Gone or forgotten? The rise and fall of Zika virus

The rise of Zika virus, from a little known pathogen to an internationally recognised cause of birth defects, was swift and devastating. Not present in the western hemisphere before 2015, over 800 000 people have since been reported to be infected with Zika virus in the region; however, this number is most likely an underestimate since the infection typically causes a mild febrile illness in less than 20% of patients.[1] Moreover, the Asian lineage of Zika virus, which is responsible for the 2015–16 epidemic, has been associated with severe congenital defects in children born to women infected during pregnancy,[2] leading to thousands of children with congenital Zika syndrome. Furthermore, the combination of asymptomatic infection, the potential for extended latent seminal and sexual transmission,[3] and a predilection to cause birth defects has presented substantial challenges to disease control for inhabitants of endemic regions and travellers.[3]

As the scale of the epidemic and its complications came into focus, the public health community developed a multipronged response that included WHO declaring a public health emergency of international concern to encourage the development of surveillance networks, diagnostics, risk communication strategies, and vector-control measures. Yet, even before a substantial response was realised, the incidence of Zika virus infections in the western hemisphere began to fall almost as fast as it had risen. Seasonal variation was not to blame. Most of Latin America and the Caribbean had a massive decline in cases in 2017 compared with similar periods in 2016. Birth defects associated with Zika virus also declined by over 50%. Before the end of 2016, WHO called an end to the international Zika emergency.

So, what is to be made of these sizeable fluctuations in the epidemiology of Zika virus disease? And how should the public—most notably women of childbearing age—and public health planners prepare for the future? The best predictors of the future course of Zika virus disease will most likely include: the duration of protective immunity after infection, and the potential effect of non-neutralising, cross-reactive antibodies to co-circulating flaviviruses, such as dengue virus. Regarding protective immunity, early data suggest that Zika virus infection induces serological protection from reinfection;[4] although, the duration of such protection remains unknown. Zika virus vaccination studies have also shown the production of neutralising antibodies that appear to be protective both in vitro and in mouse models.[5] Zika virus shares substantial genetic homology, structural features, and cross-reactive antibodies with dengue virus and other flaviviruses. The immune responses in people infected at some point by more than one of these viruses is not yet fully understood.[6] Might some cross-protection exist? Does the order of infection matter? Might priming with one virus actually make congenital or other outcomes more or less likely? In the best case scenario, Zika virus infection will induce lifelong immunity independent of dengue virus infection, which would greatly increase the likelihood that the western hemisphere epidemic will protect much of the current population from local reinfection and provide herd immunity to others.

However, even if Zika virus immunity proves durably protective, complete eradication remains an unlikely scenario because it would only be possible if an enzootic sylvatic cycle is not sustained and no threat of re-introduction exists. Although Zika virus is believed to exist within a sylvatic cycle in Africa and Asia, a reservoir in animals in Latin America has not yet been clearly documented. Nonetheless, environmental factors and mosquito vectors support the potential for endemicity and spread to more temperate climates. Ultimately, time will tell if Zika virus behaves more like yellow fever virus, which is sustained in enzootic sylvatic cycles in South America, or dengue virus, which is largely sustained by transmission between people via mosquito vectors.[7] The history of Zika virus elsewhere shows that a sylvatic cycle is more likely to be established, and consequently that long-term vector control, disease surveillance, and, ideally, widespread vaccination programmes will be required.

Perhaps the most important future development for both travellers and residents of endemic settings is the promise of effective vaccines. To date, vaccine safety and immunogenicity studies have largely enrolled residents of non-endemic regions. However, women of childbearing age in areas affected by Zika virus are the population that will most likely benefit from such vaccines and should be prioritised in vaccine evaluation, licensing, and distribution.

Although the decline in reported cases of disease and congenital defects is a welcome sign, it should not be a cause for diverting efforts away from Zika virus control efforts. Crucial questions remain unanswered, particularly related to the safety of pregnant women. For example, does the near disappearance of cases in Latin America mean that these areas are now free from transmission, or that herd immunity is protecting the local population? How will severe weather patterns affect the risk of disease re-emergence? Will better diagnostic tests become widely available in a timely manner? And will these tests change recommendations to promote testing for women trying to conceive, or, more importantly, their partners who might carry the virus in their semen for months after infection? Until these questions are answered, the virus might appear to be gone, but should not be forgotten.

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