

**PACIFIC JOURNAL OF MEDICAL SCIENCES**

**{Formerly: Medical Sciences Bulletin}**

**ISSN: 2072 – 1625**



**Pac. J. Med. Sci. (PJMS)**

[www.pacjmedsci.com](http://www.pacjmedsci.com). Email: [pacjmedsci@gmail.com](mailto:pacjmedsci@gmail.com).

---

**ZIKA: A RE-EMERGING INFECTIOUS VIRUS DISEASE OF PUBLIC HEALTH CONCERN**

**CLEMENT E. ANYIWO**

MD, M.Sc, Zeugnis Immun., FMCPATH; FWACP, FICS

Professor of Medical Microbiology & Immunology

American International Institute of Graduate Studies, San Antonio, Texas USA

[caemenike@gmail.com](mailto:caemenike@gmail.com)

**ZIKA: A RE-EMERGING INFECTIOUS VIRUS DISEASE OF PUBLIC HEALTH CONCERN****CLEMENT E. ANYIWO**

MD, M.Sc, Zeugnis Immun., FMCPATH; FWACP, FICS  
Professor of Medical Microbiology & Immunology  
American International Institute of Graduate Studies, San Antonio, Texas USA  
[caemenike@gmail.com](mailto:caemenike@gmail.com)

**ABSTRACT:**

Zika is caused by a flavivirus transmitted by mosquitoes of the *Aedes* species, mainly *Aedes aegypti*. It causes a mild self-limiting illness in people that it infects, leaving most people asymptomatic. However, the recent rise in the spread of Zika virus predominantly in Latin America has been accompanied by unprecedented rise in a number of children being born with abnormally small heads-identified as microcephaly. In addition several countries, including Brazil, which has experienced the world largest Zika outbreaks, reported a steep increase in Guillain Barre Syndrome- a neurological autoimmune disorder that could lead to paralysis and death. Although it has not been definitively proven, evidence is growing that Zika virus causes both microcephaly and Guillain Barre Syndrome. Obviously, these reports made the World Health Organization to declare Zika as a significant global public health concern. Apart from using insecticides to control the spread of mosquitoes, several other approaches are being implemented to prevent Zika virus infection. These include vaccine development and impairing egg-laying female mosquito's ability to transmit infection and also genetic modification and sterilization of male *Aedes aegypti*.

**Keywords:** Zika Virus, Public Health Concern, Brain Damage, Preventive Strategies

*Submitted March 2016; Accepted May 2016*

**INTRODUCTION:**

Nature abhors vacuum and so as the frenzy of Ebola appears to be in recess, the void has to be filled with the advent of Zika, a re-emerging infectious disease spreading explosively around the world and predominantly transmitted by mosquitoes of the *Aedes* species such as the tiger mosquito *Aedes aegypti*, which also transmits Yellow Fever,

(Figure 1) and potentially *Aedes albopictus*.

The Zika virus (ZIKV) is an RNA arbovirus that belongs to the virus family Flaviviridae and the genus Flavivirus and is therefore related to the Dengue, Yellow Fever, Japanese Encephalitis, Chikungunya and West Nile viruses. It is an enveloped virus with icosahedral symmetry and non-segmented single-stranded RNA genome [1, 2]. ZIKV has also been isolated from *Aedes*

*africanus*, *Aedes apicoargentus* and *Aedes vittatus*, to mention a few. Zika virus derived its name from the Zika forest of Uganda, just as Ebola got its name from the Ebola River in Zaire and Lassa from a town in North Eastern Nigeria. It was first isolated in 1947 from a rhesus macaque monkey by scientists of Yellow Fever Research Institute [3 - 5]. A second isolation from *Aedes africanus* followed at the same time at the same site in 1948. When the monkey developed a fever,

researchers isolated from its serum a “filterable transmissible agent” that was named Zika virus in 1948 [6]. ZIKV, like other arboviruses, such as Yellow Fever, Dengue or Chikungunya is maintained in enzootic transmission cycles in the forested areas of Africa, Asia, South America and French Polynesia with the vertebrate hosts as primarily monkeys in the so-called monkey-mosquito-monkey cycle, with occasional transmission to humans.



