Nebraska Department of Health and Human Services
HEALTH ALERT NETWORK
Advisory

TO: Primary care providers, emergency rooms. OB/Gyn, pediatrics, pathology, microcoordinators, neurology, infection control, infectious disease, and public health

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RE: **Zika Virus Background and Recommendations**

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Background:

Zika virus (ZIKV) is a mosquito-borne virus related to Dengue and West Nile viruses. Zika virus was first recognized in 1947. The first outbreaks occurred in 2007 and 2013 in the Pacific Islands. In 2015, outbreaks occurred in Brazil and other countries. Mosquitoes continue to spread the virus: countries currently affected can be found here (this map is very dynamic and may change frequently): http://www.cdc.gov/zika/geo/index.html

In the Americas, ZIKV is primarily transmitted to people by the bite of *Aedes aegypti* mosquitoes, but *Aedes albopictus* mosquitoes may also be competent vectors. Anyone living in or traveling to an area where ZIKV is found and not already infected with ZIKV is at risk. ZIKV can be transmitted from a pregnant mother to her fetus during pregnancy or around the time of birth. It is not known how often ZIKV perinatal transmission occurs. Transmission via blood transfusion and sexual contact has been reported.

Last week the Nebraska Department of Health and Human Services received reports of two cases of travel-related Zika virus, one form Douglas and one from Sarpy County. These are the first cases in the state. Both people are females in their 20s who recently traveled to Zika-affected countries. Neither was hospitalized.

With the current outbreaks in the Americas, we will see an increasing number of cases among U.S. travelers. Viral introduction and local spread in limited parts of the U.S. where the mosquito vector is endemic may occur.

Clinical characteristics:

Only about 1 in 5 people infected with ZIKV become symptomatic. Characteristic clinical findings are acute onset of fever with maculopapular rash, arthralgia, or conjunctivitis. Clinical illness is usually mild with symptoms lasting for several days to a week. While cases of Guillain-Barré syndrome have been reported in patients following suspected ZIKV infection the relationship between ZIKV infection and Guillain-Barré syndrome needs definitive study.

Congenital risks:

There have been reports of congenital microcephaly in babies of mothers who were infected with ZIKV while pregnant. ZIKV infections have been confirmed in several infants with microcephaly. It is not known how many of the microcephaly cases are associated with ZIKV infection. Studies are under way to investigate the association of ZIKV infection and microcephaly, including the role of other contributory factors (e.g., prior or

concurrent infection with other organisms, nutrition, and environment). **CDC recommends that any pregnant woman regardless of trimester should consider postponing travel to an area where ZIKV transmission is ongoing. If a pregnant women is considering travel to one of these areas, she should talk with her healthcare provider. If she travels, she should strictly follow steps to avoid mosquito bites during the trip.**

Sexual Transmission:

Sexual transmission of ZIKV is possible, and is of particular concern during pregnancy. Current information about possible sexual transmission is based on reports of three cases. In all three cases, the men developed symptomatic illness. Whether infected men who never develop symptoms can transmit ZIKV to their sexual partners is unknown. Sexual transmission of ZIKV from infected women to their sex partners has not been reported.

CDC is recommending that men who reside in or have traveled to an area of active ZIKV transmission who have a pregnant partner should abstain from sexual activity or correctly use condoms during sex for the duration of the pregnancy. Pregnant women should discuss their male partner's potential exposures to mosquitoes and history of ZIKV-like illness (http://www.cdc.gov/zika/symptoms) with their health care provider. Providers can consult CDC's guidelines for evaluation and testing of pregnant women.

For men and their nonpregnant sex partners CDC's recommendation is that men who reside in or have traveled to an area of active ZIKV transmission who are concerned about sexual transmission of ZIKV consider abstaining from sexual activity or using condoms consistently and correctly during sex. Couples considering this decision should take several factors into account. Most infections are asymptomatic, and when illness does occur, it is usually mild with symptoms lasting from several days to a week; severe disease requiring hospitalization is uncommon. The risk for acquiring vector-borne ZIKV in areas of active transmission depends on the duration and extent of exposure to infected mosquitoes and the steps taken to prevent mosquito bites (http://www.cdc.gov/zika/prevention). After infection, ZIKV might persist in semen when it is no longer detectable in blood. How long ZIKV might persist in semen is currently unknown and being studied.

At present, ZIKV testing for the assessment of risk for sexual transmission is of uncertain value, because current understanding of the incidence and duration of shedding in the male genitourinary tract is limited to one case report in which ZIKV persisted longer than in blood. At this time, testing of men for the purpose of assessing risk for sexual transmission is not recommended.

Prevention:

There is no vaccine or specific medicine to treat Zika virus. The best way to prevent Zika or other diseases spread by mosquitoes is to prevent mosquito bites:

- Use an EPA registered mosquito repellent containing DEET, picaridin, oil of lemon eucalyptus, or IR3535
- Dress in long-sleeved shirts, pants and socks when you're outside.
- Stay in places with air conditioning or that use window and door screens to keep mosquitoes outside.

