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Review article

ZIKA VIRUS PATHOGENESIS: A GLOBAL BIOTERRORISM FOR PUBLIC HEALTH

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ABSTRACT

Zika virus is a newly developing virus that has been confirmed to have potential of spreading across a wide area. Aedes mosquito is considered to be responsible for the evolution of the virus. Till today, more than 44 countries have reported the transmission of the disease. The virus can also spread from human origin even after clinical recovery because the virus has a long viraemia or due to clogging of the virus in the semen even after viraemia is cleared. Zika virus contributes to several neurological abnormalities mainly Barre syndrome which have symptoms like weakness of the arms and legs usually on both side of the body. Recent research has suggested that the virus causes Microcephaly, a condition where neonates' brain and head is smaller than normal and may also occur some other brain defects. No approved vaccines or treatment procedure is available for Zika virus presently. Though FDA has approved Focus diagnostics, Inc'sZika virus RNA Qualitative Real-Time TR-PCR test for diagnostics of the virus. Zika virus is an arbovirus from the family Flaviviridae, genus Flavivirus. Zika virons are enveloped, icosahedral and contain a non-segmented, single-stranded, positive-sense RNA genome, which encode 3 structural and 7 nonstructural proteinsthat are expressed as a single polyprotein that undergoes cleavage. Zika genomic RNA replicates in the cytoplasm of infected host cell. According to estimation of The World Health Organization, smaller Caribbean economics almost loses 1 to 2% of their total GDP due to Zika virus monthly. The estimated total wastage on the Latin America and the Caribbean region is $3.5 billion USD which is approximately 0.06% of the GDP. The actual concept of the virus is still unclear with some human cases reported in Asia and Africa. Very concentrated public health surveillances is necessary to control and prevent the disease. Preparation for prevention and control includes capacities and capabilities for early detection, response and communication.

Keywords: Zika Virus , Discovery, Neurological Complications, Genomic Evolution And Pathogenesis, Pregnancy, Birth Defects, Prevention, Transmission, Control , Vaccine ,Travel-Related Zika.

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INTRODUCTION

Zika is a mosquito - borne viral disease originated by Zika virus (ZIKV), a Flavivirus from the Flaviviridae family, that has the title of a forest near Kampala in Uganda, where it was recognized in rhesus monkeys in 1947 [1,2]. It was subsequently isolated in humans several years after in 1952 in Uganda and another country in East Africa - Tanzania [1]. Genomic comparison showed various sub-clades and the continuation of 2 different lineages the African and

the Asian lineage [2]. The virus is inherited by mosquitoes, and so far, only Aedes mosquitoes are known to be the vector. The Aedes species that can transfer the virus includes Aedes apicocoargenteus, Aedes africanus, Aedes furcifer, Aedes luteocephalus, Aedes vitattus and Aedes aegypti [3]. Clinical symptoms in patients include fever, transient arthritis or arthralgia with possible joint swelling and maculo-papular rash, conjunctival hyperaemia (red sclerae) or bilateral non-purulent conjunctivitis with non-specific symptoms such as headaches, weakness, and muscle pain. These symptoms become visible after an incubation period that lasts between 3 to 12 days [1]. Indications are usually snsetive and infection may go unrecognized or be misdiagnosed as dengue, chikungunya or other arboviral and sticky disorders like malaria, and other hemorrhagic viral disease. There are reports of perinatal transmission, most probably transplacental or during delivery .Transfusion-derived transmission may occur as reported during the rush in French Polynesia, from November 2013 to February 2014 where 3% of blood donors found positive for zika virus by PCR [4]. A possible sexual transmission has been reported in 2011 .The presence of viable virus has also been reported in semen more than two weeks after recovery from an infection . The above-described modes of transmission are uncommon. Diagnosis of zika virus is primarily based on viral RNA detection from clinical specimens. Detection of the virus can only be done on the first 3 to 5 days after onset of clinical symptoms [5,6]. Specific assays have been created for both African and Asian Zika virus strains targeting the NS5 region or the envelope gene [5]. Currently, there is no vaccine to prevent Zika virus infection [7]. Travelers going to countries where cases of Zika virus infection have been reported are advised to use insect repellents and wear long-sleeved shirts and long pants. The study aimed to review the epidemiology of Zika virus infection and to describe the recent epidemics and reported travel-related infection.

Discovery of the Zika Virus

The Zika virus was first recognised in the Zika Forest ofUganda in 1947. It was located at the Virus Research Institute in a rhesus monkey that had been placed in an enclosure on a sentinel platformin the forest. The Zika Forest consisted then as nowof a small dense belt of lake shore (Lake Victoria) high canopy growth containing large clumps of trees that runs parallel to the road between Entebbe and Kampala [8]. At the time of the isolation of the Zika virus, the Virus Research Institute was maintained by the Rockefeller Foundation. The Institute was later re-named the East African Virus Research Institute and then the Uganda Virus Research Institute in 1977.

In 1960, a 120-foot-high steel tower was shifted from the Mpanga Forest to the Zika Forest to research the vertical Issues of mosquito species in the forest. This writer walked up to the diverse levels of this tower in 1961 while on a visit to the Zika Forest and the East African Virus Research Institute. Mosquito traps were strategically placed at diverse levels of the tower. This facilitated both the identification of mosquito species and isolation of arboviruses from them. The mosquito tower was located close to the Kampala-Entebbe road. On the other side of the road was the Kisubi Catholic Mission, then the largest of its kind in East Africa. The mission school was staffed by a teaching order of brothers, the Brothers of Christian Instruction, most of whom wereFrench Canadians. The mission also had across the road in the Zika Forest.

Epidemiology and current situation

Human cases of Zika virus has been reported since 1951. The first large outbreak occurred in Yap Island [Federated state of Micronesi, Northwest of Indonesia] in 2007 [2,9]. The second outbreak occurred in French Polynesia in 2014 [2,9]. Many African and Asian countries such as Uganda, Tanzania, Egypt, India, Malaysia, the Philippines, Thailand, Vietnam, and Indonesia have reported Zika virus infected cases . World Health Organization has reported presence of Zika virus in 40 countries from 2007 to February 2016. Out of these 40 countries, 33 have Zika virus transmission in the year 2015 .[10] The recent Zika outbreak is largest of its kind with 1.4 million cases in Brazil alone. Whereas the second leading number of 20000 cases are reported from Colombia and Cape Verde [10].

Clinical features

The symptoms and signs of patients who are affected by Zika virus are similar to dengue virus and other viral diseases. The patient presents with fever, body aches, joint pains, fatigue,malaise and conjunctivitis. Maculopapular rash can also occur with it like other viral illnesses [11]. Total duration of illness can lasts up to 5–7 days . Almost all cases reported yet have shown mild symptoms but some neurological and autoimmune complications are also reported in some patients. But these patients were having concomitant dengue virus infection. So whether Zika virus alone or dual infection by these viruses are responsible for these complications this needs further evaluation and studies . During Zika virus outbreaks many cases of Guillain-Barre (GB) syndrome are also reported [11]. Many viruses are thought to be playing their role as causative agents for GB syndrome but whether Zika virus is also causative agent or not, this needs further documentation [11].

