidance for the diagnosis, evaluation, and management of infants
- Overview of key changes since previous guidance

What Have We Learned About Zika Virus Infection?



Zika virus can cause serious brain abnormalities, microcephaly, and potentially other birth defects



Pattern of birth defects associated with Zika virus infection called **congenital Zika syndrome**



Estimated risk of congenital Zika syndrome from congenital Zika virus infection **5-10%^{1,2}**

References:

1. Honein MA, Dawson AL, Petersen EE et al. Birth Defects Among Fetuses and Infants of US Women With Evidence of Possible Zika Virus Infection During Pregnancy. *JAMA*. 2017;317(1):59-68. doi:10.1001/jama.2016.19006
2. Shapiro-Mendoza CK, Rice ME, Galang RR, et al. Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy — U.S. Territories, January 1, 2016–April 25, 2017. *MMWR Morb Mortal Wkly Rep* 2017;66:615-621. DOI: <http://dx.doi.org/10.15585/mmwr.mm6623e1>

Photo sources:

Moore CA, Staples JE, Dobyns WB, et al. Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians. *JAMA Pediatr*. Soares de Oliveira-Szeinfeld P, Levine D, Suely de Oliveira Melo A, et al. Congenital brain abnormalities and zika virus: What the radiologist can expect to see prenatally and postnatally. *Radiology* 2016;281:203-218.

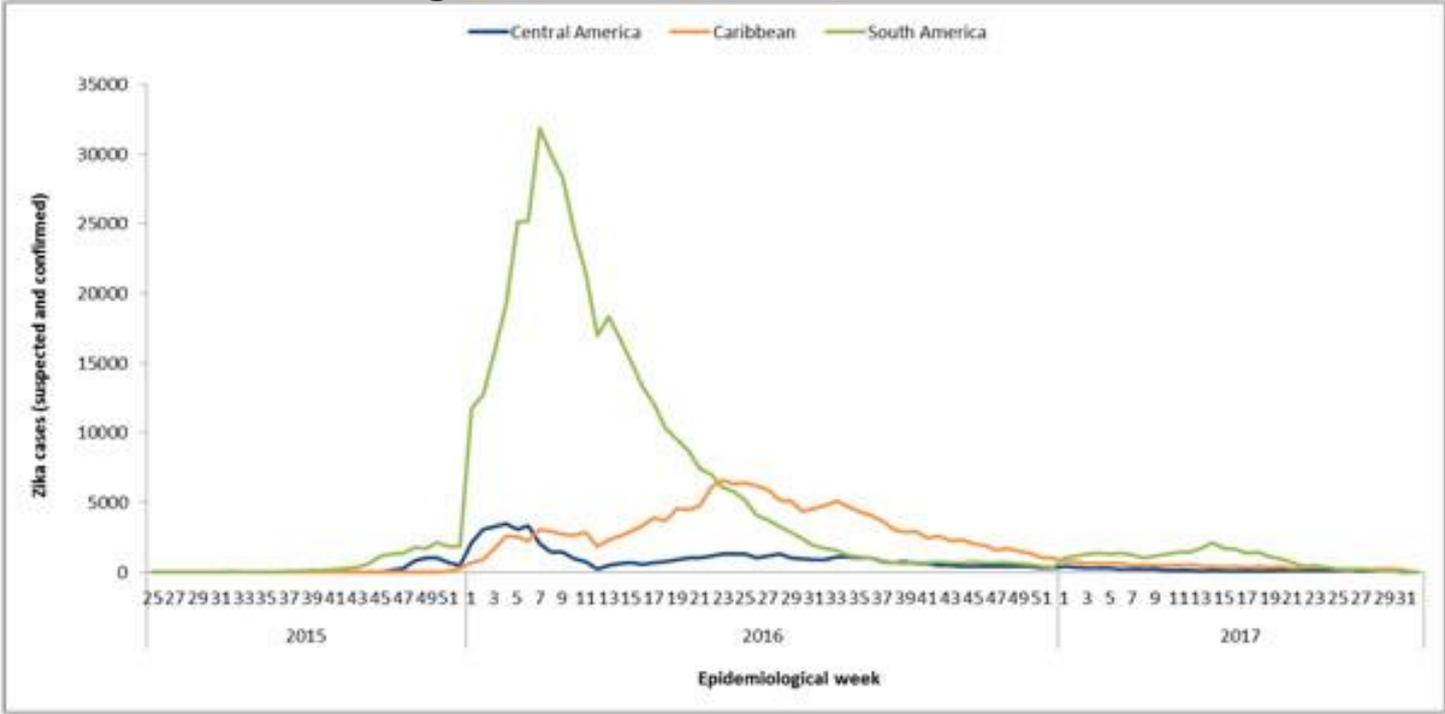
Testing for Zika Virus Infection

Laboratory testing for Zika virus has several limitations:

