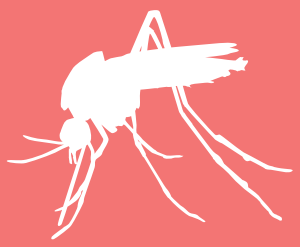
CDC US ZIKA PREGNANCY REGISTRY

HEALTHCARE PROVIDER TOOLKIT FOR HEALTH DEPARTMENTS

FOR OBSTETRICIANS



CENTERS FOR DISEASE CONTROL AND PREVENTION
1600 CLIFTON ROAD
ATLANTA, GEORGIA 30329

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

Welcome

The success of the US Zika Pregnancy Registry (USZPR) depends on the voluntary collaboration of healthcare workers and local health departments to report complete and accurate case information. This toolkit is a suite of tools and resources to help health departments educate and inform healthcare providers to identify, counsel, report, and follow pregnant women and their infants who have tested positive for Zika virus infection. We invite you to use this toolkit to raise awareness about the USZPR and improve reporting and completeness of data collected.

The USZPR was established in collaboration with state, tribal, local, and territorial health departments to collect information about pregnancy and infant outcomes following Zika virus infection during pregnancy. This information will be used to update recommendations for clinical care, to plan for services for pregnant women and families affected by Zika virus, and to improve prevention of Zika virus infection during pregnancy.

We hope you find these materials useful.

If you have any further questions, please email zikapregnancy@cdc.gov.

Using Materials in this Toolkit

This toolkit includes resources to assist obstetricians with **Identification**, **Diagnosis,** and **Reporting** of Zika virus infection in pregnant women. All factsheets and infographics can be printed, shared, and distributed as needed. The following materials are included in this toolkit:

- **Identification:** These materials can assist providers with recognizing potential Zika virus cases.
    - Clinical Guidance*:* CDC updated its interim guidance for US health care providers caring for pregnant women with possible Zika virus exposure, to include the emerging data indicating that Zika virus RNA can be detected for prolonged periods in some pregnant women.
    - Zika Screening Tool: Pregnant women should be asked at each prenatal care appointment if they may have been exposed to Zika. This material can help providers screen their patients and identify if Zika virus testing is indicated.
    - Updated Interim Pregnancy Guidance (Algorithm & Widget): These materials are intended to help healthcare providers apply the updated recommendations for Zika virus testing during clinical practice, assist with interpretation of results, and inform clinical management for a pregnant woman with possible exposure to Zika virus.
- **Diagnosis:** These materials can assist providers with diagnostic testing to determine if a pregnant woman is infected with Zika and provide counseling to women and families.
    - Specimen Collection Factsheets: These resources provide detailed information on what type of specimens to test, how, when and why to test, and storage and shipping instructions.
        - For collection and submission of fetal tissue
        - For collection and submission of specimens at time of birth
    - Pretesting Counseling Materials & Provider Scripts: These materials assist providers to counsel pregnant women about Zika virus testing and what they might expect. Three factsheets apply to different testing scenarios: presenting for care 1) within two weeks of possible exposure, 2) two to twelve weeks after possible exposure, or 3) for those living in area where Zika is spreading.
    - Congenital Zika Syndrome Factsheets for families: These materials can assist providers' conversations with pregnant women if microcephaly or other abnormalities are suspected during pregnancy.
        - If your doctor suspects microcephaly during pregnancy
        - If your baby was born with congenital Zika Syndrome
        - If your baby may have been affected by Zika but has no related health conditions at birth
- **Reporting:** These materials can assist with improved reporting of pregnancy and birth defects data.
    - Registry Factsheets: This resource explains the purpose of the registry, who should be included, and how the information is stored and used.
        - For Obstetricians
        - For pregnant women
- **Additional resources:** Available to guide providers to supplemental information

INTRODUCTION

Dear [Obstetric Healthcare Provider/Practice],

As you know, Zika virus infection during pregnancy can cause microcephaly and other severe brain defects and has been linked to a number of other adverse pregnancy outcomes. The Centers for Disease Control and Prevention (CDC) US Zika Pregnancy Registry seeks to track all pregnancies with laboratory evidence of possible Zika virus infection, whether or not the mother has symptoms.

The goals of the US Zika Pregnancy Registry are to obtain the information CDC needs to estimate the risk of congenital infection among fetuses and infants of pregnant women with possible Zika infection and to identify factors that may influence pregnancy outcomes. This information will be used to update clinical guidance, plan for services for pregnant women and families affected by Zika virus, and improve prevention of Zika virus infection during pregnancy.

Healthcare Providers' Roles

You can help. As your [state, tribal, local, or territorial health department], we may contact your practice to request prenatal and delivery information on a pregnant woman with possible Zika virus infection. We may also contact you to request this information if a neonate is later identified to have possible congenital Zika virus infection. The information we gather and send to CDC represents the minimum necessary to carry out the public health purposes of the US Zika Pregnancy Registry.

Patient Confidentiality

As a healthcare provider, you are considered a covered entity under the Health Insurance Portability and Accountability Act (HIPAA). Under the HIPAA Privacy Rule (45 CFR § 164.501), you may disclose, without prior authorization, protected health information to public health authorities, such as CDC, which are authorized by section 301 of the Public Health Service Act to collect or receive identifiable information for the purpose of preventing or controlling disease. However, per federal standards established in the HIPAA Privacy Rule, people have the right to receive an accounting of disclosures of their protected health information made by a covered entity.

CDC has developed fact sheets that you may wish to give to your patients to let them know how their information is being used: http://www.cdc.gov/zika/hc-providers/registry.html. These fact sheets also contain information on the Assurance of Confidentiality that CDC has obtained. This Assurance is a formal confidentiality protection authorized under Section 308(d) of the Public Service Act that stipulates that CDC cannot be compelled to release protected health information for any reason without authorization from you and your patient. Because of this Assurance, information collected for the US Zika Pregnancy Registry may only be used to better understand Zika virus infection during pregnancy and its outcomes.

Resources

We appreciate your time and attention to this important public health issue. For up-to-date tools and resources, please visit the US Zika Pregnancy Registry Healthcare Provider website, https://www.cdc.gov/zika/reporting/registry.html. This website includes patient checklists, trainings for healthcare providers, clinical guidance, print-ready counseling resources, and other helpful tips.

[**Insert appropriate jurisdiction signature**]

IDENTIFICATION

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

Titilope Oduyebo, MD[1]; Irogue Igbinosa, MD[2]; Emily E. Petersen, MD[1]; Kara N.D. Polen, MPH[2]; Satish K. Pillai, MD[3]; Elizabeth C. Ailes, PhD[2]; Julie M. Villanueva, PhD[3]; Kim Newsome, MPH[2]; Marc Fischer, MD[4]; Priya M. Gupta, MPH[5]; Ann M. Powers, PhD[4]; Margaret Lampe, MPH[6]; Susan Hills, MBBS[4]; Kathryn E. Arnold, MD[2]; Laura E. Rose, MTS[3]; Carrie K. Shapiro-Mendoza, PhD[1]; Charles B. Beard, PhD[4]; Jorge L. Muñoz, PhD[4]; Carol Y. Rao, ScD[7]; Dana Meaney-Delman, MD[8]; Denise J. Jamieson, MD[1]; Margaret A. Honein, PhD[2]

On July 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 pregnant women with possible Zika virus exposure, to include the emerging data indicating that Zika virus RNA can be detected for prolonged periods in some pregnant women. To increase the proportion of pregnant women with Zika virus infection who receive a definitive diagnosis, CDC recommends expanding real-time reverse transcription–polymerase chain reaction (rRT-PCR) testing. Possible exposures to Zika virus include travel to or residence in an area with active Zika virus transmission, or sex* with a partner who has traveled to or resides in an area with active Zika virus transmission without using condoms or other barrier methods to prevent infection.† Testing recommendations for pregnant women with possible Zika virus exposure who report clinical illness consistent with Zika virus disease§ (symptomatic pregnant women) are the same, regardless of their level of exposure (i.e., women with ongoing risk for possible exposure, including residence in or frequent travel to an area with active Zika virus transmission, as well as women living in areas without Zika virus transmission who travel to an area with active Zika virus transmission, or have unprotected sex with a partner who traveled to or resides in an area with active Zika virus transmission). Symptomatic pregnant women who are evaluated <2 weeks after symptom onset should receive serum and urine Zika virus rRT-PCR testing. Symptomatic pregnant women who are evaluated 2–12 weeks after symptom onset should first receive a Zika virus immunoglobulin (IgM) antibody test; if the IgM antibody test result is positive or equivocal, serum and urine rRT-PCR testing should be performed. Testing recommendations for pregnant women with possible Zika virus exposure who do not report clinical illness consistent with Zika virus disease (asymptomatic pregnant women) differ based on the circumstances of possible exposure. For asymptomatic pregnant women who live in areas without active Zika virus transmission and who are evaluated <2 weeks after last possible exposure, rRT-PCR testing should be performed. If the rRT-PCR result is negative, a Zika virus IgM antibody test should be performed 2–12 weeks after the exposure. Asymptomatic pregnant women who do not live in an area with active Zika virus transmission, who are first evaluated 2–12 weeks after their last possible exposure should first receive a Zika virus IgM antibody test; if the IgM antibody test result is positive or equivocal, serum and urine rRT-PCR should be performed. Asymptomatic pregnant women with ongoing risk for exposure to Zika virus should receive Zika virus IgM antibody testing as part of routine obstetric care during the first and second trimesters; immediate rRT-PCR testing should be performed when IgM antibody test results are positive or equivocal. This guidance also provides updated recommendations for the clinical management of pregnant women with confirmed or possible Zika virus infection. These recommendations will be updated when additional data become available.

Introduction

Zika virus continues to spread worldwide, and as of July 21, 2016, 50 countries and territories reported active Zika virus transmission (locations with mosquitoes transmitting Zika virus to persons in the area).¶ Although most persons with Zika virus infection are asymptomatic or have mild clinical disease, infection during pregnancy can cause congenital microcephaly and other brain defects (*1*). Zika virus has also been linked to other adverse pregnancy outcomes, including miscarriage and stillbirth (*1,2*). The U.S. Zika Pregnancy Registry (USZPR)** and the Puerto Rico Zika Active Pregnancy Surveillance System (ZAPPS)†† were established in collaboration with state, tribal, local, and territorial health departments to monitor pregnant women with confirmed or possible Zika virus infection to determine the risk for Zika virus infection during pregnancy and the spectrum of conditions associated with congenital Zika virus infection (*3*). As of July 14, 2016, a total of 400 women in the 50 U.S. states and the District of Columbia, and 378 women in

* Sex is specifically defined as vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys.

† Barrier methods include male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina).

§ Zika virus disease is defined as having at least one of the following signs or symptoms: acute onset of fever, rash, arthralgia, conjunctivitis, and laboratory confirmation of Zika virus infection.

¶ http://www.cdc.gov/zika/geo/active-countries.html.

** http://www.cdc.gov/zika/hc-providers/registry.html.

†† http://www.cdc.gov/zika/public-health-partners/zapss.html.

all U.S. territories (aggregated territories' data from the USZPR and ZAPSS) were determined to have laboratory evidence of confirmed or possible Zika virus infection during pregnancy.[§§]

Data from the USZPR and published case reports indicate that Zika virus RNA can persist in serum of some pregnant women longer than had been previously reported; the longest documented duration of Zika virus RNA detection in serum is 10 weeks after symptom onset (*4–7*). In addition, recent data indicate that Zika virus RNA might be detected in the serum or urine of some asymptomatic pregnant women (*7*). The frequency of this finding is unknown, but the detection of Zika virus RNA in serum or urine provides a definitive diagnosis of Zika virus infection. Preliminary data suggest that plaque reduction neutralization testing (PRNT) might not discriminate between Zika virus and other flavivirus infections, particularly in persons with previous flavivirus exposure (*8*), which complicates interpretation of serologic testing (IgM antibody test and PRNT). Given these challenges, expanded rRT-PCR testing might provide a definitive diagnosis for more pregnant women who are infected with Zika virus.

CDC has revised its interim guidance for U.S. health care providers caring for pregnant women with possible Zika virus exposure. The revised testing recommendations extend the timeframe for rRT-PCR testing of serum and include rRT-PCR testing for some asymptomatic pregnant women. CDC continues to evaluate all available evidence and will update recommendations as new information becomes available.

Updated Recommendations for Evaluating and Testing of Pregnant Women with Possible Zika Virus Exposure

All pregnant women in the United States and U.S. territories should be assessed for possible Zika virus exposure at each prenatal care visit. CDC recommends that pregnant women not travel to an area with active Zika virus transmission (*9*,*10*). Pregnant women who must travel to one of these areas should strictly follow steps to prevent mosquito bites during the trip.[¶¶] In addition, it is recommended that pregnant women with a sex partner who has traveled to or lives in an area with active Zika virus transmission use condoms or other barrier methods to prevent infection or abstain from sex for the duration of the pregnancy (*11*).

