

ZIKA VIRUS: SYMPTOMS, AFFECTED COUNTRIES, DIAGNOSIS AND TREATMENT

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ABSTRACT

Zika virus is a mosquito-borne disease that is spread by the *Aedes* species of mosquito, the mosquito also responsible for the transmission of dengue and chikungunya viruses. Unlike malaria-carrying mosquitos, this species is mostly active during the day and so barrier methods, such as mosquito nets, are less effective. Zika virus (ZIKV) has two lineages: African and Asian. Mosquito-borne flaviviruses are thought to replicate initially in dendritic cells and then spread to lymph nodes and the blood stream. Risk for infection through blood transfusion, sexual practices and perinatal transmission exists. The possible routes of perinatal transmission are during delivery, breastfeeding and by close contact between the mother and her newborn. There are two types of ZIKV infection; Zika fever and congenital infection. Laboratory tests are needed for diagnosis of ZIKV infection, because there is no known pathognomonic clinical, biochemical or radiological features.

KEYWORDS: Zika Virus, *Aedes* Species, Treatments, Prevention, microcephaly.

INTRODUCTION

Zika virus is a mosquito-borne illness that is spread by the *Aedes* species of mosquito, the mosquito also responsible for the transmission of dengue and chikungunya viruses. Unlike malaria-carrying mosquitos, this species is mostly active during the day and so barrier methods, such as mosquito nets, are less effective. These mosquitos can survive in both indoor and outdoor environments. The two known species responsible for Zika transmission are the *Aedes albopictus*, known as the Asian tiger mosquito, and the *Aedes aegypti*, known as the yellow fever mosquito. The Zika virus was first identified in monkeys, in Uganda in 1947. The first human cases were detected in Uganda and the United Republic of Tanzania in 1952. Since then, there have been further outbreaks in Africa, South East Asia, and the Pacific Islands. The Zika virus is linked to an increase in microcephaly in children which may be caused by exposure during pregnancy, and an increase in Guillain-Barré syndrome. The virus has been found in saliva and other bodily fluids, but scientists are not sure if it can be transmitted through these. There is no vaccination or cure for the Zika virus, so measures to control or eradicate mosquito populations and bites are the most effective response.^[1-3]

Zika virus Affected countries

The majority of Zika virus cases occur in tropical regions, such as Brazil, Colombia, Paraguay, Suriname, Venezuela, and French Guiana, there is the possibility of

mosquito infection in tropical-like climates in some cities in the U.S. Transmission by mosquito has been confirmed in both Texas and Florida. Areas within the U.S. that are of concern for potential Zika-infected mosquitos are those with wet lowlands, warmer temperatures, and higher levels of poverty. Infection in the U.S. is most frequently linked to exposure of travelers who return from other countries, but is thought in a select few cases to be the result of mosquito transmission. Due to the fact that the species of mosquito that transmits Zika virus can be found throughout the world, the CDC believe it is likely that outbreaks of the disease will spread to new countries. WHO expects the virus to rapidly spread through the whole of the Americas and some virologists and epidemiologists also believe that Asia will be at risk. Countries with Zika outbreaks have also seen a rise in cases of this rare disorder that affects the immune system. Guillain-Barre syndrome can cause muscle weakness in the arms and legs and, in severe cases, the muscles you use to breathe. Scientists aren't sure what the link is to Zika, though so far, only a few people have gotten it after their infection. Symptoms can last for a few weeks or months, but most people fully recover.^[14-16]

What Is the Connection Between Zika, Microcephaly, and Pregnancy?

