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Ross River virus antibody prevalence in the Fiji Islands, 2013-2015

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COVER LETTER

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Papeete, Tahiti, April 24, 2018

Dear Editor,

Please find enclosed a manuscript entitled: "**Ross River virus antibody prevalence in the Fiji Islands, 2013-2015**" we submit for publication as a letter in "Emerging Infectious Disease" journal.

Ross River virus (RRV, *Alphavirus* genus, *Togaviridae* family) is endemic to Australia where it causes ~5,000 cases of infection annually. Outside Australia, RRV outbreaks were reported during 1979-1980 in several Pacific countries including the Cook Islands, American Samoa, New Caledonia, Wallis and Futuna, and the Fiji Islands. Although RRV has not been locally detected in those countries after 1980, cases of RRV infection were reported in travelers returning from Fiji between 1997 and 2009.

To investigate the possible undetected endemic circulation of RRV in Fiji, blood samples collected as part of a previous typhoid/leptospirosis seroprevalence study in 2013, and samples re-collected from a subset of the same participants in 2015, were tested for the presence of anti-RRV IgG antibodies. Among the participants who were born after 1982 (post-outbreak), 37.4% and 29.6% were seropositive for anti-RRV antibodies in 2013 and 2015, respectively. Moreover, 10.9% of the participants who had no detectable anti-RRV antibodies in 2013 had seroconverted to RRV by 2015.

Our findings confirm the continuous silent transmission of RRV in Fiji after 1980, and at least until 2015. In addition to previous serosurveys conducted in American Samoa in 2010 and in French Polynesia during 2011-2013 and 2014-2015, the present study strongly supports the endemic circulation of RRV in the Pacific region during the past decades without the need of marsupials as main reservoirs, and raises questionings on the potential for RRV to emerge in other parts of the world.

Please consider that this manuscript has not been submitted or accepted for publication elsewhere. We hope you will find our work of interest and our manuscript suitable for publication in Emerging Infectious Disease.

Yours sincerely

Van-Mai Cao-Lormeau

1 **Title Page**

2 Running title: Ross River virus seroprevalence, Fiji, 2013-2015

3 Title: Ross River virus antibody prevalence in the Fiji Islands, 2013-2015

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Abstract – 49 words

A unique outbreak of Ross River virus (RRV) infection was reported in Fiji in 1979. In 2013, RRV seroprevalence among residents was 46.5%. Of those born after 1982, 37.4% had anti-RRV antibodies. Between 2013-2015, 10.9% of residents had seroconverted to RRV suggesting ongoing endemic circulation of RRV in Fiji.

Text - 797 words

Ross River virus (RRV) is an *Alphavirus* of the family *Togaviridae* and is transmitted to humans by *Aedes (Ae.)* and *Culex* (*Cx.*) mosquitoes, with marsupials considered as significant reservoirs (1). Clinical manifestations of RRV infections include fever, rash, and arthralgia which commonly last 30-40 weeks. RRV is endemic to Australia where it causes ~5,000 cases of epidemic polyarthritis annually, and to Papua New Guinea where incidence is unknown (2). Outbreaks of RRV infection were reported between 1979-1980 in Fiji, the Cook Islands, American Samoa, New Caledonia, and Wallis and Futuna (1,3,4). Subsequently, RRV infections were detected in travelers returning from Fiji between 1997-2009 (4).

The Republic of Fiji comprises 322 islands distributed among 4 administrative divisions (Central, Western, Eastern and Northern) and has a population of ~830,000. Apart from RRV, the four serotypes of dengue virus were the only mosquito-borne viruses known to circulate in Fiji until the recent emergence of Zika and chikungunya viruses (5). We report evidence of endemic RRV circulation in Fiji based on the serological analysis of blood samples collected in 2013 and 2015.

