Zika Virus Disease: A Global Health Challenge

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ABSTRACT

Zika virus is a flavivirus that belongs to the family Flaviviridae. It is a mosquito-transmitted infection related to dengue, yellow fever, and West Nile virus. It was first discovered in 1947, during a study of yellow fever from the blood of a sentinel rhesus monkey that had been placed in the Zika Forest of Uganda. There are three strains of Zika virus in circulation, Nigerian Cluster, MR766 Cluster, and the Asian genotype.

To date, Zika virus remain in relative obscurity for 60 years; then, it spread from Africa and Asia to cause the first large outbreak in humans on the Pacific island of Yap, in the Federated States of Micronesia in 2007. Prior to this event, no outbreaks and only 16 cases of human Zika virus disease had been documented worldwide. Thereafter, Zika virus was introduced into Brazil from the Pacific Islands where it causes the largest outbreak ever in humans and spread swiftly throughout the America.

Today, Zika Virus is commanding worldwide attention recently because researchers have found evidence that Zika may be linked to birth defects and neurological conditions like microcephaly and Guillain-Barré syndrome in adults. Thus, this review explicates in detail the available information on the virology, epidemiology, pathogenesis, transmission, clinical manifestation and diagnosis. Proactive measures to curtail the spread of Zika virus infection are also highlighted.

(Keywords: MR766 cluster, Flaviviridae, Zika virus infection, sentinel rhesus monkey, Asian genotype)

INTRODUCTION

Zika virus (ZIKV) is a flavivirus that belongs to the family Flaviviridae. It is a mosquito-transmitted infection related to dengue, yellow fever and West Nile virus. It was discovered in Zika forest in Uganda in 1947 and is common in Africa and Asia. Thereafter, Zika virus was isolated on several occasions from *Aedes africanus* mosquitoes and was not known to cause human disease. Until the twentieth century, the virus did not cause meaningful infections in humans (Knipe and Kuno and Chang, 2007; Hayes, 2009; Cao-Lormeau *et al.,* 2014; Faye *et al.*, 2014; WHO, 2016).

However, as of late 2007, vectored by *Aedes aegypti* mosquitoes, ZIKV caused the first noteworthy epidemic on the Yap Island in Micronesia. Patients experienced fever, skin rash, arthralgia and conjunctivitis (Lanciotti *et al.,* 2008). From 2013 to 2015, the Asian lineage of the virus caused further massive outbreaks in New Caledonia and French Polynesia. In 2015, ZIKV reached Brazil, later spreading to other countries in South and Central America (Faria *et al.,* 2016).

Scientific concern in this population is focused on women who become infected while pregnant and those who develop a temporary form of paralysis after exposure to Zika virus. In pregnant women, Zika virus causes brain damage in infants termed microcephaly usually characterized by small heads and damaged brains that emerged only in October 2015 when doctors in northern Brazil noticed a surge in babies with the condition. Experts were not certain how it happens or even whether the virus is to be blame (WHO, 2016).

Zika virus is spread by mosquitoes of the Aedes genus, which can bread in tiny pool of water and usually bite during the day. The aggressive yellow fever mosquito, *Aedes aegypti,* has spread most Zika cases. The mosquito is found in Nigeria and some other countries. In February, 2016 as infection moved rapidly through the range occupied by *Aedes* mosquitos in the America, WHO declared that Zika virus infection

associated with microcephaly and other neurological disorders constitutes a Public Health Emergency of International Concern (PHEIC) (WHO, 2016).

Today, Zika Virus is commanding worldwide attention recently because researchers have found evidence that Zika may be linked to birth defects and neurological conditions like microcephaly and Guillain-Barré syndrome in adults. Thus, this review explicates in detail the available information on the virology, epidemiology, pathogenesis, transmission, clinical manifestation and diagnosis. Proactive measures to curtail the spread of Zika virus infection are also highlighted.

VIROLOGY

Zika virus is icoshahedral, enveloped nonsegmented, single-stranded and positive-sense RNA. It is most closely related to the Spondweni virus (Knipe and Howley, 2007; Kuno and Chang, 2007; Hayes, 2009; Cao-Lormeau *et al.,* 2014; Faye *et al.*, 2014).

