

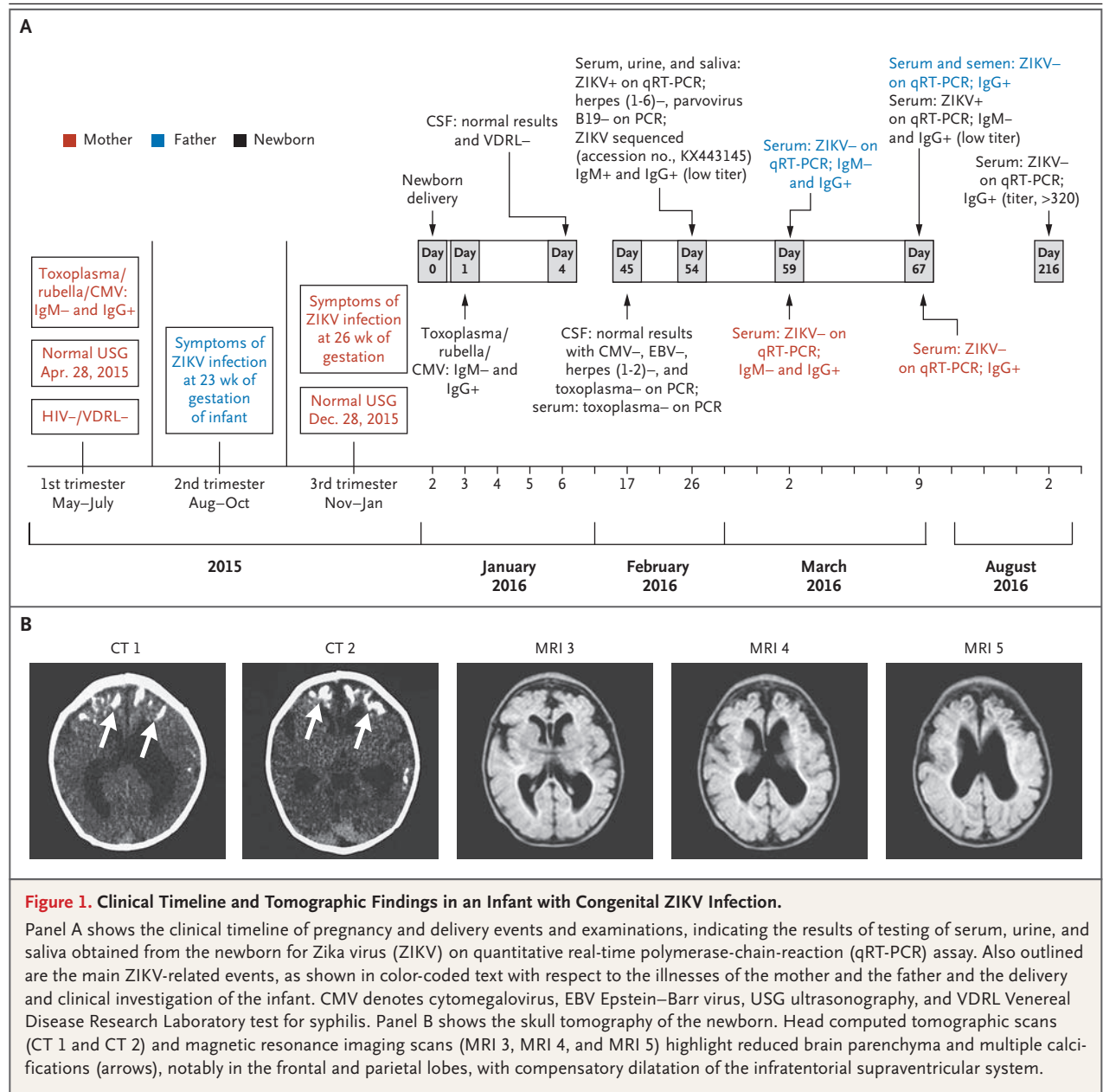
CORRESPONDENCE

Prolonged Shedding of Zika Virus Associated with Congenital Infection

**TO THE EDITOR:** The presence of Zika virus (ZIKV) infection has been associated with microcephaly in multiple studies,<sup>1-3</sup> although little is known about ZIKV shedding in congenitally infected in-

fants. We report a case of a newborn who had continued viremia with ZIKV for at least 67 days after birth.

