

CDC US ZIKA PREGNANCY REGISTRY

HEALTHCARE PROVIDER TOOLKIT FOR HEALTH DEPARTMENTS

FOR OBSTETRICIANS



CENTERS FOR DISEASE CONTROL AND PREVENTION
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**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 in July 2017 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 (Algorithms & 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. CDC's updated interim guidance presents the recommendations in two algorithms—one for pregnant women with Zika symptoms and one for pregnant women without Zika symptoms.
- **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 placental and 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) for asymptomatic pregnant women with ongoing exposure to Zika 2) for asymptomatic pregnant women without ongoing exposure to Zika 3) for symptomatic pregnant women with recent exposure to Zika.
 - 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
 - Roadmaps for Parents: These materials can help parents of babies with birth defects related to congenital Zika infection and parents whose babies were infected with Zika before birth and appear healthy with navigating the series of screenings and tests recommended during their baby's first year of life.
 - Roadmap for Parents of Babies with Congenital Zika Syndrome
 - Roadmap for Parents of Babies Infected with Zika Before Birth Who Appear Healthy
- **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.

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IDENTIFICATION

Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories), July 2017

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On July 24, 2017, this report was posted as an MMWR Early Release on the MMWR website (<https://www.cdc.gov/mmwr>).

CDC has updated the interim guidance for U.S. health care providers caring for pregnant women with possible Zika virus exposure in response to 1) declining prevalence of Zika virus disease in the World Health Organization's Region of the Americas (Americas) and 2) emerging evidence indicating prolonged detection of Zika virus immunoglobulin M (IgM) antibodies. Zika virus cases were first reported in the Americas during 2015–2016; however, the incidence of Zika virus disease has since declined. As the prevalence of Zika virus disease declines, the likelihood of false-positive test results increases. In addition, emerging epidemiologic and laboratory data indicate that, as is the case with other flaviviruses, Zika virus IgM antibodies can persist beyond 12 weeks after infection. Therefore, IgM test results cannot always reliably distinguish between an infection that occurred *during* the current pregnancy and one that occurred *before* the current pregnancy, particularly for women with possible Zika virus exposure before the current pregnancy. These limitations should be considered when counseling pregnant women about the risks and benefits of testing for Zika virus infection during pregnancy. This updated guidance emphasizes a shared decision-making model for testing and screening pregnant women, one in which patients and providers work together to make decisions about testing and care plans based on patient preferences and values, clinical judgment, and a balanced assessment of risks and expected outcomes.

For these recommendations, **the definition of possible Zika virus exposure has not changed and includes travel to, or residence in an area with risk for mosquito-borne Zika virus transmission or sex with a partner who has traveled to or resides in an area with risk for mosquito-borne Zika virus transmission.** These areas can be found on the CDC “Zika Travel Information” webpage.*

Key recommendations include the following:

1) All pregnant women in the United States and U.S. territories should be asked about possible Zika virus exposure before and during the current pregnancy, at every prenatal care

visit. CDC recommends that pregnant women not travel to any area with risk for Zika virus transmission. It is also recommended that pregnant women with a sex partner who has traveled to or lives in an area with risk for Zika virus transmission use condoms or abstain from sex for the duration of the pregnancy.

2) Pregnant women with possible Zika virus exposure and symptoms[†] of Zika virus disease should be tested to diagnose the cause of their symptoms. The updated recommendations include concurrent Zika virus nucleic acid test (NAT) and serologic testing as soon as possible through 12 weeks after symptom onset.

3) Asymptomatic pregnant women with ongoing possible Zika virus exposure[§] should be offered Zika virus NAT testing three times during pregnancy. IgM antibody testing is no longer routinely recommended because IgM can persist for months after infection; therefore, IgM results cannot reliably determine whether an infection occurred during the current pregnancy. The optimal timing and frequency of testing of asymptomatic pregnant women with NAT alone is unknown. For pregnant women who have received a diagnosis of *laboratory-confirmed* Zika virus infection (by either NAT or serology [positive/equivocal Zika virus or dengue virus IgM and Zika virus plaque reduction neutralization test (PRNT) ≥ 10 and dengue virus PRNT < 10 results]) any time before or during the current pregnancy, additional Zika virus testing is not recommended. For pregnant women without a prior laboratory-confirmed diagnosis of Zika virus, NAT testing should be offered at the initiation of prenatal care, and if Zika virus RNA is not detected on clinical specimens, two additional tests should be offered during the course of the pregnancy coinciding with prenatal visits.

4) Asymptomatic pregnant women who have recent[¶] possible Zika virus exposure (i.e., through travel or sexual exposure)

[†] Symptoms of Zika virus disease include acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis.

[§] Persons with ongoing possible Zika virus exposure include those who reside in or frequently travel (e.g., daily or weekly) to an area with risk for Zika virus transmission.

[¶] For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/ flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period (i.e., 8 weeks before conception or 6 weeks before the last menstrual period).

* <https://wwwnc.cdc.gov/travel/page/world-map-areas-with-zika>.

but *without ongoing possible exposure are not routinely recommended to have Zika virus testing*. Testing should be considered using a shared patient-provider decision-making model, one in which patients and providers work together to make decisions about testing and care plans based on patient preferences and values, clinical judgment, a balanced assessment of risks and expected outcomes, and the jurisdiction's recommendations. Based on the epidemiology of Zika virus transmission and other epidemiologic considerations (e.g., seasonality), jurisdictions might recommend testing of asymptomatic pregnant women, either for clinical care or as part of Zika virus surveillance. With the decline in the prevalence of Zika virus disease, the updated recommendations for the evaluation and testing of pregnant women with recent possible Zika virus exposure but *without ongoing possible exposure* are now the same for all areas with any risk for Zika virus transmission.

5) Pregnant women who have recent possible Zika virus exposure and who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus syndrome should receive Zika virus testing to assist in establishing the etiology of the birth defects. Testing should include both NAT and IgM tests.

6) The comprehensive approach to testing placental and fetal tissues has been updated. Testing placental and fetal tissue specimens can be performed for diagnostic purposes in certain scenarios (e.g., women without a diagnosis of laboratory-confirmed Zika virus infection and who have a fetus or infant with possible Zika virus-associated birth defects**). However, testing of placental tissues for Zika virus infection is not routinely recommended for asymptomatic pregnant women who have recent possible Zika virus exposure but *without ongoing possible exposure* and who have a live born infant without evidence of possible Zika virus-associated birth defects.

7) Zika virus IgM testing as part of preconception counseling to establish baseline IgM results for nonpregnant women with ongoing possible Zika virus exposure is not warranted because Zika virus IgM testing is no longer routinely recommended for asymptomatic pregnant women *with ongoing possible Zika virus exposure*.

CDC continues to evaluate all available evidence and will update recommendations as new information becomes available.

** Possible Zika virus-associated birth defects that meet the CDC surveillance case definition include the following: brain abnormalities and/or microcephaly, intracranial calcifications, ventriculomegaly, neural tube defects and other early brain malformations, eye abnormalities, or other consequences of central nervous system dysfunction including arthrogryposis (joint contractures), congenital hip dysplasia, and congenital deafness (<https://www.cdc.gov/zika/geo/pregnancy-outcomes.html>). In all cases, infants or fetuses with possible Zika virus-associated birth defects should also be evaluated for other etiologies of congenital anomalies.

Zika Virus Infection

Zika virus is a mosquito-borne flavivirus that is closely related to dengue, West Nile, Japanese encephalitis, and yellow fever viruses (1). During 2015–2016, Zika virus spread rapidly and caused outbreaks across the Americas; 47 countries and territories in the Americas reported Zika virus outbreaks. However, since early 2017, the reported incidence of Zika virus disease in the region has declined (2).

The World Health Organization uses a country classification scheme that describes the epidemiology of Zika virus transmission to aid in geographic risk assessment. Some areas (e.g., American Samoa) have been reclassified to indicate that Zika virus transmission has been interrupted (3,4), which is reflective of the declining trends in the prevalence of Zika virus disease. As of July 23, 2017, 95 countries and territories have been designated by CDC as areas with any possible risk for Zika virus transmission.

Although the understanding of the consequences of Zika virus infection is improving, diagnosing Zika virus infection accurately continues to present challenges. First, Zika virus is present in body fluids only transiently, which makes confirming the presence of the virus difficult. Second, serologic testing, based on the immunologic response, cannot always reliably determine when infection occurred. Finally, serologic tests are prone to false-positive results and cross-reactivity with other flaviviruses (5). With declining prevalence of Zika virus disease (2), the probability of false-positive test results increases (6). The changing epidemiology further limits the diagnostic capability of currently available Zika virus tests. In this context, CDC has updated the interim guidance for health care providers caring for pregnant women with possible Zika virus exposure to provide new information and highlight current testing limitations.

Persistence of Zika Virus Nucleic Acid and Immune Response

Data from outbreaks before 2015 indicated that Zika virus RNA was detected in serum for up to 7 days after symptom onset (1,7). However, in some persons, Zika virus RNA can be detected in body fluids longer than has been documented previously. The Zika Virus Persistence (ZiPer) Study of persons with NAT-confirmed Zika virus disease, recently reported detection of viral RNA in serum 8–15 days after symptom onset in 36% (10 of 28) of participants, 16–30 days after symptom onset in 21% (27 of 129), and >60 days after symptom onset in 4% (three of 79) (8). Prolonged detection of Zika virus RNA in serum obtained from pregnant women was also reported; three of the five pregnant women included

in the ZiPer study had detectable RNA 46 days after symptom onset, and one had detectable RNA 80 days after symptom onset. This finding is consistent with other small case series (<20 pregnant women in total) that have demonstrated detection of Zika virus RNA for longer than had been previously reported, up to 107 days after symptom onset and 53 days after last exposure (9–15).

Zika virus IgM antibodies typically become detectable within the first 2 weeks after symptom onset (1,8,16). Published data on the duration of detection of IgM antibodies following Zika virus infection are limited. In the ongoing ZiPer study, IgM antibodies were detected in 34% (17 of 50) of participants at 0–7 days after symptom onset, 100% (28 of 28) at 8–15 days after symptom onset, and 87% (52 of 60) >60 days after symptom onset (8). In addition, consistent with what is known about other flaviviruses (17), unpublished preliminary data from this study indicate a median of 4 months (122 days, [range = 8–210 days]) to the first negative Zika virus IgM result (18). Thus, detection of IgM antibodies might not indicate an infection that occurred during the current pregnancy. Inability to determine the timing of infection through IgM testing is a major challenge for pregnant women and their health care providers, making it difficult for health care providers to counsel pregnant women about the risk for congenital Zika virus infection.

Neutralizing antibodies develop shortly after IgM antibodies and likely persist for many years (19). Based on experience with other flaviviruses, previous Zika virus infection is likely to confer prolonged, possibly lifelong, immunity (20). Testing is not routinely recommended for pregnant women with a previous diagnosis of **laboratory-confirmed** Zika virus infection by either NAT or serology (positive/equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥ 10 and dengue virus PRNT <10 results). However, in light of the limitations of serologic testing (e.g., cross-reactivity and false-positive test results), for pregnant women without a previous diagnosis of laboratory-confirmed Zika virus infection, including those with laboratory evidence of flavivirus infection or laboratory evidence of presumptive Zika virus or flavivirus infection (Table 1), decisions about testing during a subsequent pregnancy should be made using a shared patient-provider decision-making model. If the decision is made to test, only NAT testing is recommended, because IgM antibody testing might not be able to determine the timing of infection among pregnant women who have had exposure to Zika virus before the current pregnancy.

Zika Virus Diagnostic Testing

Diagnostic testing for Zika virus infection can be accomplished using molecular and serologic methods; several NAT and serology assays have received Emergency Use Authorization (EUA) from the Food and Drug Administration (FDA) for use

on nontissue clinical specimens.^{††,§§} Zika virus NAT is used to identify viral RNA in clinical or pathologic specimens, and for most persons with suspected Zika virus disease, a positive NAT result confirms acute Zika virus infection. However, despite the high specificity of NAT, false-positive results can occur (1,8,16). In addition, because Zika virus RNA is cleared from blood and other body fluids and tissues, a negative NAT result does not exclude acute Zika virus infection.

Several assays can be used to detect Zika virus IgM antibodies in serum or cerebrospinal fluid. Zika virus IgM tests can be difficult to interpret because of false-positives and cross-reactivity with other flaviviruses, especially in persons who were previously infected with or vaccinated against a related flavivirus (5,21). Additionally, a negative IgM test result does not rule out Zika virus infection when an IgM test is performed before the development of IgM antibodies or after the antibodies have waned.

PRNT measures virus-specific neutralizing antibody titers and should be performed for Zika and dengue viruses in NAT-negative, IgM-nonnegative (i.e., positive, equivocal, presumptive positive, or possible^{¶¶}) specimens (21). In primary flavivirus infections (i.e., a person's first flavivirus infection), PRNT can often identify the infecting virus (21). PRNT can also assist in identifying false-positive IgM. However, PRNT might not discriminate between anti-Zika virus antibodies and cross-reacting antibodies in persons who have been previously infected with or vaccinated against a related flavivirus (i.e., secondary flavivirus infection) (22,23). In addition, if areas with risk for Zika virus transmission experience increasing levels of dengue virus transmission, the difficulty in differentiating between cross-reactive Zika virus and dengue virus antibodies will further complicate interpretation of test results and diagnosis of Zika virus infection. This is especially concerning at this time, as epidemiologic trends suggest a reduced likelihood of Zika virus transmission in the Americas, compared with 2016 (2,24).

Efforts to develop and validate Zika virus serologic assays with improved specificity for Zika virus infection and the ability to distinguish a recent infection from a previous infection are ongoing. CDC is currently working with multiple manufacturers to validate tests in development and will update testing recommendations as new information becomes available.

^{††} <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika>.

^{§§} <https://www.cdc.gov/zika/laboratories/lab-guidance.html>.

^{¶¶} Terms listed here are only examples of assay interpretation terminology because nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under the "Labeling" tab for the specific assay.

TABLE 1. Interpretation^{*,†} of results of nucleic acid and antibody testing^{§,¶} for suspected Zika virus infection — United States (including U.S. territories), July 2017

Zika virus NAT (serum)**	Zika virus NAT (urine)**	Zika virus IgM ^{††}	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Positive	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <ul style="list-style-type: none"> Repeat testing on original urine specimen If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM testing on a serum specimen collected ≥ 2 weeks after symptom onset or possible exposure or specimen collection date <ul style="list-style-type: none"> If repeat IgM result is positive,^{§§} interpret as evidence of acute Zika virus infection If repeat IgM result is not positive, interpret as no evidence of Zika virus infection
Positive	Negative or not performed	Positive	Not indicated	Not indicated	Acute Zika virus infection
Positive	Negative or not performed	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <ul style="list-style-type: none"> Repeat testing on original serum specimen If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM testing on a serum specimen collected ≥ 2 weeks after symptom onset or possible exposure or specimen collection date <ul style="list-style-type: none"> If repeat IgM result is positive, interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive,^{§§} interpret as no evidence of Zika virus infection
Negative	Negative or not performed	Any nonnegative result ^{¶¶}	≥ 10	< 10	Zika virus infection; timing of infection cannot be determined <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection
Negative	Negative or not performed	Any nonnegative result ^{¶¶}	< 10	Any result	No evidence of Zika virus infection
Negative	Negative or not performed	Any nonnegative result ^{¶¶}	≥ 10	≥ 10	Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection.
For areas where PRNT is not recommended[¶]					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended		Presumptive Zika virus infection; timing of infection cannot be determined***
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended		Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined***
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended		Insufficient information for interpretation <ul style="list-style-type: none"> Consider repeat testing
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended		No laboratory evidence of Zika virus infection

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

* Final interpretations of results of Zika virus tests should be performed after all testing is completed.