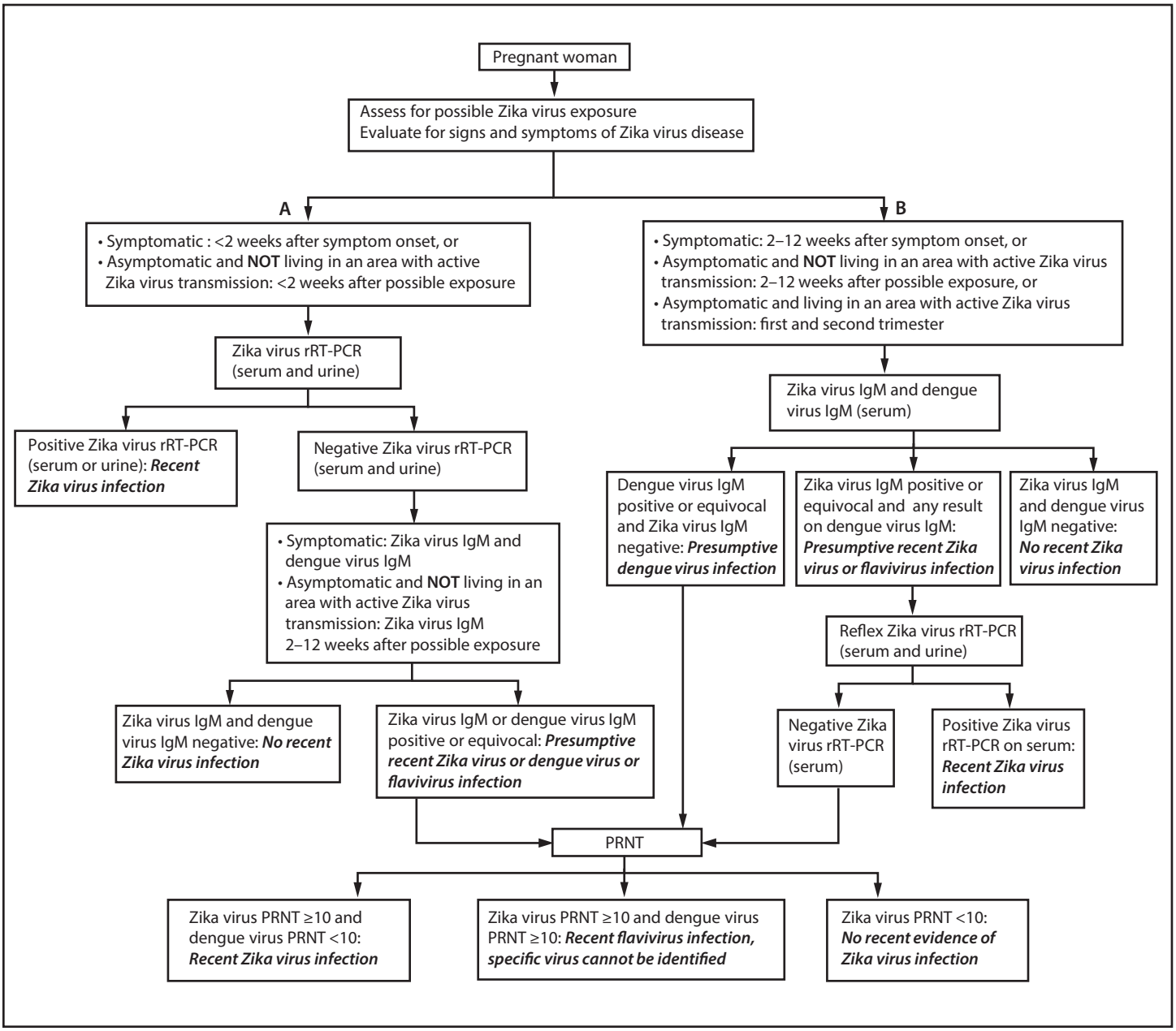
Symptomatic pregnant women. Pregnant women who report signs or symptoms consistent with Zika virus disease (acute onset of fever, rash, arthralgia, conjunctivitis) should be tested for Zika virus infection (Figure). The testing recommendations for symptomatic pregnant women are the same regardless of the circumstances of possible exposure; however, the type of testing recommended varies depending on the time of evaluation relative to symptom onset. Testing of serum and urine by rRT-PCR is recommended for pregnant women who seek care <2 weeks after symptom onset. This recommendation extends the previous recommendation for testing of serum from <1 week after symptom onset to <2 weeks (Figure). A positive rRT-PCR result confirms the diagnosis of recent maternal Zika virus infection. Symptomatic pregnant women with negative rRT-PCR results should receive both Zika virus IgM and dengue virus IgM antibody testing. If Zika virus rRT-PCR testing is requested from laboratories that do not have IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of a negative rRT-PCR result (*12*). If either the Zika virus or dengue virus IgM antibody test yields positive or equivocal results, PRNT should be performed on the same IgM-tested sample or a subsequently collected sample to rule out false-positive results (*8*).

Symptomatic pregnant women who seek care 2–12 weeks after symptom onset should first receive Zika virus and dengue virus IgM antibody testing (Figure). If the Zika virus IgM antibody testing yields positive or equivocal results, reflex rRT-PCR testing should be automatically performed on the same serum sample to determine whether Zika virus RNA is present. A positive rRT-PCR result confirms the diagnosis of recent maternal Zika virus infection. However, if the rRT-PCR result is negative, a positive or equivocal Zika virus IgM antibody test result should be followed by PRNT. Positive or equivocal dengue IgM antibody test results with a negative Zika virus IgM antibody test result should also be confirmed by PRNT. Interpretation of serologic results has been described (*8*).

Asymptomatic pregnant women. Testing recommendations for asymptomatic pregnant women with possible Zika virus exposure differ based on the circumstances of possible exposure (i.e., ongoing versus limited exposure) and the elapsed interval since the last possible Zika virus exposure (Figure). Asymptomatic pregnant women living in areas without active Zika virus transmission who are evaluated <2 weeks after possible Zika virus exposure should be offered serum and urine rRT-PCR testing (Figure). A positive rRT-PCR result confirms the diagnosis of recent maternal Zika virus infection. However, because viral RNA in serum and urine declines over time and depends on multiple factors, asymptomatic pregnant women with a negative rRT-PCR result require additional testing to exclude infection. These women should return 2–12 weeks after possible Zika virus exposure for Zika virus IgM antibody testing. A positive or equivocal IgM antibody test result should be confirmed by PRNT.

[§§] https://www.cdc.gov/zika/geo/pregwomen-uscases.html.
[¶¶] http://wwwnc.cdc.gov/travel/page/avoid-bug-bites.

FIGURE. Updated interim guidance: testing and interpretation recommendations*,†,§,¶ for a pregnant woman with possible exposure to Zika virus — United States (including U.S. territories)**



Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (acute onset of fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported. A pregnant woman is considered asymptomatic if these symptoms are not reported.

† Testing includes Zika virus rRT-PCR on serum and urine samples, Zika virus and dengue virus IgM, and PRNT on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

§ Dengue virus IgM antibody testing is recommended only for symptomatic pregnant women.

¶ If Zika virus rRT-PCR testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of an rRT-PCR negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (http://wwwnc.cdc.gov/travel/notices/), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission.

Asymptomatic pregnant women living in an area without active Zika virus transmission, who seek care 2–12 weeks after possible Zika virus exposure, should be offered Zika virus IgM antibody testing (Figure). If the Zika virus IgM antibody test yields positive or equivocal results, reflex rRT-PCR testing should be performed on the same sample. If the rRT-PCR result is negative, PRNT should be performed.

As recommended in previous guidance (*9,13*), IgM antibody testing is recommended as part of routine obstetric care during the first and second trimesters for asymptomatic pregnant women who have an ongoing risk for Zika virus exposure (i.e., residence in or frequent travel to an area with active Zika virus transmission) (Figure). Reflex rRT-PCR testing is recommended for women who have a positive or equivocal Zika virus IgM antibody test results because rRT-PCR testing provides the potential for a definitive diagnosis of Zika virus infection. Negative rRT-PCR results after a positive or equivocal Zika virus IgM antibody test result should be followed by PRNT. The decision to implement testing of asymptomatic pregnant women with ongoing risk for Zika virus exposure should be made by local health officials based on information about levels of Zika virus transmission and laboratory capacity.

Symptomatic and asymptomatic pregnant women who seek care >12 weeks after symptom onset or possible Zika virus exposure. For symptomatic and asymptomatic pregnant women with possible Zika virus exposure who seek care >12 weeks after symptom onset or possible exposure, IgM antibody testing might be considered. If fetal abnormalities are present, rRT-PCR testing should also be performed on maternal serum and urine. However, a negative IgM antibody test or rRT-PCR result >12 weeks after symptom onset or possible exposure does not rule out recent Zika virus infection because IgM antibody and viral RNA levels decline over time. Given the limitations of testing beyond 12 weeks after symptom onset or possible exposure, serial fetal ultrasounds should be considered.

Updated Recommendations for Prenatal Management of Pregnant Women with Laboratory Evidence of Confirmed or Possible Zika Virus Infection

Laboratory evidence of a confirmed recent Zika virus infection includes 1) detection of Zika virus or Zika virus RNA or antigen in any body fluid or tissue specimen or 2) positive or equivocal Zika virus or dengue virus IgM antibody test results on serum or cerebrospinal fluid with a positive (≥10) PRNT titer for Zika virus together with a negative (<10) PRNT titer for dengue virus (*8*). However, given that serology test results can be difficult to interpret, particularly in persons who were previously infected with or vaccinated against flaviviruses, and because the adverse outcomes caused by Zika virus infection during pregnancy are not fully described, pregnant women with laboratory evidence of recent flavivirus infection are considered to have possible Zika virus infection and should be monitored frequently (Table).

Pregnant women with confirmed or possible Zika virus infection should be managed in accordance with the updated CDC Interim Guidance (Table). In addition, pregnant women with presumptive recent Zika virus or flavivirus infection (i.e., positive or equivocal Zika virus or dengue virus IgM antibody test result that needs to be confirmed by PRNT) should also be managed in accordance with this updated guidance (Table) until final results are available. Serial fetal ultrasounds (every 3–4 weeks) should be considered to assess fetal anatomy, particularly neuroanatomy, and to monitor growth. Ultrasound findings that have been associated with congenital Zika virus syndrome include microcephaly, intracranial calcifications, ventriculomegaly, arthrogryposis, and abnormalities of the corpus callosum, cerebrum, cerebellum, and eyes (*1,14*). Consideration of amniocentesis should be individualized, because data about its usefulness in diagnosing congenital Zika virus infection are limited (*13*). The presence of Zika virus RNA in the amniotic fluid might indicate fetal infection (*5,15*); however, a negative result does not exclude congenital Zika virus infection (*13*). In addition, persistent detection of Zika virus RNA in serum has been reported during pregnancy (*7*). The clinical implications of prolonged detection of Zika virus RNA in serum are not known; however, repeat rRT-PCR testing has been performed in some cases (*5,7*).

Updated Recommendations for Postnatal Management of Pregnant Women with Laboratory Evidence of Confirmed or Possible Zika Virus Infection

Infants born to women with laboratory evidence of confirmed or possible Zika virus infection should be evaluated for congenital Zika virus infection in accordance with CDC interim guidance for health care providers caring for infants with possible Zika virus infection. (*16*). Zika virus testing is recommended for these infants regardless of the presence or absence of phenotypic abnormalities (*14*). Previous published guidance recommended that testing be performed on cord blood or infant serum; however, the use of cord blood to diagnose other congenital viral infections, such as HIV and syphilis, has sometimes yielded inaccurate results (*17–20*). Maternal blood can contaminate cord blood specimens leading to false-positive results, whereas Wharton's jelly in the umbilical cord can yield false-negative results (*19,20*). Cord blood samples

TABLE. Clinical management of a pregnant woman with suspected Zika virus infection

Interpretation of laboratory results*	Prenatal management	Postnatal management
Recent Zika virus infection	Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth.† Decisions regarding amniocentesis should be individualized for each clinical circumstance.§	*Live births:* Cord blood and infant serum should be tested for Zika virus by rRT-PCR, and for Zika IgM and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. Zika virus rRT-PCR and IHC staining of umbilical cord and placenta are recommended.¶ *Fetal losses:* Zika virus rRT-PCR and IHC staining of fetal tissues is recommended.¶
Recent flavivirus infection; specific virus cannot be identified		
Presumptive recent Zika virus infection**	Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth.† Amniocentesis might be considered; decisions should be individualized for each clinical circumstance.	*Live births:* Cord blood and infant serum should be tested for Zika virus by rRT-PCR, and for Zika virus IgM and dengue virus IgM antibodies. If CSF is obtained for other reasons, it can also be tested. Zika virus rRT-PCR and IHC staining of umbilical cord and placenta should be considered.¶ *Fetal losses:* Zika virus rRT-PCR and IHC staining of fetal tissues should be considered.¶
Presumptive recent flavivirus infection**		
Recent dengue virus infection	Clinical management in accordance with existing guidelines.††	
No evidence of Zika virus or dengue virus infection	Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.† *Fetal abnormalities present*: repeat Zika virus rRT-PCR and IgM test; base clinical management on corresponding laboratory results. *Fetal abnormalities absent*: base obstetric care on the ongoing risk for Zika virus exposure risk to the pregnant woman.	

Abbreviations: CSF = cerebrospinal fluid; IgM = immunoglobulin M; IHC = immunohistochemical; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* Refer to the previously published guidance for testing interpretation (http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm).

† Fetal abnormalities consistent with congenital Zika virus syndrome include microcephaly, intracranial calcifications, and brain and eye abnormalities.

§ Health care providers should discuss risks and benefits of amniocentesis with their patients. It is not known how sensitive or specific rRT-PCR testing of amniotic fluid is for congenital Zika virus infection, whether a positive result is predictive of a subsequent fetal abnormality, and if it is predictive, what proportion of infants born after infection will have abnormalities.

¶ Refer to pathology guidance for collection and submission of fetal tissues for Zika virus testing for detailed information on recommended specimen types (http://www.cdc.gov/zika/laboratories/test-specimens-tissues.html).

** rRT-PCR or PRNT should be performed for positive or equivocal IgM results as indicated. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms and areas where other viral illnesses are endemic, evaluate for possible dengue or chikungunya virus infection.

†† http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf.

can also become clotted, which does not allow for appropriate serologic testing. Therefore, although collection and testing of cord blood for Zika virus testing can be performed, these results should be interpreted in conjunction with infant serum results. Pathology evaluation of fetal tissue specimens (e.g., placenta and umbilical cord)*** is another important diagnostic tool to establish the presence of maternal Zika virus infection and can provide a definitive diagnosis for pregnant women with Zika virus infection whose serology results indicate recent unspecified flavivirus infection. In addition, pathology findings might also be helpful in evaluating pregnant women who seek care >12 weeks after symptom onset or possible exposure; Zika virus RNA has been reported to persist in tissue specimens including placenta and fetal brain (*21*). A positive rRT-PCR or immunohistochemical staining on the placenta indicates the presence of maternal infection (*21*).

Pregnant women with laboratory evidence of confirmed or possible Zika virus infection who experience a fetal loss or stillbirth should be offered pathology testing for Zika virus infection; testing includes rRT-PCR and immunohistochemical staining of fixed tissue (*21*). This testing might provide insight into the etiology of the fetal loss, which could inform a woman's future pregnancy planning. Additional information is available at http://www.cdc.gov/zika.

*** http://www.cdc.gov/zika/laboratories/test-specimens-tissues.html.

Acknowledgments

Aron J. Hall, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC; Amy J. Lambert, Ronald M. Rosenberg, Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Diane Morof, Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; Evelyn M. Rodriguez, Division of Global HIV/AIDS and Tuberculosis, Center for Global Health, CDC; Gail Thompson, Toby L. Merlin, Division of Preparedness and Emerging Infections, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Heather J. Menzies, Division Of Global Health Protection, Center for Global Health, CDC; John R. Sims, Division of Congenital and Developmental Disorders, National Center on Birth Defects and Developmental Disabilities, CDC; Angela D. Aina, Karen R. Broder, Division Of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC; Rita M. Traxler, Division Of High-Consequence Pathogens and Pathology, National Center for Emerging and Zoonotic Infectious Diseases, CDC.

[1]Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; [2]Division of Congenital and Developmental Disorders, National Center on Birth Defects and Developmental Disabilities, CDC; [3]Division of Preparedness and Emerging Infections, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [4]Division of Vector-Borne Diseases, National Center for Emerging and Zoonotic Infectious Diseases, CDC; [5]Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion, CDC; [6]Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; [7]Division Of Global Health Protection, Center for Global Health, CDC; [8]Office of the Director, National Center for Emerging and Zoonotic Infectious Diseases, CDC.

Corresponding author: Titilope Oduyebo, 770-488-7100, ZikaMCH@cdc.gov.

