Preventing Zika Virus Infection and its Consequences: Update and Guidance for Clinicians

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Keeping up with Zika has been a challenge for health care providers. The areas affected by Zika outbreaks have expanded and recommendations for diagnosis and management have changed as our understanding of the disease increased and new lab tests became available. As we move into the high-risk summer season when more people travel and the mosquito vectors that transmit Zika increase, it is a good time to review current recommendations for diagnosis and prevention.

Background

In 2016, Zika virus outbreaks spread throughout Latin America and the Caribbean. Travel notices currently are posted for 60 countries and territories including in Asia and the Pacific. The large majority of Zika infections identified in the U.S. have occurred among travelers to affected areas but local outbreaks also have occurred in South Florida and Brownsville, Texas, resulting in 218 and 6 cases, respectively. Numbers of reported Zika cases, however, are certainly a substantial underestimate of the true burden of infection as 80% of infections are asymptomatic and persons with mild symptoms may not seek care or be diagnosed. In Puerto Rico, for example, over a period during which about 25,000 cases were reported, screening of blood donors suggested that 13% of the population had been infected, translating to over 475,000 people, consistent with only 1 in 19 cases being reported. Although no mosquito-borne Zika transmission has occurred in Los Angeles County or anywhere in California, conditions sufficient for a local outbreak (introduction of the virus by travelers and the presence of Aedes species mosquitoes that transmit infection) are present. The Centers for Disease Control and Prevention (CDC) have identified LA County as one of the U.S. jurisdictions at highest risk for an outbreak.

Zika infection during pregnancy is the greatest concern due to adverse pregnancy and birth outcomes. Microcephaly associated with disruption of brain development has been identified in 4% of U.S. infants whose mothers were infected during pregnancy, similar to estimates from Brazil and other earlier outbreaks. Recent data from a Brazilian cohort study, however, suggests that Zika infection can cause a much broader range of defects and affect a much higher proportion of infants. From a cohort of 134 Brazilian women with symptomatic Zika infection during pregnancy, defects were identified by clinical examination or imaging in 42% of infants. Defects occurred in 55% of infants whose mothers were infected during the first trimester, 51% in the second, and 29% in the third. Abnormalities on exam included hypertonicity, clonus, hyperreflexia, abnormal movements, spasticity, contractures, seizures, abnormal fundoscopic exams, and abnormal hearing tests. Imaging showed cerebral calcification, cerebral atrophy, ventricular enlargement, hypoplasia of cerebral structures, and parenchymal brain hemorrhages. While the complete spectrum of congenital Zika virus disease and its long-term consequences are not yet known, the impacts on infants and their families are likely to be far greater than previously recognized.

With the onset of summer in LA County, Zika-associated risks increase. Warmer weather will lead to increased density of the Aedes mosquito vectors in Mexico and Central America, where in 2016, 76% of LA County’s reported Zika cases acquired the infection. Increased summer travel to other areas with Zika virus will also increase Zika cases in Los Angeles. More than half of the 98 Zika cases reported in the county last year were acquired during travel in July and August. And during summer, the risk of a local outbreak increases as more infections among travelers coincides with an expanding indigenous Aedes mosquito population.

What can health care providers do to reduce the threat to individuals and public health?

Reducing Individual Zika Risk

Travel-Related Risk

CDC recommends that pregnant women not travel to areas with Zika virus infection risk. If a pregnant woman must travel to a Zika affected area, she should be counseled to strictly follow steps to prevent mosquito bites and sexual transmission of Zika during the trip.

Precautions for all travelers to Zika-affected areas to reduce the risk of mosquito bites include:

- Consistently using insect repellent with an EPA-registered ingredient (all of which are safe for use during pregnancy when following manufacturers’ instructions);
- Avoiding areas where mosquitoes are most prevalent;
- Wearing long sleeved shirts and pants; and
- Keeping mosquitoes outside the house by staying in a residence with screens or air conditioning.

