# Zika Virus Infection Among U.S. Pregnant Travelers — August 2015–February 2016

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After reports of microcephaly and other adverse pregnancy outcomes in infants of mothers infected with Zika virus during pregnancy, CDC issued a travel alert on January 15, 2016, advising pregnant women to consider postponing travel to areas with active transmission of Zika virus. On January 19, CDC released interim guidelines for U.S. health care providers caring for pregnant women with travel to an affected area (*1*), and an update was released on February 5 (*2*). As of February 17, CDC had received reports of nine pregnant travelers with laboratory-confirmed Zika virus disease; 10 additional reports of Zika virus disease among pregnant women are currently under investigation. No Zika virus–related hospitalizations or deaths among pregnant women were reported. Pregnancy outcomes among the nine confirmed cases included two early pregnancy losses, two elective terminations, and three live births (two apparently healthy infants and one infant with severe microcephaly); two pregnancies (approximately 18 weeks' and 34 weeks' gestation) are continuing without known complications. Confirmed cases of Zika virus infection were reported among women who had traveled to one or more of the following nine areas with ongoing local transmission of Zika virus: American Samoa, Brazil, El Salvador, Guatemala, Haiti, Honduras, Mexico, Puerto Rico, and Samoa. This report summarizes findings from the nine women with confirmed Zika virus infection during pregnancy, including case reports for four women with various clinical outcomes. U.S. health care providers caring for pregnant women with possible Zika virus exposure during pregnancy should follow CDC guidelines for patient evaluation and management (*1*,*2*). Zika virus disease is a nationally notifiable condition. CDC has developed a voluntary registry to collect information about U.S. pregnant women with confirmed Zika virus infection and their infants. Information about the registry is in preparation and will be available on the CDC website.

Zika virus is a mosquito-borne flavivirus that was first isolated from a rhesus monkey in Uganda in 1947 (*3*). For several decades, only sporadic human disease cases were reported from Africa and Southeast Asia. In 2007, an outbreak was reported on Yap Island, Federated States of Micronesia (*3*), and outbreaks subsequently were reported from several Pacific Island countries (*4*). Local transmission of Zika virus was first identified in the Region of the Americas (Americas) in Brazil in May 2015 (*5*). Since that time, transmission of Zika virus has occurred throughout much of the Americas; as of February 18, a total of 32 countries and territories worldwide have active transmission of Zika virus (http://www.cdc.gov/zika/geo/active-countries.html). Interim guidelines for evaluation and management of pregnant women who have traveled to areas with ongoing local transmission of Zika virus include offering laboratory testing after return from travel (*2*).

During August 1, 2015–February 10, 2016, CDC received 257 requests for Zika virus testing for pregnant women. Among these requests, 151 (59%) included information indicating that the woman had a clinical illness consistent with Zika virus disease (i.e., two or more of the following signs or symptoms: acute onset of fever, rash, conjunctivitis, or arthralgia). The remaining requests did not document an illness compatible with Zika virus disease, but reporting of symptom information might have been incomplete.

Laboratory confirmation of recent Zika virus infection includes detection of 1) Zika virus, viral RNA, or viral antigen, or 2) Zika virus immunoglobulin M (IgM) antibodies with Zika virus neutralizing antibody titers ≥4-fold higher than neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred. Among the 257 pregnant women whose specimens were tested at CDC, 249 (97%) tested negative for recent Zika virus infection and eight (3%) had confirmed Zika virus infection. In addition to the eight patients with laboratory testing performed at CDC, one confirmed case was reported to CDC from a state health department with capacity to test for Zika virus infection.

Among nine pregnant women with confirmed Zika virus disease, no hospitalizations or deaths were reported. All nine women reported at least one of the four most commonly observed symptoms (fever, rash, conjunctivitis, or arthralgia), all women reported rash, and all but one woman had at least two symptoms. Among the six pregnant women with Zika virus disease who reported symptoms during the first trimester, outcomes included two early pregnancy losses, two elective pregnancy terminations, and delivery of a live

born infant with microcephaly; one pregnancy is continuing. Among two women with Zika virus infection who had symptoms during the second trimester of pregnancy, one apparently healthy infant has been born and one pregnancy is continuing. One pregnant woman reported symptoms of Zika virus infection in the third trimester of pregnancy, and she delivered a healthy infant.

## Selected Case Reports

**Patient A.** In January 2016, a pregnant woman in her 30s reported symptoms of fever, rash, arthralgia, myalgia, and malaise at 6–7 weeks' gestation. She had traveled to a Zika-affected area at approximately 5 weeks' gestation. Serologic testing confirmed recent Zika virus infection. She experienced a spontaneous early pregnancy loss and underwent a dilation and curettage at approximately 8 weeks' gestation. Products of conception were sent to CDC for testing, and Zika virus RNA was detected by reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemical (IHC) staining (*6*).