The virus has caused panic in Brazil since it first appeared there in May 2015. More than 2,100 babies in Brazil have been born with microcephaly or other birth

defects linked to Zika. Brazil and several other nations have advised women to postpone pregnancy. Although there are many causes of microcephaly in babies, including infections during pregnancy, genetic problems, and exposure to toxic substances during pregnancy, the CDC says research has provided enough evidence to show that Zika is among those causes. Research has suggested that infection during the earliest stages of pregnancy, when a baby's organs are still forming, seems to be linked to the worst outcomes. However, some studies are showing that fetuses can be harmed by infection later in pregnancy, and evidence is emerging that microcephaly isn't the only birth defect linked to Zika. In a November report, the CDC describes five types of birth defects, including severe microcephaly, that are unique to Zika or rarely occur with other infections in pregnant women. They are:

- Decreased brain tissue with calcium deposits indicating brain damage
- Damage to the back of the eye
- Limited range of motion in joints, such as clubfoot
- Too much muscle tone, which restricts movement.

Those effects in babies are called congenital Zika syndrome. As of Feb. 21, the CDC had confirmed Zika infections in more than 1,500 pregnant women in the U.S. and more than 3,200 pregnant women in U.S. territories. Forty-seven U.S. babies have been born with Zika-linked birth defects, and five pregnancy losses have been linked to the virus. In May 2016, the agency set up registries in the U.S., including Puerto Rico, to track pregnant women infected with Zika.^[6,7] The agency advises that women and men who have lived or traveled in areas with Zika infections and have a pregnant sex partner either use condoms or abstain from sex during the pregnancy.^[8] People who live in South Florida or near Brownsville, TX, or must travel there should protect themselves from mosquito bites, the CDC says. All pregnant women in the U.S. should be evaluated for possible Zika exposure during each prenatal care visit, the CDC says, and all pregnant women with possible exposure should be offered Zika testing. Pregnant women who must travel, as well as women who are thinking about becoming pregnant, should talk to their doctor first and "strictly follow steps to avoid mosquito bites" during their trip, the CDC says. Couples planning pregnancies "in the near future" should consider avoiding areas with active Zika transmission. Scott C. Weaver, PhD, director, Institute for Human Infections and Immunity, University of Texas Medical Branch at Galveston, is particularly concerned about pregnant women travelers. "Especially in the first trimester or early second trimester, going to an area with Zika virus circulating is pretty risky," he says. "... I certainly would not recommend that pregnant women travel to areas where epidemics are ongoing." Couples who are trying to have a baby should wait a few months to get pregnant if either partner has traveled to an area where Zika is spreading -- even if they did not have a confirmed

infection, the CDC says. The agency advises women to wait 2 months and men to wait at least 6 months after possible exposure, even if the man did not have symptoms. Men and women who have traveled to areas where Zika is spreading are advised to practice safe sex or abstinence for 6 months upon returning. The recommendation applies whether or not they are trying to get pregnant and whether or not they showed symptoms of Zika.^[5-9]

How Are You Tested for Zika?

There are two ways to test for Zika. One test looks for pieces of the virus's genetic code in people with active infections. But after the body clears the infection, which takes about 2 weeks after symptoms appear, that test won't work.

The FDA has OK'd the emergency use of a more advanced version of this test that can distinguish whether a person has dengue, chikungunya, or Zika, rather than having to do three different tests. The new version will be sent to qualified labs, the CDC says.

Since 80% of people with Zika don't have symptoms, many people don't know when they were infected and would not be eligible for this test.

Another test looks for proteins called antibodies made by the immune system to fight the virus. It can find antibodies in the blood up to 3 months after a person is infected. But this test isn't very specific. It may mistakenly show a person has had Zika if they've been infected with other viruses, including dengue and chikungunya. A positive or inconclusive test result means a follow-up test is done by the CDC or a CDC-authorized lab. The FDA has approved the first phase of the second test, and the CDC is distributing it to qualified labs. Testing of amniotic fluid in pregnant women can also be done, although it's not clear how well this test would work for Zika, according to the CDC.

TRANSMISSION AND RISKS OF ZIKA VIRUS

Through mosquito bites

Zika virus is transmitted to people primarily through the bite of an infected *Aedes* species mosquito (*Ae. aegypti* and *Ae. albopictus*). These are the same mosquitoes that spread dengue and chikungunya viruses. These mosquitoes typically lay eggs in and near standing water in things like buckets, bowls, animal dishes, flower pots and vases. They prefer to bite people, and live indoors and outdoors near people.