This study included 778 participants recruited between September-November 2013 from the Central, Western and Northern divisions for a typhoid/leptospirosis community-based serosurvey (6). Among the residents from the Central division who had participated in the 2013 survey, 333 were re-bled during October-November 2015 including 311 whose serum sample collected in 2013 was available to test. All blood samples were tested for the presence of anti-RRV IgG using a recombinant antigen-based microsphere immunoassay (7). Data were analyzed with GraphPad Prism 6.03 using the Fisher or Chi-square tests. P values <0.05 were considered significant. The study was approved by the Fiji National Health Research Ethics Review

Committee (FNRER/N°2015.114.NW & FNRER/N°2015.45.MC), the University of the South Pacific (FSTER/2015/10/Research Proposal Approval) and the London School of Hygiene & Tropical Medicine Observational Research Ethics Committee (6344 & 10207).

The prevalence of anti-RRV antibodies among all 2013 participants was 46.5%, and was lower in the Central (38.1%) than the Western (58.6%, p<0.0001) and Northern (55.9%, p=0.0108) divisions (Table). The prevalence of anti-RRV antibodies among the participants sampled in the Central division in 2015 was similar (37.2%) to results from this division in 2013 (38.1%). In 2013, 37.4% of the participants born after 1982 (post-outbreak) had anti-RRV antibodies and in 2015 this rate (26.9%) was not significantly different (p=0.0685). The prevalence of anti-RRV antibodies increased with age (p<0.0001 in 2013, p=0.0020 in 2015) and was higher in rural than in urban (p<0.0001 in 2013, p=0.0197 in 2015) and peri-urban areas (p=0.0060 in 2013). There was no difference between genders. Among the 311 participants with available serum samples collected in 2013 and 2015, 21 of the 192 (10.9%) participants who had no detectable anti-RRV antibodies in 2013 had seroconverted to RRV by 2015.

A serosurvey conducted after the RRV outbreak in Fiji in 1979 detected anti-RRV antibodies in 92% of the participants from the Western division (3). In the study reported here, which was conducted in 2013, anti-RRV antibody prevalence in the Western, Central and Northern divisions ranged from 38.1% to 58.6%, and 37.4% of the people born after 1982 had anti-RRV antibodies, suggesting that RRV circulated in all three divisions after the 1979 outbreak. The report of RRV infection in travellers returning from Fiji between 1997-2009 (4), the observations that 10.9% of the participants in this study seroconverted to RRV between 2013-2015 and the increase in the prevalence of anti-RRV antibodies with age, suggest endemic RRV transmission in Fiji.

The finding that RRV seroprevalence was higher in rural than in urban and peri-urban environments suggests increased transmission risks in the rural areas, potentially due to (i) higher risk occupations of rural residents including farming and outdoor work, (ii) greater exposure related to rural housing or other environmental factors, and/or (iii) to the fact that non-domestic mosquito species in Fiji such as *Ae. vigilax*, *Ae. polynesiensis*, *Ae. pseudoscutellaris*, *Ae. albopictus*, and *Cx. annulirostris* may be more competent vectors of RRV than peridomestic mosquitoes such as *Ae. aegypti* (8).

Serosurveys conducted in American Samoa in 2010 (1), in French Polynesia between 2011-2013 (9) and 2014-2015 (7), and the present study in Fiji during 2013-2015 suggest that endemic circulation of RRV in the Pacific region continued, or re-commenced, after 1979-1980. These data provide further evidence for endemic transmission of RRV in areas where marsupials are absent (10). Due to extensive travel between Australia and the Pacific islands, it is plausible that RRV is repeatedly seeded into the Pacific region. Whether this plays an important role in perpetuating local transmission in the Pacific islands is unknown. As previously illustrated with Zika and chikungunya viruses, there is a risk for emerging arboviruses to be imported from the Pacific to other parts of the world and RRV could be the next unexpected threat.

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Author Biographical sketch

Dr Aubry is a research scientist at the Institut Louis Malardé, Tahiti, French Polynesia. Her research interests include the prevalence, epidemiology, and genetic evolution in the Pacific region of various arboviruses such as dengue, Zika, chikungunya and Ross River viruses.

