



## Study Finds Zika Virus Replicates and Persists in Fetal Brains and Placentas

Direct evidence of link between Zika and microcephaly

Zika virus can make thousands of copies of itself in fetuses' brains and in the placentas of pregnant women, which may help explain how the virus causes devastating birth defects and pregnancy losses even if a woman had only a minor illness. A new study by the Centers for Disease Control and Prevention (CDC) is the first to show Zika virus RNA (genetic material of the virus) replicating in brain tissues of infants with microcephaly who later died and in placentas of women who suffered pregnancy losses.

CDC scientists found Zika virus RNA persisted in fetal brains and in placentas for more than seven months after the mothers contracted Zika. The researchers also found evidence of the virus replicating in an infant with microcephaly who died two months after birth. The RNA levels were about 1,000 times higher in the infants' brains than in the women's placentas, according to the study published today in CDC's *Emerging Infectious Diseases* journal.

"Our findings show that Zika virus can continue to replicate in infants' brains even after birth, and that the virus can persist in placentas for months – much longer than we expected," said Julu Bhatnagar, Ph.D., lead of the molecular pathology team at CDC's Infectious Diseases Pathology Branch and the study's lead author. "We don't know how long the virus can persist, but its persistence could have implications for babies born with microcephaly and for apparently healthy infants whose mothers had Zika during their pregnancies. More studies are needed to fully understand how the virus can affect babies."

The study sheds light on how the virus can cross the placenta and infect the fetus's brain. The researchers found Zika virus infects and proliferates in Hofbauer cells, a type of migratory

immune cell in the placenta. Because the Hofbauer cells can move freely throughout the placenta, they may help transfer the virus to the fetus's brain. Once there, the virus can infect various types of brain cells.

The CDC researchers tested tissues from 52 patients with suspected Zika virus infection, including brain tissues (tested postmortem) from eight infants who had microcephaly and later died. They also tested placental tissues from 44 women: 22 who had adverse pregnancy or birth outcomes (miscarriage, elective termination, stillbirth or babies born with microcephaly) and 22 who had babies who appeared healthy. Most of the women were U.S. residents who had traveled to countries with Zika outbreaks during their pregnancies. The eight infants with microcephaly who died were from Brazil and Colombia.

### **More evidence that Zika is most dangerous during early pregnancy**

Brain tissues from all eight infants were positive for Zika virus, and Zika virus was detected in placentas of nearly three-quarters (16/22) of women who had an adverse pregnancy or birth outcome. Mothers of all the infants with fatal microcephaly and all of the women with positive test results contracted Zika virus during their first trimester of pregnancy. Zika virus RNA was also detected in the placentas of more than one-third (8/22) of the women who had apparently healthy infants. All of these women had Zika infection during their third trimester of pregnancy, but the babies who were tested for Zika after birth tested negative. These findings further confirm that Zika virus infection during the first trimester of pregnancy poses more danger for pregnancy and fetal development than infection contracted during the third trimester.

As part of the Zika response, CDC's Infectious Disease Pathology Branch developed a variety of tests to detect Zika virus in human tissue samples. The molecular tests used in this study can show evidence of Zika virus in tissues long after the virus would be undetectable by blood tests, which typically can only be used during the 12 weeks following infection.

"Our molecular tests for tissues extend the timeframe to detect Zika virus," Bhatnagar said.

"For women who contracted Zika virus during early pregnancy but were never diagnosed, these tests could help determine whether Zika virus may have caused their miscarriage, pregnancy loss, or adverse birth outcome."

CDC recommends monitoring babies born to mothers who had Zika virus infection during their pregnancy. CDC established the US Zika Pregnancy Registry (USZPR), in collaboration with state, tribal, territorial, and local health departments, to monitor the effects of Zika virus infection during pregnancy on fetal and infant outcomes. The data collected through the

USZPR is used to update [recommendations](#) for clinical care, to plan for services and support for pregnant women and families affected by Zika virus, and to improve prevention of Zika virus infection during pregnancy.

CDC continues to recommend that pregnant women not travel to areas with Zika. If a pregnant woman travels to or lives in an area with active Zika virus transmission, she should talk with her healthcare provider and strictly follow steps to prevent mosquito bites and sexual transmission of Zika virus. For more information, please visit [www.cdc.gov/zika/pregnancy/](http://www.cdc.gov/zika/pregnancy/).

As of Dec. 12, 2016, Zika virus outbreaks have been reported in 50 countries and territories in the Americas. More than 4,000 travel-associated cases of Zika have been reported in the United States. A total of 1,172 pregnant women in the United States have had evidence of Zika virus infection.

The EID article is available at [http://wwwnc.cdc.gov/eid/article/23/3/16-1499\\_article](http://wwwnc.cdc.gov/eid/article/23/3/16-1499_article). For more information about Zika, please visit [www.cdc.gov/Zika](http://www.cdc.gov/Zika).