CORRESPONDENCE

Evidence of Sexual Transmission of Zika Virus

TO THE EDITOR: Zika virus (ZIKV), an emerging flavivirus, generally causes mild infection in humans but is associated with severe neurologic complications and adverse fetal outcomes. ZIKV is transmitted to humans primarily by aedes mosquitoes. However, there is some evidence of sexual transmission.[1,2] Two studies have shown the presence of infectious ZIKV in semen.[3] A recent article described detection of ZIKV RNA in semen 62 days after the onset of illness, but infectious virus was not cultured.[4]

We report a case of ZIKV infection in a previously healthy 24-year-old woman (Patient 1) who was living in Paris and in whom acute fever, myalgia, arthralgia, and pruritic rash developed on February 20, 2016. She was not receiving any medication, had not received any blood transfusions, and had never traveled to a region where Zika was epidemic or to tropical or subtropical areas. Her last trip outside France was to Okinawa, Japan, from December 21, 2015, to January 1, 2016. A clinical examination on February 23 showed a maculopapular rash on the patient's abdomen, arms, and legs and a temperature of 36.6°C. The illness lasted approximately 7 days.

Patient 1 reported sexual contact between February 11 and February 20, 2016, with a man (Patient 2, the index patient) who had stayed in Brazil from December 11, 2015, through February 9, 2016. The sexual contact involved seven episodes of both vaginal sexual intercourse, without ejaculation and without the use of a condom, and oral sex with ejaculation.

Patient 2, a 46-year-old man, reported fever, asthenia, myalgia, chills, and a cutaneous rash that began on February 7, while he was in Rio de Janeiro. The symptoms had resolved on the day he arrived in France on February 10. The clinical examination of Patient 2 was normal on February 23 (details are provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org).

Populations of *Aedes aegypti* and *A. albopictus* mosquitoes are not established in the city of Paris. Moreover, in France, the diapause period of aedes species extends from December to May.

Three days after the onset of her symptoms, on February 23, samples of urine and saliva were obtained from Patient 1. The urine sample tested positive for ZIKV RNA by reverse-transcriptase polymerase chain reaction (RT-PCR) at a viral count of 3.5×10^3 copies per milliliter, and the saliva tested positive at a viral count of 2.1×10^4 copies per milliliter. A plasma sample tested negative for ZIKV RNA by RT-PCR, but serum IgM antibodies to ZIKV were detected (see the Supplementary Appendix). A vaginal swab obtained on March 1 was negative for ZIKV RNA by RT-PCR.

In Patient 2, a urine sample obtained 16 days after the onset of symptoms tested positive for ZIKV RNA by RT-PCR with a viral count of 4×10^3 copies per milliliter, but plasma and saliva samples tested negative. The first and second urine stream samples obtained on day 24 were positive for ZIKV RNA with a viral count of 2.1×10^4 copies per milliliter. Semen samples tested positive for ZIKV RNA by RT-PCR with a high viral load of 2.9×10^8 copies per milliliter in the sample obtained on day 18 and 3.5×10^7 copies per milliliter in the sample obtained on day 24. ZIKV was isolated by means of culture from semen samples on days 18 and 24. Timelines are shown in Figure 1A.

A complete ZIKV genome was sequenced from saliva samples obtained from Patient 1 and semen samples obtained from Patient 2 (see the Supplementary Appendix). Only four mutations, all of them synonymous, differentiate the se-

