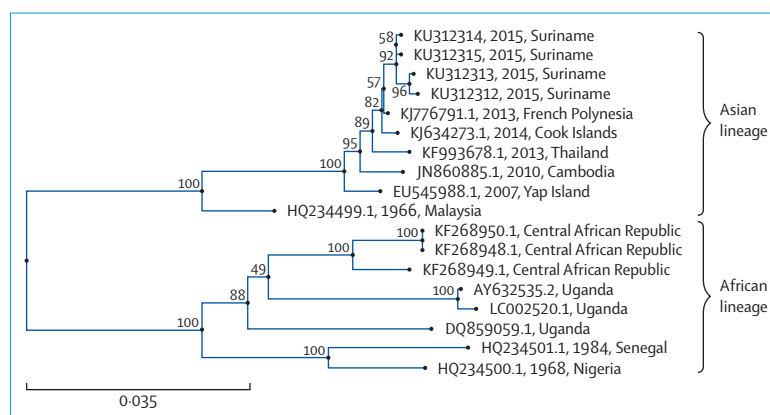


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## Zika virus genome from the Americas

On Oct 1, 2015, a 52-year-old man was hospitalised with exanthema and conjunctivitis at the Academic Hospital in Paramaribo, Suriname. During the next few days, four patients were admitted with mild symptoms including exanthema. Sera from these patients were negative for dengue and chikungunya viruses but positive for Zika virus (ZIKV) by specific real-time reverse transcription PCR.<sup>1</sup>

ZIKV is an emerging arthropod-borne virus of the family Flaviviridae. It is transmitted by aedes mosquitoes, as are dengue and chikungunya viruses. First isolated in April, 1947, in Uganda, it was until recently considered to cause sporadic benign human infections in Africa and Asia. After the first documented outbreak on Yap Island, Micronesia, in 2007, however, ZIKV caused a large epidemic in French Polynesia in 2013–14, before spreading throughout the Pacific.<sup>2</sup> This large epidemic occurred concomitantly with circulation of dengue viruses and unusual increases in severe neurological complications, such as Guillain-Barré syndrome<sup>3</sup> and congenital neurological malformations. Also during 2013–14, chikungunya emerged and spread in the Americas. Soon after, the first evidence was found of the emergence of ZIKV in the Americas, in northeast Brazil in May, 2015.<sup>4</sup> Autochthonous circulation of ZIKV in other countries started on Oct 16, 2015, in Colombia,



**Figure:** Phylogenetic relations between the envelope gene sequences of Suriname ZIKV and other ZIKV. Maximum likelihood phylogenetic tree was inferred for sequences from envelope genes of Zika viruses with the GTR+G+I model with four Suriname ZIKV strains (GenBank accession numbers: KU312312 to KU312315, complete genome sequence was obtained for KU312312) and 14 reference ZIKV sequences from GenBank (eight references from the African lineage [accession numbers: KF268948, KF268950, KF268949, LC002520, AY632535, DQ859059, HQ234500, HQ234501] and six references from the Asian lineage [accession numbers: KJ776791, KJ634273, KF993678, JN860885, EU545988, HQ234499]). The contig sequences, obtained from de-novo assembly of Suriname strain sequences and multiple sequence alignments were done with CLC Main Workbench 6.9 Beta 4 software (CLC bio, Aarhus, Denmark). Bootstrap values are indicated at nodes. Scale is shown at the bottom as substitutions per site. ZIKV=Zika virus.

followed by Suriname on Nov 12, 2015.

The first five autochthonous cases detected in Suriname were confirmed by the French National Reference Centre for arboviruses, located at the Pasteur Institute in French Guiana. Viral sequencing was done directly from the sera of four of these viraemic patients. Complete coding of the ZIKV sequence was obtained for one patient and envelope protein coding sequences for the three others.

Few complete genomes are available for ZIKV and, until this analysis, none for ZIKV circulating in the Americas. Phylogenetic analyses were conducted for the NS5 protein coding region, the envelope protein coding region, and the complete coding region, against the sequences available in databases: all the phylogenetic trees showed the same topology. The Suriname strains belong to the Asian genotype and seem to be most closely related to the strain that was circulating in French Polynesia in 2013, with which they share more than 99.7% and 99.9% of nucleotide and amino acid identity, respectively (figure).

