Zika Virus in the Americas: An Environmental Health Perspective

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Phylogenetic studies suggest that ZIKV may have been introduced to Brazil, and therefore to the Americas, in 2014 during the World Spring Canoe Championship held in the city of Rio de Janeiro. Since then the virus has spread across Latin America, Caribbean, and North America. It seems clear that Aedes aegypti and, to a lesser extent, Aedes albopictus are the main vectors of the pathogen. ZIKV infection symptoms are similar to other flaviviruses such as a dengue infection and therefore can be easily confounded. Currently, the ZIKV maintains two life cycles. The first, and the original one is the sylvatic/enzootic cycle that occurs in Africa. The second life cycle is the suburban-urban transmission cycle that emerged through natural evolution. ZIKV has gained the ability to maintain this human-endemic cycle in urban and suburban areas. ZIKV has never been isolated from non-primates, so it is not clear whether other species can act as reservoir hosts. Several reports have been made of non-vector ZIKV transmission including breast-milk feeding, blood transfusion, sexual intercourse, saliva, urine, and physical contact (sweat, tears). A major global concern with ZIKV infection is the reported increase in cases of microcephaly and Guillain-Barre Syndrome (GBS) in the Americas after the recent ZIKV outbreak. Currently, there is no available vaccine for ZIKV. Therefore, prevention of ZIKV infection must be emphasized by local public health authorities promoting collective responsibility and engagement for integrated vector management through environmental management, biological control, and as a last resource chemical control. [*P R Health Sci J 2018;37(Special Issue):S5-S14*]

Key words: ZIKV, Aedes aegypti, Americas

I. Discovery and original distribution

The first isolation of the ZIKA virus (ZIKV) was made in April 1947 from the serum of a sentinel rhesus monkey from the ZIKA forest in Uganda during surveillance for yellow fever virus (YFV) (1). Subsequently, the virus was isolated from various species of *Aedes* mosquitoes including Aedes africanus (2). During the following years, the virus expanded its original African geographic distribution to the Asian continent. ZIKV is an arbovirus belonging to the Flaviviridae family, is an emerging pathogen that is currently spreading rapidly across the Americas raising concerns about the possible impacts to public health (3). The term arboviruses define viruses maintained in nature through biological transmission between a vertebrate host and a hematophagous arthropod mainly mosquitoes (4).

II. Phylogeny of ZIKV

The ZIKV belongs to the Flavivirus genus (RNA viruses of a single-strand), that includes some tropical viruses like the West Nile virus (WNV), dengue virus (DENV), and the yellow fever virus (YFV) (5). The genus contains 53 species divided into 3 clusters: tick-borne viruses, mosquito-borne viruses, and viruses with no known vector (6, 7). The ZIKV first major outbreaks, outside continental Africa and Asia, occurred in the Yap Island (part of the Federated States of Micronesia) in 2007 and the French Polynesia in 2013. Regarding phylogeny, the ZIKV French Polynesian strain is closer to the strain isolated in Cambodia, Asia, in 2010 than to the ZIKV 2007 Yap strain (7,8). Both of them belong to the Asian lineage (9). The analyses of two isolates collected during the French Polynesian epidemic evidenced genomic microevolution during the outbreak (10).

In the Americas, ZIKV samples were available from Brazil (11) Puerto Rico, Guatemala, and Colombia (12). All of the sequences showed more than 99% nucleotide identity with the French Polynesian strain. These American strains can constitute a "Western Hemisphere group" within the Asian genotype (13).

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III. Arrival to the Americas

In 2015, a ZIKV outbreak was reported in Brazil and henceforth has spread across the Latin America, Caribbean, and North America (5). Phylogenetic studies suggest that ZIKV may have been introduced to Brazil in 2014 during the sporting event World Spring Canoe championship in Rio de Janeiro (14). In that event participated the following four Pacific countries, in which the ZIKV was already present: French Polynesia, New Caledonia, the Cook Islands, and Easter Island (7).

The scenario in Brazil was ideal for ZIKV emergence because the vectors Aedes aegypti and Aedes albopictus are widely distributed within the country (15). In December 2015, autochthonous ZIKV infections were reported in 12 additional countries of the Americas that included El Salvador, French Guiana, Guatemala, Haiti, Honduras, Martinique, Mexico, Panama, Paraguay, Puerto Rico, Suriname, and Venezuela (16). During January 2016, ZIKV was also present in Barbados, Bolivia, Dominican Republic, Ecuador, Guadeloupe, Guyana, Nicaragua, and the U.S. Virgin Islands (17).

By November 17, 2016, 48 countries in the Americas had reported local mosquito-borne transmission of ZIKV. To that date, the total number of confirmed cases was 171,553 (18). During the same month, 4, 444 confirmed ZIKV cases were reported in the United States of America to the database ArboNET. Of that total, thirty-six cases were the result of sexual intercourse with a person infected with the ZIKV. Also, 182 were local cases from the state of Florida. Precisely, the state where the first local reported case, in the United States, occurred in July 2016 (12). Unfortunately, by November 17, 2016, 33 newborn infants and pregnancy losses with birth defects were reported to the United States ZIKA Pregnancy Registry (12).

In summary, until August 25, 2017, 48 countries and territories in the Americas confirmed autochthonous, vector-borne transmission of ZIKV disease (19). Also, since October 2015, a total of 27 countries and territories in the Americas have reported confirmed cases of congenital syndrome associated with ZIKA virus infection (19). Also, five countries reported sexually transmitted ZIKA cases since the beginning of 2015 (20). Finally, regarding the ZIKV capacity to cause congenital damage, Ali and collaborators indicate that unlike other flaviviruses the ZIKV makes efficient use of the cell-surface receptor AXL to enter the fetal bloodstream to reach fetal tissues and lead to microcephaly in neonates (21).

IV. Ecology of the ZIKV

ZIKV life cycles

Most arboviruses are perpetuated in transmission cycles independent of human hosts. However, those with sylvatic cycles often infect people who invade their natural habitats (22). In the case of ZIKV, previous studies indicate that non-human primates were the primary vertebrate hosts, with the sporadical participation of humans in the transmission cycle. Currently, the ZIKV maintains two life cycles (23, see Figure 1).

The first and the original one, is the sylvatic/enzootic cycle that occurs in Africa. This cycle is thought to be maintained primarily between non-human primates (apes and monkeys) and mosquitoes. In this cycle, humans are incidental hosts. But in Asia, some scientists believe that humans have become the principal host for the Asian ZIKV lineage (24,25).

Figure 2 depicts more details concerning both the sylvatic and urban cycles of the ZIKV (24) and also of the potential modes of human to human transmission of the virus.