- Mosquitoes that spread chikungunya, dengue, and Zika are aggressive daytime biters, but they can also bite at night.
- Mosquitoes become infected when they feed on a person already infected with the virus. Infected mosquitoes can then spread the virus to other people through bites.

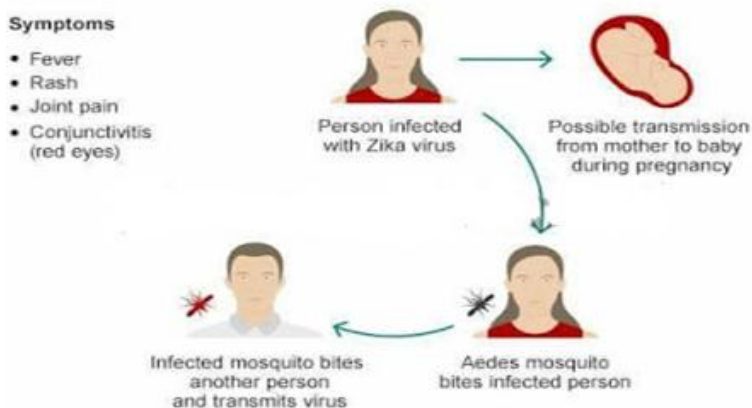


Fig. 1: Zika Virus Transmission Cycle.

From mother to child

- A pregnant woman can pass Zika virus to her fetus during pregnancy. Zika is a cause of microcephaly and other severe fetal brain defects. We are studying the full range of other potential health problems that Zika virus infection during pregnancy may cause.
- A pregnant woman already infected with Zika virus can pass the virus to her fetus during the pregnancy or around the time of birth.
- To date, there are no reports of infants getting Zika virus through breastfeeding. Because of the benefits of breastfeeding, mothers are encouraged to breastfeed even in areas with risk of Zika.

Through sex

- Zika can be passed through sex from a person who has Zika to his or her partners. Zika can be passed through sex, even if the infected person does not have symptoms at the time.

Through blood transfusion

- To date, there have not been any confirmed blood transfusion transmission cases in the United States.
- There have been multiple reports of blood transfusion transmission cases in Brazil. These reports are currently being investigated.
- During the French Polynesian outbreak, 2.8% of blood donors tested positive for Zika and in previous outbreaks, the virus has been found in blood donors.^[16,17]

Risks

Anyone who lives in or travels to an area with risk of Zika and has not already been infected with Zika virus can get it from mosquito bites. Once a person has been infected, he or she is likely to be protected from future infections. Zika infection during pregnancy can cause fetuses to have a birth defect of the brain called microcephaly. Other problems have been detected among fetuses and infants infected with Zika virus before birth, such as defects of the eye, hearing deficits, and impaired growth. There have also been increased reports of

Guillain-Barré syndrome, an uncommon sickness of the nervous system, in areas affected by Zika.

Zika causes microcephaly in babies born to infected pregnant women, the CDC confirmed this year. Microcephaly stunts a baby's head growth, causing devastating, sometimes fatal brain damage, and it can result in miscarriage or stillbirth.

Symptoms

Signs and symptoms of Zika virus are vague and can last for up to 1 week. Diagnosis of the virus is typically confirmed with a blood test.

Symptoms of Zika virus include

Fever, rash, joint pain, conjunctivitis (red eyes), muscle pain, headache, pain behind the eyes, vomiting. Zika is usually mild with symptoms lasting for several days to a week. People usually don't get sick enough to go to the hospital, and they very rarely die of Zika. For this reason, many people might not realize they have been infected. Symptoms of Zika are similar to other viruses spread through mosquito bites, like dengue and chikungunya. Infection with the Zika virus is rarely severe enough to warrant hospitalization, and it is rarer still for an individual to die as a result.