Figure 1: Adult female yellow fever mosquito, *Aedes aegypti* (Linnaeus), in the process of seeking out a penetrable site on the skin surface of its host Photograph by James Gathany, Courtesy: Center for Disease Control Public Health Image Library [www.cdc.gov/features/stop](http://www.cdc.gov/features/stop)

As of February, 2016 there are no confirmed cases of ZIKV transmission through blood transfusions, although a potential risk is suspected based on a study conducted between November 2013 and February 2014 during the Zika outbreak in French Polynesia, in which 42 (2.8%) blood donors tested positive for ZIKV RNA and were asymptomatic at the time of blood donation [7, 8]. As a safety

measure to protect blood and transplant recipients, the Centers for Disease Control and Prevention (CDC) recommends that blood, tissues or organs should not be obtained from donors diagnosed with ZIKV within six months from date of diagnoses, travelled to a ZIKV hotspot or had sex with a patient diagnosed with ZIKV [9].

**Is it possible for the Zika virus to be transmitted through urine, saliva and semen?**

Brazilian Research Institute recently found active ZIKV in the urine and saliva of some infected patients, but the ability of the virus to infect people through these two body fluids requires to be established through further research [10, 11]. The story with semen is different. In 2016 three cases of sexual transmission were reported. ZIKV was grown from semen. Zika antibodies were demonstrated in a United States biologist studying mosquitoes in Senegal [10], also in 2016 the Dallas County Health and Human Services Department reported a person contacted Zika fever after having sexual contact with an infected person. Fourteen additional cases of possible sexual transmission are being investigated. Reports also showed that ZIKV can stay in the semen indefinitely [11]. This is why men should be more concerned about Zika than women. Common sense therefore dictates that they should be having protected sex to prevent a possible transmission to their partners.

**There are two lineages of the ZIKV:** African and Asian. Phylogenetic studies indicate that the ZIKV spreading in the Americas is mostly closely related to the Asian strain, whereas Western ZIKV is found to be 89% identical to African genotypes, but is most closely related

to the strain found in French Polynesia during the 2013 - 2014 Zika outbreaks [12].

**Symptomatology:** As in malaria, when a person is bitten by a mosquito that has the ZIKV they harbor the virus in their blood, (just as the Anopheles mosquito transmits plasmodia in the blood). When they get bitten by another mosquito, the virus is passed along. Symptoms of ZIKV infection are usually mild. Majority of people (80%) are asymptomatic. Infection manifests as fever, maculopapular rash, muscle and joint pain, malaise, headache and conjunctivitis. These symptoms generally last for 2-7 days [9].

**Treatment:** There is no specific treatment for Zika. Symptoms are palliatively alleviated with over-the-counter medications: Analgesics and antipyretics. Patients are advised to rest and take enough fluids to prevent dehydration and to avoid taking specific non-steroidal anti-inflammatory drugs (NSAIDs), such as, Ibuprofen and Aspirin until the diagnosis of Dengue is ruled out to reduce the risk of bleeding. Acetaminophen (Tylenol) or Paracetamol are recommended [13]. There are no vaccines currently available.

**Complications:** Zika fever is mild but not its complications. Unfortunately babies have to bear the brunt of this seemingly innocuous infection. New research associates the ZIKV

with a condition in which the immune system attacks nerves of fetuses causing muscle weakness, paralysis and even death. This autoimmune disorder is called Guillain Barre Syndrome. In pregnant women also, the virus has been linked to an alarming increase in the rate of birth defect known as microcephaly-an abnormally small head which may cause brain damage, mental retardation, delays in speech, movement and growth. It is suspected that this can only occur during the first trimester of pregnancy when the brain is being formed. However, this relationship has not been established by researchers [4]. More than 4000 new microcephaly cases are suspected to be Zika-related. CDC recommends that pregnant women delay travel to areas where Zika is active; these areas have been expanded to include 37 countries of the Americas, Oceania and the Pacific Islands. CDC current guidelines recommend that pregnant women returning from these areas get tested for Zika. More of the cases in the USA of pregnant travelers are being investigated by CDC [14]. In 2015, Zika virus was detected in the amniotic fluid of 2 pregnant women, whose fetuses had microcephaly, indicating that the virus had crossed the placenta and could have caused mother-to-child infection [14]. In a cohort study of pregnant women in Brazil, Zika infection was associated with growth retardation and fetal death, placental insufficiency and CNS injury and abnormally small heads [15].

