EC BACTERIOLOGY AND VIROLOGY
Mini Review

Zika Virus Vaccine Initiatives and Proactive Vector Control Strategies: Key to Halting the Ongoing Pandemic

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Abstract

Zika virus (ZIKV) is an emerging arboviral infection, affecting approximately 2 million residents in 45 countries since 2015, and is primarily transmitted by *Aedes aegypti* mosquitoes through a mosquito to human transmission cycle [1]. ZIKV, recently declared by the WHO as a "Public Health Emergency of International Concern" may affect approximately 4 million people by the end of 2016 and a "coordinated international response" is required to minimize the threat in affected countries and reduce the risk of further international spread [2]. Currently, "3.97 billion people residing in 128 countries are at risk for infection" as *aedes* mosquitoes typically circulates in these regions and as 80% of ZIKV cases are asymptomatic, individuals with in appararent infections are considered vehicles for ongoing disease transmission as they can potentially infect other *aedes* mosquitoes [3]. The potential for asymptomatic ZIKV cases to infect *aedes* mosquitoes and the subsequent ability of these mosquitoes to potentially infect 4-5 additional individuals within a single blood meal is of particular concern as it can facilitate ongoing ZIKV transmission and impact high risk groups. The purpose of this paper is to discuss potential ZIKV vaccines, evaluate proactive vector control strategies, and implement preventative measures in order to halt the spread of the ongoing pandemic.

Keywords: *Zika virus; Aedes mosquitoes; CDC; WHO*

Potential ZIKV Vaccines

To date, there are no available and approved vaccines to prevent ZIKV. Prior to the ongoing pandemic, no vaccines existed to prevent ZIKV since it is a novel arboviral infection, and supporting studies highlighting epidemiological patterns associated with this disease remained scant. Prior to 2007, only 14 human cases were identified and during the first outbreak that occurred in Polynesia, 82% of ZIKV cases were asymptomatic posing a minute threat to the public [4]. However, the massive increases in ZIKV cases identified in South America, risk it poses to travelers visiting endemic countries, unique modes of disease transmission (e.g., sexual & vertical) and birth/neurological complications including: microcephaly, spontaneous abortions, and Guillain-Barre syndrome has prompted researchers to initiate development of the first vaccine [4]. The geographical distribution of ZIKV is increasing due to foreign travel and climate change and to date, a total of 193 travel-associated cases were identified in the Continental United States and 173 locally acquired cases were detected in United States territories [5]. Of the 193 ZIKV cases detected in the Continental United States, the majority (N=49) were identified in Florida, 25 cases were detected in New York, and 19 cases were confirmed in Texas [5]. Approximately, 15 research groups are currently investigating potential vaccines and Table 1 depicts selected research companies that are involved in the planning phases of vaccine development [6].

Manufacturer	Type
Bharat Biotec	Recombinant live
	Inactivated
Inovio Pharmaceuticals	DNA
Sanofi Pasteur	DNA
National Institutes of Health	DNA

Table 1: *Zika Virus Vaccine Candidates.*

Challenges to ZIKV Vaccine Development

One of the challenges in developing a ZIKV vaccine is that the final approval and marketing of the vaccine may take up to several years, which may be too late to halt the rapid spread of this disease [6]. By the time vaccines are available for use, ZIKV will most likely become endemic in regions that are currently non-endemic and the epidemiological situation related to the current pandemic may change. Another challenge in vaccine development involves identifying the appropriate piece of the virus to use and identifying a piece of the virus that will be common to most ZIKV strains [6]. Finally, the development of novel vaccines can be expensive, time-consuming, and risky, as years of research, licensing, and production costs may exceed $1 billion [7].

ZIKV Alternative Preventative Strategies

An effective ZIKV response strategy involves policy change, federal funding, aggressive testing of potentially infected ZIKV cases, proactive vector control measures, and targeted public health messaging towards high risk groups. Aggressive rapid testing of ZIKV is a priority at this stage of the pandemic as it will accelerate ongoing surveillance efforts and several biotech companies are in the process of developing different tests [6]. One of the tests involves detection of the virus in an infected person and determining which body fluid it was identified in, the second is an antibody-based test to allow individuals to determine if they have previously been infected with ZIKV, and the third is a rapid diagnostic test which provides immediate results on a test stick [6]. The antibody tests are critical to detecting additional cases which may go unreported due to asymptomatic clinical presentation in many individuals [8]. Antiviral medications and prophylactic drugs that could prevent infection in pregnant women are also under investigation [6].

