

Zika virus in the dock

In October, 2015, the Ministry of Health in Brazil reported an unexplained increase in cases of microcephaly, a congenital malformation normally associated with incomplete brain development, in newborn babies (4783 cases vs 150 in the previous year). The reported cases have caused widespread fear among pregnant women all over South and Central America, to the point that some nations such as Ecuador have recommended that their citizens postpone pregnancy to 2018, to give time to investigate the causes of the increase of microcephaly cases. In response to the growing concern of the international community, on Feb 1, 2016, WHO declared the recent cluster of microcephaly cases and other neurological disorders reported in Brazil a Public Health Emergency of International Concern.

Microcephaly can be caused by a variety of infectious agents, diabetes, drug use, and alcohol misuse, but in this case Zika virus, which recently arrived in the Americas, has been implicated as the prime suspect. Zika virus was first reported in Brazil in May, 2015, and it then rapidly spread throughout Central and South America, facilitated by its widely dispersed natural vector, the mosquito *Aedes aegypti*, and the lack of existing immunity in the local population. To limit the spread of the virus, Brazil has activated a strengthening of existing eradication measures against mosquitoes that are the vector for Zika, dengue, chikungunya, and yellow fever viruses. Meanwhile, WHO has supported the hypothesis that Zika virus could be a cause of microcephaly by indicating that specific research on the transmission, diagnosis, and treatment of Zika virus infection should be a priority.

However, evidence of a link between Zika virus and microcephaly is limited. Zika virus is usually associated with mild symptoms such as fever, rash, joint pain, or conjunctivitis, and it has not previously been linked with microcephaly. Moreover, diagnosis of Zika virus infection in the laboratory is challenging. Immunological assays are not specific because serological cross-reactivity exists between Zika and dengue viruses. Molecular detection in acute specimens would be the best available option, but the virus usually remains in the blood of an infected person for only 4–5 days after symptoms have appeared, which restricts the available time for diagnosis. In the current cluster of microcephaly cases in Brazil, Zika virus

infection has been mainly suspected because of “non-specific” symptoms in pregnant mothers and presence of the virus in babies with microcephaly has been confirmed by RT-PCR in only 17 cases.

Understanding the reasons behind the increase of microcephaly cases in Brazil is further hampered by inherent difficulties in reporting the malformation: the most recent figures released by Brazil’s Health Ministry have shown that only 404 of 1313 suspected cases already investigated were confirmed to be microcephaly. First, active searches for a specific congenital malformation always result in an increase of at least two-thirds in the number of cases usually recorded. Then, the discrepancy between reported cases and real cases of microcephaly stems from the fact that the reporting system for microcephaly in Brazil is not standardised, so different criteria were applied in each state resulting in the registration of cases that do not fit the definition. There is not even uniformity for the definition of microcephaly: in the current cluster of cases, microcephaly was defined by a head circumference more than two standard deviations below the average for that sex and age. Yet, head circumference varies across populations, so a specific threshold, such as the lower limit of 32 cm set to identify the current cases in Brazil, cannot be generally applied, considering that 40% of babies are born before term in the country, which has the highest caesarean section rate in the world.

At the moment, the causal link between Zika virus and microcephaly is speculative. The position taken by WHO on the reported microcephaly cases will help to guarantee accurate investigations based on standardised parameters, to promote case-control studies, and to accelerate development of diagnostic tests, potential vaccines, and therapies for Zika virus infection. The precautionary approach taken by WHO and national governments is sensible. Care of pregnant women who might be at risk is essential, as is providing adequate access to birth control. Nevertheless, at this stage caution should be exerted by the media in linking Zika virus to the microcephaly cases to avoid unjustified fears, and investigations on alternative causes of microcephaly should continue in parallel with studies on Zika virus. ■ *The Lancet Infectious Diseases*



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For [The Lancet Zika Resource Centre](#) see <http://www.thelancet.com/campaigns/zika>

For the [WHO statement on Zika virus and observed increase in neurological disorders and neonatal malformations](#) see <http://www.who.int/mediacentre/news/statements/2016/1st-emergency-committee-zika/en/>