

[Primary Care]

Update on Zika Virus: Considerations for the Traveling Athlete

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As public health experts work to contain the outbreak of Zika virus in South America and minimize the devastating prenatal complications, the international sports community prepares for the 2016 Summer Olympic and Paralympic Games in Rio de Janeiro, Brazil. Athletes have publicly expressed concern regarding the health risks of competition in Zika-endemic areas.³³ Ensuring the safety of the athletes during training and competition is the primary role of the team physician. Special consideration is needed for sports teams preparing for travel to areas affected by Zika virus.

Keywords: Zika virus; infectious disease; travel medicine; Olympic athletes; Paralympic athletes

Zika virus is an arthropod-borne virus (arbovirus) that is a single-stranded positive RNA flavivirus. It was named for the forest where it was initially identified in rhesus monkeys in Uganda in 1947. The first reported cases in humans were in 1952, although no outbreaks of Zika virus occurred until recently.^{8,15,23}

The first outbreaks of Zika virus occurred in Yap State, Federated States of Micronesia and 2010 in Cambodia.^{9,15} Subsequently in 2013-2014, an outbreak occurred in French Polynesia, which later spread to surrounding Pacific Islands, including New Caledonia, the Cook Islands, Easter Island, Vanuatu, and Solomon Islands.^{9,16,21} An estimated 28,000 cases were reported in French Polynesia, representing 11% of the population.^{5,9} The infection is also associated with Guillain-Barré syndrome, which increased 20-fold during this particular outbreak.²³

Zika virus may have been brought to Brazil during the 2014 FIFA World Cup. Although no Pacific Island teams competed in World Cup, foreign spectators from French Polynesia and the Pacific Islands may have traveled to Brazil during an acute infection with or without symptoms.³⁴ Additionally, shortly after the World Cup, the Va'a World Sprint Championship canoe race was held in Rio de Janeiro, where Pacific Island teams competed and could have contributed to the spread of Zika virus.³⁴

The first identified cases of Zika virus in Brazil were in March 2015, when a cohort of patients in Bahia, Brazil with symptoms

of an acute viral illness were tested for various viruses by serum reverse transcription polymerase chain reaction (RT-PCR); 29% were found to have Zika virus and 13% found to have chikungunya. The strain of Zika virus was later determined to be nearly identical to that found in French Polynesia and the Pacific Islands.⁸ Since then, the virus has spread throughout South America and the Caribbean. By December 2015, Brazil's Ministry of Health estimated 440,000 to 1,500,000 cases of Zika virus infection.¹⁹

Apart from Brazil, the Zika virus has been detected in more than 34 countries. While mosquito-borne transmission of the Zika virus has not occurred in the continental United States during the 2015-2016 outbreak, the first case of sexually transmitted infection was reported in Texas in February 2016.¹³

OVERVIEW OF ZIKA VIRUS

Transmission

Zika virus is primarily transmitted to humans by the bite of an infected mosquito. Several species of mosquitos have been identified as carriers of the virus, including an *Aedes* species mosquito that is endemic in the tropics and subtropics (Figure 1).²³ Additional methods of transmission include sexual intercourse, perinatal, in utero, and potentially, blood transfusion.^{5,17} A case report of a semen sample positive by RT-PCR 2 months after the onset of febrile illness suggests prolonged potential for sexual transmission, although the

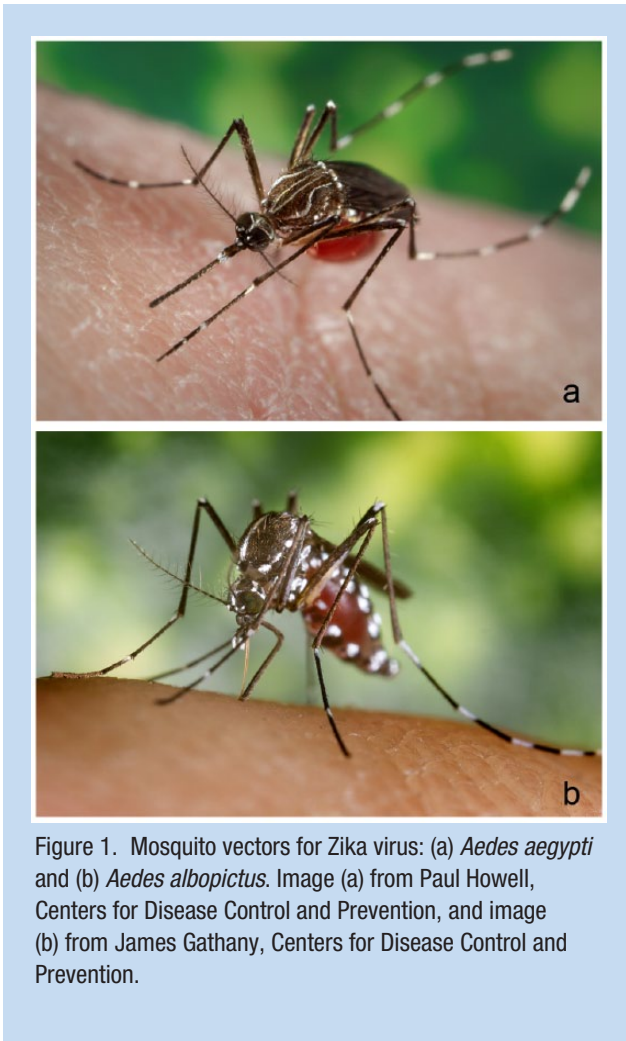
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duration of infectivity for this mode of transmission is unknown.³