References

1. Rasmussen SA, Jamieson DJ, Honein MA, Petersen LR. Zika virus and birth defects—reviewing the evidence for causality. N Engl J Med 2016;374:1981–7. http://dx.doi.org/10.1056/NEJMsr1604338
2. Meaney-Delman D, Rasmussen SA, Staples JE, et al. Zika virus and pregnancy: what obstetric health care providers need to know. Obstet Gynecol 2016;127:642–8. http://dx.doi.org/10.1097/AOG.0000000000001378
3. Simeone RM, Shapiro-Mendoza CK, Meaney-Delman D, et al.; Zika and Pregnancy Working Group. Possible Zika virus infection among pregnant women—United States and Territories, May 2016. MMWR Morb Mortal Wkly Rep 2016;65:514–9. http://dx.doi.org/10.15585/mmwr.mm6520e1
4. Bocanegra C, Sulleiro E, Soriano-Arandes A, et al. Zika virus infection in pregnant women in Barcelona, Spain. Clin Microbiol Infect. In press 2016.
5. Driggers RW, Ho CY, Korhonen EM, et al. Zika virus infection with prolonged maternal viremia and fetal brain abnormalities. N Engl J Med 2016;374:2142–51. http://dx.doi.org/10.1056/NEJMoa1601824
6. Pacheco O, Beltrán M, Nelson CA, et al. Zika virus disease in Colombia—preliminary report. N Engl J Med 2016;NEJMoa1604037. http://dx.doi.org/10.1056/NEJMoa1604037
7. Meaney-Delman D, Oduyebo T, Polen KND, et al. Prolonged detection of Zika virus RNA in pregnant women. Obstet Gynecol In press 2016.
8. Rabe IB, Staples JE, Villanueva J, et al. Interim guidance for interpretation of Zika virus antibody test results. MMWR Morb Mortal Wkly Rep 2016;65:543–6. http://dx.doi.org/10.15585/mmwr.mm6521e1
9. Oduyebo T, Petersen EE, Rasmussen SA, et al. Update: interim guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:122–7. http://dx.doi.org/10.15585/mmwr.mm6505e2
10. Petersen EE, Staples JE, Meaney-Delman D, et al. Interim guidelines for pregnant women during a Zika virus outbreak—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:30–3. http://dx.doi.org/10.15585/mmwr.mm6502e1
11. Oster AM, Russell K, Stryker JE, et al. Update: interim guidance for prevention of sexual transmission of Zika virus—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:323–5. http://dx.doi.org/10.15585/mmwr.mm6512e3
12. CDC. CDC Recommendations for subsequent Zika IgM antibody testing. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. http://emergency.cdc.gov/han/han00392.asp
13. Petersen EE, Polen KN, Meaney-Delman D, et al. Update: interim guidance for health care providers caring for women of reproductive age with possible Zika virus exposure—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:315–22. http://dx.doi.org/10.15585/mmwr.mm6512e2
14. Franca GV, Schuler-Faccini L, Oliveira WK, et al. Congenital Zika virus syndrome in Brazil: a case series of the first 1501 livebirths with complete investigation. Lancet 2016. Epub June 29, 2016. http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)30902-3.pdf
15. Meaney-Delman D, Hills SL, Williams C, et al. Zika Virus infection among U.S. pregnant travelers—August 2015–February 2016. MMWR Morb Mortal Wkly Rep 2016;65:211–4. http://dx.doi.org/10.15585/mmwr.mm6508e1
16. Fleming-Dutra KE, Nelson JM, Fischer M, et al. Update: interim guidelines for health care providers caring for infants and children with possible Zika virus infection—United States, February 2016. MMWR Morb Mortal Wkly Rep 2016;65:182–7. http://dx.doi.org/10.15585/mmwr.mm6507e1
17. Lo YM, Lo ES, Watson N, et al. Two-way cell traffic between mother and fetus: biologic and clinical implications. Blood 1996;88:4390–5.
18. Masuzaki H, Miura K, Miura S, et al. Labor increases maternal DNA contamination in cord blood. Clin Chem 2004;50:1709–11. http://dx.doi.org/10.1373/clinchem.2004.036517
19. Chhabra RS, Brion LP, Castro M, Freundlich L, Glaser JH. Comparison of maternal sera, cord blood, and neonatal sera for detecting presumptive congenital syphilis: relationship with maternal treatment. Pediatrics 1993;91:88–91.
20. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep 2015;64(RR-03).
21. Martines RB, Bhatnagar J, de Oliveira Ramos AM, et al. Pathology of congenital Zika syndrome in Brazil: a case series. Lancet 2016. Epub June 29, 2016. http://thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)30883-2.pdf

CDC's Response to **Zika**

ZIKA SCREENING TOOL FOR PREGNANT WOMEN

(To be administered by nurse, check-in receptionist, or other healthcare provider)

All pregnant women should be assessed for possible Zika virus exposure[1] at each prenatal care visit. Use this tool to evaluate pregnant women for exposure to Zika virus and for signs and symptoms of Zika virus disease to determine whether testing is indicated.

NOTE: If your pregnant patient has questions about Zika testing, educational factsheets are available on CDC's website: http://www.cdc.gov/zika/hc-providers/pregnant-woman.html

Assess for Possible Exposure[1] to Zika Virus Infection

(See references on back for more information.)

Circle response:

Do you live in or do you frequently travel (daily or weekly) to an area with active Zika virus transmission[2]?	**YES** | **NO**
Have you traveled to an area with Zika[2] during pregnancy or just before you became pregnant [8 weeks before conception or 6 weeks before your last menstrual period]?	**YES** | **NO**
Have you had sex (vaginal, anal, or oral sex) without a condom or shared sex toys with a partner(s) who lives in or has traveled to an area with Zika[2]?	**YES** | **NO**

➡ If your pregnant patient answered **"NO"** to ALL questions, she is at low risk for exposure to Zika.

If Pregnant Patient Answered "Yes" to Any Question, Assess for Signs and Symptoms of Zika Virus Disease

Circle response:

Do you currently have or have you had (in the last 12 weeks) fever, rash, joint pain, or conjunctivitis (red eyes)?	**YES** | **NO**

➡ If your pregnant patient answered **"YES"** to having any of these signs or symptoms, she might have symptomatic Zika virus infection. Test in accordance with CDC guidance for symptomatic persons[3].

➡ If your pregnant patient answered **"NO"** to having any signs or symptoms, she has been exposed and might have an asymptomatic Zika virus infection. Test in accordance with CDC guidance for asymptomatic pregnant women[3].

References:

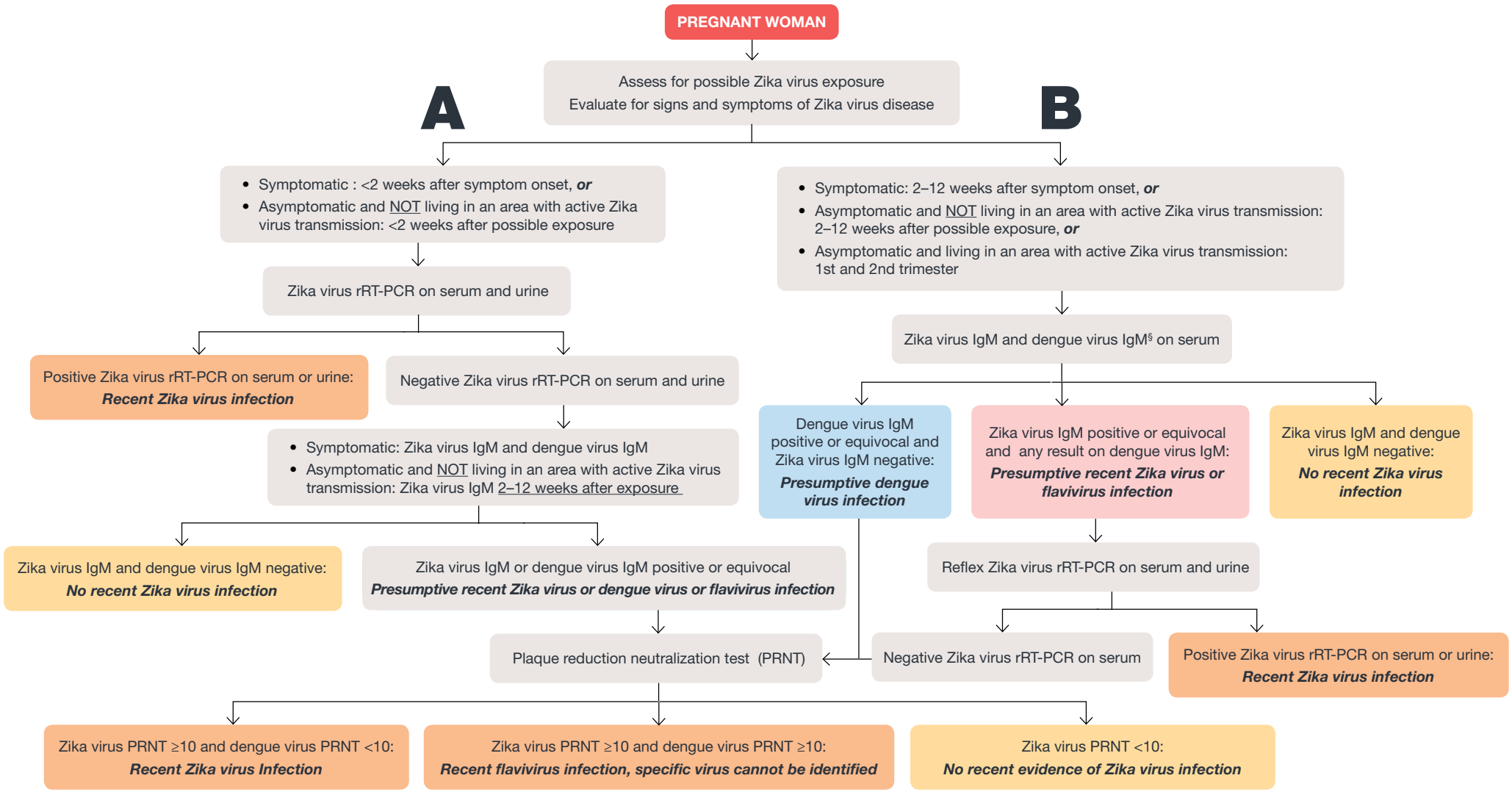
1. Possible exposure to Zika virus that warrants testing includes one or more of the following:
   a. Living in an area with active transmission
   b. Travel to an area with active transmission
   c. Sex (vaginal, anal, and oral sex) without a condom or the sharing of sex toys with a person who traveled to or lives in an area with Zika.
2. Visit CDC's website to see areas with active Zika transmission: http://www.cdc.gov/zika/geo/index.html
3. **Please see the algorithm on the back from CDC's Updated Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure to guide testing and interpretation of results.** (http://www.cdc.gov/mmwr/volumes/65/wr/mm6529e1.htm?s_cid=mm6529e1_e)

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

CS270355A October 4, 2016

CDC's Response to **Zika**

Testing and interpretation recommendations[*,†,§,¶] for a pregnant woman with possible exposure to Zika virus[**] — United States (including U.S. territories)



Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; rRT-PCR = real-time reverse transcription–polymerase chain reaction.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported whereas a pregnant woman is considered asymptomatic if symptoms are NOT reported.

† Testing includes Zika virus rRT-PCR on serum and urine samples, Zika virus and dengue virus Immunoglobulin M (IgM), and plaque reduction neutralization test (PRNT) on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

§ Dengue IgM antibody testing is recommended only for symptomatic pregnant women.

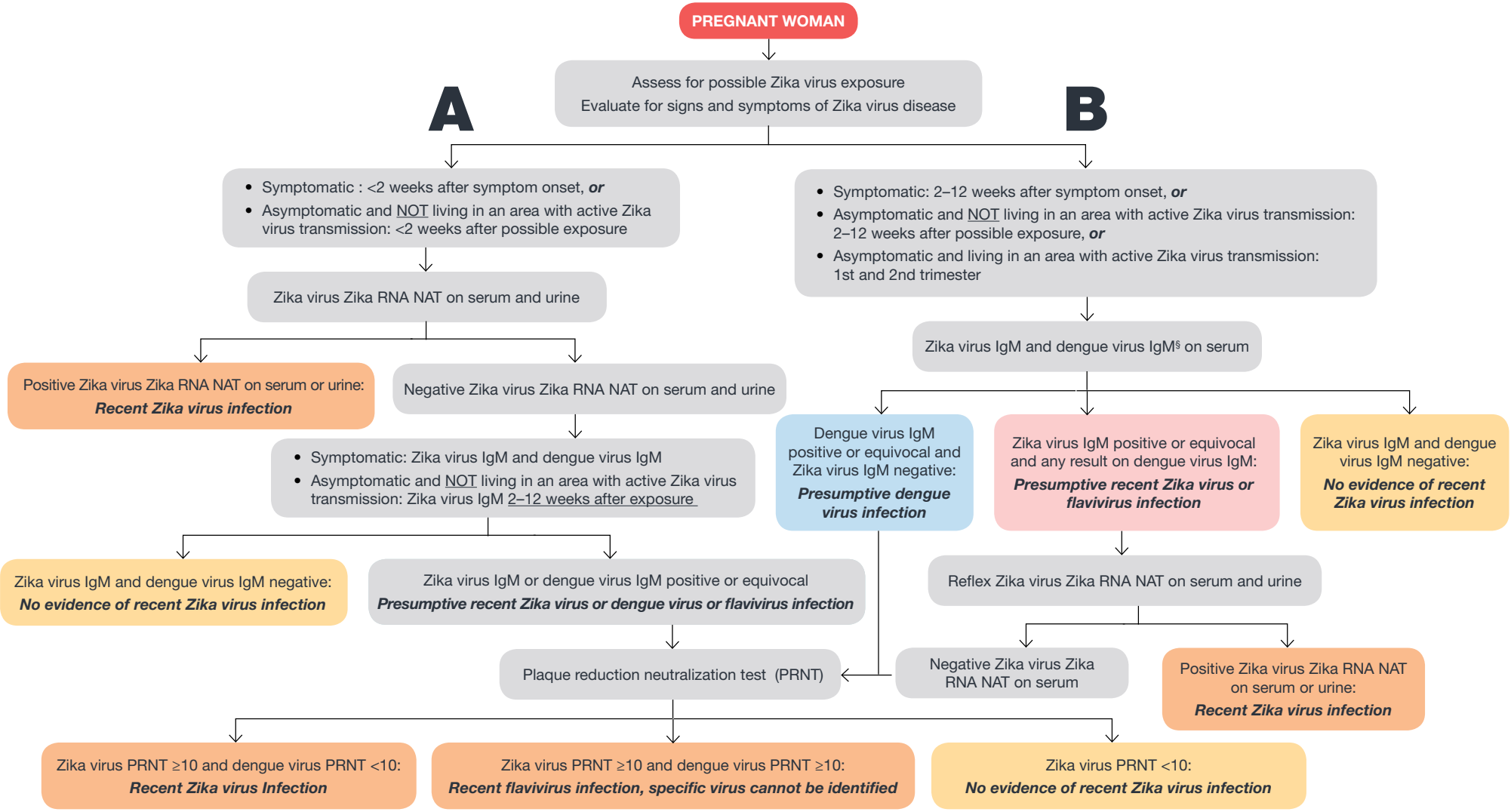
¶ If Zika virus rRT-PCR testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of a rRT-PCR negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (http://wwwnc.cdc.gov/travel/notices/), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission.