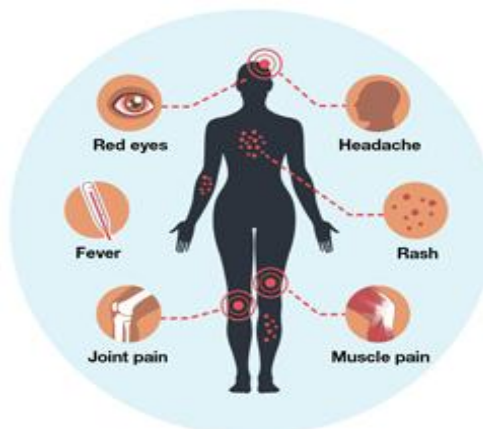


Fig. 2: Symptoms of Zika virus.

The symptoms of Zika typically pass within the space of 1 week. However, there have been recent concerns about the virus due to a link between Zika and birth defects, such as microcephaly. In light of this, on 1 February 2016, the World Health Organization (WHO) declared that the Zika virus outbreak constituted a Public Health Emergency of International Concern. On 31 March 2017 the Centers for Disease Control and Prevention (CDC) issued travel warnings for people traveling to certain countries and other areas where Zika virus transmission is ongoing. Travelers, particularly those who are pregnant, who are heading to certain regions should be aware of these warnings.^[1-3]

Diagnosis

Your doctor will likely ask about your medical and travel history. Be sure to describe international trips in detail, including the countries you and your partner have visited and the dates, as well as any contact you may have had with mosquitoes. Talk to your doctor about which tests for Zika virus — or similar diseases such as dengue or chikungunya viruses, which are spread by the same type of mosquitoes — are available in your area.

A pregnant woman with no symptoms of Zika virus infection with a history of recent travel to an area with active Zika virus transmission can be offered testing two to 12 weeks after her return.

Following positive, inconclusive or negative test results, care providers may:

- Perform an ultrasound to detect microcephaly or other abnormalities of the brain
- Offer to take a sample of amniotic fluid using a hollow needle inserted into the uterus (amniocentesis) to screen for Zika virus.^[45-46]

Virus detection

Zika virus can be identified by RT-PCR in ill patients and from day 5 post onset of fever by serology through detection of specific IgM antibodies. Serological cross-reactions with closely related flaviviruses such as Dengue fever are possible.^[2,5]

Antibody detection

ZIKV-specific IgM antibodies can be detected by ELISA or immunofluorescence assays in serum specimens from day 5 after the onset of symptoms. Since a single serum in the acute phase is presumptive, it is recommended by the WHO that a second sample be taken 1–2 weeks after the first sample to demonstrate seroconversion (negative to positive) or a fourfold increase on the antibody titer (with a quantitative test).^[5-6]

Zika Testing

Doctors can test your blood or urine to look for signs of the virus. If you have symptoms and you live or have traveled in an area with Zika, or you've had sex with someone who has, you should get tested. The virus usually stays in blood for about a week, but it can stay in

other body fluids, like semen, long after that. Scientists need more research to know exactly how long someone is contagious.^[35-36]

Treatment

There is no specific medicine or vaccine for Zika virus.

- Treat the symptoms.
- Get plenty of rest.
- Drink fluids to prevent dehydration.
- Take medicine such as acetaminophen (Tylenol®) to reduce fever and pain.
- Do not take aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) until dengue can be ruled out to reduce the risk of bleeding.
- If you are taking medicine for another medical condition, talk to your healthcare provider before taking additional medication.^[24]

If you think you may have or had Zika tell your doctor or healthcare provider and take steps to protect others.

If you are caring for a person with Zika: Take steps to protect yourself from exposure to the person's blood and body fluids (urine, stool, vomit). If you are pregnant, you can care for someone with Zika if you follow these steps.

- Do not touch blood or body fluids or surfaces with these fluids on them with exposed skin.
- Wash hands with soap and water immediately after providing care.
- Immediately remove and wash clothes if they get blood or body fluids on them. Use laundry detergent and water temperature specified on the garment label. Using bleach is not necessary.
- Clean the sick person's environment daily using household cleaners according to label instructions.
- Immediately clean surfaces that have blood or other body fluids on them using household cleaners and disinfectants according to label instructions.