Neurological complications

The degree of Guillain-Barre syndrome during the current Zika virus outbreak changed the medical denomination. It is deliberated that the Zika virus is occuring GB syndrome which is acute medical state leading the patient towards death because of respiratory muscles collaboration or can left the patient with life time residual inability[12]. The point to consider at this stage is the participation of many viruses as causative agents for GB syndrome but whether Zika virus alone or in conjunction with other viruses is causative agent or not, needs further verification. The most under controversy topic of Zika virus which has become alarming signal for the global health authorities is its proven organization with microcephaly . Mothers of infants with marked microcephaly have history of travelling to Zika virus infected areas during pregnancy. They receive this infection during their travel and then this virus gets dispatched to fetus and end in microcephaly.

This transmission is proven after separating virus from not only amniotic fluid of these mothers but also from cerebrospinal fluids of these babi [13] . But how it is causing microcephaly in newborn? One hypothesis has mentioned that Zika virus infects primary progenitor cells of neurological system and prevents their growth. In Brazil alone 4000 cases of microcephaly have been suspected due to Zika virus. In America, presence of Zika virus is confirmed by Centre of Disease Control in 9 pregnant females who visited virus infected areas during their pregnancy [14]. One of them gave birth to microcephalic child, two ended in miscarriages and two underwent medical termination of their pregnancy after finding microcephalic infants [15]. World Health Organization has released its statement in late February that the Zika virus is infecting infants and is causing notonly microcephaly but also a number of complications resulting in bad outcomes of pregnancy like placental insufficiency, early abortions, fetus mental and body growth retardation .This is the reason that CDC has developed guidelines to take care of pregnant females during Zika virus outbreaks.

Recently CDC has forbidden the pregnant females to travel to areas where Zika virus is largely reported particularly Brazil which is endemic for Zika virus [15]. Philippines ministry urged their females to delay their pregnancy so that chances of microcephaly can be minimized [17].Zika virus has proven transmission from mother to infants during pregnancy; there are also chances of Zika transmission to new borne infants from infected mother by lactation. This route of transmission is not studied yet and it is not under debate. We are purposing that the transmission through lactation should be considered, so that the Zika virus transmission to new born wil lbecome minimum.

Temporary Recommendations of the World Health Organization (WHO)

Following the direction of the Emergency Committee on Zika Virus and Observed multiplication in Neurological Disorders and Neonatal Malformations, the Director General of the World Health Organization (WHO) provied short-time Recommendations on 1 February 2016. These recommendations, while essentially focused on the clusters of microcephaly and other neurological diseases and their possible interconnection with Zika virus, also address measures to inhibit and control the epidemic [17]. Self-motivation will hopefully help in containing the spread of the virus .Following the short-time directions, WHO strongly recommended the use of contraception for women in Zika-infected areas. WHO also called for approch to emergency contraception for women who had contaminated sex and were concerned about contracting the Zika virus. Pope Francis later stated that contraception would be permissible to inhibit the spread of the Zika epidemic disorders. This was a remarkable declaration given that the Roman Catholic Church has in extensive opposed birth control [18].

NEUROLOGICAL SEQUELAE OF ZIKA VIRUS: MICROCEPHALY/GUILLAIN-BARRÉ SYNDROME

The public health significance of Zika virus lies in the expanding body of evidence linking it to microcephaly in neonates and Guillain-Barre syndrome in adults. In September 2015, researchers reported a substantial increase in the number of cases of neonatal microcephaly among women giving birth in northeastern Brazil [19] and subsequently an increase was also reported in southeast Brazil [19]. Zika virus has been isolated from the amniotic fluid of women who were pregnant with infants with confirmed microcephaly and from the brain of a fetus with abnormalities of the central nervous system [20]. Perhaps the strongest evidence to date linking Zika to microcephaly comes from a study by Brasil et al of the Fundacao Oswaldo Cruz who followed patients in Rio de Janeiro with regard to clinical manifestations of acute Zika virus infection in mothers and the consequences in fetuses. Pregnant women were enrolled in whom a rash indicative of possible Zika infection had developed within the preceding 5 days and specimens of blood and urine were taken and tested for the Zika virus by RT-PCR assays. The women were followed prospectively and clinical and ultrasonographic data collected. Eight-eight women were examined, and of these 72 (82%) tested positive

for the Zika virus in blood, urine or both. The timing of acute viral infection fell in ma range from 5-38 weeks of gestation. Forty-two Zika-positive women (58%) and all Zikanegative women were examined using fetal ultrasonography. Twelve of the 42 Zika-positive women (29%) and none of the 16 Zika virus-negative women had fetal abnormalities that were detectable by Doppler ultrasonography. Adverse findings included 2 fetal deaths occurring at 36 and 38 weeks of gestation, 5 fetuses showed in utero growth restriction occurring with or without microcephaly, 7 fetuses had ventricular calcifications or other lesions of the central nervous system and 7 fetuses had an abnormal amniotic fluid volume or cerebral or umbilical artery flow. Cordeiro et al collected blood and cerebrospinal fluid (CSF) samples from 31 neonates with microcephaly in the state of Pernambuco, Brazil. Zika-specific IgM was detected in 30 (97%) of 31 CSF samples and in 28 (90%) of 31 serum samples. It performed prenatal brain MRI of fetuses with Zika virus infection and observed severe cerebral damage with indirect findings that suggested the germinal matrix is the principal target for Zika virus with lesions resembling to severe forms of congenital cytomegalovirus and lymphocytic choriomeningitis virus infections. In another study, Cavalheiro et al [21] observed decreased brain parenchymal volume associated with lissencephaly, ventriculomegaly secondary to lack of brain tissue and calcifications while de Fatima Vasco Aragao et al reported severe cerebral damage with brain calcifications in the junction between cortical and subcortical white matter and malformations of cortical development, Brasil et al [22] concluded that Zika virus infection during pregnancy is associated with several kinds of serious outcomes, including fetal death, fetal growth restriction, placental insufficiency and injury to the fetal central nervous system. In another study, Cauchemez et al [23] reported a lower incidence of microcephaly of about 1% and suggested that the biggest risk is in the first trimester based on the outbreak in French Polynesia, 2013–15.

In April 2016, the Centers for Disease Control and Prevention concluded that a causal relationship exists between prenatal Zika virus infection and microcephaly and other serious brain anomalies. Zika virus infection has also been linked to the development of Guillain-Barre syndrome in adults. Guillain-Barre syndrome is a rapid-onset muscle weakness caused by the immune system damaging the peripheral nervous system. Coincident with the largest Zika virus outbreak ever described at that time, 42 patients presented at a hospital in French Polynesia with Guillain-Barre syndrome between November, 2013 and February, 2014, compared to reports of five, ten, three, and three, in 2009, 2010, 2011, and 2012, respectively .

