Long Term Prospects for a Vaccine against Zika Virus Hold Promise but Imminent Expectation should be Tempered by Reality

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Abstract

The rapid rise in the number of reported clinical cases of Zika in South and Central America over the span of a few months in late 2015 and early 2016 presents a real risk of a global epidemic of this *Aedes* mosquito-transmitted viral infection. This threat is exacerbated by the globalisation of the human population which promotes the movement of asymptomatic carriers between nations in the same or separate continents. Pregnant women are considered at highest risk since microcephaly in the developing foetus is strongly associated with, if not yet proven as caused by, Zika infection. The possibility of additional modes of virus transmission, vertical and sexual, if confirmed, suggests the life cycle of the virus to be very complex and thus limits the scope of predictive models, which in turn may impede control efforts. Currently, no anti-Zika vaccine is available and while this has now been prioritised by multiple funding agencies, it may take several years to come to commercial fruition. The fact that Zika is closely related to yellow fever and Japanese encephalitis viruses, for both of which effective vaccines exist, offers hope that the fast-tracked preparation of a candidate vaccine is feasible. However, performing clinical trials on pregnant women would provide ethical and practical challenges to overcome before licensure is granted for administration to the general public. In the meantime, alternative public health management strategies, such as vector control programs to target mosquito breeding, are required in order to limit the global spread of this re-emerging disease.

The *Aedes* mosquito-borne viral disease of humans Zika was first recognized in 1947 and takes its name from the Ugandan rainforest where it was originally isolated from rhesus macaques [1]. For decades Zika occurred at a very minor prevalence and thus hitherto it represented a footnote to tropical medicine of specialist interest only to arbovirus researchers. All that has changed over the past few months, following an explosive Zika epidemic in many countries across Latin America and the Caribbean [2]. This includes an estimated 1,400,000 clinical cases in Brazil, the initial focus of the outbreak [3]. Moreover, the World Health Organization now predicts that by the end of 2016 the Zika virus could infect up to 4 million people in the Americas [4]. While the impact on the vast majority of these individuals will be minimal, for some, especially infants, the effect will be severe and long-lasting.

The epidemic is causing public concern at a time shortly before the attention of the world will turn to the summer Olympic Games in Rio de Janeiro this August. Beyond the immediate focus on Brazil, it has fuelled an already increasing media frenzy regarding the possibility of the global spread of Zika, and the impact this may have on public health in those regions that are presently not affected [5]. With increased globalization and in an age of mass international travel, it is uncertain where the virus may establish next. Hence, the consequences, both real and perceived, of a possible introduction of this disease in developed countries are a matter for anxiety for their resident populations and are thus an important subject for discussion.

While there are varied and diverse reasons for the current epidemic in South America [6], inadequate vector control of a sudden population explosion of mosquitoes is suspected as a causal factor. It is appropriate to consider Zika as a re-emerging infectious disease; that is one which is established but displayed in a novel setting, in much the same way as the recent upsurge of Ebola cases in West Africa [7].

Zika is a member of the *Flavivirus* genus of positive sense, single-stranded RNA viruses [8]. This includes yellow fever, Japanese encephalitis and dengue viruses, but also etiological agents of other less familiar yet debilitating mosquito-borne diseases, such as Ross River fever, Murray Valley encephalitis and Kokobera encephalitis, that occur especially along the north east coast of Australia [9]. Vertical, sexual and blood-borne transmission of Zika has been suggested [10,11], which, if confirmed, may provide auxiliary routes to enable viral persistence in regions that are not endemic for *Aedes* mosquitoes.

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Compared to the closely related viruses yellow fever, Japanese encephalitis and dengue, infection with each of which can be severely incapacitating for a person of any age, four in every five adults infected with Zika are thought not to show any clinical manifestations [12]. Thus, for a period of several days after being bitten by an infectious mosquito they may act as asymptomatic carriers of infection. If a person does become ill, the main symptoms may last for up to one week and are similar but less severe than other related febrile illnesses – a mild fever, myalgia, arthralgia, conjunctivitis and maculopapular rash [13]. Infrequently, Zika is associated with Guillain-Baré syndrome, a neural demyelination syndrome that is considered to be an autoimmune sequela of infectious disease [14,15].