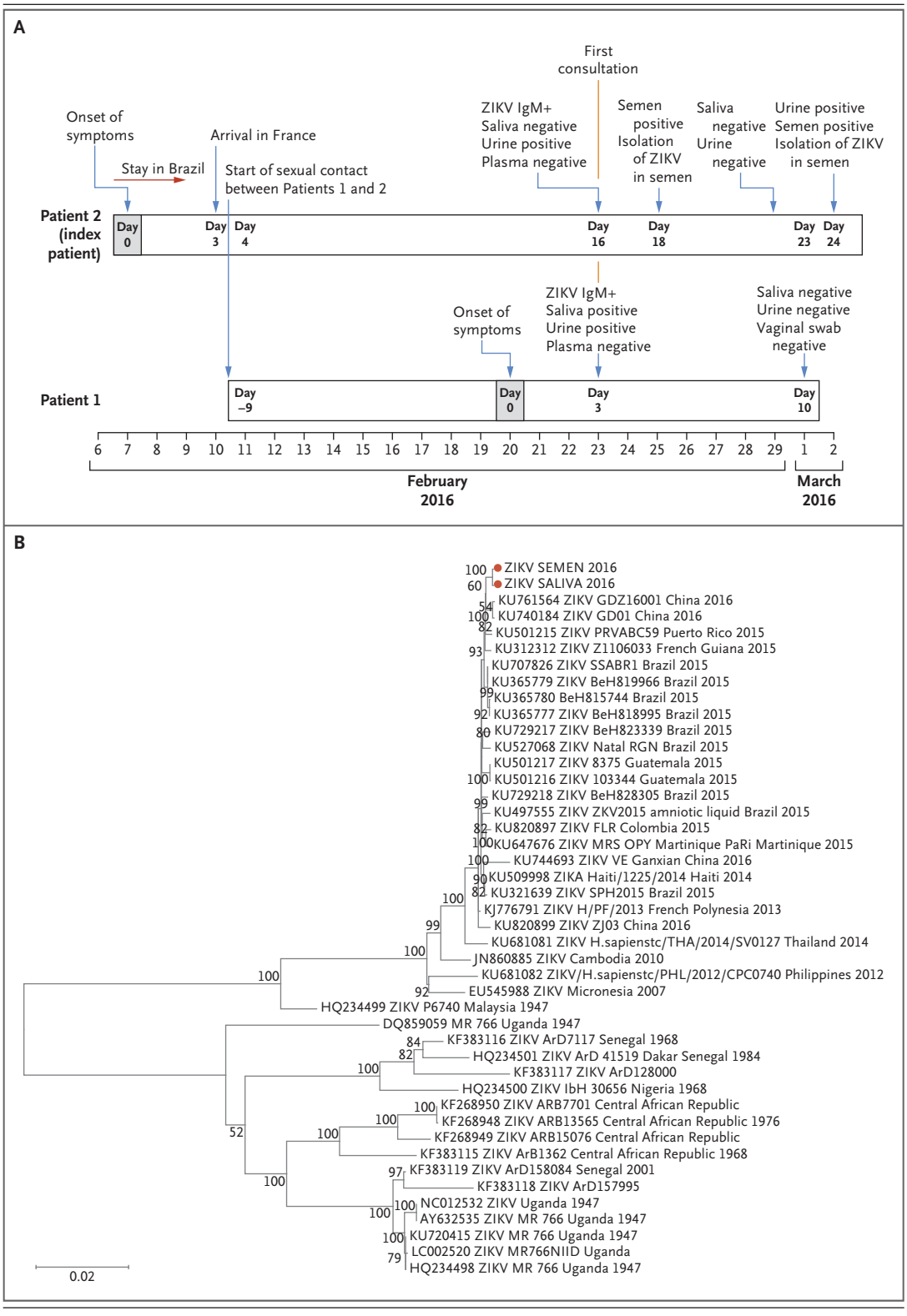

Figure 1 (facing page). Clinical Events and Phylogenetic Analysis of Zika Virus in the Patients.

Panel A shows clinical timelines with the key dates of exposure to Zika virus (ZIKV), the onset of symptoms, the results of reverse-transcriptase–polymerase-chain-reaction tests of plasma, urine, saliva, semen, and vaginal swab samples, and the results of ZIKV IgM from serum in Patient 1 and the index patient (Patient 2). Panel B shows the ZIKV strains (red dots) that were characterized directly from the semen (obtained from Patient 2) and saliva (obtained from Patient 1) at the top of a phylogenetic tree. Available sequence information regarding the virus GenBank number, strain name, country of isolation, and date of isolation is shown. Sequences of the Zika viruses identified in the semen and saliva samples are labeled beside the taxon names. The scale bar shows the nucleotide sequence divergence.

quences of the two patients. The complete nucleotide coding sequences of ZIKV identified in these semen and saliva samples cluster together within the phylogenetic tree (Fig. 1B).

These data support the hypothesis of sexual transmission (either oral or vaginal) of ZIKV from Patient 2 to Patient 1. We cannot rule out the possibility that transmission occurred not through semen but through other biologic fluids, such as pre-ejaculate secretions or saliva exchanged through deep kissing. The saliva of Patient 2 tested negative on day 10 after the onset of his symptoms, but it was not tested earlier. ZIKV has been detected in saliva,[5] but, to our knowledge, no cases of transmission through saliva have been documented.

The current outbreaks of ZIKV infection should be an opportunity to conduct studies to understand the natural history of ZIKV. We need to better define recommendations to prevent transmission of the virus. In particular, guidelines regarding how long men who are returning from an area where active ZIKV transmission is occurring should continue to use condoms during sexual contact with pregnant women and those of child-bearing age are lacking. In addition, recommendations regarding the possibility of oral transmission of the virus through semen are needed.

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