In a case-control study by Cao-Lormeau [24], patients with Guillain-Barre syndrome diagnosed at the Centre Hospitalier de Polynesie Francaise (Papeete, Tahiti, French Polynesia) during the outbreak period were compared to controls who were age-matched, sex-matched, and residence-matched patients who presented at the hospital with a non-febrile illness. In this study, virological investigations included RT-PCR for Zika virus and both microsphere immunofluorescent and seroneutralisation assays for Zika and dengue viruses. Forty-two patients were diagnosed with Guillain-Barre syndrome during the study period and 41 (98%) patients with Guillain-Barre syndrome had anti-Zika virus IgM or IgG, and all (100%) had neutralising antibodies against Zika virus compared with 54 (56%) of 98 in control group 1 ($p<0.0001$). 39 (93%) patients with Guillain-Barre syndrome had Zika virus IgM and 37 (88%) had experienced a transient illness in a median of 6 days (IQR 4–10) before the onset of neurological symptoms, suggesting recent Zika virus infection. Patients with Guillain-Barre syndrome had electrophysiological findings compatible with acute motor axonal neuropathy and showed a rapid evolution of disease. Twelve (29%) patients required respiratory assistance. No patients died. This study by Cao-Lormeau [25] was the first study to provide evidence for Zika virus infection causing Guillain-Barre syndrome. Fontes et al [26] reported magnetic resonance imaging findings in Guillain-Barre syndrome caused by Zika virus infection. The features described were attributed to demyelination, ischemia, inflammation and breakdown of the bloodbrain barrier, as occurs in autoimmune polyneuropathy. Recently, Paploski et al [27] investigated temporal correlations and time lags between outbreaks of acute exanthematous illness (AEI) attributed to Zika virus, Guillain-Barre syndrome and microcephaly occurred in 2015 in Salvador, Brazil. Number of Guillain-Barre syndrome cases peaked after a lag of 5-9 weeks from the AEI peak while the number of cases of microcephaly peaked after a lag of 30-33 weeks from the AEI peak. This corresponds to a time of potential infection during the first trimester and these findings support association of Guillain-Barre syndrome and microcephaly with Zika virus infection. As well as Guillain-Barre syndrome, Zika virus has also been detected in cerebrospinal fluid from patients with encephalopathy and meningoencephalitis.

The suspected link between Zika virus infection and microcephaly and Guillain-Barre syndrome is an urgent global health concern and has prompted new laboratory research into the neurotropic and neuropathic potential of the Zika virus. It has been

known since the 1950s that Zika virus will grow in mouse brain when injected intracranially. Bell et al [28] infected newborn mice with Zika virus injected intracranially and observed necrosis in hippocampal neurons, inflammation and active replication of virus. Of particular note were the remarkably prominent enlarged astrocytes with extended processes and containing cytoplasmic virus factories throughout the cortex of the infected mouse brains. Interestingly, astrocyte pathology is also observed in post-mortem analysis of neonatal brain from Zika virus-associated microcephaly where diffuse astrogliosis was present with focal astrocytic outburst into the subarachnoid space. It was also reported that Zika virus can cause disease and mortality in mice lacking the interferon (IFN) alpha receptor, which might a potential model system to test antivirals and vaccines [29]. Recently, Lazear et al described a mouse model for Zika virus infection in which mice lack interferon signaling and develop neurological disease succumbing to infection with high viral loads in the CNS, spinal cord and testes, consistent with severe Zika disease in humans. Similarly, Dowall et al the effect of Zika virus infection in type-I interferon receptor deficient mice using subcutaneous challenge in the lower leg to mimica mosquito bite and severe symptoms with striking histological changes and widespread Zika viral RNA detection in the blood, brain, spleen, liver and ovaries of these animals. Recently, Tang et al [30] reported that Zika virus directly infects human cortical neural progenitor cells with a high efficiency resulting in stunted cell growth and transcriptional dysregulation. Zika virus was found to efficiently infect neural progenitor cells derived from induced pluripotent stem cells and release infectious progeny Zika virus.

Zika virus infection increased cell death, dysregulated cell-cycle progression and attenuated growth [30]. Analysis of global gene expression revealed transcriptional dysregulation especially of genes related to of cell-cycle pathways [30]. These data identify neural progenitor cells as a direct Zika virus target and importantly establish cultures of these cells to be a tractable experimental model system to investigate the impact and mechanism of Zika virus on human brain development.

Cultured neural progenitor cells also constitute a potential platform to screen therapeutic compounds against Zika virus. Another recently developed alternative is to use human neurospheres and brain organoids, which support Zika virus infection and show reduced viability
and growth resembling microcephaly [31,32].

DESCRIPTION OF THE PATHOGEN

ZIKV, is a single-stranded RNA virus found within the Flaviviridae family and Flavivirus genus.10 Within this same genus and family, Zika virus is related to yellow fever, dengue, West Nile, and Japanese encephalitis virus. The ZIKV is divided into 2 genetic lineages, an African lineage and an Asian lineage. These lineages are historically linked with the geography for which they are named. As for the virus that is spreading within the Western Hemisphere, recent genetic series and comparisons of viruses collected from autochthonous cases in Suriname in November 2015 were described genetically similar to the Asian lineage viruses. The virus is receptive to and eliminated by potassium permanganate, ether, and temperatures above 60°C. Use of 10% ethanol is reported to be fruitless to kill or inactivate the virus.

PATHOGENESIS

Little is known about the pathology of the ZIKV. A 2015 study showed that ZIKV is introduced by the mosquito vector in the skin and skin immune cells, including dermal fibroblasts, epidermal keratinocytes, and immature dendritic cells. The virus clones, leading to activation of an antiviral innate immune response and type I interferons in the cells. Viral replication occurs in cellular cytoplasm or in the infected cell nuclei. It is theorized that the virus reaches in the bloodstream to the lymph nodes. A recent study described that ZIKV directly spread disease to human cortical neural progenitor cells, resulting in stunted growth and cell death, which recommends that ZIKV may stimulate human brain development. An additional report detected ZIKV in brain tissues of infants with microcephaly and in placental tissues from early miscarriages. Detection of ZIKV in the blood has been transported to occur as early as infection onset and to continue up to 11 days after onset. The virus has been found in blood, urine, semen, amniotic fluid, breast milk, and cerebrospinal fluid.

ZIKV Genomic Evolution and Pathogenesis

Owing to the motility of sequencing technology, various ZIKV segregates from this prevalence are already reported and are attainable for analysis and differentiation with past sequester. A current analysis of the molecular evolution of ZIKV segregates throughout the elevation of the virus in the 20th century stated various insights. Based on phylogenetic analysis, ZIKV likely first flourished in Uganda almost1920 followed by 2 independent ZIKV induction into West and Central Africa from the eastern part of the continent and then a third induction event into Malaysia around 1945. During its emergence, ZIKV undergo 13 recombination events, which is an unnatural characteristic for a flavivirus

since these viruses are often genetically confined by the need to replicate in evolutionarily different invertebrate (mosquitoes) and vertebrate hosts.

