



IN THIS ISSUE: Zika Testing Guidance for Healthcare Providers

**CDC'S UPDATE ON ZIKA TESTING FOR PREGNANT WOMEN AND
RECOMMENDATIONS FOR HEALTHCARE PROVIDERS (HCPs)**

Introduction

On July 24, 2017, the Centers for Disease Control and Prevention (CDC) released an MMWR with updated testing recommendations for Zika virus. Zika cases have declined since the initial increase was first seen in 2015-2016. Due to the declining prevalence of Zika there is the possibility of false-positive results occurring. Therefore, CDC made changes to the testing recommendations. With the updated testing recommendations and availability of commercial laboratories to conduct Zika testing, the Washoe County Health District (WCHD) will be changing how we manage testing patients for Zika virus. In the past, WCHD approved patients to be tested for Zika using the Nevada State Public Health Laboratory. A majority of those tested through WCHD were asymptomatic pregnant women with possible exposure through travel or sex. Testing of asymptomatic pregnant women is one of the major changes made in this latest update and is no longer recommended. WCHD will no longer be the "gatekeeper" for Zika testing, but will be available to consult with physicians on individual cases. This issue of Epi News is to inform healthcare providers of the latest testing recommendations and what commercial labs offer Zika testing.

Recommendations for HCPs¹

The MMWR article goes over in detail the updated recommendations. See below for key points. Please refer to the article for more information.

1. All pregnant women in the United States and U.S. territories should be asked about possible Zika exposure before and during the current pregnancy, at every prenatal visit.
2. Pregnant women with possible Zika virus exposure and symptoms of Zika virus disease should be tested to diagnose the cause of their symptoms. Testing for Dengue and Chikungunya would also be advised. WCHD can assist with testing symptomatic individuals.
3. Asymptomatic pregnant women with ongoing possible Zika virus exposure should be offered Zika virus NAT testing three times during their pregnancy. This would include those who reside in or frequently travel to an area with a risk of Zika virus transmission. To date, Washoe County does not have the vector that transmits Zika virus.
4. Asymptomatic pregnant women who have recent possible Zika virus exposure (i.e. through travel or sexual exposure) but without ongoing exposure are not routinely recommended to have Zika virus testing.

¹ https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w

Healthcare providers (HCPs) will need to have a conversation with patients meeting this criteria to determine if testing is necessary. Please see below for commercial lab testing information.

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 birth defects. WCHD can assist in these situations with testing for Zika virus.
6. The comprehensive approach to testing placental and fetal tissues has been updated. Certain scenarios may warrant testing of these tissues by CDC.

Testing Algorithms

CDC has put together two testing algorithms (Page 2 and 3) for HCPs to follow when determining if Zika testing is necessary for pregnant women. WCHD strongly suggests HCPs of pregnant women print out these two important algorithms from the CDC's website to use as a reference to determine testing needs.

1. Updated Interim Pregnancy Guidance for Symptomatic Pregnant Women
https://www.cdc.gov/zika/pdfs/testing_algorithm.pdf
2. Updated Interim Pregnancy Guidance for Asymptomatic Pregnant Women
<https://www.cdc.gov/zika/pdfs/testing-algorithm-asymptomatic.pdf>

Zika Testing through Commercial Laboratories

Zika testing is offered through LabCorp, Quest and ARUP. If you decide to test a patient for Zika Virus (ZV) please be sure to follow CDC's testing algorithms so the appropriate test is ordered.

Lab	Test Name	Specimen	Test Code
LabCorp	ZV Comprehensive Profile, NAA	Serum, Urine	139600
LabCorp	ZV IgM, MAC-ELISA	Serum	163049
Quest	ZV RNA, Qualitative, Real-Time RT-PCR Panel	Serum/Urine	CPT: 87798 (x2)
Quest	ZV Antibody (IgM), MAC-ELISA	Serum	CPT: 86790
ARUP	ZV by PCR	Blood	2014069
ARUP	ZV by PCR	Urine	2014065
ARUP	ZV Antibody (IgM), MAC-ELISA	Serum	2013942

For a consultation, you may email your questions to ZikaMCH@cdc.gov, or call CDC's Zika Pregnancy Hotline at 770-488-7100 or CDC-INFO (800-232-4636) or WCHD at 775-328-2447.

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

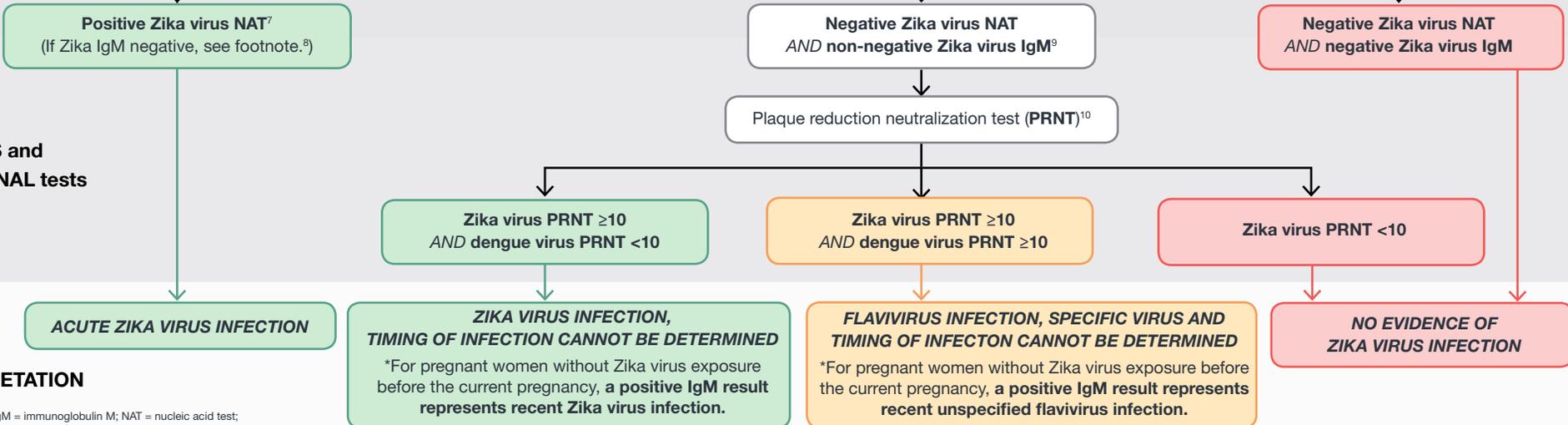
WHEN to test?

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://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.
- 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.



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

- 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.
- 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.
- 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).
- 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.
- 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 healthcare providers should perform IgM antibody testing on a specimen collected ≥2 weeks after the initial specimen collection. For laboratory interpretation, see [Table 1](#).
- 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.



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