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ZIKA VIRUS OUTBREAK: THE GLOBAL ENDEMIC TO PANDEMIC

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ABSTRACT

Zika virus is a member of the Flaviviridae family and is transmitted to humans by mosquitoes. It is related to other pathogenic vector borne flaviviruses including dengue, West-Nile and Japanese encephalitis viruses but produces a comparatively mild disease in humans. Since 2007 Zika virus has caused several outbreaks in the Pacific and since 2015 it further spread in the Americas. These were the first documented transmissions outside of its traditional endemic areas in Africa and Asia. Zika virus is considered an emerging infectious disease with the potential to spread to new areas where the Aedes mosquito vector is present. Zika virus is related to the dengue, yellow fever, Japanese encephalitis and West Nile viruses. Since the 1950s, it has been known to occur within a narrow equatorial belt from Africa to Asia. From 2007 to 2016, the virus spread eastward, across to the Americas, leading to the 2015-16. The infection, known as Zika fever or Zika virus disease, often causes no or only mild symptoms, similar to a very mild form of dengue fever. While there is no specific treatment, paracetamol (acetaminophen) and complete rest may help with the symptoms. As of 2016, the illness cannot be prevented by medications or vaccines. Zika can also spread from a pregnant woman to her fetus. This can result in microcephaly, severe brain malformations and other birth defects. Zika infections in adults may result rarely in Guillain-Barré syndrome (demyelination). In January 2016, the United States CDC issued travel guidance on affected countries, including the use of enhanced precautions and guidelines for pregnant women including considering postponing travel. Other governments or health agencies also issued similar travel warnings, while Colombia, the Dominican Republic, Puerto Rico, Ecuador, El Salvador and Jamaica advised women to postpone getting pregnant until more is known about the risks. Like other flaviviruses, Zika virus is enveloped and icosahedral and has a non-segmented, single-stranded, 10 kilobase positive-sense RNA genome. It is most closely related to the Spondweni virus and is one of the two known viruses in the Spondweni virus clade.

KEYWORDS: Aedes mosquito, Guillain-Barré syndrome, RT-PCR, Flavivirus, Capsid, Genome, CDC, Microcephaly, Zika fever.

INTRODUCTION

Aedes aegypti, the yellow fever mosquito, is a mosquito that can spread dengue fever, chikungunya, Zika fever, Mayaro and yellow fever viruses and other diseases. The mosquito can be recognized by white markings on its legs and a marking in the form of a lyre on the upper surface of its thorax. This mosquito originated in Africa, but is now found in tropical and subtropical regions throughout the world. The average wing length of female *A.aegypti* mosquitoes varies greatly (1.67–3.83 mm in a Peruvian habitat). It was first identified in monkeys in Uganda in 1947. The first human case was detected in Nigeria in 1954 and there have been further outbreaks in Africa, South East Asia and the Pacific Islands. Most were small and Zika has not previously been considered a major threat to human health.[1]