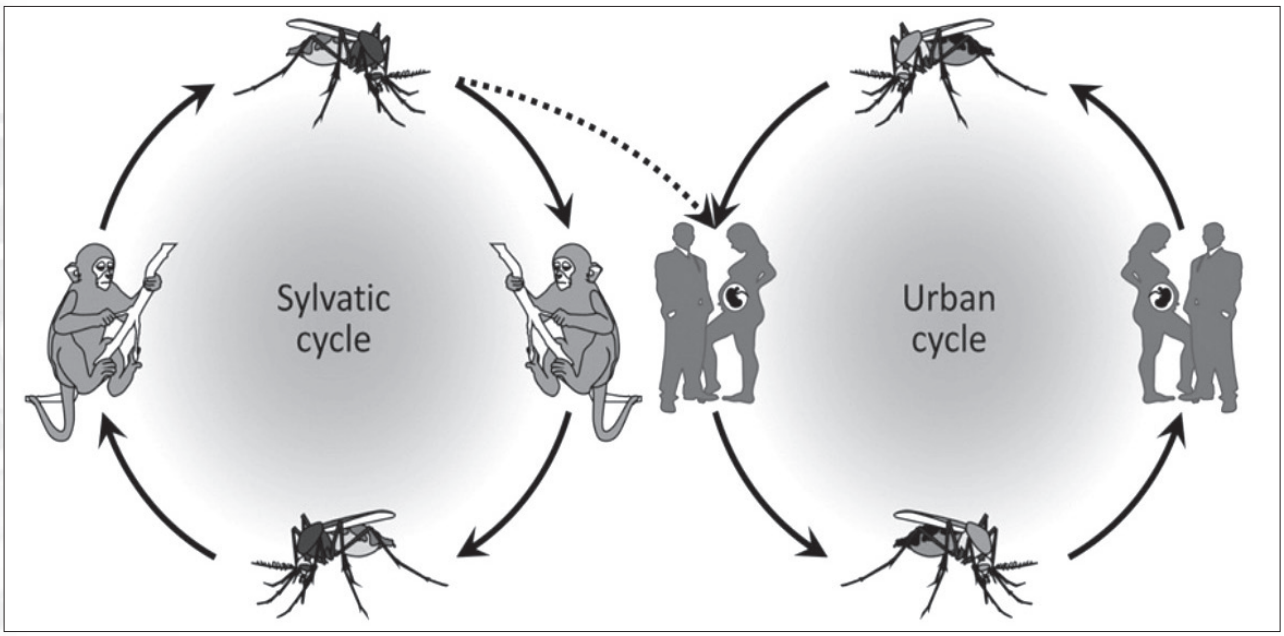

Figure 1. Vector-borne transmission of ZIKV. The two mosquito-driven transmission cycles: a. the sylvatic cycle –the virus cycles between non-human primates and arboreal mosquitoes, b. the urban cycle, the virus cycles between humans and urban mosquitoes. Reproduced with permission (23).

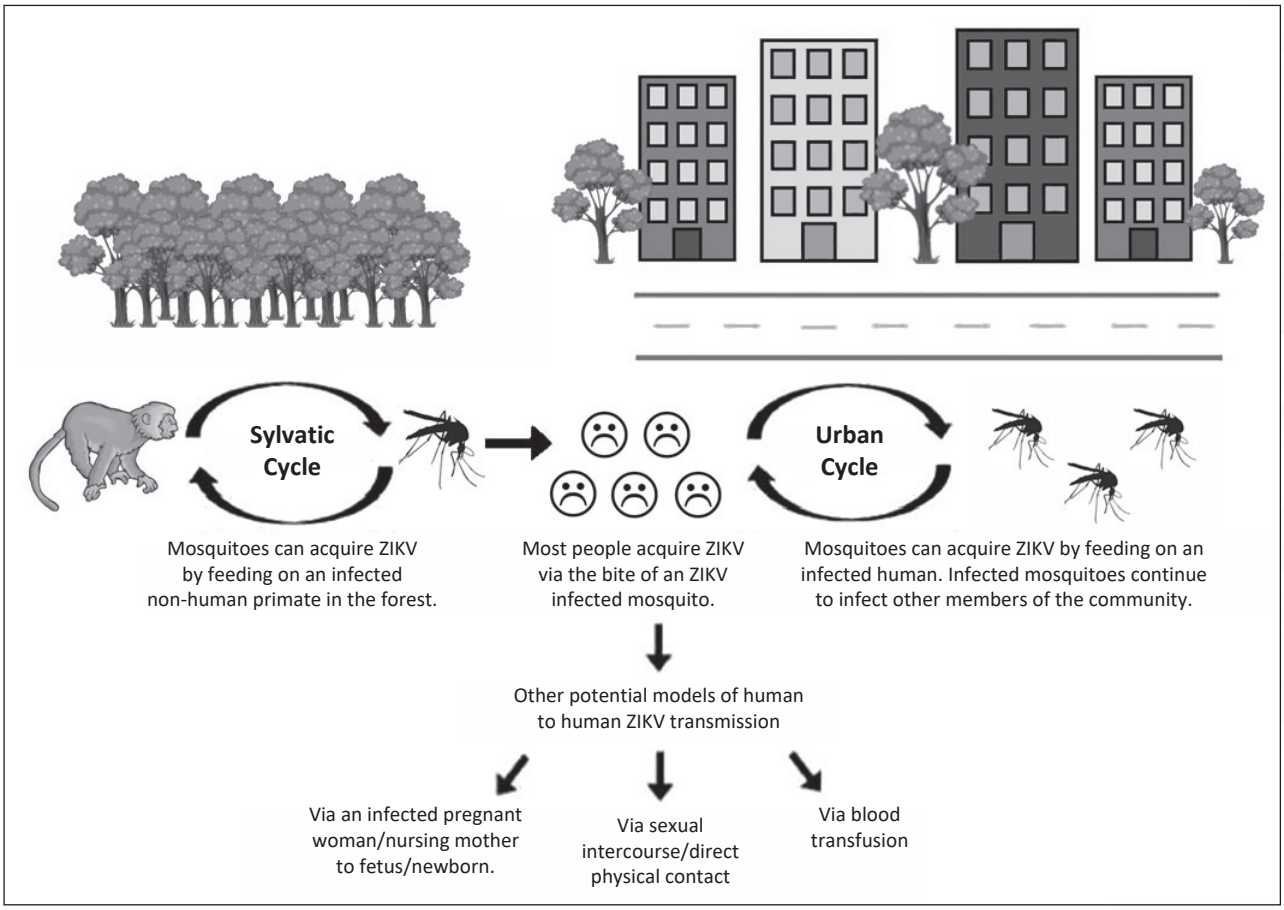

Figure 2. Sylvatic/enzootic and urban transmission cycles of ZIKV. Reproduced with permission (24).

The second life cycle is the suburban-urban transmission cycle that emerged through evolution (24). ZIKV has gained the ability to maintain this human-endemic cycle in urban and suburban areas. In this scenario, humans serve as the source, carrier, and multiplier of ZIKV for non-infected mosquitoes (22). This last, human-adapted cycle, can cause and sustain ZIKV outbreaks (5).

In places without non-human primates, such as the Island of Yap (in Micronesia) and French Polynesia (25, 26), the ZIKA virus is most probably maintained in a human to mosquito to human cycle, implying that the virus has adapted to humans as a reservoir host (7).

Mosquitoes in the transmission cycle

The ZIKV was first isolated from Aedes africanus (1) and, several years later from Aedes aegypti which is the main and natural vector for the virus (27, 28). Until recently, the virus has been isolated from17 different Aedes mosquitoes' species as well as Culex perfuscus, Mansonia uniformis, Anopheles coustani, and Anopheles gambiae mosquitoes (3, 22, 24). In recent years Aedes albopictus was also confirmed as a competent vector (22). In the Americas, the principal vector species, responsible for spreading ZIKV, are Aedes aegypti and Aedes albopictus (29).