On January 2, 2016, a male child was born with



**Figure 1. Clinical Timeline and Tomographic Findings in an Infant with Congenital ZIKV Infection.**

Panel A shows the clinical timeline of pregnancy and delivery events and examinations, indicating the results of testing of serum, urine, and saliva obtained from the newborn for Zika virus (ZIKV) on quantitative real-time polymerase-chain-reaction (qRT-PCR) assay. Also outlined are the main ZIKV-related events, as shown in color-coded text with respect to the illnesses of the mother and the father and the delivery and clinical investigation of the infant. CMV denotes cytomegalovirus, EBV Epstein–Barr virus, USG ultrasonography, and VDRL Venereal Disease Research Laboratory test for syphilis. Panel B shows the skull tomography of the newborn. Head computed tomographic scans (CT 1 and CT 2) and magnetic resonance imaging scans (MRI 3, MRI 4, and MRI 5) highlight reduced brain parenchyma and multiple calcifications (arrows), notably in the frontal and parietal lobes, with compensatory dilatation of the infratentorial supraventricular system.

microcephaly in São Paulo, Brazil, at 40 weeks of gestation to a mother who had reported having symptoms associated with ZIKV infection during the 26th week of pregnancy. At birth, the weight was 3095 g, the length 48 cm, and the head circumference 32.5 cm. The neurologic abnormality was not detected during an initial physical examination.

An analysis of cerebrospinal fluid and ophthalmologic and otoacoustic evaluations were normal. Magnetic resonance imaging (MRI) showed a reduced brain parenchyma, notably in the frontal and parietal lobes, foci of calcification in the subcortical area, and compensatory dilatation of the infratentorial supraventricular system (Fig. 1). At day 54, serum, saliva, and urine were tested for ZIKV on quantitative real-time polymerase-chain-reaction (qRT-PCR) assay. All three assays were positive for ZIKV RNA, with  $1.4 \times 10^5$  copies per milliliter in the serum,  $4.1 \times 10^4$  in the saliva, and  $5.4 \times 10^3$  in the urine. (Details of all analyses are provided in the Methods section in the Supplementary Appendix, available with the full text of this letter at NEJM.org.)

RNA sequencing of a urine sample obtained from the infant showed a high degree of similarity with samples isolated in the Americas with 98.5% bootstrap support (Fig. S3 in the Supplementary Appendix). ZIKV-specific IgM and IgG were positive as well. On day 67, ZIKV RNA in the serum continued to be detected on qRT-PCR, with  $2.8 \times 10^4$  copies per milliliter. On day 216, ZIKV RNA was no longer detected in the serum on qRT-PCR; the ZIKV-specific IgG titer was high ( $>320$ ) in comparison with the first and second samples (average titer,  $<99$ ).

When the infant was examined on day 54, he had no obvious illness or evidence of any immunocompromising condition. However, by 6 months of age, he showed neuropsychomotor developmental delay, with global hypertonia and spastic hemiplegia, with the right dominant side more severely affected.

During the third trimester of pregnancy, the infant's mother had presented with fever, pruritic maculopapular rash, headache, conjunctival hyperemia, and swelling and pain in the joints of the hands and feet at 26 weeks of gestation; all the symptoms had resolved spontaneously. Although the mother had not left the city of São Paulo during the pregnancy, it was suspected that ZIKV could have been sexually transmitted from the

father, who had traveled to the northeast region of Brazil (state of Paraíba) and reported having had the same symptoms as the mother 3 weeks before the onset of her symptoms. Recently, some cases of sexual transmission of ZIKV have been reported but none in pregnant women.<sup>4,5</sup> Samples obtained from the mother and father at days 59 and 67 were positive for ZIKV-specific IgG and negative for IgM. As shown in the timeline of events in this case in Figure 1, ZIKV infection persisted in a congenitally infected newborn for more than 2 months.

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1. Mlakar J, Korva M, Tul N, et al. Zika virus associated with microcephaly. *N Engl J Med* 2016;374:951-8.
2. Sarno M, Sacramento GA, Khouri R, et al. Zika virus infec-

tion and stillbirths: a case of hydrops fetalis, hydranencephaly and fetal demise. *PLoS Negl Trop Dis* 2016;10(2):e0004517.

3. Martines RB, Bhatnagar J, Keating MK, et al. 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.

4. McCarthy M. Zika virus was transmitted by sexual contact in Texas, health officials report. *BMJ* 2016;352:i720.

5. D'Ortenzio E, Matheron S, de Lamballerie X, et al. Evidence of sexual transmission of Zika virus. *N Engl J Med* 2016;374:2195-8.

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