† Serology test results that indicate flavivirus infection should be interpreted in the context of circulating flaviviruses.

§ Dengue virus IgM testing is recommended for symptomatic pregnant women as well as for asymptomatic pregnant women residing in areas where PRNT is not recommended.

¶ Currently, PRNT confirmation is not routinely recommended for persons living in Puerto Rico.

** Serum must be submitted for all persons tested for Zika virus infection; a urine specimen for Zika virus NAT testing should always be submitted concurrently with a serum specimen.

†† For laboratory interpretation in the presence of dengue virus IgM results refer to <https://www.cdc.gov/dengue/clinlab/laboratory.html>.

§§ **Positive** results include "positive," "presumptive Zika virus positive," or "possible Zika virus positive." These are examples of assay interpretations that might accompany test results; positive serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under the "Labeling" for the specific assay.

¶¶ **Nonnegative** results include "positive," "equivocal," "presumptive positive," or "possible positive." These are examples of assay interpretations that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under "Labeling" for the specific assay.

*** Zika virus IgM positive result is reported as "presumptive positive or flavivirus infection" to denote the need to perform confirmatory PRNT titers against Zika virus, dengue virus, and other flaviviruses to which the person might have been exposed to resolve potential false-positive results that might have been caused by cross-reactivity or nonspecific reactivity. In addition, ambiguous test results (e.g., inconclusive, equivocal, and indeterminate) that are not resolved by retesting also should have PRNT titers performed to rule out a false-positive result. However, PRNT confirmation is currently not routinely recommended for persons living in Puerto Rico.

Updated Interim Guidance for Laboratory Testing of Pregnant Women with Exposure to Areas with Risk for Zika Virus Transmission

As many areas in the Americas move into a subsequent (e.g., a second or third) mosquito season after introduction of Zika virus, testing becomes more complex. Given the evolving situation and the many uncertainties, the updated testing algorithms for symptomatic and asymptomatic pregnant women (Figure 1) (Figure 2) emphasize a shared patient-provider decision-making model. Counseling is recommended before *and* after testing, and Zika virus test results should be interpreted in the context of several limitations (Box). To address new and emerging data, the laboratory interpretations of Zika virus testing (Table 1) have also been updated.

Health care providers should continue to ask pregnant women at each prenatal visit about possible Zika virus exposure (e.g., travel to, or residence in an area with risk for mosquito-borne Zika virus transmission or sex with a partner who has traveled to or resides in an area with risk for mosquito-borne Zika virus transmission), specifically *before* and *during* the current pregnancy. Health care providers should ask about presence of symptoms of Zika virus disease (e.g., fever, rash, arthralgia, and conjunctivitis) and place, duration, and type of travel to assess a woman's potential for Zika virus exposure. Data from other mosquito-borne illnesses indicate that intensity of transmission, duration of travel, and type of travel influence the likelihood of infection (25,26); these factors might also affect the likelihood of Zika virus acquisition. Knowledge of a pregnant woman's possible exposure to Zika virus *before* and *during* pregnancy is critical contextual information that should be used to tailor pretest and posttest counseling and interpretation of test results (Box). Zika virus IgM test results might be difficult to interpret for pregnant women who have had exposure to any area with risk for Zika virus transmission before the current pregnancy, and this difficulty underscores the importance of shared patient-provider decision-making.

Pregnant women with recent possible Zika virus exposure and symptoms of Zika virus disease. Testing for Zika virus infection is still recommended for pregnant women with symptoms of Zika virus disease and possible Zika virus exposure, with the main goal of establishing a diagnosis that accounts for their symptoms, or ruling out Zika virus infection so that an alternative diagnosis can be considered. Negative test results should prompt evaluation for other causes, which might include dengue virus or chikungunya virus infection, depending on the symptoms and epidemiology of circulating viruses.

Concurrent NAT (serum and urine) and serologic testing (serum) is recommended for pregnant women as soon as possible, through 12 weeks after symptom onset (Figure 1).

Reports of prolonged detection of Zika virus RNA in symptomatic pregnant women support longer time frames for the performance of molecular diagnostic testing (8–11,13–15). However, the proportion of pregnant women with this finding is unknown. Expanding the time frame for NAT testing through 12 weeks after symptom onset allows for a longer period in which to make a NAT-confirmed diagnosis of Zika virus infection in some pregnant women. However, because of the potential for false-positive NAT results (6,27),*** updated recommendations include NAT testing of both serum and urine and concurrent Zika virus IgM antibody testing to confirm the diagnosis of acute Zika virus infection with more than one test (Table 1).

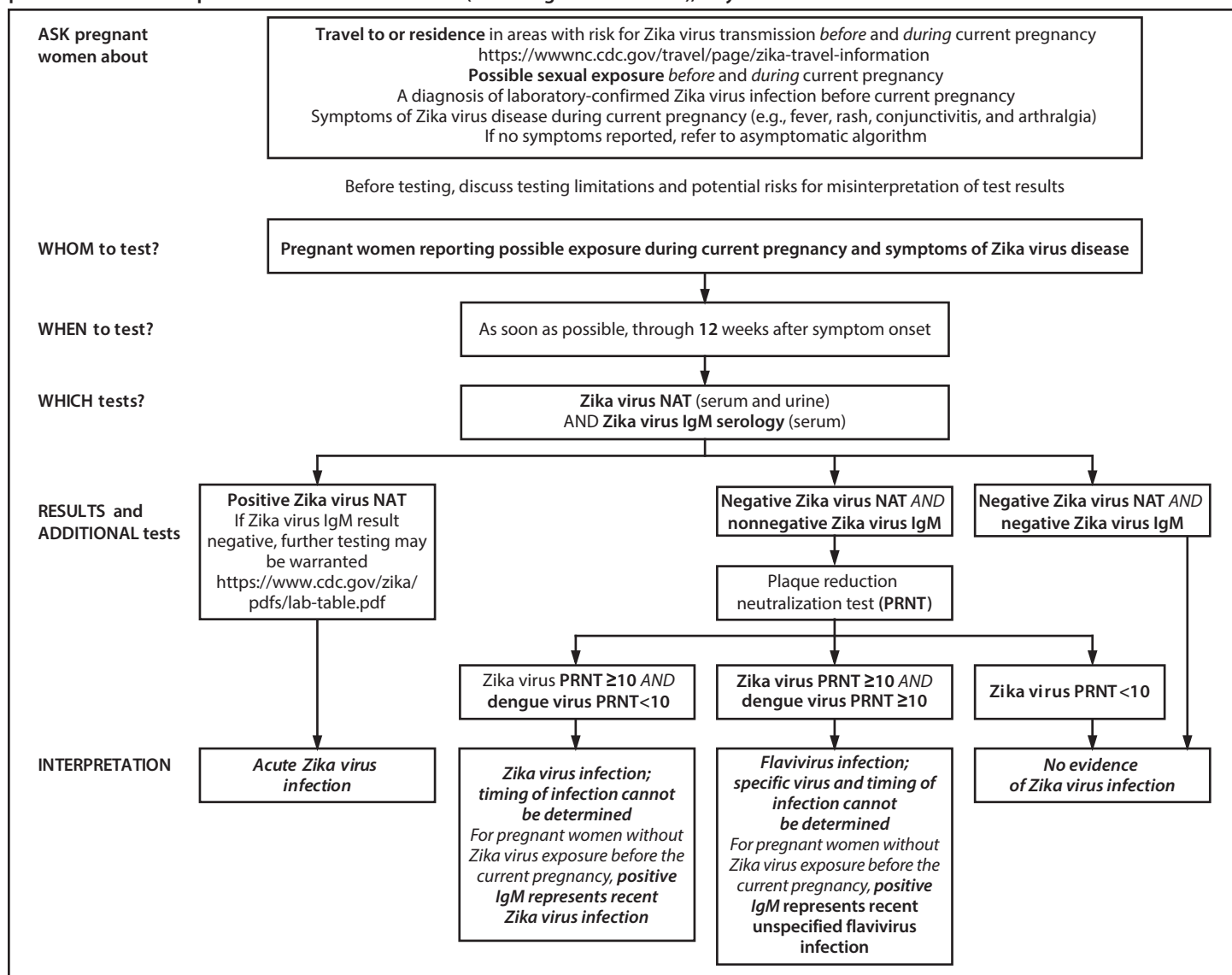
For women who seek care >12 weeks after symptom onset, Zika virus IgM testing might be considered; however, a negative result does not rule out an infection during pregnancy because IgM levels decline over time. A positive result should be interpreted within the context of the known limitations of serologic testing.

Asymptomatic pregnant women with ongoing possible Zika virus exposure. For asymptomatic pregnant women *with ongoing* exposure to Zika virus, testing for Zika virus infection should be offered as part of routine obstetric care because it might identify acute infection during pregnancy (Figure 2). Previous guidance recommended IgM testing with reflex NAT once during the first and second trimester of pregnancy for women with *ongoing* possible Zika virus exposure (28). IgM testing is no longer routinely recommended because of the limitations of IgM tests and the difficulty in interpreting results.

The optimal timing and frequency for testing asymptomatic pregnant women with NAT alone is unknown; NAT for asymptomatic pregnant women should be informed by jurisdictional trends in Zika virus transmission, the duration of ongoing possible exposure during pregnancy, and data on the duration of Zika virus RNA detection in body fluids. For pregnant women who have received a diagnosis of **laboratory-confirmed** Zika virus infection any time *before* or *during* the current pregnancy, additional Zika virus testing is not recommended. For women without a prior laboratory-confirmed diagnosis of Zika virus, NAT should be offered at the initiation of prenatal care, and if Zika virus RNA is not detected on clinical specimens, two additional NAT tests should be offered during the course of the pregnancy coinciding with prenatal visits. The proportion of fetuses and infants with Zika virus-associated birth defects is highest among women with first and early second trimester infections (29); therefore, conducting all NAT during the first and second trimesters might

*** Page 52 at <https://www.fda.gov/downloads/MedicalDevices/Safety/EmergencySituations/UCM491592.pdf>.

FIGURE 1. Updated interim testing recommendations^{*,†,§,¶,**,††,§§} and interpretation of results^{¶¶} for symptomatic pregnant women with possible Zika virus exposure^{***,†††} — United States (including U.S. territories), July 2017



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

* Ask about type and duration of Zika virus exposure before and during current pregnancy. Exposure before the current pregnancy might limit interpretation of Zika virus IgM results; pretest counseling can help inform testing decisions. Some patients may choose not to receive Zika virus IgM testing.

† Zika virus testing is not routinely recommended for pregnant women with a previous diagnosis of laboratory-confirmed Zika virus infection by either NAT or serology (positive/equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥10 and dengue virus PRNT <10 results).

§ This algorithm also applies to pregnant women with possible Zika virus exposure who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus syndrome.

¶ The duration of detectable Zika virus RNA in pregnant women following infection is not known. Preliminary data suggest that NAT might remain positive for several weeks after symptom onset in some pregnant women. Zika virus IgM antibodies are most likely to be detected within 12 weeks after infection; however, IgM antibodies might be detected for months after infection, limiting the ability to determine whether infection occurred before or during the current pregnancy.

** Dengue virus IgM antibody testing is recommended for symptomatic pregnant women. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dengue/clinlab/lab-table.html>.

†† Nonnegative results include “positive,” “equivocal,” “presumptive positive,” or “possible positive.” These are examples of assay interpretation that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under the “Labeling” tab for the specific assay.

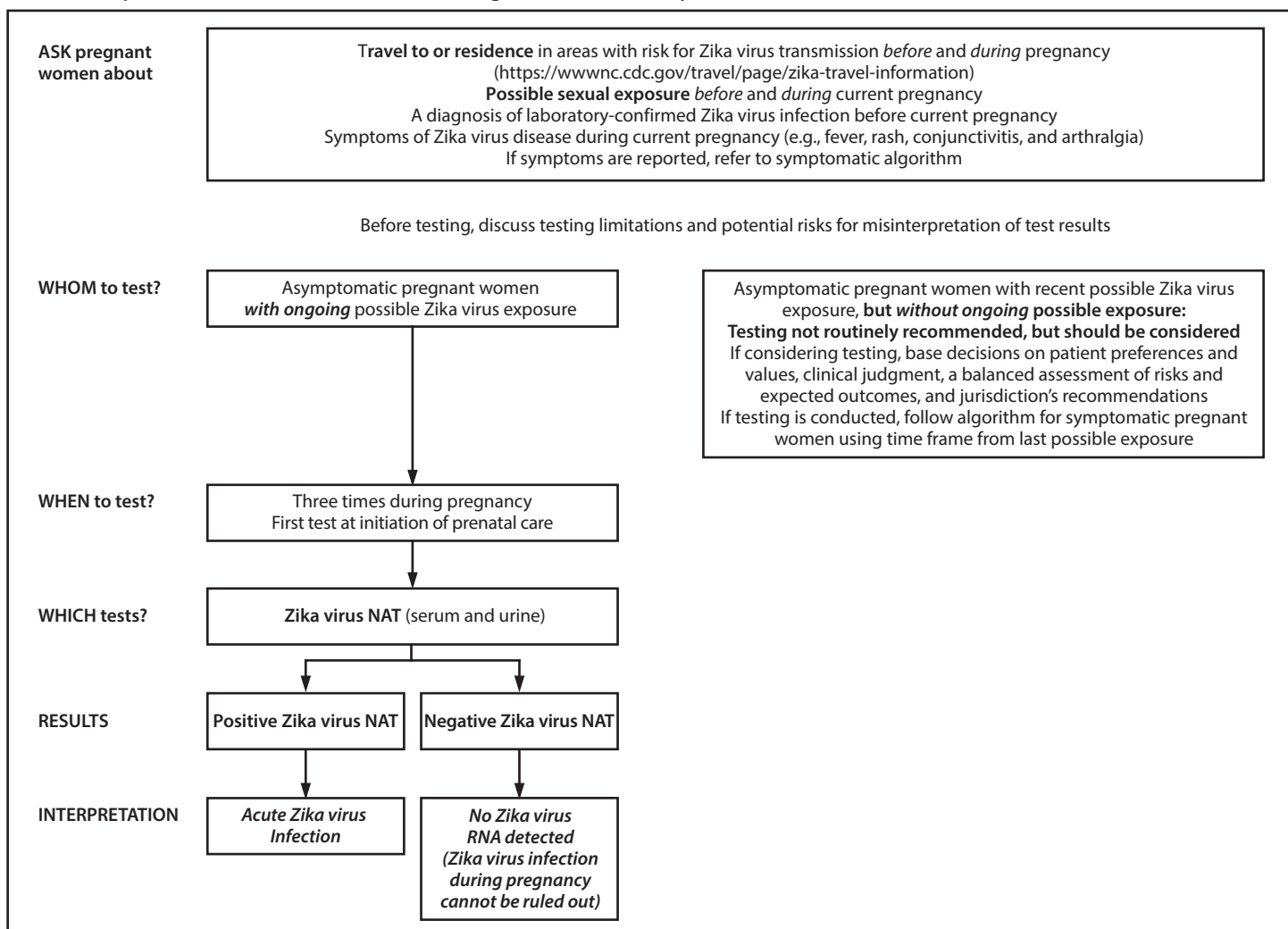
§§ Currently, PRNT confirmation is not routinely recommended for persons living in Puerto Rico. For laboratory interpretation in the absence of PRNT testing, refer to <https://www.cdc.gov/zika/pdfs/lab-table.pdf>.