Clinicians should ask their patients if they or any of their family members intend to travel and, if they are traveling to a Zika-affected area, provide appropriate education and counseling. Patient education materials can be downloaded from the Los Angeles County Department of Public Health (DPH) Zika Education and Outreach webpage and the CDC’s Mosquito Bites Prevention webpage.

http://rx.ph.lacounty.gov/RxZika0717
Understanding the epidemiology of Zika in pregnant women in the county may assist providers to better target their counseling efforts to women at highest risk of travel-associated Zika. Of 15 Zika cases among pregnant women in 2015-2016, 87% of these women were Latina. The large majority of these women were born outside of the U.S., most spoke Spanish as their first language, half owned a residence in the country to which they traveled, another quarter were visiting family, and the median duration of their travel exceeded one month. Clinicians should be particularly diligent in promoting behavior change when they identify pregnant women who fit this highest-risk profile. However, modifying travel behavior of women who may be “bi-national,” who want to be with family during their pregnancy, or who have financial reasons to travel is a substantial challenge and will require cultural sensitivity and time. While DPH is working with community partners to educate women who are at high risk, the most effective intervention is likely to be a recommendation from a trusted healthcare provider.

**Sexual Transmission**

Zika can be transmitted sexually. It is important to counsel patients about reducing the risk of sexual transmission, particularly to pregnant women and to those trying to conceive. In contrast to travel-associated Zika infections in the U.S., the number of confirmed Zika infections transmitted through sex is small (in 2016, only 46 of 5,102 symptomatic Zika cases in the U.S. were sexually transmitted). The CDC recommendations regarding reducing sexual transmission to pregnant women or those trying to conceive are summarized below. All other guidance regarding reducing sexual transmission can be found on the CDC’s Sexual Transmission and Prevention webpage.

- If a pregnant woman or her partner travel to a Zika-affected area, the couple should either consistently use condoms every time they have sex, or not have sex, for the entire pregnancy, even if the traveler does not have symptoms of Zika or feel sick.
- Couples who are interested in pregnancy where one person traveled to a Zika-affected area, should consider delaying conception until the risk of Zika transmission is passed:
  - If the male partner traveled: the couple should use condoms or not have sex for at least 6 months after the male partner returns, even if he doesn’t have symptoms, or from the start of his symptoms or the date he was diagnosed with Zika, whichever period is longest. The 6 months is based on the duration of time that the virus may be identified in semen.
  - If the female partner traveled: the couple should use condoms or not have sex for at least 8 weeks after the female partner returns even if she doesn’t have symptoms, or from the start of her symptoms or the date she was diagnosed with Zika, whichever period is longest.

**Why is the diagnosis of Zika important when there is no treatment and the clinical illness is usually mild and self-limited?**

**Improving Zika Diagnosis**

For pregnant women, appropriate screening, counseling, and care all depend on making a diagnosis of Zika. CDC guidelines for testing pregnant women and for clinical management are available online and in a recent issue of the MMWR. Diagnosis of Zika infection in non-pregnant symptomatic persons is also important. Diagnosis facilitates counseling to reduce the risk of sexual transmission (especially to women who are pregnant or may become pregnant) and to avoid local mosquito bites for 3 weeks to decrease the risk of transmitting the Zika virus to local Aedes mosquitoes, potentially igniting a local outbreak. Identification of Zika also triggers an immediate public health and vector control response to reduce the chance of a local outbreak.

Clinical characteristics of Zika infection include acute onset of fever, maculopapular rash, arthralgia and conjunctivitis. Recently, the CDC has also described headache and myalgia as Zika-associated symptoms. Laboratory testing for Zika is recommended for all persons who have one or more symptoms consistent with Zika and who have an exposure history through travel or sexual contact with a traveler. Providers should consider travel both to foreign locations as well as U.S. locations experiencing Zika outbreaks; in 2016, one LA County case had been exposed in South Florida. The clinical presentation of Zika is similar in both adults and children; therefore, recommendations do not differ for pediatric patients.