The virus originated in East Africa and subsequently spread to West Africa and then to Asia, thus resulting in distinct lineages (Nigerian Cluster, MR766 Cluster, and the Asian genotype). All strains currently associated with the outbreak in America are of the Asian genotype and are most closely related to strains from Yap, Cambodia, Thailand, and French Polynesia. Phylogenetic studies indicates that the virus spreading in the America States is 89% identical to African genotypes, but is most closely related to the Asian strain that circulated in French Polynesia during the 2013–2014 outbreak (Lanciott *et al*., 2008; Faye *et al*., 2014; Lanciott *et al*., 2016; Enfissi *et al.,* 2016; Zanluca *et al.*, 2016).

ZIKA VIRUS TRANSMISSION

Mosquito-Borne Transmission

Zika virus circulates in a sylvatic transmission cycle between nonhuman primates and enzootic vector, certain forest-dwelling species of aedes mosquitoes, with only occasional transmission to humans (Figure 1). In Asia, a sylvatic transmission cycle has not yet been identified. The Likely enzootic vectors in Africa and Asia primarily belong to the stegomyia and diceromyia subgenera of aedes, and including *A. africanus*, *A. luteocephalus*, *A. furcifer*, and *A. taylori* (Marchette *et al.,* 1969; Diallo *et al.,* 2014).

In suburban and urban settings, Zika virus is transmitted in a human–mosquito–human transmission cycle, mostly involving *A. aegypti* mosquitoes (figure 2.1). Two species in the stegomyia subgenus of aedes — *A. aegypti* and, to a lesser extent, *A. albopictus* — have been connected with nearly all known Zika virus outbreaks, though two other species, *A. hensilli* and *A. polynesiensis*, were thought to be vectors in the Yap and French Polynesia outbreaks, respectively (Musso *et al.,* 2014; Ledermann *et al.,* 2014; Grard *et al.,* 2014).

Despite the association of *A. aegypti* and *A. albopictus* with outbreaks, both were found to have unexpectedly low but similar vector competence (i.e., the intrinsic ability of a vector to biologically transmit a disease agent) for the Asian genotype Zika virus strain, as determined by a low proportion of infected mosquitoes with infectious saliva after ingestion of an infected blood meal. However, *A. aegypti* is thought to have high vectorial capacity (i.e., the overall ability of a vector species to transmit a pathogen in a given location and at a specific time) because it feeds primarily on humans, often bites multiple humans in a single blood meal, has an almost imperceptible bite, and lives in close association with human habitation (Gubler, 2002).

Other mosquito species, with low potential for transmission of the virus include *A*. *unilineatus*, *Anopheles coustani*, and *Mansonia uniformis*. Moreover, Zika virus has been reported only once in any culex species, which suggests that mosquitoes in this genus have a low vectorial capacity (Gubler, 2002).

Non-Mosquito Transmission

Considerable facts now indicate that Zika virus can be transmitted from the mother to the fetus during pregnancy. These findings include identification of Zika virus RNA in the amniotic fluid of mothers whose fetuses had cerebral