- Zika virus RNA transiently present in body fluids
- Serologic testing:
 - » Affected by timing of sample collection
 - » IgM may be detectable for months after the initial infection
 - » Cross-reactivity of Zika virus IgM antibody tests with other flaviviruses
- Limitations of Zika virus IgM tests approved under an Emergency Use Authorization (EUA)

Testing for Zika Virus Infection – cont.

Suspected and Confirmed Zika Virus Cases reported to PAHO – Region of the Americas, 2015-2017



http://www.paho.org/hq/index.php?option=com_content&view=article&id=11599:regional-zika-epidemiological-update-americas&catid=8424:contents&Itemid=41691&lang=en

Updated Guidance for Testing of Pregnant Women with Possible Zika Virus Exposure

Symptomatic pregnant women with possible Zika virus exposure

- Recommend testing to diagnose cause of symptoms
- Tests: Concurrent NAT & IgM

Updated Guidance for Testing of Pregnant Women with Possible Zika Virus Exposure

Symptomatic pregnant women with possible Zika virus exposure

- Recommend testing to diagnose cause of symptoms
- Tests: Concurrent NAT & IgM

Asymptomatic pregnant women with ongoing possible Zika virus exposure

- Recommend testing given ongoing exposure to Zika
- Tests: NAT testing 3x during routine prenatal care visits

Updated Guidance for Testing of Pregnant Women with Possible Zika Virus Exposure

Symptomatic pregnant women with possible Zika virus exposure

- Recommend testing to diagnose cause of symptoms
- Tests: Concurrent NAT & IgM

Asymptomatic pregnant women with ongoing possible Zika virus exposure

- Recommend testing given ongoing exposure to Zika
- Tests: NAT testing 3x during routine prenatal care visits

Asymptomatic pregnant women with possible Zika virus exposure but without ongoing exposure

- Testing not routinely recommended
- Should be considered as a shared decision between patients and providers and in line with jurisdictional recommendations

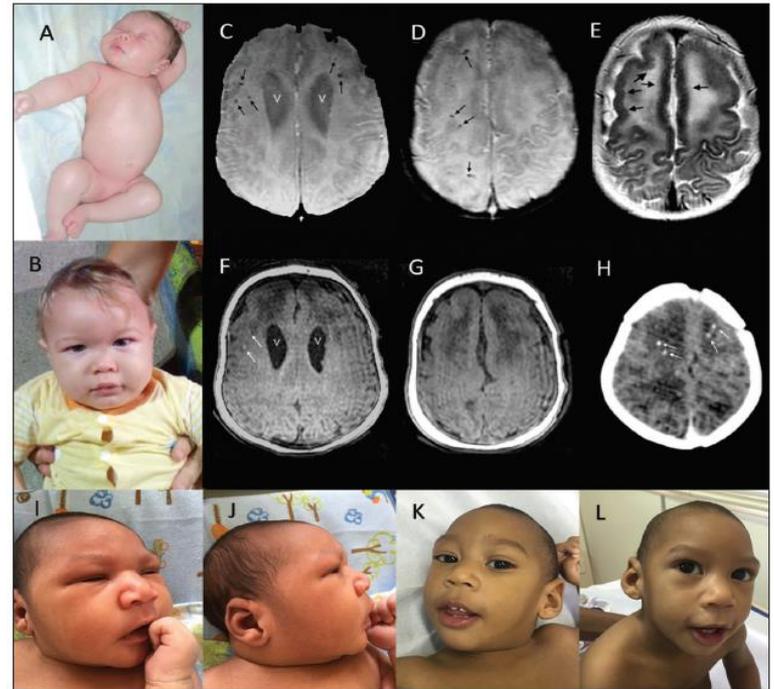
Bottom Line of the Updated Pregnancy Guidance

- » **Intended to reduce possibility of false positive results**
- » **Might delay identification of some infants who might have complications from congenital Zika virus infection**

Emerging Data on Congenital Zika Virus Infection

- Eye problems in infants without microcephaly or other brain anomalies
- Postnatal-onset microcephaly in infants
- Postnatal-onset hydrocephalus
- Abnormalities on sleep electroencephalogram (EEG) without recognized seizures
- Diaphragmatic paralysis

FIGURE. Clinical photographs and magnetic resonance (MR) and computed tomography (CT) images of two infants with congenital Zika syndrome* — Brazil, October 2015–October 2016



Postnatal-onset microcephaly

Van Der Linden et al., MMWR Morb Mortal Wkly Rep 2016;65(47):1343-1348.

