

Zika Virus

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Purpose

The purpose of this course is to explain the transmission, diagnosis, symptoms, complications (including congenital syndrome), treatment, and precautions for Zika infection.

Goals

Upon completion of this course, one should be able to:

- Describe the history of Zika outbreaks.
- Describe transmission of the Zika virus.
- Describe at least 5 symptoms associated with Zika infection.
- Describe 2 major complications: Guillain-Barré syndrome and congenital syndrome/
- Discuss diagnostic tests for different populations.
- Discuss treatment and patient care.
- Discuss precautions against infection.
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Introduction

The Zika virus isn't actually new. It was first isolated in Africa in 1947. There was a brief outbreak in Yap in 2007 with no neurological impairments and another in French Polynesia in 2013 to 2014 with increased number of Guillain-Barré, but no one anticipated the havoc it would wreak until 2015, when reports of increased cases of microcephaly began emerging from Brazil. An outbreak of Zika virus had been reported in northeastern Brazil in April; and by October, the cases of microcephaly were multiplying. In February 2016, the CDC and WHO considered proclaiming Zika a public health emergency (1, 2).



Rates of infection have recently fallen in areas that were severely impacted in 2015 and 2016, such as Brazil and Puerto Rico, because infection confers immunity so there are fewer active infections, but this doesn't mean there is no risk, especially if the virus moves into new areas or mutates.

To date, congenital syndrome associated with Zika infection has been confirmed in 48 countries and territories throughout the Americas with thousands of cases of microcephaly. In 2016 in the United States, there were 5102 cases of Zika virus infection cases reported with 4830 from travelers, 224 cases through local transmission in Florida and Texas, and 48 through other routes (such as sexual transmission). From 2016 to June 13, 2017, 1654 pregnancies of women infected with Zika were completed with 80 of those involving birth defects.

Transmission

Eight pregnancies were lost with evidence of birth defects (3, 4).

The *Aedes aegypti* mosquito becomes infected by feeding on a person or animal that is already infected and then spreads the virus during subsequent feedings, making the mosquito the primary vector. This is the most common mode of infection although the disease can also be spread from mother to fetus during pregnancy, through sex, through blood transfusion, and through laboratory/healthcare exposure (4, 5).

While currently infections have only been locally-transmitted in Texas and Florida, the *Aedes* mosquito is found in the Southern States and Hawaii, so there is a potential for transmission in those areas (6).

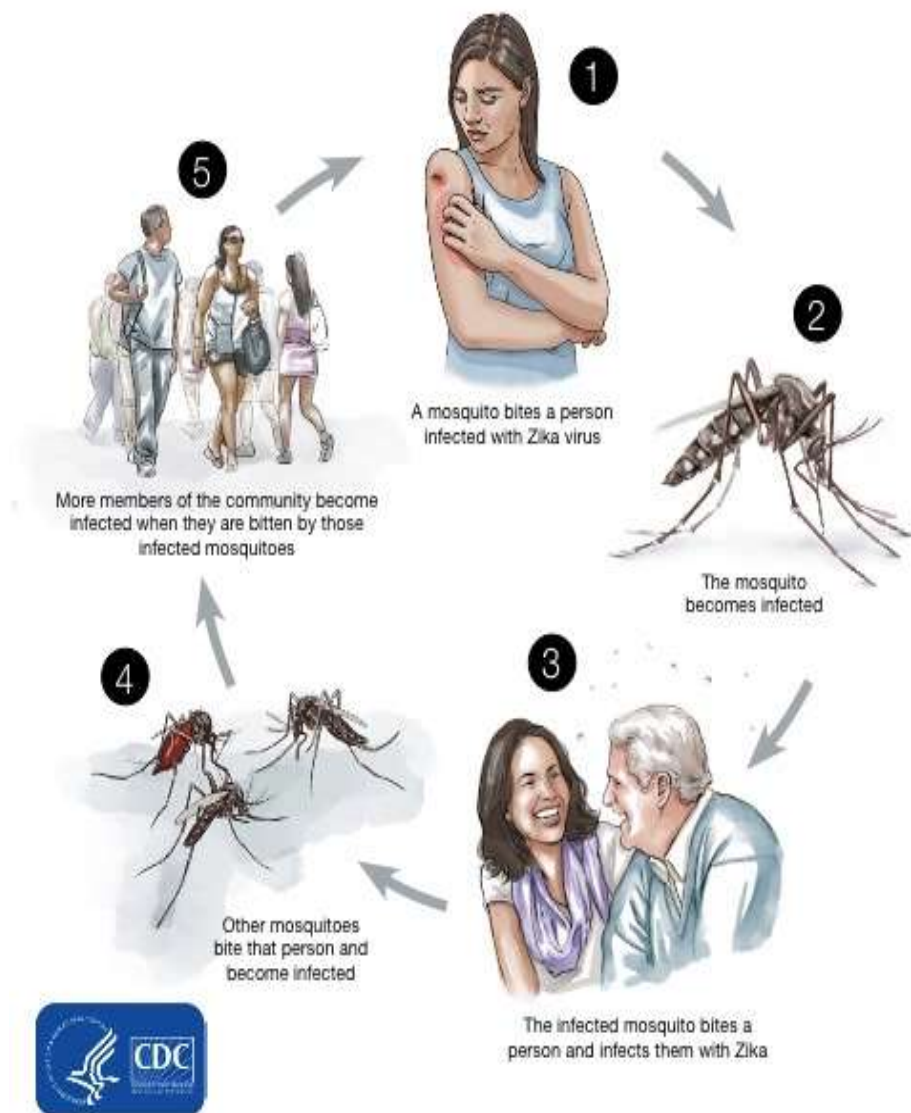
Another member of the *Aedes* family, *Aedes albopictus*, which is commonly known as the Asian tiger mosquito, is also capable of spreading the Zika virus. This mosquito is a native of Southern Asia but has spread to many countries. In August 2017, the Asian tiger mosquito was found in Wayne County, Michigan. The mosquito has also been found in Nebraska, Connecticut, Indiana, Ohio, Minnesota, and Wisconsin. While there is no present evidence that these mosquitos are spreading Zika, there is increasing concerns that the virus could spread to further areas (17).