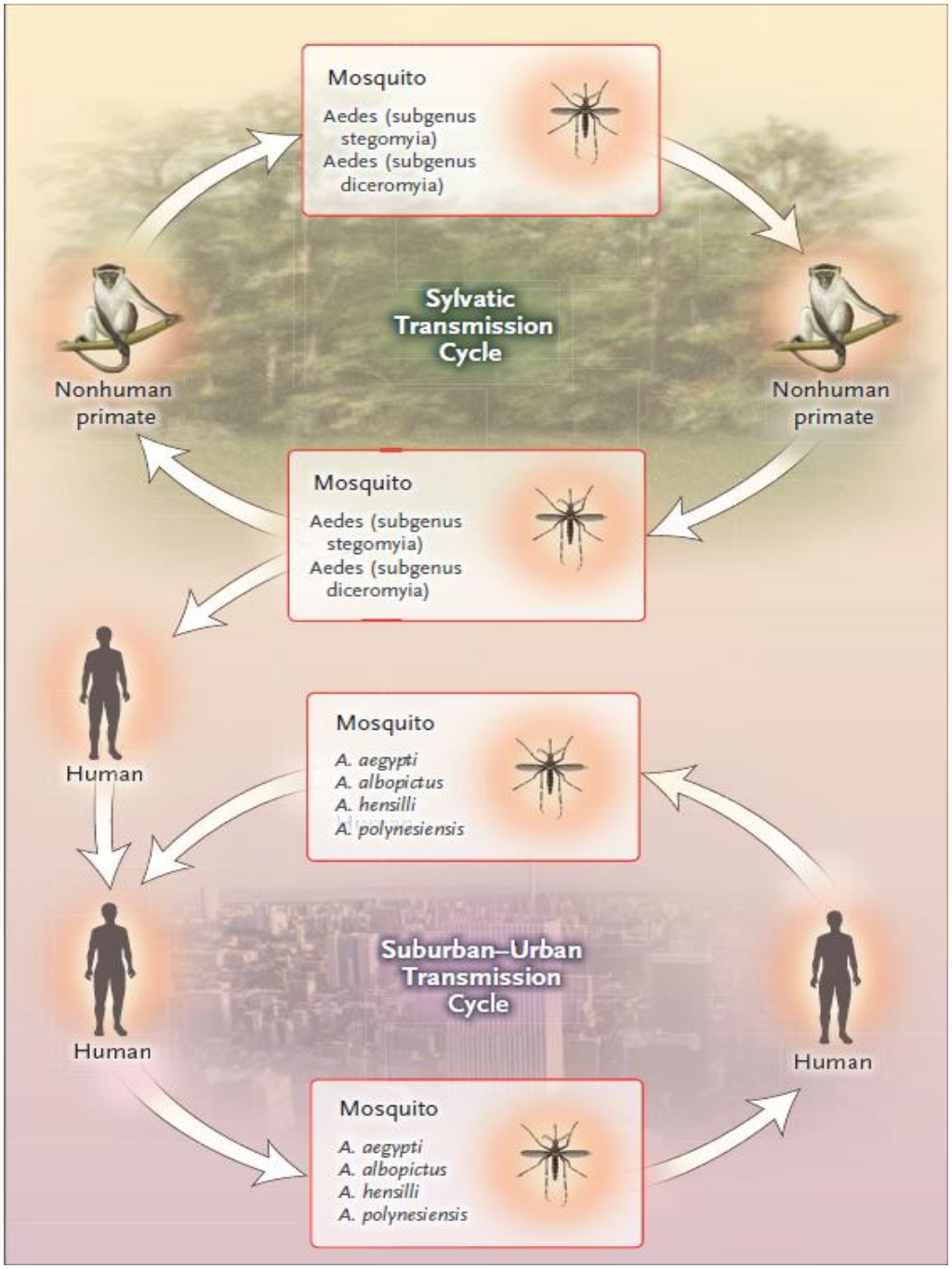

Figure 1: Zika Virus Transmission Cycle
Source: (Petersen *et al.*, 2016).

abnormalities detected by ultrasonography and ZIKV viral antigen and RNA have been identified in the brain tissue and placentas of children who were born with microcephaly and died soon after birth, as well as in tissues from miscarriages. The frequency and risk factors for transmission are unknown (Oliveira *et al.*, 2016; Calvet *et al.*, 2016; Jouannic *et al.*, 2016). Two cases of peripartum transmission of Zika virus have been reported among mother–infant pairs. Zika virus

RNA was detected in both infants; one infant had a mild rash illness and thrombocytopenia, whereas the other was asymptomatic (Besnard *et al.*, 2014).

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, which can then infect humans. Information regarding pathogenesis of Zika virus is scarce but recent finding by researcher at John Hopkin University and Florida State University showed that Zika virus may target and infect neural stem cells (NSCs) - the cells that divide to create neurons and other brain cells (Cui *et al.,* 2016). Also, Institute for research and education in Brazil independently found the same result; they equally learned that ZIKV affects neural cell growth and survival (Cugola *et al*., 2016).

To mimic embryonic development, the researcher grew some NSCs in the laboratory in two different forms. In one experiment the scientists infected some of the NSCs with Zika virus and grew them as neurospheres- flat circular clusters that contain NSCs and other brain cells. At six days, the infected NSCs grew into hundreds of healthy, round neurospheres but the infected neurosphere were all strangely lopsided with jagged edges, the cells started separating from each other and all of them died (Cui *et al.,* 2016).