Updated Interim Guidance for Infants with Possible Congenital Zika Virus Infection

Centers for Disease Control and Prevention

MMWR

Morbidity and Mortality Weekly Report

Weekly / Vol. 66 / No. 41

October 20, 2017

Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017

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Forum on the Diagnosis, Evaluation, and Management of Zika Virus Infection among Infants



Updated interim guidance based on:

- Current, limited data about the clinical aspects of Zika virus infection
 - Individual expert opinions collected during the Forum
 - Knowledge about other congenital infections

Diagnosis of Congenital Zika Virus Infection



Serum

Zika virus NAT
Zika virus IgM



Urine

Zika virus NAT



CSF (if obtained for other purposes)

Zika virus NAT
Zika virus IgM

Perform as early as possible, preferably within the first few days after birth

Testing specimens within the first few weeks to months after birth might still be useful

Zika Virus Infection Based on Infant Test Results

NAT	IgM	Interpretation
Positive	Any result	Confirmed congenital Zika virus infection
Negative	Nonnegative	Probable congenital Zika virus infection*
Negative	Negative	Congenital Zika virus infection unlikely

If Zika virus plaque reduction neutralization test (PRNT) is negative, this suggests that the infant's Zika virus IgM test is a false positive

Updated Interim Guidance

For infants born to women with possible Zika virus exposure during pregnancy

Infants **with** clinical findings consistent with congenital Zika syndrome

Updated Interim Guidance

For infants born to women with possible Zika virus exposure during pregnancy

Infants **with** clinical findings consistent with congenital Zika syndrome

Infants **without** clinical findings consistent with congenital Zika syndrome born to mothers **with** laboratory evidence of possible Zika virus infection during pregnancy

Updated Interim Guidance

For infants born to women with possible Zika virus exposure during pregnancy

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Infants **without** clinical findings consistent with congenital Zika syndrome born to mothers **without** laboratory evidence of Zika virus infection during pregnancy

Standard Evaluation for Infants with Possible Congenital Zika Virus Exposure

- Comprehensive physical examination (includes growth parameters)
- Age-appropriate vision screening and developmental monitoring and screening using validated tools
- Standard newborn hearing screen at birth, preferably using auditory brainstem response (ABR) methodology



Updated Interim Guidance

For infants born to women with possible Zika virus exposure during pregnancy

Infants **with** clinical findings consistent with congenital Zika syndrome

Infants with Clinical Findings Consistent with Congenital Zika Syndrome: Initial Evaluation

- Standard evaluation
- Zika virus NAT and IgM testing
- Testing for Zika virus NAT and IgM on CSF should be considered
- Head ultrasound by 1 month of age
- Comprehensive ophthalmologic exam by 1 month of age
- Automated ABR (If newborn hearing screen passed using otoacoustic emissions [OAE] methodology)
- Evaluate for other causes of congenital anomalies

- Refer to developmental specialist and early intervention services
- Family support services

Consider additional consultations with

- Infectious disease specialist
- Clinical geneticist
- Neurologist
- Other clinical specialists based on clinical findings of infant

Consider fewer consultations for the evaluation of severely affected infants who are receiving palliative care

Infants with Clinical Findings Consistent with Congenital Zika Syndrome: Follow-up Care

- Standard evaluation with routine preventive care and immunizations at every well-child visit
- Follow-up visits with ophthalmology should occur based on ophthalmology recommendations
- Continue subspecialty care

Updated Interim Guidance

For infants born to women with possible Zika virus exposure during pregnancy

Infants **with** clinical findings consistent with congenital Zika syndrome

Infants **without** clinical findings consistent with congenital Zika syndrome born to mothers **with** laboratory evidence of possible Zika virus infection during pregnancy

Infants without Clinical Findings Consistent with Congenital Zika Syndrome Born to Mothers with Laboratory Evidence of Possible Zika Virus Infection during Pregnancy: Initial Evaluation

- Standard evaluation
- Zika virus NAT and IgM testing
- Head ultrasound by 1 month of age
- Comprehensive ophthalmologic exam by 1 month of age
- Automated ABR (If newborn hearing screen passed using OAE methodology)

