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Review

Rapid Spread of Zika Virus in The Americas - Implications for Public Health Preparedness for Mass Gatherings at the 2016 Brazil Olympic Games

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SUMMARY

Mass gatherings at major international sporting events put millions of international travelers and local host-country residents at risk of acquiring infectious diseases, including locally endemic infectious diseases. The mosquito-borne Zika virus (ZIKV) has recently aroused global attention due to its rapid spread since its first detection in May 2015 in Brazil to 22 other countries and other territories in the Americas. The ZIKV outbreak in Brazil, has also been associated with a significant rise in the number of babies born with microcephaly and neurological disorders, and has been declared a 'Global Emergency by the World Health Organization. This explosive spread of ZIKV in Brazil poses challenges for public health preparedness and surveillance for the Olympics and Paralympics which are due to be held in Rio De Janeiro in August, 2016. We review the epidemiology and clinical features of the current ZIKV outbreak in Brazil, highlight knowledge gaps, and review the public health implications of the current ZIKV outbreak in the Americas. We highlight the urgent need for a coordinated collaborative response for prevention and spread of infectious diseases with epidemic potential at mass gatherings events.

1. Mass gatherings and transmission of infectious diseases

Sporting events attract millions of international travelers and residents from the host country. These mass gatherings of people are put at risk of acquiring imported and locally prevalent infectious diseases.[1,2] Brazil is to host the 2016 Olympic and Paralympic Games in Rio De Janeiro in August 2016 [3] where millions of people from within Brazil and from all over the world, are expected to attend. Recent media and World Health Organization (WHO) attention has focused on the unexplained rapid spread of the mosquito-borne Zika Virus (ZIKV) across South and Central America and the Caribbean Islands.[4] On February 1st 2016 the WHO announced that the ZIKV outbreak constitutes a '*Public Health Emergency of International Concern*'.[5] The term 'public health emergency of international concern (PHEIC)' is defined in the International Health Regulations as "an extraordinary event which is determined to constitute a public health risk to other States through the international spread of disease and to potentially require a coordinated international response".

The first ever case of ZIKV disease in Brazil was reported in May 2015,[6] and since then, the virus has rapidly spread within Brazil[7] and across 22 other countries and territories in the region.[8,9] The

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ZIKV outbreak in Brazil is unusual, in that, alarmingly it has been associated with a large rise in the number of babies born with microcephaly and other neurological complications.[4,5,7,10–12] The rapid spread of ZIKV in Brazil and the Americas is also of great concern since it joins the growing list of re-emerging infectious diseases[13], and its epidemic potential poses challenges for public health preparedness and surveillance for the 2016 Olympics and Paralympic Games. We review the epidemiology and clinical features of the current ZIKV outbreak in Brazil, highlight knowledge gaps, and highlight the need for enhanced public health preparedness for the 2016 Olympic Games.

2. ZIKV epidemiology and global spread

ZIKV is a single stranded RNA arbovirus member of the genus Flavivirus and is related to other mosquito-borne viruses such as Dengue, Yellow Fever, Japanese B encephalitis, and West Nile Fever viruses. ZIKV was named as such because it was first identified in a rhesus monkey in the Zika Forest of Uganda in 1947.[14] ZIKV was later found in humans with febrile illnesses in West Africa[15] in 1954. It then to spread to Indonesia[16], Micronesia[17], Thailand,[18] the Philippines,[19] French Polynesia,[20] and Easter Island-South Pacific in 2014.[21] ZIKV was not documented on mainland South America until the first report of autochthonous transmission in Brazil in May 2015. The conclusion at that time was that ZIKV was introduced into Brazil during the 2014 World Cup Football.[6] This was not supported due to the fact that no Pacific countries with documented ZIKV had competed in the World Cup competition. However, Pacific countries had participated in the August 2014 Va'a World Sprints canoe championship which was held in Rio de Janeiro, suggesting that introduction of ZIKV into Brazil could have occurred then.[23,23] Another possibility was the introduction of ZIKV to Brazil by travelers from Chile.[24] Since its introduction into Brazil in May 2015, ZIKV has subsequently spread rapidly across Brazil and the Americas. As of January 28th 2016, autochthonous cases of ZIKV infection have been reported from 26 countries in the Americas: Barbados, Bolivia, Brazil, Colombia, Curaçao, Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Martinique, Mexico, Nicaragua, Panama, Paraguay, Puerto Rico, Saint Martin, Suriname, Venezuela, Virgin island.[11] No autochthonous ZIKV transmission has been reported from EU countries, and a heightened state of global alert is in place in Europe and USA to screen for ZIKV in travelers with fever returning from ZIKV-endemic countries.[4,5]