The unusual evolutionary plasticity of the ZIKV genome is likely due in part to vertebrate host preferences for the virus, which may contribute to ZIKV genomic adaptation to specific vector–vertebrate host environments. This likely resulted in an increased frequency of ZIKV activity every 1 to 2 years when compared with other arbo viruses, which exhibit an activity frequency of 5 to 8 years for dengue virus and yellow fever virus. The unique genomic features of ZIKV likely contributed to the rapid emergence of the virus over a very large geographic area. Very little is currently known about the biology and pathogenesis of ZIKV. The envelope protein for flaviviruses is largely responsible for host range due to receptor binding and immune responses. The ZIKV envelope gene underwent several selective changes mainly associated with negative selection, implying an important role for this gene in vertebrate host selectivity and emergence. Acute ZIKV infection in 6 human cases was characterized by robust, acute polyclonal T-cell activation and acute increases inseruminter leukin (IL) responses (IL-1β, IL-2, IL-4, IL-6, IL-9, IL-13, and IL-17). Also, acute infection in these patients was associated with increases in RANTES (regulated on activation, normal T cell expressed and secreted), macrophage inflammatory protein 1α, and vascular endothelial growth factor. These data provide some initial information to characterize the acute
inflammatory response in these patients.

Cell culture and mouse models of ZIKV are not well established at this stage. Recent data have shown that human dermal fibroblasts, epidermal keratinocytes, human neurospheres, and immature dendritic cells are permissive to recent ZIKV isolates and that several entry or adhesion factors (DC-SIGN, AXL, Tyro3, and TIM-1) permitted ZIKV entry, implying that the virus can use a range of host receptors to gain entry into different cell types. During acute infection in cell culture, ZIKV induced transcription of Toll-like receptor 3 (TLR3), retinoic acid-inducible gene 1 (RIG-I), and melanoma differentiation-associated protein 5(MDA5) as well as several common interferon-stimulated genes, implying that the innate immune response found to be important for control of other flaviviruses also plays an important role in the detection and control of ZIKV. Zika viruswas also sensitivetotypeIandII interferons in these cell culture systems. These data are consistent with what is known about other flaviviruses and help to characterize the role of the immuneresponse for this virus.Abetter understanding of the mechanisms of immune control of ZIKV will enable targeted vaccination or therapeutic treatments in the future.

A recent mouse model of ZIKV brain infection was developed in interferon signaling–deficient mice.Work with classic ZIKV isolates in suckling mice revealed neurotropism and 100% mortality by day 10 following intracerebral injection.These studies revealed neuronal injury especially in the hippocampus characterized by astrocyte activation and new virions on ultrastructural examination in networks of the endoplasmic reticulum of neurons. Adult mice in these studies seemed to be more resistant to peripheral infection with ZIKV but did develop neurologic disease following intracerebral infection. Further development of animal models for modern ZIKV isolates is needed to understand the complex pathogenesis and immune responses required to prevent disease.

Symptoms

Actually, the principal clinical symptoms of zika virus infection consist of low-grade fever (< 38 °C), maculo-papular rash, arthralgia , conjunctival hyperaemia as well as general symptoms such as asthenia and headaches. [33]. zika virus infection symptoms are generally mild and can be misdiagnosed as dengue,chikungunya and many arboviral infections which cause fever and rash.

Furthermore, numerous studies have strongly suggested that there is an association between zika virus infection and neurological complications like Guillain – Barré syndrome. However, this finding still under investigations [34].

DIAGNOSIS

Diagnosis is performe by testing the blood, urine, or saliva for the presence of Zika virus RNA when the person is infacted[35] .It can be identified by reverse transcriptase polymerasechain reaction (RT‑PCR) in acutely sick patients. However, the span of viremia can be reduced. The World Health Organization consults that RT‑PCR testing should be done on the collected serum within 1–3 days of syndrome onset or on saliva or urine samples poised during the first 3–5 days. Zika virus was indentified more repeated in saliva than serum when appreciating paired samples.

The longest period of detectable virus has been 11 days and Zika virus does not appear to establish evanescence .besides, serology for the identification of specific IgM and IgG antibodies to Zika virus can be used. IgM antibodies can be detectable within 3 days of the onset of sickness [36]. Serological cross‑reactions with closely related

flaviviruses such as dengue and West Nile virus as well as vaccines to flaviviruses are possible.

Screening during pregnancy

The Centers for Disease Control and Prevention (CDC) consults screening of pregnant women even if they do not have indications of affliction. Pregnant women who have traveled to infected areas should be turned between 2 and 12 weeks after their return from journey. For women living in infected places, the CDC has consulted testing at the first prenatal call with a doctor as well as in the mid‑second trimester, though this may be regulate based on local staffs and the local burden of Zika virus. Another testing should be done if there are any symptoms of Zika virus disease. Women with positive test outcome for Zika virus contamination should have their fetus observed by ultrasound for every 3–4 weeks to monitor fetal anatomy and growth[40].

Infant testing

For infants with suspected inherent Zika virus disorder, the CDC consult testing with both serologic and molecular test such as RT‑PCR, IgM ELISA, and plaquereduction neutralization test. Newborns with a mother who was potentially unprotected who had positive blood assay, microcephaly, or intracranial calcifications should be develop including a detail edphysical inquisition for Neurologic abnormity, dysmorphic features, splenomegaly, hepatomegaly, and rash or other skin lesions. Moreover, the consulted tests are cranial ultrasound, hearing evaluation, and eye examination. Analyzing should be done for any malformations encountered as well as for other Inherent infection such as syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic chorio meningitis virus infection, and herpes simplex virus.

Testing Pregnant Women

For asymptomatic pregnant women, testing can be offered 2 to 12 weeks for protection from Zika virus infection. For asymptomatic pregnant women who live in areas of ongoing disease transmission, IgM testing is recommended at the beginning of prenatal care with follow-up testing mid-second trimester. For symptomatic pregnant women, testing is recommended during the first week of illness. ZIKV testing of maternal serum includes RT-PCR and IgM and plaque reduction neutralizing antibody testing on specimens collected at 4 or more days after onset of symptoms.

Pregnant Women and Birth defects

The fetus can be infected in womb from the pregnant mother and recently after careful review of the documentary evidence the scientists at CDC decided that Zika virus causes Microcephaly a condition in which the size of baby's brain and head is smaller than the normally expected. In addition to that there may be other critical brain defects in the new born baby. This indicates that the Zika can be transmit during pregnancy has an increased risk of having baby with some problems and not all women who have Zika virus infection during pregnancy will have babies with problems since some infected women have delivered babies that appear to be healthy.

Zika virus infection in Southeast Asia

Southeast Asia is a tropical territory where many tropical diseases are endemic. Focusing on arboviral diseases, dengue and chikungunya fever are seen in this area. Abundance of mosquito vector (Aedes species) is responsible for infection in this area. Of interest, the same vector is also able to transmit Zika virus and might be the new big problem in this area. Southeast Asian countries might be the next target of Zika virus transmission. The data on the present situation of disease in this area can be useful for global monitoring of the disease. Here, the author will summarize the situation in each Southeast Asian country.