Given the importance of diagnosis, all pregnant women, regardless of symptoms, should be tested for Zika if they or their sexual partner have a history of traveling to, or living in, a Zika affected area (see algorithm). Asymptomatic men and non-pregnant women do not need to be tested, although precautions against sexual transmission should be followed.

**CDC Algorithm for Testing Pregnant Women with Possible Exposure to Zika Virus**

http://rx.ph.lacounty.gov/RxZika0717
Complete guidance for Zika laboratory testing is beyond the scope of this article and can be found on the CDC Diagnostic Tests webpage. In brief, two types of tests are available for diagnosis: nucleic acid testing by real-time reverse transcription polymerase chain reaction (rRT-PCR) and serology. rRT-PCR should be done on serum and urine samples collected within 14 days of symptom onset or for asymptomatic pregnant women, within 14 days of the last possible exposure. A positive test confirms Zika infection; a negative test does not exclude Zika and CDC recommends an IgM serology test.

Serum IgM antibody generally develops toward the end of the first week of illness and remains positive for about 12 weeks. Specimens collected between 14 days and 12 weeks after exposure should be tested for Zika virus IgM. Because antibody to other flavivirus infections (e.g., dengue, chikungunya) may cross-react with Zika antibodies, a positive IgM test must be confirmed with a plaque reduction neutralization test (PRNT). Interpreting serology results may be challenging because the PRNT titer may be elevated for Zika and another flavivirus. CDC guidance on interpreting Zika antibody test results can be found in the June 3, 2016 issue of the MMWR.¹⁰

Both Zika rRT-PCR and IgM tests are available at commercial laboratories and at the DPH laboratory. PRNT testing is done at the California Department of Public Health (CDPH). Specimens are forwarded to CDPH for testing by the laboratory that obtained the positive IgM result and the PRNT test result is reported by that laboratory. Confirmatory test results likely will take several weeks to become available.

Reducing Public Health Risk

Evidence of local, mosquito-borne transmission of Zika virus in LA County would likely lead to a number of significant consequences: enhanced investigation, possibly including house-to-house testing of residents living near a case; widespread and recurrent testing of pregnant women; expanded vector control measures including application of pesticides to kill larvae and adult mosquitoes; possible economic impacts from avoidance of affected areas; and increased levels of anxiety among pregnant women, couples wanting to become pregnant, and those living in the outbreak area.

Aedes albopictus and Aedes aegypti mosquitoes were first introduced into the county in 2011 and 2014, respectively, they have spread widely (see map

http://rx.ph.lacounty.gov/Rx Zika0717
and listing of cities below). In 2016, new areas of infestation were identified in the San Fernando Valley, the eastern San Gabriel Valley, and in the City of Los Angeles west of downtown. Some areas on the map not showing infestation may, in fact, have Aedes mosquitoes, but testing has not yet detected their presence.

**Location of Aedes Aegypti and Aedes Albopictus Mosquitoes in Los Angeles County**

Click images to expand view

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**Map of Los Angeles County, December 2016**

*Aedes aegypti* locations are shown in red and *Aedes albopictus* locations are shown in blue.

Zip codes with one or more Zika case are highlighted in yellow

**List of Cities in Los Angeles County, June 2017**

*Aedes aegypti* locations are shown in red and *Aedes albopictus* locations are shown in blue.

Cities with both types of mosquito are shown in purple

Adapted from [www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/AedesDistributionMap.pdf](http://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/AedesDistributionMap.pdf)

*Aedes albopictus* and *Aedes aegypti* mosquitoes have also been detected elsewhere in California (see map below).

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**Aedes aegypti and Aedes albopictus Mosquitoes in California Detection Sites by County/City Updated June 23, 2017**

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**Counties with Aedes aegypti only**: Fresno, Imperial, Madera, Riverside, San Mateo, Tulare

**Both Aedes aegypti and Aedes albopictus**: Kern, Los Angeles, Orange, San Bernardino, San Diego.

Click the image to view the full size map and a listing of Aedes detections by city or census-designated place in each county.