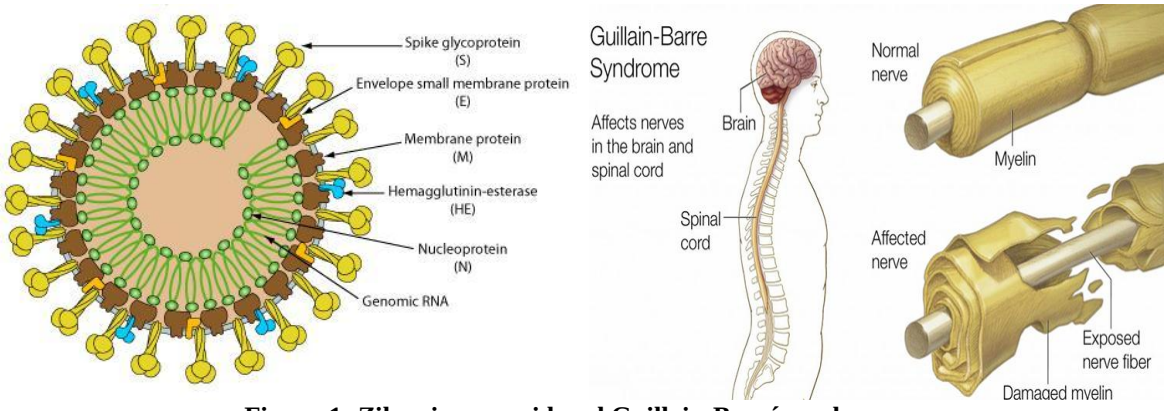

Figure-1: Zika virus capsid and Guillain-Barré syndrome

In 1947, scientists researching yellow fever placed a rhesus monkey in a cage in the Zika Forest (zika meaning *overgrown* in the Uganda language), near the East African Virus Research Institute in Entebbe, Uganda. The monkey developed a fever and researchers isolated from its serum a transmissible agent that was first described as Zika virus in 1952. It was subsequently isolated from a human in Nigeria in 1954. From its discovery until 2007, confirmed cases of Zika virus infection from Africa and Southeast Asia were rare. In 2007, however, a major epidemic occurred in Yap Island, Micronesia. More recently, epidemics have occurred in Polynesia, Easter Island, the Cook Islands and New Caledonia.

Figure-2: Zika virus genome from mosquito

The first outbreak of the disease outside of Africa and Asia was in April 2007, on the island of Yap in the Federated States of Micronesia. The condition was characterized by rash, conjunctivitis and arthralgia and was initially thought to be dengue. The Chikungunya and Ross River viruses were also suspected. However, serum samples from patients in the acute phase of illness contained RNA of Zika virus. The Zika fever disease process was relatively mild: there were 49 confirmed cases, 59 unconfirmed cases, no deaths and no hospitalizations.[2]

Since April 2015, a large, ongoing outbreak of Zika virus has spread too much of South and Central America and the Caribbean. In January 2016, the CDC issued a level 2 travel alert for people traveling to regions and certain countries where Zika virus transmission is ongoing. The agency also suggested that women thinking about becoming pregnant should consult with their physicians before traveling. According to the CDC, Brazilian health authorities reported more than 3,500 microcephaly cases between October 2015 and January 2016. Some of the affected infants have had a severe type of microcephaly and some have died. A recent larger outbreak of Zika virus outside Africa and Asia was confirmed in April 2015, in Brazil.

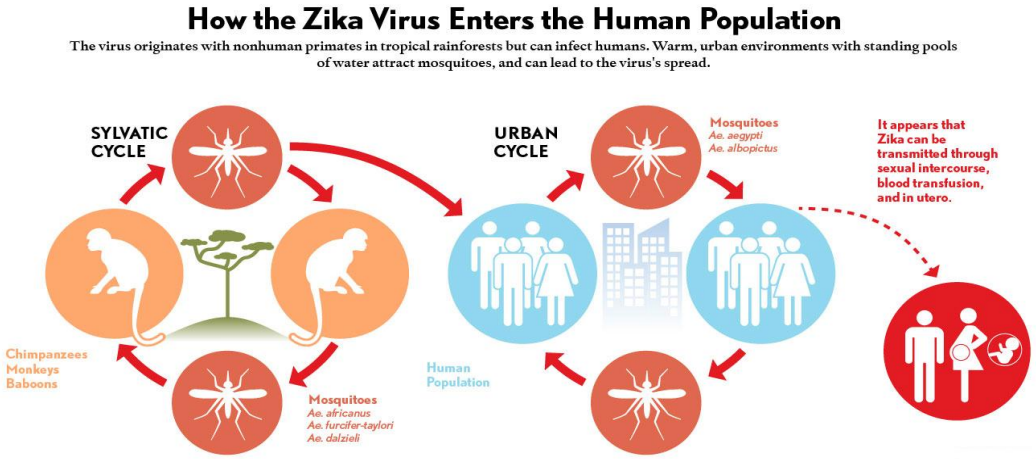

Figure-3: Zika virus cycle

In the district of Camaçari and the neighbor Salvador city, capital of the state of Bahia, healthcare authorities confirmed that a previously unknown disease affecting around 500 patients with flu-like symptoms followed by rash and arthralgia is indeed an ongoing outbreak of Zika fever, as proved by RT-PCR technique by researchers from Federal University of Bahia. Local authorities link the outbreak to recent increased flow of foreign visitors prompted by the 2014 FIFA World Cup, coupled with the large population of insect vectors such as *Aedes aegypti* and *Aedes albopictus* mosquitoes that inhabit the region. The spread follow a similar pattern to the also recent outbreak of chikungunya virus in the same region.[3]

