Zika virus

Investigative Guidelines
December 2018

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

1. To characterize the epidemiology, modes of transmission, and clinical aspects of the disease.
2. To monitor disease trends and recognize outbreaks.
3. To identify local transmission within Oregon, should it occur.
4. To identify cases during their infectious period and to prevent transmission to local mosquito vectors and other humans.

1.2 Laboratory and Physician Reporting Requirements

Healthcare providers and laboratories are required to report Zika virus, as an infection that is typically "arthropod vector-borne," to the local public health department **within one local public health authority working day**

1.3 Local Health Department Reporting and Follow-Up Responsibilities

1. Report confirmed and presumptive cases to the Oregon Health Authority (OHA) as soon as possible but no later than by the end of the calendar week of initial physician or lab report.
2. Begin follow-up investigation within one working day. Submit all data electronically to ACDP within seven days of initial report.
3. Advise healthcare providers on testing as needed for individuals meeting Zika testing criteria.
4. Coordinate testing at birth as needed for neonates who are thought to have possible congenital Zika infection.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

Zika virus is a flavivirus transmitted primarily by *Aedes aegypti* and *Aedes albopictus* (the same mosquitoes that transmit dengue, chikungunya and yellow fever viruses). In May 2015, local transmission of Zika virus was confirmed in Brazil. Zika virus infections have been documented in travelers returning to the continental United States and have been locally acquired in isolated areas of the continental U.S. A current list of regions with risk of Zika, including areas with

active mosquito transmission and endemic areas, is available here: www.cdc.gov/zika/geo/.

2.2 Description of Illness

Symptomatic infections are generally mild and characterized by fever, maculopapular rash, arthralgia and non-purulent conjunctivitis. Maternal infection during pregnancy can result in intrauterine infection and is associated with fetal loss, microcephaly and other fetal anomalies.[1] The full spectrum of congenital Zika syndrome is not yet known, but it is estimated that about 14% of infants born to Zika-infected mothers have Zika-associated health problems.[2] Zika virus infection might also lead to Guillain-Barré syndrome (GBS).

2.3 Reservoirs

Humans and non-human primates can serve as reservoirs. Humans are thought to be the primary reservoir during an outbreak.

2.4 Sources and Routes of Transmission

Zika is transmissible via mosquitoes, sexual exposure, from a pregnant woman to her fetus or infant, and via blood-borne exposure.

Aedes aegypti and *Aedes albopictus,* the mosquitoes that transmit Zika, become infected when they feed on a person already infected with the virus, and then spread the virus to other people through bites. These mosquitoes are not found in Oregon.

Zika virus can also be transmitted via sexual exposure, defined as vaginal sex (penis-to-vagina sex), anal sex (penis-to-anus sex), oral sex (mouth-to-penis sex or mouth-to-vagina sex), or sharing of sex toys without a condom. It is unknown how long Zika can persist in semen or vaginal secretions. For updated information, visit CDC's *Zika and Sexual Transmission* web page.

A pregnant woman infected with Zika virus can pass the virus to the fetus or to the newborn at the time of birth (i.e., vertical transmission). To date, there are no reports of infants getting Zika virus through breastfeeding. Because of the benefits of breastfeeding, mothers are encouraged to breastfeed, even in areas where Zika virus is found.

Zika appears to be transmissible through transfusion of blood products. FDA recommends universal screening of blood products for Zika.[3] FDA also recommends that people wait to donate blood for 120 days from onset of Zika-compatible symptoms or from the date of a positive Zika test, whichever is longer.

2.5 Incubation Period

In persons experiencing symptoms, onset of illness typically occurs 3–14 days after exposure.

2.6 Period of Communicability

The periods of communicability for sexual or maternal-fetal transmission are not known. Typically, PCR evidence of Zika virus can be found in the blood of an ill, non-pregnant person for at least a week after the onset of symptoms and for two weeks in urine.[4] Zika virus RNA has been documented in a pregnant woman up to 80 days after clinical onset, but not after delivery.[5, 6] Zika virus RNA has been detected in semen for as long as 370 days after symptom onset; however, the estimated mean time to clearance of Zika virus RNA from semen is 54 days, and detection for long periods is rare.[7]

Sexual transmission of Zika virus is possible and is of particular concern during pregnancy. The longest period reported from symptom onset in the index case to potential sexual transmission to a partner was between 32 and 41 days.[7] Although maternal-fetal transmission occurs, it is unclear whether there are particular stages during the pregnancy when transmission is more likely. Lest one be tempted to conclude that congenital Zika infections linked with birth defects are confined to early pregnancy (first trimester), a Brazilian cohort study of pregnant women with Zika infection reported manifestations of congenital Zika infection with maternal infection occurring as late as gestational week 27.[8]

2.7 Treatment

There is no specific treatment for Zika virus; treatment is supportive.