¶¶ Despite the high specificity of NAT, false-positive NAT results have been reported. **If both serum and urine specimens are NAT-positive, regardless of IgM antibody results, results should be interpreted as evidence of acute Zika virus infection. If either serum or urine specimen is NAT-positive in conjunction with a positive Zika virus IgM, results should be interpreted as evidence of acute Zika virus infection.** If NAT is only positive on serum or urine and IgM testing is negative, repeat testing on the original NAT-positive specimen. **If repeat NAT is positive, results should be interpreted as evidence of acute Zika virus infection.** If repeat NAT testing is negative, results are indeterminate and health care providers should repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset. **If subsequent IgM antibody test is positive, interpret as evidence of acute Zika virus infection,** but if negative, interpret as no evidence of Zika virus infection.

*** Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://wwwnc.cdc.gov/travel/page/zika-travel-information>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period]), or sex without a condom during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission.

††† For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/ flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.

FIGURE 2. Updated interim testing recommendations^{*,†,§} and interpretation of results^{¶,**} for asymptomatic pregnant women with possible Zika virus exposure^{††,§§,¶¶} — United States (including U.S. territories), July 2017



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

* Ask about type and duration of Zika virus exposure before and during the current pregnancy. Exposure before the current pregnancy might limit interpretation of Zika virus IgM results; pretest counseling can help inform testing decisions.

† Zika virus testing is not routinely recommended for pregnant women with a previous diagnosis of laboratory-confirmed Zika virus infection by either NAT or serology (positive/equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥ 10 and dengue virus PRNT < 10 results).

§ The interval for Zika virus NAT testing during pregnancy is unknown. Preliminary data suggest that NAT might remain positive for several weeks after infection in some pregnant women. For women without a prior *laboratory-confirmed* diagnosis of Zika virus, NAT testing should be offered at the initiation of prenatal care, and if Zika virus RNA is not detected on clinical specimens, two additional tests should be offered during the course of the pregnancy coinciding with prenatal visits. The proportion of fetuses and infants with Zika virus–associated birth defects is highest among women with first and early second trimester infections; therefore, conducting all NAT testing during the first and second trimesters might be considered to help identify infections early in pregnancy. However, adverse outcomes have been associated with infection diagnosed in the third trimester; therefore, testing every trimester might be considered.

¶ Despite the high specificity of NAT, false-positive NAT results have been reported. **If both serum and urine specimens are NAT-positive, interpretation should be acute Zika virus infection.** If NAT is only positive on serum or urine, testing should be repeated on the original NAT-positive specimen. **If repeat NAT is positive, results should be interpreted as evidence of acute Zika virus infection.** If repeat NAT testing is negative, results are indeterminate and health care providers should perform IgM testing on a specimen collected ≥ 2 weeks after initial specimen collection. For laboratory interpretation, refer to <https://www.cdc.gov/zika/pdfs/lab-table.pdf>.

** A negative Zika virus NAT result does not exclude infection during pregnancy because it represents a single point in time. Zika virus RNA levels decline over time, and the duration of the presence of Zika virus RNA in serum and urine following infection varies among pregnant women. Despite Zika virus IgM antibody test limitations (e.g., cross-reactivity with other flaviviruses and prolonged detection for months, presenting challenges in determining the timing of infection), which should be discussed as part of pretest counseling, patients may still choose to receive Zika virus IgM testing.

†† Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://wwwnc.cdc.gov/travel/page/zika-travel-information>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period]), or sex without a condom, during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission.

§§ Persons *with ongoing* possible Zika virus exposure include those who reside in or frequently travel (e.g., daily or weekly) to an area with risk for Zika virus transmission.

¶¶ For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.

BOX. Key information needed for deciding whether to test and how to interpret serology results

- Pregnant women with possible Zika virus exposure should be asked about their risk for exposure both before and during the current pregnancy. Health care providers should ask about the presence of symptoms of Zika virus disease (e.g., fever, rash, arthralgia, and conjunctivitis), and place, duration, and type of travel to assess a woman's potential for exposure to Zika virus and other flaviviruses (e.g., dengue or West Nile viruses).
- It is important to ascertain whether a woman had exposure to Zika virus before the current pregnancy because Zika virus immunoglobulin M (IgM) antibodies can be detected for months after an infection. A positive Zika virus IgM result could indicate antibodies from infection before the current pregnancy, thus limiting the ability to distinguish between an infection that occurred *before* the current pregnancy and one that occurred *during* the current pregnancy.
- It is important to ascertain whether a woman had exposure to flaviviruses other than Zika virus before the current pregnancy because a positive IgM result might have been caused by cross-reactivity from a previous flavivirus exposure.
- Health care providers and counselors should provide appropriate pretest counseling to inform decisions on whether to test; Zika virus test results should be interpreted within the context of known limitations.
- A negative Zika virus IgM test result, if performed during the recommended time frame, in the setting of a negative Zika virus nucleic acid test (NAT) result, provides some reassurance of absence of Zika virus infection during the current pregnancy. However, a negative Zika virus IgM test result should be interpreted within the context of the limitations of the assay.
- When plaque reduction neutralization testing (PRNT) is indicated and performed during the recommended time frame, a negative PRNT result in the setting of a negative NAT result indicates that there is no laboratory evidence of Zika virus infection.

be considered to help identify infections early in pregnancy. However, adverse outcomes have been associated with infection diagnosed in the third trimester (28); therefore testing every trimester might also be considered.

Serologic testing is not routinely recommended for asymptomatic pregnant women with ongoing possible Zika virus exposure because of the potential for prolonged detection of Zika virus IgM, which poses challenges in determining whether the infection and therefore

the risk of congenital Zika virus infection, occurred during the current pregnancy. In addition, in areas with ongoing dengue virus transmission, a positive Zika virus IgM result might occur because of serologic cross-reactivity. Despite these limitations, which should be discussed as part of pretest counseling, patients may still choose to receive Zika virus IgM testing (Table 1).

Although a recommendation to consider Zika virus IgM testing as part of preconception counseling to establish baseline IgM results for nonpregnant women *with ongoing* possible Zika virus exposure was previously issued, Zika virus IgM is no longer routinely recommended for asymptomatic pregnant women *with ongoing* possible Zika virus exposure, and therefore baseline preconception testing is not warranted. Zika virus testing is not recommended to determine timing of conception or pregnancy for couples in which one or both partners has had possible Zika virus exposure. Zika virus testing for this purpose is of uncertain value because: 1) IgM testing has diagnostic limitations; 2) Zika virus NAT testing of serum does not reflect persistence in other body fluids (e.g., semen). The current understanding of Zika virus shedding in genital secretions is limited (30); testing semen and vaginal fluids for Zika virus is not currently available outside research settings.

Asymptomatic pregnant women with recent possible Zika virus exposure (i.e., through travel or sex) but *without ongoing* possible exposure. For asymptomatic pregnant women with recent possible Zika virus exposure (i.e., through travel or sex), but *without ongoing* possible exposure, testing for Zika virus infection is not routinely recommended. However, testing should be considered using a shared decision-making model, one in which patients and providers work together to make decisions about testing and care plans based on patient preferences and values, clinical judgment, a balanced assessment of risks and expected outcomes, and the jurisdiction's recommendations. Health care providers should consider potential exposure risk factors when deciding whether to advise testing. These include symptoms, type and length of possible exposure, Zika virus transmission trends at location of possible exposure and the use of prevention measures (e.g., insect repellent, appropriate clothing, and condom use). Jurisdictional recommendations may take into account the epidemiology of Zika virus transmission and other epidemiologic considerations (e.g., seasonality and mosquito surveillance and control factors) in areas with risk for Zika virus transmission and, therefore, might include a routine recommendation to test asymptomatic pregnant women either for clinical care or as part of Zika virus infection surveillance.

Although preliminary data indicate that the risk for Zika virus-associated birth defects does not differ by maternal symptom status, testing is not routinely recommended for asymptomatic pregnant women with recent possible Zika virus exposure but

without ongoing possible exposure to address the increased probability of false positive results in the setting of the declining prevalence of Zika virus disease (28,29). The limitations of currently available tests and the lack of a vaccine or an effective therapy to prevent congenital infection or mitigate sequelae of Zika virus infection during pregnancy, or in the neonate, underscore the importance of shared patient-provider decision-making. The decision about Zika virus testing should take into account the patient's unique circumstances and should allow pregnant women to make an informed decision about the utility of testing. If testing is conducted for asymptomatic pregnant women *with recent possible Zika virus exposure, but without ongoing possible exposure*, the testing algorithm for symptomatic pregnant women with possible Zika virus exposure (Figure 1) should be used, applying time frames from last possible Zika virus exposure.

Pregnant women with possible Zika virus exposure who have a fetus with prenatal ultrasound findings consistent with congenital Zika virus syndrome. Maternal Zika virus NAT and IgM testing should be performed. Consideration of amniocentesis should be individualized because data about its usefulness in diagnosing congenital Zika virus infection are limited. If amniocentesis is performed as part of clinical care, NAT testing should be performed on amniocentesis specimens. A recent study reported that detection of Zika virus RNA in amniocentesis specimens from pregnancies with a fetus with Zika virus–associated birth defects indicate fetal infection. However, data also suggested that detection of Zika virus RNA in amniotic fluid could be transient and that Zika virus RNA might not always be detectable in amniotic fluid after fetal infection (13).

Updated Interim Guidance for Prenatal Management of Pregnant Women with Laboratory Evidence of Possible Zika Virus Infection^{†††}

For pregnant women with laboratory evidence of possible Zika virus infection, serial fetal ultrasounds (every 3–4 weeks) should be considered to assess fetal anatomy, particularly fetal neuroanatomy, and to monitor growth. A study of 17 pregnancies in symptomatic women with laboratory-confirmed Zika

virus infection and adverse fetal outcomes in Colombia and a summary of eight published studies of 37 pregnancies reported a median of 18 weeks from symptom onset to prenatal diagnosis of microcephaly (31). This finding is consistent with other reports about prenatal diagnosis of microcephaly. Among 37 pregnancies with confirmed or suspected Zika virus infection, a median of 21 weeks (range = 3–29 weeks) from maternal symptom onset to prenatal diagnosis of microcephaly was observed (31). Given the length of time for the detection of prenatal microcephaly, prenatal ultrasounds should carefully evaluate the fetal anatomy, particularly the neuroanatomy, to identify brain or structural abnormalities that might occur before microcephaly.

Decisions about performing amniocentesis should be individualized because there is a paucity of data regarding the usefulness of amniocentesis in diagnosing congenital Zika virus infection. The presence of Zika virus RNA in the amniotic fluid might indicate fetal infection; however, a negative result does not exclude congenital Zika virus infection. The optimal time to perform amniocentesis to diagnose congenital Zika virus infection is not known; health care providers should discuss the risks and benefits of amniocentesis with their patients.

This guidance also applies to pregnant women with laboratory evidence of presumptive Zika virus or flavivirus infection; timing of infection cannot be determined (Table 1).

Updated Interim Guidance for the Evaluation of Placental and Fetal Tissue Specimens for Zika Virus Infection

Detection of Zika virus RNA has been reported in placental tissues and in fetal and infant brain tissue 15–210 days (mean = 81 days) and 119–238 days (mean = 163 days), respectively, from maternal symptom onset (32). Among 546 live births with travel-associated possible maternal Zika virus exposure in the 50 U.S. states and the District of Columbia in 2016 for which placental specimens were submitted to CDC, 60 (11%) were positive for Zika virus RNA (33). When restricted to live births without a laboratory-confirmed Zika virus infection based on maternal or infant Zika virus testing of serum or urine, 47 of 482 (10%) were positive for Zika virus RNA (33). Although, the proportion of live births with positive placental reverse-transcription polymerase chain reaction (RT-PCR) results was relatively low, these results provided definitive evidence of maternal Zika virus infection during that pregnancy. As with serologic and NAT testing of serum and urine, the proportion of pregnancies with a positive Zika virus RT-PCR on tissue specimens is expected to decrease in the setting of declining prevalence of Zika virus disease in the Americas.

^{†††} Laboratory evidence of possible Zika virus infection during pregnancy is defined as 1) Zika virus infection detected by a Zika virus RNA nucleic acid test (NAT) on any maternal, placental, or fetal specimen (referred to as NAT-confirmed) or 2) diagnosis of Zika virus infection, timing of infection cannot be determined or unspecified flavivirus infection, timing of infection cannot be determined by serologic tests on a maternal specimen (i.e., positive/equivocal Zika virus immunoglobulin M [IgM] and Zika virus plaque reduction neutralization test [PRNT] titer ≥ 10 , regardless of dengue virus PRNT value; or negative Zika virus IgM, and positive or equivocal dengue virus IgM, and Zika virus PRNT titer ≥ 10 , regardless of dengue virus PRNT titer). The use of PRNT for confirmation of Zika virus infection, including in pregnant women and infants, is not routinely recommended in Puerto Rico (<https://www.cdc.gov/zika/laboratories/lab-guidance.html>).

Testing placental tissue specimens from pregnancies with possible Zika virus exposure that result in live births can be considered for diagnostic purposes in certain scenarios. It may be considered for symptomatic pregnant women and women with infants with possible Zika virus–associated birth defects, without a definitive diagnosis of laboratory-confirmed Zika virus infection during pregnancy (Table 2). Similar to the updated testing recommendations for asymptomatic pregnant women who have recent possible Zika virus exposure but *without ongoing* possible exposure, testing of placental tissues is not routinely recommended; however, it should be considered for women who have a fetus or infant with possible Zika virus–associated birth defects.

Finally, testing of placental and fetal tissues may be considered in selected scenarios for pregnancies resulting in a miscarriage or fetal loss/stillbirth (and testing of autopsy tissues in the event of an infant death) to provide insight into the potential etiology of the fetal loss or infant death (Table 2), which could inform a woman’s future pregnancy planning. Additional information is available at <https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html>.

Implications of Updated Interim Guidance for Laboratory Testing of Pregnant Women with Possible Zika Virus Exposure for the Evaluation and Care of Infants with Possible Congenital Zika Virus Exposure

Interim guidance for the evaluation of infants with congenital Zika virus exposure has been previously published; infants who meet one or more of the published criteria for testing for congenital Zika virus infection should be tested and evaluated in accordance with the updated CDC interim guidance for the evaluation and management of infants with possible Zika virus infection (34). However, in light of the updated recommendations that will likely reduce routine Zika virus testing of asymptomatic pregnant women with recent possible Zika virus exposure but *without ongoing* possible exposure, it is critical that pediatric health care providers inquire about possible maternal and congenital Zika virus exposure for every newborn. Infants born to mothers with possible Zika virus exposure during pregnancy but who did not receive testing, including asymptomatic pregnant women

with recent possible Zika virus exposure but *without ongoing* possible exposure, should receive a comprehensive physical examination, including standardized measurement of head circumference and newborn hearing screen, as part of routine pediatric care. In addition, based on the level of possible Zika virus exposure (e.g., duration and type of exposure, use of prevention measures, intensity of Zika virus transmission at the location of travel), the provider should consider whether further evaluation of the newborn for possible congenital Zika virus infection is warranted, in which case, a head ultrasound, and ophthalmologic assessment should be considered. Based on results of the evaluation, testing of the infant for Zika virus infection could be considered.