Symptoms

Zika symptoms are often very mild and usually fade on their own within days. However, because the virus is also sexually transmitted and has been linked to serious birth defects when contracted by pregnant women, it's more important than ever for the public to recognize the signs of Zika and if infected, avoid sexual contact with pregnant women. Here is what you need to know about the early symptoms of the Zika virus. Deaths are rare and only one-in-five people infected is thought to develop symptoms. These include: mild fever, conjunctivitis (red, sore eyes), headache, joint pain, a rash. A rare nervous system disorder, *Guillain-Barré syndrome* that can cause temporary paralysis has been linked to the infection. There is no vaccine or drug treatment so patients are advised to rest and drink plenty of fluids. But the biggest concern is the impact it could have on babies developing in the womb and the surge in microcephaly.[4]

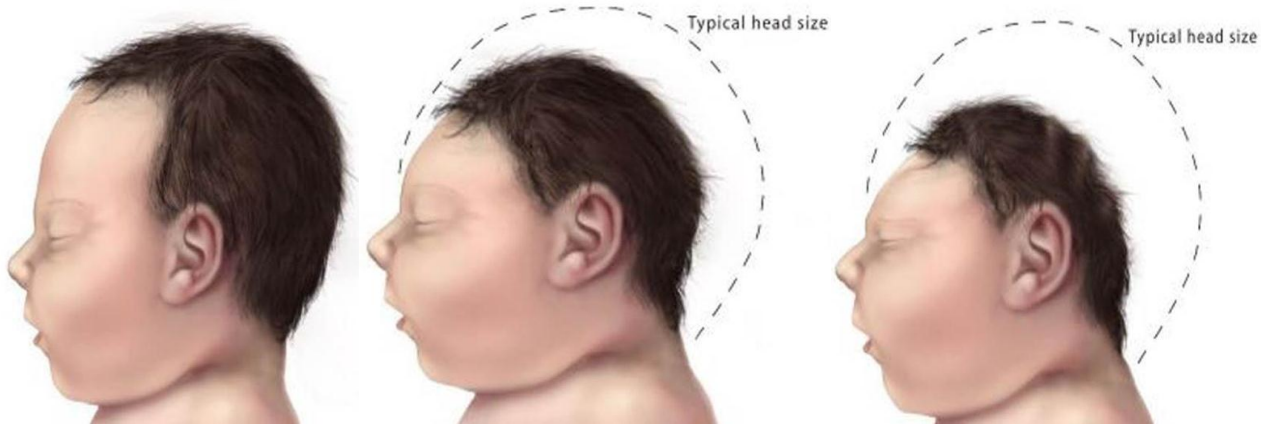

Figure-4: Microcephaly

It is when a baby is born with an abnormally small head, as their brain has not developed properly. The severity varies, but it can be deadly if the brain is so underdeveloped that it cannot regulate the functions vital to life. Children that do survive face intellectual disability and development delays. It can be caused by infections such as rubella, substance abuse during pregnancy or genetic abnormalities. WHO says that Zika causes microcephaly as well as *Guillain-Barré syndrome*. Some babies who died had the virus in their brain and it has been detected in placenta and amniotic fluid too.[5]

