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Notes on Zika virus – an emerging pathogen now present in the South Pacific

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There has never been a confirmed indigenously acquired case of mosquito-borne disease in humans in New Zealand.[1] It has been proposed that it is just a matter of time before such an outbreak occurs,[2] particularly in light of the increased connectivity and movement of people and pathogens around the globe.

In the past few years, the emergence of Chikungunya virus is posing a threat to public health in NZ.[3] This risk has increased with the Chikungunya outbreaks in New Caledonia and Papua New Guinea,[4] and more recently in Tonga,[5] Samoa, American Samoa,[6] French Polynesia,[7] and Tokelau Islands (a NZ territory).[8] Recent outbreaks of Zika virus disease (family *Flaviviridae*, genus *Flavivirus*) in the South Pacific[9,10] and associated imported cases to NZ raise concerns about the likelihood of this virus reaching NZ.

Geographical distribution, recent outbreaks, and imported cases

Zika virus was first isolated from a rhesus monkey in the Zika Forest of Uganda in 1947, and over the next 35 years it was reported from a number of countries throughout Africa and Asia.[11] In 2007, an outbreak of Zika virus in Yap Islands (Micronesia) constituted the first reported outbreak of the disease anywhere, as well as the first reported cases outside those two continents.[12] Genetic analyses suggested that the outbreak was caused by a Zika virus strain from Southeast Asia,[13] which was probably introduced to Yap Islands by an infected mosquito or a viraemic human.[12] Surprisingly, prior to the Yap Islands outbreak, there had been only 14 cases of Zika virus disease reported in the literature.[12]

Lately, Zika virus has emerged in the South Pacific with outbreaks in French Polynesia, New Caledonia[10] and Cook Islands.[9] As of 7 March 2014, there were 30,000 suspected cases of Zika virus disease in French Polynesia, with a further 169 autochthonous cases reported in New Caledonia.[10] In the Cook Islands, as of 4 April 2014 there had been 760+ cases of Zika virus disease reported by doctors since the outbreak began on 13 February 2014 (Rangiau Fariu, personal communication, 2014). Of 80 samples tested, 49 were positive for Zika virus, but none were positive for dengue viruses. It seems that Zika virus disease has been mild compared to the symptoms of dengue fever, and there have been no associated hospitalisations in the Cook Islands (Rangiau Fariu, personal communication, 2014). Further, an outbreak of Zika virus has occurred in Easter Island, constituting the first locally acquired cases in the Americas.[14]

Recently, there have also been imported cases of Zika virus infection reported in a number of countries around the world. These include Japan,[15] the US,[16] Canada,[17] Germany,[18] France,[19] Norway,[20] Australia[21] and NZ. To 30 June 2014, Australia had 12 confirmed imported cases of Zika virus infection (Department of Health, Canberra, personal communication, 2014). In 2012 and 2013 a resident of South Australia and one from the Northern Territory, respectively, acquired Zika virus in Indonesia. In the first half of 2014, two New South Wales residents and seven Queensland residents acquired Zika virus from the Cook Islands, and one Victorian resident acquired the disease from an unknown place. In comparison, as of 1 July 2014 NZ has had 29 laboratory-confirmed imported cases – all in 2014 – with 27 cases acquired from the Cook Islands, one from Vanuatu, and one case where the place of acquisition was unknown (Institute of Environmental Science and Research, Wellington, personal communication, 2014). The higher number of confirmed cases in NZ compared to Australia may reflect the proximity and cultural links between the Pacific Islands and NZ, and the associated frequent exchange of travellers. No cases of local Zika virus transmission have been reported in Australia or NZ.

Clinical presentation

The symptoms of Zika virus disease are generally described as an illness similar to influenza, accompanied by skin rash.[22] In the Yap Islands outbreak, the most common symptoms reported were rash, fever, arthritis or arthralgia, and conjunctivitis, as well as myalgia, headache, retro-orbital pain, oedema and vomiting.[12] In 2009, Hayes warned that although Zika virus disease had been mild and self-limiting until then, West Nile virus was also considered a relatively innocuous pathogen once.[23] Hayes' prediction seems to have become reality to some extent, as there have been 70 cases of Zika virus infection with neurological or auto-immune complications during summer 2013–2014 in French Polynesia.[24]

The literature describes a case of Guillain-Barré syndrome associated with Zika virus infection,[22] but a report by the European Centre for Disease Prevention and Control cites 38 cases of this syndrome.[24] Other described complications following initial Zika virus infection include encephalitis, meningo-encephalitis, paraesthesia, facial paralysis, myelitis and immune thrombocytopenic purpura, as well as ophthalmologic and cardiac complications.[24]