This guidance also applies to infants born to mothers with negative maternal testing in the setting of ongoing possible Zika virus exposure or a possible Zika virus exposure that occurred more than 12 weeks before maternal testing (<https://www.cdc.gov/zika/hc-providers/infants-children/evaluation-testing.html>). Recommendations for outpatient management during the first 12 months of life include monitoring of head circumference and development and are provided in the updated CDC interim guidance for the evaluation and management of infants with possible Zika virus infection (34).

Prevention of Zika Virus Infection

CDC recommends that pregnant women avoid travel to any area with risk for Zika virus transmission. To prevent Zika virus infection during pregnancy, all pregnant women and their partners should receive counseling on prevention measures including strategies to prevent mosquito bites and sexual transmission of Zika virus (35). If pregnant women must travel, CDC recommends strict adherence to strategies to prevent mosquito bites and sexual transmission. Pregnant women living in areas with risk for Zika virus transmission should also follow these strategies. Couples wishing to conceive should receive preconception counseling about how to minimize risks for Zika virus infection (30). Other persons at risk for Zika virus exposure should receive information on travel and strategies to prevent mosquito bites and sexual transmission. §§§

§§§ <https://www.cdc.gov/zika/prevention/index.html>.

TABLE 2. Interim guidance for Zika virus testing* of formalin-fixed, paraffin-embedded placental, fetal, or infant autopsy tissues† for completed pregnancies with possible Zika virus exposure‡ during pregnancy¶ — United States (including U.S. territories), July 2017

Pregnancy outcome	Maternal Zika virus test results on nontissue clinical specimens (e.g., serum, urine)				
	Acute Zika virus infection**	Zika virus infection; timing of infection cannot be determined††	Flavivirus infection; timing of infection cannot be determined	>12 weeks after symptom onset or exposure,§§ with either negative maternal Zika virus IgM, or no maternal testing conducted	No evidence of Zika virus infection¶¶
Testing of placental tissues					
Live birth, possible Zika virus–associated birth defects***	Not indicated†††		Should be considered to aid in maternal diagnosis		Not indicated†††
Live birth, no obvious Zika virus–associated birth defects at birth	Not indicated		May be considered to aid in maternal diagnosis on a case-by-case and jurisdictional basis. Not routinely recommended for asymptomatic women with possible Zika virus exposure but <i>without ongoing</i> possible exposure		Not indicated
Testing of placental and fetal tissues					
Pregnancy loss, possible Zika virus–associated birth defects	May be considered to aid in fetal diagnosis		May be considered to aid in fetal and maternal diagnosis		Not indicated†††
Pregnancy loss, no obvious Zika virus–associated birth defects	May be considered to aid in fetal diagnosis		May be considered to aid in fetal and maternal diagnosis		Not indicated†††
Testing of placental and infant autopsy tissues					
Infant death following live birth	Should be considered to aid in infant diagnosis		Should be considered to aid in infant and maternal diagnosis		Not indicated†††

Abbreviations: IHC = immunohistochemistry; NAT = nucleic acid test; RT-PCR = reverse-transcription polymerase chain reaction.

* Zika virus testing on formalin-fixed, paraffin embedded tissue specimens is conducted at CDC's Infectious Diseases Pathology Branch (IDPB) and includes Zika virus RT-PCR on placental and fetal/infant tissues. Zika virus IHC may be performed on placental tissues into the second trimester, fetal tissues from any gestational age, and infant autopsy tissues.

† Placental tissues include placental disc, umbilical cord, and fetal membranes. Zika virus RNA can be focal within placental tissues, and testing of three sections of placenta, one section of umbilical cord, and one section of fetal membrane is recommended (<https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html>). For pregnancy losses and infant deaths, submission of placental tissues in addition to fetal or infant autopsy tissues, if available, is preferred, but if not available will not preclude placental testing.

‡ Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://www.cdc.gov/zika/geo/index.html>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period]), or sex without a condom, during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission.

¶ Zika virus testing is not routinely recommended for asymptomatic pregnant women with recent possible Zika virus exposure but *without ongoing* exposure and who have a fetus or infant without Zika virus–associated birth defects.

** In the event of a confirmed maternal acute Zika virus infection or confirmed congenital Zika virus infection in the infant (e.g., a positive NAT), placental testing from live births is not indicated. Currently, placental testing does not routinely provide additional diagnostic information in the setting of a maternal or infant diagnosis of acute or congenital Zika virus infection, respectively.

†† For women with no possible Zika virus exposure before the current pregnancy, a positive IgM result likely represents acute Zika virus infection, and placental testing is not indicated.

§§ All or part of possible maternal Zika virus exposure, or symptom onset occurred >12 weeks before maternal serum specimen was collected.

¶¶ Includes pregnant women with negative Zika virus NAT and negative Zika virus IgM ≤12 weeks after symptom onset or exposure.

*** Possible Zika virus–associated birth defects that meet the CDC surveillance case definition include the following: brain abnormalities and/or microcephaly, intracranial calcifications, ventriculomegaly, neural tube defects and other early brain malformations, eye abnormalities, or other consequences of central nervous system dysfunction including arthrogyrosis (joint contractures), congenital hip dysplasia, and congenital deafness (<https://www.cdc.gov/zika/geo/pregnancy-outcomes.html>). In all cases, infants or fetuses with possible Zika virus–associated birth defects should also be evaluated for other etiologies of congenital anomalies.

††† Testing may be considered on a case-by-case basis, consult CDC for case-specific questions at <https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html>.

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Conflict of Interest

No conflicts of interest were reported.

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SCREENING PREGNANT WOMEN FOR ZIKA TESTING



To Be Administered by a Nurse or Other Healthcare Provider

Pregnant women should be asked about any possible Zika virus exposure, before and during their pregnancy, at each prenatal visit. Use this tool to evaluate pregnant women for exposure to Zika virus and symptoms of Zika virus disease to determine whether testing is indicated. Visit CDC's map to determine [areas with risk of Zika](#).



Questions to ask your patient to determine if she needs Zika testing:

- ✓ Have you traveled during pregnancy?
 - Where did you travel?
 - How long did you stay?
- ✓ Have you lived in any area where mosquitoes are spreading Zika during your pregnancy?
- ✓ Has your partner lived in or traveled to any area where mosquitoes are spreading Zika during your pregnancy?
 - When and where did your partner travel?
 - Did your partner have any signs or symptoms of Zika (including fever, rash, headache, joint pain, red eyes, or muscle pain) when he or she were on the trip, or after returning?
 - Did you have sex without a condom with your partner after they returned from the trip?
- ✓ Have you had any symptoms of Zika during your pregnancy?
 - Use the chart on page 2 of this document to discuss Zika symptoms. The most common symptoms of Zika are fever, rash, headache, joint pain, red eyes, and muscle pain.

Use the responses to the questions above to determine if Zika testing is indicated.

Testing is recommended for

- Symptomatic pregnant women possibly exposed to Zika (who lived in or traveled to or have unprotected sex with a partner who lived in or traveled to an area with risk of Zika), and
- Asymptomatic pregnant women who have ongoing exposure (who live in or frequently travel to) to areas with risk of Zika.

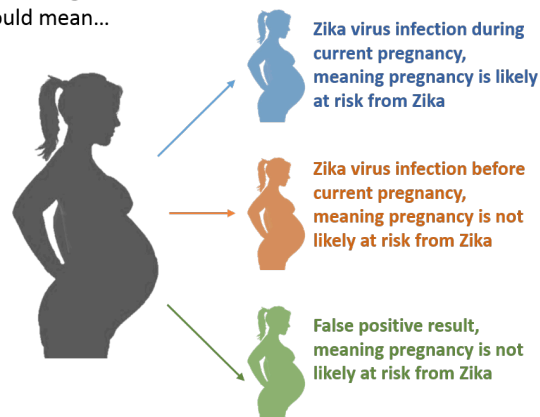
Testing is not routinely recommended for asymptomatic pregnant women with recent possible Zika exposure but without ongoing possible exposure. However, testing may be considered as a shared decision between patients and providers, according to patient preferences and clinical judgement, or if a state or local area recommends it.

Other considerations that might affect interpretation of Zika test results:

- ✓ Did you live in any area where mosquitoes were spreading Zika before you became pregnant?
- ✓ Have you frequently traveled (for example, daily or weekly) to one of these areas before you became pregnant?
- ✓ If you did visit one of these areas before pregnancy, did you protect yourself from mosquito bites?
 - Did you wear long sleeves and pants?
 - Did you use insect repellent through the day and night? Did you follow the instructions on the label?
 - Did you stay somewhere with window and door screens or air conditioning?

If your patient reports exposure to any area with risk of Zika before her current pregnancy, the test that looks for Zika IgM antibodies may be difficult to interpret and may have limited usefulness for clinical decision-making. The patient may choose not to be tested. For more information, visit [CDC's website](#).

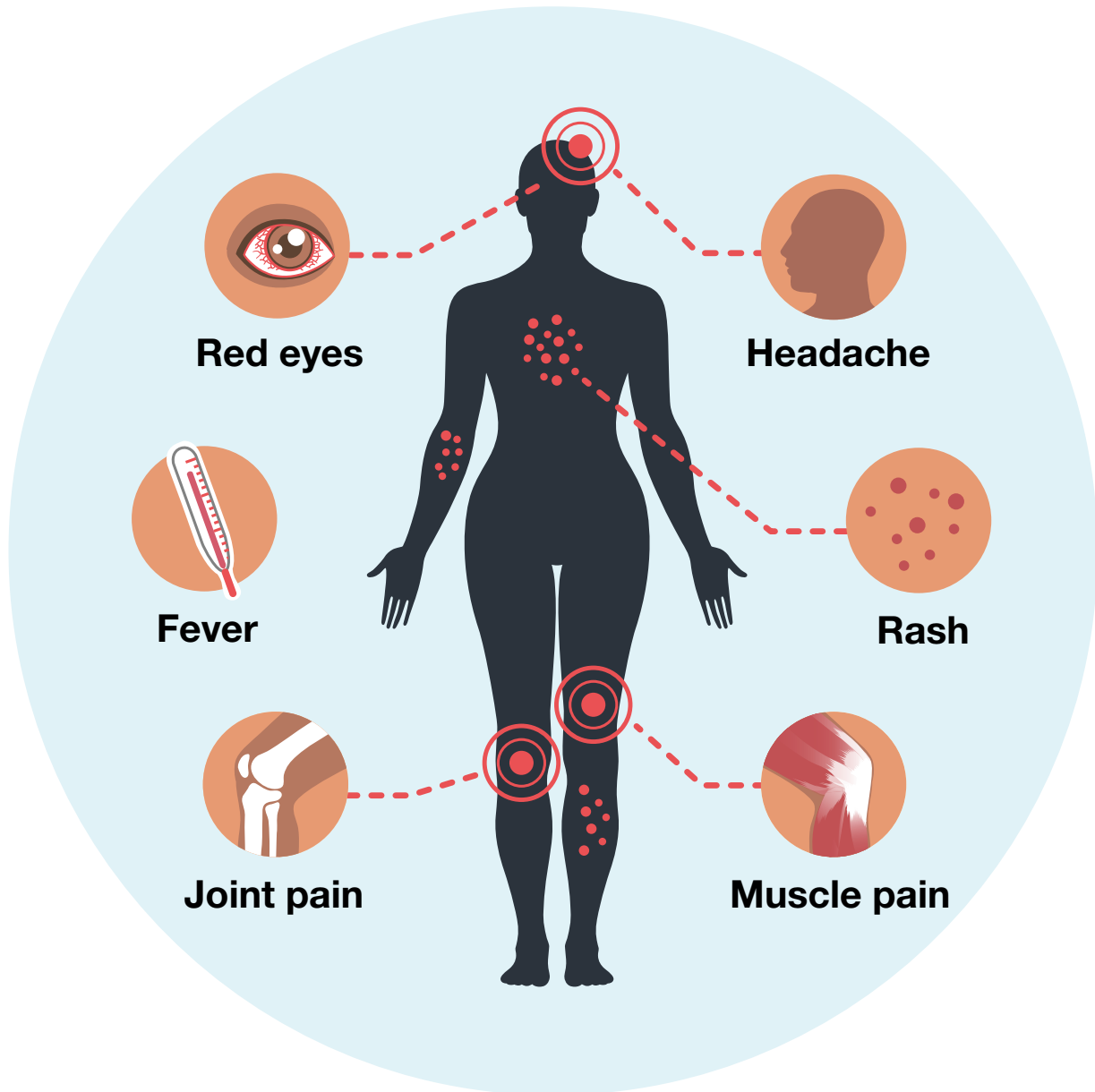
A positive Zika IgM test result could mean...



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

Zika Symptoms

The most common symptoms for Zika are fever, rash, headache, joint pain, and muscle pain.



UPDATED INTERIM PREGNANCY GUIDANCE: SYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE



Testing Recommendations and Interpretation of Results for Healthcare Providers

ASK PREGNANT WOMEN ABOUT

Travel to or residence in any areas with risk for Zika virus transmission *before and during* the current pregnancy^{1,2} • Possible sexual exposure *before and during* the current pregnancy
A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy³ • Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia)
If no symptoms reported, refer to asymptomatic algorithm.

Before testing, discuss testing limitations and potential risks for misinterpretations of test results.

WHOM to test?

Pregnant women reporting possible exposure during current pregnancy and symptoms of Zika virus disease⁴

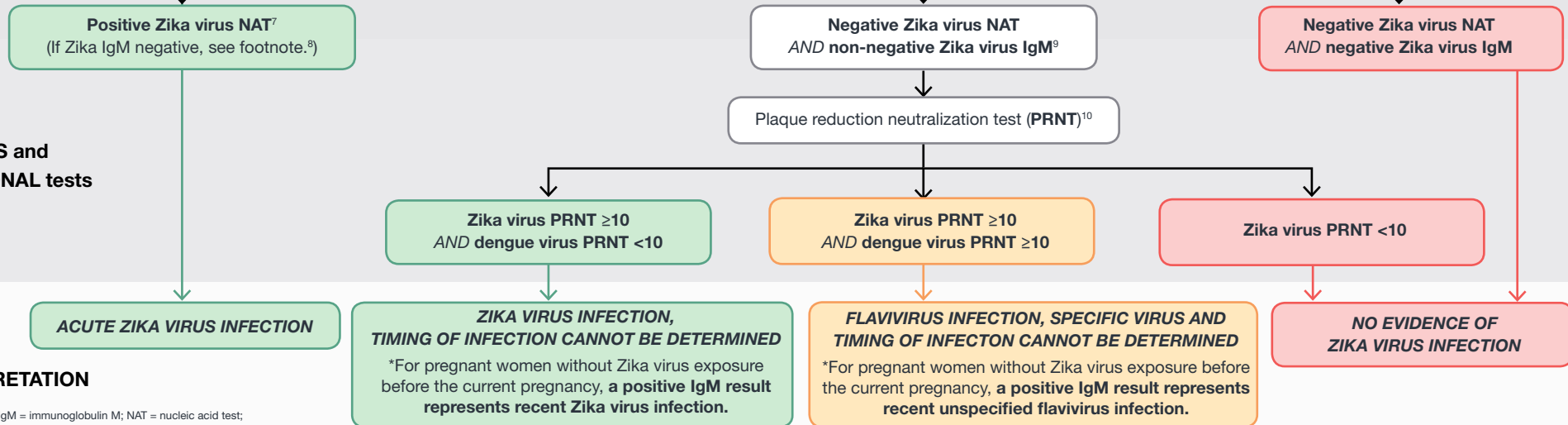
WHEN to test?