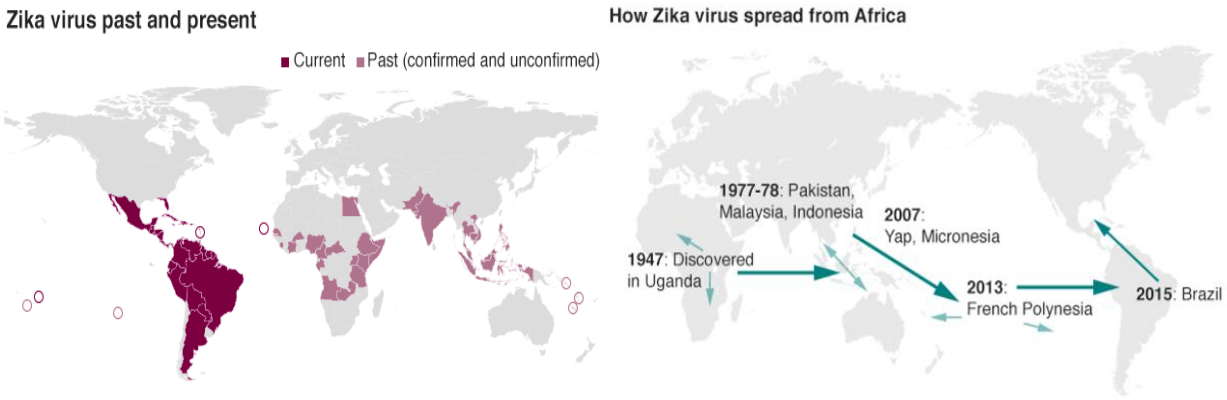

Figure-5: Zika virus spread

Some patients may also go on to develop joint pains in their wrists, knees and ankles, as well as muscle pain and pain behind the eyes. These symptoms can last for up to a week and usually appear within two weeks of the initial infection, CBS reported and, unlike the mosquitoes that spread malaria, they are mostly active during the day, so bed nets offer limited protection. If they drink the blood of an infected person they can then infect subsequent people they bite. The WHO says sexual transmission is also possible.[6]

Virology

A positive-sense RNA genome can be directly translated into viral proteins. As in other flaviviruses, such as the similarly sized West Nile virus, the RNA genome encodes seven nonstructural proteins and three structural proteins. One of the structural proteins encapsulates the virus. This protein is the flavivirus envelope glycoprotein that binds to the endosomal membrane of the host cell to initiate endocytosis. The RNA genome forms a nucleocapsid along with copies of the 12-kDa capsid protein. The nucleo-capsid, in turn, is enveloped within a host-derived membrane modified with two viral glycoproteins. Viral genome replication depends on the making of double stranded RNA from the single stranded positive sense RNA ssRNA(+) genome followed by transcription and replication to provide viral mRNAs and new ssRNA(+) genomes.

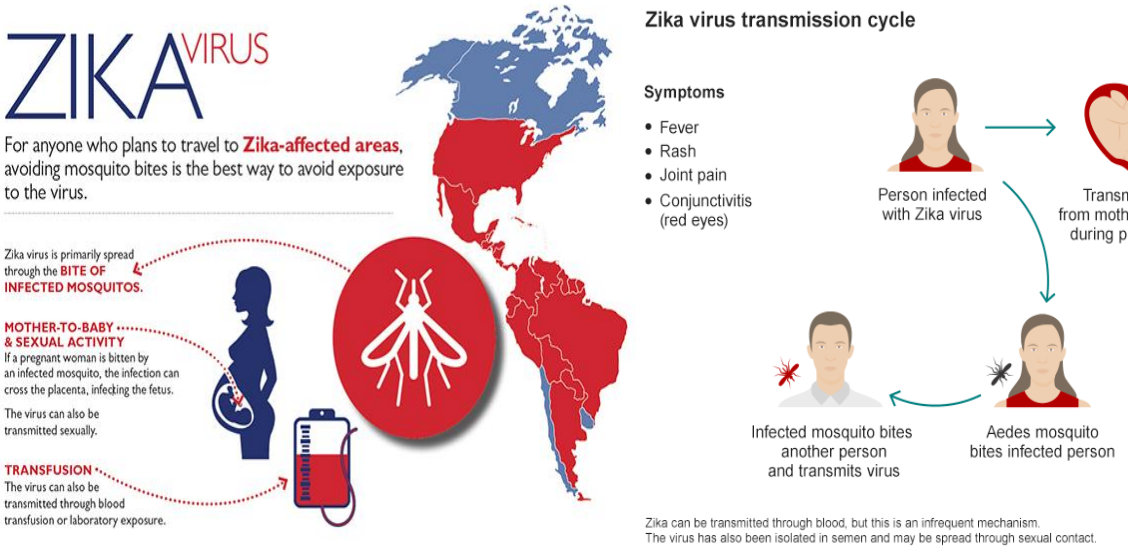

Figure-6: Zika virus cycle

There are two Zika lineages: the African lineage and the Asian lineage. Phylogenetic studies indicate that the virus spreading in the Americas is 89% identical to African genotypes, but is most closely related to the Asian strain that circulated in French Polynesia during the 2013–2014 outbreaks.[7]

Where Is Zika Virus Found?

