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ZIKA VIRUS (ZIKV)

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ABSTRACT
Zika virus (ZIKV) is an emerging arthropod-borne virus (arbovirus) related to yellow fever, dengue, West Nile, and Japanese encephalitis viruses. Zika virus is a mosquito-borne first isolated in Uganda from a sentinel monkey in 1947, In 2007 ZIKV caused an outbreak of relatively mild disease characterized by fever, rash, arthralgia, headache and myalgia. It has generally been associated with *Aedes* mosquitoes. Serologic surveys suggest that Zika virus is widely distributed in humid areas of tropical Africa, Southeast Asia, the Philippines and Zap Island in the South Pacific and the Americas. The disease is probably more common than currently recognized, because of its clinical similarity to dengue and the high prevalence of heterologous flavivirus antibodies where it occurs. The observation that severe clinical complications, its appearance across the globe, mosquito-driven transmission cycle and possible spread via sexual contact make ZIKV an emerging virus.

KEYWORDS: Zika virus, Flavivirus, Arboviruses, Emerging disease, Microcephaly.

INTRODUCTION
The family Flavivirus within the genus Flaviviridae contains some of the most important mosquito transmitted viruses that affect humans and animals. Particularly important mosquito transmitted viruses in this family include Dengue virus (DENV), Yellow fever virus, Japanese encephalitis virus (JEV) and West Nile virus, which combined cause millions of infections every year around the world. However, many of the other viruses in this family also cause disease in humans or animals, but are generally believed to have a more limited geographical range and to cause few infections annually.[1]

Zika virus (ZIKV) is a member of the Spondweni serocomplex within the genus *Flavivirus*, family *Flaviviridae* phylogenetically related to dengue viruses. Following its first isolation in 1947 from a sentinel rhesus monkey placed in the Zika forest near Entebbe in Uganda[1,2], a second isolation from the mosquito *Aedes africanus* followed at the same site in 1948[3], whose natural transmission cycle involves mainly vectors from the Aedes genus (*A. furcifer, A. taylori, A. luteocephalus, A. africanus and A. aegypti*) and monkeys[4], Its genome was sequenced in 2006. Other mosquito borne flaviviruses of public health importance include yellow fever, dengue, West Nile, and Japanese encephalitis viruses. Although research efforts have focused on many of these viruses, other medically important members of the mosquito borne flaviviruses, such as ZIKV, have received far less attention.

MORPHOLOGY OF ZIKA VIRUS
The structure of ZIKV belongs to the Flaviviridae, which is a large family of enveloped, single-stranded, positive sense RNA-viruses with a genome of ~11 kb which encodes three structural and seven non-structural proteins. Viral pathogen that are responsible for causing severe disease and mortality in humans and animals each year.[6,7] It contains a nucleocapsid approximately 25-30 nm in diameter surrounded by a host-membrane derived lipid bilayer that contains envelope proteins E and M. The virion is approximately 40–55 nm in diameter with surface projections that measure roughly 5-10 nm.[8] The surface proteins are arranged in an icosahedral-like symmetry.[9]

GENES AND PROTEINS OF ZIKA VIRUS
The ZIKV genome consists of a single-stranded positive sense RNA molecule with 10,794 kb of length (encoding 3,419 amino acids) with 2 flanking noncoding regions (5' and 3' NCR) and a single long open reading frame encoding polyprotein 5'-C-prM-E-NS1-NS2A-NS2B-NS3-NS4A-NS4B-NS5-3', that is cleaved into capsid (C), precursor of membrane (prM), envelope (E) and seven non-structural proteins (NS).[10,11] The E protein (≈53 kDa) is the major virion surface protein. E is involved in various aspects of the viral cycle, mediating binding and membrane fusion.[12] The NS5 protein (≈103

kDa) is the largest viral protein whose C-terminal portion has RNA-dependent RNA polymerase (RdRP) activity and the N-terminus is involved in RNA capping by virtue of its processing due to methyl transferase activity.[12] The 3'NCR of the ZIKV genome contains about 428 nucleotides, including 27 folding patterns, virus replication occurs in the cellular cytoplasm.[11]

EPIDEMIOLOGY OF ZIKA VIRUS IN HUMANS

The mosquito transmitted Zika virus, subsequently, sporadic human infections were reported in Africa and Asia. In 2007, the first large documented ZIKV outbreak was reported from Yap State, Federated States of Micronesia and more recently in French Polynesia and New Caledonia with this last outbreak causing more than 8000 suspected cases.[13,14] Then spread to many countries in Oceania, before arriving in the Americas in 2014‑15, probably via Easter Island with an estimated 440000‑1300000 cases currently in Brazil alone.[15,16] Isolated cases have been reported in parts of Asia including Philippines, Cambodia, and Indonesia.[17-19] Also, two imported cases of ZIKV infection of travelers, from Indonesia and the Cook Islands to Australia, and two cases imported from Thailand, to Europe and Canada, were described recently.[20] Emphasizing the capacity of ZIKV to spread to areas where it is not endemic but where the proper mosquito vector might be present.