CDC's Response to **Zika**

UPDATED INTERIM PREGNANCY GUIDANCE:

Testing and interpretation recommendations[*,†,§,¶] for a pregnant woman with possible exposure to Zika virus[**] — United States (including U.S. territories)



Abbreviations: IgM = immunoglobulin M; PRNT = plaque reduction neutralization test; Zika RNA NAT = nucleic acid test.

* A pregnant woman is considered symptomatic if one or more signs or symptoms (fever, rash, arthralgia, or conjunctivitis) consistent with Zika virus disease is reported whereas a pregnant woman is considered asymptomatic if symptoms are NOT reported.

† Testing includes Zika virus Zika RNA NAT on serum and urine samples, Zika virus and dengue virus Immunoglobulin M (IgM), and plaque reduction neutralization test (PRNT) on serum samples. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/lab-guidance.html). Because of the overlap of symptoms in areas where other viral illness are endemic, evaluate for possible dengue or chikungunya virus infection.

§ Dengue IgM antibody testing is recommended only for symptomatic pregnant women.

¶ If Zika virus Zika RNA NAT testing is requested from laboratories without IgM antibody testing capacity or a process to forward specimens to another testing laboratory, storing of additional serum samples is recommended for IgM antibody testing in the event of a Zika RNA NAT negative result.

** Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission (http://wwwnc.cdc.gov/travel/notices/), or sex (vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), and the sharing of sex toys) without a barrier method to prevent infection (male or female condoms for vaginal or anal sex, male condoms for oral sex (mouth-to-penis), and male condoms cut to create a flat barrier or dental dams for oral sex (mouth-to-vagina) with a partner who traveled to, or lives in an area with active Zika virus transmission.

Clinical management of a pregnant woman with suspected Zika virus infection

Interpretation of Laboratory Results*	Prenatal Management	Postnatal Management
Recent Zika virus infection	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth[†] • Decisions regarding amniocentesis should be individualized for each clinical circumstance[§]	**LIVE BIRTHS:** • Infant serum and infant urine should be tested for Zika virus Zika RNA NAT. Infant serum should be tested for Zika IgM. If CSF is obtained for other reasons, it can also be tested.** • Zika virus Zika RNA NAT and IHC staining of umbilical cord and placenta is recommended.[¶] **FETAL LOSSES:** • Zika virus Zika RNA NAT and IHC staining of fetal tissues is recommended.[¶]
Recent flavivirus infection; specific virus cannot be identified		
Presumptive recent Zika virus infection* **	• Consider serial ultrasounds every 3–4 weeks to assess fetal anatomy and growth[†] • Amniocentesis might be considered; decision should be individualized for each clinical circumstance[§]	**LIVE BIRTHS:** • Infant serum and infant urine should be tested for Zika virus Zika RNA NAT. Infant serum should be tested for Zika IgM. If CSF is obtained for other reasons, it can also be tested. ** • Zika virus Zika RNA NAT and IHC staining of umbilical cord and placenta should be considered.[¶] **FETAL LOSSES:** • Zika virus Zika RNA NAT and IHC staining of fetal tissues should be considered.[¶]
Presumptive recent flavivirus infection* **		
Recent dengue virus infection	• Clinical management in accordance with existing guidelines (http://apps.who.int/iris/bitstream/10665/44188/1/9789241547871_eng.pdf).	
No evidence of Zika virus or dengue virus infection	• Prenatal ultrasound to evaluate for fetal abnormalities consistent with congenital Zika virus syndrome.[†] ◆ Fetal abnormalities present: repeat Zika virus Zika RNA NAT and IgM test; base clinical management on corresponding laboratory results. ◆ Fetal abnormalities absent: base obstetric care on the ongoing risk of Zika virus exposure to the pregnant woman.	

Abbreviations: CSF = cerebrospinal fluid; IgM = immunoglobulin M; IHC = immunohistochemical; PRNT = plaque reduction neutralization test; Zika RNA NAT = nucleic acid test.

* Refer to the previously published guidance for testing interpretation (http://www.cdc.gov/mmwr/volumes/65/wr/mm6521e1.htm).

† Fetal abnormalities consistent with congenital Zika virus syndrome include microcephaly, intracranial calcifications, ventriculomegaly, arthrogryposis, and abnormalities of the corpus callosum, cerebrum, cerebellum, and eyes.

§ Health care providers should discuss risks and benefits of amniocentesis with their patients. It is not known how sensitive or specific Zika RNA NAT testing of amniotic fluid is for congenital Zika virus infection, whether a positive result is predictive of a subsequent fetal abnormality, and if it is predictive, what proportion of infants born after infection will have abnormalities.

¶ Refer to pathology guidance for collection and submission of fetal tissues for Zika virus testing for detailed information on recommended specimen types (http://www.cdc.gov/zika/laboratories/test-specimens-tissues.html).

** Refer to the previously published guidance for evaluation and management of infants with possible congenital Zika virus infection (http://www.cdc.gov/mmwr/volumes/65/wr/mm6533e2.htm?s_cid=mmv6533e2_w)

*** Zika RNA NAT or PRNT should be performed for positive or equivocal IgM results as indicated. PRNT results that indicate recent flavivirus infection should be interpreted in the context of the currently circulating flaviviruses. Refer to the laboratory guidance for updated testing recommendations (http://www.cdc.gov/zika/laboratories/ lab-guidance.html). Because of the overlap of symptoms and areas where other viral illnesses are endemic, evaluate for possible dengue or chikungunya virus infection.

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

CS267383A December 15, 2016

DIAGNOSIS

CDC's Response to **Zika**

ZIKA VIRUS: COLLECTION AND SUBMISSION OF FETAL TISSUES FOR ZIKA VIRUS TESTING

General Information

The following information applies to fetal tissue collection and submission. For cord blood and amniotic fluid analysis, please see CDC's web page on testing body fluid specimens.

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

- **Healthcare Providers:** Please make sure that your state, territorial, tribal, or local health department has been notified and has received pre-approval from CDC for submission and shipment of specimens before they are collected and sent.
  - » **Institutions with surgical pathology available:** Please consult surgical pathology regarding appropriate collection and processing of specimens for Zika virus testing.
  - » **Institutions without surgical pathology available:** Please see table below for general guide on collection of tissue specimens for Zika virus testing.
  - » **Specimens should ONLY be sent to CDC from health departments.**
- **Health Departments:** Pre-approval is required prior to the submission of specimens to CDC. Information required for the pre-approval process includes:
  - » Maternal/neonatal state and specimen identification numbers, maternal age, Zika virus test results, travel locations and dates, illness onset (if applicable), estimated date of delivery, gestational age at delivery, pregnancy outcome, age and sex of infant, birth anthropometric measurements, any additional testing/imaging.
  - » Please specify cases that have been reported to the US Zika Pregnancy Registry and for which this information has already been provided during the pre-approval process.
- **Please Note:** CDC Form 50.34 is required to be submitted with all specimens. Please write "Zika virus" in test order name after it is printed as this is not yet an option on the drop drown menu.
  - » Select Test Order CDC-10371 for infant deaths (pathologic evaluation of infant death due to infection)
  - » Select Test Order CDC-10372 for pregnancy losses (pathologic evaluation of illness due to infection)

Collection of Fetal or Neonatal Tissues

- Appropriate consent from the parents or guardian must be obtained by the healthcare provider prior to collection and submission of specimens for Zika virus testing.
- To optimize evaluation of possible Zika virus infection in fetal tissues, send fixed tissues. Submission of frozen tissues may be considered on a case by case basis, please email pathology@cdc.gov and ZIKA_EPI_ADB@cdc.gov for consultation.

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

CS268552A August 5, 2016

- The type of tissues available for evaluation will depend on the gestational age of the fetus and the collection procedure that is performed. Effort should be made to maintain the tissue architecture, and to minimize any dissection or disruption of the tissues.
- For situations in which individual organs or tissue types cannot be identified, please provide any available tissue with minimal disruption.
- CDC Infectious Diseases Pathology Branch (IDPB) accepts microscopic or gross photos from health departments as part of either telediagnosis consultation or routine tissue specimen submission for diagnostic evaluation. Photos should not contain patient names or medical record numbers. Visit the CDC ePathology telediagnosis (http://www.cdc.gov/ncezid/dhcpp/idpb/epathology/index.html) page for more details.
- Staff who collect and handle specimens should refer to Zika biosafety guidelines for laboratory and pathology procedures www.cdc.gov/zika/state-labs/biosafety-guidance.html.

Specimen Type	Fixed Specimens	When to Consider	General Notes
Products of conception (POC)	• 4 or more specimens	Generally less than 12wks gestational age	For early pregnancy loss/ miscarriage, please send POCs fixed in formalin.
Placenta and fetal membranes	• Several full thickness pieces including at least 3 full thickness pieces (0.5–1 cm x 3–4 cm in depth) from middle third of placental disk and at least 1 from the placental disk margin • One 5 x 12 cm strip of fetal membranes	Any gestation for which placenta is available	Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible. Please include information about placenta weight and sample both maternal and fetal side of the placenta. Label all specimens to identify location of sample.
Umbilical cord	• 2.5 cm segments of cord • 4 or more specimens	Any gestation for which placenta is available	Umbilical cord segments should be obtained proximal, middle, and distal to umbilical cord insertion site on the placenta. Label all specimens to identify location of sample.
Brain and spinal cord	• 0.5–1.0 cm3 each • 5 or more specimens from different parts of brain and spinal cord	Fetal demise	It is critical to maintain the tissue architecture to evaluate viral pathology. Certain fetal tissues require longer fixation, please fix brain specimens for 48-72 hours.
Solid organ (heart, lung, liver, kidneys, skeletal muscle, eyes, bone marrow)	• 0.5-1.0 cm3 each • 1 representative specimen from each solid organ	Fetal demise	Submission of eyes is highly recommended.

Fixed Tissues

- Histopathology, immunohistochemical staining, and reverse transcription-polymerase chain reaction (RT-PCR) will be performed on fixed tissues, as needed. Fixed tissues may include formalin fixed and/or paraffin embedded tissues.
- The volume of formalin used to fix tissues should be 10x the volume of tissue. Place tissue in 10% buffered formalin for a minimum of three days or until fully fixed. After fixation, tissue can be transferred to 70% ethanol for long term storage.
- If stored prior to shipping, please transfer fixed tissues to 70% ethanol after 72 hours.
- Fixed tissues should be stored and shipped at room temperature. Additional instructions for collecting, handling, and shipping formalin-fixed tissues are also available. Paraffin blocks should be submitted in accordance with these instructions for formalin-fixed specimens.
- DO NOT FREEZE samples that have been fixed in formalin.

Submission and Shipping of Specimens

- [CDC Form 50.34] is required with all specimen submissions and specimens should ONLY be sent to CDC directly from health departments. Please see introduction above for further details.
- Fixed specimens can be shipped at ambient temperature to:
  Infectious Diseases Pathology Branch
  Centers for Disease Control and Prevention
  1600 Clifton Rd. NE, MS G-32
  Atlanta GA 30329-4027
- More information on shipping can be found here: http://www.cdc.gov/ncezid/dhcpp/idpb/specimen-submission/cns.html.

Reporting of Results

- Test results will be reported to the state health department and the submitting healthcare provider.
- Turnaround time will vary, depending on testing volume.
- Considerations for interpreting pathology results include maternal/infant epidemiologic risk factors, maternal/infant Zika testing results, and clinical presentation. For assistance with interpretation of pathology reports results please contact pathology@cdc.gov.

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 virus test results.

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.

Healthcare Providers:

- Please contact your state, tribal, local, or territorial health department to facilitate laboratory testing and pathology specimen submission.
  - » If available in your hospital/institution, please consult surgical pathology to ensure appropriate collection and processing of tissue specimens for Zika 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; or email zikapregnancy@cdc.gov) 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 questions regarding specimen submission.

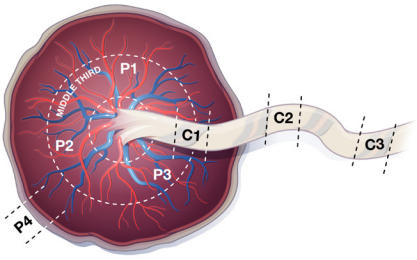


Figure: Collecting placental specimen

Health Departments:

- 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 eocevent189@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.

Reporting of Results:

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

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

Specimen Type	General Instructions	Notes	Storage	Shipping
Infant serum	At least 1.0 ml Transfer serum to a plastic tube measuring approximately 50 mm tall and 15 mm in diameter (e.g., 1.8 mL cryotube or 2.0 mL microtube) with screw cap and secure with thermoplastic, self-sealing lab film.	For antibody and rRT-PCR testing, specimens should be kept cold (2–6 °C) or frozen (-70 °C). For virus isolation testing, specimens should be frozen as soon as possible (-70 °C).	For cold specimens, the sample should be placed in an insulated container with adequate ice packs to ensure specimen ("cold chain") integrity. For frozen specimens, ship the sample on enough dry ice to ensure specimens remain frozen until received.	Arboviral Diseases Branch Diagnostic Laboratory Centers for Disease Control and Prevention 3156 Rampart Road Fort Collins, Colorado 80521 More information about collecting, handling, and shipping is available here.
Placenta and fetal membranes	Several full thickness pieces including at least 3 full thickness pieces (0.5–1 cm x 3–4 cm in depth) from middle third of placental disk and at least 1 from the placental disk margin 5 x 12 cm strip of fetal membranes Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible. *(Please reference the figure on page one.)*	Please include information about placenta weight and sample both maternal and fetal side of the placenta. Label all specimens to identify location of sample.	Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days. Once fully fixed the tissue can be transferred to 70% ethanol for long term storage. Storage and shipping at room temperature.	Infectious Diseases Pathology Branch Centers for Disease Control and Prevention 1600 Clifton Rd. NE, MS G-32 Atlanta GA 30329-4027 More instructions can be found here.
Umbilical cord	2.5 cm segments of cord 4 or more specimens	Umbilical cord segments should be obtained proximal, middle, and distal to umbilical cord insertion site on the placenta. Label all specimens to identify location of sample.	Fix specimens in formalin Volume of formalin used should be about 10x mass of tissue. Place in 10% neutral buffered formalin for a minimum of 3 days. Once fully fixed the tissue can be transferred to 70% ethanol for long term storage. Storage and shipping at room temperature.	Infectious Diseases Pathology Branch Centers for Disease Control and Prevention 1600 Clifton Rd. NE, MS G-32 Atlanta GA 30329-4027 More instructions can be found here.
Infant urine	Provide 0.5–1.0 mL of the specimen in a sterile screw capped vial secured with a small piece of thermoplastic, self-sealing lab film. Please ensure a tight seal as leaking specimens cannot be accepted.	Sterile specimen is not required	For rRT-PCR testing, specimens should be kept cold (2–8 °C) or frozen (-≤ 20 °C) for storage and shipping. For frozen specimens, ship the sample on enough dry ice to ensure specimens remain frozen until received.	Arboviral Diseases Branch Diagnostic Laboratory Centers for Disease Control and Prevention 3156 Rampart Road Fort Collins, Colorado 80521 Get more information about collecting, handling, and shipping.