As a mosquito-borne virus, Zika moves with the insects and populations. This has allowed the virus to spread throughout South and Central America. The following countries have had Zika outbreaks in the last year or are at risk of a Zika outbreak: Barbados, Bolivia, Brazil, Cambodia, Cape Verde, Chile, Colombia, Cook Islands, Dominican Republic, Ecuador, El Salvador, French Guiana, French Polynesia, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Indonesia, Martinique, Mexico, Panama, Paraguay, Puerto Rico, Saint Martin, Samoa, Suriname, Tahiti, Thailand, Vanuatu and Venezuela. Zika virus outbreak: America: 2016, Asia:

2016, Uganda: 1947-1983, Federated States of Micronesia: 1947, United States: 2008, Africa & Asia: 2012, French Polynesia: 2013-2014, Japan: 2013, New Caledonia: 2014, Cook Islands: 2014, Easter Island: 2014, Bangladesh: 2016, Solomon Islands: 2015, Brazil: 2015.

Transmission

The vertebrate hosts of the virus were primarily monkeys in a so-called enzootic mosquito-monkey-mosquito cycle, with only occasional transmission to humans. Before the current pandemic began in 2007, Zika rarely caused recognized 'spillover' infections in humans, even in highly enzootic areas. Infrequently, however, other arboviruses have become established as a human disease and spread in a mosquito–human–mosquito cycle, like the yellow fever virus and the dengue fever virus (both flaviviruses) and the chikungunya virus (a togavirus). Though the reason for the pandemic is unknown, dengue, a related arbovirus that infects the same species of mosquito vectors, is known in particular to be intensified by urbanization and globalization. Zika is primarily spread by *Aedes aegypti* mosquitoes and can also be transmitted through sexual contact or blood transfusions. In 2015, news reports drew attention to the rapid spread of Zika in Latin America and the Caribbean. At that time, the Pan American Health Organization published a list of countries and territories that experienced local Zika virus transmission comprising Barbados, Bolivia, Brazil, Colombia, the Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Guyana, Haiti, Honduras, Martinique, Mexico, Panama, Paraguay, Puerto Rico, Saint Martin, Suriname and Venezuela. By August 2016, more than 50 countries had experienced active transmission of Zika virus.[8]

Figure-7: Control of Zika virus

Pathogenesis

Zika virus replicates in the mosquito's midgut epithelial cells and then its salivary gland cells. After 5–10 days, the virus can be found in the mosquito's saliva. If the mosquito's saliva is inoculated into human skin, the virus can infect epidermal keratinocytes, skin fibroblasts in the skin and the Langerhans cells. The pathogenesis of the virus is hypothesized to continue with a spread to lymph nodes and the bloodstream. Flaviviruses replicate in the cytoplasm, but Zika antigens have been found in infected cell nuclei.[9]

Zika fever

Zika fever (also known as Zika virus disease) is an illness caused by the Zika virus. Most cases have no symptoms, but when present they are usually mild and can resemble dengue fever. Symptoms may include fever, red eyes, joint pain, headache and a maculopapular rash. Symptoms generally last less than seven days. It has not caused any reported deaths during the initial infection. Infection during pregnancy causes microcephaly and other brain malformations in some babies. Infection in adults has been linked to *Guillain–Barré syndrome* (GBS). Diagnosis is by testing the blood, urine, or saliva for the presence of Zika virus RNA when the person is sick. Prevention involves decreasing mosquito bites in areas where the disease occurs and proper use of condoms. Efforts to prevent bites include the use of insect repellent, covering much of the body with clothing, mosquito nets, and getting rid of standing water where mosquitoes reproduce. There is no effective vaccine. Health officials recommended that women in areas affected by the 2015–16 Zika outbreak consider putting off pregnancy and that pregnant women not travel to these areas. While there is no specific treatment, paracetamol (acetaminophen) and rest may

help with the symptoms. Admission to hospital is rarely necessary.[10]