Importantly, as the symptoms of Zika virus disease are generally similar to those of dengue fever and other arboviral infections, differential diagnosis of febrile and subfebrile patients with rash should include Zika virus infection, particularly in those who have visited regions where the virus is known to occur.[15] The common laboratory tests are serological tests for the presence of specific antibodies, reverse-transcription PCR (RT-PCR) and virus isolation (the 'gold standard').[25] Given the cross-reactivity of diagnostic flavivirus antibody assays, it is speculated that Zika virus infection is greatly misdiagnosed and under-reported.[13] As a result, a recently developed rapid real-time RT-PCR assay that can detect a wide range of Zika strains may be a useful tool for diagnosis where clinically similar arboviruses (such as dengue and Chikungunya) are endemic.[25]

Vectors

The primary vectors of Zika virus appear to be *Aedes* spp., with reported viral isolations from nine different *Aedes* and one *Anopheles* species.[25,26] Little is known about the vector

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competence of most *Aedes* species for the virus. For example, the culprit of the Yap Islands outbreak has not been identified.[12] *Aedes aegypti* is a laboratory vector of Zika virus,[27] and there have been viral isolations from the species in the wild.[25,28] Thus, it is believed to be the main vector of Zika virus in a number of countries.[24,27] *Aedes aegypti* is widespread in most of the South Pacific, including the Cook Islands,[29] so it is a potential vector of the recent outbreaks. *Aedes albopictus* has also been shown to be an efficient laboratory vector of Zika virus,[30] with viral isolations recorded in the wild.[26] In addition, *Ae. polynesiensis* may be involved in Zika virus transmission in the South Pacific, with preliminary results suggesting its possible role as a vector.[24]

In Australia, the Zika virus vector *Ae. aegypti* is established in Queensland, where seven of the 12 imported cases of Zika virus infection were recorded.[21] *Aedes aegypti* and *Ae. albopictus* are also found in the Torres Strait, and there is concern that *Ae. albopictus* may become established in Australia's mainland.[31]

None of the three mosquito species described above are present in New Zealand.[29] However, the introduced *Ae. notoscriptus* is abundant and widespread in northern parts of the country, where it thrives in human-modified environments, including urban areas.[32] The vector competence of *Ae. notoscriptus* for Zika virus is unknown, but the species is a laboratory vector of related flaviviruses such as dengue and Japanese encephalitis viruses.[33-35] Importantly, Faye and colleagues evaluated the molecular evolution of Zika virus, and their results suggest that this virus might have experienced recombination in nature as it spread throughout Africa and into Asia, without clear associations with any host or vector species.[11] Consequently, the potential role of *Ae. notoscriptus* as a vector of Zika virus in NZ cannot be disregarded.

There have been reports of non-vector-born transmission of Zika virus.[16,36] In the US, strong circumstantial evidence suggests that a scientist returning from Senegal with the disease transmitted the virus to his wife during sexual intercourse.[16] In French Polynesia, there have been two reported cases of perinatal transmission of the virus from mother to child, mostly likely via transplacental transmission or during delivery.[36] Blood transfusion has been identified as another potential pathway for Zika virus transmission, with many donors asymptomatic at the time of blood donation.[37]

Long term in the South Pacific

Little is known about the disease ecology of Zika virus. Animal reservoirs appear to be mostly primates,[13,23,24] with rare reports of Zika antibodies in non-primates. One study in Pakistan identified Zika antibodies in rodents, sheep, and goats,[38] with Henderson et al.[39] cited as having detected antibodies in many large wild African mammals.[13] According to Haddow and colleagues, humans may "serve as primary amplification hosts and potentially as reservoir hosts if their viraemia is sufficient in duration and magnitude".[13] Importantly, overseas experience shows that Zika virus disease can have a transmission cycle in urban environments[26] and, as previously discussed, there are abundant and widespread mosquito vector species throughout the South Pacific. As a result, it is likely that there will be new outbreaks of Zika virus disease in the region, as well as ongoing imported cases to other South Pacific countries.

Conclusion

The likelihood of Zika virus transmission in the subtropical climate of NZ's northernmost areas (including Auckland, the country's largest city) is unknown, but the risk of an outbreak is compounded by a population that is immunologically naive to exotic arboviruses.[3] Vigilance may be particularly important for Zika virus, as the disease can have relatively mild symptoms and may not hinder the international travel of viraemic people into NZ. If symptoms are well-tolerated, infected persons may not seek medical attention in a timely manner to minimise the chances of transmission to possible mosquito vectors. In addition, with similar symptoms to dengue fever and other arboviruses as well as the cross-reactivity of assays, ongoing public health vigilance is required.