Test as soon as possible; through 12 weeks after symptom onset

WHICH tests?

Zika virus NAT (serum and urine) AND Zika virus IgM serology (serum)^{5,6}

RESULTS and ADDITIONAL tests



INTERPRETATION

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

- Ask about type and duration of Zika virus exposure before and during the current pregnancy. Exposure before the current pregnancy might limit interpretation of Zika virus IgM antibody results; pretest counseling can help inform testing decisions. Some patients may choose not to receive Zika virus IgM testing.
- Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://www.cdc.gov/travel/page/zika-travel-information>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period]), or sex without a condom during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission.
- Zika virus testing is not routinely recommended for pregnant women with a previous diagnosis of laboratory-confirmed Zika virus infection by either NAT or serology (positive/equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥10 and dengue virus PRNT <10 results).
- This algorithm also applies to pregnant women with possible Zika virus exposure who have a fetus with prenatal ultrasound findings consistent with congenital Zika syndrome.
- The duration of detectable ZIKA virus in pregnant women following infection is not known. Preliminary data suggest NAT may remain positive for several weeks after symptom onset in some pregnant women. Zika virus IgM antibodies are most likely to be detected within 12 weeks after infection however IgM antibodies

- might be detected for months after infection, limiting the ability to determine whether infection occurred before or during the current pregnancy.
- Dengue virus IgM antibody testing is recommended for symptomatic pregnant women. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dengue/clinicallab/laboratory.html>
- Despite the high specificity of NAT, false positive NAT results have been reported. **If both serum and urine specimens are NAT-positive, regardless of IgM antibody results, results should be interpreted as evidence of acute Zika virus infection. If either serum or urine specimen is NAT positive in conjunction with a positive Zika virus IgM (see Table 1), results should be interpreted as evidence of acute Zika virus infection.**
- If NAT is only positive on serum or urine and IgM antibody testing is negative, repeat testing on the original NAT positive specimen. **If repeat NAT is positive, results should be interpreted as evidence of acute Zika virus infection.** If repeat NAT testing is negative, results are indeterminate and healthcare providers should repeat Zika virus IgM antibody testing on a serum specimen collected ≥ 2 weeks after symptom onset. **If subsequent IgM antibody test is positive, interpret as evidence of acute Zika virus infection but if negative, interpret as no evidence of Zika virus infection.**

- Non-negative results include positive, equivocal, presumptive positive, or possible positive. These are examples of assay interpretations that might accompany test results; non-negative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika>, under the "Labeling" for the specific assay.
- Currently, PRNT confirmation is not routinely recommended for individuals living in Puerto Rico. For laboratory interpretation in the absence of PRNT testing, refer to Table 1.
Note: For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/ flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.



TABLE 1. Interpretation of results¹ of nucleic acid and antibody^{2,3} testing for suspected Zika virus infection — United States (including US territories), 2017

Zika NAT (serum) ⁴	Zika NAT (urine) ⁴	Zika virus IgM ⁵	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Positive	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original urine specimen</i> <ul style="list-style-type: none"> If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date <ul style="list-style-type: none"> If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Positive	Negative or not performed	Positive	Not indicated	Not indicated	Acute Zika virus infection
Positive	Negative or not performed	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original serum specimen</i> <ul style="list-style-type: none"> If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date <ul style="list-style-type: none"> If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥10	<10	Zika virus infection; timing of infection cannot be determined. <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥10	≥10	Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection
Negative	Negative or not performed	Any non-negative result ⁷	<10	Any result	No evidence of Zika virus infection
For areas where PRNT is not recommended³					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended		Presumptive Zika virus infection; timing of infection cannot be determined⁸
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended		Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined⁸
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended		Insufficient information for interpretation <ul style="list-style-type: none"> Consider repeat testing
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended		No laboratory evidence of Zika virus infection

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

1 Final interpretations of results of Zika virus tests should be performed after all testing is complete.

2 Serology test results that indicate flavivirus infection should be interpreted in the context of circulating flaviviruses.

3 Currently, PRNT confirmation is not routinely recommended for persons living in Puerto Rico.

4 Serum must be submitted for all persons tested for Zika virus infection; a urine specimen for Zika virus NAT testing should always be submitted concurrently with a serum specimen.

5 Dengue virus IgM antibody testing is recommended for symptomatic pregnant women, as well as for asymptomatic pregnant women residing in areas where PRNT confirmation is not recommended. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dengue/clinlab/lab/assay.html>.

6 Positive results include "positive," "presumptive Zika virus positive," or "possible Zika virus positive." These are examples of assay interpretations that might accompany test results; positive serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific

assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under the "Labeling" for the specific assay.

7 Non-negative results include "positive," "equivocal," "presumptive positive," or "possible positive." These are examples of assay interpretations that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under "Labeling" for the specific assay.

8 Zika virus IgM positive result is reported as "presumptive positive or flavivirus infection" to denote the need to perform confirmatory PRNT titers against Zika virus, dengue virus, and other flaviviruses to which the person might have been exposed to resolve potential false-positive results that might have been caused by cross-reactivity or nonspecific reactivity. In addition, ambiguous test results (e.g., inconclusive, equivocal, and indeterminate) that are not resolved by retesting also should have PRNT titers performed to rule out a false-positive result. However, PRNT confirmation is currently not routinely recommended for persons living in Puerto Rico.

UPDATED INTERIM PREGNANCY GUIDANCE: ASYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE



Testing Recommendations and Interpretation of Results for Healthcare Providers

ASK PREGNANT WOMEN ABOUT

Travel to or residence in any areas with risk for Zika virus transmission before and during the current pregnancy^{1,2}
Possible sexual exposure before and during the current pregnancy • A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy³ • Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia) • If symptoms are reported, refer to symptomatic algorithm.

Before testing, discuss testing limitations and potential risks of misinterpretations for test results.

WHOM to test?

Asymptomatic pregnant women **with ongoing** possible Zika virus exposure⁴

Asymptomatic pregnant women with recent possible Zika virus exposure, **without ongoing exposure:**
Testing not routinely recommended, but should be considered.
 If considering testing, base decisions on patient preferences and values, clinical judgment, a balanced assessment of risks and expected outcomes, and jurisdiction's recommendations
 If testing is conducted, follow algorithm for symptomatic pregnant women using timeframe from last possible exposure.

WHEN to test?

Three times during pregnancy⁵
 First test at initiation of prenatal care.

WHICH tests?

Zika virus NAT (serum and urine)

RESULTS

Positive Zika virus NAT⁶

Negative Zika virus NAT

INTERPRETATION

ACUTE ZIKA VIRUS INFECTION

NO ZIKA VIRUS RNA DETECTED. ZIKA VIRUS INFECTION DURING PREGNANCY CANNOT BE RULED OUT.⁷

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

- 1 Ask about type and duration of Zika virus exposure before and during the current pregnancy. Exposure prior to the current pregnancy may limit interpretation of Zika IgM antibody results; pretest counseling can help inform testing decisions.
- 2 Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://wwwnc.cdc.gov/travel/page/zika-travel-information>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period]), or sex without a condom during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission.
- 3 Zika virus testing is not routinely recommended for pregnant women with a previous diagnosis of laboratory-confirmed Zika virus infection by either NAT or serology (positive/equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥10 and dengue virus PRNT <10 results).
- 4 Persons with ongoing possible exposure include those who reside in or frequently travel (e.g., daily or weekly) to an area with risk for Zika virus transmission.
- 5 The interval for Zika virus NAT testing during pregnancy is unknown. Preliminary data suggest that NAT might remain positive for several weeks after infection in some pregnant women. For women without a prior laboratory-confirmed diagnosis of Zika virus, NAT testing should be offered at the initiation of prenatal care, and if Zika virus RNA is not detected on clinical specimens, two additional tests should be offered during the course of the pregnancy coinciding with prenatal visits. The proportion of fetuses and infants with Zika virus-associated birth defects is highest among women with first and early second trimester infections; therefore, conducting all NAT testing during the first and second trimesters might be considered

to help identify infections early in pregnancy. However, adverse outcomes have been associated with infection diagnosed in the third trimester; therefore, testing every trimester might be considered.

- 6 Despite the high specificity of NAT, false positive NAT results have been reported. **If both serum and urine specimens are NAT positive, interpretation should be acute Zika virus infection.** If NAT is only positive on serum or urine, testing should be repeated on the original NAT-positive specimen. **If repeat NAT is positive, results should be interpreted as evidence of acute Zika virus infection.** If repeat NAT testing is negative, results are indeterminate and healthcare providers should perform IgM antibody testing on a specimen collected ≥2 weeks after the initial specimen collection. For laboratory interpretation, see [Table 1](#).
- 7 A negative Zika virus NAT result does not exclude infection during pregnancy because it represents a single point in time. Zika virus RNA levels decline over time, and the duration of the presence of Zika virus RNA in serum and urine following infection vary among pregnant women. Despite Zika virus IgM test limitations (e.g., cross-reactivity with other flaviviruses and prolonged detection for months, presenting challenges in determining the timing of infection), which should be discussed as part of pretest counseling, patients may still choose to receive Zika virus IgM testing.

Note: For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/ flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.



TABLE 1. Interpretation of results¹ of nucleic acid and antibody^{2,3} testing for suspected Zika virus infection — United States (including US territories), 2017

Zika NAT (serum) ⁴	Zika NAT (urine) ⁴	Zika virus IgM ⁵	Zika virus PRNT	Dengue virus PRNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Positive	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original urine specimen</i> <ul style="list-style-type: none"> If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date <ul style="list-style-type: none"> If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Positive	Negative or not performed	Positive	Not indicated	Not indicated	Acute Zika virus infection
Positive	Negative or not performed	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original serum specimen</i> <ul style="list-style-type: none"> If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date <ul style="list-style-type: none"> If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥10	<10	Zika virus infection; timing of infection cannot be determined. <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥10	≥10	Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection
Negative	Negative or not performed	Any non-negative result ⁷	<10	Any result	No evidence of Zika virus infection
For areas where PRNT is not recommended³					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PRNT is not recommended		Presumptive Zika virus infection; timing of infection cannot be determined⁸
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PRNT is not recommended		Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined⁸
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PRNT is not recommended		Insufficient information for interpretation <ul style="list-style-type: none"> Consider repeat testing
Negative	Negative or not performed	Negative on both assays	Not performed because PRNT is not recommended		No laboratory evidence of Zika virus infection

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

1 Final interpretations of results of Zika virus tests should be performed after all testing is complete.

2 Serology test results that indicate flavivirus infection should be interpreted in the context of circulating flaviviruses.

3 Currently, PRNT confirmation is not routinely recommended for persons living in Puerto Rico.

4 Serum must be submitted for all persons tested for Zika virus infection; a urine specimen for Zika virus NAT testing should always be submitted concurrently with a serum specimen.

5 Dengue virus IgM antibody testing is recommended for symptomatic pregnant women, as well as for asymptomatic pregnant women residing in areas where PRNT confirmation is not recommended. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dengue/clinlab/lab/assay.html>.

6 Positive results include "positive," "presumptive Zika virus positive," or "possible Zika virus positive." These are examples of assay interpretations that might accompany test results; positive serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under the "Labeling" for the specific assay.

7 Non-negative results include "positive," "equivocal," "presumptive positive," or "possible positive." These are examples of assay interpretations that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm#zika> under "Labeling" for the specific assay.

8 Zika virus IgM positive result is reported as "presumptive positive or flavivirus infection" to denote the need to perform confirmatory PRNT titers against Zika virus, dengue virus, and other flaviviruses to which the person might have been exposed to resolve potential false-positive results that might have been caused by cross-reactivity or nonspecific reactivity. In addition, ambiguous test results (e.g., inconclusive, equivocal, and indeterminate) that are not resolved by retesting also should have PRNT titers performed to rule out a false-positive result. However, PRNT confirmation is currently not routinely recommended for persons living in Puerto Rico.

DOCTOR'S VISIT CHECKLIST:



For Pregnant Women Who Traveled to an Area with Risk of Zika*

If you are pregnant and might have been exposed to Zika, talk to your healthcare provider (even if you don't feel sick). You might have been exposed to Zika if:

- You or your sex partner have traveled to an [area with risk of Zika](#)* during your pregnancy, or
- You or your sex partner traveled to one of these areas before you became pregnant (up to 8 weeks for women, up to 6 months for men).



Here are some topics and questions you may want to discuss with your healthcare provider:

INFORMATION TO SHARE:

- ✓ When did you travel to an area with risk of Zika?
 - Where did you travel?
 - How long did you stay?
- ✓ In what trimester was your pregnancy when you traveled to an area with risk of Zika?
- ✓ Did you have any symptoms of Zika during your trip or within 2 weeks of returning?
 - The most common symptoms of Zika are fever, rash, headache, joint pain, red eyes, and muscle pain.
- ✓ Did your partner travel to an area with risk of Zika?
 - When and where did your partner travel?
 - Did your partner have any signs or symptoms of Zika (including fever, rash, joint pain, red eyes, muscle pain or headache) when they were on the trip, or after returning?

QUESTIONS TO ASK:

- ✓ Should you be tested for Zika virus?
 - Pregnant women with possible exposure to Zika virus should be tested for Zika infection, if they have symptoms.
 - ✓ Do you need an ultrasound?
 - ✓ Do you need to be referred to a maternal-fetal medicine specialist or a high-risk obstetrics specialist?
 - ✓ How can you prevent sexual transmission of Zika virus?
- Be sure to ask any other questions or mention concerns you may have about Zika and your pregnancy.

*Check <https://wwwnc.cdc.gov/travel/page/zika-travel-information> for the most up-to-date travel recommendations.