2.8 Prevention

There is no vaccine against Zika virus. Currently, the two best ways to prevent Zika virus infection are avoiding exposure to mosquitoes in areas of ongoing transmission and avoiding unprotected sexual activity with partners who have recently traveled to a Zika-affected area. The main prevention messages are:

- Pregnant women and women seeking pregnancy should not travel to Zika-affected areas.
- People visiting a Zika-affected area should avoid mosquito bites and unprotected sexual contact while there.
- All people returning from regions with active Zika virus transmission should avoid mosquito bites for at least three weeks after returning.
- After possible Zika exposure, people and their sexual partners should avoid unprotected sexual contact for 8 weeks to 3 months, depending on who traveled (See §5). Those with pregnant partners should avoid unprotected sexual activity for duration of the pregnancy. For more information about Zika for people considering pregnancy, visit the CDC webpage 'Women Trying to Become Pregnant.'

3. CASE DEFINITIONS, DIAGNOSIS AND LABORATORY SERVICES

3.1 Possible Exposure to Zika and Window for Testing

Possible exposure to Zika

- Recent travel to a Zika-affected area; OR
- Unprotected sex with a person who recently traveled to a Zika-affected area or has evidence of Zika infection

Window for testing

Specimens should be collected within 12 weeks of symptom onset or possible Zika exposure since testing methods may not be reliable outside of this 12-week window. If a pregnant woman misses the window for testing, serial fetal ultrasounds are an option (every 3–4 weeks). The woman would become eligible for maternal PCR and IgM testing if any Zika-compatible abnormalities are identified by ultrasound. Amniotic fluid may be considered for Zika testing if amniocentesis is planned for other reasons. (See § 3.5).

3.1 Under Investigation Case Definition (meets recommendation for testing)

Individuals who:

- Are asymptomatic pregnant women (including women who became pregnant within 8 weeks of exposure) with ongoing exposure. Ongoing exposure includes frequent (e.g., at least monthly) travel to a Zika-affected area or unprotected sex with a partner who frequently travels to a Zika-affected area; OR.
- Are born to a mother with Zika infection, but who don't have evidence of infection themselves.

NOTE: *Testing for asymptomatic pregnant women without ongoing exposure or prenatal ultrasound findings consistent with congenital Zika virus syndrome is no longer routinely recommended. Healthcare providers should discuss with their patients the limitations of testing and provide prevention guidance, including avoiding unprotected sex for the duration of the pregnancy.*

3.2 Suspect Case Definition (meets recommendation for testing)

Individuals who:

- Develop clinically compatible illness, which includes one or more of the following symptoms: fever, rash, arthralgia, or conjunctivitis within 2 weeks of possible exposure to Zika; OR
- Are diagnosed with Guillain-Barré syndrome (GBS) within 2 months of possible exposure to Zika; OR
- Are pregnant with or who deliver an infant with abnormalities consistent with congenital Zika syndrome (e.g., microcephaly, intracranial calcifications, or other brain or eye abnormalities) or who experience adverse pregnancy outcomes, including fetal loss following possible exposure to Zika.

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3.3 Presumptive Case Definitions

Any person who has presumptive serologic evidence of infection as determined by CDC.

3.4 Confirmed Case Definition

Any person who has Zika virus RNA sequence as determined by RT-PCR **OR** confirmatory serologic evidence of Zika virus infection as determined by CDC.

3.5 Services Available at the Oregon State Public Health Laboratory (OSPHL)

The OSPHL does not perform Zika virus testing as of January 1, 2019. Zika virus IgM and rRT-PCR testing are available at commercial laboratories. As of the date of these guidelines, ARUP, Quest, LabCorp, and Mayo are some of the laboratories that offer Zika virus testing. Providers pursuing Zika virus testing should consult with their clinical laboratory for guidance on specimen collection and transport.

CDC laboratory testing guidance is available here: www.cdc.gov/zika/laboratories/lab-guidance.html

OSPHL can receive and forward specimens to CDC for confirmatory testing, neonates, fetal losses, or other special cases. If needed, coordinate collection of tissue specimens of neonates and fetal losses who are born to women with suspected, presumptive or confirmed Zika infection: www.cdc.gov/zika/hc-providers/test-specimens-at-time-of-birth.html

CDC recommends placental tissue testing only in select circumstances, e.g., when maternal testing was not performed or done outside the 12-week window, and the infant has clinical findings consistent with congenital Zika syndrome. If providers are interested in placental tissue testing, review the CDC guidance to determine if testing is recommended (found here: www.cdc.gov/pregnancy/zika/testing-follow-up/documents/PlacentalTesting_Guidance_v4-508.pdf).