Source: [www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/AedesDistributionMap.pdf](http://www.cdph.ca.gov/Programs/CID/DCDC/CDPH%20Document%20Library/AedesDistributionMap.pdf)
Health care providers can take several actions to reduce the risk of a local Zika outbreak, especially by providing information and education, and promoting behavior change (see ‘key actions’ below).

**Key Actions for Clinicians to Reduce Individual and Community Risk of Zika in LA County**

- **Provide health education materials**
  - Make posters/flyers available on travel-associated Zika, reducing mosquito breeding sites, and preventing mosquito bites.

- **Ask patients about upcoming travel to a Zika affected area**

- **Recommend pregnant women defer travel to Zika affected areas**
  - Provide culturally sensitive counseling.

- **Recommend travelers to a Zika affected area take precautions to reduce the risk of mosquito bites during their trip and for 3 weeks after they return**
  - Educate all returning travelers, regardless of symptoms, to avoid mosquito bites for 3 weeks to reduce the risk of initiating a local outbreak.

- **Provide guidance for pregnant women and couples wanting to become pregnant**
  - Recommend that they abstain from sexual contact or use condoms consistently for defined time periods after either partner travels to an affected area.

- **Encourage all patients to “tip and toss” to reduce mosquito breeding sites around their residences**
  - Use materials and reinforce messages to eliminate standing water and get rid of containers where *Aedes* mosquito eggs may be laid.

If locally acquired Zika infections do occur, early identification will facilitate a quick response to contain spread of infection and eliminate *Aedes* mosquitoes. Because current guidelines limit Zika diagnostic testing to individuals who have traveled to Zika-affected areas or had sexual contact with a traveler, local transmission would most likely not be identified in a person who lacks these exposures. In Texas, to increase the likelihood of detecting local transmission of the Zika virus, public health officials have recommended testing non-travelers for Zika if they live in the Lower Rio Grande Valley and have rash and at least one other common Zika symptom. Because LA County is an area at increased risk of local, mosquito-borne transmission, providers should consider a diagnosis of Zika in a patient who has not traveled to an affected area or had sex with a traveler if the patient meets all of the following criteria:

- Lives or works in an area with documented *Aedes aegypti* mosquitoes* (see map and listing of cites above);
- Has a maculopapular rash AND at least one other symptom consistent with Zika (fever, joint pain, or conjunctivitis);
- Is ≥18 years old (febrile rash illness frequently occurs in children associated with viral infection; not testing children will substantially improve the specificity of surveillance for Zika); and
- No other diagnosis is identified that could cause the observed symptoms.

* *Aedes aegypti* transmit Zika much more effectively than *Aedes albopictus* and therefore guidance for testing to detect potential local transmission is focused on areas with *Aedes aegypti*.

As the patient would be acutely symptomatic, an rRT-PCR would be the appropriate diagnostic test. In the absence of known local infection, confirmation of a negative test with serology would not be needed. Clinicians who suspect Zika infection in a patient who has not travelled to a Zika-affected area may consult with the DPH Acute Communicable Disease Control Program (ACDC) at 213-240-7941. Confirmed locally acquired disease should be reported immediately by telephone to ACDC.

**Conclusions**

Health care providers play a critical role both in reducing their patients’ risk of Zika infection as well as preventing an outbreak in the community. Through effective counseling, diagnosis and prevention, the impacts of Zika, particularly for pregnant women and their families, can be reduced. It is important that providers remain up-to-date on the clinical aspects of this infection as well as on the evolving outbreak.

Changes in geographical areas affected by Zika are likely to occur throughout the year. Similarly, recommendations and algorithms for diagnosis, laboratory testing, and prevention may change as additional knowledge is gained. Therefore, it is recommended that providers periodically refer to the DPH and CDC Zika webpages to ensure optimal practices to address this emerging infection.

http://rx.ph.lacounty.gov/RxZika0717
Additional Resources

- DPH - Zika webpage www.publichealth.lacounty.gov/acd/VectorZika.htm

Patient Resources

- DPH - Zika education and outreach materials http://publichealth.lacounty.gov/acd/ZikaMaterials.htm

Continuing Medical Education

To obtain CME click here

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