**Epidemiology:** Zika was first reported in one of the African countries, and as was earlier mentioned, was discovered in rhesus monkeys in the Zika forest of Uganda in 1947 [3 – 5]. Researchers found that it lived in mosquitoes. First evidence of human ZIKV infection was published in 1952 following the results of serological studies in Uganda, Tanzania and Nigeria. Among 84 people of all ages, 50 individuals had antibodies to ZIKV, all above 40 years old were immune [16]. But it was not until 1954 that the isolation of the ZIKV from humans was published [16]. Subsequently outbreaks have been reported from 1957 - 1981 throughout Africa and Asia and in French Polynesia in 2007 and spread to Latin America in 2014. To date there have been ZIKV outbreaks in 41 countries. Some 312 travel-associated cases in the United States with Zika-viremia have been reported, including 27 pregnant women and 6 sexually transmitted, and also a total of 352 locally acquired cases in the United States territories, including a case of Guillain-Barre Syndrome [11]. Since Brazil reported the ZIKV in May 2015, infections have occurred in about 24 countries of the Americas. The disease now has explosive pandemic potential. A German biotechnology company- Genekam- claims to have developed a DNA-based test that can detect ZIKV in the blood and this can determine if a person is a carrier of ZIKV [17]. If it proves to be true it will be a

great tool in epidemiological studies and an adjunct to detection of Zika antibodies.

**Prevention and Control:** Prevention of ZIKV infection is completely dependent on the control of the mosquito vector and limiting person-person contact, the goal of mosquito-based surveillance is to quantify human risk by determining local vector presence and abundance. In order to quickly identify and mitigate a mosquito-borne disease outbreak, establishing and maintaining a local surveillance program is critical. The vector for Zika, *Aedes aegypti*, is an "urban mosquito" which likes to feed on people and breed in water-filled habitats like plant containers, bird-bath and pools of standing water which we too often leave around our dwellings. First line of approach in getting rid of mosquitoes is to get rid of their habitats. Spraying of insect repellents is another strategy. Some people use a combination of 20% Picaridin and 30% oil of lemon eucalyptus. Chemical pesticides ("larvicides" and "adulticides") are effective in killing mosquito eggs, larvae, pupae and adult mosquitoes. It is also advisable, just as it is recommended in the case of West Nile virus, to wear long sleeve shirts and trousers when outside during dusk and dawn when mosquitoes are most active [9, 18].

As it has always been the case in diseases that have no vaccine, Non-governmental organizations (NGOs) should be involved in

ZIKV awareness by mobilizing community members to take specific actions, as has been advised, to prevent further infections with the ZIKV. One of WHO's responses to the reduction of mosquito population and thus contain Zika is providing training on clinical management, diagnosis (strengthening capacity of laboratories to detect the virus) and vector control (providing larvicide to treat standing water sites) through a number of its collaborating centers [9].

Forrest innovations- an Israeli-based biotech company has another solution to contain the spread of disease-carrying mosquitoes, especially *Aedes aegypti* that transmits the ZIKV. They plan to breed and release sterile mosquitoes to prevent reproduction and eventually reduce its population. The company's mosquito control program called "NoMoreMos" uses a technique- "sterile insect technique" that sterilizes male mosquitoes at a larval stage by applying a topical solution that renders them sterile but does not modify their genetic code. The company targets Rio de Janeiro, Brazil which has seen the world's largest Zika outbreaks and will host the 2016 Summer Olympics. Its more immediate concern is to prevent transmission among visitors and athletes. To achieve this, the company plans to release some 25 million sterile mosquitoes starting in June and through the Olympics in August [19]. The choice of male mosquitoes is

justified because sterilized male mosquitoes can no longer fertilize female eggs and male mosquitoes do not bite.

Another approach to contain the Zika disease was pioneered by a British biotech firm, Oxitec working with Brazil has genetically modified the *Aedes* mosquito in such a way that the males produce off-springs that cannot reproduce. “The USA FDA has granted preliminary approval for Oxitec to release the insects in Florida, after determining that there would be no significant impact to human, animal and plant life from the experiment or reducing mosquito populations that spread Dengue, Chikungunya and Zika virus” [20].

The Australian approach to contain the spread of mosquitoes is to infect them with *Wolbachia* bacterium that lives only in insect cells and impairs the mosquito ability to transmit infections such as Dengue and Zika. If mosquitoes cannot become infected with ZIKV, they cannot transmit the virus between people [19].