As with other mosquito-borne diseases, travellers should be advised to practise mosquito-avoidance behaviour, such as using insect repellent, protective clothing, bed nets or sleeping in screened accommodation. It would be wise for NZ to continue to assist its South Pacific neighbours with mitigating measures to manage existing outbreaks and prevent future outbreaks of Zika virus and other arboviruses. Otherwise, these nations could act as sources of Zika virus and other emerging infectious diseases into NZ.[40]

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References

1. Derraik JGB, Maguire T. Mosquito-borne diseases in New Zealand: Has there ever been an indigenously acquired infection? *N Z Med J*. 2005;118(1222):U1670. PubMed PMID: 16222361.
2. Derraik JGB, Calisher CH. Is New Zealand prepared to deal with arboviral diseases? *Aust N Z J Public Health*. 2004;28:27-30.
3. Derraik JGB, Slaney D, Nye ER, Weinstein P. Chikungunya virus: A novel and potentially serious threat to New Zealand and the South Pacific islands. *Am J Trop Med Hyg*. 2010;83:755-9.
4. Horwood P, Bande G, Dagina R, Guillaumot L, Aaskov J, Pavlin B. The threat of chikungunya in Oceania. *Western Pac Surveill Response J*. 2013;4:8-10.
5. ProMED-mail [Internet]. Chikungunya (27): Tonga, New Caledonia ex Tonga. *ProMED-mail 20140417.2409660*. Brookline (MA): ProMed-mail; 2014 April 17 [cited 2014 Dec 2]. Available from: http://www.promedmail.net/
6. ProMED-mail [Internet]. Chikungunya (57): Samoa, American Samoa. *ProMED-mail 20140926.2809338*. Brookline (MA): ProMed-mail; 2014 September 26 [cited 2014 Dec 2]. Available from: http://www.promedmail.net/
7. ProMED-mail [Internet]. Chikungunya (69): French Polynesia. *ProMED-mail 20141127.2995033*. Brookline (MA): ProMed-mail; 2014 November 27 [cited 2014 Dec 2]. Available from: http://www.promedmail.net/
8. ProMED-mail [Internet]. Chikungunya (62): Pacific, Tokelau Islands. *ProMED-mail 20141019.2878897*. Brookline (MA): ProMed-mail; 2014 October 19 [cited 2014 Dec 2]. Available from: http://www.promedmail.net/
9. ProMED-mail [Internet]. Zika virus - Pacific (09). *ProMED-mail 20140328.2365267*. Brookline (MA): ProMed-mail; 2014 March 28 [cited 2014 Dec 2]. Available from: http://www.promedmail.net/
10. European Centre for Disease Prevention and Control. Communicable Disease Threats Report. *CDTR Bull*. 2014; March 9-15(Week 11):1-17.
11. Faye O, Freire CC, Lamarino A, et al. Molecular evolution of Zika virus during its emergence in the 20th century. *PLoS Negl Trop Dis*. 2014;8:e2636. doi: 10.1371/journal.pntd.0002636.
12. Duffy MR, Chen TH, Hancock WT, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. *N Engl J Med*. 2009;360:2536-43.
13. Haddow AD, Schuh AJ, Yasuda CY, et al. Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. *PLoS Negl Trop Dis*. 2012;6:e1477. doi: 10.1371/journal.pntd.0001477
14. Ministerio de Salud de Chile. *Virus Zika: Informe de Situación*. Santiago (CHL): Departamento de Epidemiología División de Planificación Sanitaria; 2014 March 20 [cited 2014 Dec 2]. Available from: http://www.sochinf.cl/sitio/templates/sochinf2008/documentos/2014/Informe_situacion_Zika_Isla_de_Pascua.pdf
15. Kutsuna S, Kato Y, Takasaki T, et al. Two cases of Zika fever imported from French Polynesia to Japan, December 2013 to January 2014. *Euro Surveill*. 2014;19:pii=20683.
16. Foy BD, Kobylinski KC, Chilson Foy JL, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. *Emerg Infect Dis*. 2011;17:880-2.
17. ProMED-mail [Internet]. Zika virus - Canada ex Thailand. *ProMED-mail 20130529.1744108*. Brookline (MA): ProMed-mail; 2013 May 29 [cited 2014 Dec 2]. Available from: http://www.promedmail.net/
18. Tappe D, Rissland J, Gabriel M, et al. First case of laboratory-confirmed Zika virus infection imported into Europe, November 2013. *Euro Surveill*. 2014;19:pii=20685.

