



Surveillance of Zika virus infection and microcephaly in Brazil

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Zika virus has been spreading rapidly in Brazil and the Americas, with a sharp increase in the number of notified microcephaly cases since September, 2015.^{1,2} Based on the high number of cases, and the association between Zika virus infection and microcephaly,^{3,4} WHO on Feb 1, 2016, declared a Public Health Emergency of International Concern.⁵ Recently, animal models have shown that the Brazilian Zika virus strain causes intrauterine growth restriction and microcephaly.⁶

An emerging disease such as Zika virus infection, with severe consequences for newborn babies, is already a major challenge for public health authorities for countries as large as Brazil. But the effect of the current epidemic is expected to be even more devastating, considering the current Brazilian economic crisis and its potential impact on the already chronically underfunded Brazilian health system.⁷ Effective evidence-based health surveillance systems are needed.

In the context of several scientific and public health uncertainties regarding Zika virus infection, Giovanni França and colleagues⁸ paper in *The Lancet* is welcome. Using data from the Brazilian Ministry of Health surveillance system for microcephaly, the study describes clinical and anthropometric characteristics of the largest case series of suspected Zika virus infection reported so far. Among a total of 5554 liveborn infants with suspected microcephaly, the study includes data for all 1501 suspected cases (27%) with a complete investigation.

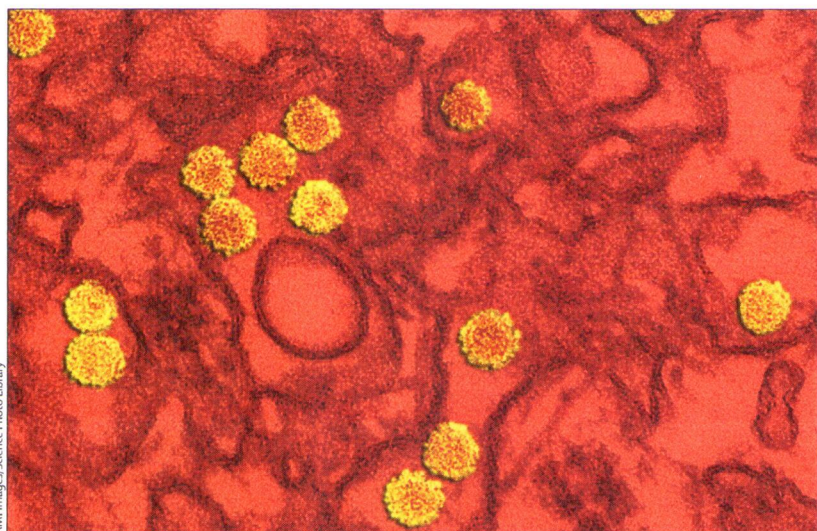
Compared with discarded cases (all cases that were not included in the categories as probable cases; n=899), definite and probable cases (n=602) showed smaller head circumference and their mothers were more likely to refer rash during pregnancy. Interestingly, some 20% of the definite or probable cases had normal head circumference values, and for a third of them, a rash had not occurred during pregnancy. Based on these results, the authors recommend that a surveillance system aimed at detecting all affected newborn babies should not simply focus on microcephaly and rash during pregnancy.

The paper by França and colleagues⁸ is an important contribution for improving the surveillance system for congenital Zika virus infection. However, caution should be taken in interpreting results of this case series based on routinely collected data with missing information for many cases and an unknown degree of under-reporting.

Based on the cutoff for head circumference below -2 SD (Z values, InterGrowth standards), the study provides a sensitivity estimate of 83% for identifying definite or probable cases. There is potential bias in the estimates provided for sensitivity and specificity due to the way that participants were selected for the study. Most participants included in the analyses were reported on the basis of a preselection screening for microcephaly, a predictor of congenital Zika virus syndrome. Because small head circumference is being evaluated as an indicator, the incorporation of a correlate (microcephaly) in the selection of participants might have overestimated sensitivity. Systematic follow-up studies during pregnancy and the first years of life will be needed to provide more accurate sensitivity estimates of the proposed criterion.

Concerning specificity, the authors' estimate of 98% is also debatable. Based on the InterGrowth standards, one would truly expect 2% of normal newborn babies having microcephaly using the proposed cutoff. However, 98% is not the expected specificity for ruling out congenital Zika virus syndrome among suspected cases, but the specificity for pathological microcephaly.

For incorporating new information besides microcephaly and rash during pregnancy to detect all affected cases, neurological signs and symptoms could be eligible, but might be difficult to obtain in most settings because of insufficient specialised personnel. The development of an accurate serological test that



could be incorporated into routine prenatal care will be essential, and its validation a research priority.

Besides all these issues, the main message of the paper is important for health surveillance measures: focusing only on microcephaly is insufficient to detect all affected newborn babies, and a revision of the procedures should be accomplished. While the current outbreak is a paradigmatic example of how quickly evolving systematic scientific evidence can (and should) change the view on a disease within months, it can be expected that public health authorities, and also the scientific community, will struggle for many years with Zika epidemics and its consequences in Brazil and elsewhere.

*Jörg Heukelbach, Guilherme Loureiro Werneck

Department of Community Health, School of Medicine, Federal University of Ceará, Rodolfo Teófilo, 60430-140 Fortaleza, CE, Brazil (JH); Anton Breinl Centre for Public Health and College of Public Health, Medical and Veterinary Sciences, Division of Tropical Health and Medicine, James Cook University, Townsville, QLD, Australia (JH); and Department of Epidemiology, Social Medicine Institute,

State University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil (GLW) heukelbach@web.de

We declare no competing interests.

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