CDC's Response to **Zika**

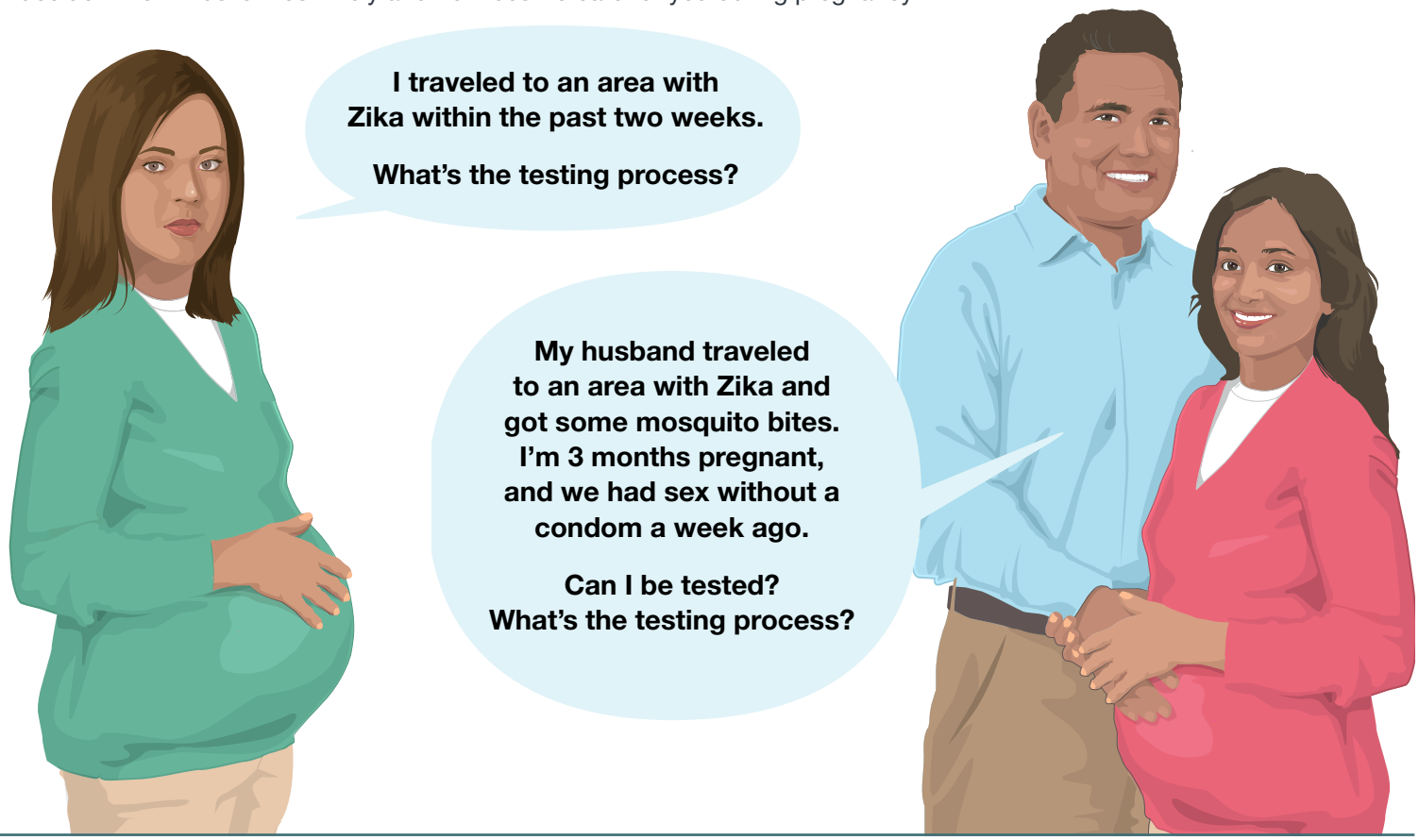
WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING

For Pregnant Women Who May Have Been Exposed to Zika within the Past Two Weeks

If you or your sex partner live in or recently traveled to an area with Zika, you may have been exposed to Zika. You may have questions about Zika and how to find out if you've been infected. Keep reading to learn more about what you might expect if you have Zika virus during pregnancy.

Zika testing is complex

- **You may need more than one Zika test:** You may find out if you have Zika after one test. However, finding out if you have Zika can require up to three different tests, because the result of one test may require more testing to find out if you recently had a Zika virus infection. You may wait different amounts of time for results of each test to come back.
- **Understanding test results can be challenging:** Zika virus is similar to other viruses that are carried by mosquitoes. Testing for Zika may also detect these other mosquito-borne viruses. Sometimes even after testing, we may not know which type of virus you were infected with. Each test result is important, because it helps your doctor or other provider decide which virus is most likely and how best to care for you during pregnancy.



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

CS272943 December20,2016

Testing Process

Testing is recommended for pregnant women who may have been exposed to Zika, even if they haven't had symptoms. You may have been exposed if you traveled to an area with Zika or had sex without a condom with a partner who lived in or traveled to an area with Zika. Whether or not you had symptoms (fever, rash, joint pain, or red eyes) within the past two weeks, the steps for testing are the same.

Step One

Your doctor or other provider will start by ordering a test that looks for Zika genetic material, called RNA, which can be in blood and urine.

- A positive result means that you have Zika.
- A negative result means another test is needed. A negative test may mean that you had Zika, but your body cleared the virus from your system.

Step Two

If you tested negative for Zika RNA, your doctor or other provider will order a test to look for antibodies, which the body makes to fight infections. This test should occur 2-12 weeks after you may have been exposed, because these antibodies are usually in your body for 2-12 weeks after infection.

- If you were tested in this 2-12 week window and your antibody test is negative, it means there is no evidence you were recently infected with Zika.
- If your antibody test is positive, more testing is needed to be sure. The antibody test (step 2 test) can sometimes show results that are positive even when a person isn't actually infected. For example, the test might detect antibodies to a similar mosquito-borne infection, such as dengue.

Step Three

If your antibody test was positive, a third test is needed to confirm the antibodies are for Zika. This test takes the longest for results. Your doctor or other provider will work with your state or local health department to interpret your test results.

At any time during the testing process, if your doctor doesn't have a sample of your blood or urine, you may have to give another sample.

Testing Results

Positive test results

Testing positive for Zika during pregnancy lets your doctor or other provider know to watch your pregnancy more closely. This means you might have more ultrasounds or other tests to check the growth and development of your fetus and check for Zika infection.

Inconclusive (not positive or negative) test results

Sometimes, if the tests aren't clearly positive or negative, the results are considered "inconclusive," meaning we're not sure if you had the virus. If the test results are inconclusive, your doctor or other provider may choose to follow the CDC recommendations for a positive test result, meaning he or she might do more ultrasounds or other tests to monitor the pregnancy.

Negative test results

Your doctor or other provider may check the growth and development of your fetus during an ultrasound and check for any signs of Zika virus infection. If there are no signs of Zika virus infection, you will get routine prenatal care, which is what CDC recommends. If your doctor or other provider sees signs of Zika virus infection during an ultrasound, then you may need additional tests.

PRETESTING COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

For Pregnant Women with Possible Exposure to Zika or Symptom Onset within the Past Two Weeks

This guide describes recommendations for conducting pretesting counseling for pregnant women if they or their sex partner live in or recently traveled to an area with active Zika transmission. CDC recommends testing for pregnant women who may have been exposed to Zika, whether or not they have symptoms. This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy to understand information, avoiding technical terms, and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation	Sample Script
Provide the patient with information on the complexity of Zika testing.	Use one or both of the two following sentences to begin the discussion depending on the clinical scenario: 1) You may be at risk of having Zika since you or your sex partner recently traveled to (replace "recently traveled to" with "live in" as appropriate) an area where Zika virus is spreading by mosquitoes within the past two weeks. (For those without symptoms: You could be at risk even if you or your partner do not have symptoms). OR/AND 2) You may be at risk of having Zika because within the past two weeks you had sex without a condom with a person who traveled to (replace "traveled to" with "lives in" as appropriate) a Zika affected area. (For those without symptoms: You could be at risk even if you or your partner do not have symptoms). Based on what you've told me, I think it is best to move forward with testing you for Zika. Before we begin, I would like to provide you with some helpful information on what to expect throughout this process.
Patients should be informed that more than one Zika test may be required before a final result is determined.	You may only need one test to find out whether you have Zika. However, you may need up to three different tests before we can find out whether you have Zika or not because the result of one test may not tell us the whole story, and you may need to get additional tests to find out if you recently got Zika. We want to be sure we take all of the necessary steps to make sure your results are accurate. Each test can take different amounts of time to receive results, which I know can be frustrating. As your healthcare provider I am here to answer any questions you may have. • Reassure the patient that this method of testing is normal. • Consider providing the fact sheet "What You Should Know about Zika Virus Testing for Pregnant Women Who May Have Been Exposed to Zika within the Past Two Weeks."
Patients should be informed that it can be challenging to understand test results	It can be hard to understand Zika test results for a number of reasons. Mosquitoes can carry many viruses, like dengue virus, which is very similar to Zika. So if someone has been infected with these other viruses in the past, it may be difficult to know which virus you have been infected with. It is possible that the test will: 1) detect signs that your body cleared one of these viruses, other than Zika, from your system, 2) detect signs that your body recently cleared Zika virus from your system, or 3) detect that you currently have Zika. Therefore, we may need to do additional testing to figure out whether you actually had or have Zika. Once I know which virus is most likely the cause I will know how best to care for you during your pregnancy. • Ask the patient if she has any questions before you move forward with providing information on the testing process.

Recommendation	Sample Script
Discuss each step of the testing process with the patient	There could potentially be up to three steps of testing before I can determine whether you have Zika or not.
Step one- Let the patient know that you will be ordering a test to look for antibodies. Define this term as it may be unfamiliar and inform the patient of what to expect next.	I am going to start step one of the testing process by ordering a test for the genetic material of Zika, known as RNA. This material from the virus can be found in blood and urine. If your Zika RNA test comes back with a positive result, it means that you have Zika. If this test comes back negative, it is still not be certain that you were not infected with Zika. It may mean that you had Zika but your body cleared the virus from your system. It could also mean that you had an infection with a virus similar to Zika like dengue virus. We want to be sure whether or not you have Zika so we can give you proper treatment during your pregnancy. We will need to do one more round of testing to figure out whether or not you actually have or recently had Zika. • Ask the patient if they have any questions before you move forward with providing information on step two of testing.
Step two- If the patient requires further testing, inform the patient that positive antibody test results will require further testing and provide them with information on what to possibly expect next.	If you test negative for Zika RNA, I will order a second test to look for evidence that your body fought off a recent Zika infection. This test looks for antibodies, which are proteins that your body makes usually 2–12 weeks after an infection. If your antibody test comes back with a negative result, that means you were not recently infected with Zika, and we will continue our original plan of care for your pregnancy. If your antibody test comes back positive, I will need to do more testing to determine whether you have or recently had Zika. The antibody test may be positive even when a person isn't actually infected with Zika for many reasons. It could be because the test may be detecting antibodies to another virus that is similar to Zika, like dengue virus or West Nile virus. • Ask the patient if they have any questions before you move forward with providing information on step three of testing.
Step three- If the patient requires further testing after the Zika RNA test, inform patients that further testing will be needed if they test negative for Zika RNA.	If your second test for antibodies was positive, I will need to order a third test to confirm whether the antibodies are for Zika or a similar virus. This test takes the longest to receive results because I will have to send the results to a specialized lab and then work with the state or local health department to interpret the results. • Ask the patient if they have any questions on what to expect during each step of the testing process.
Inform patients of each what each test result could mean for their pregnancy.	Now we'll go over what each test result could mean for your pregnancy.
If Zika test results are positive.	If you test positive for Zika, I will need to watch your pregnancy more closely. I may do more ultrasounds or other tests to check for your fetus's growth and development.
If Zika test results are inconclusive.	Sometimes test results will not come back as a clear negative or positive. When this happens the results are considered "inconclusive". If this happens, I'd rather be more cautious and still do more ultrasounds and other tests to closely monitor your pregnancy.
If Zika test results are negative.	If your test results are negative, I will do an ultrasound to check the growth and development of your baby and check for any signs of Zika virus infection. If I see any signs of Zika during the ultrasound, then I may order additional tests. If there are no signs of Zika, we will continue with routine prenatal care.