CDC requires the health department to submit a pre-approval request for any tissue testing. Contact the ACDP Zika Epi so that we can request pre-approval from CDC for tissue testing. The request may not be approved until the infant is born, so placenta specimens may need to be collected, formalin fixed per CDC recommendations, and held until approval is given. There are additional (non-specimen collection) recommendations to plan for as well (see § 6.2).

Please follow the instructions provided on the OSPHL website at www.bitly.com/or-cdc-testing for submission of specimens and required forms for testing at the CDC.

3.6 Interpreting Test Results

Of the two tests conducted for Zika virus infection, only positive rRT-PCR results are considered definitive for confirming Zika infection. IgM may cross-react with *other* flaviviruses (dengue, yellow fever), requiring a confirmatory test. Commercial labs should be following the CDC testing algorithms. Based on testing algorithms, specimens may be sent to the CDC for confirmatory testing after initial

tests are completed. The purpose of CDC's confirmatory test, called a Plaque Reduction Neutralization Test (PRNT), is to identify *which* flavivirus was responsible for recent infection. It works relatively well unless someone was infected by two or more flaviviruses or was previously infected by a flavivirus, in which case the infection with Zika cannot be accurately confirmed. PRNT results should be interpreted in the context of the currently circulating flaviviruses in the region where exposure occurred. For more information on testing and interpretation, see: www.cdc.gov/zika/laboratories/lab-guidance.html

4. CASE INVESTIGATION

4.1 Follow-up for Presumptive and Confirmed Cases

A case with lab evidence of infection requires investigation and follow-up with the case and provider (particularly if the case is pregnant).

- Pregnant women
  - Follow-up with provider to review results.
  - Provide patient education. Here are some CDC links for reference:

    www.cdc.gov/zika/pregnancy/protect-yourself.html

    www.cdc.gov/pregnancy/zika/testing-follow-up/patient-counseling-pregnant-women.html
  - Patient materials are provided in multiple translations.
  - Complete clinical and risk (including travel and sexual exposure history) questions in Orpheus, and provide country of birth, race and ethnicity (needed for CDC reporting). Discuss (typically with the case's medical provider) specimen and tissue testing recommendations at time of birth. Contact ACDP epi to discuss tissue testing at CDC.
- Non-pregnant women and all others
  - Follow-up with provider to review results.
  - Provide patient education (avoiding mosquito bites and providing information about pre-conception planning). Here are some CDC links for reference:

    www.cdc.gov/zika/symptoms/diagnosis.html

    www.cdc.gov/pregnancy/zika/women-and-their-partners.html
  - Patient materials are provided in multiple translations.
  - Complete clinical and risk (including travel and sexual exposure history) questions in Orpheus and provide country of birth, race and ethnicity (needed for CDC reporting).

5. CONTROLLING FURTHER SPREAD

5.1 Environmental and Infection Control

Prevent secondary/local transmission by urging those who have returned from a Zika-affected area (or a chikungunya or dengue-affected area for that matter) to avoid mosquito bites for three weeks after travel or onset of symptoms. Also remind people to hold off on giving blood for 6 months if they are symptomatic or have lab-confirmed Zika infection.

Pregnant couples are encouraged to use guidance outlined in §6.1 below. Couples who are not pregnant are encouraged to use the guidelines below (regardless of their plans for conception).

Suggested timeframe to wait to seek pregnancy following Zika exposure	
Possible exposure via recent travel or sex without a condom with a person infected with Zika	
Women	Men
Wait at least 8 weeks after symptoms start or last possible exposure, whichever is longer	Wait at least 3 months after symptoms start or last possible exposure, whichever is longer

6. MANAGING SPECIAL SITUATIONS

6.1 Pregnancy

Zika infection during pregnancy is associated with problems in fetal development. Congenital infection may be characterized by a pattern of birth defects, classified as congenital Zika syndrome. These features include severe microcephaly, decreased brain tissue, eye defects, joint contractures, and increased muscle tone, restricting body movement. Infants with Zika infection who do not have microcephaly at birth may experience slow head growth and develop microcephaly postnatally.

If ultrasounds or infants at birth show clinical findings consistent with congenital Zika syndrome, there may be additional testing recommendations, including testing infant urine and serum, as well as placental tissue. Placental testing can help to confirm maternal Zika infection in women who have not previously been tested or who were tested outside the 12-week window following possible Zika exposure. Review the CDC guidance for clinical management and evaluation of infants, including testing recommendations:

www.cdc.gov/pregnancy/zika/testing-follow-up/documents/PlacentalTesting_Guidance_v4-508.pdf

Healthcare providers should screen pregnant women for risk of Zika exposure and symptoms of Zika. Pregnant women should not travel to areas where Zika

virus transmission is ongoing. Pregnant women or women seeking pregnancy who do travel to these areas should talk to their healthcare providers and take steps to avoid mosquito bites. Healthcare providers should counsel pregnant women on the interpretation of test results and the limitations of IgM and PCR testing. See CDC guidance here: www.cdc.gov/zika/hc-providers/testresults.html

Pregnant women or their partners who have lived in or traveled to an area with active Zika virus transmission should abstain from sexual activity or should use condoms and other barrier methods, e.g., dental dams, during any sexual activity for the duration of the pregnancy. Click on clinical management to access CDC guidance for care of pregnant women with possible Zika virus exposure.