Humans and other primates are likely the primary reservoirs of the disease; however, the virus has been detected in both wild and domestic animals, including goats, sheep, horses, cows, rodents, bats, rodents, ducks, and orangutans (5).

PROTECT YOUR FAMILY AND COMMUNITY

HOW ZIKA SPREADS

Most people get Zika from a mosquito bite



Other ways people get Zika



The Zika virus can be transmitted prior to the onset of symptoms and after symptoms have subsided and can persist in semen for longer periods of time than in blood or other body fluids.

Because Zika virus occurs in areas in which chikungunya and dengue viral infections are also common, there is some concern that mosquitos may transmit more than one virus simultaneously, resulting in co-infections. Co-infections have occurred during various outbreaks in North and South America, including during the recent Zika outbreaks.

The symptoms of chikungunya and dengue are similar to those of Zika infection but also include increased bruising, nose and gingival bleeding, and joint and bone pain. It is not clear at this time whether co-infection increases the risk of neurological complications because some studies indicate it does and others not (14).

Infection

Many people infected with Zika are asymptomatic or have mild flu-like symptoms:

- Fever
- Rash
- Headache
- Joint pain
- Muscle pain
- Conjunctivitis.

Guillain-Barré

Symptoms usually recede within a week. Because of the mildness of the disease, many may be unaware that they are infected.

Some patient, however, develop complications, including Guillain-Barré syndrome, an autoimmune neurological disorder characterized by bilateral ascending flaccid paresis/paralysis, which can progress to respiratory failure and death. Symptoms of GBS can include:

- Weakness.
- Cranial nerve involvement with facial/oropharyngeal weakness.
- Pain in the back and legs.

- Dysesthesias, such as numbness, tingling, and shock-like sensations.
- Autonomic nervous system abnormalities, such as dysrhythmias, tachycardia, bradycardia, anhidrosis, diaphoresis, hypertension or hypotension, paralytic ileus, and urinary retention.
- Respiratory impairment, which may progress to respiratory failure and need for endotracheal intubation and mechanical ventilation. (12)

Treatment includes supportive care and plasmapheresis or Intravenous immunoglobulin (IVIg), which helps to reduce the severity of symptoms by about 50% if symptoms are recognized early and treatment initiated, so healthcare providers caring for Zika patients should be alert for symptoms of GBS.