By now, it seems clear that Aedes aegypti and, to a lesser extent, Aedes albopticus are the main vectors implying that humans probably serve as primary amplification hosts when their viremia is sufficient in duration and magnitude (26). Apparently, as in other flaviviral infections, virus dynamics is related to: a specific mosquito species, the mosquito's population density, competence, and behavior in a specific geographical area (30).

Aedes aegypti vs Aedes albopictus

Aedes albopictus has a great advantage over Aedes aegypti in terms of expanding its geographical limits. This mosquito species, contrary to Aedes aegypti, can hibernate and survive in cool temperature regions of the world (31). It can also transmit the virus very efficiently. This was shown during a ZIKV epidemic that occurred in the Central Africa country of Gabon in 2007. In that event, among all the tested mosquito species the virus was also detected, in addition to Aedes aegypti, in Aedes albopictus (32). This is an indication that Aedes albopictus can play an important role in the virus transmission.

The fact that both Aedes mosquito species can effectively transmit ZIKV represents a big obstacle for their prevention and control measures. Part of the problem is that both species grow very close to human populations, and also feed on humans.

A difference, between them, is that while Aedes aegypti feed almost exclusively on humans, during daylight hours (typically resting indoors). Aedes albopictus is usually exophagic and (in addition to humans) it also bites domestic and livestock animals (33, 7), However, it has been observed that in some occasions Aedes albopictus prefers to feed on humans. Some scientists believe that this species can also display an anthropophilic behavior similar to that of Aedes aegypti (34).

Therefore, the methods of control for a species may not be as effective to control the other. Moreover, in case of a population reduction of Aedes aegypti, in a geographical zone, Aedes albopictus may quickly invade the area due to its opportunistic nature (35).

ZIKV vector and host preferences

The isolation of a virus from a mosquito is not evidence that it is a vector of the virus. To demonstrate that a mosquito is a vector, first it must be shown to be capable of transmitting a pathogen (36). For example, the competence of Aedes aegypti to transmit ZIKV depends on the mosquito strain (37).

However, Aedes aegypti, with a poor competence nature but high population density, has been found to be a vector of viral epidemics (38). In the case of Aedes albopictus, the results from experiments have found that this mosquito species is capable of transmitting 27 arboviruses, including the ZIKV (39). All the previous data, tend to indicate that ZIKV lacks a clear pattern of preference for animal species and a specific mosquito vector species.

Reservoir species

ZIKV antibodies have been detected in several monkey species in Africa and Asia (40) and human and monkey serum samples have been examined. Researchers found that ZIKV seroprevalence was higher in humans (44.1%) than in orangutans (8.5%). Finally, they concluded that orangutans possibly were infected with ZIKV from a human reservoir or recently established sylvatic cycles (7, 40) and that nonhuman primates may be reservoir hosts for the ZIKA virus in Asia.

Other possible reservoir species

Several studies detected antibodies for ZIKV in sheep, bats, rodents, and goats (41). The accumulated evidence indicates that there is no clear association between ZIKV and a particular animal species. However, ZIKV has never been isolated from non-primates, so it is not clear whether other species can act as reservoir hosts (7, 42).

V. Environmental factors

The following environmental factors can enhance an arbovirus epidemic: disruption and destruction of terrestrial and aquatic ecosystems, urban sprawl, international travel, urban population growth, and climate change. Those factors can also trigger the emergence of yet unknown pathogens (43). Therefore, to better understand the complex dynamic processes of the ecosystems that allow the coevolution of arboviruses with their respective vectors, there is an urgent need to conduct comprehensive and integrated research in those areas.

Also, is very important to determine the possible establishment of a sylvatic cycle within the Americas, including susceptible animal populations that can serve as reservoirs of the ZIKV. This can have a significant impact on public health in the New World (25).

Factors in the emergence and resurgence of arboviruses

There are several extrinsic environmental and intrinsic genetic factors associated with the emergence and resurgence of arboviruses (7). These factors include: overuse and uncontrolled spraying of insecticides; degradation and destruction of natural ecosystems by human activities (42, 43); human population growth with the associated urbanization (44, 45); climate change (44); expansion of the geographic distribution of mosquito vectors (46); adaptation to new reservoir hosts (47); genetic changes for CHIKV (48), DENV (49), and WNV(50); lack of effective mosquito control (51); and increased travel around the world (52).

VI. General symptoms

ZIKV infection symptoms are similar to other flaviviruses such as a dengue infection and therefore can be easily confounded (21). Around 80% of human ZIKV infections are asymptomatic, with a small group of cases presenting mild clinical symptoms similar to the flaviviral and influenza infections (24). Clinical manifestation in symptomatic cases tends to appear after an incubation period of 3 to 12 days and are reported to be characterized by fever, skin rashes (exantherma), myalgia, arthralgia, conjunctivitis, gastrointestinal disturbance, and headaches (21). The most common systemic manifestations include a febrile episode (≤ 37.9°C) followed by maculopapular rash involving the face, trunk, limbs, hand palms and feet soles, which can be pruritic and may persist from 2 to 14 days (42). Conjunctivitis has frequently been described and is usually non-purulent. Arthralgia and myalgia typically affect hands, knees and ankle joints with average duration 3.5 days (8). Some non-specific symptoms can occur, but they are less frequent, including anorexia, headache, dizziness, cough, sore throat, loose bowels, nausea, vomiting, retinal abnormalities, hypertensive iridocyclitis, and retro-orbital pain. Severe disease is uncommon, and most cases do not require hospitalization. Table 1 compares the most common symptoms of Dengue, ZIKA, and Chikungunya viruses (21).

VII. Non-vector ZIKV transmission

Maternal transmission or prenatal transmission

ZIKV has been detected in microcephalic neonates born to mothers with a history of ZIKV infection during pregnancy (53). It is postulated that ZIKV can cross the placenta and subsequently, infect fetal nervous tissues. This statement is supported by the following evidence: detection of ZIKV RNA

Table 1. Common clinical manifestations of Dengue, Zika, and Chikungunya viruses*

Symptom	DENV	ZIKV	CHIKV
Onset post infection	4-7 d	1 and 5 d become ill	3-7 d
Fever	>38°C	No or mild fever	High fever > 38°C
Headache	More common	Common	Common
Exantherma	Common	Very Common	More Common
Itch	Common	Common	Common
Arthralgia	Yes	Common	Very common
Myalgia	More common	Common	Common
Conjunctivitis	None	Very common	Yes/none
Thrombocytopenia	Very common	Less common	None
Low levels of blood cells and platelets	Very common	None	Common
Bleeding disorders	Very common	None	Yes/none
Shock	Yes/none	None	None
Recovery	6-7 d, only DF	4-7 d	< 1 week

*(21) Modified by Luis A. Bonilla-Soto. Legend: d = days; DF = dengue fever.

and antigens in the amniotic fluid, placenta, and fetal brain tissue and the observation of ZIKV particles in fetal brain via electron microscopy (5, 29). The accumulated evidence suggests the potential ability of ZIKV to be transmitted to the fetus and the possible role of ZIKV in the development of microcephaly (5).