Transmission routes:

Mosquito-borne route

Zika virus is a mosquito-borne virus. It completes its zoonotic cycle between mosquitoes and nonhuman primates. The first identified route of transmission of Zika virus was mosquito belonged to *Aedes aegypti* specie. Later on presence of Zika virus was confirmed by PCR in ten species of genus Aedes, Mansonia uniformis, Anopheles coustani, and Culex perfuscus [41]. After entering the body of human, Zika virus replicates in dendritic cells and then spreads in the body through lymphatic channels and blood. Recently it is reported that the Zika virus is not only transmitted by blood but also by other body fluids. Sexual transmission of this disease came under discussion when one person during outbreak in French Polynesia came to seek medical advice after noticing blood in semen. Zika virus was isolated from his semen raising the possibility of sexual transmission of this infection. Recently, France has confirmed first case of sexually transmitted Zika virus in a lady who has acquired the infection from her partner who recently visited Brazil. CDC is recently investigating 14 possible sexually acquired Zika virus cases.

Animal bites

Transmission of Zika virus through animal's saliva during bite is also possible. This route of

transmission came under discussion when Zika virus was isolated from person's blood after monkey bite.

Rarer routes of transmission

Mosquito bites, sexual intercourse and animal bites are documented routes of Zika virus transmission .There is dire need to evaluate the other possible route of Zika transmission like blood transfusion, lactation and contact with body fluids so that the spread of this virus through these invisible routes can be minimized.

Transmission

Zika virus is transmitted by Aedes mosquitoes, including several species such as Aedes.hensilli, Aedes.africanus, Aedes. Luteocephalus and Aedes [42]. Aegypti zika virus was first isolated from Ae. Africanus, these mosquitoes were the most abundant and widely distributed in Africa as reported by many scientists. Numerous researches have showed that Aedes. Aegyptiin as principal vector responsible for zika virus transmission outside Africa [43]. Recently, Wong and co-workers have performed an experiment in based on the fact that Ae. Albopictus was able to transmit more than 20 arboviruses. Therefore, scientists have orally infected mosquito with Zika virus. After few days later, Wong and co-workers have ascertained the transmissibility of zika virus using qRT-PCR.As the result about 73% of mosquitoes infected contain Zika virus in their saliva. The Aedes spp. mosquitoes have been pointed out as having the ability to transmit the virus for up to 60 days. For the Western Hemisphere, Aedes aegypti and Aedes albopictus are common vectors. Within these mosquitoes, from the time a blood meal is taken, the incubation period until a mosquito is infective is from 5 to 10 days. There is evidence of perinatal and in utero transmission reported from earlier outbreaks, and the suspected connection of microcephaly as well as the identification of ZIKV in amniotic fluid suggests transformation between mother and fetus. A recent report established infective ZIKV particles in breast milk from a mother postpartum as a possible source of transmission, although her baby remained healthy. To date, 3 reports have proposed that ZIKV transmission by sexual contact is possible. In one case, a male working in Senegal returned to the United States and became ill 6 days after return. His spouse also became ill 4 days after he had become ill. Both had had sexual contact prior to any clinical symptoms developing. In another statement , ZIKV was isolated from semen. In further case a patient had sexual contact with a returning male traveler. Reports commend that ZIKV may be detectable in semen from 2 to 10 weeks after infection onset. Sexual transformation from infected women to sex partners is unknown and not recorded. Through blood transfusion appears plausible and recent investigations and documentations are ongoing to reported.

ZIKV transmission via transfusion process. On 7 February 2016, the Brazilian Ministry of Health reported 2 possible ZIKV cases of blood transfusion transmission from 2015. Transfusion risk due to ZIKV is unclear. During the French Polynesian outbreak, 2.8% of blood donors tested positive for Zika RNA, which suggests that transfusion transmission is possible. As of1 February 2016, the American Association of Blood Banks released recommendations to reduce the risk of transfusion transmission. By recommendation of the American Association of Blood Banks , blood donors who have traveled to Mexico, the Caribbean, or Central or South America during the 28 days before donation should not donate. Presently, there are no legal blood donor screening tests in the United States to identify Zika RNA.

Prevention

There is no specific treatment available for Zika virus, the best strategy is to block viral transmission [44]. The common ways of protection include protecting oneself from mosquito bites by using mosquito repellents, mosquito nets, cooling rooms by using air conditions, covering body with full sleeves and pants and using permethrin-treated clothes [45]. Vector can be controlled by preventing water pooling and spraying on larval breeding places. The emergence of permethrin resistant strains has urged the need of other alternative routes of controlling vectors. The virus is mainly spread by mosquitoes, so avoidance and control of mosquitoes are important elements for Zika virus disease prevention.

Measures for mosquito avoidance

- Cover exposed skin by wearing long‑sleeved shirts and long pants
- Use an insect repellent
- Stay and sleep in screened‑in or air‑conditioned rooms
- Use a bed net if the area where you are sleeping is exposed to the outdoors.

Measures for mosquito control

- Control mosquitoes such as eliminating standing water where
they replicate
- Repairing septic tanks
- Using screens on doors and windows
- Spraying insecticide which is used to kill flying mosquitoes and larvicide can be used in water containers.

Measures to control the spread of sexual transmission

Sexual transmission of Zika virus is possible. All people who have been infected with Zika virus and their sexual partners should practice safer sex by following the measures mentioned below:

● Use condoms correctly and consistently

● Pregnant women's sex partners living in or returning from areas where local transmission of Zika virus occurs shoul practice safer sex, wear condoms, or abstain throughout the pregnancy

● People living in areas where local transmission of Zika virus occurs should practice safer sex or abstain from sexual activity

● People returning from areas where local transmission of Zika virus occurs should adopt safer sexual practices or consider abstinence for at least 4 weeks after their return to reduce the risk of onward transmission.[16-19]

Furthermore, an integrated prevention and vector control approach combined with timely detection of illness, communication of current and correct information, and development of a rapid response that involves the community is recommended.

Prevention and Control

Surveillance:

All possible measures should be undertaken to reduce exposure to virus and prevent transmission in a health care setting [48]. For planning more effective disease control and prevention activities for Zika fever there is great need for a functional and intensified Public Health Surveillance system that can be based on the same system for Dengue and Chikungunya fever. As per the recommendations of PAHO/WHO (Epidemiological Alert, PAHO/WHO 7 May 2015), the surveillance for Zika fever should be focused to

i. Determine if the virus is autochthonous or has been introduced to an area

ii. Monitor the Zika virus in case if its introduced and

iii. Monitor the disease process once it has been established.

iv. Monitor for neurological and autoimmune complications

Considering the broad distribution of Aedes mosquito in the Americas and the high mobility of people in and outside of this region in this globalized world it poses a great risk for the spread of Zika virus with in the Americas.

The recommendations for the public health authorities in countries without autochthonous transmission of Zika virus:

1. Test for Zika virus from patients presenting with fever and arthralgia or fever and arthritis with no known etiology where malaria, dengue and chikungunya are ruled out.
2. Health authorities but be on high alert for the clusters of rash febrile syndrome of unknown etiology where dengue, chikungunya, measles, rubella and parvovirus B 19 have been ruled out
3. Early detection will help to identify the viral strains in circulation and also enhances proper response of the outbreak.