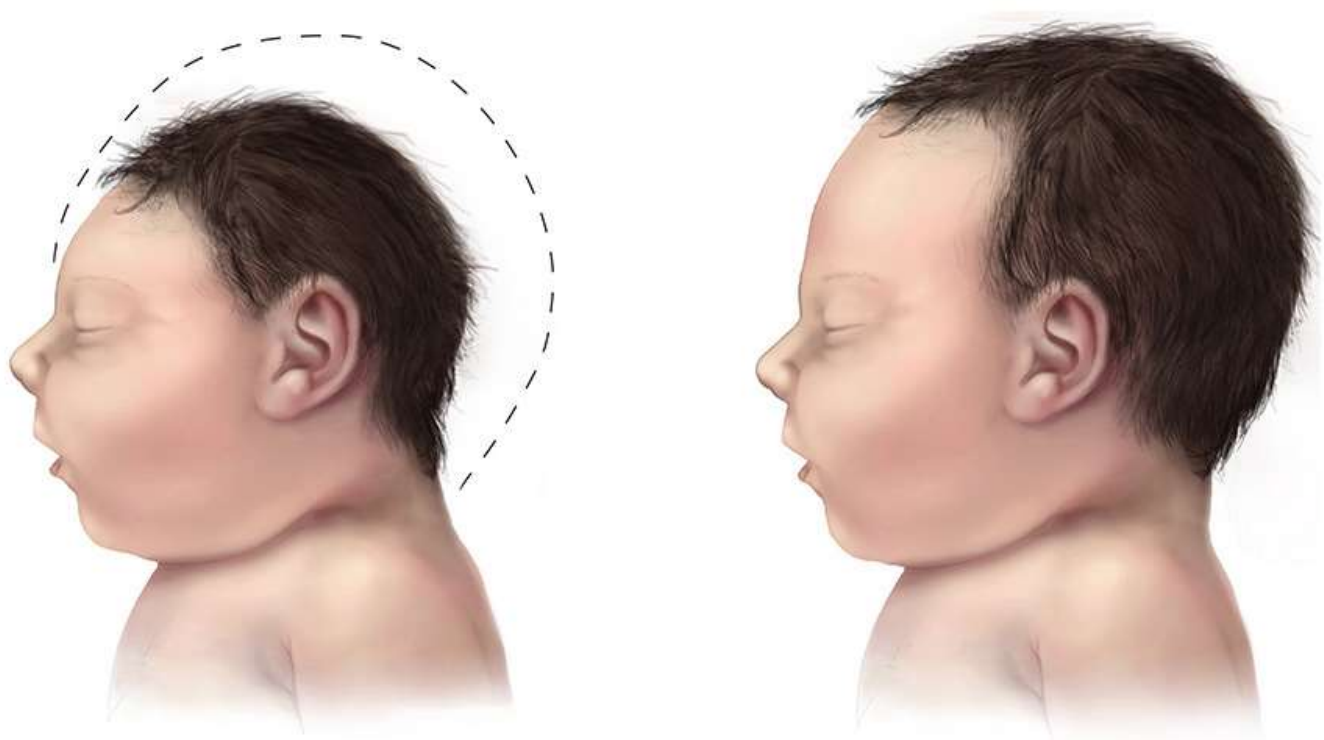
According to a study in 7 countries (primarily in South America), while the incidence of Zika infections was 75% higher in females (20 to 49), the incidence of GBS was 28% higher in males (7). However, in Puerto Rico, the incidence was higher in females (8).

Additionally, the subtype of GBS may vary from one area to another. For example, in a Zika-associated outbreak of GBS in French Polynesia, the subtype was acute motor axonal neuropathy while in Puerto Rico the subtype was acute inflammatory demyelinating polyneuropathy (8). Risk of developing Zika-associated GBS is highest for those over age 50.

Congenital syndrome

One of the most serious complications is the effect that the virus has on the developing fetus. At present, much is still unknown about Zika congenital syndrome. Some infants of infected mothers are born with obvious abnormalities, such as microcephaly, but others may develop problems during later development.

Comparison of infant with microcephaly to an infant with normal development



Source: CDC

According to the CDC, infants born with congenital syndrome may have all or some of the following:

- Microcephaly.
- Impaired brain development.
- Dysphagia and other feeding problems.
- Loss of hearing.
- Seizure disorders.
- Impaired vision.
- Contractures.
- Hypertonic muscles. (9)

Scientists are only recently learning more about how the virus causes microcephaly and other neurological impairments. According to a study at the University of Cambridge, the Zika virus enters neural stem cells, attaches to the Musashi-1 protein (MSI1) (produced in neural stem cells and necessary for proper development), replicates in, and kills the cells or prevents MSI1 from working correctly. Because MSI1 is essential for neuron development, the neurological system cannot produce enough neurons for normal brain development and size (10).

Additionally, the Zika virus attacks the pregnant woman's immune system, which usually serves to protect the fetus, increasing fetal susceptibility to the Zika infection. The virus attacks and white blood cells that normally become macrophages. These macrophages, instead of fighting the invading virus then send out signals to inactivate the immune response (16).

Diagnosis

Diagnostic studies usually include serum and urine tests to detect virus, viral nucleic acid, or Zika virus immunoglobulin M. Testing guidelines (CDC)

include:

- Testing infants at birth if mothers had evidence of Zika infection during pregnancy or the child has signs or symptoms that suggest congenital syndrome. Infant testing includes Zika virus serum and urine RNA NAT test and Zika virus immunoglobulin M (IGM) serum test. Testing should be done with 2 days of birth although there may be value in testing for several weeks or months if symptoms are delayed. CDC's Infectious Diseases Pathology Branch will test placental tissue specimens by Zika virus RT-PCR for infants born with possible Zika-associated birth defects.
- Pregnant women with possible exposure to Zika virus (recent travel to endemic areas or sexual exposure with a person traveling or living in an endemic area) should be tested at each prenatal visit.
- Adults and children with symptoms of Zika and possible exposure should be tested during the first 2 weeks and 2 to 12 weeks after onset.