CDC also recommends that people who are not pregnant but have recent possible Zika exposure wait 8 weeks (if female) or 3 months (if male) before trying to get pregnant. See §5 and additional pre-pregnancy guidance here: www.cdc.gov/zika/pregnancy/women-and-their-partners.html

6.2 Newborn Care

Healthcare providers should screen pregnant women for risk of Zika exposure, such as travel to a Zika-endemic area or unprotected sex with a partner who has traveled to a Zika-endemic area. If no maternal Zika virus exposure is identified, infants should receive routine pediatric care.

All infants who have possible maternal Zika virus exposure should receive a standard evaluation at birth and at each subsequent well-child visit. A standard evaluation includes a comprehensive physical examination, including growth parameters, age-appropriate vision screening, developmental monitoring, and screening using validated tools.

Testing and clinical evaluation beyond a standard evaluation is not routinely recommended for healthy kids (no abnormal findings on ultrasound or at birth) born to moms who had no laboratory evidence of possible Zika virus infection. This includes moms who had negative test results as well as those who were never tested or tested outside of the appropriate window.

Additional testing and follow-up is recommended if maternal or infant Zika test results are positive or if the infant is born with abnormalities consistent with congenital Zika syndrome and there was possible maternal Zika virus exposure. New findings suggest that around 14% of infants born to Zika-infected mothers have Zika-associated health problems, including birth defects such as microcephaly and neurodevelopmental abnormalities. Additionally, some infants with no abnormal findings at birth may have brain or other abnormalities later, so healthcare providers should ensure that these children receive the recommended care and evaluations.[9]

For further information see:

Updated Recommendations for Infants with Zika

www.cdc.gov/pregnancy/zika/testing-follow-up/evaluation-testing.html

www.cdc.gov/pregnancy/zika/testing-follow-up/documents/PlacentalTesting_Guidance_v4-508.pdf

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UPDATE LOG

December 2018: Updated to reflect testing changes at OSPHL and impacts on LHD responsibilities and Orpheus case management. Removed section on specimen collection and appendices. Updated time frame for sexual transmission for males. Information updated on extent of Zika-associated birth defects. (Takeuchi, Leman)

October 2017: Incorporated new CDC guidance for infants (§6.2). Minor edits for clarity (Takeuchi, Leman)

August 2017: Incorporated new CDC guidance regarding testing of pregnant women. Minor edits for clarity (Takeuchi, Leman)

June 2017: Incorporated new CDC testing guidance for asymptomatic pregnant women. Edits for clarity in case definitions, specimen collection, and congenital Zika syndrome. (Takeuchi, Boyd)

October 2016: Incorporated new CDC guidance on pre-conception planning. Edits for clarity in case definitions. Added Appendix A. (Takeuchi, Boyd, Leman)

August 2016: Incorporated new CDC guidance on testing. Updated to reflect occurrence of isolated mosquito-borne transmission on U.S. Mainland. Edits for clarity in case definitions. (Takeuchi, Boyd, Leman)

July 2016: Updates about urine testing, availability of testing through OSPHL, how to handle Zika testing results from commercial labs, new CDC guidance on testing of asymptomatic pregnant women, Tables added to clarify interpretation of test results (§3.7), timing of specimen collection in different situations (§4.1), and recommended time to wait before attempting pregnancy after potential Zika exposure (§6). Updated to reflect potential sexual transmission by women. Updated references. Minor edits for clarity. (Boyd, Takeuchi, Leman)

May 2016: Updated testing of urine, and GBS case definition. Specified that testing criteria now include suspect cases with epidemiologic risk factors and a single Zika-compatible symptom. (Fisher, Ellingson, Leman)

April 2016: Updated evidence and guidance regarding transmission and testing (Fisher, Ellingson, Leman)

February 26, 2016: Incorporated updated CDC guidance on sexual transmission (Ellingson, Fisher, Leman)

February 18, 2016: Incorporated new CDC guidance regarding testing of asymptomatic pregnant women with appropriate travel history, as well as sexual transmission. (Ellingson, Fisher, Leman)

January 2016: Created (Ellingson, Fisher, Leman)