Perinatal transmission

Additional evidence, from perinatal transmission, comes from two babies born in French Polynesia during the ZIKV epidemic. However, infection during delivery was not discarded (53). Sera from the mothers were positive for ZIKV within 2 days post-delivery and those of their newborns within 4 days after birth (24). A high ZIKV RNA load was found in breast milk samples.

Sexual transmission

In Tahiti, French Polynesia, a high ZIKV RNA load was confirmed in semen of patient who sought treatment of hepatospermia during outbreak that occurred in December 2013 (54). Female to male transmission of ZIKV was reported in New York City as a result of unprotected sexual intercourse (55). Some other cases of sexual transmission of ZIKV were documented in Texas, USA (56), and in the city of Florence in Italy (57).

Blood transfusion transmission

Also, ZIKV has high potential to be transmitted via blood transfusions. This was observed during the French Polynesian epidemic. Around 3% (42/1505) of blood donors, asymptomatic at the time of donation, were found positive for ZIKV infection by specific RT-PCR (24).

Transmission through saliva and urine

Another non-vector transmission route of the ZIKV is through saliva. The virus has been detected in saliva samples (53) with higher frequency than in blood samples (58). Therefore, saliva is another transmission source that must be taken into account.

The transmission of the ZIKV though urine has also been reported. In Rio de Janeiro, Brazil, five saliva samples and nine urine samples were collected from nine patients with acute phase symptoms. ZIKV was isolated from a saliva sample and also from a urine sample. The researchers found that the viral load was higher in urine samples than in saliva samples (59).

Transmission through breast-milk

ZIKV has also been detected and transmitted through breast milk. This was the case of three lactating mothers that transmitted the virus to two of the three newborns (53). However, more evidence is still needed to support this conclusion of transmission of ZIKV through breast milk (60). ZIKV RNA and infectious viral particles have been detected in high loads in the breast milk of infected mothers (61). Flavivirus transmission, such as DENV and WNV, via breastmilk have been previously reported (62).

Transmission by physical contact

The first case of ZIKV transmission via physical contact was reported in the United States during September 2016 (63). The report informed the transmission of ZIKV from an infected 73-year-old man (living in Salt Lake City, Utah) to his healthy 38-year son. The old man returned to the United States from southwest Mexico (a ZIKV region). Several days later he was hospitalized and tested positive for ZIKV. During his hospitalization, he was visited by his son. Posteriorly, the son also developed ZIKV symptoms. The old man died four days after his admission. The man's son informed that during the hospitalization period he wiped with his bare hands his father's watery eyes. None of the healthcare workers who had contact with the patient, but were wearing protective gloves, reported having symptomatic illness.

VIII. Modes of detection

During ZIKV testing, cross-reactivity to the Flaviviruses often occurs due to close-relatedness and co-circulation of other Flaviviruses in ZIKV endemic regions. Thus, a high proportion of the ZIKV infections in the region will be secondary flavivirus infections with complicated serology (64). Detection of ZIKV is best during the acute-phase. However, it is difficult to determine the period of onset of symptoms as the majority of the cases are asymptomatic.

Reverse Transcription Polymerase Chain Reaction (RT-PCR) Detection

Real-time and conventional RT-PCR are the most common approaches utilized in diagnostic labs owing to their specificity and ability to differentiate ZIKV from other flaviviral infections (65). RT-PCR allows for rapid, specific, and reliable ZIKV RNA detection during the acute-phase, as compared to other modes of detection.

ZIKV RNA has been reported to be detected in the saliva of infected individuals, often more readily compared to blood samples (58). The choice and combination of samples chosen for testing are highly dependent on the stage of infection. It is recommended to perform RT-PCR on both blood and saliva/urine samples to increase test sensitivity, particularly during the late stage of infection (66, 58). In addition, alternative sampling of urine or saliva reduces invasiveness and hence, is advantageous for diagnosis in neonates and infants (64). For prenatal testing, amniotic fluid is predominantly collected for molecular analysis.

Antibody detection

Immunoglobulin (Ig) G/M Enzyme-Linked Immunosorbent Assay (ELISA) IgM/IgG ELISA involves the detection of ZIKV-specific antibodies in the serum (67). IgM antibodies are known to develop within a few days' post onset of symptoms and can last up to 3 months. But, regarding the IgG antibodies, they develop after IgM and can last from a few months to years. IgM specific to ZIKV has been developed at the Centers for Disease Control and Prevention, Atlanta (42). However, studies have reported complications during diagnosis due to sera cross-reactivity of ZIKV IgM to antibodies against other Flaviviruses, often in patients with a history of flaviviral infection or vaccination (64). According to Hayes (2009), cross-reactivity was predominantly noted with DENV, as compared to other Flaviviruses (42).

Plaque Reduction Neutralization Test (PRNT)

PRNT is used for virus-specific neutralizing antibody titer quantification (68). The test is reported to have improved specificity compared to ELISA. Hence, it is often used in addition to ELISA to rule-out false positive antibody response (42, 64).

IX. Diagnosis of ZIKV

Serum

The detection of viral RNA through RT-PCR in serum is the most sensitive and specific method, and the current gold standard test for the diagnosis of the ZIKV infection (69).

RT-PCR is very useful in areas where different arboviruses are present. It is recommended to perform immunoglobulin M (IgM) antibodies and plaque reduction neutralization test (PRNT) on samples collected 4 days after onset of symptoms. Also, IgG antibodies should be looked for in serum in the acute and convalescent phase of patients (70).

Saliva

Molecular techniques can also be used to test for ZIKV RNA presence in fluids like saliva and urine (54, 66). The use of saliva increases the rate of molecular detection of ZIKV at the acute phase of the disease. Saliva can be used when blood is difficult to collect like with neonates and children (54).

Urine

Urine samples are useful for diagnosis of ZIKV infections. The analyzed sample tested positive for ZIKV more than 10 days after onset of disease (66). This was a longer period compared to that for serum samples.

Clinical diagnosis

ZIKV outbreaks in areas where other flavivirus species are endemic can represent a diagnostic challenge due to cross-reactivity (71).

Differential diagnosis

DENV and CHKV can easily be misdiagnosed with ZIKV because of an inconclusive clinical diagnosis due to an unreliable serological analysis. Therefore, it is recommended to perform a differential diagnosis to distinguish between the viruses which are mainly determined with DENV and CHKV.

X. Neurological complications

A major global concern with ZIKV infection is the reported increase in cases of microcephaly and Guillain-Barre Syndrome (GBS) in the Americas after the recent ZIKV outbreak (2). Microcephaly is associated with diverse determinants including: genetic factors, and environmental factors like: exposure to diverse infectious agents (during pregnancy), prenatal care, pregnant women lifestyle and/or behavior (smoking or alcohol drinking habits) are known to contribute to the onset of microcephaly.

Regarding the GBS, it is considered a rare autoimmune disorder of the peripheral nervous system. This condition can cause muscle weakness, paralysis, and, in some complicated cases, even the death of the patient. (24, 5).