Infants without Clinical Findings Consistent with Congenital Zika Syndrome Born to Mothers with Laboratory Evidence of Possible Zika Virus Infection during Pregnancy: Follow-up Care

- Standard evaluation with routine preventive care and immunizations at every well-child visit
- Follow-up visits with ophthalmology should occur based on ophthalmology recommendations
- If findings consistent with congenital Zika syndrome are identified, further evaluation should follow recommendations for **infants with clinical findings consistent with congenital Zika syndrome**

Infants without Clinical Findings Consistent with Congenital Zika Syndrome Born to Mothers with Laboratory Evidence of Possible Zika Virus Infection during Pregnancy: Follow-up Care

- Standard evaluation with routine preventive care and immunizations at every well-child visit
- Follow-up visits with ophthalmology should occur based on ophthalmology recommendations
- If findings consistent with congenital Zika syndrome are identified, further evaluation should follow recommendations for **infants with clinical findings consistent with congenital Zika syndrome**

Laboratory evidence of possible congenital Zika infection

- Follow recommendations for infants with clinical findings even in the absence of clinically apparent abnormalities

Infants without Clinical Findings Consistent with Congenital Zika Syndrome Born to Mothers with Laboratory Evidence of Possible Zika Virus Infection during Pregnancy: Follow-up Care

- Standard evaluation with routine preventive care and immunizations at every well-child visit
- Follow-up visits with ophthalmology should occur based on ophthalmology recommendations
- If findings consistent with congenital Zika syndrome are identified, further evaluation should follow recommendations for **infants with clinical findings consistent with congenital Zika syndrome**

No laboratory evidence of possible congenital Zika infection

- Congenital Zika virus infection is unlikely
- Infant should continue to receive routine care, and healthcare providers should remain alert for any new findings of congenital Zika virus infection

Updated Interim Guidance

For infants born to women with possible Zika virus exposure during pregnancy

Infants **with** clinical findings consistent with congenital Zika syndrome

Infants **without** clinical findings consistent with congenital Zika syndrome born to mothers **with** laboratory evidence of possible Zika virus infection during pregnancy

Infants **without** clinical findings consistent with congenital Zika syndrome born to mothers **without** laboratory evidence of Zika virus infection during pregnancy

Infants without Clinical Findings Consistent with Congenital Zika Syndrome Born to Mothers without Laboratory Evidence of Zika Virus Infection during Pregnancy

- Laboratory testing and clinical evaluation beyond a standard evaluation **are not routinely recommended.**
- If findings suggestive of congenital Zika syndrome are identified at any time, refer to appropriate specialists and evaluate for congenital Zika virus infection.

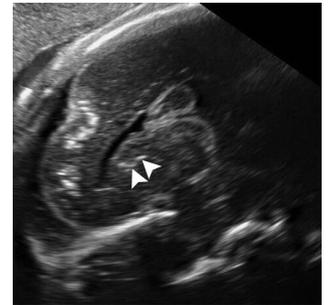
Special Considerations for the Prenatal Diagnosis of Congenital Zika Virus Infection

Prenatal Ultrasound

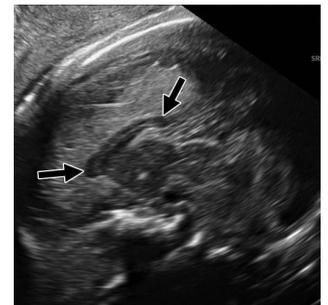
- Prenatal ultrasound findings associated with congenital Zika virus infection:
 - » Brain abnormalities
 - » Microcephaly
 - » Limb anomalies
- Length of time for detection of abnormalities has varied

Amniocentesis

- Decisions to test amniotic fluid for Zika virus should be individualized, and considered as part of an evaluation for abnormal prenatal findings in the context of possible exposure



Intracranial calcifications



Small corpus callosum

Soares de Oliveira-Szejnfeld P, et al. *Radiology* 2016;281:203–18

Key Changes from the Previous Guidance

- Initial evaluation can occur before or after hospital discharge
- **Infants with laboratory evidence of congenital Zika virus infection**
 - » Repeat ABR is no longer recommended at age 4-6 months if the newborn hearing screen was passed using ABR methodology or if automated ABR at 1 month is passed
- **Infants with clinical findings consistent with congenital Zika syndrome**
 - » Maintain vigilance for emerging findings associated with congenital Zika virus infection
 - » Transfer to a hospital with subspecialty care is not necessary unless there is an urgent clinical need
 - » No set recommendation to perform thyroid screening

Key Changes from the Previous Guidance – cont.