Laboratory Testing:

ZIKV testing can be performed by the CDC on patients who meet the following criteria:

- Two of the following symptoms: acute fever, rash, myalgia, or arthralgia, AND travel to an area with ongoing transmission within the previous 2 weeks of symptom onset;
- Pregnant women with clinical illness consistent with ZIKV disease (two or more of the above symptoms) AND history of travel to an area with ongoing ZIKV transmission the previous 2 weeks;
- Pregnant women without clinical illness consistent with ZIKV disease with history of travel to an area with ongoing ZIKV disease (testing should be performed 2-12 weeks after travel).
- Suspected fetal infection

There are four ways to test for ZIKV. None are available commercially. Except for a few states, all ZIKV testing is currently performed at the CDC Arbovirus Diagnostic Laboratory. Our Nebraska Public Health Lab is collaborating with CDC to establish testing but will not have that testing operational for 3-4 months. Healthcare providers in Nebraska should contact their local public health department (http://www.dhhs.ne.gov/lhd) to arrange for testing.

The four tests for ZIKV:

1) During the first week of illness, ZIKV disease can be diagnosed by performing reverse transcriptase-polymerase chain reaction (RT-PCR) on serum. A RT-PCR test may not demonstrate ZIKV RNA in a person with ZIKV infection if the period of viremia has passed. Specimens should be collected within the first seven days following symptom onset.
2) An IgM ELISA assay can detect ZIKV IgM antibody. The specimen should be collected between four and 30 days following the onset of symptoms.
3) Because of the potential for IgM ELISA cross-reactivity with related flaviviruses (e.g., dengue, West Nile, yellow fever and St. Louis encephalitis viruses) plaque-reduction neutralization testing (PRNT) is required on IgM (+) samples to differentiate between these viruses. Cross-reactivity between these flaviviruses, including persons vaccinated against yellow fever or Japanese encephalitis remains a concern.
4) IgG ELISA is not currently available at CDC, but needs to be developed for persons who are beyond the 30-day window for IgM ELISA/PRNT.

Laboratory Specimen Collection:

Instructions for Physicians:

1) Collect blood in three separate 6.0 mL serum separator tubes (may be red or gold/tiger top). Providers can refer to their laboratory for guidelines on collecting serum. It may differ depending on where they get their tubes, or their procedures.

Note: The NPHL will coordinate the submission of specimens to the CDC Arbovirus Branch laboratory for testing.

Pre-approval is required from state or local public health before submitting a specimen for testing.

Supplemental Forms Required: A NPHL Special Microbiology Requisition must accompany the specimen. In addition, a CDC clinical investigation form (CDC DASH form) must include the following information: **complete patient information-name, date of birth, date of onset of symptoms, pregnancy status, signs and symptoms and underlying illness; travel history; and vaccine history.**

Instructions for Labs:

1) Laboratory should separate the serum, at least 0.5 mL, but more is better in case more testing is needed, and send it to NPHL in a separate, sealed tube. For further information please see the table below.

Specimen:	Serum and cerebrospinal fluid (CSF)
Collection Device:	Clot (Red) or SST(Gold) tube, CSF collection tube **Specimen Labeling:** Test subject to CLIA regulations and required 2 patient identifiers on specimen container and requisition forms
Volume:	Serum:1 mL; Minimum:0.25 mL (additional testing for dengue and chikungunya requires separate containers); CSF 1.0 mL
Storage/Transport	Centrifuge and aliquot serum into sterile leakproof tube, ASAP. Place both CSF and serum at 4°C. **Shipping instructions, including specimen handling requirements during transport:** Sender should contact the NPHL by email or phone before shipping. Ship specimen Monday -Thursday overnight to avoid weekend deliveries. Refrigerated, specimen should be shipped on cold packs. Package and ship as Category B, Biological Substance, UN3373. See instructions and shipping address: http://nphl.org/. Do not send directly to CDC.
Unacceptable:	Severely lipemic, icteric or hemolyzed samples; heat-inactivated serum; multiple freeze thaw cycles
Specimen Stability:	2-8°C for 72 hours, if > 3 days, freeze

Zika Virus Resources:

CDC Zika Virus Landing Page http://www.cdc.gov/zika/

PAHO/WHO Zika Virus Landing Page
http://www.paho.org/hq/index.php?option=com_content&view=article&id=11585&Itemid=41688&lang=en

Updated Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women Reproduction Age with Possible Zika Virus Exposure- United States, 2016
http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm?s_cid=mm6505e2er.htm_w

Interim Guidelines for the Evaluation and Testing of Infants with Possible Congenital Zika Virus Infection- United States, 2016 http://www.cdc.gov/mmwr/volumes/65/wr/mm6503e3.htm

Interim Guidelines for Prevention of Sexual Transmission of Zika Virus- United States, 2016
http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e1er.htm?s_cid=mm6505e1er_w.htm

Questions and Answers for Obstetrical Healthcare Providers: Pregnant Women and Zika Virus Infection
http://www.cdc.gov/zika/hc-providers/qa-pregnant-women.html

Questions and Answers for Pediatric Healthcare Providers: Infants and Zika Virus Infection
http://www.cdc.gov/zika/hc-providers/qa-pediatrician.html

Question and Answers: Zika and Sexual Transmission http://www.cdc.gov/zika/hc-providers/qa-sexual-transmission.html