If you visit a family member or friend with Zika in a hospital, you should avoid contact with the person's blood and body fluids and surfaces with these fluids on them. Helping the person sit up or walk should not expose you. Make sure to wash your hands before and after touching the person. The CDC recommends infected people get plenty of rest, drink fluids to prevent dehydration and take acetaminophen for fever and pain. Aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs) should not be taken until dengue is ruled out, to reduce bleeding risk, the agency says. There is no vaccine against Zika, but the National Institutes of Health is testing one in humans.^[25,29]

Prevention

Avoiding mosquito bites is vital to preventing transmission of Zika virus.

The CDC recommend:

- Using insect repellents
- Wearing long-sleeved garments and long pants
- Placing mosquito nets over beds (in some cases)
- Using window and door screens
- Running an air conditioner
- Wear light-colored clothing, since mosquitos are thought to be more attracted to darker colors
- Avoid the use of scented skin care products.^[28]

It is also recommended that people empty any areas with collected standing water, as this is a common environment in which mosquitos can lay their eggs. It is recommended specifically that pregnant women traveling



to countries that pose a risk for contracting Zika virus avoid mosquito bites. When choosing an insect repellent, the CDC recommend: Using products that contain oil of lemon eucalyptus and para-methane-diol, which can also provide long-lasting protection. They also recommend applying insect repellent:

- After the application of sunscreen
- Onto clothes - for example, treating or wearing clothes treated with permethrin
- To under clothing.^[35,38]

Always check the instructions for the particular brand of repellent or sunscreen for guidance on use.



Fig. 3: Zika virus prevention through mosquito control and insect repellent.

Common insect repellents include

- **DEET:** (N, N-diethylmetatoluamide) blocks a mosquito's ability to find people who've applied it. Apply repellent with a 10% to 30% concentration of DEET to your skin and clothing. Choose the concentration based on the hours of protection you need - the higher the concentration of DEET, the longer you are protected. A 10% concentration protects you for about two hours. Keep in mind that chemical repellents can be toxic, and use only the amount needed for the time you'll be outdoors. Don't use DEET on the hands of young children or on infants younger than age 2 months
- **Picaridin:** This repellent, also called KBR 3023, offers protection that's comparable to DEET at similar concentrations. It also blocks a mosquito's ability to find people who've applied it. Picaridin is nearly odorless, which may make it a good alternative if you're sensitive to the smells of insect repellents.
- **Oil of lemon eucalyptus:** This plant-based chemical may offer protection that's comparable to low concentrations of DEET. Don't use this product on children younger than 3 years.
- **Others:** Shorter acting repellents that may offer limited protection generally contain plant-based oils such as oil of geranium, cedar, lemon grass, soy or citronella.^[42]

CONCLUSIONS

Avoiding mosquito bites is vital to preventing transmission of zika virus. as there is no specific medicine or vaccine for zika virus. Zika virus can be identified by RT-PCR in ill patients and from day 5 post onset of fever by serology through detection of specific IgM antibodies. vaccination against zika viruses are fields that require further research.

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REFERENCE

1. M. Ginier, A. Neumayr, S. Günther, J. Schmidt-Chanasit, J. Blum Zika without symptoms in returning travellers: what are the implications? *Travel Med Infect Dis*, 2016; 14(1): 16–20.
2. S.D. Speer, T.C. Pierson Diagnostics for Zika virus on the horizon *Science*, 2016; 353(6301): 750–751.
3. C. Shan, X. Xie, A.D.T. Barrett, M.A. Garcia-Blanco, R.B. Tesh, P.F. da Costa Vasconcelos, *et al* Zika virus: diagnosis, therapeutics, and vaccine *ACS Infect Dis*, 2016; 2(3): 170–172.
4. M. Besnard, S. Lastere, A. Teissier, V. Cao-Lormeau, D. Musso Evidence of perinatal transmission of Zika virus, French Polynesia,