Resource List:

- Areas with Zika Virus: www.cdc.gov/zika/geo/
 Facts About Microcephaly: www.cdc.gov/ncbddd/birthdefects/microcephaly.html
 Zika Virus and Pregnancy: www.cdc.gov/zika/pregnancy/index.html
 Pregnant Women: How to Protect Yourself: www.cdc.gov/zika/pregnancy/protect-yourself.html
 Mother-To-Baby Website: www.mothers-to-baby.org/
 Zika Virus Prevention: www.cdc.gov/zika/prevention/index.html
 Zika and Sexual Transmission: www.cdc.gov/zika/transmission/sexual-transmission.html



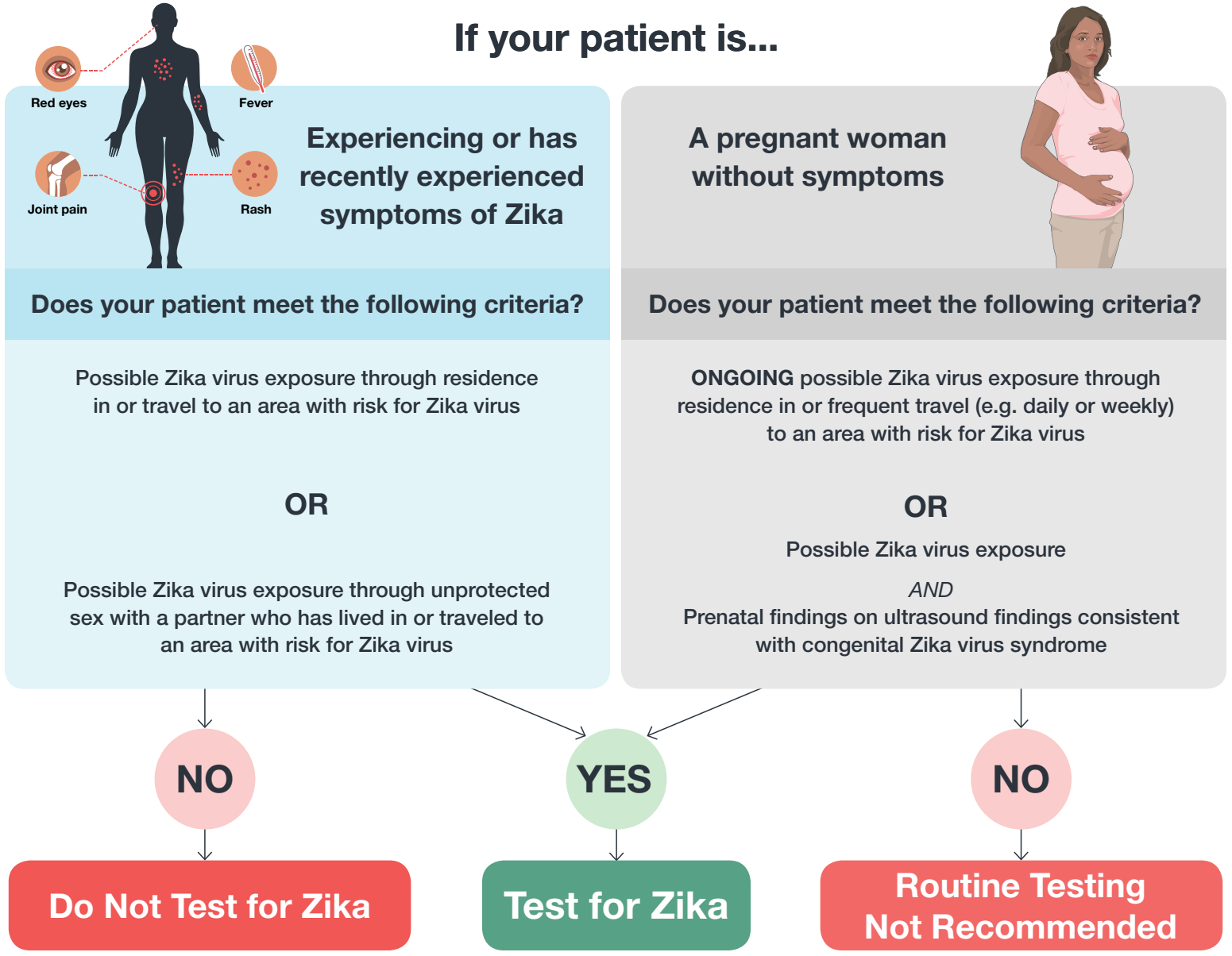
U.S. Department of Health and Human Services
 Centers for Disease Control and Prevention



WHEN TO TEST FOR **ZIKA VIRUS**



As a healthcare provider, you decide if a patient should be tested for Zika virus infection. The algorithm below will help you determine whether or not to test your patient for Zika virus infection.



- NOTE:**
- Asymptomatic pregnant women with recent possible Zika virus exposure (i.e. through travel or sexual exposure) who do not have ongoing exposure are not routinely recommended to have Zika virus testing. Testing should be considered using a decision-making model, one in which patients and providers work together to make decisions about testing and care plans based on a balanced assessment of risks and expected outcomes, clinical judgement, patient preferences and values, and the jurisdiction's recommendations.
 - Healthcare providers should review their local and state health jurisdiction guidelines regarding testing of patients with clinically compatible illness without known travel or sexual exposures.
 - Find full testing algorithms and details on which tests to order at <https://www.cdc.gov/zika/hc-providers/testing-guidance.html>.

CDC does not recommend Zika virus testing for asymptomatic

- Men
- Children
- Women who are not pregnant



DIAGNOSIS

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



General Information

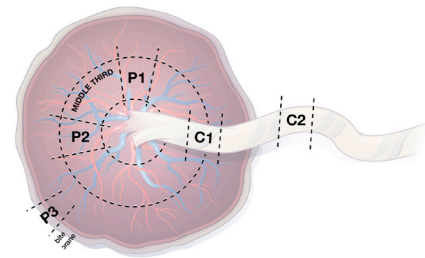
The following information applies to placental (e.g., placental disk, umbilical cord, and fetal membranes) and fetal or infant autopsy tissue collection and submission. For serum, urine, cerebrospinal fluid (CSF), and other body fluid analysis, please see [CDC's web page on testing body fluid specimens](#).

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

For guidance regarding for which Zika virus testing on placental tissues should be considered, please see [Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States \(Including U.S. Territories\)](#).

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. **Minimum information required** for the pre-approval process includes the following:
 - » Maternal/infant state and specimen identification numbers, maternal age, maternal and infant Zika virus test results (if available), dates of possible maternal Zika virus exposure and locations of exposure (if applicable), illness onset (if applicable), estimated date of delivery, gestational age at delivery, pregnancy outcome, sex of infant, birth anthropometric measurements (head circumference, weight, and length) and significant physical exam findings, any additional testing/imaging.
 - » Pre-approval and specimen processing can be delayed if required information is missing.
- **Please Note:** [CDC Form 50.34](#) is required to be submitted with all specimens. **One hard copy (per case)** of the CDC 50.34 form should be submitted with the formalin-fixed wet tissues or formalin-fixed paraffin-embedded tissue blocks at ambient temperature. Please do not submit multiple copies of the CDC 50.34 per case.
 - » Select Test Order CDC-10365 “Pathologic Evaluation of Tissues for Possible Infectious Etiologies.”
 - » Select “Zika Virus” as the suspect agent from the drop down menu.
 - » The remaining items must be completed electronically and then printed.
 - » If the placenta is submitted to surgical pathology, or a fetal or infant autopsy is conducted, a copy of the preliminary or final surgical pathology and/or fetal or infant autopsy report should be enclosed with the specimen submission paperwork.



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Collection of Placental, Fetal, or Infant Autopsy Tissues

1. To optimize evaluation of possible Zika virus infection, **send fixed tissues**. CDC's Infectious Diseases Pathology Branch is not accepting fresh or frozen tissues for Zika virus testing at this time.
2. Staff who collect and handle specimens should refer to [Zika biosafety guidelines](https://www.cdc.gov/zika/laboratories/lab-safety.html) (https://www.cdc.gov/zika/laboratories/lab-safety.html) for laboratory and pathology procedures.
3. **For fetal or infant autopsy 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.
 - » The types 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.

Specimen Type	Fixed Specimens	When to Consider	General Notes
Products of conception (POC)	<ul style="list-style-type: none"> • 4 or more specimens 	Generally less than 12 weeks gestational age	For early pregnancy loss/miscarriage, please send POCs fixed in formalin (wet tissues, not formalin-fixed paraffin-embedded tissue blocks), if possible.
Placenta and fetal membranes	<ul style="list-style-type: none"> • At least 2 full thickness sections (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 taken from the area of rupture and including a small bite of the edge of the disk. 	Any gestation for which placenta is available	<p>Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible.</p> <p>Sample both maternal and fetal side of the placenta.</p> <p>Label all specimens to identify location of sample.</p>
Umbilical cord	<ul style="list-style-type: none"> • At least 2.5 cm segments of cord 	Any gestation for which placenta is available	Label specimen to identify location of sample (e.g., if proximal, middle or distal to umbilical cord insertion site on placenta).
Brain and spinal cord	<ul style="list-style-type: none"> • 0.5–1.0 cm³ each • 5 or more specimens from different parts of brain and spinal cord 	Fetal loss, stillbirth, or infant death.	It is critical to maintain the tissue architecture to evaluate viral pathology.
Solid organ (heart, lung, liver, kidneys, skeletal muscle, eyes, bone marrow)	<ul style="list-style-type: none"> • 0.5-1.0 cm³ each • 1 representative specimen from each solid organ 	Fetal loss, stillbirth or infant death.	Submission of eyes is highly recommended.

Fixed Tissues

1. The approach to Zika virus testing on fixed tissue specimens continues to evolve as more is learned regarding this emerging virus. Currently, Zika virus testing on fixed tissues includes Zika virus reverse transcription-polymerase chain reaction (RT-PCR) on placental and fetal tissues. Zika virus immunohistochemistry (IHC) is performed on selected cases, including placental tissues from 1st and early 2nd trimester pregnancy losses, fetal tissues from pregnancy losses, and autopsy tissues from infant deaths. Microscopic examination of submitted tissues is also performed in selected cases.
2. Fixed tissues may include formalin-fixed wet tissues and/or formalin-fixed paraffin-embedded tissues. Formalin-fixed paraffin-embedded tissue blocks are preferred if formalin-fixation of the wet tissues has exceeded two weeks. Wet tissues fixed in formalin for more than four weeks **are not acceptable** for Zika virus testing.
3. Collecting tissues with the recommended dimensions provided in the table above will allow formalin to penetrate the specimen and increase the chances for appropriate tissue fixation.
4. The volume of formalin used to fix tissues should be 10x the volume of tissue. Place tissue collected according to the dimensions provided above in 10% buffered formalin for three days (72 hours). After fixation, if not paraffin-embedded, tissues **SHOULD** be transferred to 70% ethanol for long term storage and for shipping.
5. 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.
6. **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
Phone: (404) 639-3133
- 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 as well as the submitting healthcare provider if adequate contact information is provided on the CDC Specimen Submission form.
- Turnaround time will vary, depending on testing volume and individual case complexity.
- 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.

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, neurologic assessment as well as newborn hearing screen should be performed. In addition, based on the level of possible maternal Zika virus exposure (e.g., duration and type of exposure, use of prevention measures, intensity of Zika virus transmission at the location of travel), the provider should consider whether

further evaluation of the newborn for possible congenital Zika virus infection is warranted, in which case a head ultrasound and ophthalmologic assessment should be considered. Based on results of the evaluation, testing of the infant for Zika virus infection could be considered.

Testing of placental tissue specimens by Zika virus reverse-transcription polymerase chain reaction (RT-PCR) is conducted at CDC's Infectious Diseases Pathology Branch (IDPB). Zika virus RT-PCR on placental tissues from women with possible Zika virus exposure can be considered for diagnostic purposes for symptomatic pregnant women and women with infants with possible Zika virus-associated birth defects without a definitive diagnosis of laboratory-confirmed Zika virus infection during pregnancy. For asymptomatic pregnant women who have recent possible Zika virus exposure but without ongoing possible exposure, similar to the updated recommendations for testing of non-tissue clinical specimens (e.g., serum and urine), testing of placental tissues is not routinely recommended.

IMPORTANT: Pre-approval is required prior to submission of any tissue specimens. For pre-approval please contact pathology@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 tissue specimens before they are collected and sent.
 - » Institutions with surgical pathology available: Please consult surgical pathology regarding appropriate collection and processing of tissue 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 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.

Health Departments:

- When submitting specimens, please submit [CDC Form 50.34](#) with all specimens.
 - » Select Test Order Code CDC-10365 "Pathologic Evaluation of Tissues for Possible Infectious Etiologies."
 - » Select "Zika Virus" as the suspect agent from the drop down menu.
 - » The remaining items must be completed electronically and then printed.

- **Pre-approval is required** prior to submission of all tissue specimens (i.e., placenta, umbilical cord). Please contact pathology@cdc.gov to obtain pre-approval. Additional clinical and epidemiologic information may be requested, see <https://www.cdc.gov/zika/laboratories/test-specimens-tissues.html> for minimum required information for 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.

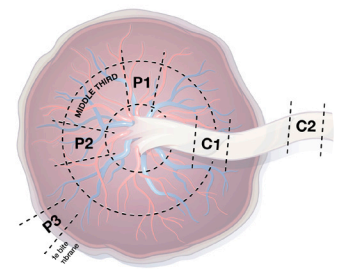


Figure: Collecting placental specimen

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
<p>Infant serum</p>	<p>At least 1.0 ml</p> <p>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.</p>	<p>For antibody and rRT-PCR testing, specimens should be kept cold (2–6 °C) or frozen (-70 °C).</p> <p>For virus isolation testing, specimens should be frozen as soon as possible (-70 °C).</p>	<p>For cold specimens, the sample should be placed in an insulated container with adequate ice packs to ensure specimen (“cold chain”) integrity.</p> <p>For frozen specimens, ship the sample on enough dry ice to ensure specimens remain frozen until received.</p>	<p>Arboviral Diseases Branch Diagnostic Laboratory Centers for Disease Control and Prevention 3156 Rampart Road Fort Collins, Colorado 80521</p> <p>More information about collecting, handling, and shipping is available here.</p>
<p>Placenta and fetal membranes</p>	<p>At least 2 full thickness sections (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</p> <p>One 5 x 12 cm strip of fetal membranes taken from the area of rupture and including a small bite of the edge of the disk.</p> <p>Please include sections of the placental disk, fetal membranes, and pathologic lesions when possible.</p> <p><i>(Please reference the figure on page one.)</i></p>	<p>Please sample both maternal and fetal side of the placenta.</p> <p>Label all specimens to identify location of sample.</p>	<p>Fix specimens in formalin</p> <p>Volume of formalin used should be about 10x the volume of tissue. Place in 10% neutral buffered formalin for 3 days (72 hours). After fixation, if not paraffin-embedded, tissues should be transferred to 70% ethanol for long term storage and shipping.</p> <p>Storage and shipping at room temperature.</p>	<p>Infectious Diseases Pathology Branch Centers for Disease Control and Prevention 1600 Clifton Rd. NE, MS G-32 Atlanta GA 30329-4027</p> <p>Get more instructions regarding collecting and shipping tissue specimens.</p>
<p>Umbilical cord</p>	<p>At least two representative 2.5 cm segments of cord</p>	<p>Label specimen to identify location of sample (e.g., if proximal, middle, and distal to umbilical cord insertion site on the placenta).</p>	<p>Fix specimens in formalin</p> <p>Volume of formalin used should be about 10x the volume of tissue. Place in 10% neutral buffered formalin for 3 days (72 hours). After fixation, if not paraffin-embedded, tissues should be transferred to 70% ethanol for long term storage and shipping</p> <p>Storage and shipping at room temperature.</p>	<p>Infectious Diseases Pathology Branch Centers for Disease Control and Prevention 1600 Clifton Rd. NE, MS G-32 Atlanta GA 30329-4027</p> <p>Get more instructions regarding collecting and shipping tissue specimens.</p>
<p>Infant urine</p>	<p>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.</p>	<p>Sterile specimen is not required</p>	<p>For rRT-PCR testing, specimens should be kept cold (2–8 °C) or frozen (≤ 20 °C) for storage and shipping.</p> <p>For frozen specimens, ship the sample on enough dry ice to ensure specimens remain frozen until received.</p>	<p>Arboviral Diseases Branch Diagnostic Laboratory Centers for Disease Control and Prevention 3156 Rampart Road Fort Collins, Colorado 80521</p> <p>Get more information about collecting, handling, and shipping.</p>

WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING



For Pregnant Women Who Have Ongoing Exposure to Zika but No Symptoms

If you or your sex partner live in an area with risk of Zika or frequently travel to such an area, you may have been exposed to Zika during pregnancy or before you became pregnant. You may have questions about Zika and you may want to know how to find out if you've been infected. Keep reading to learn more.