Another experiment involved cerebral organoids, which are these apple- seed sized mini brain that kind of look and act like brain of a first trimester fetus. They infected six of these organoid with Zika and left six uninfected. When they measure the organoid after six days the infected ones were only about 60% as big as the uninfected ones. These results explains how over many months the Zika infection could cause a lot of damage to developing brain cells, and potentially leads to malformed brain condition like microcephaly (Cugola *et al*., 2016).

Clinical Manifestations

Zika virus 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 (ECDC, 2015; WHO, 2016). Symptoms may include fever, red eyes, joint pain, headache, and a maculopapular rash (Musso *et al.,* 2014; Chen and Hamer, 2016; WHO, 2016). Symptoms generally last less than seven days (Chen and Hamer, 2016)..../../../../ASKMANZANITA/Desktop/New folder/Zika virus - Wikipedia, the free encyclopedia.htm - cite_note-Ann2016-59 It has not caused any reported deaths during the initial infection. (ECDC, 2015). Infection during pregnancy causes microcephaly and other brain malformations in some babies (CDC, 2016; Rasmussen *et al.,* 2016). Infections in adults have been linked to Guillain–Barré syndrome (GBS) (ECDC, 2015).

Microcephaly in Fetuses and Newborns

Microcephaly is a condition where a baby's head is much smaller than expected (Figure 2). During pregnancy, a baby's head grows because the baby's brain grows. Microcephaly can occur because a baby's brain has not developed properly during pregnancy or has stopped growing after birth, which results in a smaller head size. Microcephaly can be an isolated condition, meaning that it can occur with no other major birth defects, or it can occur in combination with other major birth defects (WHO, 2016).

Babies with microcephaly can have a range of other problems, depending on how severe their microcephaly is. Microcephaly has been linked with the following problems: Seizures, Developmental delay, such as problems with speech or other developmental milestones (like sitting, standing, and walking), Intellectual disability (decreased ability to learn and function in daily life), Problems with movement and balance, Feeding problems, such as difficulty swallowing, Hearing loss, Vision problems,

Guillain-Barré Syndrome

Guillain-Barré syndrome (GBS) is a disorder in which the body's immune system attacks part of the peripheral nervous system. The first symptoms of this disorder include varying degrees of weakness or tingling sensations in the legs. In many instances the symmetrical

weakness and abnormal sensations spread to the arms and upper body.