Predictions of the geographical distribution and spread of ZIKV vectors are crucial to the implementation of integrated pest management strategies and development of a comprehensive mosquito control plan to eliminate *aedes* mosquitoes. A thorough understanding of the areas where *aedes* mosquitoes are typically found and knowledge regarding precipitation and climatic factors affecting particular regions will provide insight into where and when larviciding and adulticiding should occur and the expected spread of the disease. In addition, knowledge of ZIKV hot spots can guide intervention and testing efforts as rapid testing should be conducted in these areas due to the vulnerability of the population at risk. In countries where ZIKV was recently detected or has yet to be detected, vector surveillance and control should be "strengthened in all border areas and at points of entry" [2]. Development of genetically modified *Ae. aegypti* mosquitoes that reduce the populations of mosquito offspring reaching adulthood has been initiated by several researchers [9]. Recently, a field trial took place in Brazil in which *Ae. aegpti* mosquitoes were genetically modified to express lethal genes and this strategy resulted in a 95% reduction in local mosquito populations [9].

The CDC has issued travel advisories warning pregnant women not to travel to ZIKV endemic regions, women of reproductive age to postpone pregnancy for two years in disease endemic regions, and messages to ZIKV infected men to use condoms with their sexual partners to prevent sexual transmission of the virus [5]. Furthermore, typical public health messages including: applying DEET, wearing long-sleeved clothing, remaining indoors, using mosquito nets and eliminating all sources of standing water to reduce exposure to mosquito bites has been emphasized as we continue to face the ongoing pandemic [2]. Specific educational messages conveyed through interactive phone apps can educate the public about "how repellants should be applied, how to calculate the quantity of products needed for a trip, and how to erect a mosquito net" [10]. During the upcoming 2016 Rio Olympics, public health authorities should also emphas ize ZIKV prevention by conducting a massive outreach campaign with media messages recommending all spectators and athletes to exercise appropriate personal protection measures. The campaign should involve distribution of ZIKV educational brochures highlighting appropriate recommendations and testing recommendations as well as mass distribution of DEET repellant to all spectators and athletes.

Conclusion

While aggressive vector control strategies and novel interventions will reduce some ZIKV infections; the virus may reappear in non-endemic regions of the world each year, and our only hope for eliminating the spread of the infection will rely on the development of an effective vaccine. As millions of individuals plan on travelling to Brazil for the 2016 Rio Olympic Games, public health authorities are faced with the ongoing challenge of providing the public with evidence-based recommendations, and by the end of the event it is likely that the worldwide case count may double [11]. The key to halting the spread of ZIKV will depend upon the massive and routine vaccination of millions of individuals across the hemisphere and achieving an overall vaccination rate of at least 85% among high risk populations (e.g., women of reproductive age) [2].

Prior to implementation of a massive vaccination campaign, a thorough risk assessment should be conducted to identify regions and populations at highest risk of infection [2]. The risk assessment should involve the results from several epidemiological studies in different regions that depict the natural history, clinical presentation, and epidemiological patterns associated with ZIKV. Understanding mosquito to human transmission patterns in mosquito abundant areas will further increase our ability to develop novel vector control interventions and protect the public. Long-term surveillance efforts may involve evaluating the economic impact of ZIKV on the medical infrastructure, identifying novel risk factors and circulating ZIKV lineages, and detecting epidemiological and entomological changes that may impact ZIKV transmission patterns [2]. Furthermore, research efforts should evaluate the incidence of maternal-fetal transmission of ZIKV by trimester, risk of developing neurological complications and adverse birth outcomes if pregnant, and investigation of possible transmission routes.

Further analysis of epidemiological data is needed to understand the demographic distribution of ZIKV and risk factors associated with those developing co-infection with one or more arboviral diseases (e.g., dengue and chikungunya). Finally, ZIKV has been declared a "public health emergency of international concern" since "a coordinated international response" is necessary to improve surveillance and detection of infections, intensify the control of mosquito populations, and to expedite the development of diagnostic tests and vaccines to protect high risk groups [2]. Currently, there are enormous gaps in our understanding of ZIKV and it is unlikely that funding for development of vaccines will materialize before the virus has already spread to every area of the hemisphere. Advances in our understanding of potential ZIKV transmission routes, co-infection among ZIKV and other arboviral diseases, high risk groups, and epidemiological distribution of the disease will support the rational development and application of novel interventions including: vaccines, antivirals, and integrated pest control strategies.

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