In countries with autochthonous transmission of Zika virus, they are recommended:

1. To monitor the trend and geographical spread of virus to track the introduction to new areas.
2. To monitor the impact on public health and assess the clinical severity
3. To monitor potential neurological and autoimmune complications
4. To identify the risk factors those are associated with the Zika virus infection and if possible identify the virus lineages. The preventive measures are described below:

Blood transfusions may potentially contribute to the spread of the disease as reported earlier in French Polynesia. The health authorities must ensure proper screening of blood from the donors to stop the chain of transmission. Many cases of sexual transmission of Zika virus are documented in different countries and as per latest updates, Canada has reported its first case transmitted due to sexual contact recently. If the threat of sexual transmission becomes substantial then contact tracing should be considered as done for other sexually transmitted infections.

Strategy Actions:

Reduction of Mosquito density

1. Strengthen environmental management
2. Ensure no vector breeding sites in common areas like parks, schools etc. to prevent vector propagation
3. Organize mass sanitation campaigns to sensitize the public about cleanliness
4. By applying risk stratification, identify the places like schools, hospitals, transport terminals and ensure mosquitoes are removed with a radius of 400 m around these places.
5. In areas with virus, use adulticide treatment by spraying to interrupt transmission
6. Ensure proper monitoring during integrated actions for vector control (larval control and adulticide treatment)

Interruption of human vector contact / Personal prevention measures

Individual Protection

1. Rest under bed nets treated with or without insecticides
2. Appropriate clothing to cover the extremities and exposed areas of skin
3. Use repellents containing DEET, IR3535, Icaridin can be applied to exposed skin or clothing as per the instructions on the product label

Household Protection

1. Use wire-mesh screens on doors and windows
2. At least once a week, empty, clean, turn over or dispose the containers that can hold water such as buckets, flower pots, tires inside and outside of dwellings to eliminate the mosquito breeding sites.

Treatment

Zika virus disease is usually relatively mild and requires no specific treatment. People affected by Zika virus should get plenty of rest, drink enough fluids, and treat pain and fever with common medicines. If symptoms get worsen, they should seek medical care and advice. There is currently no vaccine available.

Vaccine Platforms:

The platforms being employed by Zika virus vaccine developers are quite varied (Table 1). A situation in which use of, or exposure to, a violate product is not likely to cause adverse health Consequences [48]. Most are based on other Flavivirus candidate vaccines and include live attenuated virus vaccines, whole inactivated virus vaccines, and subunit protein vaccines. Newer strategies such as DNA vaccines and as viral-vectored vaccines are also under development. Two Zika virus vaccines have recently demonstrated protection in preclinical mouse studies. A DNA vaccine encoding the full-length prM and E proteins (prM-E) of the Brazil BeH815744 Zika virus strain was developed by researchers at the Harvard Medical School, the Massachusetts Institute of Technology, the University of Sao Paulo, and the Walter Reed Institute of Research. This vaccine was evaluated in Balb/c mice.36 Mice inoculated intramuscularly (IM) with 50 μg of the DNA vaccine elicited higher anti-E antibody titers than did the same vaccine administered subcutaneously (SQ) or than DNA vaccines that did not encode the prM protein. A single dose of the prM-E DNA vaccine induced complete protection in Balb/c mice against challenge with 105 virus particles of either one of two wild-type Zika viruses of Asian lineage given at 4 or 8 weeks post vaccination. DNA vaccine constructs that did not include prM or full-length E did not elicit complete protection against challenge. IgG purified from vaccinated Balb/c and then infused intravenously was also able to protect recipient mice from challenge when the titer of anti-E antibody was _ 2.35 log10. Mice vaccine with the prM-E DNAvaccine and then depleted of CD4þ and CD8þ T cells on day 2 and day 1 prior to challenge were also protected. These studies demonstrated that protection against wild type Zika virus challenge can be mediated by antibody alone and that protection was correlated with the magnitude of the antibody response. These same investigators also evaluated the immunogenicity and protective efficacy of PIV derived from the Puerto Rico PRVAB59 strain of Zika virus. A 1 μg dose of PIV adjuvanted with alum was delivered either IM or SQ to Balb/c mice (five mice per group). Higher antibody titers were elicited when the vaccine was given by the IM route and all mice in this group were completely protected against challenge with wild-type Zika virus. Two of five mice that received the vaccine SQ had detectable levels of viremia following challenge, although viremia was of lower titer than in the control group. These results are encouraging and warrant further evaluation of these candidates in humans and to this end, Sanofi Pasteur is partnering with WRAIR for further development and evaluation of the PIV Zika virus vaccine. The U.S. National Institutes of Health (NIH) is developing two Zika virus vaccines. The Laboratory of Infectious Diseases (LID) of the NIH is developing a live-attenuated chimeric Zika virus vaccine based on one of the components of its live attenuated tetravalent dengue vaccine currently in Phase 3 clinical trial in Brazil.37,38 The candidate Zika virus vaccine virus is comprised the prM and E proteins of Zika virus and the nonstructural proteins of the DENV-2. It is expected to begin Phase 1 clinical evaluation in Flavivirus-naïve subjects in the fourth quarter of 2016. Should the vaccine prove to be immunogenic in Phase 1 clinical evaluation, the LID hopes to achieve an early efficacy evaluation of the vaccine using a Zika virus human challenge model that is currently under development. Ultimately, the LID hopes to combine this Zika virus vaccine with their live attenuated tetravalent virus (LATV) dengue vaccine to create a pentavalent vaccine that would be administered to children in endemic areas. They are partnering with the Instituto Butantan which has licensed the LATV dengue vaccine and is currently conducting the Phase 3 trial of the dengue vaccine. The Vaccine Research Center of the NIH is developing a DNA Zika virus vaccine based on the technology it used for a highly immunogenic West Nile virus vaccine. This vaccine is expected to begin human clinical trials in late Q3 or early Q4 2016. Inovio Pharmaceuticals (Pennsylvania), in collaboration with the University of Pennsylvania, the Wistar Institute of Philadelphia, and GeneOne Life Science of South Korea is developing a DNA vaccine for Zika virus, GLS-5700.40 The

vaccine elicited an immune response against Zika virus in rabbits and monkeys and the manufacturer has submitted an investigational new drug application to the U.S. FDA. It will begin a Phase 1 clinical trial in approximately 40 volunteers in the United States and Canada in Q3 2016 with safety and immunogenicity results expected by the end of the year. The vaccine is given intradermally followed by electroporation and will evaluate the safety, tolerability, and immunogenicity of the vaccine in dengue-naïve subjects. GLS-5700 is the first Zika virus vaccine to receive approval from the FDA to begin Phase 1 clinical evaluation and is registered on Clinicaltrials. gov (NCT02809443). Should these and other candidate vaccines demonstrate an acceptable safety and immunogenicity profile in denguenaïve subjects, they would then be further tested in endemic areas to evaluate the effect of preexisting dengue (or other Flavivirus) immunity on the safety and immunogenicity of the candidate vaccine. More novel vaccine platforms such as DNA vaccines would need to be more carefully evaluated for use in pregnant women if the licensure of the vaccinewere to include this population.