- **Infants without clinical findings born to mothers with laboratory evidence of possible Zika virus infection**
 - » Comprehensive eye examination by an ophthalmologist in all infants
- **Infants without clinical findings born to mothers without laboratory evidence of possible Zika virus infection**
 - » Testing and clinical evaluation for Zika virus infection beyond a standard evaluation and routine pediatric care are not routinely recommended

Thank you!

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





Zika Expert Forum (August 2017): Comments on Two Topics

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December 13, 2017

Zika Expert Forum

- **August 2017:** CDC in collaboration with the AAP and ACOG hosted a *Forum on the Diagnosis, Evaluation and Management of Zika Virus Infection Among Infants*.

Concurrent Topic Sessions

Enhancing coordination of care for the mother-infant dyad affected by Zika virus

Optimizing health systems for families affected by Zika virus

Updated Infant Guidance



“The follow-up care of infants with findings consistent with congenital Zika syndrome requires a multidisciplinary team and an established medical home to facilitate the coordination of care and ensure that abnormal findings are addressed.”

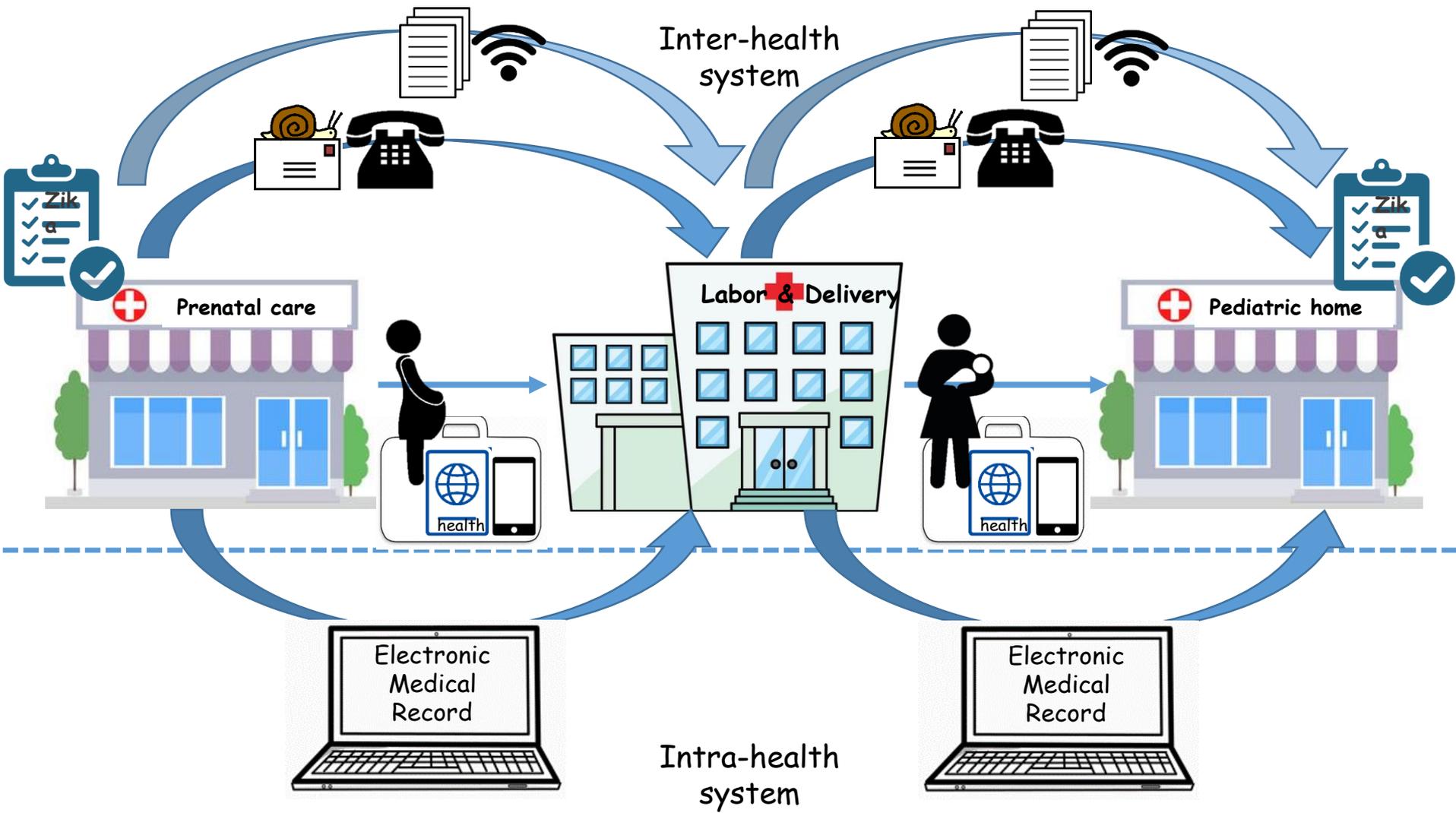
Red Topic Session

- **Focus:** How can obstetric and pediatric/neonatology providers improve communication between maternal and infant providers?
- **Action:** Explored strategies to enhance coordination of care and transfer of health information from obstetrical providers to the pediatrician at the systems-level for infants with Zika virus exposure in utero.



Outcomes

- Model of maternal/infant information sharing
- Potential infant screening tool elements
- Critical elements for Zika information sharing
- List of potential strategies for enhanced coordination



Maternal-Infant Zika Exposure and Testing Card

(Repeated in Spanish)

Please take this card with you when you see you or your child's healthcare provider. It will help make sure you both receive the care you need.

(Repeated in Spanish)

Mother's Information

Name: _____
 Date of birth: _____
 Delivery date or due date: _____

Summary of mother and infant risk for Zika (check if yes):

- Possible maternal prenatal risk factors?
- Mother tested positive or equivocal?
- Baby tested positive or equivocal?

Possible Zika risk factors during pregnancy (check all that apply):

- Rash, fever, or conjunctivitis
- Lived in or frequently traveled to an area with Zika
- Traveled to area with Zika before or during pregnancy
- Had sex without a condom with someone who lives in or traveled to an area with Zika