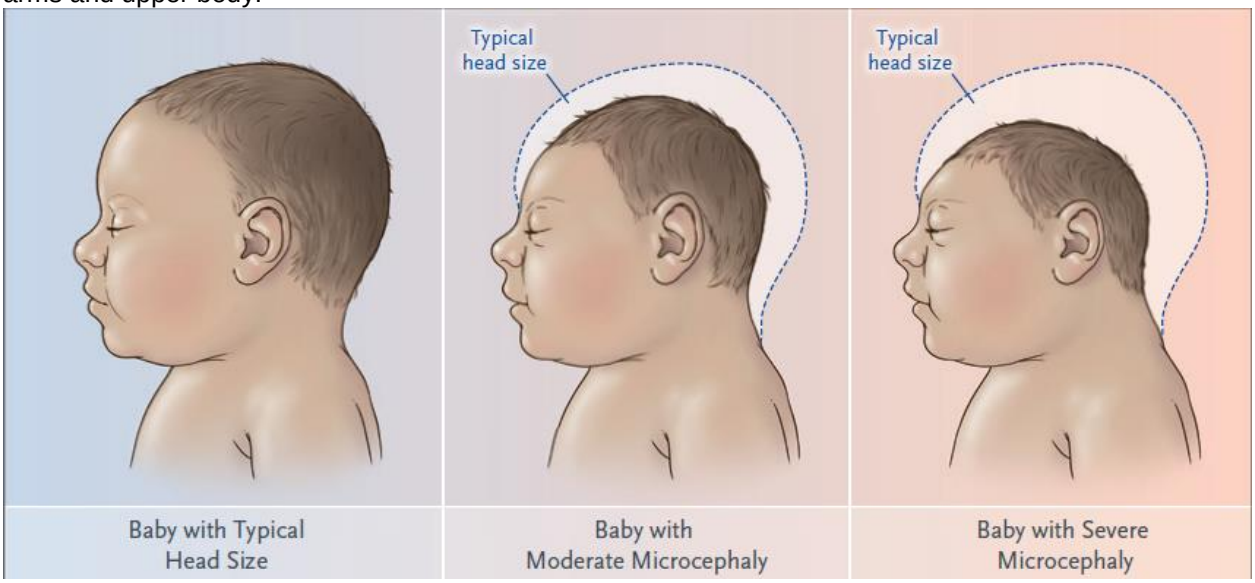

Figure 2: Infants with Moderate or Severe Microcephaly Associated with Maternal Zika Virus Infection, as Compared to a Typical Newborn.
Source: (Petersen *et al.*, 2016).

These symptoms can increase in intensity until certain muscles cannot be used at all and, when severe, the person is almost totally paralyzed. In these cases the disorder is life threatening - potentially interfering with breathing and, at times, with blood pressure or heart rate - and is considered a medical emergency (WHO, 2016).
Temporal association between Zika virus outbreaks and increases in the incidence of Guillain-Barré syndrome observed in French Polynesia, Brazil, Venezuela and El Salvador. Investigations into this association are ongoing (ECDC, 2016).

Epidemiology

The following timeline summarizes the spread of ZIKV infection, country by country, from the earliest discovery in 1947 to the latest information as of the year 2016. In 1947, Scientists conducting routine surveillance for yellow fever in the Zika forest of Uganda isolateD the Zika virus in samples taken from a captive, sentinel rhesus monkey (Dick *et al.,* 1952). Following this, it was recovered from the mosquito *Aedes* (*Stegomyia*) *africanus*, caught on a tree platform in the Zika forest in 1948 (Dick *et al.,* 1952). Initially there was no indication that the virus caused human disease, not until first human cases were detected in Uganda and the United Republic of Tanzania in a serosurvey demonstrating the presence of Zika virus neutralizing antibodies in sera in 1952 (Dick *et al.,* 1952).

In 1954, the virus was isolated from a young girl in Afikpo Division, Eastern Nigeria, while investigating outbreak of jaundice suspected of being yellow fever. Two other patients exhibited a rise in titre of serum antibodies against this virus (Macnamara, 1954). Whereas, a researcher in 1964 in Uganda who fell ill while working with Zika strains (African Zika virus, strain MR-766) isolated from mosquitoes provides the first proof, by virus isolation and re-isolation, that Zika virus causes human disease. Though a pink non-itchy rash lasting 5 days eventually covers most of his body, including the palms of his hands and soles of his feet, he reports his illness as “mild”, as he did not experience the “crippling bone pain” associated with dengue and chikungunya infections. Given the mild nature of the illness, the author concludes that “it is not surprising under normal circumstances the virus is not isolated frequently from man” (Simpson, 1964). To cap this scenario, human illness caused by

Zika virus was first recognized in Nigeria in 1968, when viral infection was confirmed in three ill persons (Moore *et al*., 1975).

In spite of recognition that Zika virus infection could produce a mild, febrile illness, only 10 naturally acquired cases were reported during the next 39 years, but such cases are rare, and the disease is regarded as benign. No deaths or hospitalizations were reported and in addition seroprevalence studies consistently indicate widespread human exposure to the virus. During this time, the geographical distribution of Zika virus expands to Portugal and Indonesia in the year 1973 and 1981, respectively, where the virus was detected in mosquitoes. Out of these ten (10) cases two (2) more from Nigeria, one (1) from Portugal and the remainder were from Indonesia (Fagbami, 1979; Filipe, 1973; Olson, 1981). 16–19 Researchers later suggested that the clinical similarity of Zika infection with dengue and chikungunya may be one reason why the disease was so rarely reported in Asia (Marchette *et al.,* 1969).

Zika virus spreads from Africa and Asia to cause the first large outbreak in humans on the Pacific island of Yap, in the Federated States of Micronesia in 2007. Prior to this event, no outbreaks and only 16 cases of human Zika virus disease had been documented worldwide. An estimated 75% (i.e. 5000 infections among the total population of 6700) of Yap residents over three years of age were infected with Zika virus. No deaths, hospitalizations, or neurological complications were reported (Lanciotti *et al.,* 2008; Duffy *et al.,* 2009). Although wind-blown mosquitoes can travel distances of several hundred kilometers over the open ocean, introduction of the virus by travel or trade involving an infected person or an infected mosquito is considered the most likely source of this outbreak, especially as no monkeys were present on the island during the outbreak (Duffy *et al.,* 2009; Haddow *et al.,* 2012).