Vaccine

Effective vaccines have existed for several viruses of the flaviviridae family, namely yellow fever vaccine, Japanese encephalitis vaccine and tick-borne encephalitis vaccine, since the 1930s and dengue fever vaccine since the mid-2010s. World Health Organization (WHO) experts have suggested that the priority should be to develop inactivated vaccines and other non-live vaccines, which are safe to use in pregnant women and those of childbearing age. As of March 2016, 18 companies and institutions internationally were developing vaccines against Zika but a vaccine was unlikely to be widely available for about ten years. In June 2016 the FDA granted the first approval for a human clinical trial for a Zika vaccine.[11-13]

CONCLUSION

The World Health Organization has declared the Zika virus a global public health emergency. The infection has been linked to thousands of babies being born with underdeveloped brains. Some areas have declared a state of emergency, doctors have described it as a pandemic in progress and some are even advising women in affected countries to delay getting pregnant. Central and South America, as well as the Caribbean, are some of the most popular destinations for American travelers. Whether you are visiting a beach in Puerto Rico or ruins in Mexico, you are likely to encounter mosquitoes. But now, a virus imported from the East is causing major problems, especially for expecting or potential mothers. The Zika virus is spread through mosquito bites with usually fairly light symptoms. Outbreaks have occurred in Africa, Southeast Asia and the Pacific Islands. In the last year, the virus gained a foothold in Brazil and since then has been slowly moving northward infecting mosquitoes and humans in 20 countries. There is no vaccine to prevent Zika and no medicine to treat it. The best protection is through preventing mosquito bites and avoiding regions where the disease is present. While Zika's symptoms are generally mild, research shows it can cause birth defects in baby's whose mothers contract the disease while pregnant. The exact nature of all defects and when they are most likely to occur is still under investigation. As a mosquito-borne disease, Zika spreads among mosquito populations and from mosquitoes to humans. Some research suggests the virus may transfer from person-to-person through sex or transfusion. But, there has only been one reported case of each type of infection. The mosquitoes that spread Zika are the same that carry Dengue fever and chikungunya. Areas affected by Dengue could potentially harbor Zika as well. Typically, a mosquito becomes infected when it feeds on a person who has Zika. This mosquito then spreads the virus to other humans through bites. Rarely, a mother infected with the virus will pass it on to her child in uterus. This form of transmission is under investigation by global health organizations. There have been no reports of infants contracting the virus through breast feeding.

Zika is a generally mild disease, though there are some possible complications. Only about 20% of those infected with the virus fall ill. Symptoms are usually mild and last anywhere from several days to a week. Severe illness is uncommon and deaths are rare. Symptoms of Zika virus include: Fever, Rash, Joint pain, Conjunctivitis (pink eye), Muscle pain, Headache. Health agencies are recommending travelers speak with a travel health specialist before visiting areas where Zika is present. If you are traveling to an affected area, schedule your appointment with Passport Health today.

Zika is a mosquito-borne disease that has neither vaccine nor cure. The best form of prevention is avoiding or repelling mosquitoes. CDC recommendations include: Use insect repellents containing DEET, picaridin, OLE or IR3535' Wear clothing treated with a repellent like permethrin; Wear long-sleeve shirts and long pants to cover exposed skin; Stay and sleep in screened or air conditioned rooms. Consider using mosquito netting depending on your itinerary. Avoid non-essential travel to areas affected by Zika if you are pregnant or may become pregnant. Many organizations are recommending travelers to these regions, whether pregnant or not, should speak with a travel health clinic like Passport Health before leaving. Research shows the Zika virus can spread from a pregnant mother to her unborn baby. It is believed the virus can cause microcephaly (the shrinking of a baby's head) and other health complications. The affects of Zika on pregnant mothers and their children are still under investigation. The CDC recommends special precautions for: **Women who are pregnant (in any trimester):** 1**.** Consider postponing travel to any area where Zika may be present. 2. If you must travel to these areas, speak to your doctor before traveling. 3. Strictly follow all methods outlined above to avoid mosquito bites. **Women who are trying to become pregnant:** 1. Talk to your doctor about your plans to become pregnant and the risks of Zika virus. 2. Strictly follow all methods outlined above to avoid mosquito bites.

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