The situation is evolving rapidly, with more countries in South and

Central America reporting cases.<sup>5</sup> This rapid spread of ZIKV strains closely related to the French Polynesian strains, raises increasing concern for public health. Furthermore, the increased frequency of Guillain-Barré syndrome and congenital neurological anomalies notified by the Brazil Ministry of Health<sup>6</sup> should provide impetus for collaborative research programmes to evaluate the relations between ZIKV and these autoimmune and neurological conditions.

We declare no competing interests.

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See Online for appendix



## Zika virus in Brazil and macular atrophy in a child with microcephaly

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Zika virus (ZIKV), a mosquito-borne Flavivirus, was first reported in human beings in 1952.<sup>1</sup> Before April, 2015, no case had been reported in Brazil. However, between April and November, 2015, 18 of the 27 Brazilian states reported ZIKV autochthonous cases.<sup>2</sup>

After ZIKV emerged in Brazil, a 20-fold annual increase of microcephaly cases was observed.<sup>3</sup> In 2015, there has been 1248 new suspected cases, a prevalence of 99·7 per 100 000 livebirths.<sup>3,4</sup>

The Brazilian Ministry of Health confirmed the relation between ZIKV and microcephaly,<sup>4</sup> and WHO issued an epidemiological alert about the association of ZIKV infection with congenital malformations and neurological syndromes.<sup>5</sup>

Here we report ophthalmic findings in three children with microcephaly born after the ZIKV outbreak in Brazil. These infants (see appendix for details) had cerebral calcifications detected by CT scans and presumable intrauterus ZIKV infection. One of the mothers reported rash and arthralgia in the first trimester. Toxoplasmosis, rubella, cytomegalovirus, herpes simplex, syphilis, and HIV were ruled out in all cases (mothers and infants), fulfilling the Ministry of Health's criteria for ZIKV vertical infection.

Mothers and infants underwent ocular examination that included biomicroscopy and fundus examination. The mothers had no ocular lesions. The three infants had unilateral ocular findings involving solely the macular region. All three infants presented with gross macular pigment mottling and foveal

reflex loss. A well defined macular neuroretinal atrophy was detected in one child (figure). To our knowledge, this is the first report of ocular findings in infants with microcephaly born after the ZIKV outbreak. All three children had fundoscopic alterations in the macular region. Although ZIKV infection was not tested by real-time PCR, cases fulfil criteria for ZIKV vertical infection. Further studies are being conducted in a larger group of infants to assess the ocular manifestations of ZIKV vertical infection.

We declare no competing interests.

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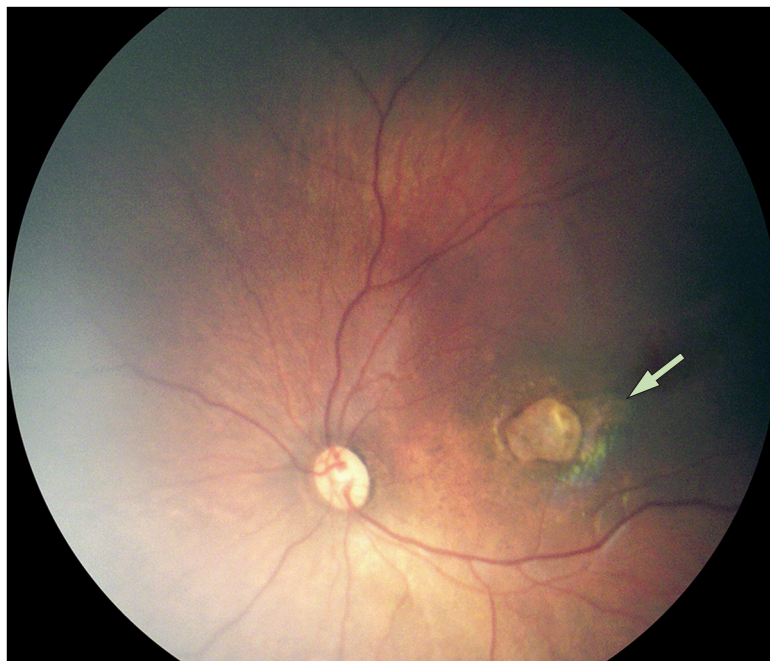


Figure: Severe macular neuroretinal atrophy in an infant with microcephaly

### Department of error

Davidson AJ, Disma N, de Graaff JC, et al. Neurodevelopmental outcome at 2 years of age after general anaesthesia and awake-regional anaesthesia in infancy (GAS): an international multicentre, randomised controlled trial. *Lancet* 2015; **387**: 239–50. In this Article, the affiliation for Liam Dorris was incorrect. This correction has been made to the online version as of Jan 14, 2016, and the printed Article is correct.