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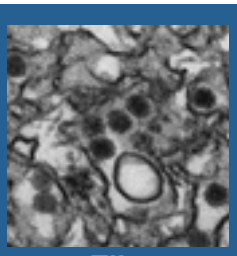
The Buzz About Zika

If you've just returned from hiking the Pacific Crest Trail for the past several months, you might be surprised to find the previously esoteric "Zika" virus very much in the news. To this point, Oregon has had nine cases, three back in 2014 among people who had traveled to Polynesia, and six in the past four months associated with travel to Zika-affected areas of the Western Hemisphere. "Sheesh," you might say, "we have more *malaria* than that!"* So what's all the buzz about? In this issue of the *CD Summary,* we review the history of Zika, its usually mild clinical presentation, the available evidence about its association with severe neurological complications, and current prevention recommendations.


Zika


Pika

Zika (not to be confused with "pika"— an adorable little rodent-like animal with cute human-like ears) is a mosquito-borne flavivirus related to West Nile and dengue. It was named after the Zika forest in Uganda, where it was first isolated in 1947 from an infected monkey.[1] Few human cases were noted until 2007, when an outbreak in Yap (Federated States of Micronesia) brought Zika to the attention of epidemiologists. In 2013, Zika was confirmed in 4 other groups of Pacific Islands: French Polynesia, Easter Island, the Cook Islands, and New Caledonia. It's unclear how much this reflected an actual increase in Zika illness, and how much it resulted from increased surveillance and the broader availability of diagnostic tests. Regardless, Zika spread to the Western Hemisphere, gaining a foothold in Brazil in 2015, and since then spreading to Mexico, Central America, northern South America, and most major islands in the Caribbean. To keep us current on the continuing spread of the virus, CDC maintains and regularly updates its map of countries with local, mosquito-borne transmission of Zika.

Zika is spread to people primarily through the bite of *Aedes aegypti* and *Aedes albopictus* mosquitoes, the only known competent vectors. These mosquitoes are found in many other countries and in some parts of the United States, but not in Oregon (figure, page 2).

*Malaria in Oregon: an average of 17 cases/year during 2011–2015, all imported.

Sexual transmission

Regrettably, the evidence is now convincing that Zika virus can also be spread through sexual activity. This is based on laboratory-confirmed infection in people who had not traveled to a Zika-affected region, and whose only known risk factor was sexual activity with a person who also had laboratory evidence of disease. As this issue goes to press, the only known cases of sexual transmission were from symptomatic, male partners. The "n," however, is small: fewer than 20 confirmed cases acquired via sexual transmission have been documented.[2]

Typical illness

Zika tends to cause mild illness, when it causes illness at all; serosurveys suggest that four out of five people who encounter the virus have no symptoms whatsoever. Those who do get sick have some combination of fever, pruritic maculopapular rash, joint pain, and conjunctivitis (usually non-purulent), commencing after an incubation period of 3–14 days; symptoms typically resolve within a week. There is no vaccine against Zika, although efforts to develop one are underway; treatment is supportive.

Figure. Estimated range of *Aedes aegypti* and *Aedes albopctus*, United States, 2016

Source: CDC

The real concern about Zika, and the reason it has attracted so much attention, is a growing body of evidence suggesting that it might lead to Guillain-Barré syndrome (GBS), and that Zika infection during pregnancy could be fatal to the fetus, or cause abnormal intrauterine brain development with resultant birth defects.

Zika and pregnancy

In Brazil, clinicians noted an increase in microcephaly (just over 5,000 suspected cases as of late March 2016) that coincided with the Zika outbreak in that country. CDC detected Zika virus RNA through polymerase chain reaction testing of brain tissue from two congenitally affected neonates who died shortly after birth, and of the products of conception from two miscarriages — compelling evidence that the virus can breach the placental barrier and infect the gestating fetus.[3] A recently published epidemiologic analysis made creative use of seroprevalence studies and retrospective surveillance for microcephaly in French Polynesia

to assess the risk of microcephaly associated with Zika infection during pregnancy. They found seven cases of microcephaly during the outbreak period — a rate of 95 per 10,000 live births — versus 2 per 10,000 during the pre-outbreak period. Based on statistical models and sensitivity analyses, the authors concluded that Zika infection during the first trimester was associated with increased risk of microcephaly, but acknowledged that more research was needed.[4] In a recent study involving symptomatic, lab-confirmed, Zika-infected pregnant women in Brazil, of 42 who had fetal ultrasounds, 12 (29%) had some abnormal finding: 3rd trimester fetal death in two, microcephaly with or without cerebral calcifications in four, cerebral calcifications in two without microcephaly, and other vascular or growth abnormalities in four others.[5] These studies don't constitute the "smoking gun" that definitely establishes a causal role for Zika infection, but CDC has taken all evidence collectively and sconcluded that Zika infection is teratogenic.[6]