Symptoms

Approximately 20% of people who are infected with Zika virus develop symptoms.²⁴ The incubation period between mosquito bite and onset of clinical manifestation is typically 2 to 14 days. In French Polynesia, where asymptomatic blood donors were screened, 3% of donors had an acute Zika virus infection.²² For those who do experience symptoms, they are typically mild and include rash, arthralgias, conjunctival injection, fatigue, malaise, retro-orbital pain, paresthesia, headache, myalgia, and lymphadenopathy (Table 1).^{7,8} The rash is often pruritic, descending, and macular or maculopapular. Symptoms can last for 1 to 7 days.^{8,24}

Differential Diagnosis

Zika virus infection can present with symptoms similar to dengue and chikungunya, which are also transmitted by mosquitos and have overlapping regions where the viruses are

Table 1. Zika virus symptoms and relative prevalence

Symptom	Prevalence, % ^{7,8}
Rash	86-100
Arthralgias	64
Conjunctival injection	58
Fatigue, malaise	49
Retro-orbital pain	49
Paresthesia	47
Headache	43-53
Myalgias	41-57
Lymphadenopathy	40
Nausea	38
Edema	36
Photophobia	31
Diarrhea	31
Fever	28-43
Respiratory	19
Anorexia	13
Bleeding, petechial, or enanthema	13
Abdominal	6
Dizziness	6

endemic. Since clinical features of Zika virus are unable to be fully differentiated from dengue and chikungunya, serologic testing is needed in suspected cases.⁸ However, features suggestive but not diagnostic of Zika virus include a febrile illness with maculopapular rash in combination with conjunctival injection and/or lymphadenopathy.⁷ Additional considerations in the differential diagnosis include adenovirus, enterovirus, group A streptococcus, leptospirosis, malaria, measles, rubella, parvovirus, and rickettsia.¹⁹

Diagnosis

During the initial 3 to 14 days of symptoms, Zika virus can be detected by RT-PCR of either blood or urine.¹⁸ In a study of 72 RT-PCR pregnant women, 47% were positive by both blood and urine, 36% by blood only, and 17% by urine only.⁷ RT-PCR is unable to rule out a Zika virus infection once viremia has resolved, which can occur within 1 week. After the first week of symptoms, virus-specific IgM and neutralizing antibodies are

needed to detect evidence of the infection.²⁵ Results of laboratory tests when performed in the United States may take up to 2 weeks to be available. If Zika virus infection is diagnosed, local health officials must be notified.²⁴

Treatment

There is no specific treatment for Zika virus. In most cases, the infection is self-limited and symptoms resolve within 1 week without intervention. Symptomatic management involves rest, hydration, and use of acetaminophen. Until dengue fever is ruled out, nonsteroidal anti-inflammatory medications and aspirin should be avoided given the risk of hemorrhage.²⁴

Neonatal Complications

In 2015, the first signs of a potential adverse effect of the Zika virus disease during pregnancy were discovered when an increased prevalence of microcephaly was identified in areas of Brazil affected by Zika virus. The virus was later detected in amniotic fluid of confirmed cases of neonatal microcephaly.^{14,29,32} Zika virus has since been implicated in cases of severe fetal neurologic abnormalities when the infection occurs in a pregnant woman. One study reported that 29% of pregnancies affected by Zika virus infection were found to have sonographic abnormalities, including intrauterine growth restriction, microcephaly, and fetal death.⁷ Initially, Brazil's Ministry of Health announced that more than 4000 cases of microcephaly had been reported since the outbreak began, but the cases are being investigated for accuracy of diagnosis and association with Zika virus.⁶ Given these potential risks, the Centers for Disease Control and Prevention (CDC) has advised pregnant women to postpone travel to affected countries.¹¹ El Salvador, which has also been affected by the Zika virus, recently recommended that women wait until 2018 to become pregnant—a recommendation not supported by the World Health Organization.¹

Guillain-Barré Syndrome

While the majority of Zika virus infections present with an influenza-like illness and cutaneous rash, there have been atypical cases that have been associated with subsequent Guillain-Barré syndrome (GBS). The first case of GBS that occurred immediately after Zika virus infection was reported in French Polynesia during coepidemics of Zika virus and dengue fever in late 2013.²⁸ A direct causal relationship has not yet been definitively established. However, there seem to be an increased number of GBS cases appearing in conjunction with the spread of Zika virus in countries across the world, and several patients with GBS in these countries were confirmed by laboratory tests to have Zika infection.¹⁰

GBS is a disease classically described as having ascending motor weakness and paralysis. If the ascending disease process reaches motor nerves to the diaphragm, a ventilator is needed for supportive therapy. Paralysis or muscle weakness can last days or weeks, but most patients recover appropriately.