The finding on Yap Island that Zika virus can cause an outbreak numbering more than one hundred confirmed and probable cases are striking. In the absence of any evidence that viral mutation can explain changes in epidemic behaviour, several other explanations are suggested including lack of population immunity, Under-reporting may also be a reason for missing previous outbreaks of infection, due to the clinical similarities of (mild) illness associated with Zika, dengue, and chikungunya infections, and the frequent co-circulation of all three viruses (WHO, 2016).

In 2008, a US scientist conducted field work in Senegal fell ill of Zika infection upon his return home to Colorado and infected his wife in what is probably the first documented case of sexual transmission of an infection usually transmitted by insects (Foy *et al.,* 2011). Subsequently, in 2012 Researchers publish findings on the characterization of Zika virus strains collected in Cambodia, Malaysia, Nigeria, Senegal, Thailand and Uganda, and construct phylogenetic trees to assess the relationships. Two geographically distinct lineages of the virus, African and Asian, were identified. Analysis of the virus from Yap Island strengthens previous epidemiological evidence that the outbreak on Yap Island originated in south-east Asia (Lanciotti *et al.,* 2008; Duffy *et al.,* 2009; Haddow *et al.,* 2012; Buathong *et al.,* 2015).

The 2007 outbreak continued to the year 2014 and spread to four other groups of Pacific islands: French Polynesia, Easter Island, the Cook Islands, and New Caledonia (Cao-Lormeau and Musso, 2014; Roth *et al.,* 2014). The results of intensive retrospective investigations was reported to WHO on 24 November, 2015 and 27 January, 2016 which indicated a possible association between Zika virus infection and congenital malformations and severe neurological and autoimmune complications (Ioos *et al.,* 2014). In particular, an increase in the incidence of Zika virus infection towards the end of 2013 was followed by a rise in the incidence of Guillain-Barré syndrome (Oehler *et al.,* 2014; Mallet *et al.,* 2015). However, because the island was also experiencing an outbreak of dengue, the link between Zika virus infection and Guillain-Barré syndrome remains suggestive but unproven. However, it became a challenge to the notion that Zika virus infection causes only mild illness (Cao-Lormeau *et al.,* 2014; Oehler *et al.,* 2014; Enserink, 2015).

The French Polynesia 2013-2014 outbreak of Zika virus infection provides evidence of additional route of transmission of Zika virus. The isolation of Zika virus from bloody semen gave the insight of possibly sexual transmission

(Musso *et al.,* 2015), also two mothers and their newborns are found to have Zika virus infection by PCR suggesting the possibility of infants' infections by transplacental transmission or during delivery (Besnard *et al.,* 2014). During the same outbreak, 1505 asymptomatic blood donors are reported to be positive for Zika by PCR. These findings alert authorities to the risk of post-transfusion Zika fever (Musso *et al.,* 2014).

By March 2015 Zika virus infection outbreak hits Brazil though Zika was not suspected at the initial stage, and no tests for Zika were carried out. Nearly 7000 cases of illness with case definition; "person having rash with or without fever, of unknown etiology, and whose clinical profile does not fit in suspected case definitions of dengue, measles or rubella." Cases were first identified in Pernambuco in December 2014. In Maranhao, Rio Grade do Norte, and Bahia, cases were identified in February and March, 2015 (WHO, 2016). In April, 2015 Bahia State Laboratory in Brazil informs WHO that samples have tested positive for Zika virus, and finally in May, 2015 Brazil's National Reference Laboratory confirms by PCR, ZIKV circulation in the country (WHO, 2016).

This is the first report of locally acquired Zika virus disease in the Americas and subsequently cases were confirmed in twelve Brazilian states. By 17 July 2015, Brazil reported detection of neurological disorders associated with a history of Zika virus infection, primarily from the north-eastern state of Bahia. Among these reports, 49 cases were confirmed as Guillain-Barré syndrome. Of these cases, all but 2 had a prior history of infection with Zika, chikungunya or dengue (WHO, 2016).