It is important to indicate that both conditions have also been implicated with other flaviviral infections like DENV and WNV (70). Recent studies suggest that ZIKV infections can be highly neurotrophic, causing bilateral macular and perimacular lesions in some cases (2). Such current complications, of a ZIKV infection, were not previously documented during the 1950s and 1960s. Therefore, apparently ZIKV has undergone a genetic evolution (through the emergence of the Asian lineage) which brought an increase in virus pathogenicity (71).

Some additional neurological disorders, associated with ZIKV infections, include: myelitis, encephalitis, optical neuritis, and meningoencephalitis (43, 72). Death from ZIKV infection in adults has been reported but is rare. However, the exact contribution of the infection to mortality has not been determined.

Intrauterine ZIKV infections have caused cerebral calcifications in fetuses' brains. The following brain anomalies have also been observed in microcephalic fetuses: hydrops fetalis and hydranencephaly. Both anomalies led to pregnancy termination. Pathological analysis of fetal images provided evidence indicating the vertical transmission of ZIKV from mother to child. This was observed during the end of the first trimester of the pregnancy period (73).

Other anomalies that have been observed include optic nerve and retinal disorders in 30% of infants with assumed ZIKV associated microcephaly. (74). This condition, including other brain and ocular abnormalities, were observed in infants in 11 studies. Seven of them were case series reports and four were observational studies (73).

Observed ocular abnormalities (associated with ZIKV) include: optic nerve abnormalities, microphthalmia, focal pigment mottling, intra-ocular calcifications, cataracts, optic disc cupping, chorioretinal macular atrophy, bilateral iris coloboma, conjunctival injections, foveal reflex loss, scarring, lens subluxation, and muscular hypoplasia (75).

XI. Treatment

Pregnant women with a ZIKV diagnosis is a complicated management issue. Actual guidelines recommend proper prenatal and postnatal attention, close monitoring of the women, exclusion of other congenital infections such as rubella, cytomegalovirus or toxoplasmosis. If abnormalities are detected, amniocentesis is recommended for virological testing. Finally, pregnancy termination is a possibility to consider, depending on the particular scenario, after the pregnant women have been thoroughly oriented by the physicians (76).

XII. Control measures

Vaccine development

Currently, there are four available flaviviruses vaccines. These are YFV (live attenuated), TBEV (inactivated), JEV (both inactivated and live attenuated), and DENV (recombinant chimeric live attenuated). At this moment, there is no ZIKV antiviral drug or vaccine in the market. Nonetheless, several vaccine platforms have entered in clinical trials (77).

Antiviral therapeutics

Currently, there is no antiviral treatment available for flaviviral infections (71). ZIKV infection treatment is symptomatic, often using analgesics and antipyretics.

Environmental health strategies

Prevention of ZIKV infection must be emphasized by the local public environmental health authorities promoting collective and community's responsibility and engagement for integrated vector management. The strategy should follow the same general strategies for other vector-borne infections like public health education to prevent mosquito bites, community involvement in eliminating mosquito breeding habitats around and inside houses, physical elimination of adult mosquitoes, patient isolation during the viremia phase (first 7 days of illness). Also, adult persons who have traveled recently to ZIKV endemic regions must prevent having unprotected sexual intercourse with their couples principally if the sexual partner is a pregnant woman (78).

Integrated Vector Management (IVM)

The World Health Organization (WHO) promotes the Integrated Vector Management (IVM) process for vector control (78). The main objectives of this approach are cost-effectiveness, sustainability, efficiency, and sound environmental health practices of disease-vector control. Obviously, the principal goal is to prevent the transmission of vector-borne diseases. The IVM method consists of the following three strategies: environmental management, biological control, and chemical control.

The environmental management strategy directs the efforts toward environment modification by preventing or reducing vector propagation (79). This can be done altering, destroying, or removing recipients that provide egg/ larval/ pupal habitats, and also by modifying human behavior. Environment management includes: installing mosquito screening on windows, doors and other entry points, and using mosquito nets while sleeping during daytime. Concerning behavior, it is important to use long-sleeved shirts and long pants to protect the body from mosquito bites (71). The use of insect repellants, to apply on the skin, made from essentials oils like eucalyptus (80), camphor (81), clove oil (82) and citronella (81, 83) are recommended instead of the commercial repellents containing the toxic chemical DEET. Finally, the employment of larvicides is considered complementary to environmental management and – except in emergencies – should be restricted to containers that cannot otherwise be eliminated or managed.

The second strategy, biological control, is based on the introduction of organisms that prey upon, parasitize, compete with or otherwise reduce populations of the target species (84). For example, against Aedes species, WHO recommends the use a selection of larvivorous fish species and predatory copepods (small freshwater crustaceans) that are effective against the immature larval stages of vector mosquitoes. Another example of this strategy is the liberation of male mosquitoes inoculated with the bacteria Wolbachia. When the male mosquitoes copulate with the females, they transfer the bacteria to the female affecting the viability of the eggs during the reproductive process. Therefore, the female produced eggs are non-viable.

Finally, the third vector control strategy, recommended by the WHO, is chemical control.

This method targets adult vectors to reduce mosquito densities, longevity, and other transmission parameters. Adulticides are applied either as residual surface treatments or as space treatments. Space spraying is recommended for control only in emergency situations to suppress an ongoing epidemic or to prevent an incipient one (85).

Public health authorities, in ZIKV endemic regions, must provide access to contraceptives, prenatal care, and good environmental health education services regarding the ZIKV life cycle, modes of transmission, and preventative measures (5).

Also, the existing disease surveillance systems of the country, should emphasize in ZIKV diagnosis and monitoring for the potential associated teratogenic and neurological complications (86).

Entomological surveillance

The entomological surveillance is a fundamental preventive strategy that allows for early detection of a potential virus outbreak, determine vector density, vector distribution, and finally, consideration and assessment of vector control methods (87).

Mosquito traps are one of the simplest and cost-effective methods for reducing the mosquito population. In a study conducted in Puerto Rico the use of mosquito traps in two urban areas reduced the population of Aedes aegypti in a range between 50–70% (88).

XIII. Conclusion

The ZIKV has become established in the Americas. Currently, the ZIKV maintains two life cycles. The first, and the original one, is the sylvatic/enzootic cycle that occurs in Africa. The second life cycle is the suburban-urban transmission cycle that emerged through natural evolution.

There are several extrinsic environmental and intrinsic genetic factors associated with the emergence and resurgence of arboviruses like ZIKV (7). These factors include: overuse and uncontrolled spraying of insecticides; degradation and destruction of natural ecosystems by human activities (44); human population growth with the associated urbanization; climate change (44); expansion of the geographic distribution of mosquito vectors; adaptation to new reservoir hosts (47, 48); genetic changes for CHIKV (48), DENV (49), and WNV (50); lack of effective mosquito control (51); and increased travel around the world.

Aedes aegypti and Aedes albopictus are the main vectors of the ZIKV in the Americas. The accumulated evidence indicates that there is no clear association between ZIKV and a particular animal species. However, ZIKV has never been isolated from non-primates, so it is not clear whether other species can act as reservoir hosts (7, 42).