**Patient B.** In January 2016, a pregnant woman in her 30s underwent laboratory testing for Zika virus infection. She reported a history of travel to a Zika-affected area at approximately 11–12 weeks' gestation. One day after returning from travel, she developed fever, eye pain, and myalgia. The next day, she developed a rash. Serologic testing confirmed recent Zika virus infection. At approximately 20 weeks' gestation, she underwent a fetal ultrasound that suggested absence of the corpus callosum, ventriculomegaly, and brain atrophy; subsequent fetal magnetic resonance imaging demonstrated severe brain atrophy. Amniocentesis was performed, and Zika virus RNA was detected by RT-PCR testing. After discussion with her health care providers, the patient elected to terminate her pregnancy.

**Patient C.** In late 2015, a woman in her 30s gave birth to an infant at 39 weeks' gestation. The infant's head circumference at birth was 27 cm (<3rd percentile), indicating severe microcephaly (http://www.cdc.gov/growthcharts/who_charts.htm). After delivery, an epidemiologic investigation revealed that the woman had resided in Brazil until 12 weeks' gestation. She reported that she had experienced fever, rash, arthralgia, and headache at 7–8 weeks' gestation. Evidence of Zika virus infection in the mother was confirmed by serologic testing. Molecular and pathologic evaluation of the placenta demonstrated Zika virus RNA by RT-PCR and IHC, respectively. The infant exhibited hypertonia, difficulty swallowing, and seizures, and computerized tomography scan demonstrated multiple scattered and periventricular brain calcifications. Funduscopic examination revealed a pale optic nerve and mild macular chorioretinitis. Newborn hearing screening was normal. The infant was discharged from the hospital with a gastrostomy feeding tube.

**Patient D.** A pregnant woman in her 30s traveled to a Zika-affected area at approximately 15 weeks' gestation. She reported symptoms of fever, rash, arthralgia, and headache beginning at the end of her travel (at approximately 17–18 weeks' gestation). Serologic testing confirmed evidence of Zika virus infection. At approximately 40 weeks' gestation, she delivered a full-term, apparently healthy infant with no reported abnormalities and a head circumference of 34.5 cm. Cranial ultrasound, newborn hearing screen, and ophthalmologic examination of the infant were all normal.

## Discussion

On January 19, 2016, CDC released interim guidelines recommending that pregnant women who had traveled to areas with ongoing local transmission of Zika virus and who had symptoms consistent with Zika virus disease be tested for Zika virus infection (*1*). These guidelines were updated and expanded on February 5 to offer Zika virus testing to all pregnant women with Zika virus exposure, regardless of the presence of symptoms (*2*). Although Zika virus testing can be performed in some state, territorial, and local health departments, most testing before mid-February 2016 was performed at CDC. Based on tests performed at CDC as of February 17, 2016, only a small number of pregnant women who reported clinical illness consistent with Zika virus disease had laboratory evidence of a recent Zika virus infection. The combination of clinical signs and symptoms consistent with suspected Zika virus disease, including fever, rash, conjunctivitis, and arthralgia, is not specific to Zika virus disease; there are other causes of this clinical presentation (*7*). Among the nine pregnant women with Zika virus infection, all reported a clinical illness, including eight women with ≥2 signs and/or symptoms, and one with a generalized rash. The finding of reported clinical illness among all women who tested positive for Zika virus might be related to the initial testing criteria for pregnant women recommended by CDC, which required the presence of clinical illness consistent with Zika virus disease. Additional testing performed as of February 24, 2016 identified no confirmed cases among 162 pregnant women without reported symptoms.

Two women with confirmed Zika virus infection experienced spontaneous pregnancy losses in the first trimester of pregnancy. Although Zika virus RNA was detected in the specimens from both of these cases, it is not known whether Zika virus infection caused the pregnancy losses. First trimester pregnancy loss is common, occurring in approximately 9%–20% of all clinically recognized pregnancies (*8*), with higher rates in older women. Pregnancy loss has been observed in association

**Summary**

What is already known about this topic?

Because of the risk for Zika virus infection and its possible association with adverse pregnancy outcomes, CDC issued a travel alert on January 15, 2016, advising pregnant women to consider postponing travel to areas with ongoing local transmission of Zika virus. CDC also released guidelines for Zika virus testing for pregnant women with a history of travel while pregnant to areas with ongoing Zika virus transmission.

What is added by this report?

This report provides preliminary information on testing for Zika virus infection of U.S. pregnant women who had traveled to areas with Zika virus transmission. As of February 17, 2016, nine U.S. pregnant travelers with Zika virus infection had been identified. No Zika virus–related hospitalizations or deaths were reported among pregnant women. Pregnancy outcomes included two early pregnancy losses, two elective terminations, and three live births (two apparently healthy infants and one infant with severe microcephaly); two pregnancies (18 weeks' and 34 weeks' gestation) are continuing without known complications.

What are the implications for public health practice?