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

CDC's Response to **Zika**

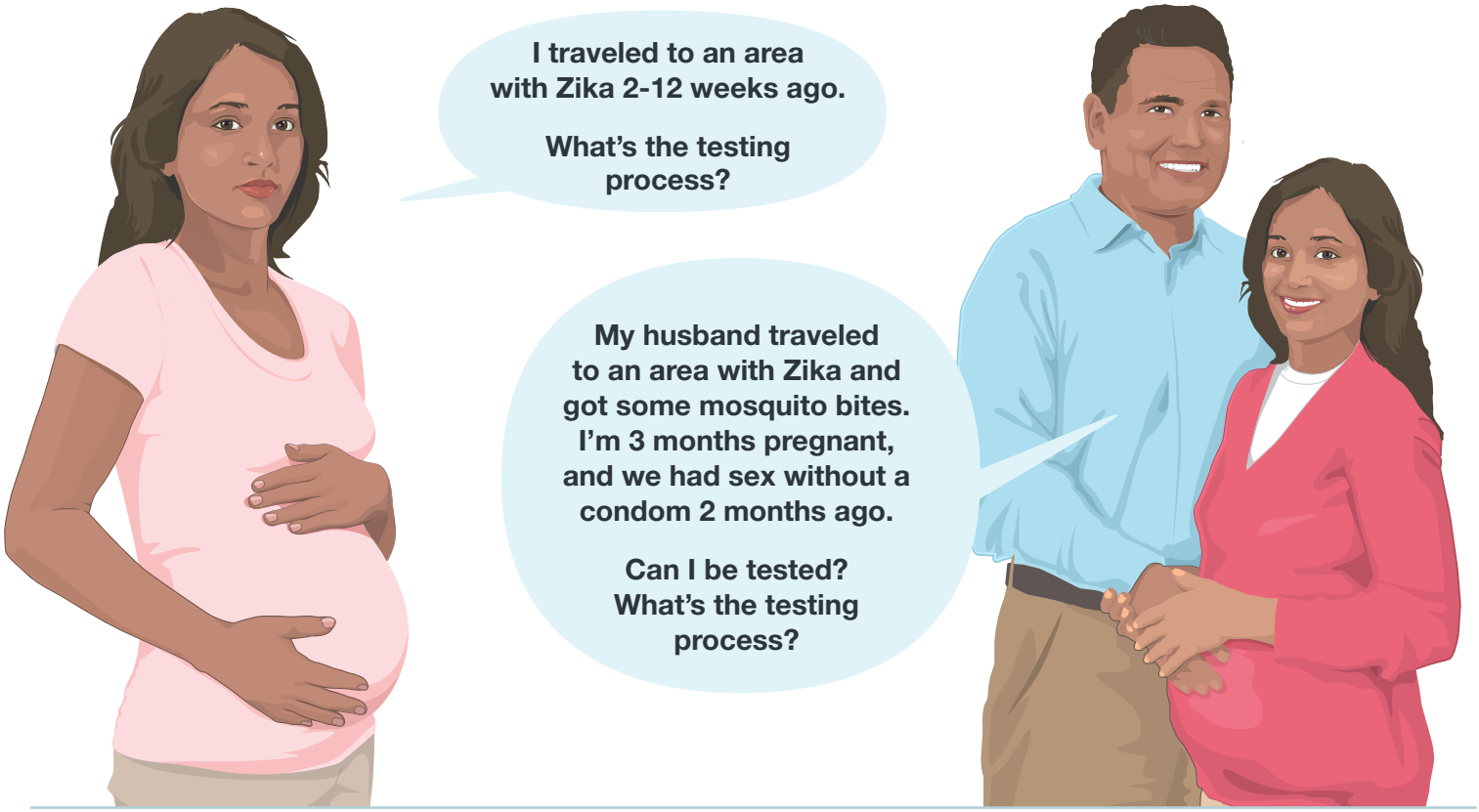
WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING

For Pregnant Women Who May Have Been Exposed to Zika 2-12 Weeks Ago

If you or your sex partner live in or recently traveled to an area with Zika, you may have been exposed to Zika. You may have questions about Zika and how to find out if you've been infected. Learn more about Zika virus testing for pregnant women and what you might expect if you have Zika virus during pregnancy.

Zika testing is complex

- **You may need more than one Zika test:** You may find out if you have Zika after one test. However, finding out if you have Zika can require up to three different tests, because the result of one test may require more testing to find out if you recently had a Zika virus infection. You may wait different amounts of time for results of each test to come back.
- **Understanding test results can be challenging:** Zika virus is similar to other viruses that are carried by mosquitoes. Testing for Zika may also detect these other mosquito-borne viruses. Sometimes even after testing, we may not know which type of virus you were infected with. Each test result is important, because it helps your doctor or other provider decide which virus is most likely and how best to care for you during pregnancy.



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

CS272943 December20,2016

Testing Process

Testing is recommended for pregnant women who may have been exposed to Zika, even if they haven't had symptoms. You may have been exposed if you traveled to an area with Zika or had sex without a condom with a partner who lived in or traveled to an area with Zika. Whether or not you had symptoms (fever, rash, joint pain, or red eyes) within the past 2-12 weeks after possible exposure, the steps for testing are the same.

Step One

Your doctor will start by ordering a test to look for antibodies, which the body makes to fight infections. These antibodies are usually in your body for 2-12 weeks after infection.

- If you were tested in this 2-12 week window and your antibody test is negative, it means there is no evidence you were recently infected with Zika.
- If your antibody test is positive, more testing is needed to be sure. The antibody test (step 1 test) can sometimes show results that are positive even when a person isn't actually infected. For example, the test might detect antibodies to a similar mosquito-borne infection, such as dengue.

Step Two

If your antibody test was positive, your doctor or other provider will order a test that looks for Zika genetic material, called RNA, which can be in blood and urine.

- A positive result means that you have Zika.
- A negative result means another test is needed. A negative test may mean that you had Zika, but your body cleared the virus from your system, or your antibody test was positive because you had an infection similar to Zika.

Step Three

If you tested negative for Zika RNA, a third test is needed to confirm the antibodies from Step 1 are for Zika. This test takes the longest for results. Your doctor or other provider will work with your state or local health department to interpret your test results.

At any time during the testing process, if your doctor doesn't have a sample of your blood or urine, you may have to give another sample.

Testing Results

Positive test results

Testing positive for Zika during pregnancy lets your doctor or other provider know to watch your pregnancy more closely. This means you might have more ultrasounds or other tests to check the growth and development of your fetus and check for Zika infection.

Inconclusive (not positive or negative) test results

Sometimes, if the tests aren't clearly positive or negative, the results are considered "inconclusive," meaning we're not sure if you had the virus. If the test results are inconclusive, your doctor or other provider may choose to follow the CDC recommendations for a positive test result, meaning he or she might do more ultrasounds or other tests to monitor the pregnancy.

Negative test results

Your doctor or other provider may check the growth and development of your fetus during an ultrasound and check for any signs of Zika virus infection. If there are no signs of Zika virus infection, you will get routine prenatal care, which is what CDC recommends. If your doctor or other provider sees signs of Zika virus infection during an ultrasound, then you may need additional tests.

PRETESTING COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

For Pregnant Women with Possible Exposure to Zika or Symptom Onset 2-12 Weeks Ago

This guide describes recommendations for conducting pretesting counseling for pregnant women if they or their sex partner live in or have recently traveled to an area with active Zika transmission. CDC recommends testing for pregnant women who may have been exposed to Zika, whether or not they have symptoms. This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy to understand information, avoiding technical terms, and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation	Sample Script
Provide the patient with information on the complexity of Zika testing.	Use one or both of the two following sentences to begin the discussion depending on the clinical scenario: 1) You may be at risk of having Zika since you or your sex partner recently traveled to (replace "recently traveled to" with "live in" as appropriate) an area where Zika virus is spreading by mosquitoes more than two weeks ago. (For those without symptoms: You could be at risk even if you or your partner do not have symptoms). OR/AND 2) You may be at risk of having Zika because within the past 2–12 weeks you had sex without a condom with a person who traveled to (replace "traveled to" with "lives in" as appropriate) a Zika affected area. (For those without symptoms: You could be at risk even if you or your partner do not have symptoms). Based on what you've told me, I think it is best to move forward with testing you for Zika. Before we begin, I would like to provide you with some helpful information on what to expect throughout this process.
Patients should be informed that more than one Zika test may be required before a final result is determined.	You may only need one test to find out whether you have Zika. However, you may need up to three different tests before we can find out whether you have Zika or not because the result of one test may not tell us the whole story, and you may need to get additional tests to find out if you recently had a Zika virus infection. We want to be sure we take all of the necessary steps to make sure your results are accurate. Each test can take different amounts of time to receive results. I know this can be frustrating, but as your healthcare provider I am here to answer any questions you may have. • Reassure the patient that this method of testing is normal. • Consider providing the fact sheet "What You Should Know about Zika Virus Testing for Pregnant Women Who May Have Been Exposed to Zika 2-12 Weeks Ago."
Patients should be informed that it can be challenging to understand test results	It can be hard to understand Zika test results for a number of reasons. Mosquitoes can carry many viruses, like dengue virus, which is very similar to Zika. So if someone has been infected with these other viruses in the past, it may be difficult to know which virus you have been infected with. It is possible that the test will: 1) detect signs that your body cleared viruses, other than Zika, from your system, 2) detect signs that your body recently cleared Zika virus from your system, or 3) detect that you currently have Zika. Therefore, we may need to do additional testing to figure out whether you actually have or had Zika. Once I know which virus infected you, I will know how best to care for you during your pregnancy. • Ask the patient if they have any questions before you move forward with providing information on the testing process.

Recommendation	Sample Script
Discuss each step of the testing process with the patient	There could potentially be up to three steps of testing before I can determine whether you have Zika or not.
Step one- Let the patient know that you will be ordering a test to look for antibodies. Define this term as it may be unfamiliar and inform the patient of what to expect next.	I am going to start step one of the testing process by ordering a test to look for evidence that your body fought off a recent Zika infection. This test looks for antibodies, which are proteins that your body makes usually 2–12 weeks after an infection. If your antibody test comes back with a negative result, that means you were not recently infected with Zika, and we will continue our original plan of care for your pregnancy. If your antibody test comes back with a positive result, I will need to do more testing to determine whether or not you have or recently had Zika. The antibody test may be positive even when a person isn't actually infected with Zika for many reasons. One reason could be that the test is detecting antibodies to another virus that is similar to Zika, like dengue virus or West Nile virus. Another could be that the test is detecting antibodies from a Zika infection your body recently fought off. • Ask the patient if they have any questions before you move forward with providing information on step two of testing.
Step two- If the patient requires further testing, inform the patient that positive antibody test results will require further testing and provide them with information on what to possibly expect next.	If your first test for antibodies is positive, I will need to order a second test to make sure it's actually Zika and not another virus that is similar to Zika, like West Nile or dengue. This test looks for the genetic material of Zika, known as RNA. This material from the virus can be found in blood and urine. If your Zika RNA test comes back with a positive result it means that you have Zika. If this test comes back negative, it may mean that you previously had Zika but your body cleared the virus from your system. It could also mean that you had an infection similar to Zika. We will need to do one more round of testing to figure out whether or not you actually have or recently had Zika. • Ask the patient if they have any questions before you move forward with providing information on step three of testing
Step three- If the patient requires further testing after the Zika RNA test, inform patients that further testing will be needed if they test negative for Zika RNA.	If your second test for Zika RNA is negative, I will need to order a third and final test to confirm whether the antibodies from the first test for Zika. This test takes the longest to receive results because I will have to send the results to a specialized lab and then work with the state or local health department to interpret the results. • Ask the patient if they have any questions on what to expect during each step of the testing process
Inform patients of each what each test result could mean for their pregnancy.	Now we'll go over what each test result could mean for your pregnancy.
If Zika test results are positive.	If you test positive for Zika, I will need to watch your pregnancy more closely. I may do more ultrasounds or other tests to check for your fetus's growth and development.
If Zika test results are inconclusive.	Sometimes test results will not come back as a clear negative or positive. When this happens the results are considered "inconclusive". If this happens, I'd rather be more cautious and still do more ultrasounds and other tests to closely monitor your pregnancy.
If Zika test results are negative.	If your test results are negative, I will do an ultrasound to check the growth and development of your baby and check for any signs of Zika virus infection. If I see any signs of Zika during the ultrasound, then I may order additional tests. If there are no signs of Zika, we will continue with routine prenatal care.

CS273696B January 10, 2017

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

CDC's Response to **Zika**

WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING

For Pregnant Women Living in an Area with Zika

As a pregnant woman who lives in an area with Zika, you may be at risk of getting Zika at any time during your pregnancy. For this reason, CDC recommends testing at the start of prenatal care and again during the second trimester. If at any time you feel sick with fever, rash, joint pain, or red eyes, you should see a doctor or other provider and be tested for Zika virus. Keep reading to learn more about what you might expect if you have Zika virus during pregnancy.

Zika testing is complex

- **You may need more than one Zika test:** You may find out if you have Zika after one test. However, finding out if you have Zika can require up to three different tests, because the result of one test may require more testing to find out if you recently had a Zika virus infection. You may wait different amounts of time for results of each test to come back.
- **Understanding test results can be challenging:** Zika virus is similar to other viruses that are carried by mosquitoes. Testing for Zika may also detect these other mosquito-borne viruses. Sometimes even after testing, we may not know which type of virus you were infected with. Each test result is important, because it helps your doctor or other provider decide which virus is most likely and how best to care for you during pregnancy.

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

Testing Process

Step One

Your doctor will start by ordering a test to look for antibodies, which the body makes to fight infections. These antibodies are usually in your body for 2-12 weeks after infection.

- If your antibody test is negative, it means there is no evidence you were recently infected with Zika.
- If your antibody test is positive, more testing is needed to be sure. The antibody testing can sometimes show results that are positive even when a person isn't actually infected. For example, the test might detect antibodies to a similar mosquito-borne infection, such as dengue.

Step Two

If your antibody test (step 1 test) was positive, your healthcare provider will order a test that looks for Zika genetic material, called RNA, which can be in blood and urine.

- A positive result means that you have Zika.
- A negative result means another test is needed. A negative test may mean that you had Zika, but your body cleared the virus from your system, or your antibody test was positive because you had an infection similar to Zika.

Step Three

If you tested negative for Zika RNA, a third test is needed to confirm the antibodies from Step 1 are for Zika. This test takes the longest for results. Your doctor or other provider will work with your state or local health department to interpret your test results.

At any time during the testing process, if your doctor doesn't have a sample of your blood or urine, you may have to give another sample.

Testing Results

Positive test results

Testing positive for Zika during pregnancy lets your doctor or other provider know to watch your pregnancy more closely. This means you might have more ultrasounds or other tests to check the growth and development of your fetus and check for Zika infection.

Inconclusive (not positive or negative) test results

Sometimes, if the tests aren't clearly positive or negative, the results are considered "inconclusive," meaning we're not sure if you had the virus. If the test results are inconclusive, your doctor or other provider may choose to follow the CDC recommendations for a positive test result, meaning he or she might do more ultrasounds or other tests to monitor the pregnancy.

Negative test results

Your doctor or other provider may check the growth and development of your fetus during an ultrasound and check for any signs of Zika virus infection. If there are no signs of Zika virus infection, you will get routine prenatal care, which is what CDC recommends.
If your doctor or other provider sees signs of Zika virus infection during an ultrasound, then you may need additional tests.

PRETESTING COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

For Asymptomatic Pregnant Women Living in an Area with Active Zika Virus Transmission

This guide describes recommendations for conducting pretesting counseling for asymptomatic pregnant women living in areas where Zika virus is spreading. For pregnant women living in an area with active Zika transmission who do not have symptoms of Zika, CDC recommends testing at the start of prenatal care and again during the second trimester. For pregnant women living in these areas who have had symptoms please see the guide for women whose symptoms started less than 2 weeks ago or the guide for women whose symptoms started in the past 2–12 weeks.