Zika testing is complex

In general, testing for Zika can include looking for Zika genetic material (pieces of the virus called RNA) and antibodies that the body would make to fight a Zika infection.

- Testing for Zika genetic material is recommended for you because it can tell your doctor if you were recently infected with Zika.
- Testing for Zika antibodies is not routinely recommended for pregnant women who have ongoing exposure to Zika but no symptoms because the results cannot be interpreted. We know that Zika antibodies can stay in the body for several months. If you lived in or frequently traveled to an area where local mosquitoes spread Zika, you may have been infected before pregnancy. This means you may have already developed antibodies against Zika before you became pregnant. Because of this, Zika antibody test results may not tell your doctor if you were infected in the past or if you were infected more recently during your current pregnancy. This means that these results would not tell us if your pregnancy is at risk from Zika infection.



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Testing Process

Testing for Zika genetic material, RNA, is recommended for pregnant women without symptoms who live in or frequently travel to an area with risk of Zika. Because you have ongoing exposure to Zika, you may receive up to three Zika tests at various points throughout your pregnancy.

Your doctor or other healthcare provider will order a test to look for Zika genetic material, RNA, which can be in blood and urine.

- If you test positive for Zika RNA, it means that you may have recently been infected with Zika.
- If you test negative, no Zika RNA was detected. A negative test may mean that you have never been infected with Zika. However, it may also mean that you had Zika, but the virus is no longer in your body. Therefore, a negative test cannot rule out a recent Zika infection.



Testing Results

Positive test results

Testing positive for Zika during pregnancy lets your doctor or other healthcare 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.

Not clearly positive or negative test results

Sometimes, the test results aren't clearly positive or negative. If this happens, your doctor or other healthcare 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 healthcare 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 infection, you will get routine prenatal care, which is what CDC recommends. If your doctor or other healthcare provider sees signs of Zika infection during an ultrasound, then you may need additional tests.



PRETEST COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

FOR ASYMPTOMATIC PREGNANT WOMEN WITH ONGOING EXPOSURE TO ZIKA



This guide describes recommendations for conducting pretesting counseling for asymptomatic pregnant women with ongoing exposure to Zika. CDC recommends Zika testing for asymptomatic pregnant women with ongoing exposure to Zika (meaning they live in or frequently travel to [an area with risk of Zika](#)). 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.

Provide the patient with information on the complexity of Zika testing.

You may be at risk for getting Zika at any time during your pregnancy because you (*replace “you” with “your sex partner” as appropriate*) live in (*replace “live in” with “frequently travel to” as appropriate*) an area with risk of Zika. 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 will test you for Zika during your pregnancy. You may be tested for Zika three times; we will perform the first test during this visit. The second and third tests will happen during routine prenatal care visits during your pregnancy.

Before we begin, I would like to tell you what to expect throughout this process.

Inform the patient that it can be challenging to understand test results and provide them with information on the type of test you will be conducting.

It can be hard to understand Zika test results for a number of reasons. The type of test that is recommended for you requires a blood and urine sample. This test will look for Zika virus genetic material. Results from this test may or may not tell us if you’ve been infected with Zika, which I’ll explain in a minute. I am going to start today’s testing process by ordering this test that looks for genetic material of Zika, known as RNA.

Ask the patient if she has any questions before you move forward with providing information on the testing process.

Inform patients of what each possible 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 RNA, this means you may have recently been infected with Zika virus and 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 not clearly positive or negative.

Sometimes test results will not come back as a clear negative or positive. If this happens, I’d rather be cautious and still do more ultrasounds and test you at least two more times during your pregnancy.

If Zika test results are negative.

If your test results are negative, it means that no Zika RNA was detected. This could mean that you have never been infected with Zika, or it could mean that you previously had Zika and the virus is no longer in your body.

A negative result does not mean that you are not at risk of becoming infected in the future. I will test you two more times during your pregnancy. If there are still no signs of Zika after these additional tests, we will continue with routine prenatal care. If you test positive at a later date (refer above to “If Zika test results are positive”).

WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING

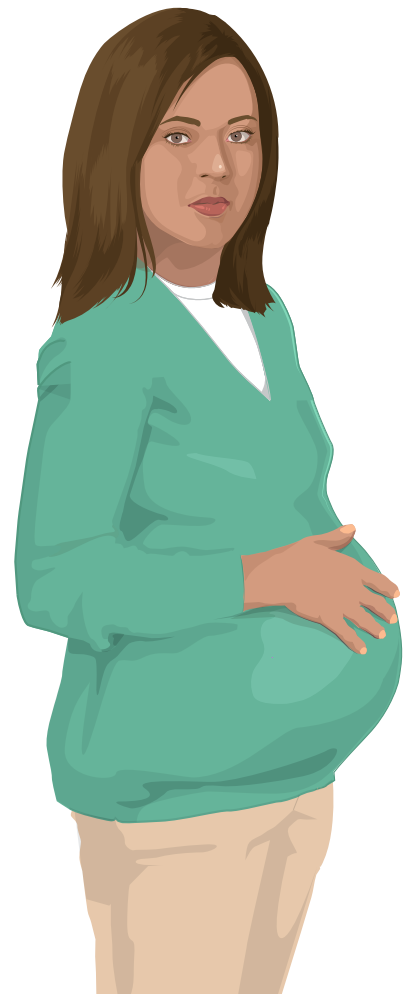


For Pregnant Women Exposed to Zika Who Have Symptoms

If you or your sex partner live in or recently traveled to an area with risk of Zika, you may have been exposed to Zika. If you have red eyes, fever, joint pain, or rash, there is a chance that these symptoms may be caused by Zika. Testing for Zika is recommended as soon as possible within 12 weeks of when your symptoms began. You may have questions about Zika and how to find out if you've been infected. Keep reading to learn more.

Zika testing is complex

- **You will need a combination of Zika tests:**
Finding out if you have Zika can require having up to three different kinds of tests. You may wait different amounts of time for the results of each test to come back.
- **Understanding test results can be challenging:**
Zika is similar to other viruses. Zika tests can sometimes detect other viruses. Sometimes even after several tests, we may not know which type of virus you were infected with. Each test result is important because it may help your doctor or other healthcare provider decide how best to care for you during your pregnancy.
- **Previous exposure to Zika could affect your current test results:**
One of the tests looks for Zika antibodies, which the body makes to fight a Zika infection. We know that these antibodies can stay in the body for several months after a person is infected. If you previously lived in or frequently traveled to an area where local mosquitoes spread Zika, you may have been infected before pregnancy. This means you may have already developed antibodies against Zika before you became pregnant. If you were infected with Zika before pregnancy, Zika antibodies may still be in your body and there would be no way to tell if you were infected in the past or if you were infected more recently during your current pregnancy. This means that these results would not tell us if your pregnancy is at risk from Zika infection.



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Testing Process

Testing is recommended for pregnant women with symptoms who may have recently been exposed to Zika. You may have been exposed if you lived in or traveled to an area with risk of Zika or had sex without a condom with a partner who lived in or traveled to an area with risk of Zika. Because you may have been exposed to Zika within the last 12 weeks, your doctor may order the following tests to look for evidence of Zika infection.

Step One

Your doctor or other provider will start by ordering two tests:

1. The first test looks for Zika genetic material, called RNA, which can be in blood and urine.
2. The second test looks for Zika antibodies.

If you test positive for Zika RNA, regardless of the test results for Zika antibodies, it means that you most likely have recently been infected with Zika.

If you test negative for Zika RNA and your antibody test is positive, more testing is needed. The antibody test can sometimes show results that are positive even when a person isn't actually infected. For example, the test might find antibodies to a similar mosquito-borne infection, such as dengue, which is why additional tests are needed.

If you test negative for Zika RNA and your antibody test is negative, it means there is no evidence you were recently infected with Zika.

Step Two

If you tested negative for Zika RNA and your antibody test is positive, the third test that is needed is a separate test to confirm the type of antibodies. This test takes the longest for results. Your doctor or other healthcare provider will work with your state or local health department or the commercial laboratory 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 provide another sample.

Testing Results

Positive test results

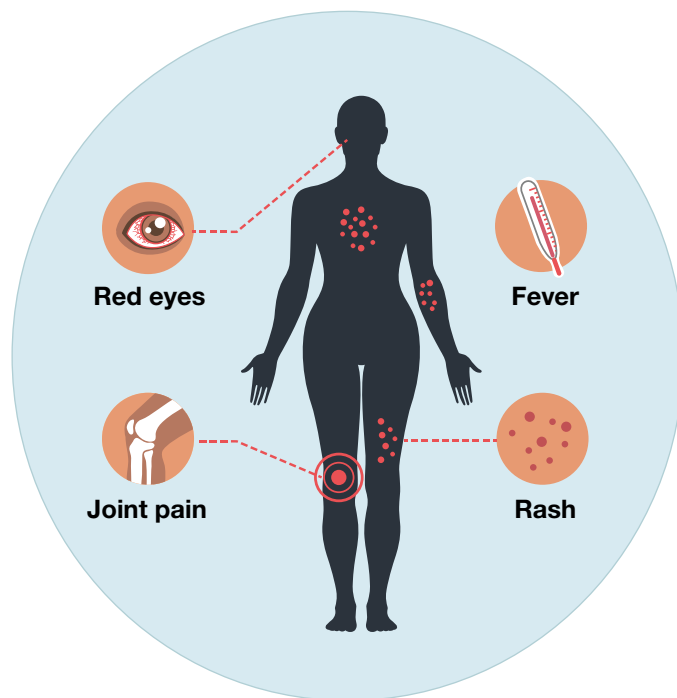
Testing positive for Zika during pregnancy lets your doctor or other healthcare provider know to watch your pregnancy more closely. This means you might have more ultrasounds or other tests to check the growth and development of your fetus and check for Zika infection.

Not clearly positive or negative test results

Sometimes, the test results aren't clearly positive or negative. If this happens, your doctor or other healthcare 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 healthcare 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 infection, you will get routine prenatal care, which is what CDC recommends. If your doctor or other healthcare provider sees signs of Zika infection during an ultrasound, you may need additional tests.



PRETEST COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

FOR PREGNANT WOMEN WITH SYMPTOMS OF ZIKA



This guide describes recommendations for conducting pretesting counseling for symptomatic pregnant women with possible recent exposure (they or their sex partner live in or recently traveled to [an area with risk of Zika](#)). Symptoms of Zika include red eyes, fever, joint pain, and rash. CDC recommends testing for pregnant women with symptoms of Zika. 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 and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation

Sample Script

Provide the patient with information on why you will be testing them for Zika and a brief overview of what to expect

Use one of the two following sentences to begin the discussion:

1. You may be at risk for having Zika since you or your sex partner recently traveled to (*replace “recently traveled to” with “live in” as appropriate*) an area with risk of Zika within the past 12 weeks and you have had (*replace ‘have had’ with “during your pregnancy you previously had” as appropriate*) symptoms of Zika.

OR/AND

2. You may be at risk of having Zika because you recently had sex without a condom with a person who traveled to (*replace “traveled to” with “lives in” as appropriate*) an area with risk of Zika within the past 12 weeks and you have had (*replace ‘have had’ with “during your pregnancy you previously developed” as appropriate*) symptoms of Zika.

Since you may have been exposed to Zika and are experiencing symptoms (*replace “are experiencing” with “during your pregnancy you previously experienced” as appropriate*), I think it is best to move forward with testing you for Zika. Before we begin, I would like to tell you what to expect throughout this process.

Patients should be informed that a combination of Zika tests will be required before a final result is determined

You will need a combination of tests to determine whether or not you have Zika. Finding out if you have Zika can require up to three different kinds of tests because the result of one test may require more testing to find out if you recently had a Zika infection. The tests we use to detect Zika can detect other similar viruses often found in the same areas with risk of Zika. Sometimes even after several tests, we may not know which type of virus you were infected with. Each test result is important, because it may help me decide how best to care for you during pregnancy.

I 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 with Symptoms of Zika](#).

Let the patient know that you will be ordering two tests; one to look for Zika RNA and one to look for Zika antibodies. Define these terms as they may be unfamiliar

I am going to start the testing process by ordering two tests:

- The first test looks for genetic material of Zika virus, known as RNA. RNA can be found in blood and urine.
- The second test looks for Zika antibodies, which are proteins that your body makes to fight off a Zika infection.

Zika test results can be difficult to interpret. If you’ve had exposure to Zika virus or another similar virus before this pregnancy, it’s possible that you’ve been infected before, and this could affect today’s test results.

Recommendation

Sample Script

Patients should be informed that it can be challenging to understand test results and that previous exposure to Zika could affect their test results

Scientists have learned that Zika antibodies can stay in your blood for several months after infection. Antibodies show evidence that your body fought off a recent Zika infection. It is possible that you may have already developed antibodies against Zika virus if you've lived in or frequently traveled to an area with risk of Zika before becoming pregnant. Because of this, it is possible that your Zika antibody test results may not tell me if you were infected in the past or if you were infected more recently during your current pregnancy. This means if you test positive, we may not know if you are currently infected or not.

Ask the patient if she has any questions before you move forward with providing information on the testing process.

Inform the patient of what the possible results of the Zika RNA and antibody tests may be

- If your Zika RNA test comes back with a positive result, regardless of your test result for Zika antibodies, it most likely means that you have recently been infected with Zika.
- If your Zika RNA test comes back negative and your antibody test is positive, we will need to do one more round of testing to figure out whether or not you actually have or recently had Zika. A positive antibody test may mean that you had Zika but the virus is no longer in your body or it could mean that you had an infection with another similar virus.
- If your Zika RNA test and your antibody test are both negative, it means there is no evidence that you have Zika or another similar virus and I will continue evaluating you to find out what may be causing your symptoms.

Ask the patient if they have any questions before you move forward with providing information on step two of testing.

If the patient requires further testing after the Zika RNA and Zika antibody test, inform the patient and provide them with information on what to possibly expect next.

If you test negative for Zika RNA and your antibody test is 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 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 not clearly positive or negative

Sometimes test results will not come back as a clear negative or positive. 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 fetus 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.

WHAT YOU SHOULD KNOW ABOUT ZIKA VIRUS TESTING



For Pregnant Women Who Were Recently Exposed to Zika and Do Not Have Symptoms

If you or your sex partner recently traveled to an area with risk of 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.