While Aedes aegypti feed almost exclusively on human's blood, Aedes albopictus is usually exophagic and (in addition to humans) it also bites domestic and livestock animals (7, 34). However, it has been observed that in some occasions Aedes albopictus prefers to feed on humans. Therefore, some scientists believe that this last species can also display an anthropophilic behavior similar to that of Aedes aegypti (35) which represents a threat to public health because, as a result, Aedes albopictus can dramatically expand its geographic distribution and therefore of the ZIKV.

Because there are no vaccines for the ZIKV, local health authorities must emphasize in sound environmental health strategies like the Integrated Vector Management method promoted by the WHO. Also, through communities' involvement in the elimination of mosquitoes breeding places in combination with other environmental and biological control strategies.

Aedes aegypti is the main vector of the ZIKV in the Americas. Because this arthropod is a domestic mosquito that lives inside and around individual houses, the communities represent the first line of defense against the transmission of the ZIKV. Therefore, a well-educated community - in preventive environmental health strategies to eradicate mosquitoes breeding places – must be the principal objective of public health campaigns and national vector control and management plans. Also, the use of insecticides must be avoided as much as possible due to the toxic effects, on human health and the environment, that such industrial substances cause. For similar reasons insect repellents containing the toxic compound DEET must not be used, principally in children and older people. Instead we recommend the use of natural insect repellents made from essential oils like eucalyptus, camphor, clove oil and citronella.

In conclusion, there are excellent environmental health control measures to prevent the transmission of the ZIKV without exposing people, animal and plant species to the hazards of pesticides and other harmful substances. Nevertheless, for this to happen, national governments must have the will and exert its constitutional power to locally prevent the improper influence of the chemical pesticides industry which history of bribery of high ranked public officials is well known around the world.

Resumen

Estudios filogenéticos sugieren que el ZIKV fue introducido a Brasil, y por tanto a las Américas, en el año 2014 durante el Campeonato Mundial de Canotaje celebrado en Río de Janeiro. Desde entonces el virus se diseminó a través de América Latina, el Caribe y Norteamérica. Parece claro que Aedes aegypti, y a menor grado Aedes albopictus, son los vectores principales. Los síntomas del ZIKV son similares a otros flavivirus, como el dengue, y por tanto pueden ser confundidos. Actualmente el ZIKV mantiene dos ciclos de vida. El primero es el ciclo selvático/enzoótico que ocurre en África. El segundo ciclo de vida es el de transmisión suburbana-urbana que surgió a través de la evolución. El ZIKV adquirió la habilidad de mantener este ciclo humano-endémico en áreas urbanas y suburbanas. El ZIKV nunca ha sido aislado en no-primates, por lo tanto, no está claro si otras especies pueden actuar de huéspedes reservorios. Existen diversos informes de la transmisión no-vectorial del ZIKV incluyendo: la lactancia, transfusiones de sangre, relaciones sexuales, saliva, orina, y el contacto físico (sudor, lágrimas). Una preocupación global es el incremento en los casos de microcefalia y del Síndrome de Guillain-Barré en las Américas. Actualmente no hay una vacuna contra el ZIKV. Por lo tanto, la prevención de la infección debe ser enfatizada por las autoridades locales de salud promoviendo la responsabilidad colectiva y la involucración en el manejo integral de vectores a través del manejo ambiental, el control biológico, y como última instancia, el control químico.

References

1. Dick GWA, Kitchen SF, Haddow AJ. Zika virus. I. Isolations and serological specificity. Trans R Soc Trop Med Hyg [Internet]. 1952 Sep [cited 2018 Feb 3];46(5):509–20. Available from: Url: http://www.ncbi.nlm.nih.gov/pubmed/12995440.