The main vector of Zika virus in Africa is the *Aedes africanus* mosquito, but *Aedes aegypti* mosquitoes, the main vector of dengue in much of Southeast Asia and elsewhere, are also capable of transmitting Zika virus[21] and it is probable that other Aedes species such as *Aedes albopictus*, *Aedes polynesiensis* and *Aedes hensilli* are also capable of transmitting Zika virus to humans.[22] The perinatal transmission[23] and potential risk for transfusion-transmitted ZIKV infections has also been demonstrated and can be a possible vector for human-to-human transmission.[24] ZIKV transmission by sexual intercourse has been suggested by Foy *et al*.[25]

PATHOGENESIS AND CLINICAL COURSE

Pathogenesis information of ZIKV is scarce but mosquito-borne flaviviruses are thought to replicate initially in dendritic cells near the site of inoculation then spread to lymph nodes and the bloodstream.[26] Although flaviviral replication is thought to occur in cellular cytoplasm, ZIKV antigens could be found in infected cell nuclei.[27]

Zika fever has significant similarities with dengue fever, although there is no abrupt clinical onset. The main symptoms are mild fever (37.8°C–38.5°C) maculopapular rash, malaise, headache, stomach ache, dizziness, anorexia, muscle and joint pain, edema of the hands and feet and non-purulent conjunctivitis while the course of the disease is believed to be relatively self-limiting and nonlethal.[28,29] However sever neurologic complications, including Guillain-Barré syndrome, have been observed.[30]

An outbreak of Zika virus infection was recognized in northeast Brazil in early 2015, In this region of an increase in the number of infants born with microcephaly, congenital infections can affect multiple organ systems, and many are associated with specific brain damage, including microcephaly, calcifications (predominantly periventricular, but also in the basal ganglia and in cerebral parenchyma), ventriculomegaly, neuronal migration disorders (pachygyria, polymicrogyria, lissencephaly and schizenchephaly), cerebellar hypoplasia and white matter anomalies.[31,32]

LABORATORY DIAGNOSIS OF ZIKA VIRUS

The detection of ZIKV in both urine and semen is consistent with the results obtained in a study of effects of Japanese encephalitis virus, Flaviviruses have also been detected in urine of persons infected with West Nile virus (WNV).[33,34] The routine diagnosis of Zika virus infection are the detection of viral nucleic acid by RT-PCR and the detection of IgM antibodies by IgM-capture enzyme-linked immunosorbent assay (ELISA). The detection of viral nucleic acid in serum provides a definitive diagnosis; however, diagnosis by RT-PCR has been most successful within 1 week after the onset of clinical illness. In contrast, viral RNA was detected in serum approximately 10 weeks after infection in a pregnant woman whose fetus had evidence of congenital infection. Zika virus testing of maternal serum includes reverse transcription-polymerase chain reaction (RT-PCR) testing, which detect viral RNA, for symptomatic patients with onset of symptoms within the previous week. Immunoglobulin M (IgM) to detect specific antibody against ZIKV in serum and neutralizing antibody testing should be performed on specimens collected ≥4 days after onset of symptoms.[35] Zika virus RT-PCR testing can be performed on amniotic fluid.[23]

TREATMENT OF ZIKA VIRUS

Emerging and re-emerging mosquito-borne diseases are considered to be major threats to global health in both developing and developed countries. Their tendency of spreading outside their known geographic range and causing large scale epidemics has been clearly demonstrated during the recent global epidemic of CHIKV.[36] Like many vector-borne diseases, the absence of vaccines and specific treatment against ZIKV means prevention and control relies heavily on vector control. Therefore, key information such as the identity of the vector, its bionomics, distribution, and density are needed in order to develop and implement sound mosquito control program. No Zika virus vaccine exists; prevention and control measures center on avoiding mosquito bites, reducing sexual transmission. Potentially effective methods of prevention that are focused on reducing infections among pregnant women include avoiding unnecessary travel to areas of ongoing Zika

virus transmission, avoiding unprotected sexual contact with partners who are at risk for Zika virus infection.[38]

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