The principal likely consequence of Zika infection arises through congenital transmission from a pregnant woman to her foetus *in utero* or newborn baby [13,15], the effects of which can be profound [16]. In Brazil alone, the virus has been associated with over 4,000 cases of microcephaly [2], a previously rare condition that as a result of abnormal brain development produces babies with small heads and, in the majority of cases, neurological impairment.

Pregnant women from non-endemic regions are currently cautioned to suspend travel to Brazil and neighbouring countries [17]. Other recommendations to prevent disease, especially microcephaly, include practicing safe sex in those territories where Zika is reported as endemic [6]. Importantly, the risks should be considered in family planning until such time as the apparent association between viral infection and microcephaly is either confirmed or refuted [18,19]. This raises the question as to what guidance is appropriate to provide in more economically developed countries distant to the present epidemic and in which Zika has not been reported. It is in such industrialized nations that there has been the loudest call for anti-Zika prophylaxis [5], such as that which could be provided by sterilizing immunization. In the short term, as anti-viral therapies are yet to be realized alternative means should be used to combat Zika. These include low technology measures that focus on vector control such as insecticide spraying, limit mosquito breeding and providing protection from mosquito bites [20]. The delivery of different interventions, singularly or in combination, should be informed by, and thereby tailored to, local settings.

Currently, there is neither a prescription medicine nor a preventive vaccine that is commercially available. As efficacious vaccines have been prepared against yellow fever and Japanese encephalitis viruses, it is anticipated that a similar therapeutic is feasible [21]. Nonetheless, despite the promised release of ring-fenced funding to support research into developing a vaccine [22], a cautionary note should be advised. It is possible that the laboratory-based design and pre-clinical testing of a candidate vaccine may be fast-tracked in a matter of months, perhaps by the end of 2016 [23]. This is especially the case if it is a DNA-based construct [21]. Both the US National Institutes of Health and the Indian company Bharat Biotech are aiming to develop a vaccine [23]. However, any clinical trials that follow may take several years to conduct and to gain full regulatory approval for public administration [6,24]. While attaining ethical approval for, and performing, tests of vaccine safety and efficacy in humans can be laboriously slow at the best of times, the due process for any prototype vaccine that is given to pregnant women is understandably subject to rigorous scrutiny [25,26]. This is especially pertinent to Zika since the gravest manifestation of infection affects pregnancy.

It is in this context that vaccine researchers, project managers and public health administrators should be mindful not to add to the wealth of misinformation surrounding Zika by suggesting, however guardedly or inadvertently, that a vaccine is imminent [5,23]. The sociopolitical backdrop to this is a Western culture in which anti-vaccination protest groups dissuade parents from having their children immunized against common childhood illnesses. Already, the recent introduction into Brazil of the triple combination vaccine used to prevent diphtheria, tetanus and pertussis is being blamed for women pregnant when vaccinated giving birth to babies with microcephaly [27]. In an era of social media, where links are shared, reposted and retweeted, journalists looking for an accessible headline can easily overlook the caveats and qualifications to the outcomes of a study that are so important to trained scientists – it is then that a story on a virus literally goes ‘viral’.

