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EDITORIAL

Search and one will find: Zika virus everywhere

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Almost one year ago, *Transactions of the Royal Society of Tropical Medicine and Hygiene* (TRSTMH) published a commentary on the potential for the establishment of new arbovirus transmission cycles in Europe.[1] The impetus for this was the remarkable emergence of chikungunya virus in the Americas and numerous travel-associated cases in many European countries. Agencies such as the European Centre for Disease Prevention and Control had developed excellent material related to chikungunya virus. There had been some discussion on the little known Zika virus, largely because of outbreaks in, for example, French Polynesia. Who could have predicted the momentum and magnitude of the ongoing Zika epidemic? Perhaps if one had perused reports published in TRSTMH over 60 years ago, then we may have been better prepared, but who knows?

On a Thursday evening in December of 1952, at what was described as an 'Ordinary Meeting' of the Royal Society of Tropical Medicine and Hygiene, Dr George Dick presented a paper entitled '*Epidemiological notes on some viruses isolated in Uganda*.' The report was based on work between 1937 and 1947.[2]

The isolations of 'yet another virus which is believed to be hitherto unrecorded' had been reported as a communication in the September issue of TRSTMH.[3] Zika virus, named after the Zika forest in the Bwamba district of Uganda, had been isolated on 20 April of 1947 from a febrile Rhesus monkey number 766, which, as part of a Rockefeller Foundation initiated survey, had been placed in a cage on a platform in the tree canopy. Mice injected intracerebrally with serum from this monkey became sick and the virus was isolated.[4] A subsequent mosquito study in January of 1948 resulted in isolation of the virus from a pool of *Aedes africanus*. In one study, antibody prevalence rates ranged from 17% in Kontagora to 45% in Ilaro.[5] Later studies resulted in a human isolate[6] and even included infection of a human volunteer.[7] At that ordinary meeting, Dick recommended that 'further studies are required of the part which *A. africanus* may play as a sylvan vector and of the way in which human beings become infected with this virus.' There were many speculations and suggestions in the report of this meeting[2]: 'While one may speculate that any of the viruses that we have been discussing may be of danger we do not know except in the case of yellow fever and Rift Valley fever how important they may be' and 'It is only time to take action against them when they begin to interfere with man's dominance over his environment.'

And so, Zika virus remained a relatively poorly studied and little understood virus for over 50 years. Studies had suggested that perhaps 14 species of mosquito might act as vectors, with isolation from *Ae. albopictus* being made for the first time in 2007. Non-human primates, for example patas and vervet monkeys, were assumed to be host for a sylvatic cycle, although Darwish *et al.*[8] reported in TRSTMH seropositive rodents and even domestic animals, the significance of which still remains unknown. Between 1947 and 2006, there were only 14 reports of human cases, but then, in 2007, an outbreak occurred on the island of Yap. At a time when chikungunya virus was rampantly spreading through the Americas and being associated with travel-related cases in countries around the globe, the 49 confirmed cases and 59 probable cases on Yap[9] did perhaps not receive the attention that it deserved. It was estimated that perhaps 75% of residents were infected but it was believed that 80% of those infected did not develop symptoms.

During 2013, an epidemic in French Polynesia infected an estimated 28 000 people, and it was during this epidemic that the question was raised regarding the possible association of Zika virus infection with hitherto unseen clinical manifestations, in this case Guillain-Barré syndrome (GBS). In 2014, cases in New Caledonia, the Cook Islands, Solomons and Easter Island tracked the march of Zika towards the Americas with the first reports for Brazil occurring in May of 2015.

In less than one year, Zika virus has been introduced throughout the region, with active transmission by *Ae. aegypti* in at least 26 countries. There is mounting evidence that Zika virus infection may indeed be associated with GBS; however, since entering the Americas another potential consequence of ZIKV infection has been reported. Dramatic increases in reports of babies born with microcephaly have led to the suggestion that Zika virus infection is responsible for these. Such speculation had been reported for

French Polynesia during 2015. Detection of Zika virus in amniotic fluid, in fetal tissues and in effected newborns has added weight to the speculation, but the evidence is mounting,[10] and a recent description of Zika virus infection of neural progenitor cells may provide the mechanism that underlies the effect.[11] The presence of virus in blood is obviously a cause for concern with respect to transfusion-related infections. However, viremias in asymptomatic cases at titers that are likely sufficient to infect mosquitoes means that a much higher proportion of infected people may contribute to the transmission cycle than previously realized. Instances of sexual transmission from men to women have increased and, with the detection of Zika virus in saliva and urine, one must wonder what other routes of Zika virus transmission may exist.

As the world once again struggles with emergence and rapid spread of a previously known pathogen, this time for over 60 years, one cannot help but reflect and ask why we are not better prepared. Zika has become a rallying point, galvanizing researchers, physicians, other health care workers, vector control experts, epidemiologists, vaccinologists, and many others from bedside to bench to administrators at the highest level, to focus on what from some perspectives is an equivalent of mosquito-borne version of Ebola, but with, dare one suggest, earlier and more coordinated responses than we have previously seen. Statements with action from national and international policy makers and organizations have been remarkably swift. Furthermore, rapid dissemination and sharing of information, ideas and data has been notable in the response to the Zika outbreak. In the spirit of this, TRSTMH has made all articles published, including invaluable archival material, freely available online (http://www.oxfordjournals.org/en/our-journals/medicine-and-health/aedes-aegypti-zika-virus.html). One would like to say read and learn, but history would suggest that this is optimistic. At least read the report presented in that ordinary meeting and see what Dick suggested and what might have helped us be better prepared.

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