2. Mlakar J, Korva M, Tul N, Popovic M, Poljsak-Prijatelj M, Mraz J, et al. Zika Virus Associated with Microcephaly. N Engl J Med 2016;374:951–8.
3. Ayres CFJ. Identification of Zika virus vectors and implications for control. Lancet Infect Dis 2016;16:278–9.
4. Arboviruses and human disease. Report of a WHO Scientific Group. World Health Organ Tech Rep Ser 1967;369:1–84.
5. Lazear HM, Diamond MS. Zika Virus: New Clinical Syndromes and Its Emergence in the Western Hemisphere. J Virol 2016;90:4864–75.
6. Gubler DJ, Kuno G, Markoff L. Flaviviruses. In: Knipe DM, Howley PM, Editors. Fields virology, 5th Ed; Philadelphia; Lippincott Williams and Wilkins, 2007:1155–1227.
7. Musso D, Gubler DJ. Zika Virus. Clin Microbiol Rev 2016;29:487–524.
8. Cao-Lormeau V-M, Roche C, Teissier A, Robin E, Berry A-L, Mallet H-P, et al. Zika virus, French polynesia, South pacific, 2013. Emerg Infect Dis. 2014;20:1085–6.
9. Nhan T-X, Cao-Lormeau VM, Musso D. Les infections à virus Zika. Rev Francoph Lab 2014:467:45–52. French.
10. Vandenbogaert M, Cao-Lormeau V-M, Diancourt L et al. Full-length genome sequencing and analysis of 3 ZIKV strains on an Ion Torrent PGM sequencer. Abstr 22.133. 63rd Am Soc Trop Med Hyg (ASTMH) Meet; New Orleans; 2014: Nov 2-6.
11. Campos GS, Bandeira AC, Sardi SI. Zika Virus Outbreak, Bahia, Brazil. Emerg Infect Dis 2015;21:1885–6.
12. CDC, 2016. Outcomes of Pregnancies with Laboratory Evidence of Possible Zika Virus Infection in the United States, 2016. Centers for Disease Control and Prevention, Atlanta, GA November 23, 2016. Available at: Url: http://www.cdc.gov/zika/geo/pregnancy-outcomes.html. Accessed July 20, 2017.
13. Lanciotti RS, Lambert AJ, Holodniy M, Saavedra S, Signor LDCC. Phylogeny of Zika Virus in Western Hemisphere, 2015. Emerg Infect Dis 2016;22:933–5.
14. Musso D. Zika Virus Transmission from French Polynesia to Brazil. Emerg Infect Dis 2015;21:1887.
15. Marcondes CB, Ximenes M de FF de M. Zika virus in Brazil and the danger of infestation by Aedes (Stegomyia) mosquitoes. Rev Soc Bras Med Trop 2016;49:4–10.
16. ProMED-mail. December, 23 2015. Zika virus—Americas, Atlantic Ocean. ProMED-mail archive no. 20151223.3886435. Available at: Url: http://www.promedmail.org. Accessed August 10, 2017.
17. ProMED-mail. January, 8 2016. Zika virus—Americas. ProMED-mail archive no. 20160108.3921447. Available at: Url: http://www.promedmail.org. Accessed August, 9 2017.
18. PAHO/WHO. Zika Suspected and Confirmed Cases Reported by Countries and Territories in the Americas (Cumulative Cases), 2015–2016; Washington, D.C. November 17, 2016. Available at: Url: http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=36937&lang=en. Accessed July 20, 2017.
19. PAHO / WHO. Zika Epidemiological Update, August 25, 2017. [PAHO/WHO Web site]. Available at: Url: http://www.paho.org/hq/index.php?option=com_content&id=11599&Itemid=41691. Accessed July 22, 2017.
20. PAHO/WHO. Zika Epidemiological Update, December 29, 2016. Available at: Url: http://www.paho.org/hq/index.php?option=com_docman&task=doc_view&Itemid=270&gid=37579&lang=fr. Accessed July 22, 2017.
21. Ali A, Wahid B, Rafique S, Idrees M. Advances in research on Zika virus. Asian Pac J Trop Med 2017;10:321–31.
22. Saiz J-C, Vazquez-Calvo A, Blazquez AB, Merino-Ramos T, Escribano-Romero E, Martin-Acebes MA. Zika Virus: the Latest Newcomer. Front Microbiol 2016;7:496.
23. Song B-H, Yun S-I, Woolley M, Lee Y-M. Zika virus: History, epidemiology, transmission, and clinical presentation. J Neuroimmunol 2017;308:50–64.
24. Sharma A, Lal SK. Zika Virus: Transmission, Detection, Control, and Prevention. Front Microbiol 2017;8:110.
25. Althouse BM, Vasilakis N, Sall AA, Diallo M, Weaver SC, Hanley KA. Potential for Zika Virus to Establish a Sylvatic Transmission Cycle in the Americas. PLoS Negl Trop Dis 2016;10:e0005055.
26. Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, Huy R, et al. Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. PLoS Negl Trop Dis 2012;6:e1477.
27. Marchette NJ, Garcia R, Rudnick A. Isolation of Zika virus from Aedes aegypti mosquitoes in Malaysia. Am J Trop Med Hyg 1969;18:411–5.
28. Diagne CT, Diallo D, Faye O, Ba Y, Faye O, Gaye A, et al. Potential of selected Senegalese Aedes spp. mosquitoes (Diptera: Culicidae) to transmit Zika virus. BMC Infect Dis 2015;15:492.
29. Petersen LR, Jamieson DJ, Powers AM, Honein MA. Zika Virus. N Engl J Med 2016;374:1552–63.
30. Martin-Acebes MA, Saiz J-C. West Nile virus: A re-emerging pathogen revisited. World J Virol 2012;1:51–70.
31. Thomas SM, Obermayr U, Fischer D, Kreyling J, Beierkuhnlein C. Low-temperature threshold for egg survival of a post-diapause and non-diapause European aedine strain, Aedes albopictus (Diptera: Culicidae). Parasit Vectors 2012;5:100.
32. Grard G, Caron M, Mombo IM, Nkoghe D, Mboui Ondo S, Jiolle D, et al. Zika virus in Gabon (Central Africa) --2007: a new threat from Aedes albopictus? PLoS Negl Trop Dis 2014;8: e2681.
33. Scott TW, Takken W. Feeding strategies of anthropophilic mosquitoes result in increased risk of pathogen transmission. Trends Parasitol 2012;28:114–21.
34. Ponlawat A, Harrington LC. Blood feeding patterns of Aedes aegypti and Aedes albopictus in Thailand. J Med Entomol 2005;42:844–9.
35. Higgs S. Zika Virus: Emergence and Emergency. Vector Borne Zoonotic Dis 2016;16:75–6.
36. Dick GW. Epidemiological notes on some viruses isolated in Uganda; Yellow fever, Rift Valley fever, Bwamba fever, West Nile, Mengo, Semliki forest, Bunyamwera, Ntaya, Uganda S and Zika viruses. Trans R Soc Trop Med Hyg 1953;47:13–48.
37. Gubler DJ, Nalim S, Tan R, Saipan H, Sulianti Saroso J. Variation in susceptibility to oral infection with dengue viruses among geographic strains of Aedes aegypti. Am J Trop Med Hyg 1979;28:1045–52.
38. Miller BR, Monath TP, Tabachnick WJ, Ezike VI. Epidemic yellow fever caused by an incompetent mosquito vector. Trop Med Parasitol 1989;40:396–9.
39. Wong P-SJ, Li MI, Chong C-S, Ng L-C, Tan C-H. Aedes (Stegomyia) albopictus (Skuse): a potential vector of Zika virus in Singapore. PLoS Negl Trop Dis 2013;7:e2348.
40. Wolfe ND, Kilbourn AM, Karesh WB, Rahman HA, Bosi EJ, Cropp BC, et al. Sylvatic transmission of arboviruses among Bornean orangutans. Am J Trop Med Hyg 2001;64:310–6.
41. Darwish MA, Hoogstraal H, Roberts TJ, Ahmed IP, Omar F. A seroepidemiological survey for certain arboviruses (Togaviridae) in Pakistan. Trans R Soc Trop Med Hyg 1983;77:442–5.
42. Hayes EB. Zika virus outside Africa. Emerg Infect Dis 2009;15:1347–50.
43. Fauci AS, Morens DM. Zika Virus in the Americas--Yet Another Arbovirus Threat. N Engl J Med 2016;374:601–4.
44. Gould EA, Higgs S. Impact of climate change and other factors on emerging arbovirus diseases. Trans R Soc Trop Med Hyg 2009;103:109–21.
45. Gubler DJ. The global emergence/resurgence of arboviral diseases as public health problems. Arch Med Res 2002;33:330–42.
46. Malkinson M, Banet C, Weisman Y, Pokamunski S, King R, Drouet M-T, et al. Introduction of West Nile virus in the Middle East by migrating white storks. Emerg Infect Dis 2002;8:392–7.
47. Weaver SC. Host range, amplification and arboviral disease emergence. Arch Virol Suppl 2005;(19):33–44.
48. Tsetsarkin KA, Vanlandingham DL, McGee CE, Higgs S. A single mutation in chikungunya virus affects vector specificity and epidemic potential. PLoS Pathog 2007;3: e201.
49. Bennett SN, Holmes EC, Chirivella M Et al. Selection-driven evolution of emergent dengue virus. Mol Biol Evol 2014;31:574-83.
50. Moudy RM, Meola MA, Morin L-LL, Ebel GD, Kramer LD. A newly emergent genotype of West Nile virus is transmitted earlier and more efficiently by Culex mosquitoes. Am J Trop Med Hyg 2007;77: 365–70.
51. Gubler DJ. Dengue, Urbanization and Globalization: The Unholy Trinity of the 21(st) Century. Trop Med Health 2011;39(4 Suppl):3–11.