- December 2013 and February 2014 Euro Surveill, 2014; 19(13): 20751.
5. Korhonen EM, Huhtamo E, Smura T, Kallio-Kokko H, Raassina M, Vapalahti O. Zika virus infection in a traveller returning from the Maldives, June 2015. Euro Surveill, 2016; 21: 30107. 10.2807/1560-7917.ES.2016.21.2.30107.
 6. Roth A, Mercier A, Lepers C, Hoy D, Duituturaga S, Benyon E, et al. Concurrent outbreaks of dengue, chikungunya and Zika virus infections - an unprecedented epidemic wave of mosquito-borne viruses in the Pacific 2012-2014. Euro Surveill, 2014; 19: 20929. 10.2807/1560-7917.ES2014.19.41.20929.
 7. Tognarelli J, Ulloa S, Villagra E, Lagos J, Aguayo C, Fasce R, et al. A report on the outbreak of Zika virus on Easter Island, South Pacific, 2014. Arch Virol, 2016; 161: 665–8. 10.1007/s00705-015-2695-5.
 8. Centers for Disease Control and Prevention. Zika virus disease in the United States, 2015–2016. 2016. Feb 10 [cited 2016 Feb 17].
 9. Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddow AD, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. Emerg Infect Dis, 2011; 17: 880–2. 10.3201/eid1705.101939.
 10. Dallas County Health and Human Services. DCHHS reports first Zika virus case in Dallas County acquired through sexual transmission, 2016. Feb 2 [cited 2016 Feb 8].
 11. Hennessey M, Fischer M, Staples JE. Zika virus spreads to new areas—region of the Americas, May 2015–January 2016. MMWR Morb Mortal Wkly Rep, 2016; 65: 55–8. 10.15585/mmwr.mm6503e1.
 12. European Centre for Disease Prevention and Control. Zika virus disease epidemic: potential association with microcephaly and Guillain-Barré syndrome (first update), 2016.
 13. Lanciotti RS, Kosoy OL, Laven JJ, Velez JO, Lambert AJ, Johnson AJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg Infect Dis., 2008; 14: 1232–9. 10.3201/eid1408.080287.
 14. Gatherer D, Kohl A. Zika virus: a previously slow pandemic spreads rapidly through the Americas. J Gen Virol, 2016; 97: 269–73. 10.1099/jgv.0.000381.
 15. Faye O, Freire CC, Iamarino A, Faye O, de Oliveira JV, Diallo M, et al. Molecular evolution of Zika virus during its emergence in the 20(th) century. PLoS Negl Trop Dis, 2014; 8: e2636. 10.1371/journal.pntd.0002636.
 16. Hamel R, Dejarnac O, Wichit S, Ekchariyawat P, Neyret A, Luplertlop N, et al. Biology of Zika virus infection in human skin cells. J Virol, 2015; 89: 8880–96. 10.1128/JVI.00354-15.
 17. Buckley A, Gould EA. Detection of virus-specific antigen in the nuclei or nucleoli of cells infected with Zika or Langkat virus. J Gen Virol, 1988; 69: 1913–20. 10.1099/0022-1317-69-8-1913.
 18. Marchette NJ, Garcia R, Rudnick A. Isolation of Zika virus from *Aedes aegypti* mosquitoes in Malaysia. Am J Trop Med Hyg, 1969; 18: 411–5.
 19. Hayes EB. Zika virus outside Africa. Emerg Infect Dis, 2009; 15: 1347–50. 10.3201/eid1509.090442.
 20. Grard G, Caron M, Mombo IM, Nkoghe D, Mboui Ondo S, Jiolle D, et al. Zika virus in Gabon (Central Africa)-2007: a new threat from *Aedes albopictus*? PLoS Negl Trop Dis., 2014; 8: e2681. 10.1371/journal.pntd.0002681.
 21. Olson JG, Ksiazek TG, Suhandiman, Triwibowo. Zika virus, a cause of fever in Central Java, Indonesia. Trans R Soc Trop Med Hyg, 1981; 75: 389–93. 10.1016/0035-9203(81)90100-0.
 22. Oehler E, Watrin L, Larre P, Leparc-Goffart I, Lestere S, Valour F, et al. Zika virus infection complicated by Guillain-Barre syndrome—case report, French Polynesia, December 2013. Euro Surveill, 2014; 19: 20720. 10.2807/1560-7917.ES2014.19.9.20720.
 23. Diallo D, Sall AA, Diagne CT, Faye O, Faye O, Ba Y, et al. Zika virus emergence in mosquitoes in southeastern Senegal, 2011. PLoS One, 2014; 9: e109442. 10.1371/journal.pone.0109442.
 24. Boorman JP, Porterfield JS. A simple technique for infection of mosquitoes with viruses; transmission of Zika virus. Trans R Soc Trop Med Hyg, 1956; 50: 238–42. 10.1016/0035-9203(56)90029-3.
 25. Musso D, Nilles EJ, Cao-Lormeau VM. Rapid spread of emerging Zika virus in the Pacific area. Clin Microbiol Infect, 2014; 20: O595–6. 10.1111/1469-0691.12707.
 26. Ledermann JP, Guillaumot L, Yug L, Saweyog SC, Tided M, Machieng P, et al. *Aedes hensilli* as a potential vector of Chikungunya and Zika viruses. PLoS Negl Trop Dis, 2014; 8: e3188.
 27. Kraemer MU, Sinka ME, Duda KA, Mylne A, Shearer FM, Brady OJ, et al. The global compendium of *Aedes aegypti* and *Ae. albopictus* occurrence. Sci Data, 2015; 2: 150035. 10.1038/sdata.2015.35.
 28. Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. Med Mal Infect, 2014; 44: 302–7. 10.1016/j.medmal.2014.04.008.
 29. Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, Huy R, et al. Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. PLoS Negl Trop Dis, 2012; 6: e1477. 10.1371/journal.pntd.0001477.
 30. Oliveira Melo AS, Malinger G, Ximenes R, Szejnfeld PO, Alves Sampaio S, Bispo de Filippis AM. Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg? Ultrasound Obstet Gynecol, 2016; 47: 6–7. 10.1002/uog.15831.
 31. Besnard M, Lestere S, Teissier A, Cao-Lormeau V, Musso D. Evidence of perinatal transmission of Zika