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19. Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. *Med Mal Infect*. 2014;44(7):302-7.
20. Wæhre T, Maagard A, Tappe D, Cadar D, Schmidt-Chanasit J. Zika virus infection after travel to Tahiti, December 2013. *Emerg Infect Dis*. 2014;20(8):1412-4.
21. Pyke AT, Daly MT, Cameron JN, et al. Imported Zika virus infection from the Cook Islands into Australia, 2014. *PLoS Currents*. 2014;6:pii: doi: 10.1371/currents.outbreaks.4635a54dbffba2156fb2fd76dc49f65e.
22. Oehler E, Watrin L, Larre P, et al. Zika virus infection complicated by Guillain-Barre syndrome - case report, French Polynesia, December 2013. *Euro Surveill*. 2014;19:pii=20720.
23. Hayes EB. Zika virus outside Africa. *Emerg Infect Dis*. 2009;15:1347-50.
24. European Centre for Disease Prevention and Control. *Rapid Risk Assessment: Zika Virus Infection Outbreak, French Polynesia*. Stockholm (SWE): ECDC; 2014 February 14.
25. Faye O, Faye O, Diallo D, Diallo M, Weidmann M, Sall AA. Quantitative real-time PCR detection of Zika virus and evaluation with field-caught mosquitoes. *Virol J*. 2013;10:311.
26. Grard G, Caron M, Mombo IM, et al. Zika virus in Gabon (Central Africa)--2007: A new threat from *Aedes albopictus*? *PLoS Negl Trop Dis*. 2014;8:e2681. doi: 10.1371/journal.pntd.0002681.
27. Li MI, Wong PS, Ng LC, Tan CH. Oral susceptibility of Singapore *Aedes (Stegomyia) aegypti* (Linnaeus) to Zika virus. *PLoS Negl Trop Dis*. 2012;6:e1792. doi: 10.1371/journal.pntd.0001792.
28. Marchette NJ, Garcia R, Rudnick A. Isolation of Zika virus from *Aedes aegypti* mosquitoes in Malaysia. *Am J Trop Med Hyg*. 1969;18:411-5.
29. Gaffigan TV, Wilkerson RC, Pecor JE, Stoffer JA, Anderson T. *Systematic Catalog of Culicidae*. Suitland (MD): Smithsonian Institution Walter Reed Biosystematics Unit; 2014 [cited 2014 Dec 2]. Available from: http://www.mosquitocatalog.org/default.aspx
30. Wong PS, Li MZ, Chong CS, Ng LC, Tan CH. *Aedes (Stegomyia) albopictus* (Skuse): A potential vector of Zika virus in Singapore. *PLoS Negl Trop Dis*. 2013;7:e2348. doi: 10.1371/journal.pntd.0002348.
31. Nicholson J, Ritchie SA, van den Hurk AF. *Aedes albopictus* (Diptera: Culicidae) as a potential vector of endemic and exotic arboviruses in Australia. *J Med Entomol*. 2014;51:661-9.
32. Derraik JGB, Slaney D. Anthropogenic environmental change, mosquito-borne diseases and human health in New Zealand. EcoHealth. 2007;4:72-81.
33. van den Hurk AF, Nisbet DJ, Hall RA, Kay BH, MacKenzie JS, Ritchie SA. Vector competence of Australian mosquitoes (Diptera: Culicidae) for Japanese encephalitis virus. *J Med Entomol*. 2003;40:82-90.
34. Maguire T. Do Ross River and dengue viruses pose a threat to New Zealand? *N Z Med J*. 1994;107:448-50.
35. Lanciotti RS, Kosoy OL, Laven JJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. *Emerg Infect Dis*. 2008;14:1232-9.
36. Besnard M, Lastère S, Teissier A, Cao-Lormeau VM, Musso D. Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. *Euro Surveill*. 2014;19:pii=20751.
37. Musso D, Nhan T, Robin E, et al. Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014. *Euro Surveill*. 2014;19(14): pii: 20761.
38. Darwish MA, Hoogstraal H, Roberts TJ, Ahmed IP, Omar F. A sero-epidemiological survey for certain arboviruses (Togaviridae) in Pakistan. *Trans R Soc Trop Med Hyg*. 1983;77:442-5.
39. Henderson BE, Hewitt LE, Lule M. Serology of Wild Mammals. *Virus Research Institute Annual Report*. Nairobi (KEN): East African Printer; 1968. p. 48–51.
40. Derraik JGB, Slaney D, Nye ER, Weinstein P. Vector-borne disease prevention: The need for a joint South Pacific approach. *N Z Med J*. 2009;122:7-12.

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