IMPLICATIONS FOR ATHLETES

Although many who are affected with Zika virus have mild or no symptoms, acute symptoms can interfere with an athlete's ability to train and compete. Symptoms of Zika virus that are common and also have the potential of preventing an athlete from participating in sport include arthralgia/myalgia, fatigue, headache, and gastrointestinal symptoms. As the duration of symptoms is often only a few days, athletes affected by Zika virus may be able to return to sport as quickly as symptoms resolve. Attempting to train and compete while experiencing acute symptoms may negatively affect the immune system and prolong symptoms.

Olympic and Paralympic athletes may be more concerned about the neonatal complications than the self-limited symptoms of the infection. As nearly all are of childbearing age, Zika virus has the potential to directly affect female athletes and indirectly affect female partners of male athletes regardless of whether the partner travels to Brazil. At least 18 female athletes have competed in the modern Olympics while pregnant.³⁰ One of the more publicized pregnancies was Kerri Walsh, who won the gold medal in beach volleyball in London 2012 when she was 5 weeks pregnant. The majority of athletes who have been known to have competed in the Olympics while pregnant were in the first trimester, a time when the risks associated with maternal-fetal transmission are potentially most significant.³⁰

Exacerbating the risk of Zika virus in Olympic athletes is the potential for non-vector-borne transmission through sexual intercourse. The prevalence of sexual activity among Olympic athletes was illustrated by reports of in excess of 100,000 condoms being dispensed to athletes in the Olympic Village in a single week.¹² Despite the prevalence of barrier contraception, unintended pregnancy is a concern and would be at risk for Zika-related complications. Development of acute symptoms as a result of sexual transmission of the Zika virus is possible and could affect an athlete's ability to compete.

Among the anticipated 5000 female athletes who will qualify to participate in the 2016 Summer Olympics, there will likely be athletes who become pregnant prior to the Games.²⁰ These athletes will face a challenging decision whether to compete though risk being infected with Zika virus or elect to forgo competing in the Olympics. For some female athletes, the 2016 Olympics and Paralympics may be their only opportunity to compete as an Olympian. Historically, there have been female athletes who have competed during the second and third trimesters.

The team physician may be consulted regarding the decision to compete. Although team physicians routinely provide return-to-play recommendations that involve considering the negative health risks to the athlete, not often are team physicians faced with guiding athletes through the ethical challenges of risk to a fetus. Both the United States Olympic Committee (USOC) and the Australian Olympic Council have instructed female athletes of childbearing age to carefully consider the risks.^{2,4} The USOC also formed an Infectious

Disease Advisory Group to provide additional guidance for the United States athletes.³¹

PREVENTION OF ZIKA VIRUS INFECTION IN ATHLETES

Currently, there is no vaccine to prevent the Zika virus. To prevent a Zika virus infection while traveling to regions of the world with known disease, certain precautions must be followed. Regions above 6500 feet (2000 m) are excluded from travel precautions, since the mosquitos that transmit Zika virus are rare in these locations and the risk for mosquito-borne transmission of Zika virus is minimal.¹¹

Vector-Borne Transmission

The mainstay for the prevention of a Zika infection is to avoid mosquito bites. The mosquitos that spread Zika mostly bite during the day, but precautions should still occur at night. Athletes and other team members should avoid potential mosquito breeding sites when possible. Mosquito larvae breed in standing water, so it is prudent to avoid standing water that could be encountered in flower pots, tires, buckets, bottles, jars, and other similar containers.²⁶ Athletes who train and compete in venues outside of the urban areas, such as marathon runners and cyclists, have increased risk of exposure to mosquitos. These athletes must take extra care to follow recommendations for insect repellent and clothing treatment.