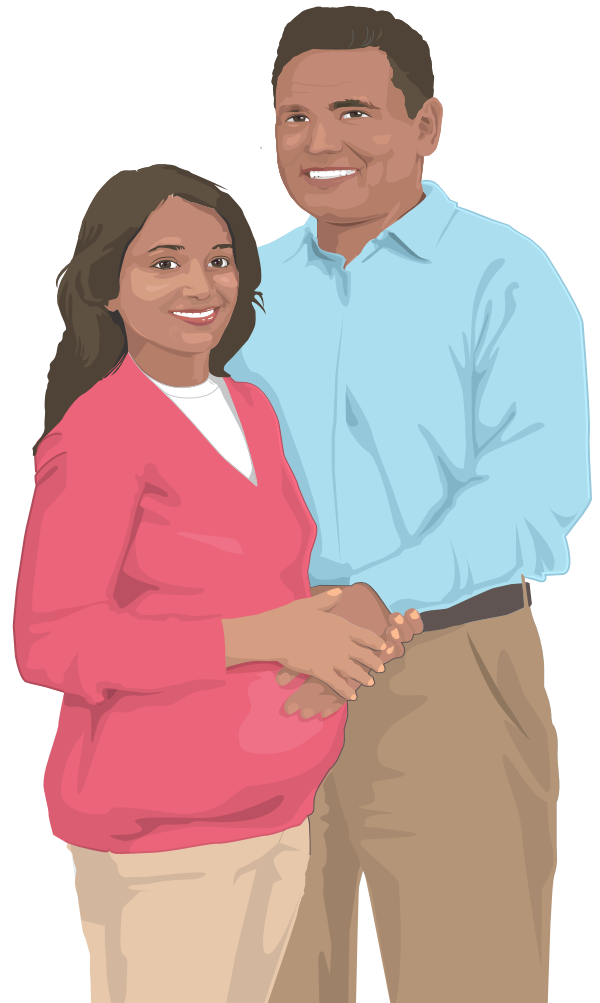
Routine testing for Zika is not recommended for you, but it can be considered if you and your healthcare provider determine it is best for your specific situation.

CDC does not recommend routine Zika testing for pregnant women who were recently exposed to Zika but did not develop symptoms and do not have ongoing exposure (for example, if you do not live in or frequently travel to an area with risk of Zika). However, you and your healthcare provider may discuss your specific situation and decide together that it is best for you to be tested. Some state or local areas may also recommend routine testing.

Why is routine testing not recommended for me?

Testing people when a disease is not spreading widely can lead to more positive tests being inaccurate (called a false positive), meaning the test might look like you have Zika when you don't actually have it.

False positive test results can cause stress and anxiety. It can also lead your healthcare provider to perform more tests and procedures than are necessary. In general, testing is recommended when it can provide necessary information for you or your healthcare provider to make informed decisions about your care during pregnancy. However, since a higher number of Zika positive results will be false, testing should only be considered on a case-by-case basis after discussing the risks and benefits of Zika testing with your healthcare provider. Despite the risks of false positive test results, some patients may still prefer to be tested.



COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

FOR ASYMPTOMATIC PREGNANT WOMEN WHO WERE RECENTLY EXPOSED TO ZIKA BUT DO NOT HAVE ONGOING EXPOSURE



This guide provides talking points for discussing why testing is not routinely recommended for asymptomatic pregnant women who were recently exposed to Zika (meaning they or their sex partner recently traveled to [an area with risk of Zika](#)) but do not have ongoing exposure. However, testing can be considered on a case-by-case basis depending on patient preferences, your clinical judgement, or if your state or local jurisdiction recommends it. This material includes sample scripts to guide discussions with your patients about why Zika testing is not recommended for asymptomatic pregnant women who do not have ongoing exposure. To increase patient understanding, it may be helpful to make additional information available to support messaging.

Pregnant women who may have been exposed to Zika may feel worried or anxious. Support them by providing them with clear and easy-to-understand information and expressing empathy by acknowledging their concerns and feelings during discussions.

Recommendation

Sample Script

Discuss with the patient why Zika testing is no longer routinely recommended for asymptomatic pregnant women without ongoing exposure

Thank you for coming in to discuss your concerns about possibly being exposed to Zika virus. Possible exposure means that you or your sex partner recently traveled to [an area with risk of Zika](#).

As you may know, the Centers for Disease Control and Prevention (CDC) issues up-to-date recommendations for pregnant women possibly affected by Zika as more continues to be learned about the virus. Currently, routine Zika testing is not recommended for pregnant women if they don't have ongoing exposure and do not have symptoms. The most common symptoms of Zika virus disease are fever, rash, joint pain, and red eyes.

Overall, the number of people with reported Zika infection in the Americas is decreasing. Testing people without symptoms when there is a smaller number of new cases occurring could increase the chances of test results being positive when they may actually be negative. This means the test might tell you that you have Zika when you actually don't.

False positive test results are a concern. They may cause stress and anxiety and lead to me performing more tests and procedures than are necessary. Testing is typically recommended when it can provide us with valuable information for us to make informed decisions about care during your pregnancy. When more positive results will be false, we should only consider testing after discussing the possibility of false positive results and what this might mean for you.

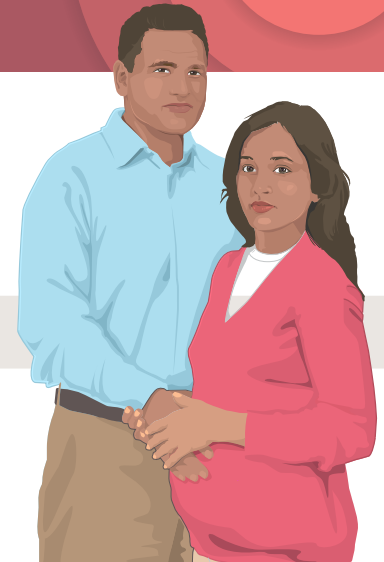
What questions do you have?

- Consider providing the fact sheet [What You should Know about Zika Virus Testing for pregnant women without symptoms who were recently exposed to an area with risk of Zika but do not have ongoing exposure](#).
- If the patient still requests to be tested, refer to [What You Should Know About Zika Virus Testing for Pregnant Women with Symptoms of Zika](#) to guide them through the steps of the testing process.

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.



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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.mothersbaby.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

www.cdc.gov/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.**



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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

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.**



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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:

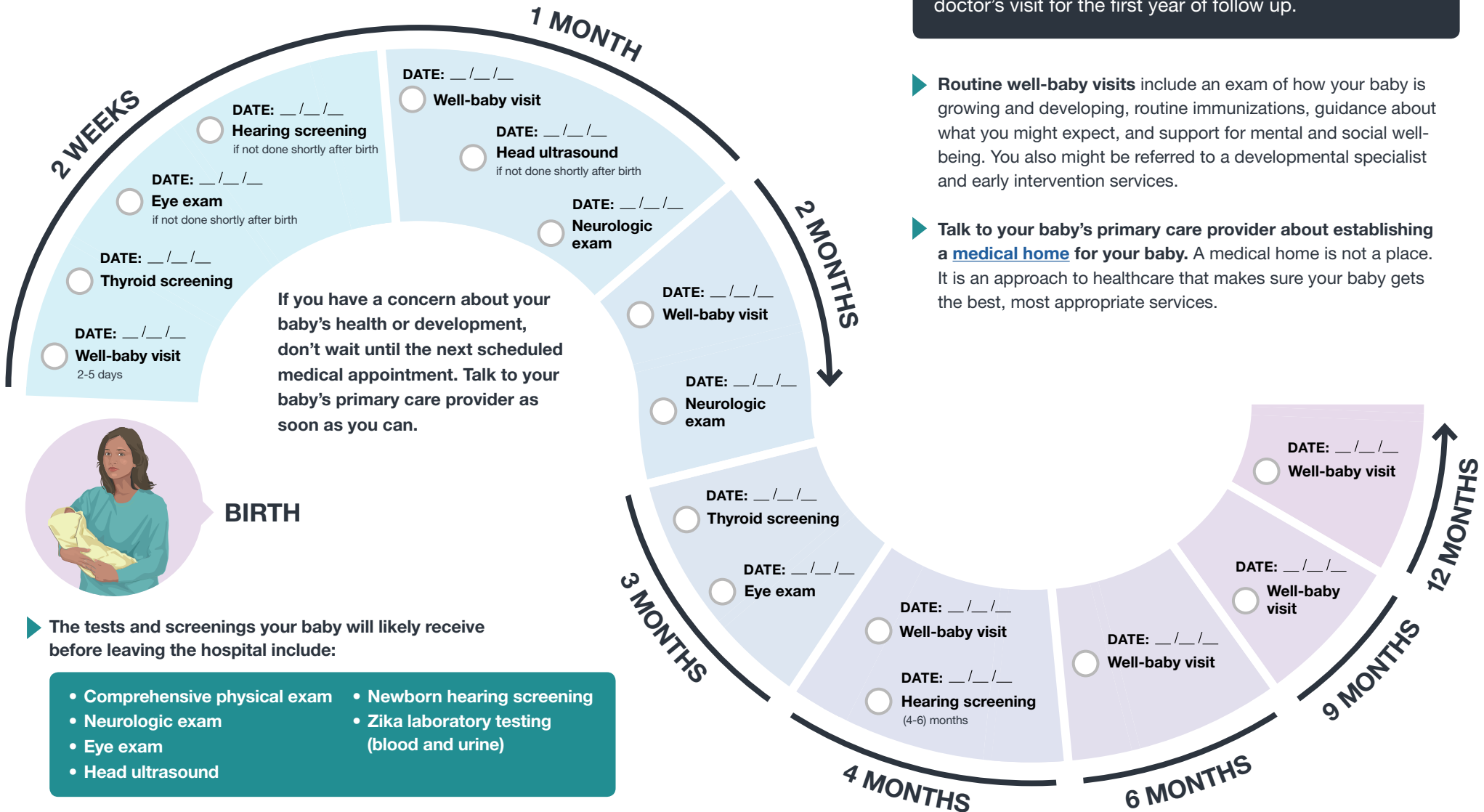
- Non-profit organizations
 - » **The Family Voices** affiliate or **Family-to-Family Health Information Center** in your state | Visit website: www.familyvoices.org/states
 - » **Parent to Parent-USA** | Visit website: www.p2pusa.org
 - » **Partnerships for Parents** | Visit website: partnershipforparents.net/

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

ROADMAP FOR PARENTS OF BABIES WITH CONGENITAL ZIKA SYNDROME

This document should be used as a guide to discuss the screening and testing your baby may receive with his or her primary care provider. Each baby is different, and it is possible that your baby may need more tests or fewer tests.



Follow the roadmap to check off each **recommended** doctor's visit for the first year of follow up.

▶ **Routine well-baby visits** include an exam of how your baby is growing and developing, routine immunizations, guidance about what you might expect, and support for mental and social well-being. You also might be referred to a developmental specialist and early intervention services.

▶ **Talk to your baby's primary care provider about establishing a medical home for your baby.** A medical home is not a place. It is an approach to healthcare that makes sure your baby gets the best, most appropriate services.



▶ The tests and screenings your baby will likely receive before leaving the hospital include:

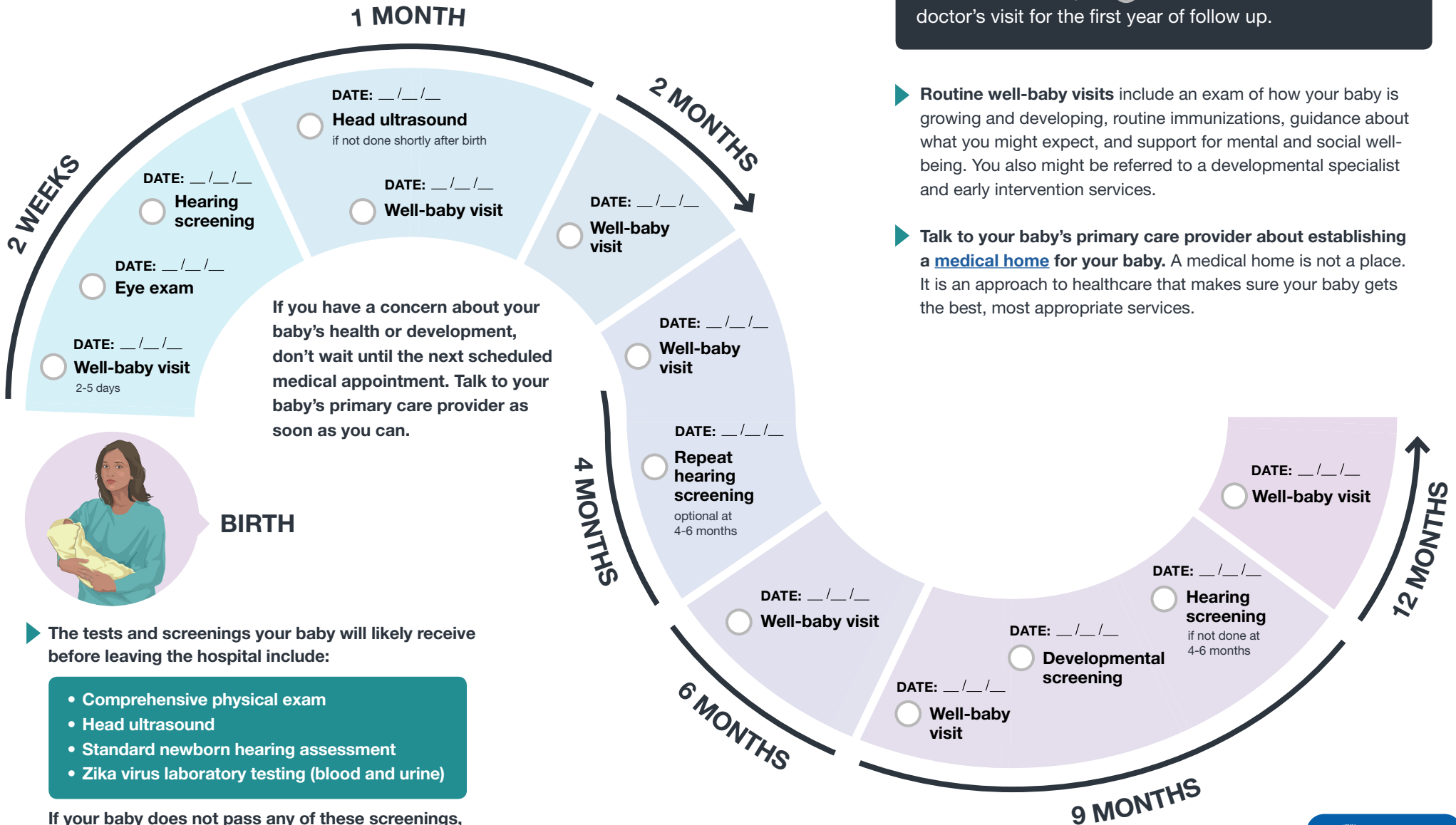
- Comprehensive physical exam
- Neurologic exam
- Eye exam
- Head ultrasound
- Newborn hearing screening
- Zika laboratory testing (blood and urine)

If your baby does not pass any of these screenings, you may be referred for additional follow-up.



ROADMAP FOR PARENTS OF BABIES INFECTED WITH ZIKA BEFORE BIRTH WHO APPEAR HEALTHY

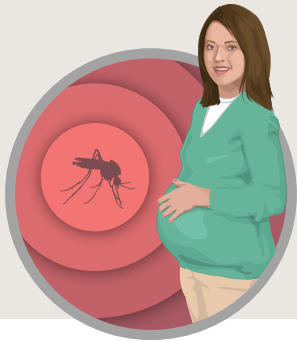
This document should be used as a guide to discuss the screening and testing your baby may receive with his or her primary care provider. Each baby is different, and it is possible that your baby may need more tests or fewer tests.



REPORTING

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



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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>

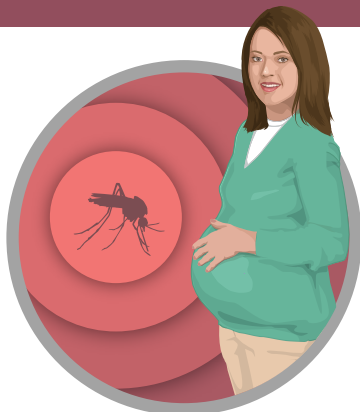
More Information about Zika

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).

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 (www.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