In stark contrast to these outbreaks, only sporadic cases of Zika virus infection was reported in other countries namely Colombia, Barbados, Mexico, Ecuador, Colombia, Bolivia, Paraguay, Guatemala, Panama, Honduras, Cabo Verde, Bolivarian Republic of Venezuela, Guyana, French Guiana and Martinique, Maldives, Haiti, France, Dominican republic, El Salvador, Nicaragua, Curacao, Suriname, Japan, Chile and territories in the Americas (PAHO, 2015; WHO, 2016; Enfissi *et al,* 2016).

By September 2015, investigators in Brazil noted an increase in the number of infants born with microcephaly in the same areas in which Zika virus was first reported, and by mid-February 2016, more than 4300 cases of microcephaly had been recorded, though may be inflated by over reporting and misdiagnosis. Subsequently, French Polynesian investigators equally retrospectively identified an increased number of fetal abnormalities, including microcephaly, after the Zika virus outbreak in that country (PAHO, 2015; Marcondes *et al.,* 2015; WHO, 2016; Branswell, 2016). Besides, Zika virus was diagnosed in the blood and tissue samples as well as amniotic fluid of a baby with microcephaly and other congenital anomalies dictating additional route of driving the infection (Olivera-Melo *et al,* 2016; Olivera-Melo *et al,* 2016).

To date, 45 countries and territories have confirmed local, vector-borne transmission of Zika virus disease and travel-associated cases in the Region of the Americas since 2015. The total case counts in US and US territories as of September 7, 2016 cumulate 2,964 and 15,869, respectively (CDC, 2016).

DIAGNOSIS

Diagnosis is by testing the blood, urine, or saliva for the presence of Zika virus RNA when the person is sick (Chen and Hamer, 2016; WHO, 2016).

Detection of Viral RNA

i. RT-PCR during the viraemic period between day 3 and 5 after onset of symptoms (serum and saliva).
ii. Detection in urine up to 10 days after onset.
iii. Specific investigation: amniotic and cerebrospinal fluids and tissues (e.g. placenta) (ECDC, 2016).

Serology: Zika-Specific IgM Antibodies

i. IgM antibodies against Zika virus detectable from day 5 after onset of symptoms.
ii. Detection of Zika virus-specific IgM antibodies requires confirmation by plaque-reduction neutralization tests because of cross-reactivity with antibodies against other flaviviruses.

iii. Vaccination status and infections with other flaviviruses must be considered when interpreting the results (ECDC, 2016).

Case number	Year	Location	Description/Notes	Reference
*	1952	Uganda and Tanzania	Serosurvey demonstrating the presence of Zika virus neutralizing antibodies in sera	Smithburn,1952
1	1954	Nigeria	10 years old African female with fever and headache	MacNamara, 1954
2	1956	Nigeria	Experimentally induced in a 34-yr-old European male, residing in Nigeria for 4 ½ months before inoculation; symptoms included headache and fever	Bearcroft, 1956
3	1964	Uganda	28 years European male researcher residing in Uganda for 2 ½ months before illness; provide first proof, by virus isolation and re-isolation, that Zika virus causes human disease	Simpson, 1964
4- 6	1968	Nigeria	Virus isolated from 3 febrile children, aged: • 10 months • 2 ½ years • 3 years No clinical details available	Moore, 1975
7- 8	1979	Nigeria	2 ½ yr-old boy with fever • 10-yr-old boy with fever, headache, and body pains 40% persons tested had neutralizing antibodies to Zika virus (more frequently in younger people), demonstrating high prevalence of immunity in Nigeria. Unreported cases likely misdiagnosed as malaria.	Fagbami, 1979
9*	1973	Portugal	Male arbovirus laboratory worker who had been vaccinated against yellow fever 2 months before infection; with chills, fever, sweating, retro-orbital pain, and pain in the back of the neck and in the joints	Filipe, 1973
10-16	1981§	Indonesia	7 cases in hospitalized patients: • 16-yr-old female • 14-yr-old male • 12-yr-old male • 32-yr-old female • 12-yr-old female • 25-yr-old female • 13-yr-old male All cases had fever; none had rash	10-16
17-5017	2007	Micronesia	75% (i.e. 5000 of 6700 population) Pacific island of Yap residents over 3 years of age were infected. An increase in the incidence of Zika infection towards the end of 2013 was followed by a rise in the incidence of Guillain-Barré syndrome.	Lanciotti *et al.,* 2008; Duffy *et al.,* 2009 Oehler *et al.,* 2014; Ioos *et al.,* 2014; Mallet *et al.,* 2015
5017-5018	2008	Colorado	US scientist conducting field work in Senegal falls ill with Zika infection upon his return home to Colorado and infects his wife ; first documented case of sexual transmission	Foy *et al.,* 2011
	2013-2014	French Polynesia	In French Polynesia;Zika virus was isolated from bloody semen, • 2 mother and their newborn were found to have Zika virus infection by PCR, and • 1505 asymptomatic blood donors are positive for Zika by PCR	Besnard *et al.,* 2014; Musso *et al.,* 2014