Locations and dates of travel: _____

Zika Testing during pregnancy (e.g., Urine PCR, Serum PCR, IgM):

Test 1: _____ Date: _____ Test 1: _____ Date: _____ Test 1: _____ Date: _____

Zika PRNT positive? Yes | No Dengue PRNT positive? Yes | No

Overall Zika test interpretation:

- Lab Positive (define) Unknown
- Lab Negative (does not exclude possible Zika)

Mother and Infant Health Care Providers

Provider 1	Provider 2	Provider 3	Provider 4
Name: _____	Name: _____	Name: _____	Name: _____
Facility: _____	Facility: _____	Facility: _____	Facility: _____
Phone: _____	Phone: _____	Phone: _____	Phone: _____

Infant's information

Name: _____ Gestational age at birth: _____
 Date of birth: _____

Date	Age	Head Circumference	Weight	Length

Zika Laboratory Test (e.g., Urine PCR, Serum PCR, IgM):

Test 1: _____ Date: _____ Test 1: _____ Date: _____

Overall Zika test interpretation: _____

Other prenatal Zika Tests (e.g., Ultrasound) and dates:

Hearing exam: _____ Date: _____

Cranial ultrasound: _____ Date: _____

Other postnatal tests (CSF)? _____

Infant symptoms (e.g. seizures, loss eye contact, fussiness?) _____

Does the mother have any concerns about her infant? _____

Child follow-up care recommendations: Recommended at:

	1 mo	3 mo	6 mo	9 mo	12 mo
<input type="checkbox"/> Comprehensive physical exam					
<input type="checkbox"/> Neurologic assessment					
<input type="checkbox"/> Hearing screen					
<input type="checkbox"/> Developmental monitoring					
<input type="checkbox"/> Postnatal head screen					
<input type="checkbox"/> Ophthalmologist assessment					
<input type="checkbox"/> Thyroid Screening					
<input type="checkbox"/> Other: _____					

Notes: _____

Examples of Potential Screening Tools

Yellow Topic Session

- **Focus:** How can systems of care be optimized to support the follow-up needs of infants with congenital Zika exposure?
- **Action:** Discussed and identified strategies that optimize communication between providers caring for an infant with congenital Zika exposure.



Outcomes

- Paradigm/mapping of services
- Potential policy implications

Paradigm/ Mapping of Services



Next Steps



Thank you!

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.



RESOURCES

- AAP Zika Virus Web Page (www.aap.org/zika)
- AAP Key Information for Pediatricians (www.aap.org/zikakey)
- CDC Zika Virus Web Page (<https://www.cdc.gov/zika/index.html>)
- CDC MMWR - Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection — United States, October 2017
(https://www.cdc.gov/mmwr/volumes/66/wr/mm6641a1.htm?s_cid=mm6641a1_w)



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