This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy to understand information, avoiding technical terms, and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation	Sample Script
Provide the patient with information on the complexity of Zika testing.	You may be at risk of getting Zika at any time during your pregnancy since you live in an area where Zika is actively being spread by mosquitoes. Many people who get infected with Zika do not have symptoms, so you could get infected and not know you have Zika. Because Zika infection during pregnancy can cause birth defects, I think it is best to test you for Zika during your pregnancy. You will be tested for Zika twice; we will perform the first test during this visit. The second test will most likely happen in the second trimester when you are about 18–20 weeks pregnant. Before we begin, I would like to provide you with some helpful information on what to expect throughout this process.
Patients should be informed that more than one Zika test may be required before a final result is determined.	You may only need one test to find out whether you have Zika. However, you may need up to three different tests before we can find out whether you have Zika or not. We want to be sure we take all of the necessary steps to make sure your results are accurate because the result of one test may not tell us the whole story, and you may need to get additional tests to find out if you recently got Zika. Each test can take different amounts of time to receive results, which I know can be frustrating. As your healthcare providerl am here to answer any questions you may have. • Reassure the patient that this method of testing is normal. • Consider providing the fact sheet "What You Should Know about Zika Virus Testing for Pregnant Women Living in an Area with Zika."
Patients should be informed that it can be challenging to understand test results	It can be hard to understand Zika test results for a number of reasons. Mosquitoes can carry many viruses, like dengue virus, which is very similar to Zika. So if someone has been infected by these other viruses in the past, it may be difficult to know which virus you have been infected with. It is possible that the test will: 1) detect signs that your body cleared one of these viruses, other than Zika, from your system, 2) detect signs that your body recently cleared Zika virus from your system, or 3) detect that you currently have Zika. Therefore, we may need to do additional testing to figure out whether you actually had or have Zika. Once I know which virus is most likely the cause, I will know how best to care for you during your pregnancy. • Ask the patient if she has any questions before you move forward with providing information on the testing process.

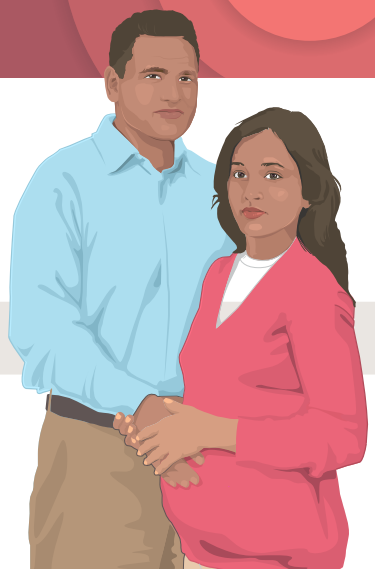
Recommendation	Sample Script
Discuss each step of the testing process with the patient	There could potentially be up to three steps of testing before I can determine whether you have Zika or not.
Step one- Let the patient know that you will be ordering a test to look for antibodies. Define this term as it may be unfamiliar and inform the patient of what to expect next.	I am going to start step one of the testing process by ordering a blood test to look for evidence that your body fought off a recent Zika infection. This test looks for antibodies, which are proteins that your body makes usually 2–12 weeks after an infection. They are produced even if you have no symptoms. If your antibody test comes back with a negative result, that means you were not recently infected with Zika, and we will continue our original plan of care for your pregnancy. If your antibody test comes back with a positive result, I will need to do more testing to determine whether or not you have Zika or recently had Zika. The antibody test may be positive even when a person isn't actually infected with Zika for many reasons. One reason could be that the test is detecting antibodies to another virus that is similar to Zika, like dengue virus or West Nile virus. Another could be that the test is detecting antibodies from a Zika infection your body recently fought off. • Ask the patient if they have any questions before you move forward with providing information on step two of testing.
Step two- If the patient requires further testing, inform the patient that positive antibody test results will require further testing and provide them with information on what to possibly expect next.	If your first test for antibodies is positive, I will need to order a second test to make sure it's actually Zika and not another virus that is similar to Zika, like West Nile or dengue virus. This next step of the testing process looks for the genetic material of Zika, known as RNA. This material from the virus can be found in blood and urine. If your Zika RNA test comes back with a positive result it means that you have Zika. If this test comes back negative, it may mean that you previously had Zika but your body cleared the virus from your system. It could also mean you had an infection similar to Zika. We will need to do one more round of testing to figure out whether or not you actually have or recently had Zika. • Ask the patient if they have any questions before you move forward with providing information on step three of testing.
Step three- If the patient requires further testing after the Zika RNA test, inform patients that further testing will be needed if they test negative for Zika RNA.	If your second test for Zika RNA is negative, I will need to order a third and final test to confirm whether the antibodies from the first test for Zika. This test takes the longest to receive results because I will have to send the results to a specialized lab and then work with the state or local health department to interpret the results. • Ask the patient if they have any questions on what to expect during each step of the testing process.
Inform patients of each what each test result could mean for their pregnancy.	Now we'll go over what each test result could mean for your pregnancy.
If Zika test results are positive.	If you test positive for Zika, I will need to watch your pregnancy more closely. I may do more ultrasounds or other tests to check for your fetus's growth and development.
If Zika test results are inconclusive.	Sometimes test results will not come back as a clear negative or positive. When this happens the results are considered "inconclusive". If this happens, I'd rather be more cautious and still do more ultrasounds and other tests to closely monitor your pregnancy.
If Zika test results are negative.	If your test results are negative, I will do an ultrasound to check the growth and development of your baby and check for any signs of Zika virus infection. If I see any signs of Zika during the ultrasound, then I may order additional tests. If there are no signs of Zika, we will continue with routine prenatal care.

CS273696A January 11, 2017

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

CDC's Response to **Zika**

WHAT TO KNOW IF YOUR DOCTOR SUSPECTS MICROCEPHALY DURING PREGNANCY



If your doctor has told you that your developing baby may have microcephaly or other health conditions related to Zika infection during pregnancy, you and your family may feel overwhelmed, worried, and unsure of what to do next. Read on to learn more about these conditions and find out where you can go for help during pregnancy.

How Might Zika Affect My Baby?

Zika infection during pregnancy can lead to a pattern of conditions, called congenital Zika syndrome, in the baby. A baby with congenital Zika syndrome, might have one or more of the conditions in the blue box.

- Smaller than expected head size, called microcephaly
- Problems with brain development
- Feeding problems, such as difficulty swallowing
- Hearing loss
- Seizures
- Vision problems
- A problem with joint movement, called contractures
- Too much muscle tone restricting body movement soon after birth

We are still learning about the effects of Zika infection during pregnancy. Some of the conditions listed in the blue box can lead to problems with a child's progress in moving, learning, speaking and playing, called "developmental delay." Babies with congenital Zika syndrome may experience different outcomes as they develop, but it's difficult to know how each baby will be affected. These answers may only come with more time. It is important for you to work with your doctors to manage your baby's medical care together.

How Will I Know How My Baby is Doing During Pregnancy?

- During pregnancy, your healthcare provider will have regular follow-up appointments with you to track how you are doing and how your baby is growing.
- Your healthcare provider may order extra ultrasound tests to check your developing baby's growth.
- It is important to know that ultrasounds can show some, but not all, problems with development during pregnancy. Microcephaly can sometimes be seen on the 18-20 week ultrasound, but is more commonly detected later in the second trimester or early in the third trimester.
- Your healthcare provider may offer you an amniocentesis between 15 -18 weeks of pregnancy. Amniocentesis is a test where the doctor collects a small amount of amniotic fluid from the area surrounding the developing baby. The fluid is then tested to look for Zika genetic material, called RNA.
- Your healthcare provider might order testing to see if you've been infected with Zika virus. Microcephaly can be caused by other exposures, such as certain infections or harmful substances (e.g., alcohol).
- Your healthcare provider may refer you to a doctor who specializes in high-risk pregnancies for close monitoring and care during pregnancy.

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

How Will I Know How My Baby is Doing After Pregnancy?

After birth, your baby's healthcare provider will perform

- A physical exam of your baby, including a measure of your baby's head size
- A hearing screening
- More exams and tests as needed

Where to Find Resources and Support During Pregnancy

If you are expecting a baby with microcephaly or other health conditions related to Zika infection during pregnancy, you may be worried and unsure of next steps. Before the baby is born, it may be helpful to learn more information about Zika and pregnancy, talk with your doctors and other specialists, and stay connected with family, friends, and support groups. Building a support system early may help once your baby is born.

FIND more information through:

- Your baby's regular doctor or a specialist whom your doctor recommends
- **Early Intervention Services** | www.cdc.gov/ncbddd/actearly/parents/states.html
- **CDC Zika Virus Website** | www.cdc.gov/zika
- **The Parent Training and Information Center** in your state | www.parentcenterhub.org/find-your-center
- Non-profit organizations
  - » **American Academy of Pediatrics** | Visit website: www.healthychildren.org
  - » **American Congress of Obstetricians and Gynecologists** www.acog.org/Patients
  - » **March of Dimes:** www.marchofdimes.org | Ask questions: www.marchofdimes.org/ask-us.aspx
  - » **Mother-to-Baby** Call 1-866-626-6847 Monday - Friday from 8am - 5pm (local time).
    Chat live or send an email through the MotherToBaby website: www.mothertobaby.org

ACCESS regular prenatal and other health care through:

- Your regular doctor
- A specialist whom your doctor recommends. Babies with microcephaly might benefit from seeing other healthcare providers who specialize in certain types of care, like treating disorders of the nervous system, eye problems, or child development.

GET support from families of children with microcephaly or other special healthcare needs through:

- Non-profit organizations
  - » **The Family Voices** affiliate or **Family-to-Family Health Information Center** in your state | Visit website: www.familyvoices.org/states
  - » **Parent to Parent-USA** | Visit website: www.p2pusa.org
  - » **Partnerships for Parents** | Visit website: partnershipforparents.net/
- Your hospital social worker. Try talking to someone about how you're feeling, be it friend or professional. Hospitals often have a social worker who can counsel you initially and connect you with additional therapeutic resources. Get the support you need to take care of yourself and your baby.

For a more complete list of resources for families, please visit
www.cdc.gov/zika/parents/families-of-newborns-affected-zika.html

Links to organizations outside of CDC are included for information only and do not indicate any form of endorsement or approval from CDC.

CDC's Response to **Zika**

WHAT TO KNOW IF YOUR BABY WAS BORN WITH CONGENITAL ZIKA SYNDROME

As a parent of a new baby with health conditions related to Zika infection during pregnancy, you may feel overwhelmed, worried, and unsure of how to care for your new baby. Read on to learn more about health conditions related to Zika and find out where you can go for help.

How Might Zika Affect My Baby?

Zika infection during pregnancy can lead to a pattern of conditions, called congenital Zika syndrome, in the baby. A baby with congenital Zika syndrome, might have one or more of the conditions in the blue box.

- Smaller than expected head size, called microcephaly
- Problems with brain development
- Feeding problems, such as difficulty swallowing
- Hearing loss
- Seizures
- Vision problems
- A problem with joint movement, called contractures
- Too much muscle tone restricting body movement soon after birth

We are still learning about the effects of Zika infection during pregnancy. Babies affected by Zika may have lasting special needs. Some of the conditions listed in the blue box can lead to problems with a child's progress in moving, learning, speaking and playing, called "developmental delay." Babies with congenital Zika syndrome may experience different outcomes as they develop, but it's difficult to know how each baby will be affected. These answers may only come with more time. It is important for you to work with your doctors to manage your baby's medical care together.

How Can I Support My Baby?

Babies with congenital Zika syndrome need support. One type of support involves getting your baby help as soon as possible for learning and developing skills, like feeding, sitting, or crawling. This type of help is called "early intervention services," and is available in the first 3 years of life. Other developmental support may be needed for any ongoing special needs. Another type of support is treatment of the conditions your baby may experience, like medication to help treat seizures.
To help your baby get the early support and services he or she might need:

- **Work with your doctor to create a coordinated care plan.**
  » Work with your doctor to organize the care your baby might need. Additional testing, like hearing and vision testing, may be needed even if the first tests were normal.
- **Keep regular appointments.**
  » Take your baby for all recommended check-ups with his or her regular doctor, nurse, or other healthcare provider or recommended specialists. This is important for your baby's doctor or other healthcare providers to monitor your baby's development.
- **Share your concerns.**
  » If you have new concerns about your baby's development at any time, talk with your baby's doctor, nurse, early intervention provider, or healthcare provider. Don't wait. Acting early could make a real difference.
- **Contact early intervention services in your community.**
  » Reach out to your state or territory's early intervention program. Your baby may be eligible for free or low cost services. Find contact information at www.cdc.gov/FindEI.
  You do not need a doctor's referral or a medical diagnosis to have your baby evaluated for services.

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

Where to Find Resources and Support

Raising a child with congenital Zika syndrome can be challenging. Thankfully, help is available for you and your baby.

The resources below can help you find more information about Zika, locate services that might help your baby, and connect with other families.

FIND more information through:

- Your baby's regular doctor or a specialist whom your doctor recommends
- **CDC Zika Virus Website** | www.cdc.gov/zika
- Non-profit organizations
  - » **American Academy of Pediatrics** | Visit website: www.healthychildren.org
    This organization is comprised of pediatricians committed to the health of infants, children, adolescents, and young adults.
  - » **March of Dimes:** www.marchofdimes.org | Ask questions: www.marchofdimes.org/ask-us.aspx
    The March of Dimes is dedicated to improving the health of babies by preventing birth defects, premature birth, and infant mortality.
  - » **The Parent Training and Information Center** in your state: www.parentcenterhub.org/find-your-center
    These centers provide information and training on early intervention and special education services to families of children with disabilities.

ACCESS regular pediatric, other health care, and early intervention services through:

- Your baby's regular doctor
- A specialist whom your doctor recommends. Babies with microcephaly might benefit from seeing other healthcare providers who specialize in certain types of care, like treating conditions of the nervous system, eye problems, or child development.
  - » State/local programs, such as early intervention and medical services for children with special healthcare needs. Call your state contact to get a free evaluation: www.cdc.gov/FindEI

GET peer support from families of children with microcephaly or other special healthcare needs through:

- Non-profit organizations
  - » **The Family Voices** affiliate or **Family-to-Family Health Information Center** in your state: www.familyvoices.org/states
  - » **Parent to Parent-USA** | Visit website: www.p2pusa.org
  - » **Partnerships for Parents** | Visit website: partnershipforparents.net/
- Your hospital social worker. Try talking to someone about how you're feeling, be it friend or professional. Hospitals often have a social worker who can counsel you initially and connect you with additional therapeutic resources. Get the support you need to take care of yourself and your baby.

Links to organizations outside of CDC are included for information only and do not indicate any form of endorsement or approval from CDC.

For a more complete list of resources for families, please visit
www.cdc.gov/zika/parents/families-of-newborns-affected-zika.html

CDC's Response to **Zika**

WHAT TO KNOW IF YOUR BABY MAY HAVE BEEN AFFECTED BY ZIKA BUT HAS NO RELATED HEALTH CONDITIONS AT BIRTH

As a parent of a new baby who may have been affected by Zika virus during pregnancy, you and your family may be worried and unsure of next steps in caring for your baby. Read on to learn more about the importance of tracking your baby's development and learn where you can go for help.

How Will Zika Virus Affect My Baby?