Zika and Guillain-Barré syndrome

In a matched case-control study of people with GBS in French Polynesia between October 2013 and April 2014, 41 of 42 patients with GBS had serologic evidence (IgG or IgM) of Zika virus infection, compared with 54 of 98 controls (odds ratio 33, $p<0.0001$). Additionally, 37 cases (88%) reported a transient illness consistent with symptomatic Zika infection a median of six days prior to onset of neurologic symptoms.[7] Although you can't prove causality through a case-control study, absent some overwhelming bias in the data, the strong association is at least highly suggestive.

Diagnosing and reporting Zika infections

Zika infection is reportable in Oregon, and public health can facilitate testing in appropriate patients. If you haven't already, please check out our Zika Virus Information for Oregon Healthcare Providers webpage. We are working to make it a one-stop resource for Oregon providers regarding Zika testing, reporting, prevention, and public health implications. Tests for Zika are not yet available commercially, and at this point all testing must be approved by your friendly local public health authority. If you are considering testing and your local health department agrees, be aware that results do not come quickly: it may be a month or more before you have any results. CDC has published recommendations for monitoring pregnant women and infants with evidence of Zika virus infection or characteristic abnormalities on ultrasound.

The low-down on prevention

The risk of mosquito-borne Zika transmission in Oregon is currently nil. Although local vector control districts have identified several species of *Aedes* mosquitoes in Oregon in recent years, these have not included *Ae. aegypti* or *albopictus* — the only ones known to carry Zika. That being said, we don't want to find out the hard way that Oregon mosquitoes can, after all, be competent vectors. If you have a patient with planned travel to a

Zika-affected area, encourage and educate them to avoid mosquito bites while there and for at least three weeks after returning to Oregon.

Given the concern about infection during pregnancy, if a pregnant woman's partner has been traveling in a Zika-affected area, they should avoid unprotected sex — vaginal, oral, or otherwise — for the duration of the pregnancy. Further, CDC recommends that pregnant women consider postponing any planned travel to Zika-affected areas. Pregnant women and those seeking pregnancy who decide to visit one of these areas should take special care to avoid mosquito bites by using insect repellent, or a treated bed net if the sleeping quarters are at all open to the outside. In fact, taking these steps to avoid mosquitoes is a good plan for anyone who visits a Zika-affected region.

It's worth noting that not all locations south of the border are equally affected. Make sure to check the CDC list. Some Caribbean islands and South American countries have hitherto been spared the scourge; and destinations at elevations of >2,000 meters (>6,500 feet) pose a negligible risk of Zika infection — at least if we can infer anything from what we know of dengue transmission. So your patient's upcoming trip to Mexico City, or Quito or Bogotá, for that matter, is unlikely to result in Zika infection. When in doubt about elevation, considering all the other nasty mosquito-borne diseases in many of these regions, we'd encourage your patients not to quibble; it's probably just as well to avoid mosquito bites.

Clinicians have relayed to us a number of questions from couples seeking pregnancy. Unfortunately, we don't yet have data about viral loads in people asymptomatically infected with Zika, and we don't know what percentage of men with symptomatic Zika infection carry the virus in semen, or for how long. From an abundance of caution,† CDC currently recommends that men wait 6 months after traveling to a Zika-affected area and women at least 8 weeks before attempting to conceive a child.

Stay tuned.

Resources

- For updated case counts and other breaking information about Zika, check out our Zika Virus Updates webpage.
- For up-to-date information geared to healthcare providers, visit www.bitly.com/zikaoregon
- For a list of countries in the Western Hemisphere affected by the current outbreak, click on http://www.cdc.gov/zika/geo/americas.html

† and a dearth of data

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