There is no specific treatment for Zika virus. Supportive care is

Treatment and patient care

provided. Patients should get adequate rest and drink plenty of fluids. Pain and

fever can be treated with acetaminophen or ibuprofen (13).

When providing care for a patient with Zika, it's important to utilize standard precautions and avoid contact with blood or body fluids.

Females who are pregnant and caring for a Zika patient must use extra precautions and be sure to wash hands with soap and water immediately after contact, clean environmental surfaces with cleaners and disinfectants, and immediately remove and wash clothes that are contaminated.

Vaccines for Zika virus are under development, and Sun Pharmaceuticals and the National Institute of Virology have announced an agreement to develop drugs for Zika (11).

Precautions

Zika infections are especially a concern for women who are pregnant or anticipate becoming pregnant. Precautions include using protection during sex, such as male and female condoms for vaginal, anal, and oral sex. Dental dams may be used for oral. People should avoid sharing sex toys. CDC precautions include:

- **Pregnant couples:** Both should use precautions.
- **Travel:** Pregnant women should avoid traveling to areas with increased risk of Zika infection. If a pregnant woman and her partner travel to a Zika area, they should use condoms every time they have sex for the entire pregnancy even if neither have symptoms of Zika.
- **Living in Zika area:** Pregnant couples should use condoms every time they have sex or should avoid sex throughout pregnancy.
- **Interested in becoming pregnant:** Couple should use precautions to protect against Zika and should discuss risk factors with physician, especially if living in area with increased risk of Zika infection.
- **Only male travels to endemic area:** Couple should use condoms for 6 months or avoid having sex for 6 months from the time of return of onset of male's symptoms as Zika persists in semen for up to 6 months.
- **Only female travels to endemic area:** Couple should use condoms or avoid sex for at least 8 weeks or the onset of Zika symptoms.

Those who live in an area with increased risk but do not plan to become pregnant may make individual decisions about condom use or avoiding sex. For most people the disease is mild, but there is increased risk of Guillain-Barré; and the more people who are infected, the greater the chance of the disease spreading (4, 6).

Mosquito control is a primary concern in preventing transmission of Zika infection. The *Aedes* mosquito lays eggs in standing water, even very small amounts. Although the female mosquito only lives about one month, it can lay hundreds of eggs during that time. The female lays the sticky eggs on the walls of water-filled containers, such as planters, and when the water rises to cover them, they hatch and mature.

Transmission can be prevented by:

- Draining standing water.
- Scrubbing mosquito eggs from containers with brush or sponge.
- Removing containers that might capture water (4, 6).

To protect against mosquito bites, people should wear light-colored clothes that cover as much of the body as possible and should ensure that homes have barriers, such as screens and bed netting. Insect repellent should be used on the skin and clothing in endemic areas. Health authorities may carry out environmental spraying to kill mosquitos.

States are considering the use of biological weapons to combat Zika. Florida is conducting a 3-month period trial release of bacteria-infected mosquitos every 2 weeks. Initially, 20,000 male mosquitos infected with Wolbachia bacteria (which is naturally occurring and non-harmful to humans) were released in the environment near Key West. The males can mate with females but the eggs don't hatch. A similar trial was carried out in California in 2016 (15).

Zika viral infection was first isolated in 1947, and periodic outbreaks have occurred, but in 2015 an outbreak in Brazil and other South American countries resulted in a marked increase in the numbers of infants born with microcephaly. The disease has spread rapidly over the last 2 years to 48 countries and territories through South, Central and North America, including the United States.

Conclusion

The Zika virus is transmitted by *Aedes* mosquitos with humans and other primates serving as the primary

reservoirs. Zika can also spread from mother to fetus during pregnancy, through sex, through blood transfusion, and through laboratory/healthcare exposure.

Infection is asymptomatic or mild for most people with some exhibiting flu-like symptoms for about a week. However, some patients develop Guillain-Barré syndrome. Which can be life-threatening. The complication of most concern is congenital syndrome, which occurs when the Zika infects the developing fetus and attacks the neurological system. Infants can be born with microcephaly or other neurological deficits.

Diagnostic studies usually include serum and urine tests to detect virus, viral nucleic acid, or Zika virus immunoglobulin M. There is no specific treatment for Zika infection other than supportive care, so precautions to prevent the infection are especially important.

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