- Zika virus infection during pregnancy can cause microcephaly and other severe brain defects in babies, but not every pregnant woman infected with Zika will have a baby with a related health condition at birth.
- While we've learned a lot about Zika in a short time, many questions remain.
- We don't yet know all of the ways Zika virus infection during pregnancy might affect a baby, including problems that may not be obvious when a baby is born.
- We also don't know how often a baby will have problems linked to Zika if a woman is infected during pregnancy.
- Children affected by Zika may have lasting special needs. Acting early to get services could make a difference.

What Should I Do After My Baby is Born?

- **Work with your baby's doctor.**
  - » Because we are still learning about the longer term effects of Zika virus infection during pregnancy, it is important for you to work with your baby's doctors to manage his or her medical care.
- **Track your baby's development.**
  - » It's important to track your baby's development as he or she grows. Tracking development helps you know what your baby should be doing at certain ages and what to expect next. This will help you and your doctors identify any problems early and get your baby any needed services or support as soon as possible.

How Can I Best Support My Baby?

To help your baby get the early support and services that might be needed:

- **Keep regular appointments.**
  - » Take your baby for all recommended check-ups with their regular doctor or recommended specialists.
- **Track your baby's development.**
  - » Between check-ups, track your baby's development using developmental milestone checklists from CDC (www.cdc.gov/Milestones).
- **Share your concerns.**
  - » If you have concerns about your baby's development at any time, talk with your child's doctor, nurse, early intervention provider, or other healthcare provider. Don't wait. Acting early can make a real difference.
- **Contact early intervention services in your community.**
  - » Reach out to your state or territory's early intervention program to find out if your baby can get free or low cost services. Find contact information at www.cdc.gov/FindEI. **You do not need a doctor's referral or a medical diagnosis to have your baby evaluated for services.**

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

Where to Find Resources and Support

As a new parent of a baby who may have been affected by Zika virus during pregnancy, you and your family may be worried and unsure of next steps in caring for your baby. Thankfully, help is available.

The resources below can help you find more information about Zika, track your baby's development, and connect with other families for support.

FIND more information through:

- Your baby's regular doctor or a specialist whom your doctor recommends
- **Early Intervention Services** www.cdc.gov/ncbddd/actearly/parents/states.html
- **CDC Zika Virus Website** | www.cdc.gov/zika
- Non-profit organizations
  - » **American Academy of Pediatrics** Visit website: www.healthychildren.org
  - » **March of Dimes** | www.marchofdimes.org Ask questions: www.marchofdimes.org/ask-us.aspx
  - » **The Parent Training and Information Center** in your state: www.parentcenterhub.org/find-your-center

ACCESS regular pediatric and other health care through:

- Your baby's regular doctor
  - » The American Academy of Pediatrics recommends that babies and children be screened for general development using standardized, validated tools at 9, 18, and 24 or 30 months or whenever a parent or provider has a concern. Ask your baby's doctor about your baby's developmental screening.
- A specialist who your doctor recommends. Babies affected by Zika during pregnancy might benefit from seeing other healthcare providers who specialize in certain types of care, like eye problems, or child development.

TRACK your baby's development through:

- CDC's "Learn the Signs. Act Early." program. CDC offers free tools and resources to help parents and other caregivers keep track of their child's development and get help if they are concerned.
  - » Order a free Parent Kit: www.cdc.gov/ActEarly/Orders
  - » See photos and videos of developmental milestones to help understand what most babies and children do by different ages: www.cdc.gov/MilestonesInAction
  - » Download fact sheets on how to get help for your baby if you have concerns: www.cdc.gov/Concerned
- The "Birth to Five: Watch Me Thrive" website: www.hhs.gov/WatchMeThrive. This site has developmental screening resources for families, including a Developmental Screening Passport.

GET peer support from families of children with special healthcare needs through:

- Non-profit organizations
  - » **The Family Voices** affiliate or **Family-to-Family Health Information Center** in your state | Visit website: www.familyvoices.org/states
  - » **Parent to Parent-USA** | Visit website: www.p2pusa.org
  - » **Partnerships for Parents** | Visit website: partnershipforparents.net/

Links to organizations outside of CDC are included for information only and do not indicate any form of endorsement or approval from CDC.

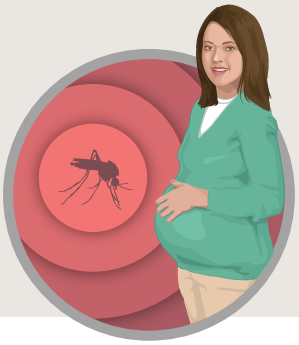
For a more complete list of resources for families, please visit
www.cdc.gov/zika/parents/families-of-newborns-affected-zika.html

REPORTING

CDC's Response to **Zika**

US ZIKA PREGNANCY REGISTRY

Obstetric Healthcare Providers: How to Participate



Zika virus infection during pregnancy has been linked to adverse outcomes including pregnancy loss and microcephaly, absent or poorly developed brain structures, defects of the eye and impaired growth in fetuses and infants. Despite these observations, very little is known about the risks of Zika virus infection during pregnancy. Information about the timing, absolute risk, and spectrum of outcomes associated with Zika virus infection during pregnancy is needed to direct public health action related to Zika virus and guide testing, evaluation, and management.

US Zika Pregnancy Registry

To understand more about Zika virus infection, CDC established the US Zika Pregnancy Registry and is collaborating with state, tribal, local, and territorial health departments to collect information about pregnancy and infant outcomes among pregnant women with laboratory evidence of Zika virus infection and their infants. The data collected through this Registry will provide additional, more comprehensive information to complement notifiable disease case reporting and will be used to update recommendations for clinical care, to plan for services for pregnant women and families affected by Zika virus, and to improve prevention of Zika virus infection during pregnancy.

How to Participate

CDC and state, tribal, local, and territorial health departments request that healthcare providers participate in the US Zika Pregnancy Registry by:

1. Reporting information about pregnant women with laboratory evidence of Zika virus infection to their state, tribal, local, or territorial health department.
2. Collecting pertinent clinical information about pregnant women and their infants on the Pregnancy and Zika Virus Disease Surveillance forms.
3. Providing the information to state, tribal, local or territorial health departments or directly to CDC Registry staff if asked to do so by local health officials.
4. Notifying state, tribal, local, or territorial health department staff or CDC Registry staff of adverse events (e.g., spontaneous abortion, termination of pregnancy).

Who to Report to the Registry

Healthcare providers should report the requested information to the health department in accordance with applicable state, tribal, local and territorial laws. Those eligible for the registry include: 1) pregnant women in the United States and US territories (with the exception of Puerto Rico) with laboratory evidence of possible Zika virus infection (regardless of whether they have symptoms) and periconceptionally, prenatally, or perinatally exposed infants born to these women and 2) infants with laboratory evidence of possible congenital Zika virus infection (regardless of whether they have symptoms) and their mothers. Healthcare providers practicing in Puerto Rico should report information to the Puerto Rico Zika Active Pregnancy Surveillance System (ZAPSS) rather than to the US Pregnancy Registry.*

*Puerto Rico has established a separate Zika Active Pregnancy Surveillance System (ZAPSS)

www.cdc.gov/zika

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

CS264086-A January 20, 2017

How To Report to the Registry

- Healthcare providers should contact their state, tribal, local, or territorial health department to arrange for laboratory testing for Zika virus infection in pregnant women and infants who meet the clinical criteria for testing as outlined in the CDC guidelines.
- Healthcare providers can contact CDC (call CDC's Emergency Operations Center watch desk at 770-488-7100; or email ZikaMCH@cdc.gov; or fax 404-718-1013) to discuss information on pregnant women with laboratory evidence of Zika virus infection. If healthcare providers contact CDC for clinical consultation, Registry staff will ensure that state, tribal, local, or territorial health departments are notified. CDC may also learn about pregnant women and infants with laboratory evidence of Zika virus infection through national surveillance of arboviral diseases.

How the Data are Collected

Depending on the preference of the state, tribal, local, or territorial health department, either health department staff or CDC Registry staff will contact healthcare providers caring for pregnant women and their infants for data collection.

CDC is requesting the collection of clinical information in identifiable form as a public health authority. As defined in the Health Insurance Portability and Accountability Act (HIPAA) and its implementing regulations, Standards for Privacy of Individually Identifiable Health Information (45 CFR § 164.501)] ("Privacy Rule"**), covered entities (e.g., healthcare providers) may disclose protected health information without patient authorization to a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease (42 CFR 164.512). Data to be collected include clinical information pertaining to the pregnant woman's health, monitoring, and testing during pregnancy, results from evaluation and testing conducted at birth, and clinical/developmental information from the infant through the first year of life. As established in the HIPAA Privacy Rule (45 CFR 164.528), individuals have the right to request from covered entities (i.e., you, the healthcare provider) an accounting of the disclosures of their protected health information.

You may wish to use the fact sheet for pregnant women to let your patients know how their information is being used. This fact sheet also contains information on the Assurance of Confidentiality that CDC has obtained.
The Assurance is a formal confidentiality protection authorized under Section 308 (d) of the Public Service Act. Under this Assurance, identifiable information about your patient and the care you provide can only be used to better understand Zika virus infection during pregnancy and its outcomes. CDC cannot share it with anyone without your permission and your patient's permission, even if an official of the court, the government or law requests it.

CDC Guidance Materials

1. Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure – United States, 2016 (April 1, 2016) http://www.cdc.gov/mmwr/volumes/65/wr/mm6512e2.htm?s_cid=mm6512e2_w
2. Interim Guidelines for Healthcare Providers Caring for Infants and Children with Possible Zika Virus Infection – United States, February 2016 (Feb. 19, 2016) http://www.cdc.gov/mmwr/volumes/65/wr/mm6507e1.htm
3. Zika Virus: Collection and Submission of Fetal Tissues for Zika Virus Testing http://www.cdc.gov/zika/hc-providers/tissue-collection-submission.html
4. Collection and Submission of Body Fluids for Zika Virus Testing http://www.cdc.gov/zika/hc-providers/body-fluids-collection-submission.html

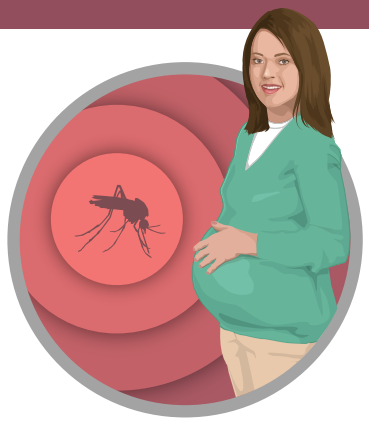
More Information about Zika

For more information, visit CDC's website, www.cdc.gov/zika.

If families would like to speak to someone about a possible Zika virus infection or diagnosis during pregnancy, Mother to Baby experts are available to answer questions in English or Spanish by phone, email, or chat: www.MotherToBaby.org. The free and confidential service is available Monday - Friday from 8am - 5pm (local time).

CDC's Response to **Zika**

US ZIKA PREGNANCY REGISTRY
WHAT PREGNANT WOMEN NEED TO KNOW



What is the purpose of the registry?

CDC developed the US Zika Pregnancy Registry to:

- Learn more about the effects of Zika virus infection (Zika) during pregnancy.
- Learn more about the growth and development of babies whose mothers had Zika while pregnant.

CDC will collect health information about Zika among pregnant women and babies across the United States for the Registry. CDC, health departments, doctors and healthcare providers will use the information from this registry to help pregnant women, children, and families affected by Zika.

Who is being included in the registry?

Pregnant women in the United States and US territories (except for Puerto Rico) with laboratory evidence of possible Zika virus infection (regardless of whether they have symptoms) and their babies can be included in the Registry. Puerto Rico has established a separate Zika Active Pregnancy Surveillance System (ZAPSS).

What will be done with the information collected?

The information your doctor or other healthcare provider shares will be added to the Registry with information about other pregnant patients with Zika, and the babies born to these mothers, to help CDC and health departments develop a clearer understanding of how Zika affects pregnant women and their babies. CDC has obtained an Assurance of Confidentiality to protect the information in this registry that could identify you or your baby. CDC cannot share this information with anyone without your permission, even if an official of the court, government, or law requests it.

What do I have to do to be in the registry?

You will not need to do extra paperwork, go to extra appointments, or have extra tests to be part of the Registry. If your healthcare provider is participating in this Registry, she/he will share information about your health with your health department and the CDC. Your health department and CDC will work with your doctor and other healthcare providers to collect all of the information needed. For this Registry, your health department and CDC will:

- Collect information about your pregnancy,
- Collect information about you and your baby around the time the baby is born, and
- Contact the baby's doctor or other healthcare provider to collect information about the baby's growth and development up to his or her first birthday.

If you change doctors or healthcare providers, please refer the new healthcare providers to CDC's US Zika Pregnancy Registry webpage.

As established in the HIPAA Privacy Rule (45 CFR 164.528), you have the right to request from your healthcare provider an accounting of the disclosure of your protected health information at any time.

What if I have questions?

- For more information about the Registry, visit CDC's Registry webpage (www.cdc.gov/zika/hc-providers/registry.html) or contact CDC-INFO by calling 800-232-4636 (TTY 888-232-6348) or submitting an online inquiry (wwwn.cdc.gov/dcs/ContactUs/Form).
- If you have questions about testing for Zika virus infection, please contact your healthcare provider.
- If you would like to speak to someone about a possible Zika virus infection or diagnosis during pregnancy, Mother to Baby experts are available to answer questions in English or Spanish by phone, email, or chat (www.MotherToBaby.org). The free, confidential service is available Monday - Friday from 8am - 5pm (local time).

How much does this cost?

Being in the Registry will not cost you any money.

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

Additional Resources

MotherToBaby

MotherToBaby is a non-profit organization that provides information to mothers, health care professionals, and the general public about medications and other exposures during pregnancy and while breastfeeding. If families would like to speak to someone about a possible Zika virus infection or diagnosis during pregnancy and risk to the baby, MotherToBaby experts are available to answer questions in English or Spanish by phone or chat. The free and confidential service is available Monday-Friday 8am-5pm (local time). To learn more, visit the MotherToBaby website.

Testing for Zika Virus

The following links provide more information about how and when to test for Zika virus:

- When to Test for Zika Virus
- Diagnostic Tests for Zika Virus
- Guidance for US Laboratories Testing for Zika Virus Infection
- Understanding Zika Virus Test Results
- Interim Guidance for Interpretation of Zika Virus Antibody Test Results

Reporting and Follow-up

Healthcare providers should report pregnant women with laboratory evidence of possible Zika virus infection (regardless of whether they have symptoms) and periconceptionally, prenatally, or perinatally exposed infants born to these women. If available, data should be collected at the time of initial identification, 2nd and 3rd trimester, and at delivery. More information about data reporting, collection, and findings can be found here.

Grand Rounds Presentations

This presentation and facilitated discussion guide provides an overview of Zika virus and pregnancy, diagnostic testing, definitions, guidelines, patient counseling, and suggestions for reporting.

Resources and Publications

- US Zika Pregnancy Registry Inclusion Criteria
- Pregnancy and Zika Testing interactive web algorithm
- Know Your Zika Risk interactive web algorithm