Table 1: Zika Virus Infection in Humans, 1952-2016.

Table 1: Zika Virus Infection in Humans, 1952-2016 (continued).

Case number	Year	Location	Description/Notes	Reference
	2015	Brazil	In march 2015, Nearly 7000 cases of illness with case definition; "person having rash with or without fever, of unknown etiology, and whose clinical profile does not fit in suspected case definitions of dengue, measles or rubella. In April 2015 Bahia State Laboratory in Brazil informs WHO that samples have tested positive for Zika virus. To date, 45 countries and territories have confirmed local, vector-borne transmission of Zika virus disease in the Region of the Americas since 2015.	WHO, 2016; PAHO, 2016
	Jan 01, 2015 – Sep 7, 2016.	US States	• Locally acquired mosquito-borne cases reported: 43 • Travel-associated cases reported: 2,920 • Laboratory acquired cases reported: 1 • Total: 2,964 • Sexually transmitted: 24 • Guillain-Barré syndrome: 7	CDC, 2016
	Jan 01, 2015 – Sep 7, 2016.	US Territories	• Locally acquired cases reported: 15,809 • Travel-associated cases reported: 60 • Total: 15,869 • Guillain-Barrésyndrome: 31	CDC, 2016

Prevention, Control and Treatment

Prevention involves decreasing mosquitoes bite in areas where the disease occurs and proper use of condoms (Chen and Hamer, 2016; Oster *et al,* 2016). 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 (WHO, 2016). There is no effective vaccine (Chen & Hamer, 2016).

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 (Chen and Hamer, 2016). While there is no specific treatment, paracetamol (acetaminophen) and rest may help with the symptoms (Chen and Hamer, 2016). Admission to hospital is rarely necessary (ECDC, 2015).

CONCLUSION

Human Zika virus infection appears to have changed in character while expanding its geographical range. The change is from an endemic, mosquito-borne infection causing mild illness across equatorial Africa and Asia, to an infection causing, from 2007 onwards, large outbreaks, and from 2013 onwards, outbreaks linked with neurological disorders including Guillain-Barré syndrome and microcephaly across the Pacific region and the Americas.

The future transmission of Zika infection is likely to coincide mainly with the distribution of *Aedes mosquito* vectors, although there may be rare instances of person-to-person transmission (other than mother to child, e.g. through semen). Beyond the range of mosquitoes, infection has been, and will continue to be, carried widely by international travel.

In areas of Africa and Asia where Zika virus is endemic, the incidence of infection, whether outbreaks will occur, and the reason for the previous lack of recorded cases of adverse pregnancy outcomes or Guillain–Barré syndrome are unknown.

RECOMMENDATIONS

Adequate resources should be directed towards identifying the incidence of Zika infection, distribution of its vector as well as the

environmental factors that can influence emergence of Outbreaks and whether it has any negative health impact in Nigeria and Africa as a whole.

Further research is required to determine whether the recently observed associations with adverse birth outcomes and Guillain–Barré syndrome simply reflect an increased incidence of infection or whether they result from a change in viral virulence.

Furthermore, identified research gaps should be addressed. These include development of discriminating diagnostic tools for flaviviruses, animals models of infection and disease pathogenesis with circulating strains, new vector control products and strategies, effective therapeutics, and vaccines to protect humans against the disease.

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