A DNA vaccine has yet to be licensed for use in people, pregnant or otherwise and as such, would have to overcome this regulatory hurdle.

Patient isolation:

A Zika virus infected person should avoid being bitten by Aedes mosquitoes during the first week of illness. It is advised to stay under the bed-net and the treating health care workers should also protect from mosquito bites by appropriate measures. Pregnant women living or traveling to areas of Zika virus transmission: It is recommended to avoid the travel to these regions and if they travel they should avoid the mosquito bites by using bed-nets, appropriate dressing and pregnant women traveling to those areas should follow the same advice as all travelers

Challenging situation

Zika virus has posed a great challenging situation not only for health and public sectors but also for economic sectors of different countries. The breakout has not only increase the expenditure on health system but has also shaken the economy by reducing travelling and tourism to Zika affected countries [15]. Brazil is going to host the Olympics 2016. Large number of participants, tourists, travellers and residents fromall over theworld will attend the event [16]. Will such mega gathering not aid in further transmission of this disease to other countrieswhen Brazil is already considered endemic for Zika? If Olympics will fail to gather mass crowding, what will be its impact on Brazil who is already facing a great economical loss due to its expenditure on health systems and reduction in tourism and travelling?

Travellers:

The health authorities should alert the citizens heading to any country with documented spread and circulation of virus and advise them regarding the protective measures.

Travel-related zika

A 27-year-old Belgian tourist coming from Tahiti was diagnosed with Zika virus infection after traveling to Easter Island, where the presence of the disease was detected [46]. In 2013, a German traveler acquired Zika virus infection in Thailand (including visits to Phuket, Krabi, Ko Jum, and Ko Lanta). This was the 1st laboratory confirmed case of zika virus reported in Germany. In September 2014, a 45-yearold woman was seen in an outpatient clinic in Heidelberg, Germany for fever and maculopapular rash covering her trunk, arms,and legs. She was diagnosed with zika virus and had returned from a vacation to peninsular Malaysia and Sabah, Malaysian Borneo [47]. In December 2013, a previously healthy 31-year-old woman from Norway was admitted to the Oslo University Hospital, Norway and diagnosed with Zika virus infection after returning from a vacation to Tahiti, where she mainly stayed in the capital, Pape'ete. The first two cases of laboratory confirmed zika virus infection was imported to Italy from French Polynesia. Both patients presented with fever, conjunctivitis, myalgia, malaise, ankle edema, arthralgia, and axillary and inguinal lymphadenopathy. One patient presented with leukopenia with relative monocytosis and thrombocytopenia. The diagnosis was based on ZIKV seroconversion for both cases and RNA detection in one patient from acute serum sample. In Canada, a woman who traveled to Thailand came to a local emergency department with a low grade fever and popular rash. This is the first documentation of zika virus in Canada.

In December, 2013, a Japanese man in his mid-20s presented with fever, headache, and arthralgia and one day of rash after visiting Bora Bora in French Polynesia. In January 2014, a previously healthy Japanese woman in her early 30s presented with retro-orbital pain, slight fever (self-reported), rash, and itches. She had travelled to Bora Bora mid-December 2013 for sightseeing. In Australia, in 2013, a traveler with fever and rash acquired Zika virus infection in Indonesia and in 2014, another traveler acquired Zika virus infection in the Cook Islands. This is the first known imported case of Zika virus infection into northern Queensland and the second reported case diagnosed within Australia.

Development of virus resistant mosquito strains

Development of virus resistant mosquito strains by using genetic engineering techniques is also under consideration. One method involves the growing of male mosquitoes in control environment with diet containing tetracycline and then these male will mate with wild females resulting in off springs who are not surviving in their adulthood [14]. The other method is the use of endosymbiotic bacteria introduced in vectors and these vectors will prevent the replication of viruses in their bodies.

FUTURE PERSPECTIVES

The current outbreak of Zika virus disease is difficult to gauge because the symptoms are nonspecific and usually mild, laboratory diagnosis is not uniformly available, and cross‐reactivity of flavivirus antibody complicates serologic assessment in areas in which dengue is endemic. There is a need to rapidly and systematically address the identified research gaps for controlling the disease. Future perspectives include a complete understanding of the frequency and full spectrum of clinical outcomes resulting from fetal Zika virus disease, the environmental factors that influence emergence, the development of discriminating diagnostic tools for flaviviruses, developing animal models for fetal developmental effects due to viral infection, new vector control products and strategies, effective therapeutics, and vaccines to protect humans against the disease.

DISCUSSION AND CONCLUSION

Zika virus disease is a vector borne disease transmitted by several Aedes species. Zika virus infection was transmitted outside Africa by Aedes Aegypti mosqueto as reported by many scientists. in fact, Aedes Aegypti is the main vector of many others tropical disease such as yellow fever and dengue virus. Moreover,this mosquito has become the major indirect cause of morbidity and mortality of human in worldwide.The presence of Aedes Aegypti have been reported in western areas of Saudi Arabia; Jeddah, Makkahand Al-Madinah [23, 24]. These findings make Saudi Arabia a potential risk infection area. Furthermore, AL ALIand co-workes have found that increased gene flow among Aedes aegypti populations occurs between Africaand Saudi Arabia. (unpublished data).

Moreover, Commercial exchange and foreign pilgrims from Zika virusendemic regions, may play critical role in disease transmission. Until now, there is no vaccine or treatment available to treat patient with Zika virus infection. However, The National Institute of Allergy and Infectious Diseases (NIAID) are currently working on a DNA based vaccine to prevent ZIKAV infection. Furthermore, the control of the disease depends on control of the vector, thus, further phylogenetic studies are required to gain more insight into the geographical distribution of Zika virus disease.

