Zika virus found to remain in some organs after disappearance from blood in macaques

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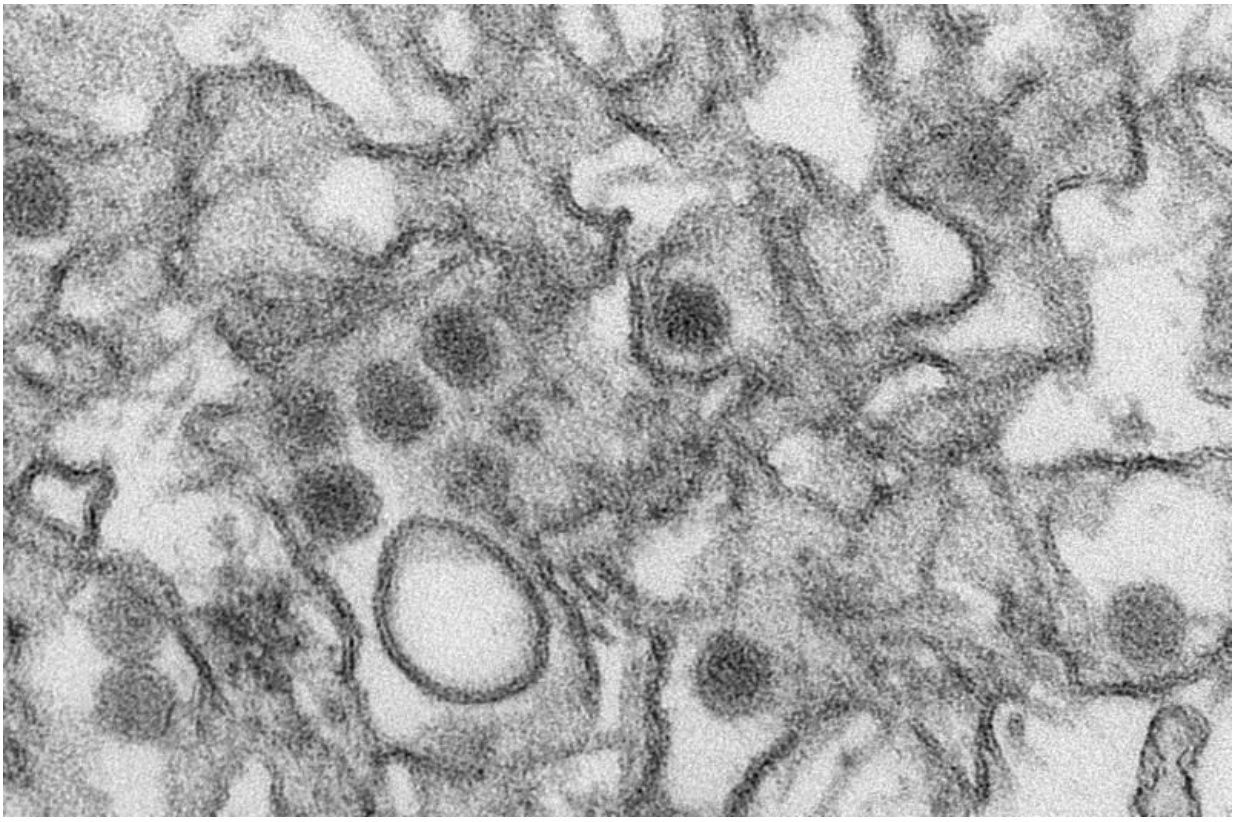

Transmission electron micrograph (TEM) of Zika virus. Credit: Cynthia Goldsmith/Centers for Disease Control and Prevention

(Medical Xpress)—A team of researchers affiliated with several institutions in the U.S. and Canada has found that the Zika virus remains in some macaques' organs and fluids, even after the immune system has

removed it from the blood stream. In their paper published in the journal *Nature Medicine*, the researchers outline their study, detail their results and offer some thoughts on what they think should be done to learn more about the infection in people.

The Zika virus has been in the news a lot over the past year after it was discovered to be causing severe birth defects in children born to infected women—mostly in South America. News that it was spreading led to research efforts to find a vaccine or a means to treat patients before it could cause more harm. In this new effort, the researchers sought to better understand the infection process in a close human substitute—macaques. They infected several subjects just under the skin with two strains of the virus, as would occur with a mosquito bite, and then watched how it traveled though the bodies of the monkeys while also tracking the immune response.

The researchers found that the virus made its way almost immediately to the lymph nodes but within five days the immune system had cleared the virus from the bloodstream. But they also found that the virus was still present in saliva, testes, prostate and semen in males and in the uterus in females for up to three weeks before it was finally overcome by the immune system. They also found that at some point, the virus had made its way to the cerebrospinal fluid around the brain, and spinal fluid, and that it had infected neurons in the cerebellum.

It is not clear at this time if the virus moves through the human body in the same way as it does with the macaques, but the researchers suggest that longer-term testing of infected humans be done to find out. If it is the case, it could mean there is a longer infectious period for such patients. They note that more research needs to be conducted to find out if the virus causes damage to the brain or the nervous system in adults, and if so, in what ways.

More information: Christa E Osuna et al. Zika viral dynamics and shedding in rhesus and cynomolgus macaques, *Nature Medicine* (2016). DOI: 10.1038/nm.4206

Abstract

Infection with Zika virus has been associated with serious neurological complications and fetal abnormalities. However, the dynamics of viral infection, replication and shedding are poorly understood. Here we show that both rhesus and cynomolgus macaques are highly susceptible to infection by lineages of Zika virus that are closely related to, or are currently circulating in, the Americas. After subcutaneous viral inoculation, viral RNA was detected in blood plasma as early as 1 d after infection. Viral RNA was also detected in saliva, urine, cerebrospinal fluid (CSF) and semen, but transiently in vaginal secretions. Although viral RNA during primary infection was cleared from blood plasma and urine within 10 d, viral RNA was detectable in saliva and seminal fluids until the end of the study, 3 weeks after the resolution of viremia in the blood. The control of primary Zika virus infection in the blood was correlated with rapid innate and adaptive immune responses. We also identified Zika RNA in tissues, including the brain and male and female reproductive tissues, during early and late stages of infection. Re-infection of six animals 45 d after primary infection with a heterologous strain resulted in complete protection, which suggests that primary Zika virus infection elicits protective immunity. Early invasion of Zika virus into the nervous system of healthy animals and the extent and duration of shedding in saliva and semen underscore possible concern for additional neurologic complications and nonarthropod-mediated transmission in humans.