

## Zika virus: following the path of dengue and chikungunya?

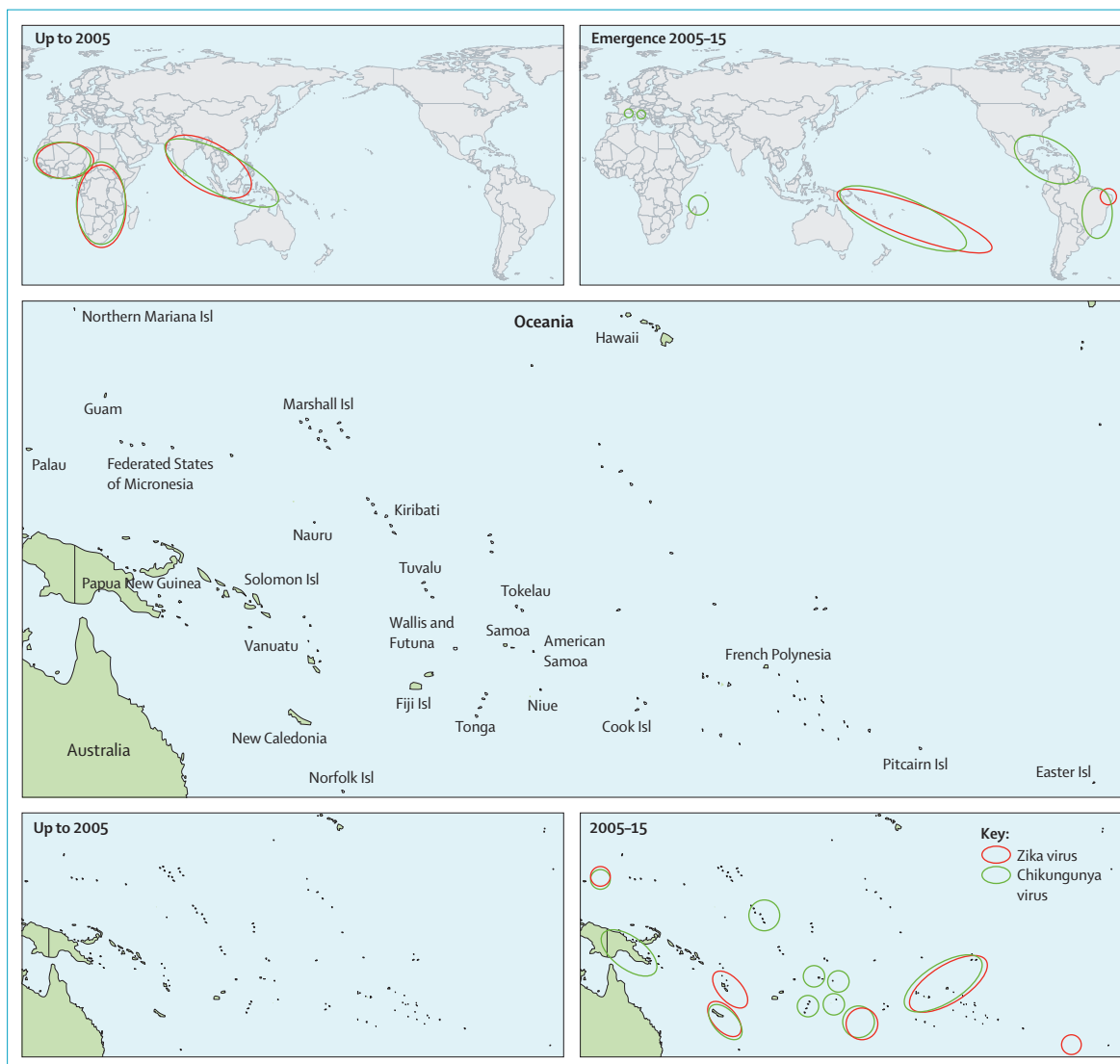
On May 7, 2015, the Pan American Health Organization issued an alert about potential Zika virus (ZIKV) transmission in northeast Brazil.<sup>1</sup> This has now been confirmed with wide spread of the disease, underscoring the potential for ZIKV to spread

globally, similar to dengue (DENV) and chikungunya (CHIKV) viruses.