As was mentioned earlier there is no vaccine or preventative drug for Zika. According to the WHO experts, the priority should be to develop inactivated vaccines that are safe to use in women of reproductive age and pregnant women. Vaccine production generally is very technically challenging, need to be pathogen-specific and also capital intensive [21]. Subsequently, as of March 2016 a total of 18

companies and institutions, including the National Institute of Health (NIH) Vaccine Research Center and India’s Bharat Biotech International that started developing Zika vaccines have faced the challenges using two approaches: “Recombinant” involving genetic engineering and “Inactivated” where the virus is incapable of reproducing itself but can still trigger immune response [21 – 25]. Some other companies involved in vaccine development are Brazil’s Butantan institute, Public Health Agency of Canada, New link Genetics, Merck & Co, Sanofi, Glaxo Wellcome and Japanese Takeda Pharmaceutical. The Director of National Institute of Allergy and Infectious Diseases (NIAID) in the USA - Anthony Fauci recently, in a CNN television interview stated that researchers on West Nile virus have developed a “platform” for a flavivirus vaccine that might be quickly adaptable to Zika if the process can skip the regulatory hurdles of the USA FDA.

#### **CONCLUSION:**

The Director-General of WHO-Margaret Chan, speaking recently in Geneva said that nobody could predict how far the ZIKV would spread, causing more and more cases of Guillain Barre Syndrome and Microcephaly in newborns when pregnant women are infected. But “if this pattern is confirmed in and beyond Latin America and the Caribbean, the world will face a severe crisis”. Subsequently on February 1,

2016 the WHO declared ZIKV infection a public health emergency of international concern [26]. In 1992 the USA National Academy of Sciences (NAS) warned that we have not yet conquered infectious disease as a consequence of human activities and we were likely to see more and more pathogens spreading beyond their ancestral ranges. In essence what NAS was saying is that human factors are responsible for human plight that we experience from time to time. Some of these factors are increasing human populations going into new places and coming in contact with new pathogens either emerging or re-emerging such as Ebola or Zika. Other factors are more and faster travels, growing urbanization and erosion of traditional public health infrastructures, such as mosquito control programs. To the list we can add climate change which can be conducive for some mosquito-borne diseases. A key lesson learned from the 2014 Ebola outbreaks is the need for galvanizing appreciable international response and avoiding panic and overreaction [28]. I think the same should be applicable in the ZIKV disease outbreaks.

In the absence of a vaccine or a preventative therapy the only option remaining is preventive strategies including public enlightenment. It is on this premise that I would like to suggest what I call the 7 “Commandments” for the prevention of ZIKV infection [27].

1. You should avoid mosquito bites, particularly at dusk and dawn when the mosquito is most active.
2. You should wear long-sleeved shirts and long pants to conceal body parts that may serve as targets.
3. You should stay in places with air conditioning or that use window or door screens to keep mosquitoes outside.
4. You should sleep under a mosquito bed net if you are in Zika-infested areas and not able to protect yourself otherwise from mosquito bites.
5. If you are suspected of having Zika then remember to wear condom if you cannot observe abstinence to prevent sexual transmission of the virus to your partner.
6. Use Environmental protection Agency (EPA) approved, and therefore safe and effective, insect repellent such as Permethrin as directed.
7. Do not use insect repellent on babies younger than 2 months of age. Instead dress infants or small children with clothing that covers arms and legs to prevent mosquito bites.

Even when vaccines become available these recommendations should still be in force as a public health norm.

#### REFERENCES:

1. Knipe DM and PM Howley. Fields Virology (5th Edit) Lippincott Williams & Wilkins 2007, pp. 1156 & 1199.
2. Faye OF, Freire CCM, Iamarino A, Faye O, de Oliveira JVC, Diallo M, Zanotto PMA, Sall AA and B Bird B. Molecular evolution of Zika virus during its emergence in the 20th century. Neglected Tropical Diseases 8 (1): 2014, e 2636.
3. Sikka V, Chattu VK, Popli RK, Galwankar SC, Kelka D, Sawicki SG, Stawicki SP and