The first travel-associated ZIKV disease case among U.S. travelers was reported in 2007. From 2007 to 2014, a total of 14 returning U.S. travelers had positive ZIKV testing performed at UC-Centers for Diseases Control (CDC). In 2015 and 2016 at least eight U.S. travelers have had positive ZIKV testing performed at CDC.[25]

3. Mode of transmission of ZIKV

The primary mode of transmission of ZIKV between humans is through the bite of an infected female mosquito of the *Aedes* species.[4,5] Apart from mosquitos, other non-vector means of transmission of ZIKV have been suggested: a) via sexual intercourse[26,27], b) blood transfusions[28], c) perinatal transmission from mother to foetus at time of delivery.[29–31]

Although it is possible that ZIKV could be passed from mother to fetus during any trimester of pregnancy[30], limited data from one study[31] has indicated that ZIKV maternal infection in the first trimester might carry a greater risk of fetal microcephaly. Of 35 infants with microcephaly, 26 (74%) of the mothers reported having had a rash; 21 in the first trimester, 5 in the second trimester. Other fetal brain abnormalities that have been reported in association with clinical maternal ZIKV infection are ventriculomegaly, cell migration abnormalities, and congenital contractures secondary to central or peripheral nervous system involvement.[29–31] There have been no reports yet of ZIKV postnatal transmission to babies through breastfeeding. Further studies are required to delineate the importance of these modes of transmission.

3.1. Mosquito-borne ZIKV transmission

Aedes spp mosquitoes are present throughout the tropics. They are known to transmit other important arboviruses that affect humans such as Chikungunya Virus, Dengue Virus and Yellow Fever Virus.[32–37] The main vector associated with transmission of ZIKV is *Aedes aegypti*. Transmission can also occur via other *Aedes* species[38] such as: *Ae.albopictus, Ae.africanus*, *Ae.luteocephalus*, *Ae.vitattus*, *Ae.furcifer*, *Ae.hensilii* and *Ae.apicoargenteus*. *Aedes aegypti* lives and breeds near people and their homes, laying their eggs in stagnant water which collects in puddles, buckets, flower pots, empty cans and other containers. They bite humans mainly during daytime, either outside or inside their houses. *Aedes aegypti* mosquitoes are widely distributed in the Americas (except for Chile) and the suitable climatic breeding conditions is partly responsible for the current ZIKV epidemic, with over a million cases reported.[4,5] *Aedes albopictus*[39] is found in the USA[40] as far north as New York and Chicago, and in parts of southern Europe. It is expected that the current ZIKV transmission will increase throughout the Americas with possibility of local transmission within the USA. Since the *Aedes* mosquito species that spread ZIKV are found in many locations throughout the world, it is likely that outbreaks will spread to new countries.

3.2. Sexual transmission

ZIKV has been isolated from semen[26,27] and possible sexual transmission has been reported.[26] Studies are needed to assess how frequently and for how long ZIKV persists in semen (or other privileged sites in the body) and whether precautions to prevent sexual transmission of ZIKV are warranted.

3.3. Blood transfusion and transmission of ZIKV

Given that the majority (80%) of persons with ZIKV infection are asymptomatic[4] and among them are blood donors, transmission of ZIKV via blood transfusion is of concern.[28] It has a parallel in the introduction of West Nile Virus in the United States and Canada, which led to the need for screening of donated blood.[41] The outbreak of Chikungunya Virus (CKV) which started in Reunion[42] and spread throughout Asia, also prompted screening of blood products. After the introduction of CKV in Italy, systematic screening by blood banks was considered, but a laboratory test for routine testing was not available[43] so blood donations from people living in the affected municipalities were discontinued. A 21-day deferral policy was introduced nationwide for blood donors who had visited the affected areas, even for a few hours. The pre-donation questionnaire was modified for an early detection of CKV infections. All stocked blood components collected from donors living in the affected area, after the identification of the first case, even those already delivered to the pharmaceutical industry, were eliminated. The impact of the CKV outbreak in Italy was later evaluated[44] with the conclusion that "Even a relatively small outbreak in Italy resulted in considerable adverse impact on blood collections and economic consequence". It is likely that blood transfusion related infection does occur in ZIKV endemic areas. To prevent blood transfusion related ZIKV infection, blood donations must also be screened for ZIKV.