ZIKV is an emerging arthropod-borne virus (arbovirus) that was first isolated from a Rhesus monkey in Uganda, in 1947. This arbovirus is related to DENV and they have similar epidemiology and transmission cycle in urban environments. Until recently, only sporadic human ZIKV infections were reported. In 2007, ZIKV emerged outside of Asia and Africa for the first

time and caused an epidemic on Yap Island in the Federated States of Micronesia,<sup>2</sup> which was followed by a large epidemic in French Polynesia in 2013–14.<sup>3</sup> Subsequently, ZIKV spread to several countries in Oceania (figure).<sup>4</sup>

The clinical presentation of ZIKV infection is not specific (mild fever, rash, arthralgia, and conjunctivitis) and can be confused with other diseases, especially dengue and



**Figure:** Distribution of Zika and chikungunya viruses before 2005 and their expansion worldwide and in Oceania between 2005 and 2015

Isl=Island. Circles represent the occurrence of an outbreak. Data are from Weaver and colleagues (2015),<sup>5</sup> Cao-Lormeau and colleagues (2014),<sup>3</sup> Nhan and Musso (2015)<sup>6</sup>, and Musso and colleagues (2014).<sup>7</sup> Data for Vanuatu are from ProMED (<http://promedmail.org>), and data for New Caledonia are from The Network of Sentinel Physicians in New Caledonia (<http://www.gouv.nc/portal/page/portal/dass/librairie/fichiers/29228252.PDF>). Other data are available from the European Centre for Disease Prevention and Control ([http://ecdc.europa.eu/en/publications/\\_layouts/forms/Publication\\_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1309](http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1309)).

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chikungunya. Prior to the French Polynesian epidemic, during which severe neurological complications (Guillain-Barre syndrome) were confirmed, ZIKV was believed to cause only mild diseases.

The history of ZIKV resembles that of CHIKV, an alphavirus.<sup>5</sup> First described in Africa in 1952, CHIKV emerged in Asia and caused major epidemics in India and southeast Asia between the 1950s and 1980s, before it disappeared epidemiologically. In 2004, CHIKV re-emerged in east Africa and spread to Asia again before spreading worldwide. CHIKV, similar to DENV, now circulates in all inhabited continents, evolving to a global public health problem in the past decade.

The adaptation of ZIKV to an urban or peri-urban cycle, involving *Aedes aegypti* and other mosquitoes of the *Stegomyia* subgenus as vectors and humans as amplification hosts, should be of great concern to public health officials. With more than half of the world's human population living in areas infested with these mosquitoes, the potential for major urban epidemics of ZIKV, DENV, CHIKV, yellow fever, epidemic polyarthritis, and other as yet unknown mosquito-borne viruses that might emerge, is overwhelming, and underscores the desperate need to develop more effective mosquito control as well as vaccines and drugs.

The future of ZIKV is unpredictable, but the worldwide spread of DENV and CHIKV—closely tied to the trends of urbanisation and globalisation, suggests that ZIKV has the potential to follow in their path.

We declare no competing interests.

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## P2X3 receptor antagonist in chronic cough

We welcome the study of a P2X3 receptor antagonist in refractory chronic cough by Rayid Abdulqawi and colleagues (March 28, p 1198),<sup>1</sup> considering the paucity of effective treatments for this disorder. However, the report raises three questions. What is the cough frequency needed to show an effect of the drug? Might inclusion of patients with chronic obstructive pulmonary disease (COPD) have affected the outcome? Did the effect of the drug on taste unmask participants?

Patients who responded were largely patients with more than 40 coughs per h. However, previous data from the authors' own group indicate that such high daytime cough frequencies are rare in chronic cough (eg, median 19.3 coughs per h [IQR 11.4–33.6]).<sup>2</sup> In our experience of acute<sup>3</sup> and chronic cough (unpublished), up to 30% of patients cough more than 40 times per h.

The authors were careful to exclude patients with “objective evidence

of an underlying cough trigger” such as “reflux disease, asthma, and postnasal drip”. However, 25% of patients had a productive cough, and patients with a forced expiratory volume in 1 s to forced vital capacity ratio less than 70% (the accepted definition for COPD) were included. Thus, in figure 2 of the Article, it would be interesting to know the identity of patients with a productive cough, and a possible diagnosis of chronic bronchitis.

P2X receptors appear to be key for taste sensation.<sup>4</sup> This might have unmasked participants and affected their subjective assessment of the active drug. However, the gustatory effect might itself have been antitussive and counterbalanced such confounding.<sup>5</sup>

This study has raised important questions, which will be valuable in the search for treatments for chronic cough.

We declare no competing interests.

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## Authors' reply

We thank Richard Turner and colleagues for their interest in our Article<sup>1</sup> and for this opportunity to clarify the patient group in our study.