References

1. Lau C, Aubry M, Musso D, Teissier A, Paulous S, Desprès P, et al. New evidence for endemic circulation of Ross River virus in the Pacific islands and the potential for emergence. Int J Infect Dis. 2017;57:73-6.
2. Aaskov JG. Ross River arthritis. In: Cherry J, Kaplan S, Demmler-Harrison G, Steinbach W, editors. Feigin and Cherry's Textbook of Paediatric Infectious Diseases. 7th edition. Saunders, Philadelphia; 2013. p. 2248.
3. Aaskov JG, Mataika JU, Lawrence GW, Rabukawaqa V, Tucker MM, Miles JA, et al. An epidemic of Ross River virus infection in Fiji, 1979. Am J Trop Med Hyg. 1981;30:1053–9.
4. Lau C, Weinstein P, Slaney D. Imported cases of Ross River virus disease in New Zealand - a

travel medicine perspective. Travel Med Infect Dis. 2012;10:129–34.

5. Cao-Lormeau V-M, Musso D. Emerging arboviruses in the Pacific. Lancet. 2014;384:1571–2.
6. Lau CL, Watson CH, Lowry JH, David MC, Craig SB, Wynwood SJ, et al. Human leptospirosis infection in Fiji: an eco-epidemiological approach to identifying risk factors and environmental drivers for transmission. PLoS Negl Trop Dis. 2016;10:e0004405.
7. Aubry M, Teissier A, Huart M, Merceron S, Vanhomwegen J, Roche C, et al. Ross River virus seroprevalence, French Polynesia, 2014–2015. Emerg Infect Dis. 2017;23:1751–3.
8. Mitchell CJ, Gubler DJ. Vector competence of geographic strains of Aedes albopictus and Aedes polynesiensis and certain other Aedes (Stegomyia) mosquitoes for Ross River virus. J Am Mosq Control Assoc. 1987;3:142–7.
9. Aubry M, Finke J, Teissier A, Roche C, Broult J, Paulous S, et al. Silent circulation of Ross River virus in French Polynesia. Int J Infect Dis. 2015;37:19–24.
10. Stephenson EB, Peel AJ, Reid SA, Jansen CC, McCallum H. The non-human reservoirs of Ross River virus: a systematic review of the evidence. Parasit Vectors. 2018;11:188.

Table. Prevalence of anti-Ross River virus antibodies in a representative subset of the Fijian population sampled during September-November 2013 (n=778) and October-November 2015 (n=333).

Variables	No. seropositive / No. tested (% [95% CI]) 2013	2015
Birth year		
< 1982	197/336 (58.6 [53.4–63.9])	68/144 (47.2 [39.6–55.7])
≥ 1982	165/441 (37.4 [32.9-42.1])	56/189 (29.6 [23.2-36.7])
1982 – 1990	58/117 (49.6 [41.1–58.9])	17/38 (44.7 [31.4–61.4)
1991 – 2000	66/146 (45.2 [37.7–53.6])	20/66 (30.3 [21.3–42.9])
2001 – 2010	40/170 (23.5 [18.1–30.7])	19/83 (22.9 [15.8–33.5])
> 2011	1/8 (12.5 [0.3–52.7])	0/2 (0.0 [0.0–84.2])
Gender		
Female	195/423 (46.1 [41.5–51.0])	73/190 (38.4 [32.1–45.8])
Male	167/354 (47.5 [42.2–52.5])	51/143 (35.7 [28.6–44.1])
Division		
Central	172/451 (38.1 [33.9–42.8])	124/333 (37.2 [32.4–42.7])
Northern	33/59 (55.9 [44.1–68.7])	–
Western	157/268 (58.6 [52.8–64.5])	–
Zone		
Rural	189/344 (54.9 [49.8–60.3])	52/113 (46.0 [37.5–55.6])
Periurban	55/135 (40.7 [33.2–49.5])	27/77 (35.1 [26.0–46.8])
Urban	117/298 (39.3 [34.1–45.1])	45/143 (31.5 [24.8–39.8])
Total	362/778* (46.5 [43.1–50.1])	124/333 (37.2 [32.4–42.7])

* For one participant, information about age and gender were not available; for another participant, information about the zone of residence was not available.

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