Figure 1. Structure of zika virus

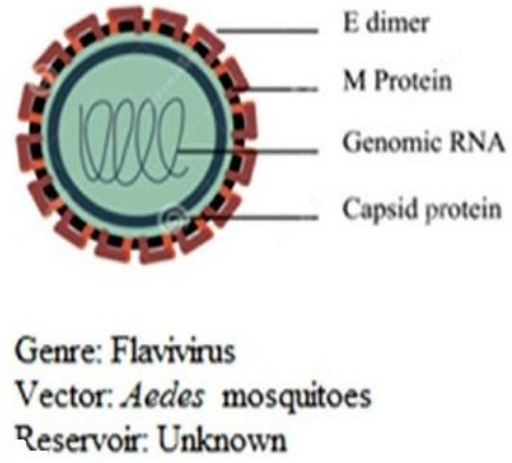

Figure 2. Clinical features of zika viruse

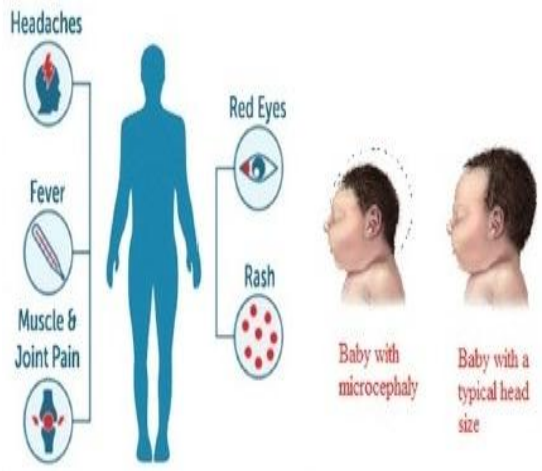

Figure 3. Testing Pregnant Women of Zika Virus

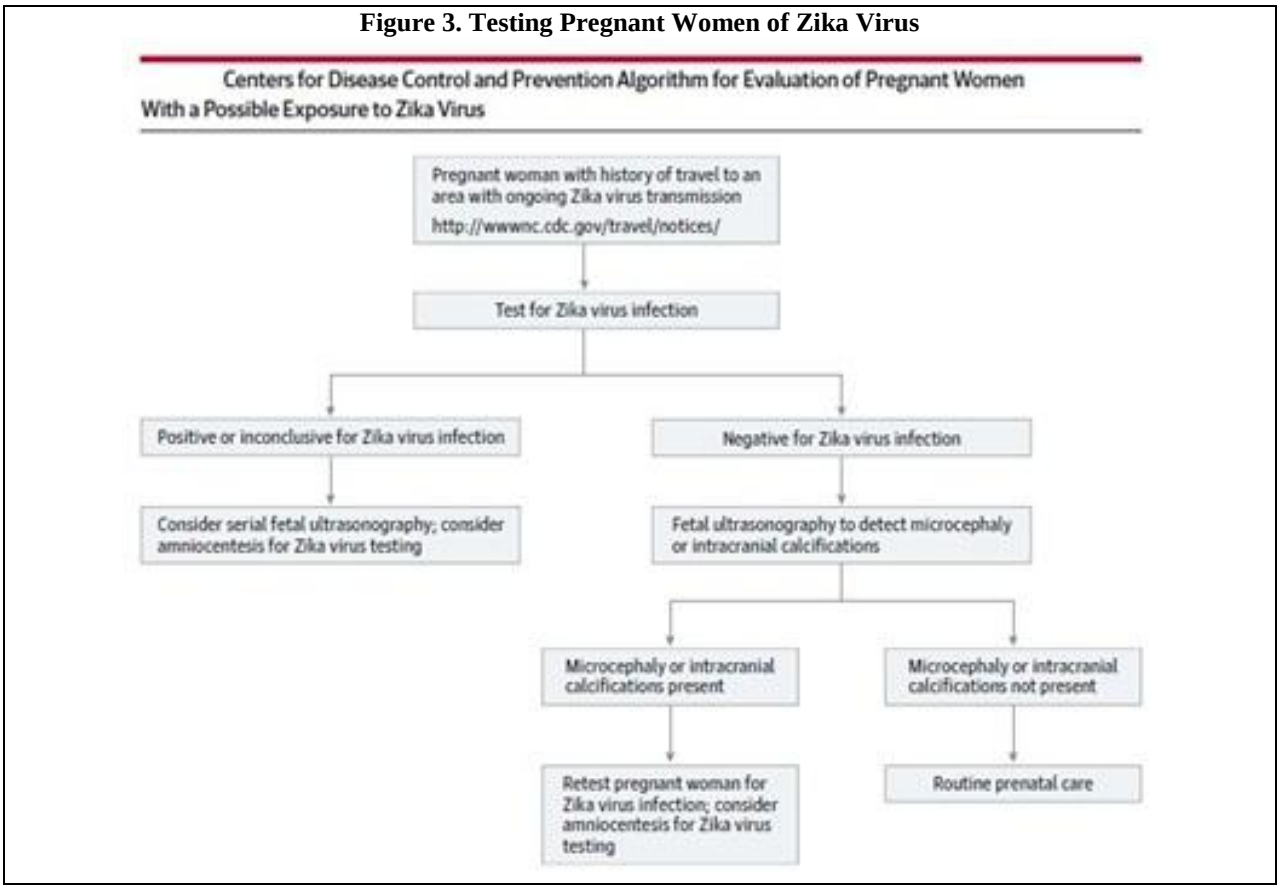

Table 1. Proposed Zika Vaccine Candidates/ Platfrom

Type	Candidate	Status
Inactivated	PaxVax, California	Preclinical
	NewLink Genetics, Massachusetts	Preclinical
	GSK, United States/Belgium	Preclinical
	Bharat Biotech, India	Preclinical
	WRAIR/Sanofi Pasteur, United States and France	Phase 1: 2016–2017
Subunit/peptide	Protein Sciences, Connecticut	Preclinical
	Hawaii Biotech, Hawaii	Preclinical
	Bharat Biotech, India	Preclinical
	Replikins, Massachusetts	Preclinical
Live	NIAID-LID/Instituto Butantan, United States/Brazil	Phase 1: Q4 2016
	UTMB/Instituto Evandro Chagas, United States/Brazil	Preclinical
	Sanofi Pasteur, France	Preclinical
Vectored	Jenner Institute (chimpanzee adenovirus), UK	Preclinical
	Harvard University (VSV), Massachusetts	Preclinical
	Themis Bioscience (measles), Austria	Preclinical
DNA/RNA	NIAID-VRC (Biojector needle-free), United States	Phase 1: Q3 2016
	Inovio Pharmaceuticals (electroporation), Pennsylvania	Phase 1: Q3 2016
	GSK (RNA), United States/Belgium	Preclinical

CONCLUSIONS

Preparedness for the prevention and control of Zika virus infection will require capacities and capabilities for early detection, response and communication. Early detection mechanisms should

ensure rapid notification of human cases, surveillance of Aedes mosquito species that transmit Zika virus and laboratory diagnosis capacity. The response mechanisms should cover organisational and planning mechanisms aimed at the prevention and control of mosquito-borne diseases, inter-sectoral and crossdisciplinary collaboration with all relevant partners, case management and safety of substances of human origin. Zika is an emerging infectious disease currently found in parts of tropical Africa, Southeast Asia, the Pacific and the Americas. Zika virus infection in humans produces an illness clinically similar to dengue fever and many other tropical infectious diseases. Thus, zika virus infection has probably been underdiagnosed and underreported in disease-endemic settings. The natural transmission cycle of zika virus involves mosquitoes, especially Aedes spp, but perinatal transmission, potential risk for transfusion-transmitted and sexually transmitted zika virus infections has also been demonstrated. Clinicians and travel medicine clinics should include zika virus infection in their differential diagnosis for travelers from those areas. The laboratory capacity to confirm suspected zika virus infections should be strengthened to differentiate zika virus infections from other arboviral dengue-like infections. Strategies for the prevention and control of zika virus infection should include the use of insect repellent and mosquito vector eradication. There is also a need for a vaccine and antiviral therapy to fight this disease.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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