- virus, French Polynesia, December 2013 and February 2014. *Euro Surveill*, 2014; 19: 20751. 10.2807/1560-7917.ES2014.19.13.20751.
32. Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. *Emerg Infect Dis*, 2015; 21: 359–61. 10.3201/eid2102.141363.
 33. Musso D, Nhan T, Robin E, Roche C, Bierlaire D, Zisou K, et al. Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014. *Euro Surveill*, 2014; 19: 20761. 10.2807/1560-7917.ES2014.19.14.20761.
 34. US Food and Drug Administration. Recommendations for donor screening, deferral, and product management to reduce the risk of transfusion transmission of Zika virus, recommendations for industry, 2016. Feb 16 [cited 2016 Feb 16].
 35. Leung GH, Baird RW, Druce J, Anstey NM. Zika virus infection in Australia following a monkey bite in Indonesia. *Southeast Asian J Trop Med Public Health*, 2015; 46: 460–4.
 36. Simpson DI. Zika virus infection in man. *Trans R Soc Trop Med Hyg*, 1964; 58: 335–8. 10.1016/0035-9203(64)90201-9.
 37. Centers for Disease Control and Prevention. Zika Virus Disease Q & A. <http://www.cdc.gov/zika/disease-qa.html> (Accessed on February 03, 2016).
 38. Ministry of Health - Manuatu Hauora. Zika virus. <http://www.health.govt.nz/our-work/diseases-and-conditions/zika-virus> (Accessed on January 13, 2016).
 39. Centers for Disease Control and Prevention. Zika Virus: For Health Care Providers: Diagnostic Testing. <http://www.cdc.gov/zika/hc-providers/diagnostic.html> (Accessed on January 13, 2016).
 40. <http://zikavirusnet.com/literature.html>.
 41. <http://www.medicalnewstoday.com>.
 42. www.cdc.gov/zika/pdfs.