- TJ Papadimos. The emergence of Zika virus as a global security threat. A review and a Consensus Statement of the INDUSEM Joint Working Group. *Journal of Global Infectious Diseases* 8(1):2016,3-15.
4. Malone RW, Homan J, Callahan MV, Glasspool-Malone J, Damodaran L, Scheinder AB, Zimler R, Talton J, Cobb RR, Ruzic I, Smith-Gagen J, Janies D and J Wilson. Zika virus: Medical countermeasure development challenges. *Neglected Tropical Diseases* 10 (3): 2016, e0004530.
  5. Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, Huy R and SC Weaver. Genetic characterization of Zika virus strains: Geographic expansion of the Asian Lineage. *Neglected Tropical Diseases* 6 (2): 2012, e1477.
  6. Enfissi A, Codrington J, Roosblad J, Kazanji M and D Rousset. Zika virus genome from the Americas. *Lancet* 387 (10015): 2016, 227-228.
  7. "Zika virus infection outbreak, Brazil and the pacific region". Stockholm: European Center for Disease Control and Prev. May 25, 2015.
  8. Musso D, Nhan T, Robin E, Roche C, Bielaire D, Zisou K, Shan Yan A, Cao-Lormeau VM and J Broult. " Potential for Zika virus transmission demonstrated during outbreak in French Polynesia, Nov. 2013-Feb. 2014. *Euro-surveillance* 19 (14): PMID 24739982, 2014.
  9. "Zika Situation Report". World Health Organization, February 5, 2016.: [www.who.com](http://www.who.com)
  10. Zanluca C, de Melo VC, Dos Santo GI and K Luz. First Report of autochthonous transmission of Zika virus in Brazil. *Memorias de Instituto Oswaldo Cruz* 110 (4): 2015, 569-572.
  11. Center for Disease Coinrol and prevention Mor. Mortal. Wkly Rep. 2016.
  12. Lanciotti RS, Lambert AJ, Holodniy M, Saavedra S and CC Leticia. Phylogeny of Zika virus in Western Hemisphere. *Emerging Infectious Diseases* 22 (5): 10. 3201, 2016.
  13. Symptoms, Diagnosis and Treatment. Center for Disease Control and Prevention, Atlanta. 4 Mach, 2016. [www.cdc.gov/features/stop](http://www.cdc.gov/features/stop)
  14. Oduyebo T, Petersen EE and SA Rasmussen. Update: Interim Guidelines for health care providers caring for pregnant women and women of reproductive age with possible Zika virus exposure-United States, 2016. *Morb Mortal Wkly Rep* 65: 1-6, 2016.
  15. Martines RB, Bhatnagar J and MK Keating. " Notes from the Field: Evidence of Zika Virus infection in Brain and Placental Tissues from Two Congenitally Infected Newborns and Two Fetal Losses-Brazil, 2015" *Morbidity Mortal Wkly Rep* 65 (06): 1-2, 2015
  16. Zika virus (06) Overview 2016-02-09 19: 58:3. Pro. MED-mail. International Society for Infectious Diseases, 2016.
  17. Ugbomoiko US. Lassa and Zika fevers: Poor disease control fuels killer viruses in Nigeria 2016.. [www.vanguardngr.com](http://www.vanguardngr.com)
  18. Mitchell C. Pan American Health Organisation (PAHO) Statement on Zika Virus Transmission and Prevention. [www.paho.org](http://www.paho.org), 2016.
  19. Mosquito control program. No More Mos. [www.forrestinnovations.com](http://www.forrestinnovations.com), 2016.
  20. Researchers release genetically modified mosquitoes in Brazil. [www.dailymail.co.uk/zikavirus](http://www.dailymail.co.uk/zikavirus), 2012.
  21. Maron DF. First Dengue Fever Vaccine Gets Green Light in 3 Countries. *Scientific American*, January, 2016.
  22. World Health Organization and experts prioritize vaccines, diagnostics and innovative control tools for Zika R&D, WHO 9 March, 2016. [www.who.com](http://www.who.com)
  23. Stemberg S. Vaccine efforts underway as Zika virus spreads. *US News and World Report*. 28 January, 2016.
  24. Bagla P. How Bharat Biotech made its breakthrough in developing a vaccine for Zika virus. *Huntington Post (India)* February, 9 2016.
  25. Siddiqi Z. Bharat Biotech says working on two possible Zika vaccines. *Reuters*, 8 February, 2016.
  26. World Health Organization declares Zika as a global emergency. *BBC online*. 1 February, 2016.
  27. Centers for Disease Control and Preventions, [www.cdc.gov/features/stop](http://www.cdc.gov/features/stop) Mosquitoes, 2016.
  28. Anyiwo CE. Ebola: Enough of the hysteria. *Pac J. Med. Sci.* vol. 14 No. 1 Jan, 2014, 30-37: [www.pacjmedsci.com](http://www.pacjmedsci.com) .