References

1. Dick GW, Kitchen SF, Haddow AJ. Zika virus. I. Isolations and serological specificity. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 1952; 46: 509-520.
2. Fauci AS, Morens DM. Zika virus in the Americas – yet another arbovirus threat. *New England Journal of Medicine*. 2016; 374: 601-604.
3. Pan American Health Organization. Zika virus infection. Washington DC: PAHO/WHO. 2016.
4. BBC News. Zika virus: up to four million Zika cases predicted. 2016.
5. BBC News. Zika virus: rumours and theories fuel ‘information war’. 2016.
6. Science/AAAS. Zika virus: your questions answered. 2016.
7. Carroll MW, Matthews DA, Hiscox JA, Elmore MJ, Pollakis G, Rambaut A, et al. Temporal and spatial analysis of the 2014-2015 Ebola virus outbreak in West Africa. *Nature*. 2015; 524: 97-101.
8. Kuno G, Chang G-J. Full-length sequencing and genomic characterization of Bagaza, Kedougou, and Zika viruses. *Archives of Virology*. 2007; 152: 687-696.
9. van den Hurk AF, Craig SB, Tulsiani SM, Jansen CC. Emerging tropical diseases in Australia. Part 4. Mosquito borne diseases. *Annals of Tropical Medicine and Parasitology*. 2010; 104: 623-640.
10. Foy BD, Kobylinski KC, Chilson Foy JL, Blitvich BJ, Travassos da Rosa A, Haddow AD, et al. Probable non-vector-borne transmission of Zika virus, Colorado, USA. *Emerging Infectious Diseases*. 2011; 17: 880-882.
11. Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. *Emerging Infectious Diseases*. 2015; 21: 359.
12. Ginier M, Neumayr A, Günther S, Schmidt-Chanasit J, Blum J. Zika without symptoms in returning travellers: what are the implications? *Travel Medicine and Infectious Disease*. 2016; 14: 16-20.
13. Centers for Disease Control and Prevention. Zika virus – symptoms, diagnosis & treatment. 2016.
14. Cao-Lormeau VM, Roche C, Teissier A, Robin E, Berry AL, Mallet HP, et al. Zika virus, French Polynesia, South Pacific, 2013. *Emerging Infectious Diseases*. 2014; 20: 1085-1086.
15. European Centre for Disease Prevention and Control. Rapid Risk Assessment. Zika virus epidemic: potential association with microcephaly and Guillain-Barré syndrome. 2016.
16. Meaney-Delman D, Rasmussen SA, Staples JE, Oduyebo T, Ellington SR, Petersen EE, et al. Zika virus and pregnancy: what obstetric health care providers need to know. *Obstetrics and Gynecology*. In Press. 2016.
17. U.S. National Library of Medicine. CDC broadens Zika virus travel alert for pregnant women. 2016.

18. Schuler-Faccini L, Ribeiro EM, Feitosa IM, Horovitz DD, Cavalcanti DP, André Pessoa, et al. Possible association between Zika virus infection and microcephaly - Brazil, 2015. *Morbidity and Mortality Weekly Report*. 2016; 65: 59-62.
19. Calvet G, Aguiar RS, Melo AS, Sampaio SA, de Filippis I, Fabri A, et al. Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study. *Lancet Infectious Diseases*. In Press. 2016.
20. Becker N, Petrić D, Zgomba M, Boase C, Minoo M, Dahl C, et al. Mosquitoes and their control. *Springer*. 2010; 509.
21. Ishikawa T, Yamanaka A, Konishi E. A review of successful flavivirus vaccines and the problems with those flaviviruses for which vaccines are not yet available. *Vaccine*. 2014; 32: 1326-1337.
22. The Guardian. Obama to seek \$1.8bn from Congress to combat Zika virus. 2016.
23. BBC News. Zika vaccine possible 'within months'. 2016.
24. Mahalingam S, Rolph M. Here's why we don't have a vaccine for Zika (and other mosquito-borne viruses). *The Conversation*. 2016.
25. Omer SB, Beigi RH. Pregnancy in the time of Zika: Addressing barriers for developing vaccines and other measures for pregnant women. *Journal of the American Medical Association*. 2016.
26. Iacobucci G. Zika highlights need for ethical framework for developing vaccines for pregnant women. *British Medical Journal*. 2016; 352: i1155.
27. BBC News. Health experts slam anti-vaxxers' Zika virus conspiracy theory as 'absurd'. 2016.