52. Kilpatrick AM, Randolph SE. Drivers, dynamics, and control of emerging vector-borne zoonotic diseases. Lancet (London, England) 2012;380:1946–55.
53. Besnard M, Lastere S, Teissier A, Cao-Lormeau V, Musso D. Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014. Euro Surveill Bull Eur sur les Mal Transm = Eur Commun Dis Bull 2014;19(13):pii: 20751.
54. Musso D, Roche C, Robin E, Nhan T, Teissier A, Cao-Lormeau VM. Potential sexual transmission of Zika virus. Emerg Infect Dis 2015;21:359-361.
55. Davidson A, Slavinski S, Komoto K, Rakeman J, Weiss D. Suspected Female-to-Male Sexual Transmission of Zika Virus - New York City, 2016. MMWR Morb Mortal Wkly Rep 2016;65:716–7.
56. McCarthy M. Zika virus was transmitted by sexual contact in Texas, health officials report. BMJ 2016;352: i720.
57. Venturi G, Zammarchi L, Fortuna C, Remoli ME, Benedetti E, Fiorentini C, et al. An autochthonous case of Zika due to possible sexual transmission, Florence, Italy, 2014. Euro Surveill Bull Eur sur les Mal Transm = Eur Commun Dis Bull 2016;21:30148.
58. Musso D, Roche C, Nhan T-X, Robin E, Teissier A, Cao-Lormeau V-M. Detection of Zika virus in saliva. J Clin Virol 2015;68:53–5.
59. Bonaldo MC, Ribeiro IP, Lima NS, Dos Santos AAC, Menezes LSR, da Cruz SOD, et al. Isolation of Infective Zika Virus from Urine and Saliva of Patients in Brazil. PLoS Negl Trop Dis 2016;10:e0004816.
60. Colt S, García-Casal MN, Pena-Rosas JP, Finkelstein JL, Rayco-Solon P, Weise Prinzo ZC, et al. Transmission of Zika virus through breast milk and other breastfeeding-related bodily-fluids: A systematic review. PLoS Negl Trop Dis 2017;11:e0005528.
61. Dupont-Rouzeyrol M, Biron A, O'Connor O, Huguon E, Descloux E. Infectious Zika viral particles in breastmilk. Lancet (London, England) 2016;387:1051.
62. Possible West Nile virus transmission to an infant through breast-feeding--Michigan, 2002. MMWR Morb Mortal Wkly Rep 2002;51:877–8.
63. Swaminathan S, Schlaberg R, Lewis J, Hanson KE, Couturier MR. Fatal Zika Virus Infection with Secondary Nonsexual Transmission. N Engl J Med 2016;375:1907–9.
64. Charrel RN, Leparc-Goffart I, Pas S, Lamballerie X, Koopmans M, and Reusken C. State of knowledge on Zika virus for an adequate laboratory response. Bull World Health Organ. 2016; doi:10.2471/BLT.16.171207.
65. Wong SS-Y, Poon RW-S, Wong SC-Y. Zika virus infection-the next wave after dengue? J Formos Med Assoc 2016;115:226–42.
66. Gourinat A-C, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M. Detection of Zika virus in urine. Emerg Infect Dis 2015;21:84–6.
67. Huzly D, Hanselmann I, Schmidt-Chanasit J, Panning M. High specificity of a novel Zika virus ELISA in European patients after exposure to different flaviviruses. Euro Surveill Bull Eur sur les Mal Transm = Eur Commun Dis Bull 2016;21(16).
68. Rabe IB, Staples JE, Villanueva J, Hummel KB, Johnson JA, Rose L, et al. Interim Guidance for Interpretation of Zika Virus Antibody Test Results. MMWR Morb Mortal Wkly Rep 2016;65:543–6.
69. Li R, Ding J, Ding G et al. Zika virus infections, a review. Radiology Infect Dis 2017;20:1-6.
70. Lanciotti RS, Kosoy OL, Laven JJ, Velez JO, Lambert AJ, Johnson AJ, et al. Genetic and serologic properties of Zika virus associated with an epidemic, Yap State, Micronesia, 2007. Emerg Infect Dis 2008;14:1232–9.
71. Weaver SC, Costa F, García-Blanco MA, Ko AI, Ribeiro GS, Saade G, et al. Zika virus: History, emergence, biology, and prospects for control. Antiviral Res 2016;130:69–80.
72. Oehler E, Watrin L, Larre P, Leparc-Goffart I, Lastere S, Valour F, et al. Zika virus infection complicated by Guillain-Barre syndrome--case report, French Polynesia, December 2013. Euro Surveill Bull Eur sur les Mal Transm = Eur Commun Dis Bull 2014;19(9):pii: 20720.
73. Ellington SR, Devine O, Bertolli J, Martinez Quinones A, Shapiro-Mendoza CK, Perez-Padilla J, et al. Estimating the Number of Pregnant Women Infected With Zika Virus and Expected Infants With Microcephaly Following the Zika Virus Outbreak in Puerto Rico, 2016. JAMA Pediatr 2016;170:940–5.
74. Petersen EE, Staples JE, Meaney-Delman D, et al. Interim guidelines for pregnant women during a Zika virus outbreak-United States, 2016. Morb Mortal Wkly Rep 2016;65:30-33.
75. Sarno M, Sacramento GA, Khouri R, do Rosario MS, Costa F, Archanjo G, et al. Zika Virus Infection and Stillbirths: A Case of Hydrops Fetalis, Hydranencephaly and Fetal Demise. PLoS Negl Trop Dis 2016;10:e0004517.
76. Oduyebo T, Petersen EE, Rasmussen SA, Mead PS, Meaney-Delman D, Renquist CM, et al. Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure - United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:122–7.
77. Villar L, Dayan GH, Arredondo-García JL, Rivera DM, Cunha R, Deseda C, et al. Efficacy of a tetravalent dengue vaccine in children in Latin America. N Engl J Med 2015;372:113–23.
78. Oster AM, Brooks JT, Stryker JE, Kachur RE, Mead P, Pesik NT, et al. Interim Guidelines for Prevention of Sexual Transmission of Zika Virus - United States, 2016. MMWR Morb Mortal Wkly Rep 2016;65:120–1.
79. WHO. Environmental management. [WHO Dengue Control Web site]. Available at: Url: http://www.who.int/denguecontrol/control_strategies/environmental_management/en/ Accessed August 12, 2017.
80. Alvarez Costa A, Naspi C V, Lucia A, Masuh HM. Repellent and Larvicidal Activity of the Essential Oil from Eucalyptus nitens Against Aedes aegypti and Aedes albopictus (Diptera: Culicidae). J Med Entomol 2017;54:670–6.
81. Nerio LS, Olivero-Verbel J, Stashenko E. Repellent activity of essential oils: a review. Bioresour Technol 2010;101:372–8.
82. Shapiro R. Prevention of vector transmitted diseases with clove oil insect repellent. J Pediatr Nurs 2012;27:346–9.
83. Hsu W-S, Yen J-H, Wang Y-S. Formulas of components of citronella oil against mosquitoes (Aedes aegypti). J Environ Sci Health B 2013;48:1014–9.
84. WHO. Biological control. [WHO Dengue Control Web site]. Available at: Url: http://www.who.int/denguecontrol/control_strategies/biological_control/en/ Accessed August 12, 2017.
85. WHO. Chemical control. [WHO Dengue Control Web site]. Available at: Url: http://www.who.int/denguecontrol/control_strategies/chemical_control/en/ Accessed August 12, 2017.
86. Pan American Health Organization. Epidemiological Alert: Neurological Syndrome, Congenital Malformations, and Zika Virus Infection. 2016; Available online at: Url: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&Itemid=&gid=32405. Accessed August 12, 2017.
87. Basarab M, Bowman C, Aarons EJ, Cropley I. Zika virus. BMJ 2016;352:i1049.
88. Barrera R, Amador M, Acevedo V, Caban B, Félix G, Mackay AJ. Use of the CDC Autocidal Gravid Ovitrap to Control and Prevent Outbreaks of Aedes aegypti (Diptera: Culicidae). J Med Entomol 2014;51:145-54.