In this small case series, Zika virus infection during pregnancy was associated with a range of outcomes, including early pregnancy losses, congenital microcephaly, and apparently healthy infants. Additional information will be available in the future from a newly established CDC registry for U.S. pregnant women with confirmed Zika virus infection and their infants.

with Zika virus infection (*6*) and after infections with other flaviviruses (e.g., dengue, West Nile, Japanese encephalitis) (*9*–*11*); however, a causal relationship has not been established. Additional histopathologic evaluation and RT-PCR testing of tissues from pregnancy losses might provide additional insight into maternal-fetal transmission of Zika virus and the link between maternal-fetal transmission and pregnancy losses.

Seven pregnant women with confirmed Zika virus infection reported fever during pregnancy. Fever has been determined to increase the risk for adverse pregnancy outcomes, including neural tube defects (*12*). It is not known whether fever might have affected pregnancy outcomes among these pregnant women with Zika virus infection. Because of the potential risks for poor outcomes associated with fever during pregnancy, acetaminophen should be used to treat fever during pregnancy (*12*).

Approximately half a million pregnant women are estimated to travel to the United States annually from the 32 (as of February 18, 2016) Zika-affected countries and U.S. territories with active transmission of Zika virus (personal communication, Bradley Nelson, February 23, 2016). These numbers might decrease if pregnant women follow CDC recommendations (*1*) and postpone travel to areas with ongoing local Zika virus transmission. Pregnant women and their partners should also be aware of the risk for Zika virus infection through unprotected sex with an infected male partner, and carefully follow CDC interim guidelines for preventing sexual transmission of Zika virus infection (*13*). Health care providers should notify their state, local, or territorial health department about women with possible exposure to Zika virus during pregnancy for assistance in arranging testing and interpreting results. CDC has developed a registry to collect information on U.S. pregnant women with confirmed Zika virus infection and their infants. Information gathered from public health officials or health care providers will include clinical information about the pregnancy and the infant at birth and through the first year of life. This voluntary registry has been determined to be a nonresearch public health surveillance activity, and as such, it is not subject to institutional review board requirements. Health care providers are encouraged to discuss participation in the U.S. registry* with pregnant women with Zika virus infection.

*For inquiries about the U.S. Pregnancy Registry, please contact the corresponding author.

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## References

1. Petersen EE, Staples JE, Meaney-Delman D, et al. Interim guidelines for pregnant women during a Zika virus outbreak—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:30–3. http://dx.doi.org/10.15585/mmwr.mm6502e1
2. Oduyebo T, Petersen EE, Rasmussen SA, et al. Update: interim guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:122–7. http://dx.doi.org/10.15585/mmwr.mm6505e2

3. Duffy MR, Chen T-H, Hancock WT, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med 2009;360:2536–43. http://dx.doi.org/10.1056/NEJMoa0805715
4. Musso D, Nilles EJ, Cao-Lormeau VM. Rapid spread of emerging Zika virus in the Pacific area. Clin Microbiol Infect 2014;20:O595–6. http://dx.doi.org/10.1111/1469-0691.12707
5. 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. http://dx.doi.org/10.15585/mmwr.mm6503e1
6. Martines RB, Bhatnagar J, Keating MK, et al. Notes from the field: evidence of Zika virus infection in brain and placental tissues from two congenitally infected newborns and two fetal losses—Brazil, 2015. MMWR Morb Mortal Wkly Rep 2016;65:159–60. http://dx.doi.org/10.15585/mmwr.mm6506e1
7. Roth A, Mercier A, Lepers C, 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. http://dx.doi.org/10.2807/1560-7917.ES2014.19.41.20929
8. Wilcox AJ, Weinberg CR, O'Connor JF, et al. Incidence of early loss of pregnancy. N Engl J Med 1988;319:189–94. http://dx.doi.org/10.1056/NEJM198807283190401
9. Chaturvedi UC, Mathur A, Chandra A, Das SK, Tandon HO, Singh UK. Transplacental infection with Japanese encephalitis virus. J Infect Dis 1980;141:712–5. http://dx.doi.org/10.1093/infdis/141.6.712
10. O'Leary DR, Kuhn S, Kniss KL, et al. Birth outcomes following West Nile virus infection of pregnant women in the United States: 2003–2004. Pediatrics 2006;117:e537–45. http://dx.doi.org/10.1542/peds.2005-2024
11. Tsai TF. Congenital arboviral infections: something new, something old. Pediatrics 2006;117:936–9. http://dx.doi.org/10.1542/peds.2005-2729
12. Rasmussen SA, Jamieson DJ, Macfarlane K, Cragan JD, Williams J, Henderson Z; Pandemic Influenza and Pregnancy Working Group. Pandemic influenza and pregnant women: summary of a meeting of experts. Am J Public Health 2009;99(Suppl 2):S248–54. http://dx.doi.org/10.2105/AJPH.2008.152900
13. Oster AM, Brooks JT, Stryker JE, et al. Interim guidelines for prevention of sexual transmission of Zika virus—United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:120–1. http://dx.doi.org/10.15585/mmwr.mm6505e1