If an athlete or health care team member is infected with Zika virus, avoiding mosquito bites during the infection is still important to prevent possible transmission to others. General precautions that the athlete health care team should advise and follow are:

- Wear long-sleeved shirts and long pants
- Stay in places with air conditioning or that use window and door screens to keep mosquitoes outside²⁶
- Sleep under a mosquito bed net
- Use Environmental Protection Agency (EPA)-registered insect repellents, which have been proven safe and effective, even for pregnant and breast-feeding women
 - Follow the product label instructions closely and reapply as directed
 - Do not spray repellent on the skin under clothing to prevent overapplication as this increases the chance for skin irritation
 - If you are also using sunscreen, apply sunscreen before applying insect repellent
- Treat clothing and gear with permethrin or advise others to purchase permethrin-treated items since a mosquito can bite through thin clothing
 - Clothing treated with permethrin may be protective after multiple washings, but read product information to learn how long the protection may last
 - If clothing items are self-treated, follow the product instructions carefully

- Be extremely cautious and do not use permethrin products directly on the skin

The active ingredients most commonly found in insect repellents are DEET, Picaridan, Bayrepel, Icaridin, oil of lemon eucalyptus (OLE), *para*-menthan-diol (PMD), and IR353. Examples of safe and commonly used insect repellents to prevent Zika include the following: Off!, Cutter, Sawyer, Ultrathon, Skin So Soft Bug Guard Plus, Autan (outside the United States), Repel, Skin So Soft Bug Guard Plus Expedition, and SkinSmart.²⁶

Non-Vector-Borne Transmission

The Zika virus can be spread during sex (vaginal, oral, or anal) by a man infected with Zika virus to partners through semen. Current evidence suggests that Zika virus can be spread when a man has symptoms, before developing symptoms, or even after symptoms subside. There are currently no known cases of women infected with Zika virus spreading the disease to her partners, and it is unknown whether other body fluids (eg, saliva or vaginal fluid) can transmit the disease from one person to another. While Zika virus blood testing is recommended for people who have been exposed to Zika virus through sex or who develop symptoms, semen analysis for Zika virus is not currently recommended because there is a limited understanding on how to interpret the results. Zika virus, however, can remain in semen longer than blood.

Based on current CDC recommendations:

1. Male athletes who have been diagnosed with Zika virus or had symptoms of Zika virus should consider using condoms or not having sex for at least *6 months* after symptoms begin. This includes male athletes who live in and traveled to areas affected by Zika virus.
2. Male athletes who have traveled to an area with Zika virus but did not develop symptoms of Zika virus should consider using condoms or not having sex for at least *8 weeks* after their return.
3. Couples who include a male athlete who lives in an area with Zika virus but have not developed symptoms should consider using condoms or not having sex while Zika virus is present in the region.

Based on current knowledge, Zika virus infection in a woman who is not pregnant would not pose a risk for birth defects for future pregnancies after the virus is cleared from the blood. Additionally, based on information gathered from similar infections, once a person has been infected with Zika virus, he or she is likely to be protected from a future Zika infection.²⁷

OTHER MOSQUITO-BORNE DISEASES AFFECTING ATHLETES

Zika virus must be distinguished from other viral diseases such as chikungunya and dengue, which can have more severe presentations.

Chikungunya

Chikungunya and Zika viruses cause very similar signs and symptoms and are also both transmitted by the same mosquito vector. However, chikungunya usually presents with a high fever and extremely intense joint pain affecting the hands, feet, knees, and back. Because of these symptoms, chikungunya can be disabling, with patients bending over and unable to walk or perform simple physical tasks. Another differentiating factor is that, unlike Zika infection, chikungunya is typically not associated with conjunctivitis.

Dengue

Dengue and Zika virus infections are also similar and transmitted by the same mosquito vector. Differentiating features for a dengue infection include a high fever, severe muscle pain, and headache. There could also be associated hemorrhagic manifestations. Similar to chikungunya and unlike a Zika infection, dengue is typically not associated with conjunctivitis.

CONCLUSION

Athlete health care team members should be cautious of potential Zika virus infection while traveling to Zika-endemic areas. While typical symptoms are mild and include acute low-grade fever, maculopapular rash, and nonpurulent conjunctivitis, severe complications can occur such as Guillain-Barré syndrome, fetal loss, and congenital microcephaly. However, once the virus is cleared from the blood, future pregnancies are not believed to be at risk of being affected. Zika virus is typically transmitted via a bite from the *Aedes* mosquito, which usually bites during the daytime and breeds in standing water, but sexual transmission from male partners to others also occurs. There is no vaccine against the disease. Prevention measures currently include personal preventative measures to prevent mosquito bites, measures to control mosquito breeding sites, and abstinence or barrier protection (eg, condoms) during sexual activity. Management of the disease is supportive and symptomatic. Traveling health care team members should review updated information from the CDC, Pan American Health Organization (PAHO), and the European Centre for Disease Prevention and Control (ECDC) prior to leaving for competition.

RESOURCES FOR THE TRAVELING PHYSICIAN

PAHO: www.paho.org/zika

CDC: cdc.gov/zika

ECDC: http://ecdc.europa.eu/en/healthtopics/zika_virus_infection

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